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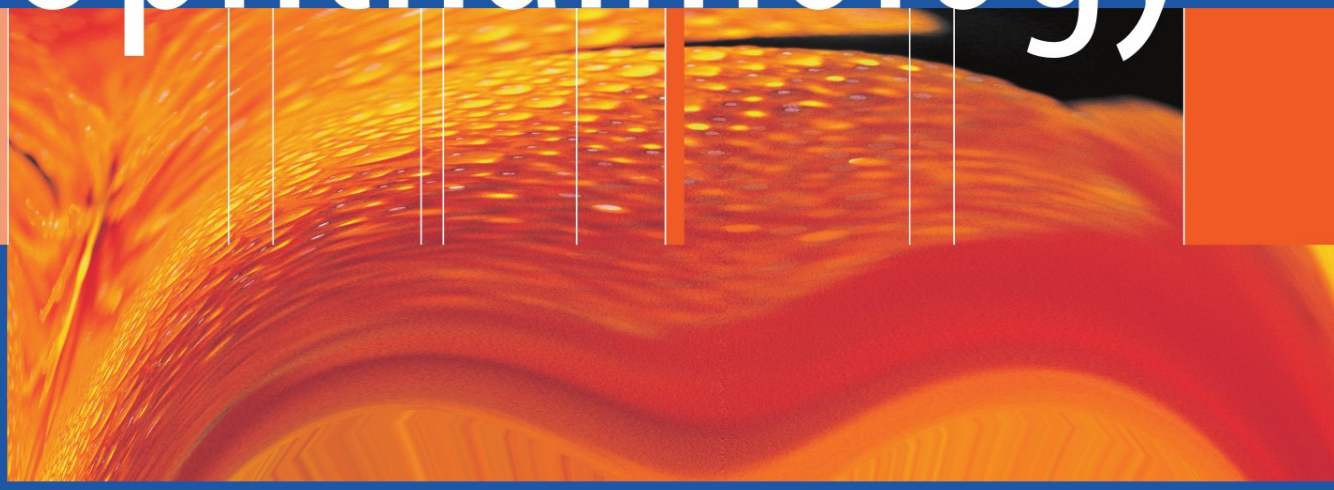
Editors

Pediatric Ophthalmology



Current Thought and A Practical Guide

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Pediatric Ophthalmology

M. Edward Wilson · Richard A. Saunders
Rupal H. Trivedi (Eds.)

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Current Thought and A Practical Guide

Springer

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Preface

There are encyclopedic reference books available in many sub-specialty areas of eye care, including pediatric ophthalmology. These large texts are most valuable when a clinician needs to quickly find a differential diagnosis, a list of treatment options, or the findings to look for when a particular syndrome is suspected. With *Pediatric Ophthalmology: Current Thought and a Practical Guide*, we have not attempted to match the breadth of those exhaustive reference texts. Instead, we bring to the pediatric-oriented ophthalmologists a book they will want to read cover-to-cover. We strived for enough depth and perspective in each chapter so that the book could be considered core reading for trainees and practitioners alike.

When I first met with Marion Philipp, Senior Editor at Springer, to discuss this project, I told her that this book would be the most well-read book in the pediatric ophthalmology field because each chapter would be written by a respected thought-leader who could give a concise overview of the most current thought and practice recommendations for that subject. I told her that each author would be recognized by the reader as one of the go-to people for that subject. I invited a true "who's who" in pediatric ophthalmology. By being very persistent and not taking "no" for an answer, I was successful in getting the most sought-after writers. Once committed, each has delivered exactly what I had hoped for. The results are chapters that display the perspective of the author's years of experience combined with the practicality needed for the busy clinician. I expect that the readers will absorb each chapter in its entirety instead of using it only to look up facts and treatments.

Each Chapter starts with a bulleted list of "Core Messages" and ends with "Take Home Pearls". The best references are included at the end of each chapter but no attempt is made to include comprehensive lists of historical references. I am thankful for this format, suggested by Springer, because it fits well with the intended scope and purpose of this work.

My Storm Eye Institute editorial partners have, more than anyone, made this project possible. Rupal Trivedi, MD, MSCR, has been with us at Storm Eye for nearly a decade. She began as a post-doctoral fellow, first with David Apple, MD and then with me. She received a Masters in Clinical Research degree here at MUSC (Medical University of South Carolina) and quickly became the go-to mentor for nearly every research project developed by one of our Ophthalmology residents or fellows. Her expertise in study design and data management is really remarkable. For this book, her attention to detail and her command of the literature gave us what we needed to bring this book to completion. The selection of index headings and sub-headings for the entire book were painstakingly selected by Dr. Trivedi singlehandedly.

Credit for this book's uniformity of style and format goes in large part to Dr. Richard Saunders. It took someone with Rick's reputation and seniority to accomplish this task. His command of written English surpasses anything that I have encountered in the field of ophthalmology, perhaps in part because he was raised by two professional editors: his father served as Executive Editor for Forbes Magazine for 20+ years; his mother was Director of Publications for the National Association of Social Workers. He gently nudged many of the authors towards the uniform content and style we had envisioned. Rick was also the first pediatric ophthalmologist in South Carolina and among the first pediatric ophthalmologists in the USA to be awarded an endowed professorship. He is respected as a leader well beyond the bounds of the state of South Carolina. His knowledge and experience are superb, especially with regard to complex strabismus and retinopathy of prematurity.

I have enjoyed working with the dedicated team at Springer. Marion Philipp, Senior Editor for Clinical Medicine was mentioned earlier. She initiated the project and shepherded it through a successful completion. Martina Himberger, Desk Editor, was in constant communication with us and gave the project her full support. I know she has many projects but she made us feel as though we were her first and only concern. Le-tex publishing services completed the copyediting (thanks to Ute Noatsch and Annegret Krap) and production editing (thanks to Petra Moews) work with precision and speed. The entire team assembled at Springer was first-rate and I thank them personally.

My final thanks must go to my family for supporting me and always trying to keep me grounded and balanced. They (my family) come first, no matter how exciting the world of ophthalmology becomes. My wife, Donna, is the "CEO" of our household, making it possible for me to run a large academic department and the Storm Eye Institute. She is an expert at motivating me to be my best for the patients I serve and yet reminding me when it is time to let it go and spend time at home. She has taught me that only with balance can there be long-lasting meaningful success. My son, Leland, has taught me more about being a good doctor than anyone in my formal education. Despite optic nerve damage and cerebral palsy, he has a way of bringing out a smile in everyone he meets. He believes, correctly, that everyone would be healthier if they had at least one hug every day.

For those in Pediatric Ophthalmology, I urge you to commit to lifelong learning, challenge conventional wisdom, and have fun. We have the privilege to take care of the eyes of children who will lead the world through many future crises. Do your job well and inspire others to follow. Don't believe the old adage that nothing new ever comes out of Pediatric Ophthalmology. The authors of the chapters in this book believe that with constant innovation and high quality clinical investigations tempered by a careful "do-no-harm" motto, the field of Pediatric Ophthalmology will be constantly evolving.

M. Edward Wilson, MD

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The Art and Science of Examining a Child

1

M. Edward Wilson

Contents

Core Messages

- The pediatric exam is not as methodical and sequenced as the adult exam. Rather, it is carefully aimed at the most important findings and it is opportunistic.
- The care giver's initial behavior should be aimed at establishing trust and making the data collection fun for the child.
- Dilating the pupils is an essential part of the complete exam of the child; however, it is used in follow-up only when it will potentially change management.
- Pediatric eye exams are done as a team. The need to see more patients in less time has eliminated the luxury of having the pediatric ophthalmologist perform the entire exam him/herself.

1.1 Introduction

I have heard it said that when it comes to the pediatric eye examination, a friendly manner, a little trickery, and a lot of praise can accomplish a great deal. These are essential elements in the art of examining a child. Residents, fellows, and geriatric ophthalmologists are usually facile and disciplined in the performance of the adult comprehensive eye examination; however, gathering useful data from an unfriendly toddler can seem as challenging as taming the wild beasts of Africa. After a few failed attempts to persuade a young patient to allow even a glimpse of the eyes, the ophthalmologist may ask how anything gets done in the pediatric ophthalmology office, at least without anesthesia.

This chapter offers advice on how to approach the pediatric eye examination. It is not meant to cover every aspect of the eye examination of children. Rather, it deals in concepts, and some details. It is assumed that the examiner already knows how to perform a complete eye exam. The reader is referred to the orthoptic chapter (Chap. 4) for well-written advice on the ocular motility examination. Here, instead, I offer practical advice to allow the examiner, the patient, and the parent to enjoy the encounter with the pediatric ophthalmology team. When dealing with a child, professional competence requires both art and science.

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1.2 Developing a Plan at the Beginning of the Encounter

Since children are not merely small adults, the temptation to proceed methodically and sequentially through each portion of the complete eye exam in each patient must be resisted. Remember that the doctor does not decide when the exam is over, the child does. Judgment must be used to pick and choose portions of the complete exam most likely to yield useful data for that patient. For example, a careful slit-lamp examination may be essential to the evaluation of childhood uveitis but could be deleted in the patient with uncomplicated intermittent exotropia. In the later, a penlight examination can quickly scan for corneal luster, pupil size and shape, anterior chamber depth, and the absence of an afferent pupillary reflex without forcing the child's head into the slit-lamp. The retinoscope or direct ophthalmoscope can assess the quality of the red reflex from an arm's length without forcing the child into a difficult position.

Use the limited attention span and cooperation of the child to perform the investigations most essential to the chief complaint and add less critical steps as patient tolerance allows. Restraint or sedation should be used only if absolutely necessary and only if the data will influence the management of the patient.

Fig. 1.1 This young boy is sitting in his mother's lap and the chair has been raised to place the child at the same or higher level compared with the examiner

Fig. 1.2 After showing this child a toy, he is allowed to hold it briefly before the exam is resumed

1.3 A Fine Line Separates Fear from Cooperation

For many children, a fine line separates fear from cooperation. The doctor's initial behavior should be aimed at establishing trust and making examination data collections seem more like "child's play". When entering the examination room, the doctor should immediately be seated, so as not to stand over the child. Invite the child to sit in the BIG chair on a parent's lap or alone. Raise the chair quickly so that the child is at least at eye level with everyone in the room (Fig. 1.1). Do not surprise the child. Tell the child you are going to make him or her TALLER and say "here we go" as the chair elevates. Talk directly to the child. Comment on his or her clothing or ask a question you know he/she can answer, such as: How old are you? What grade are you in? What are you doing this summer? When a child begins to speak, his/her anxiety level drops dramatically. It is also helpful to show the child a toy and let the child hold it (Fig. 1.2).

1.4 The Attention-span Clock is Ticking

If the chief complaint is known, begin the exam immediately, before taking additional history. The attention-span clock is ticking. Do not waste time asking

Fig. 1.3 **a** A colorful toy is used for vision testing. This one makes noise, too. **b** A colorful toy is used for vision testing. A hand on the head can promote eye movement rather than head movement. **c** A colorful toy is used for vision testing. Move quickly and remain animated using whistles and clicking sound when needed

Fig. 1.4 A colorful toy is used and changed when needed. This toy also allows corneal light reflection testing

the parents questions. Move quickly from one investigation to another. Tell the child what to do. Be animated. Have colorful toys. Whistle, make noises, and call the child by name (Figs. 1.3, 1.4). Use an age-appropriate vocabulary (e.g., phoropter = elephant glasses). Have fun and make sure the child is having fun, too. I have a foot switch that turns the overhead lights off and on. I will commonly ask the child to say "lights out" out loud. As he/she does so, I hit the foot petal and the lights go out, to the amazement of the unsuspecting child. The more curious ones will want to know how it works so I show them. They can then operate the foot petal themselves at the end of the exam if they let me do all I need to do. It is useful to have a visual acuity computer screen so you can show movies and then switch from the movie directly to ABCs, HOTV letters, or Lea symbols. We have fish, balloons, and other non-movie videos as well. It is essential to keep the child engaged and get good data. Random displays on the computer eliminate memorization so re-testing can be done at any time. We use an occlusive patch to isolate one eye for visual acuity testing. I highly recommend it. Children are experts at peaking around an occluder. We tell the child that they can take the patch off as soon as the testing is completed. That seems to comfort them somewhat. They know the patch is temporary. I like to have additional lighted noise-making animals mounted on the wall beside the computer screen. These are foot-petal

activated and are a wonderful way to get the child to look in the distance for strabismus measurements or for the evaluation of ocular torticollis (Figs. 1.5, 1.6). Some pediatric ophthalmologists have eliminated these toys because they have images on the computer visual acuity screen. I believe they still have added value to hold the attention of the child and also in visual function testing in pre-literate children. With three "barking dogs" mounted on three vertically separated shelves, I can evaluate the quality of the vertical saccade produced when I activate each toy and deactivate the previous one, using a foot petal (Fig. 1.7). This is discussed in Chap. 22 in the context of evaluating visual function in children with partial cataracts. A brisk and accurate vertical saccade to the changing "barking dogs" indicates reasonably good visual acuity in a pre-verbal child.

When slit-lamp examination is needed, I ask them to hold the "handlebars" and put their chin in the chin rest. I get them into the proper position, with the help of a parent if needed. I quickly praise them for being "grown-up" and for doing great. Then I praise them

Fig. 1.5 Foot-petal operated noise-making animals are used to direct this child's gaze into the distance

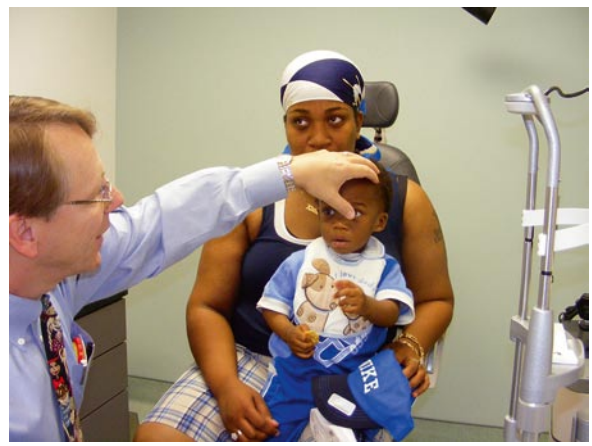

Fig. 1.6 The alternate cover test can be started with the child fixating on the distant noise-making animals

Fig. 1.7 **a** The upper foot-petal operated animal is activated. **b** The middle foot-petal operated animal is activated. **c** The lower foot-petal operated animal is activated

for having really "amazing" eyes. They will sometimes stay still if you say, "Can you see my eyes?" or "Look at my ear." I usually throw in a few "almost done" comments to keep them in the head rest. Again, at the end, more praise is warranted, even if they did not do as well as you hoped. The initial exam will build on the next one. If a child has a chronic condition and will need multiple exams, it is important to have the child feel reasonably good about the first exam, even if the evaluation was not fully accomplished. Build on that first encounter and push for a little more the next time the child is examined.

During the course of the exam, pause whenever you need a break or the child "demands" one. Remember, the child and parent will detect any hint of frustration in your voice. At the end of the initial examination, allow the child to climb down from the Big Chair. Additional history and explanation of the findings can then be completed. If pupil dilation is needed, have someone other than the examiner place the drops and make sure they are preceded with a topical anesthetic. This too can be done quickly so the child can be consoled by the parent and can retreat to the comfort of a playroom or a toy-filled sub-waiting area.

Remember that each time a decision is made to dilate a child's pupil, it adds the equivalent of one additional patient encounter to the day. These children dislike the drops and they are often tired and fussy when the drops have finally led to cycloplegia and dilated pupils. I do not discourage pupil dilation when it is necessary and when it may change the course of therapy; however, I must have a reason for dilation more than just because it has been a year since the last one.

Fundus examination and retinoscopy are usually the parts of the examination that are done after the child's pupils have been dilated. Again, as noted above, it is essential to know what information is needed. The child is often sleepy and cranky at this stage of the exam. Quickly performing an estimation of the refractive error using the retinoscope without any lenses is an invaluable skill. By learning to enhance the retinoscopic streak and then rotating it, the examiner can already know what lens with which to begin in the loose lens set. Rotating the enhanced streak gives the examiner the knowledge about whether significant astigmatism is present or not. Retinoscopy is most accurate when the central reflex is evaluated. Having the child look directly into the light is the best way to retinoscope the macula; however, when the cycloplegia is incomplete, I use the movie at the end of the examination room as the fixation target instead of the light. Care must be taken to read the reflex as centrally as possible when this occurs.

Fundus evaluation can usually be done without restraining the child if the examiner uses a low-level light and makes it fun. I point out that I am putting on a "strange hat" that can look all the way into their "brains". Then, as I view the optic nerve and macula, I often praise the child for being smart since they have "lots of brains". In fact, their head is "full of brains". When restraint is needed, having the parent help is best. Be efficient by getting the look you need as quickly as possible. I do not hesitate to schedule an examination under anesthesia if I see something that needs further study and intense examination.

1.5 The Pediatric Ophthalmology Team

Pediatric ophthalmology is, perhaps, the last holdout against the fast-paced, high-throughput, team-based approach to ophthalmic office examination. Many pediatric ophthalmologists still feel that they alone should do the majority of the gathering of data. Technicians are relegated to patient transport and dilation duties. With the need for more patients to be seen per hour, this approach is unsustainable. In addition, it is unnecessary. The modern pediatric ophthalmology office functions as a health care team. The families returning for follow-up respect the technicians, orthoptists, residents, fellows, and the pediatric ophthalmologists as care givers. Pediatric ophthalmic technicians develop a special rapport with the patients and their families. The skills they develop (accurate visual acuity, intraocular pressure measurement without squeezing, contact lens management, teaching of the care instructions) can become so refined that the physician trusts the data as much or more than if he/she had gathered it him/her self. Refracting technicians can spend time with the verbal child and get an amazingly accurate refraction once the pediatric behavior skill set is mastered. The physician need only recheck the endpoint or compare the pre-dilation finding with his/

her post-dilation finding. Orthoptists become masters of the ocular motility exam and the sensory evaluation. A combination of school-based knowledge and on-the-job training lead to the level of trust needed for the team to manage patients together.

The art of the exam discussed in this chapter must be learned by each member of the team. Using judgment, the technicians and orthoptists learn to do as much or as little as is appropriate for the particular patient and the particular complaint. Then, the physician is brought in at the correct time to do the essential things he/she really needs to do to get to the decision making at the end of the encounter. The goals are to avoid unnecessary repetition and yet avoid important omissions. The patient and the parent should recognize the value of the care team and should get the sense that the physician and the staff are all "on the same page" and have "trained together" to develop the protocols that lead to effective, efficient, and mistake-free care delivery.

1.6 Modeling Appropriate Behavior

Near the onset of ophthalmic training, residents and fellows should carefully observe practitioners who are skilled in the artful techniques of pediatric examination and develop a mindset and a game plan. Technicians and orthoptists should also model appropriate behavior they see in others. The staff should observe each other and give meaningful feedback. The team, together, should discuss the art and science of dealing with children and continuously improve their techniques. Patient and parent feedback should be taken seriously and changes made accordingly.

Each team member (physicians and staff) should take what I call an "innovation trip" periodically. The purpose of such a trip is to observe the techniques of a respected colleague in another location across the state or across the country. Pick those colleagues that have been praised for "best practices" innovation. Observe carefully and write down the details of anything you can bring home. This will help the team become a continuously learning group.

Pediatric ophthalmology is unique within ophthalmology. Those who work in pediatric ophthalmology know that "a friendly manner, a little trickery, and a lot of praise" may be a good beginning, but much more is needed for success. For those physicians or staff entering the field, success is achieved by hard work, continuous learning, and by having fun.

Early in their pediatric ophthalmology training, residents often ask why the children seem so much better behaved when the attending physician is conducting the examination. At the end of their training, after modeling the best of what they have seen in the staff and the attendings, they too can make data collection seem like "child's play". They discover that learning to tame the unfriendly toddler can produce a level of satisfaction and self-confidence not achievable by scientific mastery alone.

Take Home Pearls

- Sequence the pediatric eye exam based on what are the most important parts of the exam for that child's chief complaint.
- Learn to put the child at ease by sitting down quickly and raising the child up to where he/she is at least at eye level with everyone in the room.
- When you get a child to vocalize, his/her anxiety level goes down dramatically.
- Use pupillary dilation when necessary, but use it sparingly on follow-up visits.
- Pediatric ophthalmology is no longer a solo sport, it is a team game. Train the team so that everyone adopts the same child-friendly habits.

Refractive Error in Children

Constance E. West

2

Contents

Core Messages

- Emmetropization is guided by genetics but modified by environmental influences. No definitive treatments have emerged.
- Dynamic retinoscopy is a valuable tool in the evaluation of children (1) at risk for accommodative insufficiency, (2) with significant hyperopia, and (3) with non-physiologic visual complaints.
- Prescribing for pediatric refractive errors is complex and should take into account the child's age, current refractive error, accommodative ability, degree of anisometropia, and ocular family history.

2.1 Refractive Development and Emmetropization

Human infants are typically hyperopic at birth, with an average axial length of almost 17 mm, corneal power of 50−55 diopters, and crystalline lens power of 34 diopters; however, the range of resulting refractive error in the infant eye is significant, typically ranging from low myopic to moderate hyperopic errors, with or without astigmatism. The majority of ocular growth occurs during the first 18−24 months of life, manifested by both corneal flattening and axial elongation, and resulting in a shift from hyperopia toward emmetropia. Emmetropization continues

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after 2 years of age, albeit at a slower pace, such that most eyes are nearly emmetropic by 6–8 years of age. In some children, emmetropization fails and results in significant hyperopia, while in others emmetropia is overshot and myopia is the result.

It appears that emmetropization is guided by genetics but is modified by environmental influences. Support for genetically guided processes comes from fraternal and identical twin cohort studies, as well as from differences in refractive errors observed in prevalence studies of pediatric populations in different countries. Direct comparison of these prevalence studies is complicated by differences in methodology and definitions, but still, general patterns have emerged. It appears that there is a bias toward myopia in eastern Asian populations, particularly among the urban Chinese (as high as 75% in some studies). In comparison, Chilean children have an increased prevalence (14.5%) of significant hyperopia. Australian children of Caucasian origin also seem to have an increased prevalence of hyperopia, though not as dramatic as demonstrated in the Chilean study. In addition to hyperopia or myopia, certain populations seem to have an increased prevalence of astigmatism significant enough to cause ametropic amblyopia [1]. Genetic biases are further supported by studies that demonstrate a predictive effect of parental myopia upon the development of myopia in their offspring. The COMET study reported that children who developed high myopia during 7 years of post-study follow-up were younger and had more myopia at baseline. Children who developed high myopia were also more likely to have two myopic parents [2].

Studies of environmental influences on the development of refractive errors have primarily focused on the development of myopia, and some of the potential aggravating factors identified include sustained near work, accommodative variability, accommodative lag, and decreased time spent outdoors [3]. Urban environment [4] and increased night-time ambient lighting [5] may also have an effect on the development of myopia. In one recent report [6], parental cigarette smoking was associated with less prevalent myopia and a more hyperopic mean refraction with both prenatal and childhood exposure to tobacco smoke. Thus, the eventual refractive state of the eye depends upon *both* genetic and environmental influences. In addition, certain ocular and systemic disorders are commonly associated with ametropia (Table 2.1).

2.2 Examination

2.2.1 *Refraction Prior to Cycloplegia*

Accurate refraction of the pediatric patient is an essential element of the ophthalmic examination of the child, not only to determine the need for glasses, but also to aid in diagnosis and treatment of a variety of systemic and ocular disorders. Cycloplegic retinos-

Table 2.1 Examples of ocular and systemic disorders associated with refractive errors

Myopia	Hyperopia	Astigmatism
Stickler syndrome	Leber congenital amaurosis	Congenital ptosis
Congenital stationary night blindness	Myotonic dystrophy	Periocular hemangioma
Congenital glaucoma	Cornea plana	Limbal dermoid
Knobloch syndrome	Aarskog syndrome	Corneal scarring
Weill-Marchesani syndrome		Lens dislocation
Cornelia de Lange		Ciliary body mass
ROP		
Kniest dysplasia		
Gyrate atrophy		
Marfan syndrome and homocystinuria (with high astigmatism due to lens dislocation)		

copy is the most commonly used technique of refraction in children, but other methods of refraction, especially those used prior to cycloplegia, are important in the efficient evaluation of refractive errors in the pediatric population. Retinoscopy prior to dilation is useful in screening for large, uncorrected refractive errors that could affect measurement of acuity, stereopsis, or ocular alignment. With the child's attention directed to a non-accommodative target at distance, an estimate of the refractive error can be made.

2.2.2 Accommodation in Children

Accommodation is present at birth but does not become accurate until 4 months of age. In the pediatric eye, it is ordinarily expected that near objects can be focused onto the retina with accommodation. The pediatric patient is rarely suspected to have accommodative dysfunction, though this is probably because ophthalmologists rarely think to assess accommodation in the pediatric patient. Most ophthalmologists assess accommodative amplitudes with traditional gradient (minus lenses) or stimulus (near point) methods and limit their testing to adults and the occasional older child.

It has been increasingly recognized that certain children are at risk for accommodative insufficiency; more than half of children with Trisomy 21 [7] and cerebral palsy [8] have accommodative insufficiency. Children taking baclofen for bladder and skeletal muscle spasticity may also experience problems at near, and the pharmacologic accommodative insufficiency is often accompanied by mydriasis. Other medications may also cause accommodative insufficiency. Monocular accommodative insufficiency can also be found in some amblyopic eyes and may require an add for near to aid the amblyopia treatment. Fortunately, accommodation can be rapidly and easily assessed in most children using dynamic retinoscopy, as discussed next.

2.2.3 Dynamic Retinoscopy

Pediatric ophthalmologists, more than any other ophthalmic specialist, rely upon retinoscopy for measurement of refractive error, and are expert in static retinoscopy. Dynamic retinoscopy [9, 10] is an invaluable but much underutilized technique that allows rapid, objective assessment of accommodative ability, even in infants and young children.

With dynamic retinoscopy, neutralization of the retinoscopic reflex can be detected when the patient fixates on an accommodative target held adjacent to the peephole of the retinoscope. This rapidly performed test can (1) detect incomplete cycloplegia, (2) aid in rapid screening for astigmatism and anisometropia, and (3) guide therapy in a wide variety of patients: high hyperopia; eyes at risk for accommodative insufficiency; and non-physiologic visual loss.

Dynamic retinoscopy should not be confused with near retinoscopy, which provides a measurement of distance refraction. The technique of near retinoscopy, as described by Mohindra et al. [11], is performed under monocular conditions and uses the filament of the bulb as the target. When the filament is used as the target, there is little or no accommodative stimulus and an estimate of distance-refractive correction is obtained by empirically subtracting 1.25 diopters from the readings obtained.

During retinoscopy, the retinoscopist views the red reflex of the eye through the peephole of the retinoscope while sweeping a linear streak of divergent light across the pupil. The observed retinoscopic reflex can be described as having "with" or "against" movement, or, when the retinoscopic reflex fills the pupil, as being "neutral". Recall that the reflex observed depends upon the location of the far point of the eye. When the eye is focused beyond the peephole (behind the examiner, or even beyond infinity) the retinoscopic reflex moves in the same direction as the intercept – "with" motion. When the far point of the eye is in front of the peephole (between the patient's eye and the peephole), "against" motion is observed. Finally, when the eye is focused in the plane of the peephole, all light returning from the retina passes through the peephole, and the red reflex appears to fill with light – "neutralization." During dynamic retinoscopy, when an eye in focus at infinity ("with" movement) attends to a near target held adjacent to the peephole of the retinoscope and accommodates, the far point of the eye is brought to the peephole of the retinoscope, and a neutral reflex is observed. Dynamic retinoscopy is the process whereby the retinoscopist observes the light reflex as it attends to the near target.

In order to stimulate accommodation, it is necessary to use letters (Fig. 2.1a) or an age-appropriate picture (Fig. 2.1b) of interest to the child with little delay. When using a small picture, the author finds it helpful to pose a playful, but argumentative, question requiring the child's observation of small details on the target. Most children will quickly and gleefully respond in order to correct the mistake. Pictures, rather than letters, are also of great value when evaluating the child with difficulty reading, or presumed non-physiologic visual complaints, as the child rarely suspects that the cartoon figure is being used as an evaluation of their ability to see at near. An infant's accommodation can usually be stimulated by drawing their attention to a small toy held adjacent to the peephole of the retinoscope, sometimes using internal illumination in the base of the figure. Most infants can only be tested at near, as they are often inattentive for distance fixation.

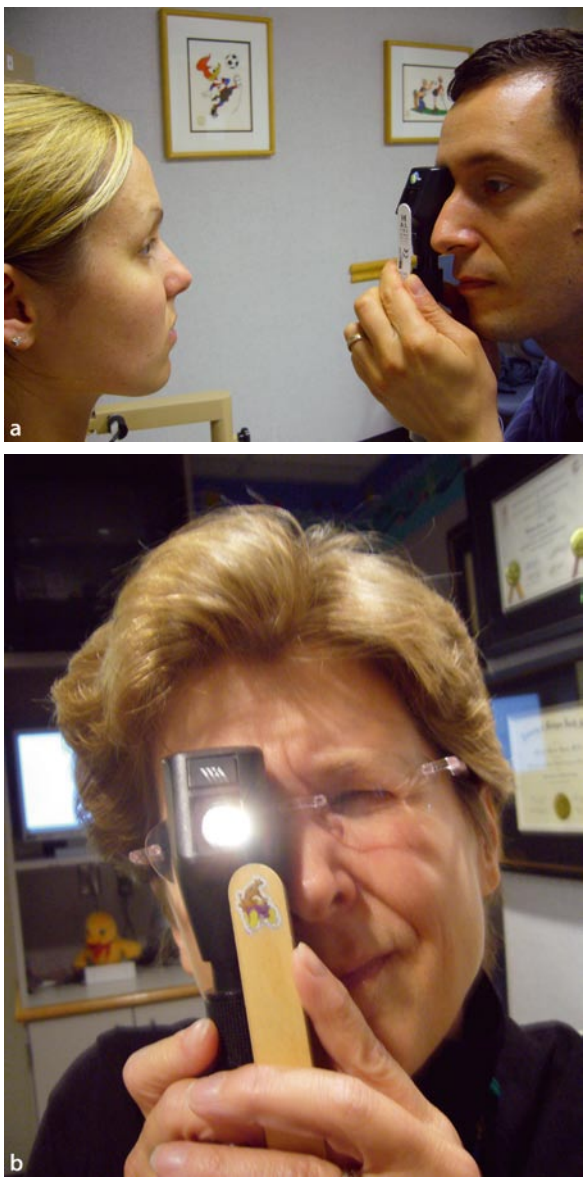


Fig. 2.1 Dynamic retinoscopy with **a** the doctor holding a lettered target close to the peephole of the retinoscope, and stimulating accommodation by moving close to the teenager and asking her to read the letters. **b** The patient's view of the retinoscope and a cartoon figure target

Except for patients with moderate to large angle strabismus, both eyes of most children can be evaluated nearly simultaneously. If refractive correction has been prescribed, it should be worn during testing. With the child attentive to a distance fixation object, and with the peephole as close to the line of sight as possible (to avoid off-axis errors), the reflex is observed in the vertical meridian of each eye, and then rotated to assess the horizontal meridian of each eye. The reflexes in the two meridians should be approximately the same width, and a difference in width of the reflex indicates that astigmatism is present. A small amount of "with" motion should be observed when the patient is in focus at distance. Larger amounts of "with" motion indicate a significant residual hyperopic error, while "against" motion indicates myopia. Next, the patient is instructed to observe details on the near target as shown in Fig. 2.1a, and the observer should see the "with" motion neutralize rapidly as accommodation brings the far point to the peephole of the retinoscope. Failure to neutralize the reflex indicates an accommodative insufficiency and/or a significant amount of hyperopia.

Attention is then directed again to the distance object, and "with" movement should be seen. Finally, attention is redirected to the near target, and the child is queried about the details of the target as the retinoscopist observes for and accurate and sustained accommodative response. The retinoscope and target are moved as a unit, and as they are moved toward the child, accommodation is further stimulated. The child should be able to sustain the accommodative effort and maintain neutralization easily as the target is studied for several seconds. When accommodation is normal, the results can be described as "rapid,

complete, and steady OU". When accommodation is abnormal, either the reflex will fail to neutralize completely or the patient will be unable to sustain the effort over time. The speed, symmetry, and sustainability of the accommodative effort should be recorded in the patient's chart. If abnormal accommodation is detected, the amount of near correction required can be determined by holding plus lenses in front of the patient and reassessing the retinoscopic reflexes at near. If dynamic retinoscopy is routinely performed on new patients and those at risk for accommodative insufficiency prior to cycloplegia, a post-cycloplegic evaluation can be avoided.

Dynamic retinoscopy can be used to evaluate how much hyperopia to correct in a patient with normal alignment and high hyperopia, and to assure that enough residual accommodation is available for near work. In a patient with strabismus that is large enough to cause off-axis errors in the retinoscopic evaluation of the non-fixating eye, it is necessary to test each eye separately and occlude the eye not being examined. Monocular evaluation is also useful in the evaluation of amblyopic eyes that are not improving with treatment of the amblyopia. Some amblyopic eyes have deficient accommodation and may require correction for near in order for amblyopia treatment to succeed.

Finally, dynamic retinoscopy is quite useful in the evaluation of the pediatric patient with complaints that may be non-physiologic in nature. Taken in conjunction with the history, other objective findings (normal papillary reactions, structural examination, and cycloplegic refraction), good stereopsis, and non-physiologic responses to stereo and color vision testing, dynamic retinoscopy can help to reassure the ophthalmologist when the findings are normal.

2.2.4 Assessment of Current Spectacles

Current spectacle correction should be measured at each visit to avoid surprise and confusion. It is always important to check that the lenses were made properly and that if the lenses have fallen out, they have been properly replaced. Sometimes children present for examination wearing old correction, a sibling's correction, or wearing glasses where the lenses have been switched. Attention to accurate measurement of current spectacles is important for ophthalmologists who prescribe using the technique of over-refraction.

Ophthalmologists who write prescriptions in plus cylinder notation should instruct their staff to be vigilant about measuring cylinder axis, as transposition errors made by opticians can result in 90° axis errors. Opticians routinely transpose prescriptions written in plus cylinder notation to minus cylinder, since lenses are manufactured with cylinder correction on the posterior surface of the lens (minus cylinder).

The accurate measurement of bifocal power, especially in hyperopic correction, should be measured with the temples oriented toward the practitioner, in contrast to typical clinical practice. The distance correction is measured first (using the least hyperopic meridian if cylinder is present), and then measuring the power in the same meridian through the near segment. The bifocal power is the difference between the two.

Some children require large astigmatic corrections, and proper cylinder axis is essential, particularly for children with amblyopia. ANSI Z80.1-2005 standards [12] require that cylinder powers 0.50-D cylinder power be dispensed within ±7°, 0.75 diopters cylinder must be within 5° the prescribed axis, correction >0.75 to ≤1.50-D cylinder within ±3°, and for greater cylinder powers its axis tolerance is ±2°.

Attention should also be given to the general location of the optical center of the lenses relative to the interpupillary distance, especially when a new or unexpected ocular deviation is present. Some frame designs have round or oval lens apertures, and the lenses can be placed in the frame with astigmatic correction at the proper axis but located temporally in the eyewire relative to its proper placement (Fig. 2.2). In a patient with high hyperopia and previously well-controlled accommodative esotropia, temporal displacement of the optical centers produces base-out prism, and can cause an exodeviation. A quick way to locate the optical centers of a lens while in the exam lane is to hold the lens below a ceiling spotlight and align the reflections of the light from the front and rear surfaces of the lens (Fig. 2.3). If a problem with the optical center of the lens is suspected based on the rapid chair-side assessment, the precise location of the optical center can be confirmed with a lens meter.

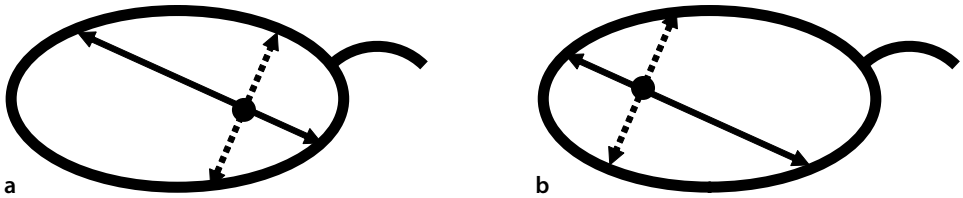
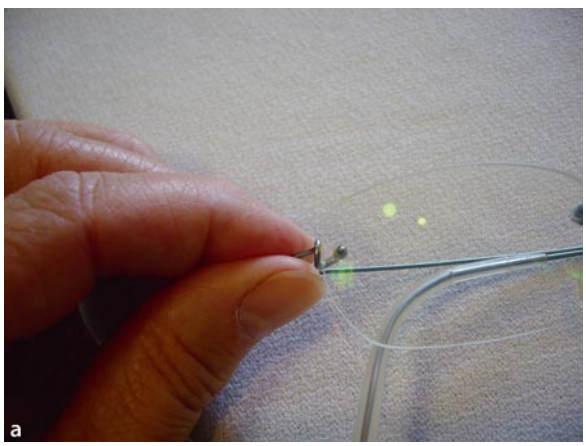
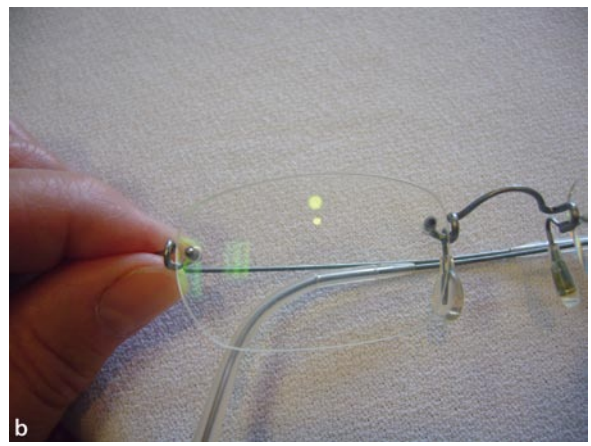


Fig. 2.2a,b Effect of 180° of lens rotation by improper replacement of the right spectacle lens in an oval frame. Typical, intended location of the optical center (*dot*). **a** Nasal of the geometric center of the eyewire; principle meridians of the spherocylindrical lens marked with *dashed* and *solid lines*. **b** With improper replacement of the lens in the frame, the axis of the spherocylindrical correction is correct, but the optical center (*dot*) is temporal to its intended location





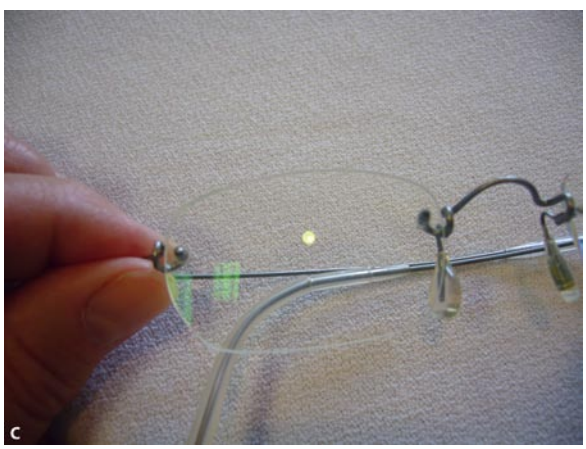


Fig. 2.3a–c Reflections from the front and rear surfaces of a spectacle lens can be used to quickly locate the optical center of a lens. **a,b** The reflections from the front and rear surfaces are separated. **c** The reflections are superimposed over the optical center of the lens

2.2.5 Subjective Refraction

Subjective refraction of teens and older children is a useful adjunct to cycloplegic retinoscopy and can be particularly helpful in children with large amounts of cylinder where very small errors in cylinder axis can make a significant difference in visual acuity. Subjective refraction can be performed either using a phoropter or in trial frames. Some children will readily accept either technique, but the author usually prefers trial frames in order to be able to watch the child's facial expressions during the refraction. A rapid and succinct subjective technique is especially important for children who may have a short attention span or who may lack self confidence when responding to the examiner. The rapidity of the response from the child is often a good indicator of her confidence in the answer: a rapid response in the anticipated

direction is usually a good indication of a reliable response. It is also helpful to have a quiet examination room, free from distraction by active siblings or a well-intentioned parent. Retinoscopic findings are usually the most efficient starting point and allow the examiner to guard against accommodation when the refraction is performed without cycloplegia. Subjective refinement of cycloplegic retinoscopic findings can help to refine axis and power.

Most children have large accommodative reserves, so special attention to control of accommodation is needed during non-cycloplegic refraction. During subjective non-cycloplegic refraction, "pushing plus" and making the child demonstrate the anticipated improvement in acuity with added minus (or reduced plus) correction can help guard against stimulating accommodation – about a line of improvement should be expected with each 0.25 diopters in the minus direction. Control of accommodation can be confirmed while performing interocular balancing in most children who are cooperative with non-cycloplegic subjective refraction using the red-green (douchrome, bichrome) test.

Subjective refinement of static retinoscopic findings prior to dilation and cycloplegia is particularly important for older children with lenticular dislocation (e.g., Marfan syndrome or ectopia lentis) or corectopia (e.g., Rieger anomaly/syndrome or after trauma). After dilation, it is difficult or impossible to tell what portion of the cornea, pupil, and lens the eye habitually uses for viewing in eyes with these disorders, so refraction with the lens and pupil in their natural positions is important.

2.2.6 Cycloplegia

Cycloplegia is essential for accurate refraction in young children. Due to their large accommodative amplitudes, a strong cycloplegic agent is indicated in the pediatric ophthalmic evaluation. Cyclopentolate is the most commonly used medication in the United States because of its rapid onset, relatively adequate cycloplegia, and short duration (compared with atropine). Cyclopentolate 1% is the most frequent strength used, and it is often combined with phenylephrine and/or tropicamide for pediatric patients with dark irides. In cases where cyclopentolate does not produce adequate cycloplegia in the office, an atropine refraction may be needed. A common regimen is atropine 1% twice a day for 2 days prior to the examination, and again on the morning of the examination. Parents should be instructed to wash their hands after instilling the eye drops in their children to avoid inadvertent self-administration of the drug.

Some pediatric ophthalmologists recommend the use of a topical anesthetic prior to the instillation of the cycloplegic drops, as the anesthetic promotes penetration of the cycloplegic agent into the eye and reduces the stinging of the cycloplegic drops. Other pediatric ophthalmologists find that the instillation of an additional set of drops is not needed, and that since the anesthetic drops sting, they feel that the extra step does not contribute to a more positive office visit.

2.2.7 Vertex Distance

Vertex distance, the distance from the cornea to the posterior surface of the refractive correction, is clinically significant for refractive errors greater than 5 diopters − a common finding in a pediatric ophthalmology practice. Vertex distance is most easily measured with a Distometer (Haag-Streit Services, Waldwick, New Jersey) and trial frames (Fig. 2.4) or the child's

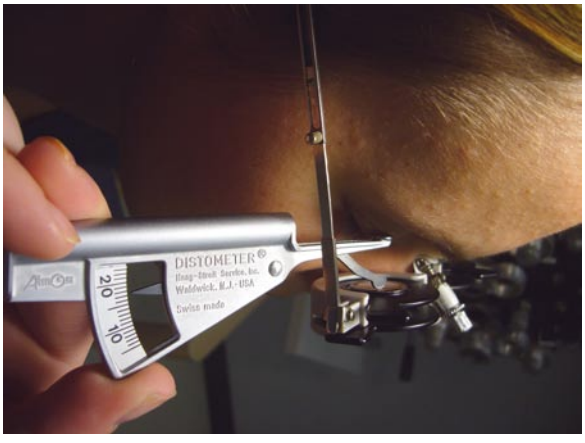


Fig. 2.4 A Distometer (Haag-Streit Services, Waldwick, N.J.) is used to measure the vertex distance in a patient with high hyperopia while wearing trial frames

current correction. Practically speaking, however, it is nearly impossible to measure vertex distance in most younger children. For children with refractive errors greater than 5 diopters, refraction over the current spectacle correction is the most accurate way to control for errors that result from vertex distance. Refractive findings can be added to the current spectacle correction (mathematically, or measured through a lensmeter) and the optician instructed to duplicate the vertex distance of the current correction. The optician will not be able to measure and duplicate the vertex distance exactly, but the optician can fit the frames so that the vertex distance of the new correction closely approximates that of the old one.

Vertex distance is very important in contact lens fitting for aphakic infants. Consider the following example of a typical aphakic infant. If the refraction with measured with retinoscopy and loose lenses is $+22.00+2.00\times80$, what should the contact lens power be? If fitting a soft contact lens, the refraction is converted to its spherical equivalent: +23.00. It is difficult, if not impossible, to measure vertex distance in a squirming infant, but if a 10-mm vertex distance is assumed, the contact lens power needed would be +29.9 diopters. If a 12-mm vertex distance is assumed instead, the contact lens power needed increases to +31.8 diopters. Note the large (2 diopters) variation in calculated lens power depending on the vertex distance. It is easy to see how small differences in vertex distance could make a significant difference in the measured refraction. The examiner should select a contact lens with a power within several diopters of the calculated power, and the refraction should be repeated and refined with the contact lens in place.

2.2.8 Refraction Under Anesthesia

Children who are refracted in the operating room while anesthetized should have cycloplegic drops instilled at an appropriate interval prior to the refraction if the eyes are phakic. Anesthesia per se does not produce cycloplegia, and accommodation may occur spontaneously. When performing retinoscopy under anesthesia, it is important to pay special attention to the eye's visual axis, and to refract that portion of the pupil that the child has been observed to use while awake. In children without corectopia, it is helpful to place the first Purkinje-Sanson image (the corneal light reflex) in a physiologic position, just nasal of the geometric center of the pupil. As a practical point, finding the position yielding the most plus (or least minus) refraction is "on-axis". Off-axis refraction will reduce the measured plus sphere (or increase the amount of minus sphere), will cause cylinder power and/or axis errors in the refraction of an astigmatic eye, or will produce an astigmatic refraction in an eye with a spherical refractive error. Care should also be taken to maintain an appropriate vertex distance, especially with larger refractive errors.

In children with difficult media and a poor retinoscopic reflex, it is often necessary to move closer to the eye to "enhance" the reflex. An assistant should measure the working distance while the doctor performs the refraction, and the working distance (in diopters) is subtracted from the retinoscopic findings. A useful distance is 20 cm, or 5 diopters from the eye. For instance, an eye with a retinoscopic reflex that is neutralized with +9.50 sphere at a working distance of 20 cm (5 diopters) would require distance-refractive correction of +4.50. It is important to measure an intentionally short working distance accurately, as small changes in a short working distance translate to larger dioptric changes in working distance compared with typical working distances.

2.2.9 Estimation Retinoscopy

Estimation retinoscopy (using sleeve position to vary the vergence of light leaving the retinoscope and estimate refractive error based on sleeve position) is a useful screening technique for children who are unable to cooperate with accurate measurement of refractive error using loose lenses. Wallace et al. demonstrated the accuracy of estimation retinoscopy in the evaluation errors less than 4 diopters of myopia and 2 diopters of hyperopia [13]. Uncooperative children with larger suspected refractive errors detected by estimation retinoscopy may warrant examination under anesthesia if accurate measurements cannot be obtained in the clinic setting.

2.3 Prescribing and Dispensing

2.3.1 Prescribing

The prescription of eyeglasses in the pediatric population is more difficult than in adults, where a prescription is usually given as a result of a visual complaint – asthenopia or blurred vision at near and/or distance. Usually, an improvement in visual acuity with correction warrants a prescription for refractive correction. While older children may present with blurred vision, younger children usually offer no subjective complaints. Prescribing for refractive errors in children is further complicated by the fact that many parents are resistant to their young child wearing glasses at all, and that children anisometropia and good uncorrected vision in the better eye may not appreciate an improvement with correction. Glasses for children are the most commonly prescribed treatment for vision disorders in children, and they can cause vision loss if improperly prescribed or can be a significant financial burden for families if not truly needed. The American Academy of Ophthalmology Pediatric Eye Evaluations Preferred Practice Pattern summarizes suggested guidelines for prescribing, and is reproduced in Table 2.2.

Table 2.2 The AAO PPP consensus guidelines for prescribing spectacles in children

	Age (years)		
	0–1	1–2	2–3
Isometropia			
Myopia	≥ −5.00	≥ −4.00	≥ −3.00
Hyperopia without strabismus	≥ +6.00	≥ +5.00	≥ +4.50
Hyperopia with esotropia	≥ +3.00	≥ +2.00	≥ +1.50
Astigmatism	≥ 3.00	≥ 2.50	≥ 2.00
Anisometropia			
Myopia	≥ −2.50	≥ −2.50	≥ −2.00
Hyperopia	≥ +2.50	≥ +2.00	≥ +1.50
Astigmatism	≥ 2.50	≥ 2.00	≥ 2.00

The unit of measure is diopters

2.3.1.1 Prescribing for Myopia: School-aged Child

Myopia is common in the school-aged population, and the prevalence in the United States and western Europe increases gradually in childhood such that about 25% of the adult population is myopic. In some clinical situations, the indications for glasses are straightforward: the school-age child with moderate myopic astigmatism that is having trouble seeing the board should receive full correction of the myopic and astigmatic error. For younger children and those needing smaller corrections, many practitioners use uncorrected distance acuity of worse that 20/40 as the threshold for prescribing; however, some children are symptomatic with better acuity, and correction should be offered for these children.

Some ophthalmologists have historically offered to undercorrect the myopic portion of the refractive error in the hope of slowing myopic progression; however, a recent study in school-aged children by Chung et al. [14] demonstrated that the myopia progression actually increased when myopia is intentionally under-corrected by 0.75 diopters. Adler and Millodot [15] undercorrected myopia by 0.5 diopters and demonstrated a slight increase in myopic progression, but the increase was not statistically significant. Thus, undercorrection of a myopic student will lead to blurred vision at distance, and may increase myopic progression, and should be avoided.

Some parents are especially concerned about myopic progression and will ask if anything can be done to slow progression in their child. The Correction of Myopia Evaluation Trial (COMET) studied the effect of progressive addition lenses versus single vision lenses on the progression of myopia in children during a 3-year randomized clinical trial. Although the trial did show a small, statistically significant reduction in myopic progression during the first year of correction only (and none during the subsequent years), the progressive addition lenses only resulted in a mean 0.2-D difference in myopia at the end of the 3-year trial [16]. Progressive addition lenses add significant cost to the spectacle correction and result in a clinically insignificant reduction in myopic progression. Thus, progressive addition lenses do not seem to be indicated in the correction of most myopic children; however, there may be some benefit for a

limited number of myopic children who have an esophoria at near, accommodative lag, or a combination of the two in association with myopia [17].

Rigid contact lenses have been proposed as a treatment for the progression of myopia, and the Contact Lenses and Myopia Progression (CLAMP) study [18] reported that rigid gas permeable contact lenses slowed myopic progression in young children when compared with soft contact lens wear. The difference in myopia progression between the rigid and the soft contact lens wearers was 0.63 diopters, but there was no difference in axial growth between the two groups. The investigators reported that the rigid contact lenses kept the cornea from changing shape more than soft contact lenses, and hypothesized that the effect of rigid lenses on myopia progression may not be permanent.

2.3.1.2 Prescribing for Myopia: Infant and Preschool Child

Myopia in infancy and the preschool years should be treated if it is of a magnitude that it is likely to cause amblyopia through large amounts of isoametropia or more modest amounts of anisomyopia. An infant and toddler's world is at near, and a younger child with symmetric amounts of mild to moderate myopia can be safely observed without correction. Miller and Harvey [19] surveyed AAPOS members and reported a prescribing threshold of 5 diopters of myopia for infants less than 1 year old, decreasing to a threshold of 3 diopters of myopia for children 2−3 years old. When anisomyopia of 2 or more diopters is present, glasses should be considered.

2.3.1.3 Prescribing for Astigmatism

Mild to moderate levels of astigmatism <1.5 diopters decrease visual acuity only slightly, and do not require correction in younger children unless accompanied by a significant myopic or hyperopic error. School-aged children have greater visual demands and may require correction for astigmatism if it is causing blurred vision at distance. Comparison of best-corrected and uncorrected visual acuity can guide the decision of whether to prescribe for an isolated astigmatic error.

Evidence-based guidelines for prescribing for infants and toddlers do not exist, but Harvey et al. [20] reported the prescribing habits of AAPOS members for astigmatism. The American Academy of Ophthalmology's Pediatric Eye Evaluations Preferred Practice Pattern [21] suggests prescribing for 3 diopters of astigmatism in a child less than 1 year old, but AAPOS members have been reported to have slightly higher thresholds for prescribing in infants and toddlers. Infants and preschoolers who require glasses for isoametropia and/or astigmatism should always receive their full astigmatic correction at the correct axis. Children do not complain about meridional distortion, and failure to fully correct astigmatic errors at the correct axis may cause amblyopia or hinder its treatment.

2.3.1.4 Prescribing for Anisometropia

Amblyopic children with anisometropia should receive balance correction of the error. If hyperopia and esotropia are present, the full hyperopic and anisometropic correction should be prescribed. In the absence of an esodeviation, hyperopia should be corrected according to the guidelines below, with symmetric reduction of the error in each eye. The recommendations for anisometropic children without amblyopia are less clear, but Donahue [22] has nicely summarized the evidence and uncertainties surrounding the correction of anisometropia in the absence of definite amblyopia. He recommended a threshold of 1−1.5 diopters of anisometropia; however, abnormal ocular findings and/or family history of amblyopia could lower threshold for spectacle prescription.

2.3.1.5 Prescribing for Hyperopia

Uncorrected hyperopia is associated with isoametropic amblyopia, accommodative amblyopia, and strabismic amblyopia. Whether to prescribe correction for hyperopia is complicated by the consideration that most young children are mildly hyperopic, and the observation that not all children with moderate levels of hyperopia develop amblyopia and/or strabismus. Atkinson [23] and colleagues have carefully studied the effects of infant hyperopia and its correction in a series of studies, summarized in a 2007

publication. The authors report that the prevalence of ≥4 diopters of hyperopia in 8- to 9-month-old Caucasian infants is around 5%. Infant hypermetropia was associated with increased strabismus and poor acuity at 4 years of age, and spectacle wear produced better visual outcome than no glasses. The prescription of glasses did not affect emmetropization. The hyperopic patients demonstrated poorer overall performance compared with emmetropic controls on visuoperceptual, cognitive, motor, and attention tests. This work was corroborated in a study [24] of 3- to 5-year-olds with a similar degree of ametropia, and the ametropic children scored significantly lower on test of visual-motor function.

Despite emerging evidence that moderate levels of uncorrected hyperopia in infancy can negatively affect ocular health and cognitive development, ophthalmologists have historically had a higher threshold for prescribing in hyperopic children without strabismus. Miller and Harvey reported that 50% of pediatric ophthalmologists would prescribe glasses for children less than 2 years old with 5 diopters of hyperopia, and the threshold decreased to 4 diopters for children older than 2 years. The AAO PPP Pediatric Eye Evaluation suggests a threshold of 6 diopters of hyperopia for infants less than 1 year old, 5 diopters for 1−2 years old, and 4.50 diopters for 2- to 3-year-olds without concurrent strabismus. When an esotropia is present, the threshold suggested by the AAO PPP changes to 3 diopters of hyperopia for infants <1 year old, 2 diopters for 1−2 years old, and 1.50 diopters for 2- to 3-year-olds.

Once a decision is made that correction is needed for hyperopia, how much of the hyperopia should be corrected? When an esotropia is present, the full hyperopic correction should be given. Children who have difficulty adjusting to their hypermetropic glasses can benefit from "pharmacologic encouragement" – one drop of atropine in both eyes daily for 5 days helps most children to accept the glasses. Children with a residual esodeviation after correction of their full hyperopic error should be refracted again to check for residual hyperopia or an increase in the error. Bifocals are indicated for children with a high clinical accommodative convergence/accommodation ratio and should be fit with the top of the segment bisecting the pupil.

In children with significant hyperopia with normal ocular alignment, most pediatric ophthalmologists will reduce the correction by a symmetric amount – typically 1.5 diopters, unless there is a family history of accommodative esotropia or evidence of accommodative insufficiency. When parents seem to resist correction of hyperopia, it can be useful to "demonstrate" the hyperopic state by putting up minus lenses in front of the parent, and directing their attention to a distance and then near target to stress their accommodation. Parents should be warned that they may begin to see an esodeviation without correction after hyperopic spectacle correction is instituted.

2.4 Dispensing Recommendations: Tints

Parents of children with albinism, aniridia, colobomata, corneal scarring, treated ROP, or other diseases associated with photophobia should be carefully questioned about light sensitivity. Children with photophobia can benefit from dark tints (80−90% tint/10−20% transmission) for outdoors, and lesser tints for indoors (20−30% tint/70−80% transmission). Opaque side shields may be needed for children with more severe photophobia, particularly those with oculocutaneous albinism. The amount of tint desired should be specified on the prescription so that the tint density will be properly made; it is unambiguous to specify both transmission and blockage percentages as noted above. A special note for the tinted lenses may be needed for school. Hats with wide brims for outdoors can also help with photophobia.

2.5 Dispensing Recommendations: Protective Eyewear and Monocular Patients

Patients with unilateral vision impairment have an increased risk of vision loss in the better eye due to disease or injury. Thus, patients who are functionally monocular (best corrected acuity in the poorly seeing eye less than 20/40) should wear protective eyewear at all times, even if refractive correction is not in-

dicated for the better eye. A frame approved by the ANSI (American National Standards Institute Standard No. Z87.1) with polycarbonate lenses should be worn for daily wear and low-eye-risk sports. Polycarbonate sports goggles complying with American Society for Testing and Materials (ASTM) should be worn for most ball and contact sports, and head and face protection should be added for higher-risk activities, as described in a Joint Policy Statement by the American Academy of Pediatrics and the American Academy of Ophthalmology (2003).

Monocular patients are at special risk for injury, and ophthalmologists should strongly recommend that athletes who are functionally one-eyed wear appropriate eye protection during all sports activities, including physical education during school. Monocular patients should not participate in full-contact martial arts or boxing, as adequate eye protection is not available. Wrestling was previously contraindicated for monocular patients, but custom eye protection can be fabricated to reduce the risk of eye injury for wrestlers.

Parents of athletes, and older student athletes themselves, should be carefully apprised of the risks associated with athletic participation and the availability of a variety of appropriate and/or certified sports eye protection. Even though eye protection cannot completely eliminate the risk of ocular injury, appropriate eye protection has been demonstrated to dramatically reduce the risk of significant eye injury. Some sports (for example, ice hockey) have mandated eye protection as a condition for sports participation, and there has been a dramatic reduction of significant eye and related injuries after institution of such policies. Sadly, not all sports have taken such a proactive stance.

Students and athletes with a history of intraocular surgery or significant eye trauma may be more susceptible to injury with even minor trauma; these children may require additional eye or face protection for athletic activity, or may need to be restricted from certain sports. It is important to inform the child's pediatrician or family medicine physician of necessary eye protection or limits on participation so that sports participation forms can be filled out properly.

2.6 Contact Lenses for Children

Contact lenses are important in the visual rehabilitation of unilaterally aphakic infants and children, and should be fit as soon after surgery as reasonably possible so that amblyopia treatment can begin. A contact lens reduces the image magnification that an aphakic spectacle lens produces, though the more important barrier to binocular vision is usually dense amblyopia due to the unilateral cataract and aphakia. Many bilateral aphakes use contact lenses with additional plus power to correct for near in infancy, graduating to bifocals as toddlers. Extended-wear soft or rigid lenses are generally well tolerated, though the frequent power changes and lost lenses are a significant financial barrier for many families. Decreased acuity secondary to corneal opacities and scarring after corneal laceration can usually be improved with a rigid contact lens if a good fit can be achieved.

Unilateral high myopia is another situation when contact lenses are sometimes recommended for young children, citing that the anisiekonia caused by the spectacle correction would prevent sensory fusion. In clinical practice, however, these children usually have dense anisometropic amblyopia that, even when successfully treated, prevents development of sensory fusion. Contact lens correction of unilateral high myopia does prevent anisophoria caused by anisometropic correction, but children are rarely bothered by this problem. Finally, children with unilateral high myopia typically have amblyopia and poor vision in the weaker eye, and so should be wearing spectacles for protection even if contacts can be successfully worn.

Take Home Pearls

- Spectacles alone improve best-corrected amblyopic eye visual acuity by about three lines, so many patients do not need additional treatment with patching or penalization.
- Penalization is a viable option to occlusive patching in most patients with amblyopia. Penalization methods include atropine eye drops, optical penalization using a plano (blank) lens or excessive plus power lens, atropine with a plano lens, and Bangerter foils.
- Atropine may successfully treat amblyopia even when there is no apparent fixation switch to the amblyopic eye and when the atropinized sound eye near visual acuity remains better than amblyopic eye acuity.
- After stopping patching or atropine, about one in four patients will lose two or more lines of amblyopic eye visual acuity over the next 1 year.
- Amblyopia treatment may have its greatest benefit in later life, when sound eyes can sustain injuries or be afflicted by diseases of the macula or optic nerve.
- The rapidity of the response from the child is often a good indicator of her confidence in the answer: a rapid response in the anticipated direction is usually a good indication of a reliable response.
- Refraction over the current spectacle correction is the most accurate way to control for errors that result from vertex distance.
- A quick way to locate the optical centers of a lens while in the exam lane is to hold the lens below a ceiling spotlight, and align the reflections of the light from the front and rear surfaces of the lens (see Fig. 2.3). If a problem with the optical center of the lens is suspected based on the rapid chair-side assessment, the precise location of the optical center can be confirmed with a lensmeter.
- In children with difficult media and a poor retinoscopic reflex, it is often necessary to move closer to the eye to "enhance" the reflex. An assistant can measure the working distance while the doctor performs the refraction, and the working distance (in diopters) is subtracted from the retinoscopic findings.
- When parents seem to resist spectacle correction of refractive errors, it can be useful to "demonstrate" the child's refractive state by placing error lenses in front of the parent. Minus lenses are used to simulate hyperopia, and parental attention is directed first to a distance, and then near, target to stress accommodation. Anisometropia can be demonstrated in a similar fashion, simulating the refractive errors with disparate lenses.

References

1. Harvey EM, Dobson V, Miller JM. Prevalence of high astigmatism, eyeglass wear, and poor visual acuity among Native American grade school children. Optom Vis Sci 2006; 83:206–12
2. Gwiazda J, Hyman L, Dong LM, Everett D, Norton T, Kurtz D, Manny R, Marsh-Tootle W, Scheiman M; Comet Group. Factors associated with high myopia after 7 years of follow-up in the Correction of Myopia Evaluation Trial (COMET) Cohort. Ophthalmic Epidemiol 2007; 14:230–7
3. Rose KA, Morgan IG, Ip J, Kifley A, Huynh S, Smith W, Mitchell P. Outdoor activity reduces the prevalence of myopia in children. Ophthalmology 2008, 20 February. [Epub ahead of print]
4. Ip JM, Rose K, Morgan I, Burlutsky G, Mitchell P. Myopia and the urban environment: findings for a sample of

12-year old Australian school children. Invest Ophthalmol Vis Sci 2008, 9 May. [Epub ahead of print]
5. Quinn GE, Shin CH, Maguire MG, Stone RA. Myopia and ambient lighting at night. Nature 1999; 399:113–4
6. Stone RA, Wilson LB, Ying GS, Liu C, Criss JS, Orlow J, Lindstrom JM, Quinn GE. Associations between childhood refraction and parental smoking. Invest Ophthalmol Vis Sci 2006; 47:4277–87
7. Woodhouse JM, Cregg M, Gunter HL, Sanders DP, Saunders KJ, Pakeman VH, Parker M, Fraser WI, Sastry P. The effect of age, size of target, and cognitive factors on accommodative responses of children with Down syndrome. Invest Ophthalmol Vis Sci 2000;41:2479–85
8. McClelland JF, Parkes J, Hill N, Jackson AJ, Saunders KJ. Accommodative dysfunction in children with cerebral palsy: a population-based study. Invest Ophthalmol Vis Sci 2006; 47:1824–30
9. Guyton DL, O'Connor GM. Dynamic retinoscopy. Curr Opin Ophthalmol 1991; 2:78–20
10. Hunter D. Dynamic retinoscopy: the missing data. Surv Ophthalmol 2001; 46:269–74
11. Mohindra I, Held R, Gwiazda J, Brill J. Astigmatism in infants. Science 1978; 202:329–31
12. ANSI Z80.1-2005 Ophthalmics – Prescription Ophthalmic Lenses – Recommendations. The Accredited Committee Z80 for Ophthalmic Standards, Optical Laboratories Assocaition, Fairfax, Virginia, 2006
13. Wallace DK, Carlin DS, Wright JD. Evaluation of the accuracy of estimation retinoscopy. J AAPOS 2006; 10:232–6
14. Chung K, Mohidin N, O'Leary DJ. Undercorrection of myopia enhances rather than inhibits myopia progression. Vision Res 2002; 42:2555–9
15. Adler D, Millodot M. The possible effect of undercorrection on myopic progression in children. Clin Exp Optom 2006; 89:315–21
16. Gwiazda J, Hyman L, Hussein M, Everett D, Norton TT, Kurtz D, Leske MC, Manny R, Marsh-Tootle W, Scheiman M. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. Invest Ophthalmol Vis Sci 2003; 44:1492–1500
17. Gwiazda JE, Hyman L, Norton TT, Hussein ME, Marsh-Tootle W, Manny R, Wang Y, Everett D; COMET Group. Accommodation and related risk factors associated with myopia progression and their interaction with treatment in COMET children. Invest Ophthalmol Vis Sci 2004; 5:2143–51
18. Walline JJ, Jones LA, Mutti DO, Zanik K. A randomized trial of the effect of rigid contact lenses on myopia progression. Arch Ophthalmol 2004; 122:1760–6
19. Miller JM, Harvey EM. Spectacle prescribing recommendations of AAPOS members. J Pediatr Ophthalmol Strabismus 1998; 35:51–2
20. Harvey EM, Miller JM, Dobson V, Clifford CE. Prescribing eyeglass correction for astigmatism in infancy and early childhood: a survey of AAPOS members. J AAPOS 2005; 9:189–91
21. American Academy of Ophthalmology. Pediatric eye evaluations, preferred practice pattern. American Academy of Ophthalmology, San Francisco, 2002
22. Donahue SP. Prescribing spectacles in children: a pediatric ophthalmologist's approach. Optom Vis Sci 2007; 84:110–4
23. Atkinson J, Braddick O, Nardini M, Anker S. Infant hyperopia: detection, distribution, changes and correlates: outcomes from the Cambridge infant screening programs. Optom Vis Sci 2007; 84:84–96
24. Roch-Levecq AC, Brody BL, Thomas RG, Brown SI. Ametropia, preschoolers' cognitive abilities, and effects of spectacle correction. Arch Ophthalmol 2008; 126:252–8

Refractive Surgery in Children

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3

Contents

Core Messages

- Anisometropic amblyopia is an important cause of visual impairment worldwide. Bilateral ametropic amblyopia can be severe enough to cause legal blindness in both eyes (20/200 or worse in the better seeing eye). Traditional treatment measures are ineffective in a significant number of affected children.
- Excimer refractive surgery is effective for correcting amblyopiogenic levels of severe anisometropia and bilateral ametropia when traditional treatment fails.
- Excimer refractive surgery in children usually requires general anesthesia. Specific modifications to the typical anesthesia protocol are needed to avoid the escape of inhalational anesthetic agents that will affect the excimer laser/tissue interaction.
- Refractive lens exchange and phakic intraocular lenses are just starting to be investigated in children with extremely high refractive errors that are outside the treatment range for excimer laser.

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3.1 Introduction

Children are born with immature visual systems, and for normal visual development to occur, they need a clear, focused image to be projected onto the retina where it is converted to neuronal signal and then transmitted to the developing occipital cortex via the optic nerve. Uncorrected refractive errors cause image blur, impeding this process, and may result in failure of normal visual maturation (amblyopia).

Amblyopia is commonly caused by anisometropia, the condition in which unequal refractive error between fellow eyes results in image blur in one eye (form vision deprivation) and/or abnormal binocular interaction via projection of dissimilar images onto the fovea of each eye [16]. In general, anisomyopia of more than 2 diopters, anisohyperopia of more than 1 diopter, and anisoastigmatism of more than 1.5 diopters can result in amblyopia [54, 55]. Studies of anisometropic amblyopia indicate a 100% prevalence of amblyopia in patients with 4 diopters or more of uncorrected hyperopia or 6 diopters or more of uncorrected myopia [26, 50]. Anisometropic amblyopia associated with anisometropia of more than 4 diopters is also less successfully treated with traditional amblyopia therapy [20]. The severity of amblyopia is directly related to the degree of anisometropia [13, 20, 26]. Successful treatment of anisometropic amblyopia with traditional therapy varies widely among practitioners and has been reported to be between 48 and 82% of children [16, 20, 23−26, 28, 56].

Bilateral uncorrected high refractive error can also cause amblyopia. This condition, called bilateral ametropic (or isoametropic) amblyopia, though less common than anisometropic amblyopia, is even more of a disability as it affects both eyes. Unsuccessfully treated bilateral ametropic amblyopia is typically a disorder that affects children with neurobehavioral disorders and high refractive error who are tactilely averse and refuse to wear their prescribed spectacles. It is becoming a more common problem today as more extremely premature infants are surviving with the sequelae of severe ROP and subsequent high myopia. Visual impairment in these children with multiple special needs further isolates them. Tychsen has coined the term “visual autism” to refer to the resultant severe visual isolation in these children [51].

Traditional therapy for anisometropic amblyopia includes refractive correction with spectacles or contact lenses, minimization of aniseikonia with contact lenses, and amblyopia management with occlusion therapy and/or pharmacologic and optical penalization of the sound eye [21, 24−26, 43]. Though these treatment strategies appear simple, they are frequently problematic and unsuccessful due to induced aniseikonia or diplopia with spectacles, psychosocial stress, unacceptable cosmesis with spectacles in which one lens is much thicker than the other, impracticality of contact management, and poor compliance with occlusion therapy [9]. Management of large magnitude bilateral ametropia is similar to anisometropia with regard to spectacles or contact lenses, though occlusion and penalization are not needed as both eyes have equal image blur.

Severe amblyopia causes a lifetime of visual handicap with its associated economic and social costs. Refractive surgery is now being used with good results for severe anisometropia and ametropia in children when traditional therapy fails.

3.2 The Excimer Laser

The excimer laser was invented in 1970 by Basov, Danilychev, and Popov in Moscow [31]. Excimer is short for “excited dimer”, as the laser uses a combination of electrically stimulated inert gas (argon, krypton, or xenon) and reactive gas (fluorine or chlorine) to create energized molecules which generate ultraviolet (UV) laser light. The UV light emitted by excimer laser is absorbed by organic material and disrupts molecular bonds, resulting in ablation, rather than burning, of surface tissues; thus, excimer lasers can remove exceptionally fine layers of surface tissue with almost no heating of or damage to the underlying tissue, which is left intact. These properties make the excimer laser well suited to precision corneal refractive surgeries.

For almost two decades, excimer refractive surgery, performed as an outpatient procedure under local anesthesia, has been an accepted method of treating myopia, hyperopia, and astigmatism in adults. Prudent selective use of excimer laser refractive surgery is now being investigated in carefully designed study protocols for children with severe anisometropia or bilateral ametropia in which traditional therapy failed and the visual results without any other treat-

ment would be effective blindness. This conservative approach is being used because of concerns regarding both the long-term refractive stability in the growing eye and the long-term corneal health.

With the advent of the excimer laser, corneal refractive surgery has evolved from incisionally based techniques to ablative procedures. Rather than altering the corneal curvature at discrete locations, photoablative procedures provide smoother and more uniform reshaping of the corneal surface. In myopia, excimer treatment flattens the central cornea to decrease its refractive power. In hyperopia, treatment indirectly steepens the central cornea by removing tissue from the periphery and flattening the peripheral cornea, which increases the cornea's focusing power. Astigmatism is corrected by differentially steepening the flattest meridian or flattening the steepest meridian.

Modern refractive surgery treatments are performed either as conventional or custom procedures. Conventional laser ablation patterns are calculated based on a patient's manifest or cycloplegic refractions, while customized (or "custom") laser ablation patterns incorporate computer-aided wavefront technology to deliver a more precise treatment. Wavefront science is a newer technology that has been incorporated into laser refractive surgery since the early twenty-first century. Using wavefront-guided techniques, a patient's subtle refractive errors, known as aberrations, which may not be detected by traditional refraction can be measured. In custom laser refractive surgery, the laser ablation pattern can be programmed to treat a patient's individual aberrations, as well as those induced by the refractive procedure itself. Unfortunately, aberration measurement requires a very cooperative patient and, for this reason, is often not possible in children. Fortunately, conventional ablation treatments still provide excellent results and are the most commonly used form of refractive surgery in the pediatric population today. Both conventional and custom treatments are available for a wide range of refractive errors (Table 3.1).

To date, approximately 270 amblyopic children (Table 3.2) who have undergone excimer refractive surgery for severe anisometropia and 15 who have undergone these procedures for bilateral severe ametropia have been reported (Table 3.3). Much more is now known about how children respond to treatment, making photorefractive keratectomy (PRK), laser in-situ keratomileusis (LASIK), and laser-assisted subepithelial keratectomy (LASEK) increasingly viable alternatives to conventional management in the subset of children with severe anisometropia or bilateral ametropia. In current practice, refractive surgery is generally considered in the severe bilateral ametropic and anisometropic pediatric population only when (1) traditional treatment measures have been exhausted

Table 3.1 Conventional ablation ranges for laser in-situ keratomileusis (*LASIK*) and photorefractive keratectomy (*PRK*)

Conventional ablation ranges				
LASIK		VISX Star S4	Alcon LadarWave	WaveLight Allegreto Wave
Myopia	Sph	≤ –14.0 D	≤ –9.0 D	≤ –12.0 D
	Cyl	–0.5 to –5.0 D	–0.5 to –3.0	≤ –6.0 D
Hyperopia	Sph	+0.5 to +5.0 D	≤ +6.0 D	≤ +6.0 D
	Cyl	≤ +3.0 D	≤ –6.0 D	≤ +5.0 D
Mixed astigmatism	Cyl	≤ 6.0 D	≤ –6.0 D	–

Conventional ablation ranges				
PRK		VISX Star S4	Alcon LadarWave	WaveLight Allegreto Wave
Myopia	Sph	≤ –12.0 D	≤ –10.0 D	
	Cyl	–0.75 to –4.0 D	–0.5 to –4.0 D	
Hyperopia	Sph	+1.0 to +6.0 D		
	Cyl	+0.5 to +4.0 D		

Table 3.2 Summary of PRK, LASIK and laser-assisted sub-epithelial keratectomy (*LASEK*) performed in children with severe anisometropic myopia. *NR* not reported, *BCVA* best-corrected visual acuity, *D* diopters, *SE* spherical equivalent

Reference	Year	Procedure	Mean age (years)	Age range (years)	No. of patients[a]	Mean Pre-SE (D)	Mean Post-SE (D)	Mean Pre-BCVA	Mean Post-BCVA
[47]	1995	PRK	12.9	10−15	9	−12.13	−2.92	20/81	20/44
[32]	1997	PRK	12.4	11−14	5	−7.9	−1.55	20/400	20/72
[4]	1998	PRK	6	5−7	6	−9.58	−2.42	20/114	20/35
[42]	1999	LASIK	9.4	7−12	14	−7.87	−0.55	20/50	20/25
[10]	1999	PRK	11.5	7−15	13	−8.9	−1.12	.51	0.61
[2]	2000	LASIK	8.4	5−11	16	−14.88	−1.44	20/37	20/37
[33]	2001	LASIK	11.5	8−15	9	−7.22	−0.22	NR	NR
[44]	2001	LASIK	NR	9−15	38	−6.00	NR	NR	NR
[34]	2001	PRK/LASIK	11.9	9−14	14	−7.96	−0.67	20/125	20/121
[6]	2002	PRK	6.3	1−6	27	−10.68	−1.37	20/70	20/40
[7]	2004	LASEK	8.27	1−17.4	25	−8.03	−1.19	20/80	20/50
[35]	2004	LASIK	NR	2−12	6	−10.2	−3.0	20/142	20/63
[36]	2004	PRK	6.1	2−11	11	−13.75	−3.3	20/316	20/126
[9]	2004	PRK/LASEK	5.4	4−7	27	−8.25	−1.61	20/95	20/26
[39]	2004	LASIK	13.4	8−19	5	−9.05	−0.90	20/30	20/30
[52]	2005	PRK/LASEK	8.4	4−16	35	−11.5	1.26	20/87	20/47
[51]	2006	LASEK	10.2	3−16	9	−16.6	−8.7	20/133	20/60

[a] A total of 269 patients

Table 3.3 Summary of PRK and LASEK performed in children with bilateral ametropia. *BCVA* best-corrected visual acuity, *D* diopters, *SE* spherical equivalent

Reference	Year	Procedure	Age (years)	No. of patients	Pre Se (D)	Post SE (D)	Mean pre BCVA	Mean post UCVA	Behavior
[51, 52]	2005, 2006	PRK, LASEK	3−16	10	−3.75 to −11.5	89% within 1 D of goal	20/133	20/60	Improved
[8]	2006	PRK, LASEK	1−7	5	+2 to −10	100% within 1 D of goal	20/100	1−2 lines BCVA in 4 patients	Improved

or fail, or (2) chronic noncompliance with, or intolerance of, traditional treatment endangers normal visual development.

Visual and refractive results of excimer laser procedures in children have been moderate to excellent depending on the study evaluated [3, 5−10, 32, 33, 35, 36, 42, 44, 51, 52]. By and large, the younger children tended to have better visual results while the refractive results were equivalent at any age. In some studies, social interaction and behavior were reported to have improved.

3.3 Excimer Surgical Procedures

PRK and LASIK are the most common ablative procedures performed in adults and children. For PRK, a topical anesthetic is first applied and the corneal epithelium in the ablation zone is removed mechanically with a spatula (which may be combined with alcohol-enhanced epithelial loosening), brush, microkeratome or, less commonly, via laser scrape. The laser is then applied to the corneal stroma to resurface it (Fig. 3.1). After the procedure, a topical antibiotic and

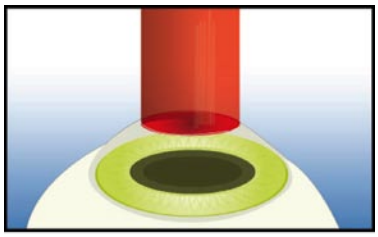

Fig. 3.1 In PRK ablation is performed directly on the corneal surface. (Courtesy of J. Van Luu)

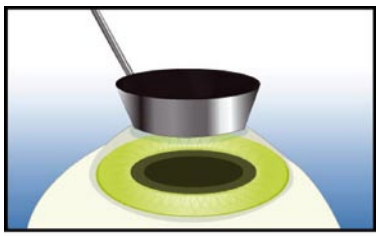

Fig. 3.2 In LASEK, the epithelium is moved over to the side after it is loosened with alcohol (shown here). Then a surface ablation like in PRK is performed and the epithelium is repositioned. (Courtesy of J. Van Luu)

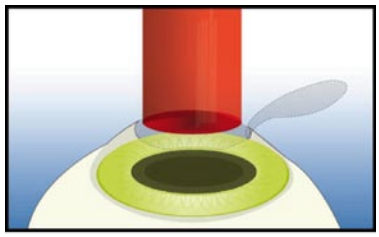

Fig. 3.3 In LASIK, the laser is applied to the stroma after a flap is cut and lifted. The flap is then replaced. (Courtesy of J. Van Luu)

steroid are applied and a disposable bandage contact lens is applied. Until the corneal epithelium recovers the patient may experience some discomfort and photophobia (3−5 days). A topical antibiotic is used for a week and topical steroid is used for 6 months in children. Visual acuity gradually improves as the epithelial defect and stroma heal and typically stabilizes by 3−6 months. Reliable refractive results are limited to 10−12 diopters of myopia, 5 diopters of hyperopia, or 4 diopters of astigmatism.

PRK carries the risk of several complications. Glare, halos, and dryness are common initially but generally diminish or resolve by the sixth postoperative month. Corneal haze is a potentially serious complication of PRK that tends to occur more often in patients with high myopia who require a larger laser ablation. The risk for developing this complication appears to be related to higher expression of collagen type-IV α3. Children may be at risk for this complication for a longer period of time postoperatively than adults. For this reason, they may require topical steroids for a longer period of time (4−6 months).

LASEK is a procedure similar to PRK. In this procedure, the corneal epithelium is first preserved with an alcohol solution and then peeled back as a single sheet to expose the corneal stroma (Fig. 3.2). The corneal stroma is then reshaped by excimer laser. After photoablation is complete, the preserved epithelium is replaced so that no corneal epithelial defect occurs. Postoperatively, patients are managed similarly to those who receive PRK. LASEK is supposed to be less painful than PRK postoperatively, though this has not been extensively studied. Visual and refractive outcomes and potential risks of LASEK are equivalent to those of PRK.

LASIK is a procedure in which a microtome or femtolaser is used to create a corneal flap typically 100−180 μm thick and 8−9 mm in diameter. This flap is reflected to reveal the underlying stroma. The excimer laser is then used to photoablate the exposed stroma to reshape the cornea (Fig. 3.3). Afterward, the flap is returned to its original position. The flap is stabilized by the natural tissue dehydration that results from the action of the corneal endothelial pump rather than by sutures. Because no corneal epithelial defect is created, patients report less postoperative pain and faster recovery. LASIK, however, carries the risk of more serious complications such as flap dislocation, corneal striae, and keratectasia [5, 14, 15, 18, 22, 27, 40, 42, 46, 48, 49]. Because children tend to rub their eyes frequently, which increases the risk of lamellar flap dislocation following LASIK, PRK and LASEK are currently preferred in the pediatric population.

The newer excimer laser models may include infrared cameras that image the eye intraoperatively. Image processing software identifies the pupil, and the excimer laser tracks the pupil margin during treatment to accurately align the ablation pattern with the cornea. The laser machine also has a fixation target for the awake patient to fixate on during the procedure. The risk of treatment decentration increases with loss of fixation or the inability to fixate. This risk is naturally higher in children who require general anesthesia and must have the eye manually centered (see below).

3.4 Setting up a Pediatric Excimer Refractive Surgery Program

3.4.1 Preoperative Guidelines

The first step in establishing a program to perform PRK, LASIK, and/or LASEK on pediatric patients must be to clearly define the criteria used to determine candidacy for such procedures. In general, refractive surgery in children should be considered for patients with anisometropia greater than 3−4 diopters when chronic noncompliance with and/or intolerance of traditional treatment endangers normal visual development or when standard therapy has failed to improve vision. The refractive treatment dose needed should ideally be within the limits of the specific excimer laser being used, typically 12 diopters of myopia, 5 diopters of hyperopia, and 4 diopters of astigmatism. Until recently, because there was no other treatment to offer, children with even higher levels of refractive error would still undergo these procedures up to the maximum dose, even though it would leave some residual refractive error because the lower residual refractive error would create less image blur which in turn would translate into less severe amblyopia. There are some new refractive surgical procedures, such as refractive lensectomy with or without lens exchange and phakic intraocular lenses, that are just beginning to be investigated in children with severe refractive error falling outside the dose range for the excimer laser. These procedure had great promise.

Absolute and relative contraindications to excimer refractive surgery include glaucoma, uveitis, recurrent conjunctivitis, tear film insufficiency, endothelial dysfunction, corneal scarring, keratitis, significant macular or optic nerve anomalies, or systemic inflammatory disease.

During the preoperative evaluation, care must be taken to ensure that patients and their families have reasonable expectations of what excimer laser surgery can achieve. During the preoperative consultation, the physician should discuss the range of visual acuity that the patient can expect to achieve but also explain that refractive surgery is not risk- or complication-free and that some patients may have some residual postoperative refractive error that would benefit from some refractive correction, especially if the amblyopia is severe and safety is an issue.

A comprehensive ophthalmologic examination should be performed on all pediatric patients being considered for refractive surgery. Special attention should be paid to the following:

1. External examination. This is necessary to rule out anatomic abnormalities and inflammatory conditions such as acne rosacea, though this is rare in young children.
2. Visual acuity. This should be measured at distance and near with and without correction, if possible.
3. Slit lamp examination. Corneal scarring within the treatment zone is a contraindication to the surgery. Herpetic viral infections can be reactivated by the ultraviolet radiation of the excimer laser.
4. Corneal pachymetry. This should be measured after the refraction has taken place to prevent surface disruption. Excimer refractive surgery may be contraindicated if the cornea is too thin to allow the needed treatment dose which varies depending on the refractive error and procedure type. Controversy exists regarding the minimal required residual thickness of the postoperative stromal bed necessary to minimize the risk of keratectasia in LASIK and haze in PRK. Currently, for LASIK, a residual stromal bed thickness of 200−300 μm with an absolute corneal thickness of 500 μm is considered reasonable. For PRK, a residual stromal bed thickness of 360 − 400 μm with an absolute residual corneal thickness of 475 − 500 μm is considered reasonable.
5. Pupils. Patients should be checked for a relative afferent papillary defect and pupil diameter should be measured in the dark, preferably using a pupillometer. Some surgeons feel that the planned treatment zone should extend beyond the edge of the dark-adapted pupil to minimize night vision symptoms such as halos and glare postoperatively.
6. Keratometry. These values are used to calculate the postsurgical corneal contour to avoid overflattening the cornea to less than 35 diopters, which will cause aberrations [19].
7. Corneal topography. This test is used to screen for an abnormal corneal contour, asymmetry in astigmatism, inferior corneal steepening, or other evidence of forme fruste keratoconus, which can be difficult to diagnose, especially in children. Patients with keratoconus should not have excimer refractive surgery as it increases the risk of postoperative keratectasia.

8. Dilated fundus examination. Patients with optic nerve or macular disease severe enough to explain their vision loss should not undergo the procedure as the likelihood of visual improvement is low. Mild abnormalities however, do not preclude proceeding with refractive surgery.

An explanation of the refractive procedures and possible complications should follow the physical examination on an initial visit, and patients and their families should have the opportunity to ask questions and consider the risks and benefits of all traditional and surgical options. Physicians should take care to emphasize that while refractive surgery is expected to improve vision and decrease dependence on refractive correction, it may not eliminate a patient's need for spectacles entirely. Furthermore, it should be emphasized to parents that long-term results of pediatric excimer laser procedures beyond 5 − 6 years are not known, and there is a possibility of unknown complications occurring later.

3.4.2 Operative Guidelines

In our practice, pediatric PRK is performed as follows: General anesthesia is usually required for children under 11 − 12 years of age. Anesthesia is first induced in an induction room using sevoflurane and nitrous oxide and oxygen by mask inhalation. An intravenous line is placed after the child is asleep, and a laryngeal mask airway is inserted into the posterior pharynx; sevoflurane is discontinued, and a propofol infusion is started. Intravenous ketorolac tromethamine and/or rectal acetaminophen are administered for analgesia. An adhesive, nonporous drape is placed over the laryngeal mask airway to minimize escape of the inhalational anesthetic agents which may interfere with laser-tissue interaction. The child is then transported to an adjacent operating room fully monitored and breathing oxygen through a Jackson-Rees circuit. Before entering the operating room, the inhalational anesthetic is discontinued.

In the operating room, the child's head is positioned in the supine position with the plane of the iris perpendicular to the laser beam. For the children requiring general anesthesia, the surgeon fixates the eye manually with forceps, taking care to avoid globe compression or rotation. For myopic PRK, laser or manual scrape is used to remove the epithelium. For hyperopic PRK, the entire epithelium is removed manually. PRK is then performed. The laser beam is centered on the entrance pupil using the laser machine's own tracking mechanism. Centration is assured by the laser tracking mechanism during the procedure. To further ensure that the iris plane remains perpendicular to the laser beam during the procedure under general anesthesia, an observer positioned on one side of the patient continually monitors the eye position.

After the procedure is completed, topical ketorolac 0.5%, fluorometholone 0.25%, and a fourth-generation fluoroquinolone are placed in the treated eye and a disposable contact lens is placed on the cornea. A fox shield is then placed over the eye.

3.4.3 Postoperative Guidelines

Postoperative medications for PRK include the fourth-generation fluoroquinolone and fluorometholone 0.25%, four times a day in the treated eye until the corneal epithelium heals (3 − 5 days). Topical ketorolac and tetracaine can be used up to four times a day as needed for discomfort for the first two postoperative days only. Hydrocodone oral elixir is also prescribed as needed for severe discomfort for the first few days. The fluoroquinolone is discontinued after 1 week, and fluorometholone 0.25% is continued four times a day for 2 months, followed by a slow taper over the next 4 months. Oral vitamin C (age-dependent dosing) is also prescribed to decrease the risk of corneal haze.

The children are examined postoperatively 4 − 7 days after the procedure, then at 1 month and 2 months postoperatively and then every 2 − 3 months for 12 months and again at 24 months following the surgery. Cycloplegic refractive correction is prescribed as needed at the 1-month postoperative examination and updated as needed thereafter. Occlusion therapy of the sound eye is recommended if needed up to full time except 2 h a day based on the child's age and visual deficit. Postoperative corneal topography is performed as indicated as patient cooperation allows to assess for centration and healing changes.

Take Home Pearls

- In current practice, refractive surgery is generally considered in the treatment of bilateral high ametropic and anisometropic pediatric population only when (1) traditional therapeutic measures have failed, or (2) chronic noncompliance with or intolerance of traditional therapy endangers normal visual development.
- A comprehensive ophthalmic examination should be performed in all pediatric patients being considered for refractive surgery with the additions of pachymetry, keratometry, and corneal topography.
- Excimer laser techniques reliably treat up to 10−12 diopters of myopia, 5 diopters of hyperopia, and 4 diopters of astigmatism.
- Setting up an excimer refractive surgery center is complex, requiring a team approach involving the ophthalmologist, anesthesiologist, nursing staff, and administration.
- Visual and refractive results with excimer laser techniques in children can be excellent. Treating earlier when the amblyopia is presumably less severe may result in better visual outcomes.
- Refractive lensectomy with or without lens exchange and phakic intraocular lenses are exciting and potentially important surgical approaches in the management of extremely high refractive error in children.

3.5 Refractive Lens Exchange and Phakic Intraocular Lenses

Refractive lensectomy with or without lens exchange and phakic intraocular lenses are just starting to be investigated in children with extremely high refractive errors that are outside the treatment range for the excimer laser or with corneas that are too thin for excimer laser treatment. These procedures have been used in adults with good results, but their use in children has been very limited to date.

Thirty three children who have undergone refractive lensectomy with or without lens exchange in one or both eyes have been published in the literature; those who had the procedure in both eyes had neurobehavioral disorders [3, 53]. The published visual and refractive results at 4+ years postoperatively in these children have been impressive with few complications. Eighty-two percent of the children achieved a refractive error within 2 diopters of the goal [3, 53]. Complications reported included one retinal detachment that was successfully repaired without visual loss and one hyphema that resolved with medical therapy. Major disadvantages of refractive lensectomy with or without lens exchange include the induction of monofocality and an increased risk of retinal detachment [37].

Recently, there have been individual case reports and pilot studies in the U.S. and abroad on phakic anterior chamber and posterior chamber intraocular lens implantation for treatment of severe anisometropic myopia [1, 12, 17, 29, 41, 45]. Implantation of a phakic anterior chamber lens without removal of the natural lens is an innovative approach in the treatment of high anisometropia, as it has the benefits of reversibility and maintenance of accommodation, and it may have fewer side effects in comparison with other currently existing and proposed surgical techniques [30, 38, 41]. Major risks of phakic intraocular lenses, however, include corneal endothelial cell damage, secondary glaucoma, and cataract. Recent studies in children demonstrate good visual and refractive results and give us reason to remain optimistic about the future of phakic intraocular lenses in the management of pediatric amblyopiogenic levels

Table 3.4 Summary of phakic intraocular lenses (*IOL*) in children. *BCVA* best-corrected visual acuity, *D* diopters, *SE* spherical equivalent

Reference	Year	No. of eyes	Mean pre-SE (D)	Mean post-SE (D)	Mean pre-BCVA	Mean post-BCVA	Follow-up time (months)	IOL type	Complication
[29]	1999	5	−12.80	+0.50	CF to 20/200	20/70	12	Post chamber Staar	None
[11]	2000	3	−12.50	−1.00	6/40	6/24	9	Post chamber Staar	One pigment dispersion
[12]	2001	1	−15.50	−4.00	NR	20/25	18	Artisan iris claw	None
[30]	2002	12	−12.70	+0.71	CF to 20/63	20/63	25	Post chamber Staar	NR
[45]	2003	1	−12.50	−2.50	20/50	20/20	36	Artisan iris claw	Endothelial cell loss

of refractive error that are outside the range for the excimer laser (Table 3.4).

Research on these procedures in children is in the early stages and further prospective case-control studies are indicated to determine the long-term safety and efficacy of these alternative refractive procedures in larger pediatric populations. If, however, found to be safe long term, these procedures could be very effective in the treatment of severe refractive errors in children who are outside the treatment range of the excimer laser [12, 17, 29, 30, 45, 51].

3.6 Summary

Refractive surgery, only a few years ago, was considered only possible for adults. Excimer laser refractive procedures have been shown to be effective for treating severe anisometropia and bilateral high ametropia associated with amblyopia in children when traditional therapy has not been successful. With follow-up now approaching 10 years, few serious complications have been reported. These procedures have resulted in improvements in vision, refractive error, and even behavior. Other refractive procedures, such as refractive lensectomy with or without lens exchange and phakic intraocular lenses, may also soon become accepted treatment alternatives for a small subset of children with extremely high refractive errors outside the range for the excimer laser. Treating earlier appears to yield better visual results; therefore, it is now more prudent to consider refractive surgery for these conditions earlier if traditional therapy is not working, rather than continuing to observe the progression toward irreversible severe ambylopia in the noncompliant or nonresponsive child. Indeed, in the near future, severe anisometropia and bilateral ametropia may be primary surgical disorders.

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References

1. Agafonov, V. V. (2007) Development of a technique for ametropia correction with phakic intraocular lenses. Vestn Ross Akad Med Nauk 8: 52−56 [in Russian]
2. Agarwal, A., Agarwal, T., Siraj, A. A., et al. (2000) Results of pediatric laser in situ keratomileusis. J Cataract Refract Surg 26: 684−689
3. Ali, A., Packwood, E., Lueder, G., et al. (2007) Unilateral lens extraction for high anisometropic myopia in children and adolescents. J AAPOS 11: 153−158
4. Alio, J. L., Artola, A., Claramonte, P., et al. (1998) Photorefractive keratectomy for pediatric myopic anisometropia. J Cataract Refract Surg 24: 327−330
5. Alio, J. L., Artola, A., Claramonte, P. J., et al. (1998) Complications of photorefractive keratectomy for myopia: two year follow-up of 3000 cases. J Cataract Refract Surg 24: 619−626
6. Astle, W. F., Huang, P. T., Ells, A. L., et al. (2002) Photorefractive keratectomy in children. J Cataract Refract Surg 28: 932−941

7. Astle, W. F., Huang, P. T., Ingram, A. D., et al. (2004) Laser-assisted subepithelial keratectomy in children. J Cataract Refract Surg 30: 2529−2535
8. Astle, W. F., Papp, A., Huang, P. T., et al. (2006) Refractive laser surgery in children with coexisting medical and ocular pathology. J Cataract Refract Surg 32: 103−108
9. Autrata, R., Rehurek, J. (2004) Laser-assisted subepithelial keratectomy and photorefractive keratectomy versus conventional treatment of myopic anisometropic amblyopia in children. J Cataract Refract Surg 30: 74−84
10. Autrata, R., Rehurek, J. and Holousova, M. (1999) Photorefractive keratectomy in high myopic anisometropia in children. Cesk Slov Oftalmol 55: 216−221 [in Czech]
11. BenEzra, D., Cohen, E. and Karshai, I. (2000) Phakic posterior chamber intraocular lens for the correction of anisometropia and treatment of amblyopia. Am J Ophthalmol 130: 292−296
12. Chipont, E. M., Garcia-Hermosa, P. and Alio, J. L. (2001) Reversal of myopic anisometropic amblyopia with phakic intraocular lens implantation. J Refract Surg 17: 460−462
13. Cobb, C. J., Russell, K., Cox, A., et al. (2002) Factors influencing visual outcome in anisometropic amblyopes. Br J Ophthalmol 86: 1278−1281
14. Davidorf, J. M., Zaldivar, R. and Oscherow, S. (1998) Results and complications of laser in situ keratomileusis by experienced surgeons. J Refract Surg 14: 114−122
15. Davis, E. A., Hardten, D. R. and Lindstrom, R. L. (2000) LASIK complications. Int Ophthalmol Clin 40: 67−75
16. de Vries, J. (1985) Anisometropia in children: analysis of a hospital population. Br J Ophthalmol 69: 504−507
17. Eleftheriadis, H. (2004) Potential complications of phakic IOLs. Br J Ophthalmol 88: 1480−1481
18. Epstein, D. and Frueh, B. E. (1995) Indications, results, and complications of refractive corneal surgery with lasers. Curr Opin Ophthalmol 6: 73−78
19. Feder R. S., Rupuano C. J. (eds) (2007) Basic LASIK and equipment. In: The LASIK handbook: a case-based approach, Lippincott Williams and Wilkins, Philadelphia, pp 1−79
20. Flynn, J. T., Schiffman, J., Feuer, W., et al. (1998) The therapy of amblyopia: an analysis of the results of amblyopia therapy utilizing the pooled data of published studies. Trans Am Ophthalmol Soc 96: 431−453
21. France, T. D. and France, L. W. (1999) Optical penalization can improve vision after occlusion treatment. J AAPOS 3: 341−343
22. Gimbel, H. V. and Levy, S. G. (1998) Indications, results, and complications of LASIK. Curr Opin Ophthalmol 9: 3−8
23. Hardman Lea, S. J., Snead, M. P., Loades, J., et al. (1991) Microtropia versus bifoveal fixation in anisometropic amblyopia. Eye 5 (Pt 5): 576−584
24. Hiscox, F., Strong, N., Thompson, J. R., et al. (1992) Occlusion for amblyopia: a comprehensive survey of outcome. Eye 6 (Pt 3): 300−304
25. Kaye, S. B., Chen, S. I., Price, G., et al. (2002) Combined optical and atropine penalization for the treatment of strabismic and anisometropic amblyopia. J AAPOS 6: 289−293
26. Kivlin, J. D. and Flynn, J. T. (1981) Therapy of anisometropic amblyopia. J Pediatr Ophthalmol Strabismus 18: 47−56
27. Knorz, M. C. (2002) Flap and interface complications in LASIK. Curr Opin Ophthalmol 13: 242−245
28. Kutschke, P. J., Scott, W. E. and Keech, R. V. (1991) Anisometropic amblyopia. Ophthalmology 98: 258−263
29. Lesueur, L. C. and Arne, J. L. (1999) Phakic posterior chamber lens implantation in children with high myopia. J Cataract Refract Surg 25: 1571−1575
30. Lesueur, L. C. and Arne, J. L. (2002) Phakic intraocular lens to correct high myopic amblyopia in children. J Refract Surg 18: 519−523
31. Basov N. G., Danilychev V. A., Popov Y. and Khodkevich D. D. (1970) Zh. Eksp. Fiz. i Tekh. Pis'ma, Red, 473; JETP Lett 12:329
32. Nano, H. D., Jr., Muzzin, S. and Irigaray, F. (1997) Excimer laser photorefractive keratectomy in pediatric patients. J Cataract Refract Surg 23: 736−739
33. Nassaralla, B. R. and Nassaralla, J. J., Jr. (2001) Laser in situ keratomileusis in children 8 to 15 years old. J Refract Surg 17: 519−524
34. Nucci, P. and Drack, A. V. (2001) Refractive surgery for unilateral high myopia in children. J AAPOS 5: 348−351
35. O'Keefe, M. and Nolan, L. (2004) LASIK surgery in children. Br J Ophthalmol 88: 19−21
36. Paysse, E. A. (2004) Photorefractive keratectomy for anisometropic amblyopia in children. Trans Am Ophthalmol Soc 102: 341−371
37. Paysse, E. A. (2007) Unilateral lens extraction for high anisometropic myopia in children and adolescents: Is this prudent? J AAPOS 11: 111−112
38. Paysse, E. A., Coats, D. K., Hussein, M. A., et al. (2006) Long-term outcomes of photorefractive keratectomy for anisometropic amblyopia in children. Ophthalmology 113: 169−176
39. Phillips, C. B., Prager, T. C., McClellan, G., et al. (2004) Laser in situ keratomileusis for treated anisometropic amblyopia in awake, autofixating pediatric and adolescent patients. J Cataract Refract Surg 30: 2522−2528
40. Piccoli, P. M., Gomes, A. A. and Piccoli, F. V. (2003) Corneal ectasia detected 32 months after LASIK for correction of myopia and asymmetric astigmatism. J Cataract Refract Surg 29: 1222−1225
41. Pirouzian, A., Bansal, P. and O'Halloran, H. (2007) Phakic IOL in children. Ophthalmology 114: 194−195
42. Rashad, K. M. (1999) Laser in situ keratomileusis for myopic anisometropia in children. J Refract Surg 15: 429−435
43. Roberts, C. J. and Adams, G. G. (2002) Contact lenses in the management of high anisometropic amblyopia. Eye 16: 577−579
44. Rybintseva, L. V. and Sheludchenko, V. M. (2001) Effectiveness of laser in situ keratomileusis with the Nidek EC-5000 excimer laser for pediatric correction of spherical anisometropia. J Refract Surg 17: S224−S228
45. Saxena, R., van Minderhout, H. M. and Luyten, G. P. (2003) Anterior chamber iris-fixated phakic intraocular lens for anisometropic amblyopia. J Cataract Refract Surg 29: 835−838

46. Schwartz, G. S., Park, D. H., Schloff, S., et al. (2001) Traumatic flap displacement and subsequent diffuse lamellar keratitis after laser in situ keratomileusis. J Cataract Refract Surg 27: 781−783
47. Singh, D. (1995) Photorefractive keratectomy in pediatric patients. J Cataract Refract Surg 21: 630−632
48. Smith, R. J. and Maloney, R. K. (1998) Diffuse lamellar keratitis. A new syndrome in lamellar refractive surgery. Ophthalmology 105: 1721−1726
49. Tabbara, K. F., El-Sheikh, H. F. and Vera-Cristo, C. L. (2003) Complications of laser in situ keratomileusis (LASIK). Eur J Ophthalmol 13: 139−146
50. Tanlamai, T. and Goss, D. A. (1979) Prevalence of monocular amblyopia among anisometropes. Am J Optom Physiol Opt 56: 704−715
51. Tychsen, L. and Hoekel, J. (2006) Refractive surgery for high bilateral myopia in children with neurobehavioral disorders: 2. Laser-assisted subepithelial keratectomy (LASEK). J AAPOS 10: 364−370
52. Tychsen, L., Packwood, E. and Berdy, G. (2005) Correction of large amblyopiogenic refractive errors in children using the excimer laser. J AAPOS 9: 224−233
53. Tychsen, L., Packwood, E., Hoekel, J., et al. (2006) Refractive surgery for high bilateral myopia in children with neurobehavioral disorders: 1. Clear lens extraction and refractive lens exchange. J AAPOS 10: 357−363
54. Weakley, D. R. (1999) The association between anisometropia, amblyopia, and binocularity in the absence of strabismus. Trans Am Ophthalmol Soc 97: 987−1021
55. Weakley, D. R., Jr. (2001) The association between nonstrabismic anisometropia, amblyopia, and subnormal binocularity. Ophthalmology 108: 163−171
56. Woodruff, G., Hiscox, F., Thompson, J. R., et al. (1994) Factors affecting the outcome of children treated for amblyopia. Eye 8 (Pt 6): 627−631

Amblyopia

David K. Wallace

4

Contents

Core Messages

- Spectacles alone are a powerful treatment for amblyopia.
- Two hours of prescribed daily patching or weekend atropine is an effective initial treatment for most children with moderate amblyopia.
- Patching is often effective in older children and teenagers, particularly if they have not previously been treated.
- Atropine and patching are equally effective as initial treatments for amblyopia.

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4.1 Introduction

Amblyopia is reduced visual acuity in one or both eyes due to reduced visual input or abnormal binocular interaction early in life. Amblyopic eyes also have deficits in contrast sensitivity, accommodation, and spatial orientation [56]. The prevalence of amblyopia is 3−5% [4]; it is usually unilateral and associated with anisometropia or strabismus (or both). Its onset is in the first decade of life, but its effects can last a lifetime [4]. Amblyopia is best diagnosed and treated as early as possible, but data from clinical trials have challenged the notion of a significant age effect of treatment [35, 36].

4.2 Types of Amblyopia

4.2.1 Anisometropic Amblyopia

Anisometropic amblyopia is reduced visual acuity in one eye due to a difference in refractive error between the eyes. Its mechanism is active inhibition within the retinocortical pathways to eliminate sensory interference from a defocused image [56]. It is usually due to anisohyperopia or anisoastigmatism, or both. Unilateral high myopia typically causes a dense form of amblyopia, and it can be associated with myelinated nerve fibers [10, 16].

4.2.2 Strabismic Amblyopia

Strabismic amblyopia is reduced visual acuity in one eye due to misalignment of the eyes. Its mechanism is active inhibition within the retinocortical pathways originating in the fovea. This mechanism is similar to that of suppression, but suppression is a binocular phenomenon, whereas amblyopia is unilateral [56]. Strabismus is not uncommonly associated with anisometropia in what has been termed “combined mechanism” amblyopia. In fact, some patients diagnosed with purely anisometropic amblyopia are found upon closer inspection to have microstrabismus.

4.2.3 Deprivational Amblyopia

Deprivational (or occlusion) amblyopia is secondary to occlusion of the visual axis early in life, resulting in a lack of foveal stimulation with well-focused images. It can be caused by problems such as cataracts, severe ptosis, hemangiomas, corneal scars or leukomas, and vitreous hemorrhage. Its onset is usually in the first year of life, and visual acuity reduction is often severe.

4.2.4 Organic Amblyopia

Organic amblyopia is associated with recognizable structural anomalies such as optic nerve hypoplasia or macular coloboma. It is important to recognize that patients with organic diagnoses may have some component of amblyopia which may improve with treatment.

4.2.5 Ideopathic Amblyopia

An unusual presentation is a patient with apparent amblyopia but with no history of strabismus, anisometropia, or visual deprivation. It has been hypothesized that such patients had an amblyopiogenic factor early in life, such as anisometropia, which resolved prior to presentation [56].

4.2.6 Bilateral Amblyopia

Bilateral ametropic amblyopia is due to uncorrected significant hyperopia or astigmatism, or both [62]. Its mechanism is presumed to be pattern vision deprivation; that is, failure of either eye to achieve a clear foveal image results in abnormal cortical development [56]. Bilateral amblyopia due to uncorrected myopia is rare because these children typically are able to achieve clear vision at near with at least one eye.

4.3 Diagnosis

4.3.1 Screening for Amblyopia

Amblyopia is best detected and treated early in life. Consequently, various screening programs have been developed for children prior to school entry, and many states sponsor these programs. Lay screeners use different tests such as assessment of visual acuity, stereopsis, and autorefraction. The Vision in Preschoolers study compared 11 commercially available screening tests and found that their performances varied widely. With 90% specificity, the best tests detected nearly 90% of children with the most important conditions [45]. They also found that nurse and lay screeners achieve similar results in detecting preschool children in need of a comprehensive eye examination [52]. Donahue reported an association between older age and depth of amblyopia, suggesting that earlier detection of amblyopia may result in better outcomes after treatment [9].

4.3.2 Preliterate Children

Several techniques are used to diagnose amblyopia in preverbal children, including assessment of fixing and following, preferential looking techniques, and tests of fixation preference. A child's ability to fix and follow is often assessed as an initial step, but this test is relatively insensitive unless amblyopia is severe. Preferential looking techniques and sweep visual evoked responses can quantify visual acuity, but they are not always readily available. Fixation preference testing is another technique which is commonly used in preverbal children.

Selecting the right test of fixation preference depends on whether a patient is strabismic or nonstrabismic. For strabismic patients, an assessment of binocular fixation pattern is performed in which the examiner determines the length of time that the nonpreferred eye can hold fixation [21, 32, 67]. Several grading schemes have been devised to quantify the results of this test, such as the one shown in Table 4.1. Şener et al. found that monocular fixation pattern correlates with visual acuity in older children [46].

For patients without strabismus or those with small angle deviations, the induced tropia test is useful [7, 12, 30, 65]. This test was originally described by Wright et al. as the 10-diopter fixation test. They reported a sensitivity of 100% (13 of 13) and a specificity of 97% (64 of 66) in the detection of amblyopia using this test. For patients with small angle tropias, they found that the 10-diopter fixation test was superior to binocular fixation pattern, which had an unacceptably high false-positive rate of 40% [64].

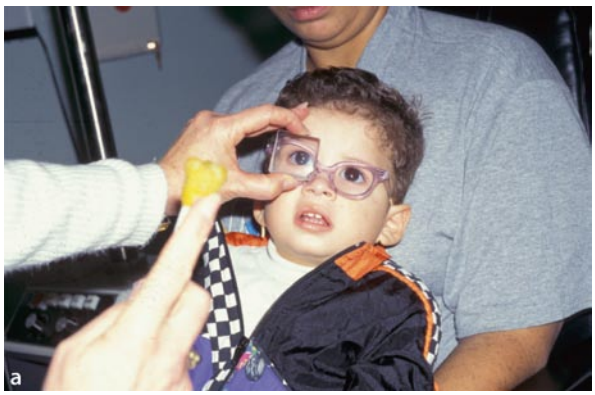
Table 4.1 A scheme for grading binocular fixation patterns in strabismic patients. (From [46, 59]

Grade	Description of response
0	Will not hold fixation with non-preferred eye
1	Holds fixation momentarily with non-preferred eye
2	Holds fixation for 2−3 seconds (or to a blink) with non-preferred eye
3	Holds fixation through a blink (or during a smooth pursuit) with non-preferred eye
4	No fixation preference; alternates spontaneously

There have been many modifications to the original description of the 10-diopter fixation test, including variations in fixation target, technique, prism power, prism orientation, and interpretation of results. The induced tropia test is typically done with the prism in the base-down position, but some examiners place the prism base-in and look for a horizontal saccade as evidence that the eye behind the prism takes up fixation. The base-up orientation is particularly useful in the presence of ptosis, because the ptotic patient is less likely to gaze upward through the prism because the eyelid may block the image from view [63]. Most examiners choose a prism power between 10 and 20 diopters. The larger prism has the advantage of inducing a larger saccade that is easier to observe, but it has the disadvantage of inducing more visual artifact in the second image. Results of the induced tropia test can be quantified using the technique shown in Fig. 4.1 and the grading scheme elaborated in Table 4.2 [59].

4.3.3 Older Children

By age 3 years, most children are able to perform tests of recognition visual acuity, such as Allen or Lea pictures, tumbling E, HOTV, or Snellen letters.



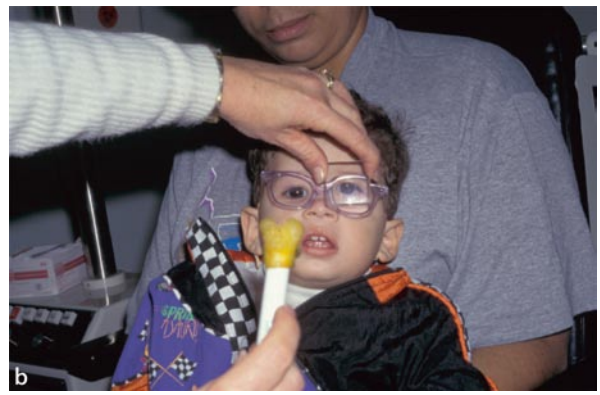


Fig. 4.1 **a** With a prism over the right eye, this child gazes upward to maintain fixation with the right eye. **b** With a prism over the left eye, he gazes straight ahead to maintain fixation with the right eye. The Induced Tropia Test Score is +2 +2 = +4, meaning that he fixes with the right eye only, and amblyopia of the left eye is very likely. (From [59])

Table 4.2 Grading scale applied to each eye for the induced tropia test. (From [59])

Grade	Fixation response
−2	Fixes with OS only
−1	Alternates but prefers OS
0	Alternates freely
+1	Alternates but prefers OD
+2	Fixes with OD only

The total induced tropia test (ITT) score equals the sum of the scores for prism placement over the right and left eyes. For example, fixation with right eye only with the prism over the right eye (+2) and then the left eye (+2) gives an ITT score of +4, indicating that amblyopia is likely

Isolated letters and those at the beginning or the end of lines are more easily identified because of the crowding phenomenon. Crowded bars can be used around individual letters to account for crowding, and such a technique along with a standard testing protocol has been used by the Pediatric Eye Disease Investigator Group (PEDIG) for amblyopia clinical trials (Fig. 4.2) [18]. When a child graduates from one testing method to another one (e.g., Allen pictures to Snellen letters), it is important to consider that visual acuity may initially appear to be worse when it is reality no different. One study found that visual acuity by Allen pictures was on average 1.5 lines better than by Snellen letters with visual acuity levels of 20/60 or better and 2.5 lines better by Allen pictures with acuity levels worse than 20/60 [24].

4.3.4 *Amblyopia Suspect*

The diagnosis of amblyopia is usually based on finding at least two lines of visual acuity difference in the presence of an amblyopia risk factor, such as anisometropia or strabismus. In the preliterate child, establishing a firm diagnosis may be difficult, since measures of visual acuity such as fixation preference are probably not as accurate [59]. In these cases, results of serial examinations are considered, and assessment of risk factors becomes more important. Some patients may be classified as "amblyopia suspects" and followed closely without occlusion or penalization treatment. Once they are able to perform recognition visual acuities, the diagnosis can be more readily established.

4.4 Treatment

4.4.1 *Elimination of Cause of Visual Deprivation*

Prompt removal of a visually significant obstruction of the visual axis is necessary in order for amblyopia treatment to be successful. Sometimes the decision of whether or not to do surgery is difficult because deprivation is not the sole cause of amblyopia, such as when a mild cataract coexists with anisometropia or

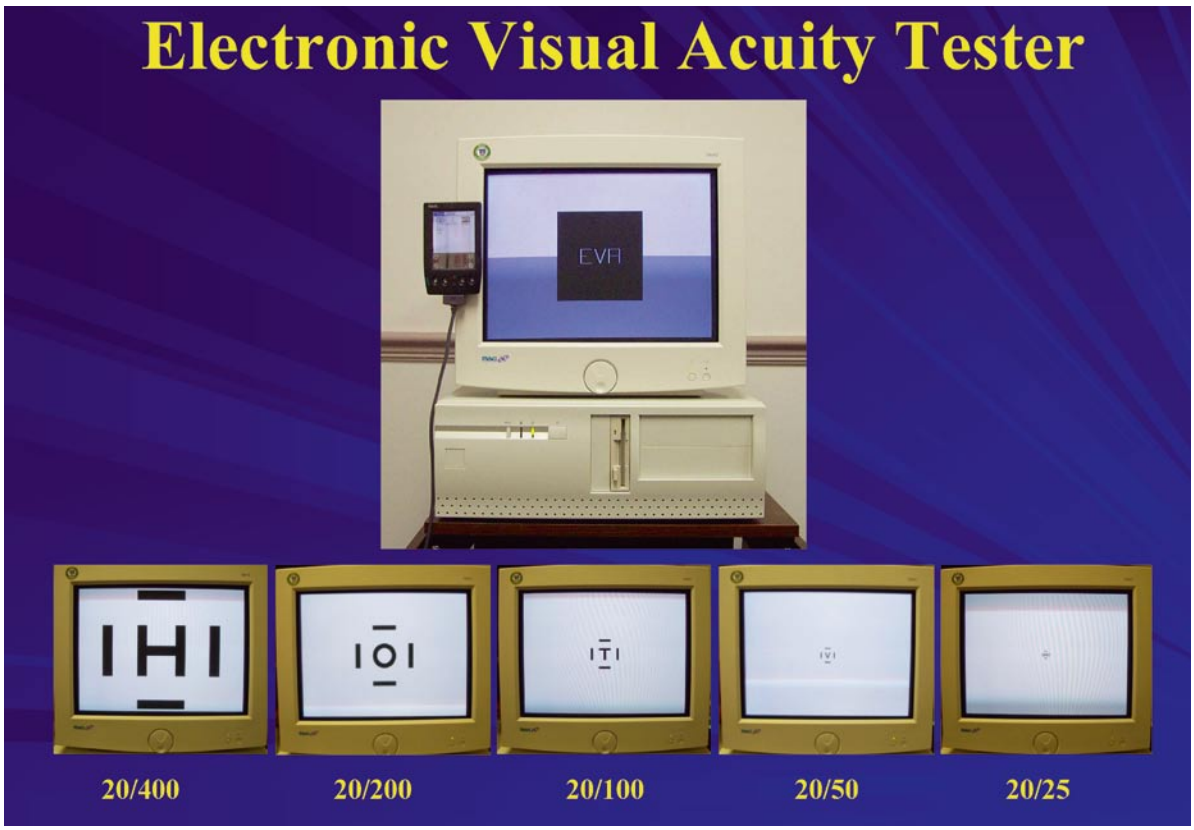


Fig. 4.2 Technique of displaying HOTV with crowded bars on a computer screen used by the Pediatric Eye Disease Investigator Group

a hemangioma partially obstructs the visual axis and induces amblyopiogenic astigmatism. In these cases, a trial of conservative treatment, such as spectacles and patching, can help to determine the amount of visual acuity reduction that is due to visual axis obstruction.

4.4.2 Spectacles

Spectacles, when needed, can be a powerful treatment for amblyopia. The spectacle phase of Amblyopia Treatment Study 5 (ATS5) enrolled 84 children age 3−7 years with previously untreated anisometropic amblyopia and treated them with spectacles alone [41]. After 5 weeks, children had improved an average of almost two lines, and 59% had improved two lines or more. Many children continued to improve for several weeks, and the mean improvement based on best measured acuity at any visit was almost three lines. One of most interesting findings of this study was that even patients with strabismus improved with spectacles alone [8].

Based on these results, one reasonable approach is to start patching immediately only if poor follow-up is expected or if parents are very anxious to start more aggressive treatment. Otherwise, spectacles alone can be used until there is resolution of amblyopia or improvement stalls. There are some advantages to this approach. Firstly, some children will not need patching or penalization because glasses alone will result in resolution of amblyopia. Secondly, if patching is needed, the visual acuity is likely to be better when patching is started compared with starting it at the same time as spectacles. A child may be more likely to wear a patch when the amblyopic eye is 20/50 rather than 20/100. Finally, it is ideal to intro-

duce one new treatment at a time, instead of initiating spectacles and patching at the same time. In this way, parents can focus on getting the best compliance with one treatment.

Bilateral amblyopia is effectively treated with spectacles. Amblyopia Treatment Study 7 (ATS7) found that binocular acuity improved almost four lines after 1 year in 113 children between 3 and 9 years old with bilateral refractive amblyopia. Children with baseline acuities of 20/100 or worse showed the greatest improvement.

4.4.3 Refractive Surgery

There may be circumstances when a child with a severe refractive error and amblyopia is unable or unwilling to wear spectacles because of behavioral problems or severe developmental delay. In these cases, unilateral or bilateral corneal refractive surgery may play a role to reduce anisometropia or severe bilateral ametropia [33, 54]. Clear lens extraction has also been performed for children with severe bilateral myopia [55]. In these select cases, the risks and benefits should be carefully evaluated prior to surgery. When considering refractive surgery for children with anisometropic amblyopia, many factors should be considered. These factors include the presence of co-existing strabismus or other causes of amblyopia, the need for post-operative patching, and the likelihood of compliance with treatment.

4.4.4 Patching and Its Effectiveness

Patching is generally considered to be the gold standard for amblyopia treatment. Most children use an adhesive patch, which has the advantage of completely occluding the sound eye as long as the child does not remove it. Disadvantages of an adhesive patch include skin irritation and cost, especially if the child removes patches frequently. An alternative is a felt patch that fits over one lens of the spectacles. It has the advantages of less cost and no skin irritation, but many children will allow their glasses to slide forward so that they can look over or around a felt patch.

Visual acuity can improve for reasons other than patching, such as concurrent spectacles wear and improving test performance with age and experience; therefore, ATS5 compared 2 h of daily patching to a control group of spectacles alone for children with baseline acuity between 20/40 and 20/400 [38]. After 5 weeks, the patching group had better acuity, with a mean improvement of 1.1 lines compared with 0.5 lines for control. A secondary cohort had only two lines of intraocular difference at randomization, or three lines of IOD with a 20/32 amblyopic eye and a 20/16 sound eye. Although it was expected that these patients would improve less because there was less room for improvement, the treatment effect relative to control was similar, reinforcing the fact that many patients who reach near-normal visual acuity wearing spectacles will benefit from the addition of patching.

4.4.5 Initial Patching Regimen

Patching has traditionally been prescribed full-time or nearly full-time, but many clinicians now prefer to prescribe 2 h daily or some other part-time regimen when initiating patching treatment. Their rationale has been that randomized clinical trials have shown similar improvement with part-time or full-time patching, and part-time patching is easier for families to accomplish. One trial randomized patients with amblyopic eye visual acuity between 20/100 and 20/400 to full-time prescribed patching versus 6 h of daily prescribed patching, and both groups improved almost five lines after 17 weeks [37]. Those children with moderate amblyopia, defined as 20/40 to 20/80, were randomized to 6 h prescribed patching vs 2 h prescribed patching daily, and both groups improved 2.4 lines after 17 weeks [36]. Although many of the patients in this effectiveness study did not wear the patch as much as prescribed, inconsistent compliance is one the factors that affects amblyopia treatment response in clinical practice, so the results are directly applicable to the "real world." Fewer daily hours of patching may work by providing sufficient stimulus for many children to reach their maximum rate of improvement, which is probably limited at the biochemical level in the ocular−cortical pathway.

4.4.6 Follow-up Patching Regimens

Figure 4.3 is a flow chart showing one method for monitoring and adjusting amounts of patching. If improvement stops after 2 h of prescribed patching, then the patching dose could be increased to 6 or more hours of prescribed patching. Some parents and children are initially enthusiastic but become fatigued after several months and compliance suffers. In these cases, switching to another treatment, such as atropine, may be useful. Some children stop improving before normal vision is achieved despite good compliance with patching. Once the maximum visual acuity has been established, treatment may be weaned while monitoring to insure that visual acuity does not worsen. For example, 6 h of daily patching might be weaned to 2 h daily patching for 6–8 weeks prior to stopping treatment. Treatment is stopped with or without weaning if amblyopia resolves, and one definition of resolution is visual acuity of the amblyopic eye within one line of the sound eye.

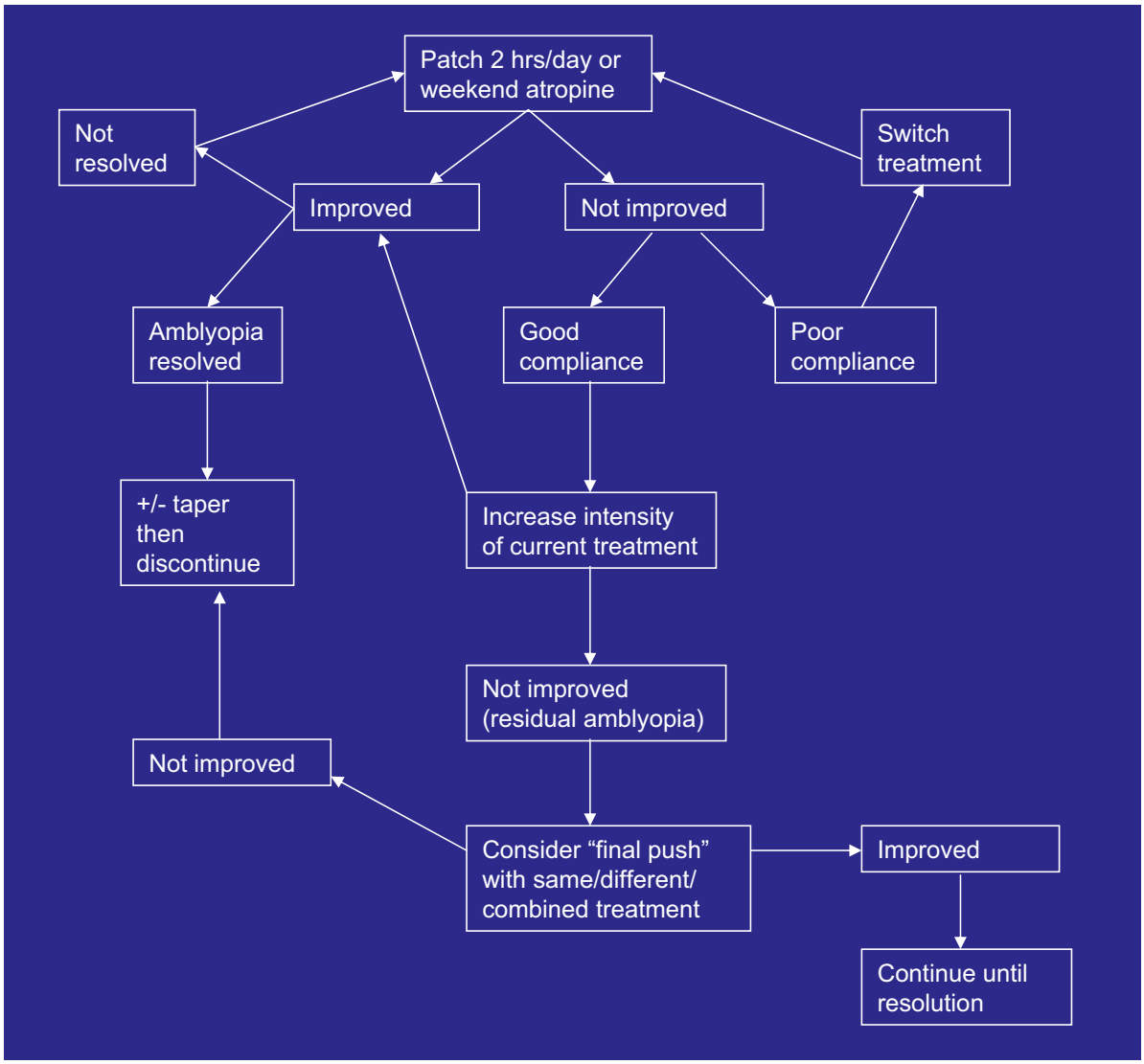


Fig. 4.3 Algorithm for treatment of moderate amblyopia in children

4.4.7 Non-compliance with Patching

The most common reason for ineffectiveness of patching is non-compliance, since many children refuse to wear an eye patch. Some children, particularly those old enough to attend school, refuse to wear a patch because of the social stigma. Others have recurrent problems with skin irritation. However, the majority of non-compliant preschool children refuse to wear a patch because they do not like it, and their parents are unable or unwilling to force them to wear it. Awan et al. included compliance data in their report of a randomized controlled clinical trial of unilateral strabismic and mixed amblyopia using occlusion dose monitors [3]. They reported mean compliance rates of 58 and 41% for 3 and 6 h of prescribed daily patching, respectively. Other authors have reported that compliance is a major problem with regard to occlusion therapy [15, 23, 29, 47, 50].

4.4.8 Penalization

As a result of poor compliance with patching among many children, other treatments collectively known as penalization are commonly used [5, 60]. Types of penalization include atropine eye drops [13, 14, 28, 43, 44, 51, 57], optical penalization using a plano (blank) lens or excessive plus power lens, atropine with a plano lens [66], Bangerter filters (or "foils") [19, 22], and translucent tape. There are several factors to consider when deciding whether to prescribe patching versus penalization, including (1) age of the child, (2) depth of amblyopia, (3) need for glasses, (4) amount of hyperopia, (5) presence or absence of strabismus, and (6) family dynamics. Age is an important consideration because penalization is used less frequently in preverbal children in whom visual acuity in the normal eye cannot be reliably measured and closely monitored. Penalization is rarely required in infants, because they are unable to successfully remove a patch. Depth of amblyopia is considered because some forms of penalization may not be successful in cases of severe amblyopia. The need for glasses is considered because some forms of penalization such as Bangerter foils rely on the patient wearing glasses. The amount of hyperopia is important when deciding whether to replace a prescription lens with a plano lens: the greater the hyperopia, the greater the reduction in vision. Strabismus is sometimes a consideration when deciding whether to use atropine or not, since some physicians prefer to avoid atropine in the presence of esotropia, particularly when it has an accommodative component. However, one study found no difference in the occurrence of new strabismus or the resolution of existing strabismus in patients treated with patching versus those treated with atropine [35]. With regard to family dynamics, the physician or orthoptist can often get a sense at the first office visit whether or not patching is likely to be successful. If the child does not follow directions from the parent(s) and/or the parent(s) express concerns about being able to get the child to wear a patch, then penalization is likely to be the best choice for initial therapy.

4.4.9 Atropine

The most commonly used form of penalization is atropine. The dosage of atropine for amblyopia treatment is one drop of 1 or 0.5% in the fellow eye as infrequently as once weekly [48] or as frequently as once daily. The best patients to consider for atropine treatment are (1) those who refuse to wear a patch, (2) those with hyperopia, and (3) those old enough to allow the sound eye visual acuity to be closely monitored. Patients with hyperopia are ideal candidates for atropine penalization. Even if glasses correct their full amount of hyperopia, their near vision is always blurred after atropine, and they cannot clear it by removing their glasses. One study found that mean visual acuity at 33 cm after cycloplegia in children wearing their full cycloplegic correction was 20/120 [61]. Conversely, myopic children using atropine can see well with their fellow eyes through their glasses at distance, and many of them can remove their glasses to see better with their fellow eyes at near, depending on the amount of myopia present.

Many clinicians now routinely use atropine as first-line amblyopia therapy. Several PEDIG studies have provided data on the effectiveness of atropine for amblyopia, and Table 4.3 summarizes the results of these and other PEDIG amblyopia studies [58]. ATS1 randomized 419 children age 3 years to <7 years with amblyopic eye acuity of 20/40 to 20/100 to at least

Table 4.3 Summary of study designs and results of randomized clinical trials conducted by the Pediatric Eye Disease Investigator Group

Short title	Ages (years)	Baseline amblyopic eye acuity	Primary outcome measure	Initial treatment prescribed	Results (improvement)	Primary conclusion
ATS1 [35]	3 to < 7	20/40 – 20/100	Lines improvement after 26 weeks	Daily atropine	2.8 lines	Atropine and patching are equally effective as primary treatment for moderate amblyopia
				At least 6 h daily patching	3.2 lines	
ATS2A [37]	3 to < 7	20/100 – 20/400	Lines improvement after 17 weeks	6 h daily patching	4.8 lines	6 h prescribed daily patching produces improvement similar to full-time patching for severe amblyopia
				Full-time patching	4.7 lines	
ATS2B [36]	3 to < 7	20/40 – 20/80	Lines improvement after 17 weeks	2 h daily patching	2.4 lines	2 or 6 h of prescribed daily patching produce similar improvement for moderate amblyopia
				6 h daily patching	2.4 lines	
ATS3 [39]	7 to < 18	20/40 – 20/400	Proportion of responders (improvement > 2 lines) after 24 weeks	2 – 6 h daily patching (+ atropine if < 12 years)	Response rates: Age ≤ 12 years: 53% Age ≥ 13 years: 25%	Older children often improve with patching ± atropine, especially when they have no prior treatment
				Spectacles alone if needed	Response rates: Age ≤ 12 years: 25% Age ≥ 13 years: 23%	
ATS4 [34]	3 to < 7	20/40 – 20/80	Lines improvement after 17 weeks	Weekend atropine	2.3 lines	Weekend and daily atropine produce similar improvement for moderate amblyopia
				Daily atropine	2.3 lines	
ATS5 [38]	3 to < 8	20/40 – 20/400	Lines improvement after 5 weeks	2 h daily patching	1.1 lines	After a period of spectacles wear, 2 h daily patching is superior to continuing spectacles alone
				Spectacles alone if needed	0.5 lines	

6 h of daily patching or to once daily atropine [35]. Treatment intensity was increased or decreased based on interim visual acuities. After 6 months, amblyopic eye acuity had improved about three lines in both groups. Improvement was initially faster with patching, but atropine was better tolerated by many families based on results of a questionnaire (the Amblyopia Treatment Index) [17]. Among the non-strabismic children, sensory outcomes were similar after 2 years [42].

Weekend or daily atropine dosing appears to provide similar improvement, and weekend dosing has the advantage of providing a short break from blur late in the week for many children. Amblyopia Treatment Study 4 found that weekend (once on Saturday and Sunday) or daily atropine improved acuity an average of about two lines after 4 months in children age 3−7 years with moderate amblyopia [34]. Interestingly, age, iris color, sound eye refractive error, and visual acuity in the sound eye after cycloplegia were not predictive of visual acuity improvement.

Some physicians believe that atropine is not effective in patients with severe amblyopia, but this premise is controversial. Traditional teaching is that

the visual acuity of the sound eye after cycloplegia must be worse than that of the amblyopic eye in order to cause the switch in fixation to the amblyopic eye necessary for visual improvement [27, 49]; however, near visual acuity after cycloplegia was measured in ATS1 and ATS4, and it was found *not* to be predictive of success with atropine treatment [34, 35]. It is possible that the dynamic accommodative demands of everyday life are not simulated well by a static test of near visual acuity. Consequently, many patients for whom the cyclopleged sound eye acuity exceeds the amblyopic eye acuity probably still switch their fixation to the amblyopic eye under certain conditions that are not simulated by a near visual acuity test.

4.4.10 Optical Penalization

Optical penalization of the sound eye can be accomplished with or without atropine. When used with atropine, optical penalization is done by reducing or eliminating the hyperopic correction for the sound eye [20]. This method is most often used in patients with significant hyperopia whose amblyopic eye visual acuity has not improved with atropine alone. In those patients who are not hyperopic but who wear glasses for other reasons, it is possible to replace the fellow eye lens with one containing more minus power; however, this may encourage non-compliant children to remove the glasses. If atropine is not used, optical penalization can be attempted by replacing the lens over the fellow eye with a fogging plus lens [11]. Another technique is sometimes useful in children with bilateral aphakia who wear contact lenses. To treat unilateral amblyopia, the contact lens of the better eye can be removed for a few weeks. The best patients to consider for optical penalization are (1) those who have stopped improving using atropine alone, (2) those already wearing glasses or contact lenses, and (3) those who are aphakic, pseudophakic, or unable to accommodate with the fellow eye for any reason (e.g., third-nerve palsy). Optical penalization can be particularly effective in patients who cannot accommodate, because they are dependent on optical correction to allow proper focus at various distances.

4.4.11 Bangerter Foils

Bangerter foils are blurring filters of different densities that can easily be placed on the back surface of a spectacle lens to degrade the visual acuity of the sound eye and promote use of the amblyopic eye [19, 22]. Clinicians use different techniques to determine the density of filter to use for amblyopia treatment. Some clinicians choose a filter that will reduce visual acuity in the fellow eye to a level below that of the amblyopic eye; others assess fixation preference and choose a filter that results in a fixation switch to the amblyopic eye. A third method is to choose the initial filter empirically, selecting, for example, a 0.2 filter as a starting point for all patients. The best patients to consider for Bangerter foils are (1) those already wearing glasses, (2) older children or teenagers who are averse to wearing a patch, (3) those with mild, residual amblyopia, and (4) those with a history of amblyopia recurring when treatment was stopped. Advocates of Bangerter foils believe that they are particularly beneficial in maintaining visual acuity improvement and in preventing recurrent amblyopia, but data are sparse comparing them to patching or atropine.

4.4.12 Penalization Treatment Regimens

In general, penalization is used for similar lengths of time (weeks to months) as occlusion therapy and is continued until visual acuity stabilizes or amblyopia resolves. Bangerter filters are often prescribed for longer periods of time than occlusion, and they are often used as a form of maintenance therapy. Eyes penalized by Bangerter filters, atropine, or other techniques should be monitored the same way that patched eyes are monitored. Assessment of visual acuity and ocular alignment should be performed at least every 2−3 months during active treatment of older children and more frequently for younger children. It is useful to discontinue atropine at least one full week prior to each examination, or its lingering cycloplegic effect can prevent accurate assessment of both visual acuity and ocular alignment. Generally, breaks from treatment are not needed when using penalization unless

reverse amblyopia is confirmed in an older child or suspected in a young child who is unable to perform recognition visual acuity.

4.4.13 Amblyopia Treatment in Older Children and Teenagers

Many ophthalmologists were taught that amblyopia treatment is not effective beyond ages 7−10 years; however, recent evidence shows that some older children and teenagers will respond to amblyopia treatment, particularly if they have had no prior amblyopia treatment. Amblyopia Treatment Study 3 randomized 507 children age 7−18 years to optical correction alone or to augmented treatment with 2−6 h of prescribed daily patching (and daily atropine for those age 12 years or less) [39]. The results showed that treatment with patching and atropine was superior to optical treatment alone in children age 7−12 years, with 53% of those who had augmented treatment improving by at least two lines. There was a significant age effect, as younger children showed a greater effect of augmented treatment relative to control than the older children. Although there was no significant difference between augmented and optical treatment in children age 13−17 years, 47% percent of teenagers without prior treatment improved by at least two lines.

4.4.14 Complications of Amblyopia Treatment

Reverse (iatrogenic or occlusion) amblyopia is uncommon [6]. Test−retest studies of visual acuity assessment in children indicate that a one-line reduction in acuity is likely due to chance [18]. A reduction in the sound eye by two or more lines may be due to reverse amblyopia or to other factors such as poor performance, residual cycloplegic effect, inadequate relaxation of accommodation, or incorrect spectacle prescription. If reduction in visual acuity of the sound eye is suspected, visual acuity can be retested after giving the child a break. Minus lenses may be held over the glasses if persistent accommodative tone is suspected in a child with hyperopia. Finally, repeating a cycloplegic refraction may be useful, and if the sound eye visual acuity is still reduced by at least two lines, then reverse amblyopia should be suspected and treatment should be discontinued. It is extremely rare for reverse amblyopia to be permanent.

Patching can cause skin irritation, particularly if the patch is frequently removed and reapplied or if the child has sensitive skin. Some brands of patches are purported to be gentler to the skin, but they have a disadvantage of coming off more easily. Skin emollients, breaks from patching, and changing the orientation of the patch may be helpful if skin irritation is problematic.

Side effects of atropine are classically described as “hot as a hare, red as a beet, dry as a bone, blind as a bat, and mad as a wet hen” [25]. More specifically, adverse effects include dryness of the mouth and skin, fever, delirium, tachycardia, and development of amblyopia in the sound eye [1, 26, 31]. Atropine should be avoided in patients with a history of a topical allergic reaction to it. Sunglasses with ultraviolet protection and/or a hat with a brim should be used when atropine-treated patients are exposed to bright sunlight, since it can make them uncomfortable and there is a hypothetical risk of lens and/or retinal damage from ultraviolet light entering the eye through a dilated pupil. For this reason, other treatments may be preferable for children who are frequently outside, such as those who go to the swimming pool often in the summer months. Atropine should also be prescribed cautiously or dosed relatively infrequently for children in school, since continuous blurring of the sound eye can significantly impact their academic performance. In such cases, a bifocal for the sound eye may be prescribed for schoolwork. Finally, Down syndrome children may be more susceptible to the side effects of atropine [2].

4.4.15 Treatment Outcomes

After treatment with spectacles, patching, atropine, and/or other modalities, many children obtain normal or near-normal visual acuity of the amblyopic eye; however, a sizable proportion fail to achieve normal vision even after increasing the dosage or

switching treatments altogether. These patients have "residual" amblyopia, and it can be frustrating to parents who view normal vision as the goal of treatment. Two years after children were randomized into ATS1, 181 of 363 (50%) still had amblyopic eye acuity no better than 20/32 [35]. It is unknown whether an intensive final push with treatment such as combined patching and atropine with or without a plano lens for the sound eye will improve visual acuity in these cases.

Some children show little or no improvement with any type of amblyopia treatment. In these cases, a dilated examination should be repeated with attention to subtle signs of organic disease, such as macular pathology or optic nerve hypoplasia or atrophy. Patients with unilateral high myopia often respond poorly to amblyopia treatment, and it is likely due to associated retinal abnormalities. If amblyopic eye visual acuity fails to reach 20/40 or better with treatment, then protective polycarbonate lenses should be prescribed if they are not already worn.

4.4.16 *Amblyopia Recurrence After Cessation of Treatment*

A sizable proportion of children get recurrence of amblyopia after treatment is stopped. Amblyopia Treatment Study 2C prospectively followed 156 children who had improved at least three lines, and for whom investigators were ready to stop amblyopia treatment [40]. During the 1-year follow-up, reduction of acuity of 2 lines or more occurred in 21% of patients, and 40% of these recurrences occurred in the first 5 weeks after treatment was stopped. For those patients who had been treated with 6–8 h of daily patching, weaning prior to cessation of treatment seemed to reduce the chance of recurrence.

4.5 Effects of Amblyopia in Adulthood

Intuitively, it is better to have excellent vision in two eyes instead of only one eye; however, binocular visual acuity (i.e., measured with both eyes open) is typically unchanged with amblyopia treatment, so some parents may wonder what effect amblyopia treatment really has on their child's quality of life. Many of the rewards of amblyopia treatment may not be recognized until much later in life. One study showed that the risk of serious injury to the normal eye is increased in patients with poor visual acuity in the other eye [53]. Older adults often develop eye diseases, such as macular degeneration or glaucoma, which reduce their functional capacity. These diseases are often asymmetrical, so that the amblyopic eye may become the eye with better visual acuity in

Take Home Pearls

- Spectacles alone improve best-corrected amblyopic eye visual acuity by about three lines, so many patients do not need additional treatment with patching or penalization.
- Penalization is a viable option to occlusive patching in most patients with amblyopia. Penalization methods include atropine eye drops, optical penalization using a plano (blank) lens or excessive plus power lens, atropine with a plano lens, and Bangerter foils.
- Atropine may successfully treat amblyopia even when there is no apparent fixation switch to the amblyopic eye and when the atropinized sound eye near visual acuity remains better than amblyopic eye acuity.
- After stopping patching or atropine, about one in four patients will lose two or more lines of amblyopic eye visual acuity over the next 1 year.
- Amblyopia treatment may have its greatest benefit in later life, when sound eyes can sustain injuries or be afflicted by diseases of the macula or optic nerve.

later life. In addition, amblyopia treatment is associated with improvement in stereopsis, which is an important component of depth perception. Finally, amblyopia often co-exists with strabismus, and it has been hypothesized that better visual acuity and stereopsis may be associated with better long-term alignment after strabismus surgery. For these and other reasons, the benefits of early screening and treatment of amblyopia are well worth the cost [4].

References

1. Altman B (1983) Drugs in pediatric ophthalmology. In: Harley RD (ed) Pediatric ophthalmology, 2nd edn. Saunders, Philadelphia
2. Apt L (1994) Pharmacology. In: Isenberg SJ (ed) The eye in infancy, 2nd edn. Mosby-Year Book, St. Louis
3. Awan M, Proudlock FA, Gottlob I (2005) A randomized controlled trial of unilateral strabismic and mixed amblyopia using occlusion dose monitors to record compliance. Invest Ophthalmol Vis Sci 46:1435–1439
4. Beauchamp GR (2007) Chronic amblyopia and strabismus in children. Arch Ophthalmol 125:821–822
5. Berard PV, Layec-Arnail M (1983) Penalization in strabismus. Int Ophthalmol 6:13–18
6. Burian HM (1966) Occlusion amblyopia and the development of eccentric fixation in occluded eyes. Am J Ophthalmol 62:853
7. Cassin B (1982) Alternate fixation in the non-strabismic child. Am Orthopt J 32:111–116
8. Cotter SA, Edwards AR, Arnold RW et al., Pediatric Eye Disease Investigator Group (2007) Treatment of strabismic amblyopia with refractive correction. Am J Ophthalmol 143:1060–1063
9. Donahue SP (2006) Relationship between anisometropia, patient age, and the development of amblyopia. Am J Ophthalmol 142:132–140
10. Ellis GS, Frey T, Gouterman RZ (1987) Myelinated nerve fibers, axial myopia, and refractory amblyopia: an organic disease. J Pediatr Ophthalmol Strabis 24:111–119
11. France TD, France LW (1999) Optical penalization can improve vision after occlusion treatment. J AAPOS 3:341–343
12. Frank JW (1983) The clinical usefulness of the induced tropia test for amblyopia. Am Orthopt J 33:60–69
13. Foley-Nolan A, McCann A, O'Keefe M (1997) Atropine penalization vs occlusion as the primary treatment for amblyopia. Br J Ophthalmol 81:54–57
14. Haase W (1975) Experiences with penalisation therapy. In: Moore S, Mein J, Stockbridge L, (eds) Orthoptics: past, present, future. Stratton, New York, pp 105–111
15. Hiscox F, Strong N, Thompson JR et al. (1992) Occlusion for amblyopia: a comprehensive survey of outcome. Eye 6:300–304
16. Hittner HM, Antoszyk JH (1987) Unilateral peripapillary myelinated nerve fibers with myopia and/or amblyopia. Arch Ophthalmol 105:943–948
17. Holmes JM, Beck RW, Kraker RT et al., Pediatric Eye Disease Investigator Group (2003) Impact of patching and atropine treatment on the child and family in the amblyopia treatment study. Arch Ophthalmol 121:1625–1632
18. Holmes JM, Beck RW, Repka MX et al. (2001) The amblyopia treatment study visual acuity testing protocol. Arch Ophthalmol 119:1345–1353
19. Iacobucci IL, Archer SM, Furr BA, Martonyi EJB, Del Monte MA (2001) Bangerter foils in the treatment of moderate amblyopia. Am Orthopt J 51:84–91
20. Kaye SB, Chen SI, Price G et al. (2002) Combined optical and atropine penalization for the treatment of strabismic and anisometropic amblyopia. J AAPOS 6:289–293
21. Knapp P, Moore S (1962) Diagnostic procedures in an orthoptic evaluation. Am Orthopt J 12:63–69
22. Lang J (1999) An efficient treatment and new criteria for cure of strabismic amblyopia: reading and Bangerter foils. Binocul Vis Strabismus Q 14:9–10
23. Leach C (1995) Compliance with occlusion therapy for strabismic and anisometropic amblyopia: a pilot study. Binocular Vis Eye Muscle Surg Q 10:257–266
24. Lueder GT, Garibaldi D, Comparison of visual acuity measured with Allen figures and Snellen letters using the B-VAT II monitor. Ophthalmology 104:1758–1761
25. Morton HG (1997) Atropine intoxication: its manifestation in infants and children. J Pediatr 1939;14:755
26. Myers TM, Wallace DK, Johnson SM (2005) Ophthalmic medications in pediatric patients. Comp Ophthalmol Update 6:85–101
27. North RV, Kelly ME (1987) A review of the uses and adverse effects of topical administration of atropine. Ophthalmol Physiol Opt 7:109–114
28. North RV, Kelly ME (1991) Atropine occlusion in the treatment of strabismic amblyopia and its effect upon the non-amblyopic eye. Ophthalmic Physiol Opt 11:113–117
29. Oliver M, Neumann R, Chaimovitch Y et al. (1986) Compliance and results of treatment for amblyopia in children more than 8 years old. Am J Ophthalmol 102:340–345
30. O'Reilly C, Smith DR (1984) The 10-diopter base-down fixation test for amblyopia: comparison of techniques. Can J Ophthalmol 19:303–305
31. Palmer EA (1986) How safe are ocular drugs in pediatrics? Ophthalmology 93:1038–1040
32. Parks MM (1963) Ocular motility diagnosis. Int Ophthalmol Clin 3:811–883
33. Paysse EA, Coats DK, Hussein MA et al. (2006) Long-term outcomes of photorefractive keratectomy for anisometropic amblyopia in children. Ophthalmology 113:169–176
34. Pediatric Eye Disease Investigator Group (2004) A randomized trial of atropine regimens for treatment of moderate amblyopia in children. Ophthalmology 111:2076–2085
35. Pediatric Eye Disease Investigator Group (2002) A randomized trial of atropine vs patching for treatment of moderate amblyopia in children. Arch Ophthalmol 120:268–278

36. Pediatric Eye Disease Investigator Group (2003) A randomized trial of patching regimens for treatment of moderate amblyopia in children. Arch Ophthalmol 121:603−611
37. Pediatric Eye Disease Investigator Group (2003) A randomized trial of prescribed patching regimens for treatment of severe amblyopia in children. Ophthalmology 110:2075−2087
38. Pediatric Eye Disease Investigator Group (2006) A randomized trial to evaluate 2 hours of daily patching for strabismic and anisometropic amblyopia in children. Ophthalmology 113:904−912
39. Pediatric Eye Disease Investigator Group (2005) Randomized trial of treatment of amblyopia in children aged 7 to 17 years. Arch Ophthalmol 123:437−447
40. Pediatric Eye Disease Investigator Group (2004) Risk of amblyopia recurrence after cessation of treatment. J AAPOS 8:420−428
41. Pediatric Eye Disease Investigator Group (2006) Treatment of anisometropic amblyopia in children with refractive correction. Ophthalmology 113:895−903
42. Pediatric Eye Disease Investigator Group (2005) Two-year follow-up of a 6-month randomized trial of atropine vs patching for treatment of moderate amblyopia in children. Arch Ophthalmol 123:149−157
43. Repka MX, Ray JM (1993) The efficacy of optical and pharmacological penalization. Ophthalmology 100:769−775
44. Ron A, Nawratzki I (1982) Penalization treatment of amblyopia: a follow-up study of two years in older children. J Pediatr Ophthalmol Strabismus 19:137−139
45. Schmidt P, Maguire M, Dobson V et al. Vision in Preschoolers Study Group (2004) Comparison of preschool vision screening tests as administered by licensed eye care professionals in the Vision In Preschoolers Study. Ophthalmology 111:637−650
46. Şener EC, Mocan MC, Gedik Ş et al. (2002) The reliability of grading the fixation preference test for the assessment of interocular visual acuity differences in patients with strabismus. J AAPOS 6:191−194
47. Simons K (1996) Preschool vision screening: rationale, methodology and outcome. Surv Ophthalmol 41:3−30
48. Simons K, Gotzler KC, Vitale S (1997) Penalization versus part-time occlusion and binocular outcome in treatment of strabismic amblyopia. Ophthalmology 104:2156−2160
49. Simons K, Stein L, Sener EC et al. (1997) Full-time atropine, intermittent atropine, and optical penalization and binocular outcome in treatment of strabismic amblyopia. Ophthalmology 104:2143−2155
50. Smith LK, Thompson JR, Woodruff G, Hiscox F (1995) Factors affecting treatment compliance in amblyopia. J Pediatr Ophthalmol Strabismus 32:98−101
51. Swann AP, Hunter CD (1974) A survey of amblyopia treated by atropine occlusion. Br Orthopt J 31:65−69
52. The Vision in Preschoolers Study Group (2005) Preschool vision screening tests administered by nurse screeners compared with lay screeners in the vision in preschoolers study. Invest Ophthalmol Vis Sci 46:2639−2648
53. Tommila V, Tarkkanen A (1981) Incidence of loss of vision in the healthy eye in amblyopia. Br J Ophthalmol 65:575−577
54. Tychsen L, Packwood E, Berdy G (2005) Correction of large amblyopiogenic refractive errors in children using the excimer laser. J AAPOS 9:224−233
55. Tychsen L, Packwood E, Hoekel J, Lueder G (2006) Refractive surgery for high bilateral myopia in children with neurobehavioral disorders: 1. Clear lens extraction and refractive lens exchange. J AAPOS 10:357−363. Erratum in: J AAPOS 2007;11:417−419
56. Noorden GK von (1996) Binocular vision and ocular motility: theory and management of strabismus, 5th edn. Mosby, St. Louis
57. Noorden GK von, Milam JB (1979) Penalization in the treatment of amblyopia. Am J Ophthalmol 88:511−518
58. Wallace DK (2007) Evidence-based amblyopia treatment: results of PEDIG studies. Am Orthop J 57:48−55
59. Wallace DK (2005) Tests of fixation preference for amblyopia. Am Orthop J 55:76−81
60. Wallace DK (2006) The role of penalization in the treatment of amblyopia. Curr Med Lit Ophthalmol 16:65−69
61. Wallace DK (1999) Visual acuity after cycloplegia in children: implications for atropine penalization. J AAPOS 3:241−244
62. Wallace DK, Chandler DS, Beck RW et al., Pediatric Eye Disease Investigator Group (2007) Treatment of bilateral refractive amblyopia in children 3 to <10 years old. Am J Ophthalmol 144:487−496
63. Whittaker KW, O'Flynn E, Manners RM (2000) Diagnosis of amblyopia using the 10-Diopter Fixation Test: a proposed modification for patients with unilateral ptosis. JPOS 37:21−23
64. Wright KW, Edelman PM, Walonker F, Yiu S (1986) Reliability of fixation preference testing in diagnosing amblyopia. Arch Ophthalmol 104:549−553
65. Wright KW, Walonker F, Edelman P (1981) 10-diopter fixation test for amblyopia. Arch Ophthalmol 99:1242−1246
66. Wu C, Hunter DG (2006) Amblyopia: diagnostic and therapeutic options. Am J Ophthalmol 141:175−184
67. Zipf RF (1976) Binocular fixation pattern. Arch Ophthalmol 94:401−405

Worldwide Causes of Blindness in Children

5

Clare Gilbert

Contents

Core Messages

- The prevalence and cause of blindness in children are related to levels of socio-economic development and the availability of primary health care and eye-care services.
- There are ten times as many blind children per million total population in poor communities compared with affluent communities.
- The major preventable causes of blindness in children are declining in poor countries as a result of large scale public health interventions and cataract is becoming a relatively more important avoidable cause.
- Retinopathy of prematurity is an important cause in Latin America and Eastern Europe and is increasing in the emerging economies of Asia.
- Control requires comprehensive eye-care services, from community interventions through to specialist tertiary levels services.

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5.1 Introduction

Although much rarer than blindness in adults, control of the avoidable causes of blindness in children is a priority of VISION2020 – the Right to Sight [15, 43]. VISION2020 is a global initiative of the World Health Organization (WHO) and the International Agency for the Prevention of Blindness, the latter being an umbrella organization which includes professional groups, organizations of, and for, the blind and international non-governmental organizations who support prevention of blindness activities. Children have been included in this initiative because the causes of blindness are so different from those in adults, and different strategies are required, from community level through to tertiary eye-care services. Another factor to consider is that most blindness is age related, whereas blind children have a lifetime of blindness ahead.

5.2 Sources of Data and Their Limitations

Designing and carrying out population-based studies of rare conditions is challenging, as large sample sizes are required. As far as blindness in children is concerned, sample sizes of 20−30,000 children would be needed to provide precise estimates of the prevalence, and the sample would need to be increased even further to obtain meaningful data on causes. There are additional challenges when studying children since measurement of visual acuity in young children in a field setting can be extremely difficult and school going children are not at home during the day except during the school holidays. For all these epidemiological and practical reasons there are only limited prevalence data from population-based surveys [8, 14, 28]. The available data are also difficult to compare and compile as some of the studies were undertaken several decades ago and different definitions of childhood and of blindness have been used. Some highly developed countries maintain registers of the blind which include children, and these can provide data on the incidence and causes of blindness in newly diagnosed children [19, 20, 31]; however, as with all registers there is likely to be under-reporting, and many observers are involved in categorizing the causes which can lead to misclassification and observer bias. In the U.K., the British Ophthalmological Surveillance Unit provides a mechanism for ophthalmologists to report new cases of rare conditions, and a recent study provided national data on the incidence and cause of blindness in children [30]. More recently, some data have become available from population-based sources in poorly developed countries, e.g. from house-to-house surveys and from studies using Key Informants who identify children who are blind in their own communities [5, 24, 47].

In 1993 a new system for classifying the causes of blindness in children was adopted by WHO which uses a descriptive, anatomical classification as well as an aetiological classification [10]. Information on the anatomical site can be obtained from all children examined but obtaining information on the underlying cause, which depends on the time of onset of the condition leading to blindness, is far more difficult. This is particularly true in poorly developed countries where the medical history may be difficult to obtain, where the child may present very late and the clinical signs may be difficult to illicit, and because facilities and expertise for diagnostic investigations are limited. Since the WHO classification system was published many thousands of blind children have been examined. Most of the data have come from examining children attending schools for the blind, the advantage being that a large number of children can be examined quickly and easily; however, these data are subject to bias, since in poorly developed countries it is estimated that less than 10% of blind children are receiving any kind of education: those who are in school may be blind from different conditions from those who do not attend school. Examining children enrolled in community-based rehabilitation programs provides community-based data on causes [37] as does data obtained from studies using Key Informants as case finders [25]. These population-based sources are likely to provide more reliable information than facility-based studies.

A major limitation of the WHO classification is that at the time of its development WHO classified blindness on the basis of “best-corrected” visual acuity rather than “presenting” visual acuity. This means that the data collected to date do not include uncorrected refractive error as a cause of blindness. To address this limitation the WHO has recently revised the categories

of visual loss, and presenting visual acuity is now being used [46]. The Refractive Error in Children Study Group used presenting and best-corrected visual acuity in their standardized population-based prevalence surveys which have been conducted in all regions of the world [27]. The sample sizes were too small to give precise estimates of the prevalence of blindness, but pooling the data across eight of the sites reveals that the prevalence of severe visual impairment and blindness (<6/60 in the better eye) due to uncorrected refractive errors was 2.5/10,000 children [18].

5.3 Prevalence of Blindness in Children

In this chapter childhood is defined as 0−15 years, and the majority of data on the causes have used a definition of blindness which also includes severe visual impairment (i.e. <6/60 in the better eye).

The prevalence of any condition in a population is determined by the rate at which new cases develop over time (i.e. the incidence) and the duration of the condition to resolution (as a result of treatment or the natural history), or death. Prevalence data can, therefore, only give a "snapshot" of the proportion of the population who are affected at any one point in time. This is of relevance when considering blindness in children, since many of the conditions that lead to blindness are also causes of child mortality. Few data are available on mortality rates among blind children, but it has been estimated that in poorly developed countries up to 60% of blind children die within 1−2 years of becoming blind and in the U.K. surveillance study mentioned above 10% of newly diagnosed children were no longer alive 1 year later [30, 43]. The implication of this is that prevalence data underestimate the magnitude of the problem, as the data cannot take account of children who have died.

The available evidence suggests that the prevalence of blindness among children is closely associated with levels of socio-economic development. In highly developed countries the prevalence is in the range 3−4/10,000 children while in the least-developed countries of sub-Saharan Africa the prevalence can be as high as 12−14/10,000 [47]. In countries with low development the prevalence is likely to be 7−9/1,000, and 5−6/1,000 in countries with medium levels of development [14, 43]. The prevalence of blindness in children correlates reasonably well with under-5-years mortality rates, which is what one would expect, particularly as under-5-years mortality rates are now being used to predict whether countries have significant levels of vitamin A deficiency [35]. Where prevalence data are not available, under-5-years mortality rates have been used as a proxy to estimate the prevalence (Fig. 5.1). Although currently limited, these estimates show that there are approximately 1.4 million children worldwide who are blind, and that sub-Saharan Africa has the largest number of blind children (almost 320,000) [23, 43]. The Former Socialist Economies of Eastern Europe is the region with the lowest number of blind children (40,000), on account of the relatively small child population and the moderately low prevalence.

5.4 Available Data on Causes

As already indicated, most of the data on the causes of blindness in children come from examining children in schools for the blind, and data are available from over 15,000 children who have been examined in 38 countries since 1993. The distribution of causes using both classification systems are shown in Tables 5.1 and 5.2. The data are presented using World Bank regions rather than any other grouping of countries, as the World Bank groups countries by levels of socio-economic development.

Retinal conditions are the commonest cause of blindness worldwide, accounting for a quarter of cases. The majority of these children are blind from retinal dystrophies, but approximately 50,000 are blind from retinopathy of prematurity (ROP). Corneal conditions are the second commonest site, the vast majority being blind from acquired conditions of childhood which lead to corneal ulceration and scarring. Congenital abnormalities of the whole eye (i.e. anophthalmos, microphthalmos and coloboma) account for 18.5% of blindness and they are a particularly important cause in Asia. Just over 200,000 children are blind from disorders of the lens, principally unoperated cataract, but also dense amblyopia following delayed surgery, complications of surgery or from associated ocular abnormalities.

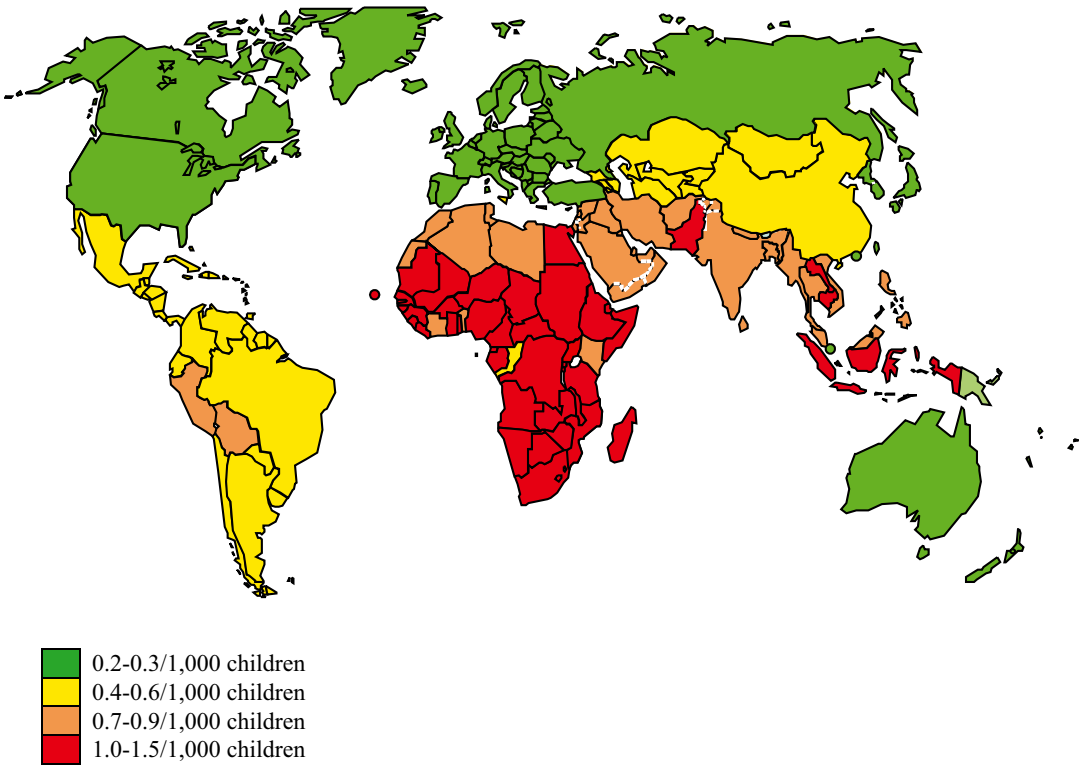

Fig. 5.1 Estimates of the prevalence of blindness in children, based on the association with under-5-years mortality rates

Table 5.1 Estimates of the proportion of children who are blind, by anatomical site and World Bank region. *EME* Established Market Economies, *MEC* Middle East Crescent, *FSE* Former Socialist Economies, *OAI* Other Asia and Islands, *LAC* Latin America and Caribbean, *SSA* sub-Saharan Africa

WB region	EME	FSE	LAC	MEC	China	India	OAI	SSA	ALL	ALL
No blind	50,000	40,000	100,000	190,000	210,000	270,000	220,000	320,000	1,400,000	
	Richest region (%)						Poorest region (%)		Number	Percentage
Retina	25.0	44.3	46.4	42.4	24.9	16.7	15.8	20.0	353,000	25.2
Cornea	1.0	2.3	8.4	5.8	4.3	24.6	24.3	36.2	265,400	19.0
Whole globe	10.0	12.0	11.0	16.0	25.4	33.3	16.5	8.8	258,900	18.5
Lens	8.0	10.8	7.5	16.7	18.9	9.7	27.4	10.0	205,400	14.7
Optic nerve	25.0	14.8	11.7	7.4	13.6	6.1	7.5	9.6	136,700	9.8
Glaucoma	1.0	2.8	8.3	6.4	9.0	2.4	4.6	6.2	77,600	5.5
Other	28.0	8.0	4.4	2.6	2.3	3.0	1.5	4.8	58,200	4.2
Uvea	2.0	5.3	2.3	2.7	1.5	4.3	2.3	4.5	44,800	3.2
Total	100	100	100	100	100	100	100	100	1,400,000	100

Compiled from a database held by C. Gilbert at the International Centre for Eye Health, LSHTM

Table 5.2 Estimates of the proportion of children who are blind, by aetiological category and World Bank region. *EME* Established Market Economies, *MEC* Middle East Crescent, *FSE* Former Socialist Economies, *OAI* Other Asia and Islands, *LAC* Latin America and Caribbean, *SSA* sub-Saharan Africa

WB region	EME	FSE	LAC	MEC	China	India	OAI	SSA	ALL	ALL
No blind	50,000	40,000	100,000	190,000	210,000	270,000	220,000	320,000	1,400,000	
	Richest region (%)						Poorest region (%)		Number	Percentage
Unknown	14.0	43.8	32.1	36.5	53.0	54.7	50.0	36.9	612,800	43.8
Hereditary	45.0	17.8	22.1	55.1	30.7	19.3	20.0	20.0	381,300	27.2
Childhood	10.0	5.0	9.9	6.1	14.0	21.7	22.6	34.6	277,000	19.8
Perinatal	24.0	27.8	27.8	1.3	2.3	1.5	6.3	5.9	95,100	6.8
Intrauterine	7.0	5.8	8.1	1.1	0.1	2.7	1.0	2.5	33,800	2.4
Total	100	100	100	100	100	100	100	100	1,400,000	100

Compiled from a database held by C. Gilbert at the International Centre for Eye Health, LSHTM

In all regions of the world an underlying aetiology cannot be determined in a large proportion of instances. This situation arises because the time of onset of the condition is often not known (e.g. congenital abnormalities can be due to chromosomal abnormalities or genetic defects, or they may be due to exposure to teratogens), and for the reasons given above (Sect. 5.1). Acquired conditions of childhood are important in the poorer regions of the world, while the consequences of prematurity are important in countries with high and medium levels of development; in the former, cortical visual impairment is more common than ROP [20, 23, 30, 38], while in middle-income countries ROP is more common than cortical impairment. Hereditary conditions predominate in countries in the Middle East Crescent [2, 12] and intrauterine causes are unusual in all regions.

Globally it is estimated that almost 45% of children are blind from avoidable causes, i.e. those that can be prevented (vitamin A deficiency, measles, ophthalmia neonatorum, use of harmful traditional eye remedies and ROP), and those that can be treated (e.g. cataract and glaucoma). In the least-developed countries the proportion that is avoidable can be as high as 70% [22] but is much lower in countries with high levels of development.

5.5 Reasons for the Variation in Prevalence

There are three main reasons why the prevalence of blindness is higher in children in countries with low and medium levels of development compared with highly developed countries:

1. Some conditions only occur in very poor communities (e.g. vitamin A deficiency; use of harmful traditional eye remedies).
2. Conditions which can lead to blindness are being prevented in highly developed countries but are not being adequately controlled in poorer countries (e.g. measles infection, ophthalmia neonatorum, congenital rubella, retinopathy of prematurity).
3. Clinical services to restore sight or prevent blindness are less well developed in poor countries, and parents may not understand the need for surgery or may not be able to afford the treatment (e.g. cataract and glaucoma).

5.6 Causes of Blindness Associated with Poverty

5.6.1 Vitamin A Deficiency Disorders

Vitamin A (retinol) has many functions apart from phototransduction, and it plays an important role in embryogenesis, haemopoesis, growth, the immune system, epithelial differentiation and as an antioxidant [34]. Preformed retinol is found in animal sources (e.g. breast milk, dairy products, fish oil) and vitamin A precursors (e.g. carotenoids and carotenes) are found in yellow and red fruit and vegetables, red palm oil and dark-green leafy vegetables. Young children have disproportionately high daily requirements for vitamin A as they are growing and this is the sector of the population most vulnerable to deficiency. They are also totally dependent on their care givers for the foods they eat. Young children can become vitamin A deficient as a result of several mechanisms which often occur in combination: poor dietary intake of vitamin A rich foods, malabsorption (diarrhoea being the commonest cause), increased demand for vitamin A due to infectious diseases and loss of retinol in the urine or feces (as can occur in measles). Severely malnourished children with protein energy malnutrition also lack carrier proteins which reduces delivery of retinol to target tissues. More distal predisposing factors include large family sizes, lack of maternal education, poor water supplies and sanitation and lack of land ownership against a backdrop of poor climate and soils, lack of infrastructure for transporting food, poor governance, political instability and displacement. The global distribution of vitamin A deficiency disorders in children is shown in Fig. 5.2 [42]. Children who are deficient in vitamin A may or may not have the clinical signs (xerophthalmia), but all those who are deficient are at increased risk of infectious diseases and higher mortality rates. Indeed, children who are deficient can enter a vicious cycle: they are more prone to infection on account of changes to the immune system and reduction in epithelial barrier

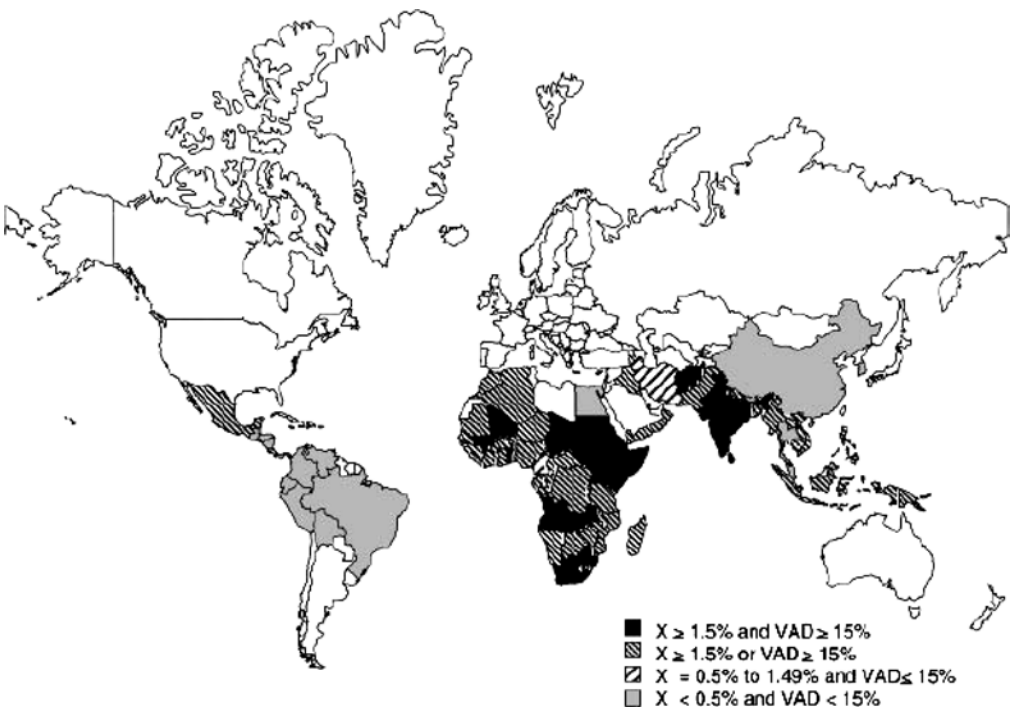

Fig. 5.2 Countries stratified by joint prevalence of vitamin A deficiency, defined by serum retinol concentrations (<0.70μmol/L), or abnormal conjunctival impression cytology, and xerophthalmia (all active stages combined) among preschool aged children. (With permission from kking@nutrition.org; West KP Jr. Extent of vitamin A deficiency among preschool children and women of reproductive age. J Nutr. 2002 132 (Suppl): 2857S–2866S)

function which, in turn, leads to increased demand for vitamin A, loss of intake an account of malaise, and possibly decreased absorption if they have diarrhoea. The child most at risk of acute, life-threatening vitamin A deficiency (and blindness) is a young child whose mother was vitamin A deficient during pregnancy, who was not adequately breast fed, who was weaned on foods low in vitamin A, who has a diet low in vitamin A and who then develops an acute infectious illness.

The ocular features of xerophthalmia are night blindness (XN), conjunctival xerosis (X1A), Bitots spots (X1B) corneal xerosis (X2), corneal ulceration and keratomalacia (X3A and B), corneal scarring (XS) and fundus changes (XF). Conjunctival xerosis and Bitots spots are signs of chronic deficiency and tend to occur in older children while the corneal changes reflect acute deficiency and usually occur in children below the age of 6 years [34]. In 2002 there were estimated to be 4.4 million children with xerophthalmia 127 million with subclinical evidence of deficiency (low serum retinol levels or with abnormal impression cytology) [42].

In the 1980s several large-scale population-based clinical trials were undertaken to determine whether vitamin A supplementation reduced child mortality and morbidity. These trials demonstrated conclusively that improving the vitamin A status of vulnerable populations of children markedly reduces child mortality [4]. These findings provided the evidence and impetus for global partnerships for control. In the long term, prevention of vitamin A deficiency requires socio-economic development and elimination of poverty in all its guises. In the medium term the following strategies are being adopted: food diversification, fortification of commonly consumed foods, promotion of home gardening, nutrition education and food supplementation for preschool age children [40]. Short-term strategies include supplementation with high-dose retinal palmitate of women immediately after delivery and of children aged 6−72 months of age. Many countries now have large-scale programs, with vitamin A being given to infants and children at the time of immunization, and targets have been set for eliminating vitamin A deficiency as a public health problem. Control of vitamin A deficiency is one of the factors responsible for declining under-5-years mortality rates in many of the least developed countries of Asia and sub-Saharan Africa [21] and for the reduction in childhood corneal blindness being observed in many of the poorer countries of the world [41].

5.6.2 Traditional Eye Remedies

The use of traditional eye remedies is an important cause of ocular morbidity in adults and children, particularly in sub-Saharan Africa; however, determining the extent to which traditional remedies contribute towards blindness is difficult, as patients are often reluctant to admit they have used them and the diagnosis is often one of exclusion.

The WHO has defined traditional medicine as "… the sum total of all the knowledge and practices, used in diagnosis, prevention and elimination of physical, mental or social imbalance and relying exclusively on practical experience and observation handed down from generation to generation, whether verbally or in writing. Traditional medicine might also be considered as solid amalgamation of dynamic medicine know-how and ancestral experience. Traditional African medicine might also be considered to be the sum total of practices, measures, ingredients and procedures of all kinds, whether material or not, which from time immemorial has enabled the African to guard against disease, to alleviate his suffering and to cure himself." [45].

People's understanding of the causes of disease vary. For example, in animist societies some conditions are believed to be supernatural in origin (e.g. angering ancestral spirits, the result of witchcraft or the "evil eye") or they may arise as a result of conflict, tension, jealousy, immoral behaviour or breaking local customs or taboos, or they may be passed down within the family (usually attributed to the mother). Other conditions are thought to arise as a consequence of lack of respect towards parents or elders, or weakness or eating unclean food. These beliefs influence whom people turn to when they become sick, and what they do about it. The use of traditional eye remedies is common, particularly in sub-Saharan Africa, where allopathic medicine has only been available for the past few generations. Indeed, it is a common practice for patients to use traditional and allopathic medicine concurrently, or they may only seek allopathic medicine once traditional remedies have failed.

Traditional practices may be benign (e.g. ritual bathing, dances), beneficial (e.g. steam baths, inhalations) or harmful. The use of harmful traditional remedies, either home remedies or prescribed by traditional healers, is an important cause of corneal blindness in children, particularly in sub-Saharan Africa [7]. Traditional remedies can lead to visual loss in children through several mechanisms: adnexal injuries (from thermal, acid or alkaline burns) can lead to exposure keratitis and secondary infection. Exposure keratitis can occur if parents hold the eyes of their child open, a practice believed to prevent blindness from measles in parts of West Africa. Mechanical damage and burns can result from objects and material being inserted into the eye (e.g. twigs and leaves, ground up cowrie shells, acidic or alkaline liquids, toxic sap or infusions made from plants). Fungal infection can occur if plant material is inserted into the eye, and gonococcal keratoconjunctivits can complicate instillation of infected urine. Even harmless traditional remedies can lead to blindness indirectly, as a consequence of delay in seeking more appropriate treatment.

The practice of traditional healing varies enormously from locality to locality and the tradition and remedies are often passed down within the family. Some healers develop specific areas of expertise (e.g. mental health) and payment is often in kind. Even in settings where eye care services are available members of the community often consult the traditional healer first, or want to discuss decisions with them having already seen an eye-care worker. Given their local standing, workshops for traditional healers have been held in countries in sub-Saharan Africa and Nepal where they have been advised regarding which harmful practices to avoid and they have been shown which cases should be referred for surgery (e.g. cataract).

5.7 Causes Where Prevention is Inadequate

5.7.1 Measles-Related Blindness

Measles can lead to corneal ulceration and scarring through a variety of mechanisms including acute vitamin A deficiency with corneal ulceration and keratomalacia, secondary bacterial infection, exposure keratitis, secondary herpes simplex virus (HSV) keratitis, measles keratitis and the use of harmful traditional eye medicines. Measles is perhaps the most important infectious disease that can precipitate a child with subclinical vitamin A deficiency into acute blinding and life-threatening deficiency. Measles increases the metabolic rate and utilization of vitamin A; intake of vitamin-A-rich foods may be low, due to anorexia, feeding taboos and customs, and painful herpetic oral ulceration; infection of the gastrointestinal tract can cause malabsorption and protein-losing enteropathy (with loss of carrier proteins), and infection of the urinary tract can lead to loss of retinol in the urine. Measles infection affects all epithelial tissues and so retinol is in great demand during epithelial repair [36].

Measles infection of the corneal epithelium usually causes a mild, self-limiting (albeit symptomatic) keratitis, but occasionally more extensive corneal erosions can occur. This loss of barrier function predisposes towards secondary bacterial infection and suppurative keratitis. Measles infection depresses cell-mediated and humoural immunity, which probably explains the secondary herpetic infection, which can become amoeboid, or involve the corneal stroma. Severe measles can lead to dehydration and prostration – the child may develop exposure keratitis and secondary infection. In Africa measles is known to be a severe condition and there is often local knowledge that measles can cause blindness. Parents try to prevent this by using traditional remedies (see Sect. 5.6.2).

In poorly developed countries measles has a far higher mortality rate than in highly developed countries (7% or higher compared with $<0.1\%$) with mortality being higher in infants and older children. The severity of measles in poorly developed countries is due to overcrowding (which increases the infecting dose of virus) [1], pre-existing malnutrition and vitamin A deficiency, and inadequate health services to manage life-threatening complications (i.e. pneumonia and diarrhoea).

Measles is also highly infectious, with a basic reproductive rate of 15 which means in "virgin", non-immune populations, one infected individual passes the infection on to 15 others, on average. To prevent epidemics, very high levels of immunity are, therefore, required. Measles immunization coverage has increased dramatically in many countries, with a concomitant drop in the number of cases of measles

and measles related deaths; however, there are still approximately 450,000 cases annually, and 15 countries (most in sub-Saharan Africa) have an incidence of ≥50/100,000 [44]. Measles immunization coverage was <50% in 5 African countries in 2004, and 50−79% in >20 other countries: measles epidemics are, therefore, still likely in these countries.

5.7.2 Retinopathy of Prematurity

Retinopathy of prematurity is emerging as an important potentially avoidable cause of blindness in children in the middle-income countries of Latin America and eastern Europe [13, 16], and it is also becoming a problem in cities in the emerging economies of Asia (e.g. Thailand, the Philippines, India, Vietnam and China) [6, 11, 29, 33, 39]. In Latin America the proportion of blindness in children due to ROP varies but can be as high as 60% (one province in Argentina), and in eastern Europe almost 50% of new cases of blindness in children in Moscow and Poland is due to ROP [32]. The available data seem to suggest that the proportion of blindness due to ROP is associated with infant mortality rates [17]. In countries with very low IMRs (<9/1,000 live births), which include North America, western Europe, Japan, Australia and New Zealand, approximately 10% of blindness in children is due to ROP. In these settings standards of neonatal care are high and there are programs in place to detect and treat babies with type-1 ROP. At the other end of the socio-economic spectrum, where IMRs are high (>60/1,000 live births), blindness due to ROP is very unusual. Most of these countries are in sub-Saharan Africa, where neonatal intensive care services are either not in place, or premature babies do survive long enough to develop severe ROP [3]. The last group are middle-income countries with IMRs in the range 9−60/1,000 live births, and it is these countries where ROP is emerging as an important cause of blindness (Fig. 5.3). This has been referred to as the "third epidemic" of ROP [13].

This "third epidemic" of ROP blindness has several explanations. Firstly, rates of preterm birth tend to be higher in middle-income countries than in high-income countries, particularly in Latin America where teenage pregnancies are common. Secondly, in mid-

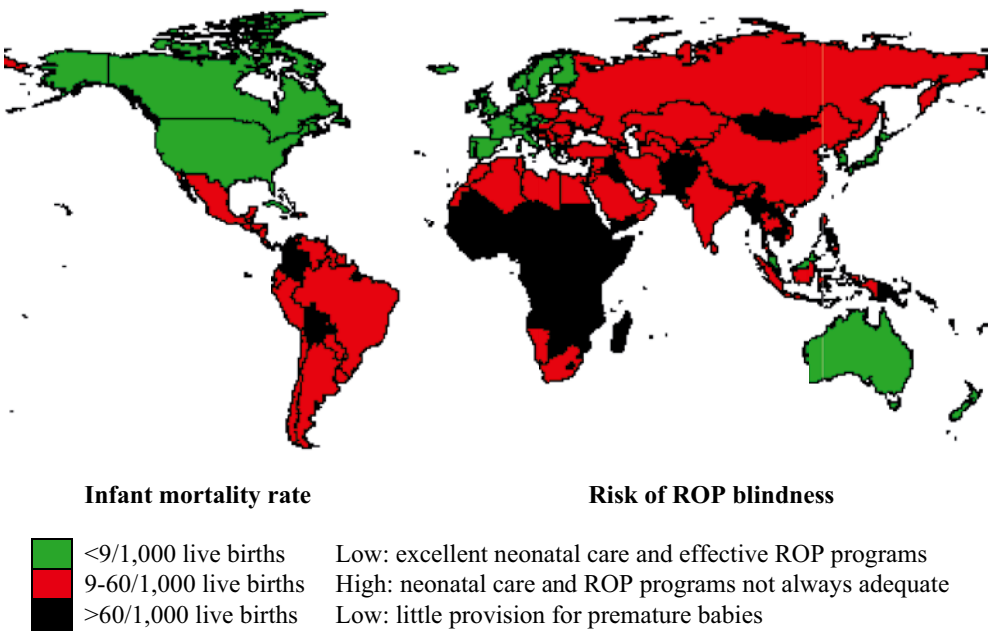

Fig. 5.3 Likelihood of retinopathy of prematurity being an important cause of blindness in children, using infant mortality rates as a proxy indicator. (Reproduced with permission from Eye (2007) 21:1338–43 by the Royal College of Ophthalmologists, London)

dle-income countries a high proportion of deliveries are in health facilities and premature babies are likely to be admitted to neonatal intensive care. Thirdly, rates of severe ROP are higher in premature babies in low- and middle-income countries, even when wider screening criteria have been used, suggesting that babies are being exposed to risk factors which are now largely controlled in highly developed countries. For example, in Latin America neonatal care is provided by a range of service providers, with some units having excellent facilities and high staff:patient ratios; however, many neonatal units in low- and middle-income countries do not have enough equipment for continuous monitoring of all babies on supplemental oxygen, and nursing shortages mean that one nurse can be responsible for several high-dependency babies. Variations in levels of neonatal care mean that some babies are cared for in "first epidemic" environments, whereas others are in "second epidemic" environments – this is why the third epidemic of ROP affects babies with characteristics of both (Fig. 5.4). The final important factor is that screening and treatment programs for ROP are not uniformly in place. Reasons for this vary: in some countries there is a real shortage of ophthalmologists while in other countries ophthalmologists are not skilled in indirect ophthalmoscopy. In many middle-income countries ophthalmologists suffer loss of income if they screen in their own time, as government employees need to work in the private sector to supplement their low incomes. Fear of litigation is also emerging as a demotivating factor; however, many countries in Latin America are expanding and improving their ROP programs, are using national guidelines and have established national ROP committees. Much more needs to be done to reduce rates of ROP in middle-income countries, by improving neonatal care for babies at risk particularly in relation to the delivery and monitoring of supplemental oxygen.

5.8 Causes Where Treatment is Inadequate

Cataract, and to a lesser extent, glaucoma, are important potentially avoidable cause of blindness in children; however, good outcomes are determined to a large extent by patient as well as provider considerations.

Most studies, including those from poorly developed countries, indicate that the majority of cataract in childhood is sporadic, which provides little opportunity for prevention. Challenges to improving outcomes in resource-poor settings are that children often present very late [26], parents may not be able to afford the inpatient and surgical costs, consumables for children are not readily available, surgical management can be sub-optimal as sub-specialty ophthalmology is not widely practiced, optical and low-vision services often do not cater to the needs of pseudo/aphakic children and children often do not return for follow-up. An additional challenge is that in many poorly developed countries many more boys present for cataract surgery than girls [9], despite there being no evidence that there are significant gender differences in the incidence. This almost certainly reflects the fact that poor parents are more willing to use their scarce resources for health care for their sons rather than for their daughters.

Reasons for late presentation include lack of awareness on the part of parents that their child has a treatable condition, and in some countries there is a belief that children who are born blind cannot have their sight restored (M. Muhit, unpublished data). There is also lack of awareness among general physicians, who are often the first point of contact, who tell parents that their child is too young for surgery, or that the cataract needs to mature. As late presentation adversely affects the visual outcome, it is important that providers of surgical services for cataract in children also provide low-vision services so that the children's residual vision can be maximized.

However, much has been achieved since the launch of VISION2020 in 1999. One of the VISION2020 targets is to establish one tertiary eye care facility for children for every 10 million population, with a well-trained, well-equipped clinical team. Training centres which offer high-volume, high-quality, hands-on clinical training have been established in India, Tanzania and Pakistan, and Child Eye Care centres are being set up, with support from the international non-governmental organizations. Resource centres which bulk purchase high-quality, low-cost equipment, consumables and low-vision devices have also been established in Hong Kong and Durban, South Africa. In Bangladesh a national program has been

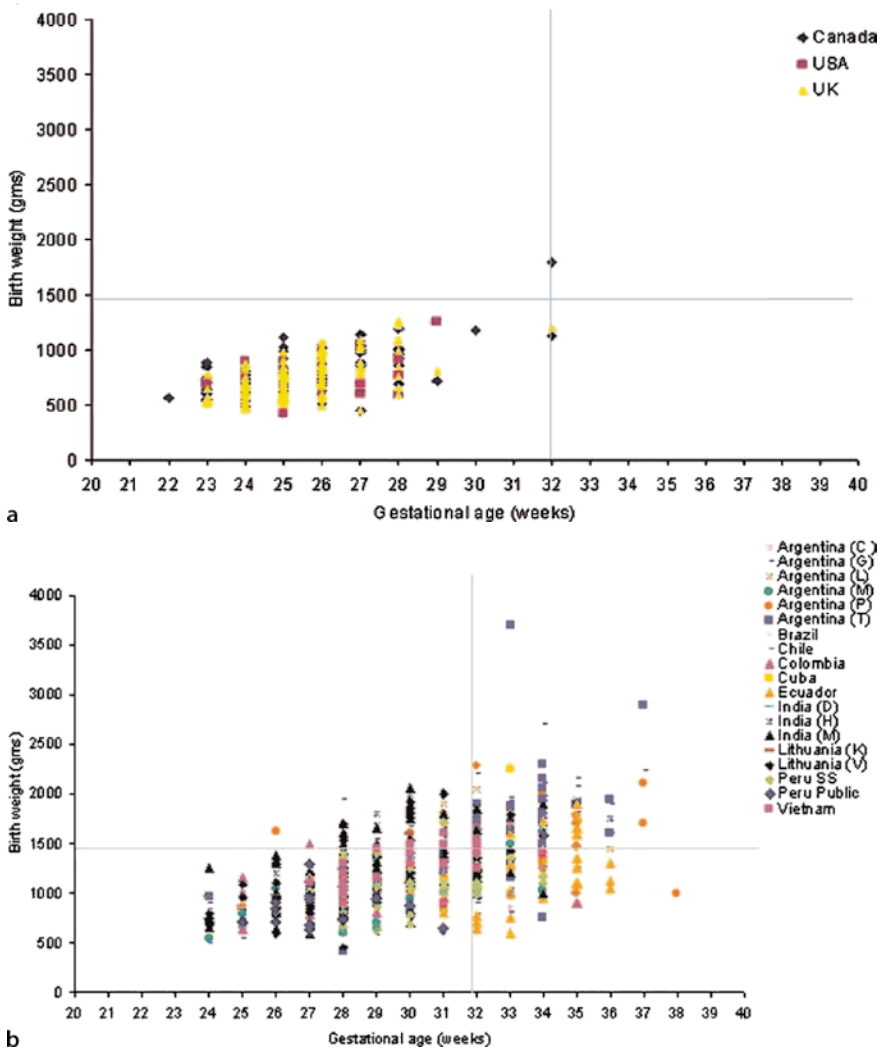

Fig. 5.4 **a** Birth weight and gestational age (GA) of infants reported with threshold disease from countries with high UNDP HDIs between 1996 and 2002. **b** Birth weight and GA of infants reported with severe retinopathy of prematurity from countries with low/middle HDIs between 1996 and 2002. The *horizontal* and *vertical lines* indicate the boundaries of the United Kingdom screening criteria. (From [16] reproduced with permission from Pediatrics (2005) 115:518–525 by the American Academy of Pediatrics)

Mean birth weights in industrialized countries	737−763 g
Mean gestational ages in industrialized countries	25.3−25.6 weeks
Mean birth weights in low- and middle-income countries	903–1.527 g
Mean gestational ages in low- and middle-income countries	26.3–33.5 weeks

(Reproduced with permission from Pediatrics 2005 115: 518–525 by the American Academy of Pediatrics.)

initiated with support from Sightsavers International in collaboration with ORBIS International. The impetus for the program came from studies using Key Informants which showed that an estimated 40,000 children were blind in the country, almost one third of whom were blind from unoperated cataract [25]. Since late 2004, six new Child Eye Care centres have been established, and active case finding of cataract-blind children is being undertaken using different approaches, including Key Informants. Between the start of the project in late 2004 and the end of 2006, 8,776 children have had cataract surgery, 3,154 of whom had bilateral cataracts.

5.9 Magnitude by Cause

Combining data on the prevalence and causes of blindness in children allows the likely magnitude of blindness by cause to be estimated (Table 5.3). There is likely to be a tenfold difference in the number of children who are blind in populations in the poorest countries of Africa compared with highly developed countries. The pattern of causes also differs. In the least-developed countries of Africa corneal scarring due to vitamin A deficiency, measles infection, use of traditional eye remedies and ophthalmic neonatorum is important, while in affluent societies the evidence suggests that the consequences of prematurity (cortical blindness as well as ROP) are the commonest potentially avoidable cause of blindness in children. Countries in Asia which are in transition can have a situation where corneal blindness is still a problem in underserved rural areas, whereas ROP is emerging as a cause in urban areas [11].

5.10 Changing Pattern of Causes

The available evidence suggests that the major avoidable causes of blindness in children are changing in response to changes in socio-economic development,

Table 5.3 Estimates of the number of blind children per 10 million population and major avoidable causes, by level of socio-economic development

	Per 10 million total population					
Level of development	Population aged 0–15 years (%)	No. of children (million)	Prevention of blindness	No. of blind	Major causes	No. affected
High income	20	2	0.3/1,000	600	Scar	0
					Cataract/glaucoma	60
					ROP	60
					Others (mainly CNS)[a]	480
Middle income	30	3	0.6/1,000	1,800	Scar	0
					Cataract/glaucoma	360
					ROP	450
					Others[a]	990
Low income	40	4	0.9/1,000	3,600	Scar	720
					Cataract/glaucoma	720
					ROP	0
					Others[a]	2,160
Very low income	50	5	1.2/1,000	6,000	Scar	3,000
					Cataract/glaucoma	900
					ROP	0
					Others[a]	2,100

Compiled from a database held by C. Gilbert at the International Centre for Eye Health, LSHTM
[a]Mostly unavoidable causes, such as congenital anomalies, optic atrophy, cortical visual impairment and retinal dystrophies

improvements in health care delivery and specific public health interventions. Over the past few decades there have been major initiatives, partnerships and programs to control vitamin A deficiency and measles. In many poorly developed countries these efforts are having a major impact not only on reducing child mortality, but they are also reducing corneal blindness in children [41]. In many countries in Africa and Asia cataract is now the leading cause of new cases of avoidable blindness in children. As already alluded to, ROP is already an important cause in Latin America and Eastern Europe, and it is likely to become a significant cause in India, China and other emerging economies of South East Asia as their provision for premature babies expand.

Take Home Pearls

- The sub-speciality of paediatric ophthalmology needs to be expanded. Well trained, well equipped teams need to be established at tertiary level for 10 million population, with provision of low vision and optical services.
- Awareness of the risk of retinopathy of prematurity needs to be increased among those caring for premature babies in neonatal intensive care in middle and low income settings. Screening programs need to use screening criteria that are based on local evidence of the population of babies at risk of type-1 retinopathy of prematurity.
- Health education and training at primary level are needed to improve early identification and referral of children with cataract for surgical management and follow up.
- Continued momentum and commitment are needed to ensure that the avoidable causes of corneal scarring are eliminated by 2020, even in the poorest countries of the world.

References

1. Aaby P, Coovadia H, Bukh J et al. (1985) Severe measles: a reappraisal of the role of nutrition, overcrowding and virus dose. Med Hypotheses 18:93–112
2. Amgad A, Kotb AA, Hammouda EF et al. (2006) Childhood blindness at a school for the blind in Saudi Arabia. Ophthal Epidemiol 13:1–5
3. Baiyeroju-Agbeja AM, Omokhodion SI (1998) Screening for retinopathy of prematurity in Idadan. Nigerian J Ophthalmol 6:23–25
4. Beaton GH, Martorell R, Aronson et al. (1993) Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in poorly developed countries. In: ACC/SCN State-of-the-art series, Nutrition Policy Discussion Paper No. 13 1993 ACC/SCN, Geneva
5. Bulgan T, Gilbert C (1992) Prevalence and causes of severe visual impairment and blindness in children in Mongolia. Ophthal Epidemiol 9:271–281
6. Chen Y, Xi L (2006) Characteristics of severe retinopathy of prematurity patients in China: A repeat of the first epidemic? Br J Ophthalmol 90:268–271
7. Courtright P, Lewallen S, Kanjaloti S et al. (1994) Traditional eye medicine use among patients with corneal disease in rural Malawi. Br J Ophthalmol 78:810–812
8. Dandona L, Gilbert CE, Rahi JS et al. (1998) Planning to reduce childhood blindness in India. Indian J Ophthalmol 46:117–122
9. Eriksen JR, Bronsard A, Mosha M et al. (2006) Predictors of poor follow-up in children that had cataract surgery. Ophthalmic Epidemiol 13:237–243
10. Gilbert C, Foster A, Negrel D et al. (1993a) Childhood blindness: a new form for recording causes of visual loss in children. Bull WHO 71:485–489
11. Gilbert C, Foster A (1993b) Causes of blindness in children attending four schools for the blind in Thailand and the Philippines: a comparison between urban and rural blind school populations. Int Ophthalmol 17:229–234
12. Gilbert C, Rahi J, Eckstein M et al. (1995) Hereditary disease as a cause of childhood blindness: regional variation. Ophthal Genetics 16:1–10
13. Gilbert C, Rahi J, Eckstein M et al. (1997) Retinopathy of prematurity in middle-income countries. Lancet 350:12–14
14. Gilbert CE, Anderton L, Dandona L et al. (1999) Prevalence of blindness and visual impairment in children: a review of available data. Ophthalmic Epidemiol 6:73–81
15. Gilbert CE, Foster A (2001) Childhood blindness in the context of VISION 2020 – the Right to Sight. Bull WHO 79:227–232
16. Gilbert C, Fielder A, Gordillo L et al., on behalf of the International NO-ROP Group (2005) Characteristics of babies with severe retinopathy of prematurity in countries with low, moderate and high levels of development: implications for screening programmes. Pediatr Electr Pages 115:518–525
17. Gilbert C (2008) Retinopathy of prematurity: a global perspective of the epidemics, population of babies at risk and implications for control. Early Hum Dev 84:77–82
18. Gilbert CE, Ellwein LB, on behalf of the Refractive Error Study in Children Study Group (in press) Prevalence and causes of functional low vision in school-age children: re-

sults from standardized population surveys in Asia, Africa and Latin America. Invest Ophthalmol Vis Sci
19. Hansen E, Flage T, Rosenberg T et al. (1992) Visual impairment in Nordic children. III. Diagnoses. Acta Ophthalmol (Copenh) 70:597–604
20. Hatton DD, Schwietz E, Boyer B et al. (2007) Babies count: the national registry for children with visual impairments, birth to 3 years. J AAPOS 11:351–355
21. Jones G, Steketee RW, Black RE et al. and the Bellagio Child Survival Study Group (2003) How many child deaths can we prevent this year? Lancet 362:65–71
22. Kello AB, Gilbert CE (2003) Causes of severe visual impairment and blindness in children in schools for the blind in Ethiopia. Br J Ophthalmol 87:526–530
23. Khan RI, O'Keefe M, Kenny D et al. (2007) Changing pattern of childhood blindness. Ir Med J 100:458–461
24. Muhit MA, Shah SP, Gilbert CE et al. (2007a). The key informant method – a novel means of ascertaining blind children in Bangladesh. Brit J Ophthalmol. 91 995–999
25. Muhit M, Shah S, Gilbert CE (2007b) Causes of severe visual impairment and blindness Bangladesh: a study of 1935 children. Br J Ophthalmol 91:1000–1004
26. Mwende J, Bronsard A, Mosha M et al. (2005) Delay in presentation to hospital for surgery for congenital and developmental cataract in Tanzania. Br J Ophthalmol 89:1478–1482
27. Negrel AD, Maul E, Pokharel GP et al. (2000) Refractive error study in children: sampling and measurement methods for a multi-country survey. Am J Ophthalmol 129:421–426
28. Nirmalan PK, Vijayalakshmi P, Sethu S et al. (2003) The Kariapatti Pediatric Eye Evaluation Project: baseline ophthalmic data of children aged 15 years or younger in southern India. Am J Ophthalmol 136:703–709
29. Phan MH, Nguyen PN, Reynolds JD (2003). Incidence and severity of retinopathy of prematurity in Vietnam, a developing middle income country. J Pediatr Ophthalmol Strab 40:193
30. Rahi J, Cable N, on behalf of the British Childhood Visual Impairment Study Group (BCVISG) (2003) Severe visual impairment and blindness in children in the UK. Lancet 362:1359–1365
31. Riise R, Flage T, Hansen E et al. (1992) Visual impairment in Nordic children. I. Nordic registers and prevalence data. Acta Ophthalmol (Copenh) 70:145–154
32. Seroczynska M, Prost ME, Medrun J et al. (2001) The causes of childhood blindness and visual impairment in Poland. Klin Oczna 1031:17–20
33. Shah PK, Navendran V, Saravanan VR et al. (2005). Fulminant retinopathy of prematurity – clinical characteristics and laser outcome. Ind J Ophthalmol 53:261–265
34. Sommer A, West K (eds) (1996) Vitamin A deficiency: health, survival and vision. Oxford University Press, Oxford
35. Sommer A, Davidson FR (2002) Assessment and control of vitamin A deficiency: the Annecy Accords. Proc XX International Vitamin A Consultative Group Meeting. Am Soc Nutr Sci (Suppl 2):845S–850S
36. Semba RD, Bloem MW (2004) Measles blindness. Surv Ophthalmol 49:243–255
37. Sil AK, Gilbert C (2001) Childhood blindness in India. J Indian Med Assoc 99:557–560
38. Steinkuller PG, Du L, Gilbert C et al. (1999) Childhood blindness. J AAPOS 3:26–32
39. Trinavarat A, Atchaneeyasakul LO, Udompunturak S (2004) Applicability of American and British criteria for screening for retinopathy of prematurity in Thailand. Jpn J Ophthalmol 48:50–53
40. Underwood B (2004) Vitamin A deficiency disorders. International efforts to control a preventable "Pox". Am Soc Nutr Sci J Nutr 134:231S–236S
41. Waddel KM (1998) Childhood blindness and low vision in Uganda. Eye 12:184–192
42. West KP (2002) Extent of vitamin A deficiency among preschool children and women of reproductive age. Am Soc Nutr Sci 132 (Suppl 9):2857S–2866S
43. World Health Organization, Geneva (1999). Preventing blindness in children. WHO/PBL/00.77
44. World Health Organization. www.who.int/.../diseases/measles/en/omdex.html
45. World Health Organization. Planning for cost-effective traditional medicines in the new century – a discussion paper. WHO Centre for Health Development. Access: http://www.who.org.jp/tm/research/bkg/3_definitions.html
46. World Health Organization (2003) Consultation on development of standards for characterization of vision loss and visual functioning. WHO/PBL/03. World Health Organization, Geneva
47. Zeidan Z, Hashim K, Muhit MA et al. (2007) Prevalence and causes of childhood blindness in camps for displaced persons in Khartoum: results of a household survey. East Mediterr Health J 13:580–585
48. Gilbert C (2007) The changing challenges of controlling blindness in children. Eye 21:1338–1343

Screening for Pediatric Ophthalmologic Disorders

6

Sean P. Donahue

Contents

Core Messages

- Screening of ocular structure and function is necessary to detect pediatric ocular disease. Screening examinations, repeated throughout childhood, detect disease when treatment is most effective.
- The sensitivity and specificity of a screening test or device may vary appropriately with respect to the severity and impact of the disease to be detected. The choice of test sensitivity should take into account the importance of timely detection, and the relative decrease in treatment effectiveness that would result from a delay in diagnosis if the pathology is missed.
- Since most pediatric eye screening is performed by the primary care physician, screening methodologies need to be coordinated between the primary care physician and a pediatric ophthalmologist.

6.1 Introduction

The pediatric population has unique ophthalmologic needs. Challenges that are intrinsic to the detection of eye disease in the pediatric population include the vast number of children (nearly 5 million children born in the United States per year), the relatively

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low number of specially trained doctors (fewer than 2000 active pediatric ophthalmologists in the United States), and the inability of children to describe symptoms that indicate pathology. These difficulties highlight the importance of vision screening in the pediatric population.

The ophthalmologic diseases that occur in the pediatric population change with the age of the child. Premature infants are at risk for retinopathy of prematurity (ROP). All neonates are at risk for congenital cataract, glaucoma, and retinoblastoma. The preschool-aged child is at risk for amblyopia, which is typically associated with anisometropia, high bilateral refractive error, or strabismus, whereas the child in elementary school may possess uncorrected bilateral refractive error that decreases acuity. The diversity of disorders in these age groups requires different techniques for screening (Table 6.1). The purpose of this chapter is to review the screening methodologies appropriate to each age group's condition, while highlighting the newer screening technologies.

6.2 Screening Guidelines

The development of screening methodologies to detect ocular pathology in children requires a consensus regarding the conditions to detect, and the best test methodologies to detect these conditions. Pathology detected using screening of the visual system should be considered to have similar guidelines as for all types of screening. The World Health Organization has mandated guidelines for a successful screening program as part of a Public Health Program (Table 6.2). Generally, the guidelines require that the condition being screened for is relatively common, a public health concern, and that successful detection

Table 6.1 Age-based disorders detectable with vision screening

Age group	Premature infant	Perinatal period	Preschool child	School-age child
Pathology	Retinopathy of prematurity	Congenital cataract, anterior segment pathology, glaucoma	Amblyopia, strabismus, anisometropia, high bilateral uncorrected refractive error	High uncorrected refractive error causing blurred vision
Location for screening detection	Neonatal intensive care unit, ophthalmology office	Newborn nursery, primary care physician office	Primary care physician office, preschool, daycare	Primary care physician office, school system
Detection methodology	Extended ophthalmoscopy using scleral depression and indirect ophthalmoscope through dilated pupil	Direct ophthalmoscopy or retinoscopy, pen light evaluation	Automated refraction, photoscreening, traditional vision screening using optotypes	Traditional optotype-based acuity

Table 6.2 World Health Organization guidelines for screening

The condition sought should be an important health problem
There should be an accepted treatment for patients with recognized disease
Facilities for diagnosis and treatment should be available
There should be a suitable latent or early symptomatic stage
There should be a suitable test or examination
The test should be acceptable to the population
The natural history of the condition, including development from latent to declared disease, should be adequately understood
There should be an agreed policy on whom to treat as patients
The cost of case finding, including diagnosis and treatment of patients diagnosed, should be economically balanced in relation to expenditures on medical care as a whole
Case finding should be a continuous process and not a "once-for-all" project

and treatment exist. These guidelines were designed to be applied to all types of screening, and most are also applicable for pediatric vision screening. Most pediatric eye diseases and test methods listed in Table 6.1 fit the WHO guidelines, although for some conditions (particularly amblyogenic factors), the natural history remains somewhat unknown, and the latent period is quite prolonged.

6.3 Retinopathy of Prematurity

A major cause of visual impairment in premature infants is ROP. In developing countries, ROP is the leading cause of visual impairment in children. While the development of cryotherapy substantially decreased the amount of ROP-related blindness in the United States and much of Europe [13], it remains the second most common cause of childhood blindness, following cortical visual impairment. Laser photocoagulation is now the primary treatment modality for severe, acute ROP (prior to retinal detachment) [29, 54]. The role of anti-VEGF medications being administered systemically or locally to aid in the treatment of advanced disease is evolving rapidly. The American Academy of Pediatrics recently revised its guidelines for screening premature infants at risk for ROP (Table 6.3) [48]. Screening for retinopathy of prematurity should be done by an experienced ophthalmologist, typically using scleral depression and indirect ophthalmoscopy, and should be performed through a dilated pupil. Children should be screened beginning at 31 weeks gestational age, but this varies depending upon the postnatal age. Screening is normally continued until there is complete maturity of the nasal retinal blood vessels (zone III) or the risk of serious disease has passed (45 weeks postconceptional age) [48]. Detailed discussion of diagnosis and treatment of ROP is given in Chap. 26.

Table 6.3 Revised screening guidelines for retinopathy of prematurity. (From [48])

All infants with birth weight < 1500 g
All infants with gestational age < 30 weeks
Selected infants with unstable clinical course
Initial screening at 31 weeks gestational age if at least 4 weeks postnatal[a]

[a] Details provided in reference

Screening for retinopathy of prematurity requires highly trained ophthalmologists and is typically done by pediatric or retinal sub-specialists. Decreasing availability of these specialists along with increasing numbers of patients meeting screening guidelines, and liability concerns by screening and treating physicians, has caused a near crisis in some geographic areas. New technologies, such as telemedicine, show promise in helping to alleviate this imbalance, however. The RetCam is a wide-angle camera that can be used in the neonatal intensive care unit, potentially by nurses or other hospital staff [19, 43, 56]. Because the new ET-ROP guidelines essentially allow the presence of "plus disease" (significant vascular dilation and tortuosity; see also Chap. 26) to guide treatment decisions [42], posterior pole retinal images obtained using the RetCam may be adequate for some screening purposes [45]; however, the lack of agreement among trained ophthalmologists about what constitutes "plus disease" [7], and the relative inability of the RetCam to view the peripheral retina (where the pathology exists) [49], are issues of significant concern. Finally, the extremely high sensitivity to detect treatable ROP that is demanded by the United States legal system (100%) currently limits the ability of telemedicine and wide-angle fundus photography to play any more than a minor role in current ROP screening.

6.4 Screening the Term Neonate

Screening of newborn infants is necessary to detect treatable anterior segment pathology, such as cataract, glaucoma, and other congenital structural abnormalities. Untreated total bilateral congenital cataracts typically cause the development of nystagmus within the first 8−10 weeks of postnatal life. The development of nystagmus is typically a poor prognostic sign, despite clearing the visual axis and correcting the aphakia. For unilateral congenital cataract, approximately age 17 weeks is the latest time a cataract can be removed and 20/20 visual acuity still regained despite adequate optical correction and institution of amblyopia therapy [6]; thus, detection of anterior segment pathology at either the nursery examination or at the 2- or 6-week well-child examination is vital.

This requires that these examinations be performed in the neonatal nursery by the admitting physician and by the primary care physician in the office setting.

Detection of congenital cataract is typically performed by red reflex testing. The current recommendation from the American Academy of Pediatrics [47] is that red reflex screening by primary care doctors occur within the first 2 months of postnatal life. In addition to the neonatal visit, the 2- and 6-week outpatient examinations are appropriate times for screening. The presence of glaucoma in the neonatal period is unusual, but observation of the anterior segment for buphthalmos, enlarged, or hazy corneas is necessary. Epiphora is a relatively late sign of congenital or acquired glaucoma.

Some pediatric ophthalmologists recommend that primary care doctors screen children for retinoblastoma using red reflex testing with pupillary dilation. This trend likely is due to the poor visual outcome expected for children who present in the classic manner (leukocoria or strabismus) with sporadic retinoblastoma [26]. Invariably, even though the affected eye with monocular retinoblastoma is retained, functional vision is almost always lost. Implementing such a screening process in the primary care office is challenging for several reasons. Firstly, the sensitivity of primary-care-physician red-reflex testing at any age to detect a small retinoblastoma before it enters the macula is unknown. The age at which the screening should optimally be performed is also unknown; although most children with sporadic retinoblastoma present before age 18 months, it is unclear when the best time for such screening should occur, and it is likely different in different individuals. Earlier screening would likely detect more patients without macular involvement, but the smaller tumor size would decrease sensitivity. Finally, the extreme rarity of sporadic retinoblastoma (in the absence of family history) makes the likelihood of detecting most children with disease, while not producing massive numbers of false-positive referrals and overwhelming the primary care eye care system, unlikely.

6.5 Preschool Vision Screening

During the preschool age period (up to 6 years), the most common ocular conditions are strabismus, anisometropia, and high bilateral uncorrected refractive error such as hypermetropia or astigmatism. All of these, if untreated, can produce amblyopia. Classic testing has involved optotype-based screening of visual acuity for these children; however, such screening is difficult in the pediatrician's office and is therefore often not performed until at least 3.5 years, if at all [53]. Thus, prior to this age a child is at risk for the development of amblyopia but it cannot be detected by traditional means. While some studies have demonstrated the ability of traditional acuity screening to detect amblyopia in 3-year-old children, most do not show good success rates until at least age 4 years.

The issue of what levels of refractive pathology should be detected with preschool vision screening is becoming clearer. The prevalence of high myopia in this population is low. Since most preschool children have a working distance of <1 m, myopic refractive errors in the range of –1.50 diopters or less are functionally irrelevant. Symmetric, low-magnitude, regular, meridional astigmatism likewise produces minimal visual blur, does not usually cause amblyopia, and also probably does not need to be detected. High-hypermetropic refractive error, high-magnitude bilateral astigmatism, as well as anisometropia represent pathology that should be detected. Studies by Atkinson and others have suggested that the risk of strabismus and amblyopia in children whose refractive error exceeds +3.5 diopters is 13 times the risk of the general population, and that spectacle correction reduces substantially the risk of strabismus and amblyopia in this population [4]; however, techniques for detecting uncorrected hypermetropia have not been perfected. In addition, the relationship between high hyperopia, accommodation, and the development of accommodative strabismus is not well understood, as some children with moderate hypermetropia do extremely well, while others with only normal or moderate magnitude hypermetropia develop strabismus and amblyopia.

Traditional optotype-based vision screening is the standard method for detecting amblyopia [9, 21]. Traditional screening programs use LEA symbols, Allen cards, Sheriden-Gardiner cards, HOTV letters, and Teller acuity cards for children who are too young to read Snellen letters. Testing personnel include trained lay volunteers, pediatricians, pediatric nurses, school nurses, and sometimes orthoptists. In addition to optotype-based acuities, tests for ocular alignment, such as a cover test or a light reflex test, and tests of stereopsis, are occasionally added to many testing

protocols. As a result, there is no standard guideline or mandate for preschool vision testing methodology. This has resulted in a relatively low compliance with published screening guidelines [21].

A significant limitation of picture-based acuity tests is that they often overestimate acuity compared with standard Snellen letters. This is important because mild and even moderate amblyopia may not be detected.

An additional limitation of all optotype-based tests used for the detection of amblyopia is the crowding phenomenon seen in amblyopic eyes; acuity is observed to be much better when isolated optotypes are shown to the child than when an entire line of optotypes is presented. The crowding phenomenon is observed with all methods of optotype-based screening; however, it is more commonly a problem when screening personnel "help" the younger child read the eye chart by isolating a single optotype in a line with hands, papers, or other objects. This well-intentioned "assistance" causes amblyopia to be missed. Therefore, acuity testing should be performed with the fellow eye occluded by a stick-on patch or adhesive paper tape to prevent peeking.

In 1998 an extensive retrospective review of preschool vision screening literature was performed by Stewart-Brown and Snowdon [5]. Their review revealed deficits in our knowledge of how amblyopic patients report their specific visual disabilities, a lack of prospective data evaluations of treatments, and the lack of natural history data. Thus, despite the multitude of retrospective studies demonstrating that vision screening could efficiently identify amblyopic children, and that amblyopia treatment could improve visual acuity, their report concluded that "screening is not effective… because there is no evidence that treatment is either effective or necessary." This report understandably created a firestorm of controversy across Europe and the United States, but served as the impetus for many studies that have since demonstrated conclusively the success of screening for and treating of amblyopia. Several of these studies are summarized below.

Kvarnstrom et al. demonstrated that a Swedish vision screening program reduced the prevalence of significant amblyopia (visual acuity less that 20/60) from 2 to 0.2%, and that 47% of amblyopic children could achieve visual acuity better than 20/30 with treatment [24]. A similar screening program using orthoptists in Haifa, Israel, compared a population screened at infancy with a population having no screening [18]. Amblyopia prevalence in the screened group was 1.0% compared with 2.6% in the unscreened group; moreover, the prevalence of 20/60 or worse amblyopia was less than 0.1% in the screened population compared with 1.7% in the non-screened population. An additional study of intensive screening using orthoptists (the ALSPAC study team) demonstrated that intensive vision screening reduced the prevalence of amblyopia at age 7.5 years to 0.6% compared with 1.8% prevalence following a single orthoptic screening at age 37 years [55].

The original report by Snowdon and Stewart-Brown also suggested that there were no data studying either the natural history of amblyopia or the effectiveness of treatment. These notions have also been debunked by multiple studies. Simons and Preslan evaluated 18 children aged 4–6 years who had been screened for amblyopia and had not complied with their prescribed treatment [51]. When re-evaluated at a repeat screening 1 year later, only one child of the 18 (who wore glasses sporadically) showed any improvement in the amblyopic eye. No other children showed any improvement; 7 of the 17 showed deterioration in acuity, and three who had no amblyopia developed it during their non-compliance.

The Pediatric Eye Disease Investigator Group (PEDIG) has performed several randomized controlled prospective masked evaluations of amblyopia treatment. Results from studies performed by this multicenter group showed that atropine and occlusion produce significant improvement in visual function of amblyopic eyes [30, 31, 32, 37]; even with limited treatment [33, 34]; that this visual improvement remains relatively stable over time [35, 37, 40]; that amblyopia can be treated, although to a lesser extent, in children older than age 7 years [36, 38]; and that amblyopia does not resolve without treatment [39].

The cost-effectiveness of amblyopia screening and treatment has also been clearly demonstrated. Konig and Berry performed an economic evaluation of several methodologies of screening and found binocular visual acuity screening to have favorable cost-effectiveness compared with other types of vision screening [23]. Membreno et al. showed that amblyopia treatment when measured by cost per quality adjusted life year gained was approximately US$2281. This compares favorably with nearly all ophthalmic interventions for all conditions, with the exception of screening and treatment of retinopathy

of prematurity [14, 27]. Membreno et al. also demonstrated that amblyopia screening and treatment would return US$22 to the economy for every US$1 spent, and that loss of vision in the fellow eye of amblyopic individuals leads to a decrease in yearly U.S. Gross Domestic Product (GDP) of US$7.4 billion. Perhaps the greatest risk of not treating amblyopia lies in the potential for loss of vision in the healthy eye at a later stage in life. A United Kingdom surveillance study of individuals with unilateral amblyopia who had acquired vision loss in their healthy eye found that the projected lifetime risk of vision loss (to 20/40 or less that precludes driving) was at least 1.2%, and that 65% of the people who lost vision in their healthy eye were unable to continue paid employment [41, 52].

It is now clear from a multitude of studies that amblyopia is a significant visual disability, that it can be detected by screening, and that treatment is both successful and cost-effective.

6.5.1 Techniques of Vision Screening

Traditional vision screening using optotypes is the time-honored technique to detect decreased acuity and amblyopia in young children. The lack of widespread acceptance of traditional screening in the primary care pediatrician's office however, implies that there are limitations to these methodologies. These limitations include the relative maturity of the child needed to perform the screening, the relatively large amount of time needed to perform it, the requirement for extensive cooperation by the child, and the lack of insurance reimbursement for most traditional screening. It should be noted that a new CPT code, 99173, for objective screening of visual acuity, has been available in the United States for approximately 3 years; but it has not yet been linked with a formal RVU value or reimbursement.

As a result of the limitations of traditional acuity screening, recent developments in technology and the desire to detect abnormalities before they cause amblyopia have led to the development of new instruments for preschool vision screening. Primarily, these instruments involve either automated retinoscopy, or photoscreening. There are several instruments which are commercially available and which have various levels of validation. The remainder of this section reviews the data regarding these instruments, recognizing that this is a rapidly evolving field.

6.5.2 The Vision In Preschoolers (VIP) Study

The Vision In Preschoolers (VIP) study was an evaluation of several, different types of traditional screening and new screening methodologies [46, 57]. The first phase of this multicenter prospective evaluation of over 1000 preschool children demonstrated four methodologies to have the best sensitivity to detect decreased visual acuity and high refractive error: non-cycloplegic retinoscopy; the Welch Allyn SureSight (Welch Allyn, Skaneatelas, N.Y.); the Nikon Retinomax (Nikon, Melville, N.Y.); and LEA symbols [46]. Non-cycloplegic retinoscopy requires the skill of a trained professional, and therefore is not an adequate technique for wide-scale screening of preschool children. The SureSight and Retinomax are examples of auto retractors, and are discussed below. The LEA symbols represent a commercially available type of optotype-based traditional acuity screening. A major difference between traditional acuity screening methodologies for vision screening is that the former detects decreases in acuity directly, whereas the latter detects problems that may lead to decreased visual acuity. These problems have been termed "amblyogenic factors" (Table 6.4). The detection of amblyogenic factors, rather than direct

Table 6.4 Amblyogenic factors to be detected by screening

Anisometropia (spherical or cylindrical) > 1.5 D
Any manifest strabismus
Hyperopia > 3.50 D in any meridian
Myopia magnitude > 3.00 D in any meridian
Any media opacity > 1 mm in size
Astigmatism > 1.5 D at 90 or 180° > 1.0 in oblique axis (more than 10°eccentric to 90 or 180°)
Ptosis ≤ 1 mm margin-reflex distance[a]
Visual acuity: per AAP (age-appropriate standards)

[a] Margin-reflex distance is the distance from the corneal light to the upper lid margin, and is the standard objective measurement of ptosis

detection of decreased acuity, points out a major limitation of these newer technologies. The natural history of amblyopia development in children with amblyogenic factors is unknown, and as a result, since some children who are at risk for amblyopia never develop it, these technologies inherently over-refer children. Factors that are recognized to contribute to the development of amblyopia include high, uncorrected refractive error (hypermetropia and astigmatism), high myopia, and anisometropia. Recently, a consensus has evolved with respect to the magnitude of such factors that should be identified using new technologies for preschool vision screening, and the Vision Screening Committee of the American Association of Pediatric Ophthalmology and Strabismus (AAPOS) has published a policy statement that mandates those refractive errors that should be detected with preschool vision screening [16]. This policy statement also allows studies of these instruments to report results uniformly, allowing for direct comparison of sensitivity and specificity data for these new techniques.

6.5.3 Photoscreening

Photorefractive screening utilizes a flash of light and the observation of the reflection of that light from the blur circle of the fundus to detect ocular misalignment and refractive blur. Several types of photoscreening instruments are available commercially. Most instruments make use of an off-axis flash, which produces an abnormality in the red reflex when the eye is not aligned, or not properly focused. The abnormality in the red reflex can be interpreted to determine if referral is appropriate. Initial techniques captured the image on color film, and evolved to utilize Polaroid film, and now digital-image capture. All systems require interpretation of the flash image, however, and concerns about interpretation limit acceptance of photoscreening. Most commercially available systems require trained personnel for interpretation, although new software is developing that automates some of the interpretation. Each of the commercially available photoscreening systems has some degree of validation (Table 6.5).

The MTI Photoscreener (MTI, Cedar Falls, Iowa) is perhaps the most well-evaluated automated visual screening instrument. There have been several large studies that have evaluated this instrument. The field studies generally report positive predictive value (since normal children are not referred) while the clinic-based studies report sensitivity and specificity (since predictive value depends upon disease prevalence). The Alaska Blind Child Discovery project utilizes the MTI photoscreener in urban and rural communities in Alaska [2, 3]. Screenings are performed by lay personnel and interpreted by a pediatric ophthalmologist, based upon the size of the flash crescent in each eye. Over 10,000 screenings have been performed thus far in Alaska, and the positive predictive value has approached 90%. Recently, the ABCD project has begun using commercially available digital cameras with standard off-axis flash photography [25]. Widespread use of such handheld digital cam-

Table 6.5 New technologies for preschool vision screening

Manufacturer/instrument	Method	Interpretation	Referral criteria	References
Photoscreener (MTI, Cedar Falls, Iowa)	Polaroid off-axis photoscreener	Centralized, manual	Various	[2, 3, 15, 17, 20, 46, 57]
Vision Research Corp. (Huntsville, Ala.)	Analog off-axis photoscreening	Centralized, manual	Proprietary	[28]
iScreen (Memphis, Tenn.)	Digital off-axis photoscreening	Centralized, manual	Proprietary	[22, 46]
Plus Optix (Munich, Germany)	Autorefractor	Automated	Can be altered	[8, 46]
Retinomax (Nikon, Melville, N.Y.)	Autorefractor	Automated	Proprietary	[12, 46, 47]
SureSight (Welch Allyn, Skaneatelas, N.Y.)	Autorefractor	Automated	Various (see text)	[44, 46, 57]

eras for photoscreening, however, is limited due to lack of uniformity in flash design.

A larger field-based vision screening program using the MTI Photoscreener™ began in Tennessee [3, 15]. This program also uses volunteer screeners and a central reading center. Referred children are evaluated by local optometrists and ophthalmologists. This program has been expanded by the Lions' Club International Foundation to include other states, and several foreign countries, and to screen over 500,000 preschool children with excellent results [17]. Nevertheless, the widespread acceptance of photoscreening with this model remains hindered by the lack of a centralized reading center, and universal agreement of criteria for referral and interpretation.

The VIP studies evaluated photoscreening with the MTI Photoscreener as one methodology in a prospective trial of over 1000 children with an enriched proportion of ocular pathology [46, 57]. In that study, photoscreening had a lower sensitivity than the Welsh Allyn SureSight and the Nikon Retinomax when specificity was fixed retrospectively at 90 or 94%; however, the relatively high sensitivity for these other instruments was likely a result of a retrospective reanalysis of the data using a set of referral criteria for the autorefractors (but not the photoscreeners) that was determined by re-evaluating the study results. Other issues with respect to the methodology of the VIP study which biased against photoscreening technology have been discussed extensively in the literature [1, 17, 20].

Vision Research Company (Huntsville, Ala.) has made photoscreening of elementary school children a commercial entity. Their company uses a 35-mm off-axis photograph to screen children for factors that can be associated with decreased visual acuity. Vision Research typically tests children enrolled in elementary school who are typically past the traditional age for amblyopia development. An anecdotal report of poorly validated results from referred children was published based upon early screening data [28]. This company remains the most commonly used photoscreening instrument. iScreen (Memphis, Tenn.) is a company which uses digital photography and a high-quality photograph with off-axis photoscreening to detect amblyogenic factors. Their marketing plan places the screening device in the primary care doctor's office, with remote image transfer to a centralized location for interpretation. The VIP study found the iScreen device to have nearly identical sensitivity as MTI photoscreening [46].

Plus Optix (Munich, Germany) has recently introduced a photoscreening instrument (the Power Refractor) which also allows detection of ocular misalignment. An earlier version of this instrument was tested in the VIP study and found to have sensitivities that exceeded the other photoscreening devices but fell short of autorefraction [46], likely due to the lack of retrospective alteration of the referral criteria for the Plus Optix (as was done with autorefraction). Field validation of this instrument is underway [8].

Several other photoscreening devices are in various levels of development and validation. These new systems will combine digital cameras with image capture and automated analysis systems that produce instant interpretation. An important step in this advance is a new CPT code for vision screening, 99174, which became effective 1 January 2008. While this code does not yet have an assigned RVU value (and therefore does not have universal reimbursement) the recognition of photoscreening as a useful adjunct in the primary care office will drive further capital investment, leading to increased research and development. A statement encouraging the use of photoscreening for preschool vision screening has also been published by the American Academy of Pediatrics [11], and is currently being updated.

Automated refraction is another method of preschool vision screening. Two autorefractors were formally validated by the VIP study [46, 57]: the Nikon Retinomax, and the Welch Allyn SureSight. Both instruments utilize ultrasonic measurements of the wavefront to estimate refractive error. These estimates can be used to predict the actual refractive error in the screened children. The biggest current limitation with the commercially available autorefractors is that the estimates of refractive error have only a good correlation (i.e., not perfect) with the measured refractive error; thus, there is an inherent over- and under-referral with these devices. Since the referral rate and predictive value as well as the sensitivity and specificity depend upon the actual criteria that have been proposed, multiple referral criteria have been proposed for each instrument. Some of the validation studies are summarized below and in Table 6.5.

The SureSight has been much more extensively studied than the Retinomax. Multiple referral criteria have been proposed for the SureSight device [44,

46, 57]. The VIP study demonstrated that the manufacturer's referral criteria have a sensitivity of over 90% [46], but the low specificity produces substantial over-referrals and a positive predictive value under 10% [44]. The VIP study proposed a second set of referral criteria for the SureSight that are commercially available as a software upgrade for the device and are called the 94% specificity VIP criteria [57]. Their implementation is associated with a higher specificity, a lower sensitivity, a much lower referral rate, and a higher predictive value than the manufacturer's criteria [44]. Raising the referral criteria for suspected astigmatism from 1.7 diopters (the 94% VIP criteria) to 2.2 diopters decreases the referral rate substantially and increases the predictive value to over 50%. This modification reduces the referral rate to under 8% and improves predictive value to over 50% [44]; however, these criteria are not currently commercially available.

It is incumbent on any purchaser of the SureSight instrument to specify the desired referral criteria software at the time of purchase. Various referral criteria may be appropriate, depending on the screening situation; specifically the suspected prevalence of the disease of the population, the availability and cost of subspecialty providers for referred patients, and the net direct and indirect cost of over referrals. Areas of the country that have low access to providers and referral subspecialists, and high direct and indirect costs of obtaining care (such as rural Alaska) need to balance a low sensitivity with extremely high specificity and low referral rates, while areas with high population density and adequate primary pediatric eye care capacity may seek a high specificity with less regard for over-referrals (false positives). Further evaluation of autorefraction and adjustment of referral criteria in the future to maximize both sensitivity and specificity will likely continue to increase acceptance of this technology.

6.5.4 *Required Eye Examinations for Preschool Children*

Comprehensive eye examinations have been mandated by state legislatures for at least three individual states in the U.S. Such legislation is usually proposed as a method for visual evaluation with extensive support from the optometry and optical manufacturing lobby. While in theory such legislation may appear appropriate, there is a lack of legislative mandate for what conditions should be detected, how they should be detected during an examination (i.e., cycloplegia or not) and how identified conditions should be treated. Finally, there is a significant issue with manpower with respect to the vast number of children needing to be evaluated. Recent data regarding the results of this vision screening law in the state of Kentucky have been published [58]. These results demonstrate that spectacles were prescribed for 14% of all children, including 11% of 3-year-olds. This is bothersome because no data demonstrate that 11% of otherwise healthy 3-year-old children require spectacles, and our anecdotal experience from seeing many of these children for second opinions is that cycloplegic refraction is only rarely performed on such children and many spectacle prescriptions are incorrect. The expense of unnecessary spectacle prescribing for such children has not been fully determined but is substantial [14].

6.6 Electrophysiologic Testing

Electrophysiologic detection of decreased acuity has been performed in laboratories for many years using visually evoked response recording. Only recently has this technique been suggested for primary vision screening. The Diopsys device is a portable screening instrument that can be placed in pediatrician offices to screen for amblyopia and other causes of decreased unilateral or bilateral visual acuity. The testing is performed by the clinic staff, and interpreted in real time by integrated software using a proprietary set of referral criteria to determine if a child should be referred. An advantage of this screening instrument to the pediatrician is that the visual evoked response testing is reimbursed by many payers. Disadvantages of this device are a relatively prolonged test time, the need to place scalp electrodes on the child's head, and the requirement for an attentive and cooperative child. Only one validation study has been published: Simon et al. found that 94% of 122 children aged 6 months to 5 years could be tested, with a sensitivity of 97% and specificity of 81% when this device was evalu-

Take Home Pearls

- Reliable processes must be in place for screening at-risk individuals for retinopathy of prematurity in the neonatal intensive care unit, and in the pediatrician's office after discharge.
- Red-reflex testing can be a valuable technique to detect congenital cataract, retinoblastoma, and other anterior segment pathology.
- New technologies for screening the preschool child are rapidly evolving and require knowledge of the referral criteria for the device, and an understanding of the relationship between the need to detect pathology (i.e., sensitivity) and the desire to avoid over referral (i.e., specificity).

ated in a pediatric ophthalmology clinic [50]. This low specificity means that most children referred with the current software will have no pathology.

6.7 Screening School-aged Children

As children reach elementary school, their visual systems are relatively well developed. Screening in this population presumes that amblyopia has been detected and treated prior to this time and, therefore, the pathology that should be detected in this age group typically is refractive error. Most myopia tends to appear and progress during elementary school. Screening for refractive error in school-age children is typically done both within the school system and the pediatrician offices. The typical test is Snellen visual acuity charts. These charts are time honored, despite the lack of formal field validation. Current standards for elementary school screening suggest referral for acuity worse than 20/30 in either eye [10]. At later ages, and in the known myopic child, relying upon subjective symptoms of blurred distance acuity, and traditional acuity screening either in the pediatrician's office, or by the optometrist or ophthalmologist, is sufficient. It is noteworthy that, in contrast to preschool children, lack of treatment of refractive error, either unilateral or bilateral, will not lead to permanent afferent visual system dysfunction such as amblyopia.

References

1. Arnold RW (2004) Vision in Preschoolers Study. Ophthalmology 111(12):2313
2. Arnold RW, Gionet EG, Jastraebski AI, et al. (2000) The Alaska Blind Child Discovery project; rationale, methods and results of 4000 screening. Alaska Med 2(3):58−72
3. Arnold RW, Donahue SP (2006) The yield and challenges of charitable state-wide photoscreening. Binocul VIS Strabismus Q 21(2):93−100
4. Atkinson J, Braddick O, Robier B, et al. (1996) Two infant vision screening programmes: prediction and prevention of strabismus and amblyopia from photo- and videorefractive screening. Eye 10:189−98
5. Stewart-Brown SL, Snowdon SK (1998) Evidence-based dilemmas in pre-school vision screening. Arch Dis Child 78:406−7
6. Cheng KP, Hiles DA, Biglan AW, et al. (1991) Visual results after early surgical treatment of unilateral congenital cataracts. Ophthalmology 98:903−1010
7. Chiang MD, Jiang L, Gelman R, Du YE, Flynn JT (2007) Interexpert agreement of plus disease diagnosis in retinopathy of prematurity. Arch Ophthalmol 125(7):963−4
8. Clausen MM, Arnold RW (2007) Pediatric eye/vision screening. Referral criteria for the pedia vision plus optix s 04 photoscreener compared to visual acuity and digital photoscreening. Kindergarten computer photoscreening. Binocul Vis Strtabismus Q 22(2):83−9
9. Cliner EB, Dobson V, Schmidt PP, et al. (1999) A survey of vision screening policy of preschool children in the United States. Surv Ophthalmol 43:445−57
10. Committee on Practice and Ambulatory Medicine of American Academy of Pediatrics Section on Ophthalmology of American Academy of Pediatrics, American Association of Certified Orthoptists, American Association for Pediatric Ophthalmology and Strabismus and American Academy of Ophthalmology (2003) Policy Statement: Eye examination in infants, children and young adults by pediatricians. Pediatrics 111(4):902−7

11. Committee on Practice and Ambulatory Medicine and Section on Ophthalmology; American Academy of Pediatrics (2002) Use of photoscreening for children's vision screening. Pediatrics 109(3):524–5
12. Cordonnier M, Kallay O (2001) Non-cycloplegic screening for refractive errors in children with the hand-held autorefractor Retinomax: final results and comparison with non-cycloplegic photoscreening. Strabismus 9:59–70
13. Cryotherapy for Retinopathy of Prematurity Cooperative Group (1988) Multicenter trial of cryotherapy for retinopathy of prematurity. Preliminary results. Arch Ophthalmol 106:471–9
14. Donahue SP (2004) How often are spectacles prescribed to "normal" preschool children? J AAPOS. 2004 8(3):224–9. Comment in: J AAPOS 8(3):222–3, author reply: J AAPOS 9(3):299–302
15. Donahue SP, Johnson TM, Leonard-Martin TC (2000) Screening for amblyogenic factors using a volunteer lay network and the MTI photoscreener. Initial results from 15,000 preschool children in a state-wide effort. Ophthalmology 107:1637–44
16. Donahue SP, Arnold RW, Ruben JB (2003) Preschool Vision Screening: What should we be detecting and how should we report it? Uniform guidelines for reporting results of preschool vision screening studies. J AAPOS 7:314–6
17. Donahue SP, Baker JD, Scott WE, et al. (2006) Lions Club International Foundation Core Four Photoscreening: results from 17 programs and 400,000 preschool children. J AAPOS 10(1):44–8
18. Eibschitz-Tsimhoni M, Friedman T, Naor J, et al. (2000) Early screening for amblyogenic risk factors lowers the prevalence and severity of amblyopia. J AAPOS 4:194–9
19. Ells AL, Holmes JM, Astle WF Williams G, et al. (2003) Telemedicine approach to screening for severe retinopathy of prematurity: a pilot study. Ophthalmology 110(11):2113–7
20. Freedman H (2004) Vision screening. Ophthalmology 111(4):1249
21. Hartmann EB, Dobson V, Hainline L, et al. (2001) Preschool vision screening: summary of a task force report. Ophthalmology 108:479–86
22. Kennedy RA, Thomas DE (2000) Evaluation of the iScreen digital screening system for amblyogenic factors. Can J Ophthalmol 35(5):258–62
23. Konig HH, Barry JC (2002) Economic evaluation of different methods of screening for amblyopia in kindergarten. Pediatrics 109:e59
24. Kvarnstrom G, Jakobsson P, Lennerstand G (2001) Visual screening of Swedish children: an ophthalmological evaluation. Acta Ophthalmol 79:240–4
25. Lang D, Leman R, Arnold AW, et al. (2007) Validated portable pediatric vision screening in the Alaska Bush. A VIPS-like study in the Koyukon. Alaska Med 49(1):2–15
26. Lueder GT (2005) The effect of initial recognition of abnormalities by physicians on outcome of retinoblastoma. J AAPOS 9(4):383–5
27. Membreno JH, Brown MM, Brown GC, et al. (2002) A cost-utility analysis of therapy for amblyopia. Ophthalmology 109:2265–71
28. Morgan KS, Kennemer JC (1997) Off-axis photorefractive eye screening in children. J Cataract Refract Surg 23(3):423–8
29. Paysse LA, Lindsey JL, Coats DK, et al. (1999) Therapeutic outcomes of cryotherapy versus transpupillary diode laser photocoagulation for threshold retinopathy of prematurity. J AAPOS 3:234–40
30. Pediatric Eye Disease Investigator Group (2002) A randomized trial of atropine vs patching for treatment of moderate amblyopia in children. Arch Ophthalmol 120(3):268–78
31. Pediatric Eye Disease Investigator Group (2003) A comparison of atropine and patching treatments for moderate amblyopia by patient age, cause of amblyopia, depth of amblyopia, and other factors. Ophthalmology 110(8):1623–8
32. Pediatric Eye Disease Investigator Group (2003) A randomized trial of prescribed patching regimens for treatment of severe amblyopia in children. Ophthalmology 110(11):2075–87
33. Pediatric Eye Disease Investigator Group (2003) A randomized trial of patching regimens for treatment of moderate amblyopia in children. Arch Ophthalmol 121(5):603–11
34. Pediatric Eye Disease Investigator Group (2004) A randomized trial of atropine regimens for treatment of moderate amblyopia in children. Ophthalmology 111(11):2076–85
35. Pediatric Eye Disease Investigator Group (2004) Risk of amblyopia recurrence after cessation of treatment. J AAPOS 8(5):420–8
36. Pediatric Eye Disease Investigator Group (2004) A prospective, pilot study of treatment of amblyopia in children 10 to <18 years old. Am J Ophthalmol 137(3):581–3
37. Pediatric Eye Disease Investigator Group (2005) Two-year follow-up of a 6-month randomized trial of atropine vs patching for treatment of moderate amblyopia in children. Arch Ophthalmol 123(2):149–57
38. Pediatric Eye Disease Investigator Group (2005) Randomized trial of treatment of amblyopia in children aged 7 to 17 years. Arch Ophthalmol 123(4):437–47
39. Pediatric Eye Disease Investigator Group (2006) A randomized trial to evaluate 2 hours of daily patching for strabismic and anisometropic amblyopia in children. Ophthalmology 113(6):904–12
40. Pediatric Eye Disease Investigator Group (2007) Stability of visual acuity improvement following discontinuation of amblyopia treatment in children aged 7 to 12 years. Arch Ophthalmol 125(5):655–9
41. Rahi JS, Logan S, Timms C, et al. (2002) Risk, causes, and outcomes of visual impairment after loss of vision in the non-amblyopic eye: a population-based study. Lancet 360:597–602
42. Reynolds JD, Dobson V, Quinn GE, et al. (2002) Evidence-based screening criteria for retinopathy of prematurity: natural history data from the CRYO-ROP and LIGHT-ROP studies. Arch Ophthalmol 120:1470–6
43. Roth DB, Morales D, Feuer WJ, et al. (2001) Screening for retinopathy of prematurity employing the RetCam 120; sensitivity and specificity. Arch Ophthalmol 119:268–72

44. Rowatt AJ, Donahue SP, Crosby C, et al. (2007) Field evaluation of the Welch Allyn SureSight vision screener: incorporating the vision in preschoolers study recommendations. J AAPOS 11(3):213−4
45. Saunders RA, Bluestein EC, Sinatra RB, et al. (1995) The predictive value of posterior pole vessels in retinopathy of prematurity. J Pediatr Ophthal Strabismus 32:82−5
46. Schmidt P, Maguire M, Dobson V, et al. (2004) Vision in Preschoolers Study Group. Ophthalmology 111:637−50
47. Section on Ophthalmology, American Academy of Pediatrics (2002) Red reflex examination in infants. Pediatrics 109(5):980−1
48. Section on Ophthalmology, American Academy of Pediatrics, American Academy of Ophthalmology and American Association for Pediatric Ophthalmology and Strabismus (2006) Screening examination of premature infants for retinopathy of prematurity. Pediatrics 117(2):572−6
49. Shah PK, Narendran V, Saravan VR Raghuram A, Chattopadhyay A, Kashyap M (2006) Screening of retinopathy of prematurity: a comparison between binocular indirect ophthalmoscopy and RetCam 120. Indian J Ophthalmol 54(1):35−8
50. Simon JW, Siegfried JB, Mills MD, et al. (2004) A new visual evoked potential system for vision screening in infants and young children. J AAPOS 8(6):549−4
51. Simons K, Preslan M (1999) Natural history of amblyopia untreated owing to lack of compliance. Br J Ophthalmol 83:582−7
52. Tommila V, Tarkkanen A (1981) Incidence of loss of vision in the healthy eye in amblyopia. Br J Ophthalmol 65:575−7
53. Wall TC, Marsh-Tootle W, Evans HH, et al. (2002) Compliance with vision-screening guidelines among a national sample of pediatricians. Ambul Pediatr 2:449−55
54. White JE, Repka MX (1997) Randomized comparison of diode laser photocoagulation versus cryotherapy of threshold retinopathy of prematurity: 3-year outcome. J Pediatr Ophthal Strabismus 34:83−7
55. Williams C, Northstone K, Harrad RA, et al. ALSPAC Study Team. (2002) Amblyopia treatment outcomes after screening before or at age 3 years. Follow-up from a randomized trial. Br Med J 324:1549
56. Wu C, Petersen RA, VanderVeen DK (2006) RetCam imaging for retinopathy of prematurity screening. J AAPOS 10(2):107−11
57. Ying Gs, Kulp MT, Maguire M, et al. (2005) Vision in Preschoolers Study Group. Sensitivity of screening tests for detecting vision in preschoolers-targeted vision disorders when specificity is 94%. Optom Vis Sci 82(5):432−8
58. Zaba JN, Johnson RA, Reynolds WA (2003) Vision examinations for all children entering public school: the new Kentucky law. Optometry 74:149−58

Evaluation of the Apparently Blind Child

7

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Contents

Core Messages

- Children with apparently poor vision can usually be divided into three categories: (1) those with abnormal ocular examination; (2) non-existent retinal findings but abnormal ERG; or (3) those with normal ocular examination.
- Common causes of non-ocular visual impairment include congenital ocular motor apraxia (saccade initiation failure), cortical visual impairment, and delayed visual maturation.
- Understanding the clinical presentation, assessment, and prognosis for each entity is essential for proper diagnoses and counseling.

7.1 Introduction

Inevitably, an ophthalmologist who cares for children will be challenged by an infant with apparently poor vision. In most cases, the causes can be divided into three categories. The first category is comprised of infants in whom the abnormality is apparent after thorough ocular examination. Anterior segment abnormalities may suggest microphthalmus, aniridia, albinism, cataract, or glaucoma. An abnormal fundus

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examination could reveal optic nerve abnormalities, abnormal vitreous or retinal pathology suggestive of Leber's congenital amaurosis, achromatopsia, or congenital stationary night blindness [6, 42]. The second category consists of those infants with subtle or non-existent retinal findings but abnormal ERG. The third category of infants present with the suspicion of blindness and a normal ocular examination. These children are particularly challenging. They are a challenge diagnostically due to frequently associated developmental or neurological deficits [26]. They are a challenge emotionally for parent and physician because the diagnosis to be given varies widely prognostically from a sighted life to one of severe visual impairment.

Caution should be used in labeling a child as blind because the definitions vary between organizations, academic and educational fields, and the public. The World Health Organization (WHO) defines blindness as a corrected visual acuity in the better eye of < 3/60 (20/400) and severe visual impairment as a corrected acuity in the better eye of < 6/60 (20/200) [15, 16]. Both of these acuity levels are far better than complete loss of sight, which can be inferred by the term "blindness." The WHO epidemiology studies of childhood blindness underscore the discrepancy between causes of visual impairment in regions with higher versus lower socioeconomic status. Westernized countries have significantly higher numbers of non-ocular, central nervous system (CNS)-related causes of blindness, a difference which has been attributed both to improved treatment of ocular disease and to perinatal intervention resulting in an increased survival rate of low-birth-weight and premature infants. This change in epidemiology brought cortical visual impairment (CVI), vision loss due to bilateral CNS damage, to the top of the list of childhood causes of blindness in the United States; however, CVI must be distinguished from other forms of visual impairment with normal ocular examinations such as congenital motor apraxia and delayed visual maturation.

This chapter focuses first on history and examination of the child who presents with suspicion of blindness. The more common entities of non-ocular visual impairment are then discussed including congenital ocular motor apraxia, CVI, and delayed visual maturation with attention to particular aspects of clinical presentation and assessment in each condition.

7.1.1 History

A thorough evaluation by the pediatrician should and most often does occur prior to ophthalmological examination. Particular attention should be paid to birth history such as prematurity, birth weight, and adverse perinatal events. Discussion of family history may uncover history of consanguinity which is helpful in investigating for evidence of autosomal-recessive retinal diseases.

7.1.2 Examination

The absence of "fix and follow" behavior is often the first clue to parent or pediatrician of a visual problem. Infants without this behavior often present after approximately 2 months of age when normally developing children lose the excused "inattention of infancy." It is an important initial physical examination finding. Fixation and pursuit may be accomplished even in most newborn infants, although its absence may be caused by the infant's state of alertness. The ideal target is the human face. The physician's face or, if unsuccessful, the face of the child's parent can be used during the examination [24]. After the human face, bright toys or patterns are useful targets. Once established that the child does not have normal visual responses, it is important to next establish if the child has nystagmus.

Careful examination for nystagmus provides a branching point for common ocular causes of severe visual impairment (Fig. 7.1) [23]. The presence of nystagmus implies anterior pathway disease with the most common anterior causes of severe vision impairment in the U.S. being Leber's congenital amaurosis, congenital stationary night blindness, bilateral optic nerve atrophy, and achromatopsia [6, 42]. An ERG may be needed to further evaluate retinal disease. Magnetic resonance imaging is useful for structural examination of optic nerve and chiasmal pathology. Only rarely is nystagmus associated with cortical visual impairment. It is important to keep in mind that it is possible for infants to have *both* posterior and anterior visual pathway damage resulting in a combined clinical picture of nystagmus and CVI. Because a relatively intact posterior visual pathway

TABLE 1. Evaluation of apparently blind infant

No Apparent Visual Response		
No Spontaneous Nystagmus		"Congenital" Nystagmus
↓		↓
Test VOR		Examine the Eye
↙	↘	↓
Normal VOR	Abormal VOR No Fast Phase	1. Anterior Segment 2. Lens 3. Retina – ERG May Be Necessary 4. Optic Nerve
↓	↓	↓
1. CVI 2. DVM	1. Ocular Motor Apraxia 2. Saccadic Palsy	
↓	↓	↓
Neuroimaging Required	Neuroimaging May Be Required	Neuroimaging May Be Necessary

VOR: vestibular ocular reflex; *CVI*: cortical visual impairment; *DVM*: delayed visual maturation; *ERG*: electroretinogram

Fig. 7.1 Evaluation of the apparently blind infant. (From [23])

is needed to generate nystagmus, the CNS damage is typically mild in these cases [11].

The importance of refraction cannot be overstated in children with apparently poor vision. High refractive error can be a cause of visual inattention in infants [44]. It can also lead the clinician to suspect a retinal or systemic abnormality [26]; therefore, careful retinoscopy should be performed after cycloplegia.

In children without nystagmus, the next step is to determine whether they can generate saccadic eye movements. Determination of the infant's ability to generate saccades may first be established by testing the vestibulo-ocular reflex. This can be done by spinning the infant at arm's length while facing the physician, and observing slow-phase nystagmus toward the infants' direction of spin with fast-phase refixation in the opposite direction. The fast phase does not develop until approximately 45 weeks gestational age [5]. Normal full-term infants of 7 days will show both slow and fast phase of nystagmus with rotation; however, premature infants may have deficient or delayed responses [5, 10]. If the infant fails to develop a fast phase, this is evidence that they cannot generate saccades and there can be no conclusions drawn from the "fix and follow" test. These children may have congenital ocular motor apraxia or forms of saccadic palsies which may be seen in children with CNS damage [24]. It is also important to consider that the vestibulo-ocular reflex can occur occasionally in the absence of vision, i.e., it is a brain-stem reflex.

If the infant without nystagmus demonstrates the ability to generate saccades and has a known history of CNS damage, the diagnosis of cortical visual impairment should be considered. Evidence by imaging of damage to the occipital cortex or radiations confirms the suspicion. The diagnosis of CVI applies only to those infants with damage limited to the visual pathways, rather than more generalized neurological disease.

Finally, in the infant with normal ocular examination, no nystagmus, and without evidence of neurological injury, application of the term delayed visual maturation is appropriate. In these children, vision improves quickly, usually within 3−5 months of age.

7.2 Congenital Ocular Motor Apraxia or Saccade Initiation Failure

7.2.1 Definition

Congenital ocular motor apraxia (COMA) is a condition described first by Cogan as a deficit in the voluntary initiation of horizontal saccades [8]. Children with COMA show an abnormality in both the initiation and amplitude of voluntary and optically induced horizontal eye movements, characterized by a failure of quick-phase nystagmus. Vertical eye movements typically remain normal, but vertical saccade initiation can occur and suggests more serious CNS disease. The term "intermittent saccadic failure" was later suggested by Harris et al. [22] due to the fact that a "true" apraxia consists of abnormal voluntary saccades but *normal* reflexive movements upon testing.

7.2.2 Clinical Presentation

Children older than 3 months with COMA exhibit a characteristic horizontal head thrust associated with attempted ocular refixation. When they attempt to look at an object, they first turn their head toward and beyond the object of interest while their eyes rotate in the opposite direction appearing "left behind." The head thrust forces the eyes to initially deviate even further away from the target, and the child must turn

the head past the object ("overshoot") in order to engage the object. When their eyes engage the object of interest, they then unwind their head counter to the direction of the thrust allowing the eyes to remain fixated on the object. A prominent blink may accompany the saccadic movement. This "synkinetic blinking" represents an adaptation used primarily in older children to aid in the initiation of saccades (Fig. 7.2) [34]. The head thrust is essentially the child's use of the vestibulo-ocular (doll's head) reflex to generate horizontal movement. The head thrust diminishes during the first decade as ability to initiate saccades improves or as the child adapts to the saccadic deficiency [35, 45] Nevertheless, virtually all children with COMA experience difficulty reading.

The diagnosis of COMA may be more difficult in infants younger than 3 months of age [14] prior to development of head control and ability to execute the head thrust. These children with COMA seem simply visually inattentive. They often present early in life with a diagnosis, from the referring physician, of poor vision or failure to fix and follow because of their lack of normal ocular refixation movements [34].

7.2.3 Assessment

Direct observation of the characteristic head and eye movements in children with COMA is often enough to make the diagnosis. Testing of vestibular-ocular reflexes and OKN drum can be helpful in confirming and differentiating the diagnosis from other entities with head thrust such as gaze palsy, slow saccades, visual field defects, or poor eccentric gaze holding [22]. The OKN drum should demonstrate normal vertical saccades and pursuit. The affected child's eyes appear "locked up" with OKN spun horizontally. This occurs as the eyes are driven toward the direction of movement but do not show normal fast-phase saccade recovery. It is important to note that testing with a handheld OKN in the clinic may give the false impression of deficient saccades because the eyes are not driven to the limit of gaze. Full-field OKN will demonstrate the characteristic deviation.

The vestibulo-ocular reflex, together with the opto-kinetic system, is responsible for holding images steady on the retina. This reflex is driven by movement of endolymph fluid in the semicircular

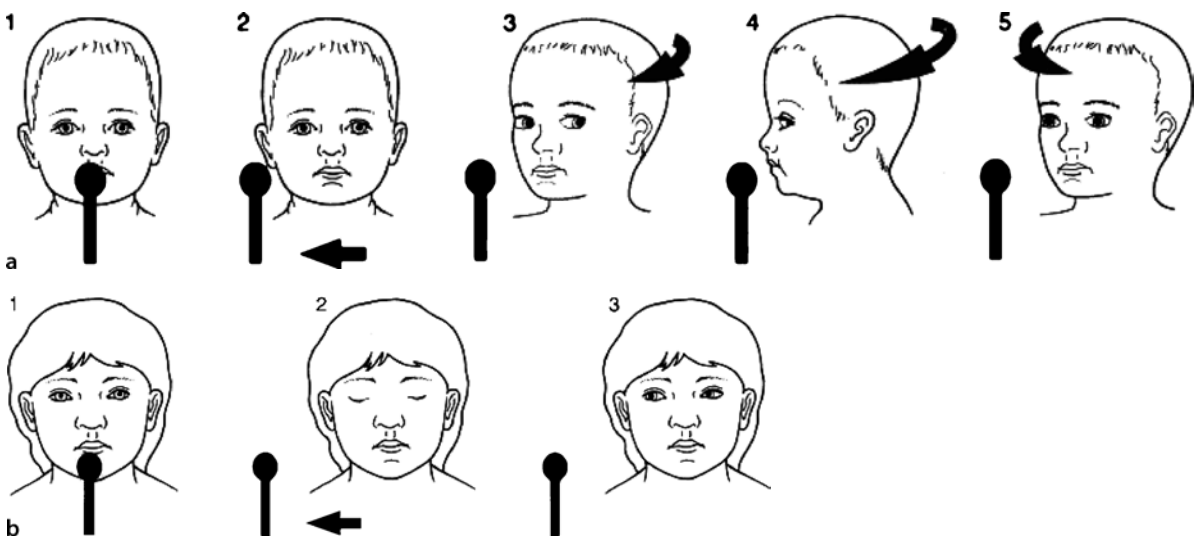

Fig. 7.2a,b Eye and head movements in congenital ocular motor apraxia. **a** Head thrusting. An abrupt turn of the head in the direction of the object (*3*) induces a vestibulo-ocular reflex and causes the eyes to rotate in the opposite direction. The head continues to rotate until the eyes are able to fixate on the object (*4*), then the head unwinds back to primary position with the eyes fixating on the object (*5*). **b** Synkinetic blinking. Older children may use an exaggerated blink to initiate saccades. (Adapted from [5])

canals and is not visually mediated; therefore, it can be elicited in the dark [5]. In children with COMA, testing of VOR by rotation of the infant will cause the eyes to deviate and remain in the furthest extent of the slow phase (toward the direction of the infant's rotation).

Vision, ERG, and VEP should be normal in children with COMA. Any abnormality on these tests should prompt further investigation for associated neurological disease [5].

7.2.4 Etiology

COMA is described as a sporadic disorder, although familial cases have been documented [9, 35, 45] including a suggested autosomal-dominant transmission pattern in one pedigree [35]. The pathophysiology of COMA is unclear. It may occur in an idiopathic form or in association with structural or systemic neurological disease. The most commonly reported structural abnormalities include agenesis of the corpus callosum and cerebellar hypoplasia [5, 8, 14, 22, 34]. Structural abnormalities in the cerebrum, cerebellar vermis, brain stem, mid-brain, and basal ganglia, as well as perinatal insults such as hypoxia, cerebral palsy, and hydrocephalus, have also been associated [8, 22, 14, 38]. The finding of vertical saccade failure suggests these more ominous conditions.

In addition to a congenital etiology, ocular motor apraxia can occasionally be acquired and associated with (1) neurodegenerative disorders such as ataxia–telangiectasia, Gaucher's disease, and linear sebaceous nevus syndrome; or (2) acquired disease such as posterior fossa tumors, ischemia, and herpes encephalitis, among others. These children initially exhibit normal development, followed by unexplained neurological decline.

7.2.5 Prognosis

As stated previously, congenital ocular motor apraxia may be idiopathic or associated with underlying structural or systemic neurological disease. In children with underlying disease, the deficits are most often attributed to the underlying abnormalities. There is evidence that even children with isolated COMA may still have associated developmental delay in motor, speech, or behavior [32, 34].

Older, school-age children tend to show less clinical signs of the condition. It is not known whether the condition itself improves or if the improvement is due primarily to the child's adaptive capabilities. There is a diminished use of the head thrust in older children, as well as use of an exaggerated blink prior to fixation on a target (synkinetic blinking) to replace or augment head movement [5, 22].

7.3 Cortical Visual Impairment

7.3.1 Introduction

Cortical visual impairment (CVI) is defined as bilateral loss of central vision due to damage to the CNS. Anterior visual pathways (globe, optic nerve, chiasm) are spared, while damage to posterior visual pathways (lateral geniculate body, optic radiations, primary visual cortex, visual association areas) produces variable visual deficits. Cortical visual impairment is the leading cause of bilateral vision impairment in children in Western countries This is believed to be due to higher survival rates of children with perinatal hypoxia and ischemia as well as improved treatment of previously lethal diseases [17, 20].

A discussion of cortical visual impairment cannot occur without clarification of terminology. Although the terms cortical or cerebral "blindness" have been used to describe patients with visual impairment related to CNS injury, it should not be used as a diagnostic term for children. Blindness implies total loss of vision and is not typical of children with CVI. In contrast to adults with acquired CNS injury, children with CVI routinely preserve residual vision. Considerable debate has also surrounded the use of cortical versus cerebral to describe the site of impairment. It can be argued that cerebral impairment is a more accurate term since the CNS damage can occur anterior to the visual cortex. At this time, "cortical visual impairment" is our preferred description of the condition due to the emphasis on the striate cortex as the ultimately disrupted endpoint of the posterior pathway.

7.3.2 Etiologies

Perinatal hypoxia/ischemia is the most common cause of CVI [4, 17, 20]. The pattern of CNS damage differs for premature infants versus full-term infants and is best explained by examination of the difference in blood supply in the developing brain.

In infants prior to 34 weeks gestation, the watershed zones between the major cerebral arteries (posterior, middle, anterior cerebral arteries) are also supplied by meningeal anastomoses [28]. This protects the area between the three major arteries, called the para-sagittal region, from infarctions. However, another watershed zone exists transiently in the premature infant in the periventricular area (choroids plexus). It is supplied by ventricular branches of deep penetrating arteries. Ischemic damage occurs to this periventricular white matter adjacent to the lateral ventricles resulting in involvement of optic radiations (Fig. 7.3). Periventricular leukomalacia (greek origin. *leuko* "white" + *malakia* "softness") is the most common form of hypoxic damage in premature infants. Risk factors in the premature infant include first-trimester hemorrhage, maternal urinary tract infections, neonatal acidosis at birth, meconium-stained amniotic fluid, and premature rupture of membranes [28]. Full-term infants manifest the para-sagittal watershed zones between the three major systems as described above, but they lack the additional meningeal anastomoses protective in the premature infant (Fig. 7.4). The areas between the parieto-occipital lobe as well as the body of the caudate nucleus are most vulnerable to both hypoxia and hypotension as they are "triple" watershed zones [4].

Causes for cerebral dysfunction after hypoxia are largely unknown. Proposed pathophysiological mechanisms include glutamate toxicity, free radical injury and macrophage-mediated cytokine damage, interruption in protein synthesis in neural or glial

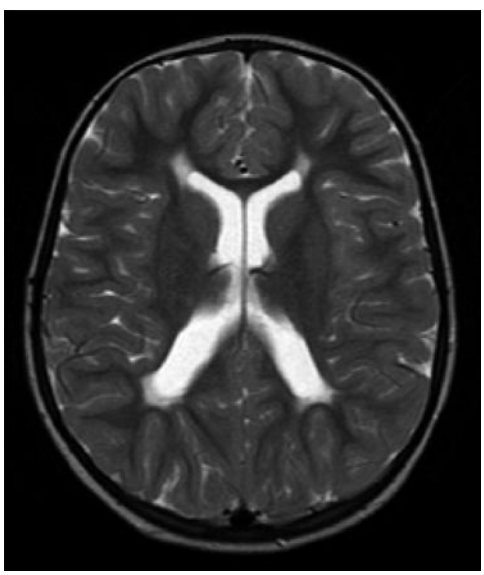

Fig. 7.3 Chronic, severe periventricular white matter injury. T2-weighted axial magnetic resonance image of the brain at the level of the lateral ventricles. Note marked white matter loss in the posterior periventricular white matter with lack of space between ventricles and overlying cortex. Ventricles are dilated posteriorly with an irregular and scalloped border. (Adapted from [46])

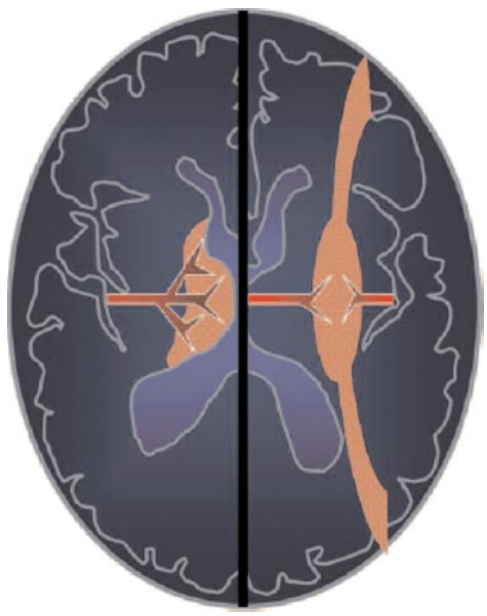

Fig. 7.4 Patterns of brain injury after hypoxic/ischemic insult. The premature infant brain (*left*) has a periventricular area, supplied by deep penetrating arteries, which is vulnerable to ischemic damage. In the term infant (*right*), the parasagittal "watershed zone" between the three major arteries is the most susceptible to injury. (Adapted from [47])

cells, abnormal myelination, and delayed dendrite formation [4, 28].

Postnatal ischemia can affect the infant brain through anatomical reasons similar to those of the term infant. Causes are many including profound hypotension, cerebral angiography, cardiac surgery, air embolism, and embolism due to congenital cyanotic heart disease. Hypertensive crisis may constrict posterior cerebral arteries. Transtentorial herniation, as may occur from hydrocephalus or ventricular shunt failure, can compress posterior cerebral arteries. Vascular malformations may also directly compress intercranial vessels. Thrombotic disorders may also cause hypoxia [4].

Periventricular/intraventricular hemorrhages occur primarily in pre-term infants before 34 weeks of gestation. These hemorrhages are a result of small vessels in the ventricular wall in which the cells that eventually become brain tissue are produced, called the subependymal germinal matrix. These vessels may hemorrhage into ventricles and brain parenchyma causing damage to posterior visual pathways. Because the matrix involutes around 34 weeks of gestation, it is a rarity in infants after this age.

Malformations of the brain, such as porencephaly (focal cavity without surrounding glial reaction occurring during first 20 weeks of gestation), encephaloceles, and Chiari malformations, may cause involvement of the posterior visual pathway [4].

Metabolic disorders, such as lead poisoning, cocaine, nitrous oxide poisoning, carbon monoxide poisoning, hemodialysis, and hypoglycemia, have been reportedly associated with acute CVI. It has also been noted in conditions such as MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke), Leigh's disease and X-chromosome-linked adrenoleukodystrophy. In these conditions anterior pathway disease may coexist and contribute to the CVI component.

Seizure-related loss of vision has been reported but is most often transient [1, 20]. Infantile spasms, which feature myoclonic seizures with deterioration of the EEG, may cause severe vision impairment which tends to recover with seizure treatment. Rarely do children remain visually impaired and profoundly developmentally delayed as a result of seizures per se.

Head trauma is a rare cause of "permanent" visual damage. More commonly it may cause transient visual loss recovering within a matter of minutes to hours. Younger children may not complain of visual loss but appear agitated, disoriented, or confused. The "shaken-baby syndrome" is a form of head trauma that may cause permanent CVI [20]. A child with the combination of CVI and unexplained trauma needs careful investigation for signs of child abuse, including retinal pathology.

Infections, such as meningitis, encephalitis, and sepsis, are rare causes of CVI.

7.4 Clinical Presentation

The most typical clinical picture of a child with CVI is the preterm infant with CNS damage that is often coexistent with other types of motor, speech, and physical developmental delay. On history, parents show concern for lack of attention to faces and objects. They may also report lack of blink response to threat, and it is important to reassure parents that this is not evidence against vision. This response is a learned behavior not present until 3 months of age and may be developed even later in children with CVI [17].

History of gazing at lights is common in children with CVI, and some flick their fingers in front of the light source or blink excessively [20, 30]. Some degree of photophobia has also been reported in children with CVI, although not as severe as may be seen in certain retinal conditions [4, 31]. Children may show a preference for brightly colored and moving objects rather than static objects [20, 29]. They may also turn their head away from a target when reaching, suggesting a preference for peripheral vision. In familiar surroundings, a relaxed and well-rested child often exhibits better vision [17]. Luminance conditions may also affect visual acuity, with a recent investigation suggesting that low luminance conditions may improve visual acuity in children with CVI [19].

While not technically CVI, unilateral cerebral damage may result in preserved visual acuity but profound visual field defects causing visual impairment. These children are usually able to adapt to their environment. They can manifest a head turn away from the affected field. Children with bilateral cerebral involvement characteristic of CVI may have asymmetric involvement and show preference for the lesser involved field [20].

7.4.1 Assessment

Careful ophthalmic examination of children with CVI typically reveals normal ocular examination with poor visual behavior. These children may exhibit other head and eye movement abnormalities such as strabismus, gaze palsies, eye movement apraxia, problems with pursuit eye movement, and visual field defects [26]. Coexistent anterior pathway disease can occur, including optic nerve atrophy, nystagmus, strabismus, and refractive error [26, 36]. Clinical judgment is then required to determine to what extent the ocular findings contribute to the overall vision deficit.

Measurement of infant vision can be accomplished by a variety of simple to extensive methods. Most children have associated severe neurological abnormalities which make traditional measurements of vision difficult. In clinic settings, techniques relying on fixation and pursuit can be used to identify both vision and basic motor and behavioral capabilities. Use of brightly colored objects, movement, or lights may increase the effectiveness of examination.

Forced-choice preferential looking is an option for quantification of infant visual acuity based on the infant's preference to look at a pattern stimulus rather than a blank stimulus of equal luminance. The test involves an observer who sits behind a screen and presents a series of cards with varied grating lines on one side and a blank field on the other. The child will usually look toward the card with grating lines until the lines presented are fine enough that they do not draw attention. Acuity is determined by estimate based on the smallest grating to which the infant showed fixation (Fig. 7.5). In children with CVI, the usefulness of this test may be limited by coexistent motor problems or inattention [3, 17]. It is, however, a commonly used tool to both quantify and evaluate progression of visual recovery in CVI.

Visual evoked potentials may also offer a quantitative tool to measure vision in pre-verbal or speech-impaired children. Its use in cortical visual impairment has focused largely on the usefulness in either confirming the diagnosis or influencing prognosis for outcome [21]. The results of flash or pattern VEP should be interpreted with caution as prior studies have shown responses even in the absence of a functioning visual cortex [24]. Steady-state (sweep) VEP measures may someday provide a means of estimating visual acuity in children with CVI [17, 19].

Fig. 7.5 Forced-choice preferential look test using Teller acuity card stage. An observer watches the behavior of the infant through a peephole as Teller cards are presented through the gray screen. Increasingly finer gratings are presented through the aperture until the infant is no longer seen to direct attention preferentially to the side with gratings. (Adapted from [48])

OKN, while still a useful tool in evaluating infant eye movements, has its limitations particularly with CVI infants. It has been shown that optokinetic nystagmus can be generated even in the absence of an intact visual cortex [24].

Neuroimaging is useful to identify the site of damage in CVI. Ultrasound is useful for initial examination of the premature infant due to portability. Computed tomography and MRI may demonstrate hypoxic–ischemic damage, infarction, or cerebral anomalies [20]. An EEG can also be used to evaluate children with CVI. The most common finding is absence of the alpha rhythm, which normally develops by 3 months of age and is elicited by eye closure and extinguished by eye opening. Patients with alpha rhythm tend to have more residual vision [20].

7.4.2 Prognosis

Improvement is seen in the majority of children with CVI, although normal vision is not regained [20, 36]. The presence of periventricular leukomalacia carries

a worse prognosis in comparison with damage to the visual cortex [17]. It is important to remain optimistic with patients and family regarding the possibility of improvement, while realizing that most children will continue to have a significant visual handicap.

7.5 Delayed Visual Maturation

7.5.1 Definitions

Delayed visual maturation (DVM) is a term introduced by Illingsworth in 1961 to describe infants who appeared blind but had improvement in their visual function with maturation [27]. In its pure form, DVM is a retrospective diagnosis given after observation of improved visual attention in a child with normal anterior and posterior visual pathways. The definition has since been expanded beyond the isolated form to include children having DVM with coexistent ocular, developmental, or systemic disorders.

7.5.2 Clinical Presentation

These children tend to present after 1−2 months with the presumption of severe visual impairment due to lack of visual responsiveness. Classically, they appear to be relatively normal infants with an abnormal delay in visual development. Many infants will show signs of general motor development delay or may have a history of prematurity or be small for gestational age [25].

Ophthalmological examination is normal, although some authors have reported gray coloration of the optic discs at presentation [2, 37]. Severity of the visual inattention can be quite variable.

7.5.3 Assessment

ERG, OKN, and VOR should be normal in children with DVM [23, 37]. By 7 days of life, normal full-term infants should demonstrate the oculo-vestibular reflex due to rotation [10]. If they do not develop nystagmus with fast phase, it may be concluded that they do not have normal oculomotor reflexes, and diagnoses, such as ocular motor apraxia, should be considered. Interestingly, in a small cohort, six of the eight infants with DVM exhibited a lack of fast-phase saccades on testing of VOR. The majority of these children were pre-term or small for gestational age and it has been suggested that these children may have had underlying neurological issues contributing to DVM, although all children did reach normal visual acuity. An overall developmental delay may be a more plausible explanation [25].

VEP may be normal or abnormal in children with DVM [4, 25, 33, 37]. Several arguments exist to explain the discrepancies. One argument includes the fact that the waveform varies even in a visually attentive infant, making establishment of "normals" a difficult process. Also, many of the infants tested were preterm or small for gestational age and were not compared with age-matched controls. It is important to note that different types of VEP were employed in each study and various testing conditions; therefore, the presence of a normal VEP is comforting, but an abnormal VEP does not reject the possibility of DVM.

Normal vernier acuity has been demonstrated in children with DVM using sweep visual evoked potential which provides a continuous patterned visual stimulus as opposed to the single flash of light used in a flash VEP [18]. During sweep VEP, the stimulus is changed gradually from perceptible to imperceptible and provides an advantage over flash VEP by allowing quantification of visual acuity thresholds.

There is evidence that hearing impairment due to delayed auditory evoked potentials may be present in children with DVM. This condition is known as auditory neuropathy/dyssynchrony and exhibits a range of hearing responses with absent or severely abnormal brain-stem auditory evoked potentials and normal cochlear function [1]. While the hearing impairment is known to be permanent when associated with other conditions, it appeared to show improvement over time in one report of a child with DVM.

Imaging studies may be warranted to investigate structural causes in infants older than 4 months presenting with the clinical picture of DVM.

7.5.4 Etiology

DVM has been associated with a number of ocular and systemic anomalies such as nystagmus, albinism, prematurity, perinatal problems, and mental retardation. As previously mentioned, the more common use of the term refers to its isolated form; however, several classification systems have been created to include those infants with associated abnormalities [13, 41]. The classification by Fielder describes four groups. Group 1 is isolated abnormality with normal ocular exam, with subdivision 1A for purely isolated and 1B for those with history of perinatal problems. Group 2 exhibits persistent neurodevelopmental problems. Group 3 includes albinism and idiopathic congenital nystagmus, and group 4 includes severe associated ocular disorders [12].

Several theories have been proposed regarding the etiology of DVM. Immaturity of the visual association areas was suggested by Lambert et al. in a study showing normal flash and pattern VEP in structurally normal, behaviorally blind children [33]. Foveal immaturity and delayed myelination of the posterior pathways have also been proposed [2, 4]. The fact that improvement in vision occurs at around the time when the early infant begins to develop certain cortical functions has led some authors to suggest a defect in the subcortical visual pathways [7, 25]. There might be some combined level of involvement in the cortex and subcortex [7] which may account for inconsistent study results. Some authors have suggested a neurochemical rather than structural problem based on the rapidity of visual recovery [7]. Given the normal ERG and VEP shown in many studies[18, 33, 43], it may also be that the problem lies in visual association areas that mediate visual attention, not in the primary visual cortex [33].

It is noteworthy that occasionally DVM has been confused with epileptic blindness in an infant [39]. These children, however, tend to exhibit normal visual behavior which then deteriorates with time.

7.5.5 Prognosis

Most infants with DVM start to demonstrate visually guided behavior between 3 and 5 months with a mean of approximately 5.5 months of age [33]. If broken down into groups 1−3, group 1 tends to show improvement by 7−24 weeks, group 2 by 22−78 weeks, and group 3 by 13−28 weeks [40]. The improvement in visual attention can occur rapidly over 1–2 weeks [37], with significant improvement seen even over a few days [7]. Children with otherwise normal developmental and neurological exam should be reassured but monitored carefully by a pediatrician and an ophthalmologist. If associated structural or developmental deficits are present, they should be dealt with appropriately. By definition, children with isolated DVM achieve normal levels of visual acuity.

Take Home Pearls

- Use caution in labeling a child as “blind” based solely on behavioral measures.
- High refractive error can be a cause of visual inattention in infants.
- Children with delayed visual maturation have rapid improvement of vision, usually by 3−5 months of age.
- Congenital oculomotor apraxia may be confused with poor vision in infants younger than 3 months prior to development of head control and ability to execute the head thrust.
- Lack of blink response to threat in children with cortical visual impairment does not indicate that the child is blind.

References

1. Aldosari M (2003) Delayed visual maturation associated with auditory neuropathy/dyssynchrony. J Child Neurol 18:358–361
2. Beauvieux J (1947) La cecite apparente chez le nouveaune la pseudo-atrophie grise du nerf optique. Arch Ophtalmol (Paris) 7:241–249
3. Birch EE, Bane MC (1991) Forced choice preferential looking acuity of children with cortical visual impairment. Dev Med Child Neurol 33:722–729
4. Brodsky MC (1996) Apparently blind infant. In: Brodsky MC, Baker RS, Hamed LM (eds) Pediatric neuroophthalmology. Springer, Berlin Heidelberg New York, pp 11–41
5. Cassidy L, Taylor D, Harris C (2000) Abnormal supranuclear eye movements in the child: a practical guide to examination and interpretation. Surv Ophthalmol 44(6):479–506
6. Casteels I (2005) Clinical investigation of bilateral poor vision from birth. In: Taylor D, Hoyt CS (eds) Pediatric ophthalmology and strabismus. Elsevier Saunders, Philadelphia
7. Cocker KD, Moseley MJ, Stirling HF, Filder AR (1998) Delayed visual maturation: pupillary responses implicate subcortical and cortical visual systems. Dev Med Child Neurol 40:160–162
8. Cogan DG (1952) A type of congential ocular motor apraxia presenting jerky head movements. Trans Am Acad Ophthalmol Otol 56(6):853–862
9. Cogan DG (1972) Heredity of congenital ocular motor apraxia. Trans Am Acad Ophthalmol Otol 76(1):60–63
10. Eviatar L, Miranda S, Eviatar A, Freeman K, Borkowski M (1979) Development of nystagmus in response to vestibular stimulation in infants. Ann Neurol 5:508–514
11. Fielder AR, Evans NM (1988) Is the geniculostriate system a pre-requisite for nystagmus? Eye 2:380–382
12. Fielder AR, Mayer DL (1991) Delayed visual maturation. Sem Opthalmol 6(4):182–193
13. Fielder AR, Russell-Eggitt IR, Dodd KL, Mellor DH (1985) Delayed visual maturation. Trans Ophtalmol Soc UK 104:653–661
14. Fielder AR, Gresty MA, Dodd KL, Mellor DH, Levene MI (1986) Congenital ocular motor apraxia. Trans Ophthalmol Soc UK 105:589–598
15. Gilbert C, Foster A (2001) Childhood blindness in the context of VISION 2020–the right to sight. Bull WHO 79(3):227–232
16. Foster GC (2001) Blindness in children: control priorities and research opportunities. Br J Ophthalmol 85:1025–1027
17. Good WV (2001) Development of a quantitative method to measure vision in children with chronic cortical visual impairment. Trans Am Ophthalmol Soc 99:253–269
18. Good WV, Hou C (2004) Normal vernier acuity in infants with delayed visual maturation. Am J Ophthalmol 138:140–142
19. Good WV, Hou C (2006) Sweep visual evoked potential grating acuity thresholds paradoxically improve in low-luminance conditions in children with cortical visual impairment. Invest Ophthalmol Vis Sci 47(7):3220–3224
20. Good WV, Jan JE, DeSa L, Barkovich JA, Groenveld M, Hoyt CS (1994) Cortical visual impairment in children. Surv Ophthalmol 38(4):351–364
21. Granet DB, Hertle RW, Quin GE, Breton ME (1993) The visual-evoked response in infants with central visual impairment. Am J Ophthalmol 116:437–443
22. Harris CM, Shawkat F, Russell-Eggitt I, Wilson J, Taylor D (1996) Intermittent horizontal saccade failure (ocular motor apraxia) in children. Br J Opthalmol 80:151–158
23. Hoyt CS (2004) Delayed visual maturation: the apparently blind infant. J AAPOS 8(3):215–219
24. Hoyt CS, Nickel BL, Billson FA (1982) Ophthalmological examination of the infant. Dev Aspects Surv Ophthalmol 26(4):177–189
25. Hoyt CS, Jastrzebski G, Marg E (1983) Delayed visual maturation in infancy. Br J Opthalmol 67:127–130
26. Huo R, Burden SK, Hoyt CS, Good WV (1999) Chronic cortical visual impairment in children: aetiology, prognosis, and associated neurological deficits. Br J Ophthalmol 83:670–675
27. Illingsworth RS (1961) Delayed visual maturation. Arch Dis Child 36:407–409
28. Jacobsen LK, Dutton GN (2000) Periventricular leukomalacia: an important cause of visual and ocular motility dysfunction in children. Surv Ophthalmol 45(1):1–13
29. Jan JE, Goenveld M, Sykanda AM, Hoyt CS (1987) Behavioural characteristics of children with permanent cortical visual impairment. Dev Med Child Neurol 29:571–576
30. Jan JE, Goenveld M, Sykanda AM (1990) Light-gazing by visually impaired children. Dev Med Child Neurol 32:755–759
31. Jan JE, Groenveld M, Anderson DP (1993) Photophobia and cortical visual impairment. Dev Med Child Neurol 35:473–477
32. Jan JE, Kearney S, Groenveld M, Sargent MA Poskitt KJ (1998) Speech, cognition and imaging studies in congenital ocular motor apraxia. Dev Med Child Neurol 40:95–99
33. Lambert SR, Kriss A, Taylor D (1989) A longitudinal clinical and electrophysiological assessment. Ophthalmol 96(4):524–527
34. Marr JE, Green SH, Willshaw HE (2005) Neurodevelopmental implications of ocular motor apraxia. Dev Med Child Neurol 47:815–819
35. Phillips PH, Brodsky MC, Henry PM (2000) Congenital ocular motor apraxia with autosomal dominant inheritance. Am J Ophthalmol 129(6):820–822
36. Roland EH, Jan JE, Hill A, Wong PK (1986) Cortical visual impairment following birth asphyxia. Pediatr Neurol 2:133–137
37. Russell-Eggit I, Harris CM, Kriss A (1998) Delayed visual maturation: an update. Dev Med Child Neurol 40:130–136
38. Sargent MA, Poskitt KJ, Jan JE (1997) Congenital ocular motor apraxia: imaging findings. Am J Neuroradiol 18:1915–1922

39. Shahar E, Hwang PA (2001) Prolonged epileptic blindness in an infant associated with cortical dysplasia. Dev Med Child Neurol 43:127−129
40. Tresidder J, Fielder AR, Nicholson J (1990) Delayed visual maturation: ophthalmic and neurodevelopmental aspects. Dev Med Child Neuro 32:872−881
41. Uemura Y, Agucci Y, Katsumi O (1981) Visual developmental delayed. Ophthalmic Paediatr Genet 1:4−11
42. van Genderen M, Riemslag F, Jorritsma F, Hoeben F, Meire F, Stilma J (2006) The key role of electrophysiology in the diagnosis of visually impaired children. Acta Ophthalmol Scand 84:799−806
43. Weiss A, Kelly JP, Phillips JO (2001) The infant who is visually unresponsive on a cortical basis. Ophthalmology 108:2076−2087
44. Winges KM, Zarpellon U, Hou C, Good WV (2005) Delayed visual attention caused by high myopic refractive error. Strabismus 13:75−77
45. Yavuz Gurer YK, Kukner S, Kunak B, Yilmaz S (1995) Congential ocular motor apraxia in two siblings. Pediatr Neurol 13:261−262
46. Saidkasimova S et al. (2007) Cognitive visual impairment with good visual acuity in children with posterior ventricular white matter injury: a series of 7 cases. J AAPOS 11(5):426−430
47. Chao CP et al. (2006) Neonatal hypoxic−ischemic encephalopathy: multimodality imaging findings. Radiographics 26:S159−S172
48. Clifford-Donaldson CE et al. (2006) Teller acuity card norms with and without use of a testing stage. J AAPOS 10(6):547−551

Comitant Esotropia

Edward L. Raab

8

Contents

Core Messages

- Age of onset, duration of the condition, and neurologic status are important factors in determining the response to surgery and the binocular sensory outcome.
- Congenital esotropia is actually "very early acquired" esotropia. Intermittency may be present initially, but only for a brief period.
- Accommodative esotropia typically begins at about age 2−2.5 years, but earlier onset is not uncommon.
- Quantitative determination of the AC/A ratio is not necessary for management. The distance-near alignment comparison remains useful as an approximation of the AC/A ratio.
- Decompensation of accommodative esotropia can occur through delayed diagnosis, poor compliance, or despite timely and excellent management.
- Decompensated esophoria has a later and more gradual onset, unlike the acute esotropia that should raise the suspicion of serious neurologic disease.

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- Undercorrected esotropia after surgery done for appropriate reasons requires completion of treatment, once it is certain that resulting alignment is not within 8 prism diopters of orthotropia.
- Initial overcorrection of exotropia is appropriate surgical strategy, but persisting overcorrection is a risk to a good binocular sensory result.
- Cyclic esotropia is distinguished from other forms of intermittent esotropia by its relatively late onset, repetitive cycle length, and lack of dependence on accommodative effort. Surgery is effective before or after the deviation becomes constant.
- *Divergence insufficiency* can either describe an unusual setting for esotropia characterized by the distance deviation being greater than that at near, or an acute presentation with diplopia suggesting a serious neurologic abnormality.

8.1 Introduction

The term *comitant esotropia* applies to several ocular motility disorders having in common (a) a convergent misalignment with no observably limited horizontal rotations, and (b) substantially the same magnitude in both lateral gazes. Not all of these entities are specific for children. When planning surgical correction of the horizontal disorders comprising this chapter, the reader should include the appropriate refinement when either an A or V pattern is part of the clinical picture. (Chap. 13 considers A and V pattern horizontal deviations and their associated features in detail.)

Guidelines for surgical quantities are provided in this volume and other texts which deal with strabismus [29], and are subject to each surgeon's variations in technique and experience. Surgical tables generally are based on the location of the original insertion, which, especially for the medial rectus, does not always conform to textbook descriptions. This has generated controversy over whether recessions should be more properly measured from the limbus rather than from the original insertion site. Neither argument has prevailed, and if the surgeon adopts the principle that experience governs the choice, the significance of this debate fades.

Botulinum toxin (Botox, Allergan, Irvine, Calif.) as a substitute for surgery has some advocates for use in comitant strabismus [12], but this agent finds its best use in paralytic deviations.

The references provide just a small sample of what is available to the interested reader. The earlier ones continue to be cited and still represent current thinking on their subjects.

8.2 Primary Classification

It is very helpful to classify the child patient with comitant esotropia with respect to two major features that guide treatment and the expected results; these are onset age and duration, and neurologic status.

8.2.1 Onset Age and Duration

While in many cases onset age and duration are difficult to ascertain reliably, precise dating allows a reasonable prediction about the likelihood of a satisfactory outcome that includes some degree of binocular cooperation. For example, an esotropia of 12−15 prism diopters (PD) that might be cosmetically acceptable without further attention would nevertheless call for a recommendation for surgical correction if a delayed age of onset suggests the probability of a better binocular sensory outcome. This may be the only information available when the patient is too young for formal sensory testing. One of the charms and burdens in the practice of children's eye care is that important decisions often must be made based on such inferences.

8.2.2 Neurologic Status

Inquiry into neurologic status essentially involves whether the child is developmentally normal or im-

paired. A familiar prototype for the latter status is cerebral palsy, one of whose characteristics is esotropia that is variable and that frustrates obtaining reliable and reproducible alignment measurements. Moreover, these patients respond unpredictably to conventional amounts of surgery [18], leading most pediatric ophthalmologists, even if advocates of early correction, to delay until the deviation stabilizes and can be properly assessed. The pediatric ophthalmologist without formal training in child neurology can gain insight by observing overall muscle tone. The normal infant will resist the effects of gravity by a visible and palpable increase in chest and limb muscle contraction when held in either position shown in Fig. 8.1.

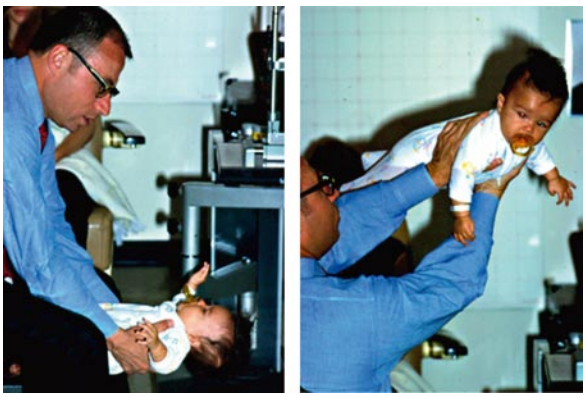

Fig. 8.1 Evaluating an infant's skeletal muscle tone

8.3 Primary Infantile (Congenital) Esotropia

"Congenital" is a misnomer, as such cases have not been encountered literally at birth [1]. The working definition of this entity for purposes of clinical research is a large, constant angle of esotropia, confirmed to be present by age 6 months, in an otherwise neurologically normal infant (Fig. 8.2). As a practical matter, cases fulfilling these criteria often first present for examination between 6 months and 1 year of age, or even later, and there may be a brief period of intermittency before the full picture is evident [17]. The more meaningful distinction is between acquired and "extremely early acquired," one which rests on the likelihood of achieving normal binocular interaction and refined stereopsis once proper alignment has been restored.

Fig. 8.2 Infant with congenital esotropia

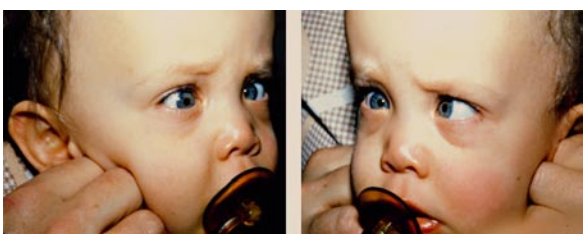

Fig. 8.3 Bilateral cross-fixation and apparent abduction deficiency

8.3.1 Features

Features include a normal refractive error for this age range (+2.00 to +2.50 D spherical equivalent) in most patients, perhaps a family history of some form of strabismus, and easily improvable amblyopia, if any. Cross-fixation of each eye (Fig. 8.3) can cause abduction to appear limited, inviting confusion with sixth-cranial-nerve palsy. Eliciting abduction when the opposite eye is occluded resolves the issue in most cases; in some, stiffer than normal or more forwardly inserted medial rectus muscles impose some degree of restriction to abduction that disappears immediately after these muscles are weakened.

Motor nystagmus, with or without a null point and a latent component, is another accompanying feature (see Chap. 18). Inferior oblique overaction and dissociated vertical deviation (DVD) are considered strong indicators of the diagnosis [39], especially when both are present. However, they usually occur closer to

age 2 years or later, whether or not there has been prior surgical correction of the horizontal deviation; therefore, they are only occasionally useful in the initial assessment. In the author's experience, these features appear with sufficient regularity in other forms of strabismus as to discount somewhat their specific diagnostic value for infantile esotropia.

8.3.2 Management

Years ago, treatment regimens stressed deferring surgery in favor of prolonged treatment of presumed abnormal binocular sensory patterns when allowed by the child having reached sufficient maturity. In most cases this led to no binocularity at all, whether or not the delayed straightening resulted in normal alignment.

Present management is based on the strong presumption that spontaneous cure of a large, constant estropia will not occur and emphasizes that satisfactory alignment should be established by about 2 years of age to afford an opportunity for the establishment of binocular sensory cooperation that includes some degree of refined stereopsis [5, 6, 34]. While some observers have advocated correction as early as age 3 months [2], the age at which proper alignment has been accomplished counts more than when efforts begin. Throughout this 2-year time frame, this scheme probably necessitates more repeated surgical procedures than would later attempts because of under- or overcorrections and the delayed appearance of the accompanying vertical deviations discussed above. The expectations from early treatment are not defeated by having to repeat surgery. When counseling the families of patients with congenital esotropia, the ophthalmologist should focus their attention on the ultimate desired outcome and not on the number of surgical steps required.

Comparative fixation ability remains the principal criterion for determining the presence or absence of amblyopia in these infants. Monitoring by preferential looking techniques has its enthusiasts, but this may not be practical in a busy setting that does not include an individual dedicated principally to this determination. Amblyopia is best addressed before operation, since occlusion when the eyes have been newly aligned frustrates the opportunity for the exercise of binocularity. (A word of caution: if occlusion of the preferred eye does not result in improvement after a brief period, the ophthalmologist should repeat the ophthalmoscopic evaluation, as subtle findings indicating an organic abnormality may not have been previously appreciated. If present, this alters both the surgical approach and the expectations from treatment.) Once equal fixation ability is apparent, whether alternation is spontaneous or demonstrated by the cover test, daily alternate-eye occlusion for brief periods as a short-term measure until surgery is carried out is helpful to maintain equal vision.

Most ophthalmologists elect recession of both medial rectus muscles. Resection of the lateral recti as a first procedure is not generally favored. When one eye has uncorrectable poor vision, monocular recession/resection is advisable to avoid exposing the good eye to serious surgical complications, although the risk is generally low.

The approach to undercorrections is discussed in Sect. 8.6 of this chapter. Overcorrections call for recession of the lateral rectus muscles when the first operation involved both eyes; otherwise, recession/resection of the horizontal recti of the previously unoperated eye usually is chosen. Resection or advancement of previously recessed medial recti is another option, but it gives less predictable results and offers no advantage when postoperative adduction is not reduced.

Can a two-muscle procedure overcome a deviation of any amount? Should the plan include recession of each medial rectus 7.0 mm or even more, or would a limit of 6.0 mm and addition of a resection of one lateral muscle be better? One study concluded that recessions up to 7.0 mm make inclusion of a third muscle unnecessary even for esotropia of more than 70 PD [38], but this is not a typical outcome in the author's experience, and recessions of 7.0 mm or more in extremely young patients present a considerable risk of limited postoperative adduction; hence, my preference for a 6.0-mm limit. If the three-muscle procedure results in an overcorrection, the operated lateral rectus muscle can be employed again as though never touched; thus, "using up a fresh muscle" is not a strong disadvantage.

Correction of inferior oblique overaction or DVD (see Chap. 12) should be done simultaneously if already present, with the caveat that weakening of only one inferior oblique often precedes, although it does

not cause, the onset of overaction in the opposite one [39]. The best explanation for such an occurrence is that the first inferior oblique weakening was done fortuitously between the non-simultaneous appearances of the components of a bilateral disorder. Alternatively, one study suggested that some inferior oblique weakening procedures involve reattachment that limits elevation in abduction, causing apparent overaction of the opposite inferior oblique by Hering's law [32].

In an otherwise typical case of congenital esotropia in which above-average hyperopia is also present, it is highly unlikely that the entire large-angle, constant deviation is the result of perpetually sustained accommodative effort at an age when the need for obtaining refined visual information is not yet well developed. Whether the customary "trial of the full refractive correction" is indicated is debatable in this setting. Postoperatively, this can change importantly. Accommodative esotropia (see Sect. 8.4) occurs as a sequel to infantile esotropia at high frequency and usually earlier than expected [3, 21], especially if hyperopia determined with cycloplegia is more than 3.50 D. The ophthalmologist should warn parents of this prominent possibility, or they will not understand the return of a deviation that, to them, seems identical to the earlier condition.

8.4 Accommodative Esotropia

Accommodative esotropia is the most common form of childhood strabismus [15]. It can be present by itself or in combination with other strabismus entities. Intermittency of the deviation in a neurologically normal child between 2 and 3 years of age strongly suggests this diagnosis, although earlier presentation is certainly not rare (Fig. 8.4). With time, the deviation in the untreated patient becomes constant as abnormal sensory adaptations become established.

8.4.1 Features

One variety of this disorder occurs because of an excessive demand for accommodation in a hyperopic patient whose innervation for accommodation and its

Fig. 8.4 Early-onset accommodative esotropia in a 1-year-old child

associated obligatory convergence (AC/A ratio) is in proper balance. The second category consists of patients whose hyperopia usually is in the normal range, but in whom the AC/A ratio results in an abnormally high convergence response. Normal and high AC/A ratios are distributed equally among patients with accommodative esotropia [21]. As a third variety, an occasional patient will present an identical clinical picture because of increased effort to overcome an insufficient accommodation ability. The extreme example of this is the aphakic child undercorrected for near vision, who despite loss of the organ of accommodation does not cease to exert neurogenic output in response to hyperopic blur.

Evaluation of accommodative esotropia requires cycloplegic refraction as well as measurement of the fusion-free alignment (e.g., by prism and alternate cover or corneal light reflex estimation). A rapid indicator that there is at least a partial accommodative component can be gained even before knowing the refractive error by observing a response to an empirically chosen +2.50 or 3.00 D that reduces the near deviation below that at distance in the uncorrected state [20].

The preferred drug for cycloplegia is still disputed, with cyclopentolate and atropine each having strong proponents. Using cyclopentolate and examining after the appropriate interval of about 45 min, dynamic retinoscopy (comparing distance and near measurements) will seldom show more than a fractional degree of residual accommodation, giving a reliable result for most patients and obviating the need for multiple instillations, prolonged blur, and systemic side effects associated with atropine.

Amblyopia is uncommon prior to decompensation (see Sect. 8.4.3), unless there is the additional caus-

ative factor of anisometropia. About 30% of cases of accommodative esotropia persist beyond the expected time of resolution of about 10−12 years of age. There are no reliable predictors of this occurrence; these cases show no differences in associated findings from those that do resolve by that time [26].

8.4.2 Management

Purists continue to debate the proper measurement of the AC/A ratio. This should be of minor concern to the practitioner. No method directly measures the simultaneous innervational events of both accommodation and convergence. It is more useful to regard the AC/A as a concept rather than as a quantity. Whether the so-called gradient method is more accurate than the commonly employed distance-near alignment comparison [35] does not stand in the way of appropriate management decisions. Much of the dispute would evaporate if users of the distance-near comparison referred to it as just that, and not as the AC/A ratio.

Discouraging accommodative innervational effort is the cornerstone of management. The goal is to reduce the esodeviation to 8 PD or fewer, a result that allows the development of at least peripheral fusion [16]. Glasses or contact lenses (less usual in the young child) that correct substantially all of the patient's hyperopia are worn during all waking hours. The author's personal guide is to "hit hard, and ease up later." It is unlikely that decompensation (see Sect. 8.4.3) will occur during the subsequent 18 months, allowing for fewer monitoring visits, e.g., every 8−9 months, than is usually advocated [27]. Less secure control requires closer scrutiny.

The controlled patient can receive periodic graded reduction of the initial prescription to facilitate acquiring a gradually expanding amplitude of fusional divergence that will maintain straight eyes under binocular conditions. Reductions are possible only unusually before age 5−6 years. They should not be arbitrary but instead determined by the measurement by simultaneous prism and cover while wearing the intended new power and with accommodation controlled. This need not be confirmed by a corresponding decrease in the cycloplegic measurement of the patient's hyperopia. It is irrelevant whether there is a corresponding change in the cycloplegic refraction, since the aim is to provide the least strength that will maintain proper alignment. It is the author's practice to limit any single reduction to 0.75−1.00 D, even if it appears that more can be tolerated. If successful, the attempt is repeated at 4- to 6-month intervals. Many parents report transitory loss of control shortly after a prescribed reduction, but only occasionally is it necessary to reverse the reduction.

Bifocal additions, initially 2.50−3.00 D, are appropriate for high-AC/A cases, and under the "hit hard" guideline should be part of the original prescription when it is clear that the distance-near comparison calls for this measure, rather than being deferred until the effect of just the distance correction can be determined. It is important that the lower segment be set at about pupillary level, and specific instructions for this should be part of the prescription. Some ophthalmologists have been enthusiastic about progressive-addition "lineless" bifocals [31], but these can cause monitoring difficulties. The bifocal strength can be periodically reduced in the same manner as indicated for the distance correction. While bifocals are no longer needed by age 10 years in many wearers, for some the need persists indefinitely [10].

Topical anticholinesterase "miotic" drugs, whose use in accommodative esotropia depends not on miosis but on facilitation of accommodation, once were considered an equally effective alternative treatment. They are less popular now, in part because of difficulty in obtaining them but also because they proved to be less reliable for diagnosis and were not useful for anisometropia or for incorporation of small degrees of vertical prism that are sometimes needed. These agents were thought to overcome non-compliance with the wearing of glasses, but this often merely substituted one parent−child conflict for another. The author considers the best indication for the use of miotics to be as a temporary measure on occasions when wearing glasses would be awkward, such as in sports or, in older children, for social events. The dangers of retinal detachment and cataract formation from the use of these agents have been overstated for this age group. Pupillary cysts are the principal adverse side effect. They usually regress when the drops are discontinued or when topical 2.5% phenylephrine is included in the regimen.

Most ophthalmologists would decline to substitute extraocular muscle surgery for cases responding to

the measures described above. Very limited exceptions may apply to the patient requiring bifocals for an accommodative esotropia present in near viewing only [13], or in indefinitely persisting cases [11].

8.4.3 Decompensation (Deterioration)

Surgery is indicated when through neglect, non-compliance, or even with all appropriate treatment measures and full cooperation, a previously controlled patient no longer maintains straight eyes. The onset of this decompensation is gradual, distinguishing it from the acute, totally non-accommodative esotropia that can strongly imply serious neurologic disease. Decompensation may not be complete, so that the esotropia still responds, but only partially, to anti-accommodative measures. Decompensation is not a complication, but rather a disappointing, although foreseeable, feature of this entity, with a reported occurrence rate between 13 and 40% in various series [9, 23]. Whether a high AC/A ratio is a predisposing factor is disputable, but onset of accommodative esotropia prior to age 2 years suggests this outcome [4]. Because of normal early binocular visual experience, the existence of the capacity for at least peripheral fusion should be presumed, even when it cannot yet be tested reliably. This reinforces the need for vigorous therapeutic efforts to restore binocular single vision.

Base-out prisms address the sensory consequences but do not restore alignment and are, at best, only a temporary measure. Surgery is required, not to replace glasses but to allow optical treatment of the residual accommodative component to continue to be effective. Medial rectus muscle recessions are the first choice of most ophthalmologists, who adjust their customary quantitative schemes somewhat upward, either adding 0.5−1.0 mm of recession to each medial rectus, averaging the distance and near deviations, or basing the amount on the near esodeviation, which generally is the larger one. Preoperative prism adaptation is useful in planning surgery, not only in this disorder but in other settings as well [28], despite its disadvantages of multiple visits and additional delays. The accommodative portion that persists after surgery has a natural course similar to that of a purely accommodative deviation [24].

8.5 Essential Intermittent Esotropia

This form of comitant esotropia presents as a recurring lapse of control of an underlying esophoria due to tonic imbalance of the horizontal rectus muscles. Fusional divergence amplitudes are unable to comfortably overcome the tendency at all times, particularly during fatigue or ill health. This condition should be distinguished from the acutely presenting esotropia in children or adults that is constant from onset and that raises the suspicion of an abnormal intracranial process calling for neurologic consultation and imaging studies.

8.5.1 Features

Patients with decompensating esophoria usually present at age 10 years or later, in contrast to the much earlier onset of accommodative esotropia. Diplopia and refined stereopsis are common and imply a long period of prior stability. Inferior oblique overaction and DVD are not prominent [14]. The monofixational fusion status occasionally seen may be an adaptation or an independent sensory state [16].

8.5.2 Management

Non-surgical treatment of decompensating esophoria has limitations. Expansion of fusional divergence through orthoptic measures is difficult due to the modest limits of even a normal amplitude and because of the prolonged rigorous effort required. Prisms base out to compensate for most or all of the esophoria can give symptomatic relief but tend to promote further erosion of the patient's own control mechanism [36]. Above-average hyperopia can add an accommodative component to the existing stress on alignment and should be relieved optically.

Surgical correction is indicated when symptoms are severe and non-operative measures are ineffective. Recession of the medial recti or a unilateral recession/resection can be chosen, planned to correct the entire deviation, regardless of whether it is becoming constant or remaining intermittent and symptomatic [14].

8.6 Undercorrected Esotropia

This designation refers to esotropia that continues after an attempt at elimination by surgery. To simplify management, if the undercorrection falls into the range where at least monofixational fusion is possible, i.e., 8 PD [16], it is for practical purposes a satisfactory result and does not require further treatment, as whatever binocular cooperation is possible is unlikely to be improved by a smaller misalignment; in addition, the cosmetic effect usually is acceptable as well.

Larger residual deviations are a different matter. If it was correct to begin the surgical task, it should be completed, provided that the conclusion that an undercorrection has occurred is deferred until it is present after the usual healing period of 6 weeks, as there is no urgency about recovering lost or slipped muscles.

If the undercorrection occurs after bilateral medial rectus weakening, lateral rectus tightening can be the follow-up operation. Prior unilateral recession/resection on one eye can call for the same procedure on the other eye. Some surgeons have supplemented a less than maximal medial rectus recession, ascertained preferably by direct exploration of its position rather than from operative reports (Fig. 8.5), by further weakening, guided by the observation that the effect of the last few millimeters of recession is more profound than that of the first several. This procedure and double marginal myotomy should be last resorts because of their unpredictable results. Posterior fixation has been suggested [33] but is technically difficult if done posteriorly enough to be effective.

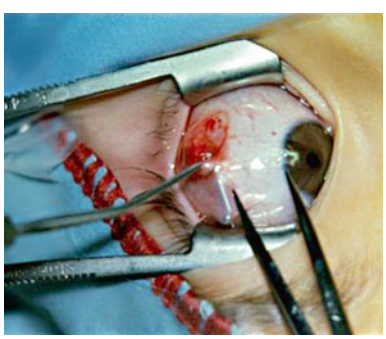

Fig. 8.5 Exploration of extraocular muscle insertion position, through a cul-de-sac incision

8.7 Consecutive Esotropia (Overcorrected Exotropia)

It is generally accepted that initial modest overcorrection of exotropia is desirable because of anticipated postoperative outward drift, and that the likelihood of persisting esotropia is far less than that of recurrent exotropia if the eyes are straight or exodeviated immediately after operation [25]. These observations were derived from patients receiving bilateral lateral rectus recession but are considered generally valid after unilateral recession/resection procedures as well. This type of overcorrection is not related to lateral rectus slippage, as abduction, although often limited just after operation, usually returns to normal quickly.

An occasional variant occurs when even successful correction of the exotropia unmasks an accommodative esotropia of the high AC/A ratio type [22]. One author has suggested that identification of these patients can be aided by determination of the AC/A ratio after occlusion has dispersed proximal fusion [8], but while this is useful for purposes of informed consent, the result is not avoidable by a modifying the surgical scheme.

Regarding management, initial overcorrection is appropriate surgical strategy, but the young patient is susceptible to a poor sensory outcome. As prevention, the author's regimen includes majority-time occlusion for a deviation of more than 20 PD at the first (2−3 days) postoperative visit. Overcorrection of 10−20 PD still present after 2-week calls for continuing occlusion, which in both instances is maintained until alignment is within the range where fusion (mono- or bifixational) is possible. Monitoring is done at 2-week intervals. Initial overcorrections of <10 PD are observed without this treatment. Trying to correct a varying alignment with prisms during this period has been less useful. Accommodation-lowering measures are not employed unless they unequivocally affect alignment immediately, an unusual occurrence.

If the overcorrection has not improved at all in the first 2 postoperative weeks, this suggests its likely permanence; however, at least 6 weeks should be allowed to pass before reaching that conclusion. Treatment requires additional corrective surgery, preferably on muscles not included in the prior pro-

Take Home Pearls

- Binocular vision and moderate grades of stereopsis are possible for congenital esotropia patients if treatment restores proper alignment by age 2 years.
- If present, oblique muscle overactions and A or V patterns should be addressed in the surgical correction of esotropia.
- About 30% of patients with accommodative esotropia retain their disorder beyond the age of expected disappearance. Such cases cannot be reliably predicted.
- Full control of accommodative esotropia should be gained before reducing optical correction to the minimum necessary to maintain straight eyes.
- Surgical correction of decompensated accommodative esotropia should be done for only the non-accommodative portion. Management of the remaining accommodative component is the same as for the patients without decompensation.
- While prism correction may have a role, surgical correction of decompensated esophoria is the most effective treatment for the patient with troublesome diplopia.
- Occlusion to avoid abnormal sensory adaptations in overcorrected exotropia is necessary until either the anticipated "exodrift" occurs spontaneously or further surgery is accomplished.
- When divergence insufficiency esotropia presents acutely, thorough investigation and imaging studies should be obtained.

cedure. Accommodative esotropia unmasked by surgery to correct exotropia is managed as described in Sect. 8.4.2.

8.8 Cyclic (Periodic) Esotropia

The hallmark of this unusual condition is a cycle of straight and crossed eyes, described as "alternate day esotropia" but often with a different interval [37]. The cycles are strictly repetitive, unlike the early variability of accommodative and essential intermittent esotropia. The condition usually is benign but has been observed in children and adults with central nervous system disease [19].

8.8.1 Features

Inferior oblique overaction, dissociated vertical deviation, and motor nystagmus are not characteristic of this entity. Abduction is not limited either in the straight or the esotropic phase. Adults may experience diplopia, but children usually have no symptoms. When the condition is still cyclic, the eyes are usually not misaligned long enough so that ambly-

opia or loss of fusion is a concern, unless there is anisometropia. Most such patients finally evolve to a constant esotropia.

8.8.2 Management

There are no effective non-surgical measures. Surgery is required and is equally effective whether done in the cyclic or the constant state [37]. The surgeon's preferred procedure for other types of esotropia is appropriate here as well.

8.9 Divergence Insufficiency

The term *divergence insufficiency* most often does not indicate a true abnormality of divergence, but rather is a shorthand description of an esodeviation that is larger at distance than at near. This is a somewhat unusual presentation in an untreated case; it is more to be expected in an undercorrected esotropia patient when the prior operation has been recession of the medial recti.

8.9.1 Features

Especially when associated with the sudden onset of diplopia, a deviation with these characteristics suggests divergence paralysis and the possibility of prior head trauma, or an intracranial abnormality with or without elevated intracranial pressure [30]. This pattern is also seen in unilateral or bilateral sixth cranial nerve paralysis, in which observable abduction deficiency is present and/or the esotropia in right and left gazes is greater than in the primary position. Unless clearly long standing and asymptomatic, this condition calls for neurologic investigation and appropriate imaging studies [7].

8.9.2 Management

Base-out prisms may be of limited help. For cases in which the designation is descriptive only, surgery is more effective and usually emphasizes lateral rectus tightening. The author has noted that such patients may also show a usually modest A pattern, for which horizontal rectus displacement upon reinsertion is appropriate.

References

1. Archer SM, Sondhi N, Helveston EM (1989) Strabismus in infancy. Ophthalmology 96:133–137
2. Birch E, Stager D, Wright K et al. (1998) The natural history of esotropia during the first six months of life. J AAPOS 2:325–328
3. Birch EE, Fawcett SL, Stager DR Sr (2002) Risk factors for the development of accommodative esotropia following treatment for infantile esotropia. J AAPOS 6:174–181
4. Dickey CF, Scott WE (1988) The deterioration of accommodative esotropia. Frequency, characteristics, and predictive factors. J Pediatr Ophthalmol Strabismus 25:172–175
5. Donahue SP (2007) Pediatric strabismus. N Engl J Med 356:1040–1047
6. Ing MR (1983) Early surgical alignment for congenital esotropia. Ophthalmology 90:132–135
7. Jacobson DM (2000) Divergence insufficiency revisited: natural history of idiopathic cases and neurologic associations. Arch Ophthalmol 118:1237–1241
8. Kushner BJ (1999) Diagnosis and treatment of exotropia with a high accommodation convergence-accommodation ratio. Arch Ophthalmol 117:221–224
9. Ludwig IH, Imberman SP, Parks MM (2005) Long-term study of accommodative esotropia. J AAPOS 9:522–526
10. Ludwig IH, Parks MM, Getson PR (1989) Long-term results of bifocal therapy for accommodative esotropia. J Pediatr Ophthalmol Strabismus 26:264–270
11. Lueder GT, Norman AA (2006) Strabismus surgery for elimination of bifocals in accommodative esotropia. Am J Ophthalmol 142:632–635
12. McNeer KW, Tucker MG, Spencer RF (1997) Botulinum toxin management of essential infantile esotropia in children. Arch Ophthalmol 115:1411–1418
13. Millicent M, Peterson W, Buckley EG (1997) Medial rectus fadenoperation for esotropia only at near fixation. J AAPOS 1:129–133
14. Molarte AB, Rosenbaum AL (1991) Clinical characteristics and surgical treatment of intermittent esotropia. J Pediatr Ophthalmol Strabismus 28:137–141
15. Mohney BG (2001) Common forms of childhood esotropia. Ophthalmology 108:805–809
16. Parks MM (1969) The monofixation syndrome. Trans Am Opthalmol Soc 67:609–657
17. Pediatric Eye Disease Investigator Group (2002) The clinical spectrum of early-onset esotropia: experience of the Congenital Esotropia Observation Study. Am J Ophthalmol 133:102–108
18. Pickering JD, Simon JW, Ratliff CD et al. (1995) Alignment success following medial rectus recessions in nor-

mal and delayed children. J Pediatr Ophthalmol Strabismus 32:225–227
19. Pillai P, Dhand UK (1987) Cyclic esotropia with central nervous system disease: report of two cases. J Pediatr Ophthalmol Strabismus 24:237–241
20. Raab EL (1972) The +3.00 test in esodeviations. J Pediatr Ophthalmol 9:207–210
21. Raab EL (1982) Etiologic factors in accommodative esodeviation. Trans Am Ophthalmol Soc 80:657–694
22. Raab EL (1985) Consecutive accommodative esotropia. J Pediatr Ophthalmol Strabismus 22:58–59
23. Raab EL (1989) Outcome of deteriorated accommodative esotropia. Trans Am Ophthalmol Soc 87:185–196
24. Raab EL (1991) The accommodative portion of mixed esotropia. J Pediatr Ophthalmol Strabismus 28:73–76
25. Raab EL, Parks MM (1969) Recession of the lateral recti. Early and late postoperative alignments. Arch Ophthalmol 82:203–208
26. Raab EL, Spierer A (1986) Persisting accommodative esotropia. Arch Ophthalmol 104:1777–1779
27. Raab EL (2001) Follow-up monitoring of accommodative esotropia. J AAPOS 5:246–249
28. Repka MX, Connett JE, Scott WE et al. (1996) The one-year outcome after prism adaptation for the management of acquired esotropia. Ophthalmology 103:922–928
29. Rosenbaum AL, Santiago AP (1999) Clinical strabismus management. Principles and surgical techniques. Saunders, Philadelphia, pp 552–555
30. Schanzer B, Bordaberry M (1998) The child with divergence paresis. Surv Ophthalmol 42:571–576
31. Smith JB (1985) Progressive-addition lenses in the treatment of accommodative esotropia. Am J Ophthalmol 99:52–62
32. Stein LA, Ellis FJ (1997) Apparent contralateral inferior oblique muscle overaction after unilateral inferior oblique muscle weakening procedures. J AAPOS 1:2–7
33. Noorden GK von (1982) An alternative to marginal myotomy. Am J Ophthalmol 94:285–289
34. Noorden GK von (1988) A reassessment of infantile esotropia. XLIV Edward Jackson Memorial Lecture. Am J Ophthalmol 105:1–10
35. Noorden GK von, Campos EC (2002) The near vision complex. In: Binocular vision and ocular motility: theory and management of strabismus, 6th edn. Mosby Year-Book, St. Louis, pp 89–92
36. Noorden GK von (ed) (2002) Esodevations. In: Binocular vision and ocular motility: theory and management of strabismus cyclic heterotropia, 6th edn. Mosby Year-Book, St. Louis, pp 313–314
37. Noorden GK von (ed) (2002) Special forms of strabismus. In: Binocular vision and ocular motility: theory and management of strabismus, 6th edn. Mosby Year-Book, St. Louis, pp 480–482
38. Vroman DT, Hutchinson AK, Saunders RA et al. (2000) Two-muscle surgery for congenital esotropia: rate of reoperation in patients with small versus large angles of deviation. J AAPOS 4:267–270
39. Wilson ME, Parks MM (1989) Primary inferior oblique overaction in congenital esotropia, accommodative esotropia, and intermittent exotropia. Ophthalmology 96:950–955

Exotropic Deviations

Burton J. Kushner

9

Contents

Core Messages

- Exotropic deviations include exophoria, infantile exotropia, sensory exotropia, consecutive exotropia, intermittent exotropia, and dissociated horizontal deviation.
- The decision whether to treat should be based on control, and how to treat is based on the magnitude of the deviation.
- Burian's classic treatment recommendations and classification of exotropia are based on some assumptions that are probably incorrect. They need not be strictly followed.
- Intermittent exotropes with a true high AC/A ratio are uncommon but do exist. Standard surgery based on the distance angle frequently results in an overcorrection at near.
- Patients with fusional convergence insufficiency are different from exotropes with accommodative convergence insufficiency; the latter have a low or absent AC/A ratio and are difficult to treat surgically; the former do well with orthoptic exercises.
- Patients with intermittent exotropia and monofixation syndrome have a poorer sensory outcome after surgery.

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9.1 Prevalence and Epidemiology

Exodeviations occur about one third as frequently as esodeviations, are more frequent in females than males, and have a higher prevalence in sunnier latitudes [18, 19, 29]. Exodeviations also occur more frequently in children with craniofacial anomalies (Fig. 9.1), neurologic impairment, or if there was a history of maternal smoking during pregnancy [13, 20]. There is probably a genetic component to the development of exotropia; however, it is most likely multifactorial [27].

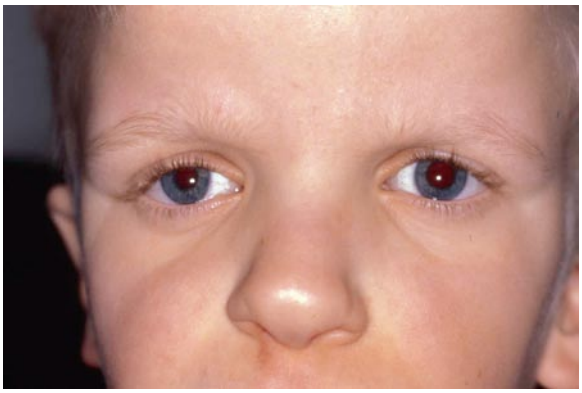


Fig. 9.1 This boy has an exotropia shown here with his right eye deviating. He was born with multiple congenital anomalies and craniofacial abnormalities

9.2 Etiology and Classification

Historically there has been disagreement about the etiology of exotropia. Theories have included an imbalance of the normal reciprocal relationship between convergence and divergence, mechanical and anatomic factors, and a combination of the two [55].

Traditionally exodeviations have been classified according to the relationship between the distance and near deviation. Burian's modification of Duane's classification is classic, [9, 10, 11, 17]; however, it implies some etiologies that are probably incorrect [34, 37, 38, 41]. In spite of this, these categories are descriptive and have some clinical utility. They are:

1. Convergence Insufficiency Pattern: The distance deviation is at least 10 prism diopters (PD) less than the near deviation.
2. Basic Exodeviation: The distance deviation is within 10 PD of the near deviation.
3. True Divergence Excess Pattern: The distance deviation exceeds the near deviation by at least 10 PD.
4. Simulated Divergence Excess Pattern: Initially the distance deviation exceeds the near deviation by at least 10 PD; however, special tests to suspend near fusion reveal a near deviation that will be within 10 PD of the distance deviation.

This classification has more recently been modified by Kushner to include the role played by the fusional mechanism as well as accommodative convergence (see Sect. 9.4.5.6 for further discussion) [34, 37, 38, 39, 41].

9.3 Sensory Adaptation

With intermittent exotropia, suppression is typically facultative. This means that when the eyes are aligned there is no suppression, and when the deviation becomes manifest the deviating eye is suppressed. The suppression scotoma may be regional in that it can include the fovea and much of the periphery. All the visual field of the deviating eye that overlaps the fixing eye may be suppressed [24, 25, 50, 51]. Of great clinical importance is the fact that most exotropic patients suppress while the image of regard falls on temporal retina of the deviating eye, but immediately see double if the image falls on nasal retina. This has important implications for the management of exotropia, as many patients will have persistent diplopia if they are permanently overcorrected surgically. Results of testing for retinal correspondence are inconsistent in exotropes. Many patients with intermittent exotropia have normal fusion with 40 s of stereopsis when they are aligned, and manifest suppression with no stereopsis when tropic.

Some patients with exotropia will experience panoramic vision (a wider binocular field) when tropic. In fact, unlike patients with esotropia who experience an expansion of their binocular visual field after surgery, some exotropes will indicate that they miss this wider field of vision after successful surgery. Von Noorden described the interesting case of an exotro-

pic rural mail carrier who was unhappy after his eyes were successfully aligned surgically [59]. Prior to surgery, he was able to watch the road with his dominant left eye, and simultaneously scan the mailboxes at the roadside with his right eye. After surgery, his binocular field was reduced to a normal range, but he missed the ability to use this panoramic vision.

9.4 Types of Exodeviations

9.4.1 Exophoria

An exophoria is a latent exodeviation that, by definition, is only manifest in the dissociated state, e.g., under cover, or with red-green glasses. Many adults have small-angle exophorias that are clinically insignificant, and they do not need treatment. Depending on the magnitude of the deviation and the patient's fusional convergence amplitudes, an exophoria may cause headache or asthenopia. In this situation, orthoptic exercises or prisms incorporated in spectacles may be helpful. It is important to optimize visual acuity with a careful refraction, and to correct any anisometropia. If a patient reports intermittent diplopia, the deviation must be intermittently manifest and hence is an intermittent tropia instead of a phoria.

9.4.2 Infantile Exotropia

Infantile (or congenital) exotropia shares many features with infantile esotropia, and some important differences. It is characterized by a constant exotropia that is present by 6 months of age. The deviation is often large, in the range of 35−60 PD; however, smaller deviations may be found. It is much less common than infantile esotropia and is much more likely to be associated with neurologic problems or developmental delay (Fig. 9.2). The child's primary care doctor should be alerted to this frequent association and should pay careful attention to the child's developmental milestones. If there is any doubt, referral to an appropriate specialist is advised. The guidelines for treating infantile exotropia are similar to those recommended for infantile esotropia; however, they are not based on as sound clinical data due to the relative infrequent occurrence of this disorder. These guidelines include providing proper optical correction if appropriate, treating amblyopia, and operating to restore alignment. This should be done between 6 months and a year of age, provided that there are no medical or neurologic issues that require prior attention. A standard surgical formula for other forms of exotropia can be used to treat infantile exotropia; however, many surgeons prefer to not exceed 7 mm for bilateral lateral rectus recessions in infants. Sensorially, patients with infantile exotropia are similar to those with infantile esotropia. They typically develop subnormal fusion with deficient stereopsis, even after successful surgical realignment, and they have a high incidence of subsequently developing dissociated vertical divergence and dissociated horizontal deviations [22, 60].

9.4.3 Sensory Exotropia

The normal anatomic configuration of the orbits tends to favor an exotropic position. If there is unilateral or bilateral vision impairment the fusion reflex will be impeded, and these anatomic factors will tend to cause an exotropia. This is referred to as a sensory

Fig. 9.2 This 5-month-old child has a constant exotropia, shown here with her right eye deviating, that was present since 2 months of age. She had been born prematurely and subsequently was found to have periventricular leukomalacia

exotropia, because it results from a sensory disruption. Sensory exotropia is seen with congenital monocular media opacity and other causes of congenital monocular vision loss. It also occurs later in life after vision loss from trauma, monocular media opacity, as well as other causes of acquired vision loss.

9.4.4 Consecutive Exotropia

When a formerly esotropic patient develops an exotropia, they are said to have a consecutive exotropia. Most commonly this occurs as a result of prior surgery for esotropia. If a patient with a consecutive exotropia has good fusion potential, and if the deviation is small, orthoptic exercises to improve convergence may be helpful. Many patients can be managed optically by a small decrease in their hyperopic correction, or overcorrecting any myopia (see Sect. 9.4.5.4 for further explanation), possibly combined with base in prism. If the deviation is large, or if the patient's age and accommodative amplitudes make this type of optical manipulation impractical, surgery is generally necessary. If a consecutive exotropia follows esotropia in a child with substantial hyperopia, decreasing the plus power of their spectacles by three or more diopters may be an appropriate temporizing measure; however, typically this is not a long-term cure [36]. As the child gets older he or she will need an increasing amount of the hyperopia corrected optically. When that happens the consecutive exotropia will recur. In addition, many patients with substantially undercorrected hyperopia or overcorrected myopia show variability of their alignment, depending on whether they are fully accommodating or relaxing their accommodation at any given moment.

In general, guidelines for operating on other types of exotropia can be applied to patients with consecutive exotropia, provided that versions are full and there are no limitations of rotation. If so, either a slippage of a previously recessed medial rectus muscle, or a restriction of a resected lateral rectus muscle, should be suspected and addressed surgically. If versions are full, the patient can often be treated as a "fresh case," and previously unoperated muscles can be operated upon as is appropriate for the patient's motility pattern. However, it has been reported that if the near deviation exceeds the distance deviation by even a few prism diopters in a consecutive exotrope, symmetric lateral rectus recession results in a high undercorrection rate [35]. This finding should be taken as a subtle sign of medial rectus underaction. The previously recessed medial rectus muscles should be explored and advanced.

9.4.5 Intermittent Exotropia

9.4.5.1 Presentation

Most cases of intermittent exotropia present between 18 months and 4 years of age; however, presentation at younger or older ages can occur. In the majority of patients it is characterized by an intermittent outward drifting of one eye, but free alternation with either eye intermittently drifting does occur. Typically the child does not report diplopia because they suppress the eye when it deviates. The deviation is characteristically worse when the child is outdoors or viewing distant objects, and initially the deviation is minimal or absent at close fixation. For this reason, intermittent exotropia is often overlooked by primary care physicians who typically do not have access to long examination lanes. Many children with intermittent exotropia tend to close their non-dominant eye in bright sunlight. This sensitivity to light is termed *photalgia.* It has been thought that eye closure is a mechanism to avoid diplopia; however, because many patients continue to exhibit photalgia with eye closure after successful surgical correction of the exotropia, this explanation is probably incomplete. Also, photalgia may be present in some individuals with normal ocular motility; however, it is more prevalent in patients with intermittent exotropia. Parents should be told prior to surgery that squinting in sunlight may persist despite a successful outcome.

Many patients with intermittent exotropia deteriorate over time, both with respect to the magnitude of the deviation and the frequency with which it manifests [1, 46]. When this occurs, it tends to do so slowly. Consequently, there is often no urgency for treatment. Although many children with intermittent exotropia are asymptomatic, some report intermittent diplopia, asthenopia, or headaches. If present, these symptoms may imply the need for earlier interven-

tion. Such complaints are more likely to be reported by adults with intermittent exotropia than children.

Most intermittent exotropes have normal visual acuity with appropriate optical correction. Amblyopia is uncommon unless anisometropia is present. Stereopsis is frequently normal when the eyes are aligned, and it is absent when the tropia is manifest (Fig. 9.3). Retinal correspondence is frequently normal; however, anomalous retinal correspondence can occur. Suppression is typically facultative in that it is present when the eyes are tropic and absent when the eyes are aligned. As discussed previously, if the image of regard falls on the temporal retina of the deviating eye, suppression is apt to occur. Once suppression is triggered, it probably involves all of the retina of the deviating eye that corresponds to the fixing eye, or else peripheral diplopia would be present. Conversely, if the image of regard falls on nasal retina of the non-fixing eye, suppression does not occur, and diplopia is present. For this reason the suppression in intermittent exotropia is described as having a hemiretinal trigger [50]. Approximately 20% of patients exhibit the findings of the monofixation syndrome (see Sect. 9.4.5.9 for more details) [3, 48].

9.4.5.2 Motility Exam

Patients with intermittent exotropia may have varying degrees of control over their deviation, depending on time of day, fatigue, and general state of health. If a child with intermittent exotropia is ill or unduly tired at the time of the examination, this should be noted to help with future assessment of progress or deterioration. Prolonged occlusion of either eye may dissociate the patient to the degree that they may have a hard time regaining control over the exotropia; thus, one should assess ocular motility before checking visual acuity.

Because many patients with intermittent exotropia have good visual acuity in both eyes and may control the deviation well during the examination, it may be difficult to determine which is the habitually deviating eye. Sometimes parents are unsure. This can be determined in most cases by observing the refixation behavior of each eye. If the habitually deviating eye is occluded and allowed to deviate, and the occluder is removed, there will be a slow refixation movement of that eye. There will be no movement of the contralateral dominant eye. On the other hand, if the habitually fixing eye is occluded and allowed to deviate, and the occluder is removed, the dominant eye will briskly adduct to pick up fixation. Simultaneously the non-dominant eye will briskly move to an exotropic position and then slowly converge to refixate.

In general, the magnitude of the deviation will determine *what* treatment is needed if the strabismus requires treatment, but the frequency of the deviation determines *if* treatment is needed. A large angle of strabismus that is infrequently manifest may not need intervention. A smaller angle of strabismus that is frequently manifest should be treated. Therefore, in addition to measuring the magnitude of the deviation with the prism and alternate cover test, some assess-

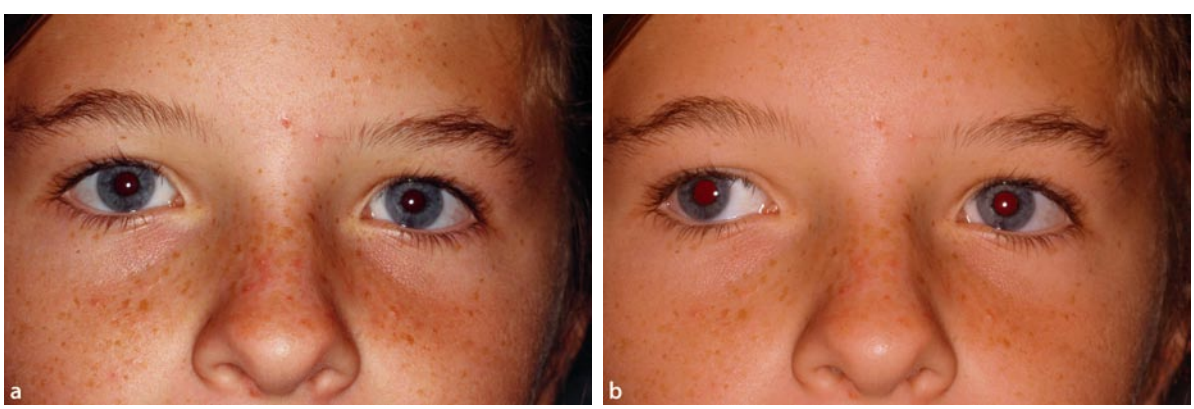


Fig. 9.3a,b This girl has an intermittent right exotropia. **a** When her eyes are aligned she has good fusion and 40 s of stereopsis. **b** When she manifests the exotropia she suppresses her right eye and has no stereopsis

ment should be made of the patient's control of the deviation. This in turn is a reflection of how often the eye deviates. Each clinician should develop his or her own set of criteria for assessing control. In addition, parental or caregiver assessment of control can be helpful in determining how frequently the deviation is manifest on a day-in day-out basis. One useful set of guidelines are listed in Table 9.1. Distance stereoacuity testing has been shown to provide an objective assessment of control and fusion [58]. Normal distance stereoacuity indicates good control and little suppression. Many clinicians, however, do not have ready access to distance stereoacuity testing. There is a need for a better objective way to assess control in patients with intermittent exotropia.

9.4.5.3 Distance–Near Differences

A comparison of the distance and near measurements plays an important role in the management of intermittent exotropia. For esotropic patients, the difference between the distance and near angle of misalignment can usually be attributed to the normal linkage between accommodation and convergence as manifest by the accommodative convergence to accommodation (AC/A) ratio. This is not the case for patients with intermittent exotropia. Many intermittent exotropes have a slow-to-dissipate fusional mechanism at near fixation which masks an underlying larger deviation and prevents it from becoming manifest with a simple cover test. This has been called *tenacious proximal fusion* (TPF) [34, 39]. In 1952 Scobee pointed that intermittent exotropes must undergo a prolonged period of monocular occlusion to unmask the full deviation at near [57]. Initially Scobee recommended 24 h of monocular occlusion; however, subsequently it was determined that 45−60 min was sufficient [32, 45]. This post-occlusion measurement must be made with one or the other eye constantly occluded. If the patient is permitted fixate binocularly for even a moment, the effect of the prolonged occlusion may be negated. Although some investigators have attributed most distance-near differences in intermittent exotropia to the AC/A ratio [6, 12, 25]. more recent studies suggest that is not the case [15, 16, 39]. Cooper and co-workers [15], and Kushner and Morton [39], have pointed out that AC/A ratios in patients with intermittent exotropia can be calculated in all the usual manners, provided that any near measurement used in the calculation be made after prolonged monocular occlusion to eliminate the contaminating effect of TPF. Consider the following patients:

Case 1. A child has an intermittent exotropia that initially measures 30 PD at 6 m and 10 PD at approximately 0.33 m. After 1 h of monocular occlusion, the near measurement is 30 PD of exotropia. Bilateral lateral rectus recessions resulted in orthophoria for distance and near. This example is a realistic representation of a very commonly encountered patient. If one calculates the AC/A ratio with the heterophoria method using the pre-occlusion near measurement of orthophoria for the calculation, the AC/A would be high. Depending on the exact size of the patient's inter-pupillary distance, it would be approximately 12/1. After surgery, the AC/A would be normal with a value of approximately 5/1. If this pre-operative calculation of the AC/A was valid, one would be left

Table 9.1 Assessment of control of intermittent exotropia

	Assessment at home by caregiver	Assessment in office examiner
Excellent	Exotropia seen rarely, is mainly with fatigue or inattention, and only at distance	Exotropia only present after cover test; recovery occurs rapidly and prior to a blink or refixation
Good	Exotropia up to five times a day, but only at distance. Eye only stays deviated for brief periods	Exotropia only present after cover test; recovery is not immediate but occurs in 5−10 s and prior a blink or refixation
Fair	Exotropia occurs more than five times a day, may persist for longer periods, but is still only at distance	Exotropia occurs spontaneously but intermittently. It does not persist past a blink Recovery often requires a blink or refixation
Poor	Exotropia is frequent, for prolonged periods, and occurs at near and distance	Exotropia occurs spontaneously and frequently and may persist through a blink

with the conundrum that weakening the lateral rectus muscles decreased the AC/A ratio. This would not make sense. However, if one uses the post-occlusion near measurement of 30 PD for the calculation, it would appear the AC/A ratio was normal before and after surgery. This is a much more credible scenario.

Much attention has been paid in the past to the use of +3.00 D lenses at near to uncover a masked deviation, and some have utilized this as a substitute for prolonged monocular occlusion for classifying intermittent exotropia [6, 7]. However, as Helveston has pointed out, monocular occlusion and +3.00 D lenses work differently [21]. Monocular occlusion suspends fusional convergence and +3.00 D lenses suspend accommodative convergence. The use of +3.00 D lenses can be useful for assessing the near measurement to calculate the AC/A ratio, provided that they are used *after* prolonged monocular occlusion. Consider this example:

Case 2. A child has an intermittent exotropia that measures 30 PD at 6 m and is orthophoric at approximately 0.33 m, which increases to 30 PD with +3.00 D lenses. After 1 h of monocular occlusion, the near measurement is 30 PD, and with +3.00 D lenses *after* prolonged occlusion, the near deviation is 35−40 PD.

If one calculated the AC/A ratio using the pre-occlusion measurements, the 30-PD increase in the near deviation with +3.00 D lenses would indicate a high AC/A ratio of 10/1; however, if one bases the calculation on the near measurement after occlusion, it only increased 5−10 PD with the additional +3.00 D lenses, and hence indicates more normal AC/A ratio. This is an example of a pseudo-high AC/A ratio.

There is a relatively uncommon subset of patients with intermittent exotropia that have a truly high AC/A ratio [34, 39, 41]. They can be diagnosed by the usual methods for calculating AC/A ratios, provided that all near measurements for the calculation be made *after* prolonged monocular occlusion. Consider the following patient:

Case 3. A child has an intermittent exotropia that measures 30 PD at 6 m and is orthophoric at approximately 0.33 m. After 1 h of monocular occlusion, he is still orthophoric at near. With +3.00 D lenses at approximately 0.33 m *after* monocular occlusion, the near measurement is 30 PD. In addition, the distance deviation decreases to 20 PD when measured with an additional –1.00 D.

Case 3 has a true high AC/A ratio as determined with both the +3.00 D lens test at near after prolonged occlusion, and the minus lens test in the distance. In addition, patients such as this often show a small esophoria if tested at a very near distance such as 3 or 4 in. Intermittent exotropes who do not have a truly high AC/A ratio typically show and exophoria at very near range, as the fixation target is closer than their near point of convergence. As is described in Sect. 9.4.5.6, it is important to identify intermittent exotropes with a high AC/A ratio before planning treatment, as they need to be managed differently than other patients.

9.4.5.4 Non-Surgical Management

Many patients with intermittent exotropia can be managed non-surgically. The first and perhaps most important step is to institute proper optical management. If a child has a low and symmetric hyperopic refractive error, no glasses are necessary. Unequal vision inputs are extremely destabilizing for patients with intermittent exotropia [28, 35]; thus, any significant astigmatism or anisometropia should be corrected. Also, myopic refractive errors should be corrected.

Many young intermittent exotropes can be managed with overcorrecting minus-lens therapy. This involves incorporating 1.5 or 2 D of additional minus-lens correction in their spectacles. This stimulates accommodative convergence and improves control over the deviation [12]. Caltreider and Jampolsky [12] initially recommended up to 3 diopters of over-minus therapy. I have found that by also incorporating 2.5 or 3 PD of base in prism in each lens, one can obtain the same control with less minus-lens power, and the latter is tolerated better by patients. Because many intermittent exotropes are myopic, and because myopia normally progresses in children, some have speculated that overcorrecting minus-lens therapy causes myopia to worsen. In my own experience, I have found this not to be the case [40].

In most children, minus-lens and prism therapy are only temporizing measures that allow one to defer surgery for several years. On occasion they provide a lasting cure. Although these treatments are useful in younger children, by the time a child is a teenager he or she often does not tolerate them.

For the same reason that anisometropia should be corrected in intermittent exotropia, monovision should be avoided [35, 42]. Consider the following two cases which point out the importance of properly balanced optical correction.

Case 4. This woman had a well-controlled intermittent exotropia since childhood. She was myopic with approximately -3.00 D in each eye and was prescribed monovision contact lenses at age 45 years to treat presbyopia. This resulted in her exotropia decompensating. She underwent strabismus surgery at 46 years of age, initially with a good result. Her strabismus recurred and within 1 year she underwent a re-operation. Again she initially had a good result which only lasted 6 months. When I saw her for the first time at 47 years of age she had a poorly controlled intermittent exotropia of 25 PD. I took her out of monovision and prescribed a bifocal. Her exotropia immediately improved and within 1 year her tropia converted to an exophoria of 10 PD which has been well controlled and asymptomatic for 9 subsequent years.

Case 5. A 4-year-old boy presented with a poorly controlled left esotropia of 20 PD. He was anisometropic with a refractive error of OD plano sph and OS -2.50 sph, which was prescribed.; however, the optician had made a mistake. He reversed the prescription and dispensed the -2.50 sph for the right eye and plano sph for the left eye. Although this had the child in over-minus therapy for his fixing eye, his angle of strabismus increased to 30 PD and his control decompensated. The deviation became constant. The error in the prescription was then corrected. One month after he received his proper glasses, he was controlling a 10 PD exophoria.

The foregoing examples point out how crucial optical management can be.

There are some high hyperopes (usually over 5 D) with intermittent exotropia who will control their deviation better if most of their hyperopia is corrected [23]. At first this seems counter-intuitive, as one would think that the accommodation needed with uncorrected hyperopia would help control the deviation; however, dynamic retinoscopy in these patients reveals that they are in fact not fully accommodating and are experiencing blur. This in turn destabilizes their fusion and worsens the deviation. Guidelines for these patients include correcting most of the hyperopia by leaving approximately one diopter uncorrected, and fully correcting astigmatism.

For younger children, occlusion therapy is very effective in improving a their control over an intermittent exotropia, even if they are not amblyopic [14, 54, 59]. A useful protocol is to start patching approximately 3−4 h a day. If the child freely alternates, it should be done on alternate eyes on alternate days. If there is a fixation preference, but no amblyopia, a program of patching 2 or 3 days over one eye and 1 day over the other, in sequence, is advised. If amblyopia is present, patching should be used to treat it in the usual manner. This treatment almost always results in an initial improvement in both the size and control of the deviation within a month or so. If so, the occlusion should be tapered over a month or two and then discontinued. Occasionally the effect is curative. More often, the deviation recurs over a number of months or years. In this case, the treatment can be repeated, and overcorrecting minus-lens therapy can be added. Although either overcorrecting minus-lens and occlusion therapy are more often temporizing than curative, there are situations in which one may wish to delay surgery, as indicated in Sect. 9.4.5.5. Also, some parents may wish to try non-surgical treatments before feeling comfortable with a recommendation for surgery. The mechanism by which occlusion therapy works is thought to be due to the anti-suppression effect of patching; however, that explanation is probably incomplete as it does not explain why the angle of deviation typically improves, as well as the control. Occlusion therapy in this manner is most useful in ages that parallel the ages at which amblyopia treatment is most successful. It usually is effective in young children and becomes less effective by 7 years of age.

In older cooperative patients with small-angle intermittent exotropia, orthoptic exercises to improve convergence can be useful.

9.4.5.5 Surgical Management

If control over an intermittent exotropia is deteriorating to an unsatisfactory level, and non-surgical means are not successful, surgery should be considered. Many people use the guideline that surgery is indicated if the deviation is present 50% of the time or more; however, this is quite hard to determine clinically [59]. The appropriate age at which to perform surgery has been the subject of some controversy.

Jampolsky recommended delaying surgery in visually immature children because even a short duration of an esotropia after surgery may result in a loss of bifoveal fusion [25, 27]. Until the child is visually mature, the deviation can be controlled with occlusion therapy and minus lenses. Other authors have recommended early surgery [31, 49, 53]. Although studies suggest poorer sensory results in children operated under 4 years of age, [4] it is impossible to tell if children who need surgery at an earlier age have a poorer underlying fusional mechanism pre-operatively than those who decompensate later. Nevertheless, at least some infants with early decompensation have the potential for bifixation after early surgery [56]. It seems prudent to defer surgery in a visually immature child if adequate control can be maintained with non-surgical means, and to operate early if it cannot be.

If a patient had been previously managed with overcorrecting minus-lens therapy, or if their hyperopia had been intentionally undercorrected, and surgery is now planned, the patient should be measured in proper optical correction prior to the operation.

The goal of surgery is to have an overcorrection of approximately 10 PD on the day after surgery [50]. This will prevent suppression from occurring in the immediate post-operative period and also compensate for the exotropic drift that typically occurs. If this desired overcorrection occurs, the patient will usually have diplopia, and patients should be advised of this possibility before surgery. Patients who are slightly undercorrected, or are in fact orthophoric immediately after surgery, have a poorer long-term prognosis than those in whom this overcorrection occurs [47]. If the overcorrection persists for more than several weeks, it can be managed by occlusion, prisms, miotics, or a combination of all three.

9.4.5.6 The Role of Distance–Near Differences in the Planning of Surgery

Burian recommended that surgery be based on his classification of distance-near differences [8–10]. Because he felt that symmetric lateral rectus recessions gave more correction at distance than near, he recommended that operation for treating divergence excess patterns. He felt that unilateral recess–resect surgery gives equal correction at distance and near, and advocated it for basic patterns. In addition, he believed that simulated divergence excess patterns really had a deviation at near that equaled the distance, albeit masked, and thus felt they also should be treated with a recess–resect procedure. For the convergence insufficiency patients he advocated bilateral medial rectus resections based on the belief that they provided more correction at near than distance. Although this is a time-honored algorithm, the validity of its recommendations has been called into question [38].

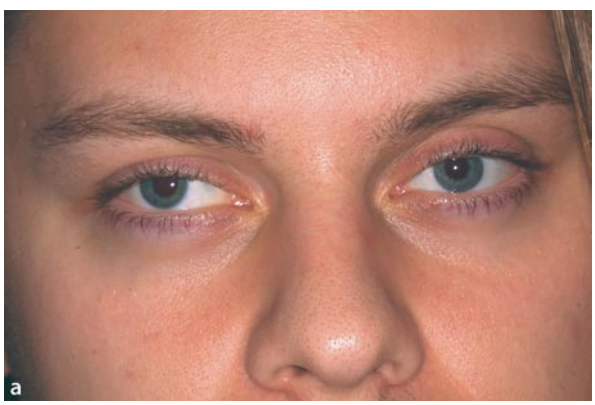
A newer classification of intermittent exotropia relies more on the role of the strength of near fusional mechanism and accommodative convergence. A comparison of the two classification systems is shown in Table 9.2. This newer system does not consider a patient in whom the distance exotropia exceeds the near deviation as having an excess of divergence, but rather as having strong near convergence or TPF that masks an underlying near deviation. There are compelling reasons that suggest such a patient does not have an excess of divergence. Typically such a patient will have approximately 30 PD more exotropia when under deep anesthesia with pharmacologic paralysis than they have in the awake state at distance fixation (Fig. 9.4) [2]. One cannot attribute the distance deviation to an excess of divergence, if the deviation is even larger when all neuromuscular tonus is eliminated.

Surgery according to this newer classification is predicated on the concept that the presence of TPF implies a stronger fusional mechanism, and allows the surgeon to choose his or her preferred operation, either lateral rectus recessions or a recess–resect procedure. On the other hand, if the distance and near deviations are the same, TPF is absent and fusion is not as strong. In this case a recess–resect procedure is preferred because of its stabilizing effect and the incomitance it produces initially. With symmetric surgery, an undercorrected patient is typically undercorrected in all gaze fields; however, with a recess–resect procedure, an undercorrected patient may still be esotropic in side-gaze toward the recessed muscle. This helps break up suppression but may induce bothersome diplopia in side-gaze. The validity of these newer surgical recommendations were confirmed in a clinical trial which revealed that patients with basic patterns had better outcomes with recess–resect procedures as Burian had advocated; however, it also

Table 9.2 Burian and Kushner's classification of intermittent exotropia

Burian's classification	Burian's treatment recommendations	Kushner's classification	Kushner's treatment recommendations
Divergence excess	Recess LROU	Proximal convergence *or* High AC/A	Recess LROU Optical management
Simulated divergence Excess (based on monocular occlusion)	Recess–resect	Tenacious proximal fusion	Recess LROU or recess–resect (surgeon's choice)
Simulated divergence Excess (based on +3.00 D at near)	Recess–resect	Tenacious proximal fusion with pseudo-high AC/A[a] *or* High AC/A[b]	Recess LROU or recess–resect (surgeon's choice) Optical management
Basic	Recess–resect	Basic	Recess–resect or recess LROU with augmented formula
Convergence insufficiency	Resect MROU	Accommodative convergence insufficiency (low AC/A)	Recess LROU for distance angle with inferior transposition, or recess–resect for distance angle

[a] If near measurement also increases with prolonged occlusion
[b] If near angle does not increase with prolonged occlusion alone but then does with +3.00 D



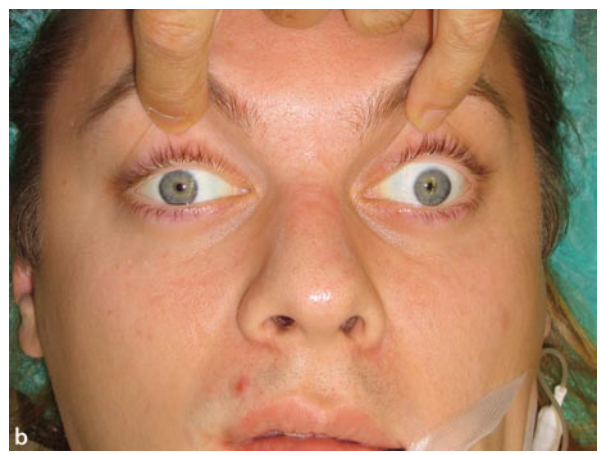


Fig. 9.4a,b This patient has an exotropia in which the distance deviation greatly exceeds the near. This is a divergence excess pattern according to the Burian classification. **a** In the awake state with distance fixation he measures 30 PD of exotropia. **b** Under anesthesia with pharmacologic paralysis his exotropia is substantially greater

showed that patients which Burian would classify as simulated divergence excess did as well with lateral rectus recessions as with recess–resect procedures [38]. A recent study suggested that patients with a basic pattern do well with lateral rectus recessions, if the standard surgical formula is augmented by increasing the usual amount of recession by 1–2 mm per muscle [43].

Patients with an intermittent exotropia and a true high AC/A ratio (if diagnosed according to the principles in Sect. 9.4.5.3) will predictably have a persistent esotropia at near fixation after surgery that cor-

rects the distance deviation [41]. They will require a bifocal after surgery to control this overcorrection at near. It is therefore important to identify this relatively uncommon type of patient before planning surgery. Because they have a high AC/A, they respond very well to overcorrecting minus-lens therapy. A small amount of minus lens corrects a lot of exotropia in these patients. They will, however, be esotropic at near with overcorrecting minus-lens correction and need a bifocal. Most of these patients normalize their AC/A by the end of adolescence, and the bifocal can be discontinued. At that time they can be treated in a standard manner. Brodsky and Fray have reported good results in exotropes with a high AC/A by performing standard lateral rectus recessions, combined with simultaneous posterior fixation of the medial rectus muscles [5].

Convergence insufficiency pattern exotropia is a special category. Unfortunately, the same term is used to describe two somewhat different groups of patients. Those who have a negligible distance deviation, a small exophoria at near (typically under 10 PD) and decreased fusional convergence amplitudes at near as measured with base-out prisms, have a fusional convergence insufficiency. They respond well to orthoptic exercises. Another group of patients have a moderate intermittent exotropia at near fixation, typically 15−25 PD, and a smaller intermittent exotropia at distance, typically 10−15 PD. They will also have what appears to be decreased convergence amplitudes at near if one simply considers the amount of base-out prism they can overcome. Consider this case:

Case 6. A patient has 10 PD of exotropia at distance and 25 PD of exotropia at near. Testing his fusional convergence amplitudes at near reveals he can overcome 8 PD of base-out prism before he is diplopic. At first glance a fusional amplitude of 8 PD seems low. However, he is also using fusional convergence to overcome his underlying 25 PD of exotropia; thus, he actually has the ability to overcome 32 PD with fusional convergence, which is a high normal amount.

If tested in the manner outlined previously, most of these patients will be found to have very low or absent AC/A ratios and should be thought of as having an accommodative convergence insufficiency. They tend to do poorly with surgery. If the near deviation is surgically corrected, they are usually overcorrected at distance; if the distance is corrected, they are typically undercorrected (but improved) at near. If one considers that these patients have very little accommodative convergence, it is not surprising that they respond poorly to surgery. Bilateral medial rectus resections have been the recommended treatment since Burian's classification was popularized. Today, many ophthalmologists prefer to treat convergence insufficiency exotropia with either lateral rectus recessions or a unilateral recess−resect procedure, using the distance deviation as the targeted angle. The residual near deviation is then managed with prisms. Edward Buckley, MD, described a useful technique for treating this patient group. He recommended performing lateral rectus recessions for the distance angle, and transposing both muscles inferiorly to induce a V pattern. This post-operative V pattern will further decrease the exotropia in down-gaze and help with reading. This approach has been found to create approximately 5−7 PD of V shift (E. Buckley, pers. commun.).

9.4.5.7 Additional Important Measurements

Many patients with intermittent exotropia will have a larger deviation if they fixate on a far distant outdoor target while looking out a window. In some patients this phenomenon is related to the increased light, in others the increased distance, and in some it is both [37]. In addition, some intermittent exotropes will increase their angle at 6 m if measured after a 1-h patch test. It has been shown that in both situations there is a higher surgical success rate if surgery targets the largest deviation found. All patients with intermittent exotropia should have a measurement made on a far distant outdoor target, and at 6 m after prolonged occlusion. Both tests should be done, as they are not interchangeable. The largest measurement found should be used for surgical planning.

9.4.5.8 Lateral Incomitance

Moore reported that if the primary position measurement exceeds the deviation in both the right and left side-gaze by more than 10 PD, there is a high incidence of overcorrection with standard surgery [44]. It

is sometimes recommended that the surgery formula be decreased by 1 or 2 mm if this degree of lateral incomitance is present. This admonition was based on patients undergoing surgery for the first time, and it is unclear how it should be applied to patients with lateral incomitance after prior exotropia surgery. The prevalence of lateral incomitance is a matter of controversy, and a more recent study has suggested that it may be an artifact of measuring [52].

9.4.5.9 Intermittent Exotropia with Monofixation

Some intermittent exotropes show the findings of the monofixation syndrome prior to surgery [3]. These patients almost invariably continue to be monofixators after surgery. It is important to identify monofixators pre-operatively, as expectations should be lower with respect to their final sensory outcome. It is unclear if the majority of patients who are monofixators after surgery are patients who were monofixators pre-operatively.

9.4.6 Dissociated Exotropia

Dissociated horizontal deviation (DHD) is usually in the form of a dissociated exotropia and is part of the dissociated horizontal complex. The DHD is characterized by a larger exotropia fixing with one eye than the other, in the absence of either uncorrected anisometropia, muscle paresis, or restriction. (It is discussed in detail in Chap. 12.)

9.5 Surgical Formula

A surgical formula for treating exotropia is presented in Table 9.3. The use of adjustable sutures may increase the success of surgery in exotropic patients if they are sufficiently cooperative [26, 30, 33].

Table 9.3 Surgical formula for treating exotropia. *PD* prism diopters

Angle (PD)	Recess LROU (mm per muscle)	Resect MROU (mm per muscle)	One LR recess/one MR resect (mm per muscle)
15	4	3	4/3
20	5	4	5/4
25	6	5	6/5
30	7	6	7/6
35	7.5	6	7/6
40	8	At 40 PD and above add lateral rectus recession	8/6
45	7 plus MR resection[a]	–	8.5/6[b]
50	7 plus MR resection[a]	–	9/6[b]
55	7 plus MR resection[a]	–	9.5/6[b]
60	7 plus MR resection[a]	–	10/6[b]
65	7 plus MR resection[a]	–	10/7[b]
70	7 plus MR resection[a]	–	10/8[b]
80	7 plus MR resection[a]	–	10/9[b]

Surgical numbers are designed to give an initial overcorrection of 5−10 PD of esotropia immediately after surgery

[a] Resect one MR 3 mm for 45 PD, and add one 1 mm per 5 PD increment in the deviation up to 6 mm. At 65 PD or greater add resection of second medial rectus

[b] For unilateral surgery in large-angle exotropia with amblyopia

Take Home Pearls

- Both simulated divergence excess and true divergence excess patterns can be treated with symmetric lateral rectus recessions. Basic patterns do better with recess−resect surgery or perhaps symmetric lateral rectus recessions with an increased surgical dose.
- Patients with intermittent exotropia with a true high AC/A are uncommon but should be identified. They do well with optical management but have a very high likelihood of developing a persistent near-gaze esotropia after surgery. This may require the use of a bifocal long term or additional surgery.
- All near-gaze measurements that are used to calculate the AC/A ratio in intermittent esotropes should be made after prolonged monocular occlusion to eliminate the effect of TPF.
- The desired alignment immediately after surgery for intermittent exotropia is 5−10 PD of esotropia; however, greater amounts of esotropia commonly resolve without further treatment.
- All intermittent exotropes should be measured while looking at a distant outdoor target and also at 6 m after 1 hour of monocular occlusion. These two tests are not interchangeable, and surgery should be done for the larger of the two measurements.
- It is important to correct anisometropia and avoid monovision in intermittent exotropes.
- Intermittent exotropes who undergo surgery at a very young age have a poorer sensory outcome than those having later surgery. It is unclear if this is a result of early surgery, or if patients needing early surgery have poorer fusion.
- Photalgia (closing one eye in sunlight) may persist after successful surgery for intermittent exotropia.

References

1. Abroms, A.D., Mohney, B.G., Rush, D.P., Parks, M.M., Tong, P.Y. (2001) Timely surgery in intermittent and constant exotropia for superior sensory outcome. Am J Ophthalmol 131, 111−16
2. Apt, L., Isenberg, S. (1977) Eye position of strabismic patients under general anesthesia. Am J Ophthalmol, 84, 574−9
3. Baker, J.D., Davies, G.T. (1979) Monofixational intermittent exotropia. Arch Ophthalmol, 97, 93−5
4. Baker, J.D., Schweers, M., Petranak, J. Is earlier surgery a sensory benefit in the treatment of intermittent esotropia? In: G. Lennerstrand, Ed. (1999) Advances in strabismology. Proceedings of the eighth meeting of the international strabismological association. Maastricht, Dept 10−12, 1998, p. 289−92. Aeolus Press, Buren, the Netherlands
5. Brodsky, M.C., Fray, K.J. (1998) Surgical management of intermittent exotropia with high AC/A ratio. J AAPOS, 2, 330−2
6. Brown, H. (1971) Accommodative convergence in exodeviations. Int Ophthalmol Clin, 11, 39−45
7. Brown, H.W. Exodeviations: their classification, diagnosis, and treatment. In: G.M. Haik, Ed. (1962) Strabismus Symposium of the New Orleans Academy of Ophthalmolgy, p. 238. Mosby, St. Louis
8. Burian, H.M., Spivey, B.E. (1964) The surgical management of exodeviations. Trans Am Ophthalmol Soc, 62, 276−305
9. Burian, H.M. (1966) Exodeviations: their classification, diagnosis, and treatment. Am J Ophthalmol, 62, 1161−6.

10. Burian, H.M., Franceschetti, A.T. (1970) Evaluation of diagnostic methods for the classification of exodeviations. Trans Am Ophthalmol Soc, 68, 56−71
11. Burian, H.M., Smith, D.R. (1971) Comparative measurements of exodeviations at twenty and one hundred feet. Trans Am Ophthalmol Soc, 69, 188−99
12. Caltreider, N., Jampolsky, A. (1983) Overcorrecting minus lens therapy for treatment of intermittent exotropia. Ophthalmol, 90, 1160−5
13. Chew, E., Remaley, N.A., Tamboli, A., Zhao, J., Podgor, M.J., Klebanoff, M. (1994) Risk factors for esotropia and exotropia. Arch Ophthalmol, 112, 1349−55
14. Chutter, C. (1977) Occlusion reatment of intermittent divergent strabismus. Am Orthopt J, 27, 80−4
15. Cooper, J., Cuiffreda, K., Kruger, P. (1982) Stimulus and response AC/A ratios in intermittent exotropia of the divergence excess type. Br J Ophthalmol, 66, 398−404
16. Cooper, J., Medow, N. (1993) Intermittent exotropia basic and divergence excess type. Binocular Vis Eye Muscle Surg Q, 8, 185−216
17. Duane, A. (1897) A new classification of the motor anomalies of the eye based upon physiologic principles, p. 84−122. J.H. Vail, New York
18. Eustace, P., Wesson, M.E., Drury, D.J. (1973) The effect of illumination of intermittent divergent squint of the divergence excess type. Trans Ophthalmol Soc U K, 93, 559−70
19. Friedman, Z., Neumann, E., Hyams, S.W., Peleg, B. (1980) Ophthalmic screening of 38,000 children, age 1 to 2 1/2 years, in child welfare clinics. J Pediatr Ophthalmol Strabismus, 17, 261−7
20. Good, W.V., Hoyt, C.S. Exotropia. In W.V. Good, C.S. Hoyt, Eds. (1996) Strabismus management, p. 93−103. Butterworth-Heinemann, Boston
21. Helveston, E.M. (1974) The use and abuse of +3.00 D lenses. J Pediatr Ophthalmol, 11, 175−6
22. Hunter, D.G., Kelly, J.B., Buffenn, A.N., Ellis, F.J. (2001) Long-term outcome of uncomplicated infantile exotropia. J AAPOS, 5, 352−6
23. Iacobucci, I.L., Archer, S.M., Giles, C.L. (1993) Children with exotropia responsive to spectacle correction of hyperopia. Am J Ophthalmol, 116, 79−83
24. Jampolsky, A. (1955) Characteristics of suppression in strabismus. Arch Ophthalmol, 54, 683−96
25. Jampolsky, A. (1970) Ocular divergence mechanisms. Trans Am Ophthalmol Soc, 68, 703−822
26. Jampolsky, A. (1979) Current techniques of adjustable sutures in strabismus surgery. Am J Ophthalmol, 88, 406−18
27. Jampolsky, A. Treatment of exodeviations. (1986) Symposium on Pediatric Ophthalmology. Tran New Orleans Acad Ophthalmol, p. 201−234. Raven, New York
28. Jampolsky, A.J. Unequal vision inputs and strabismus management: a comparison of human and animal strabismus. (1978) Symposium on Strabismus. Trans New Orleans Acad Ophthalmol, p. 358−492. Mosby, St. Louis
29. Jenkins, R. (1992) Demographics: geographic variations in the prevalence and management of exotropia. Am Orthopt J, 42, 82−7
30. Keech, R.V., Scott, W.E., Christensen, L.E. (1987) Adjustable suture strabismus surgery. J Pediatr Ophthalmol Strabismus, 24, 97−102
31. Knapp, P. Divergent deviations. In: J.H. Allen, Ed. (1958) Strabismus symposium II, p. 364−76. Mosby Year-Book, St. Louis
32. Kushner, B., Morton, G. (1983) Diagnostic occlusion in strabismus management. J Ocular Ther Surg, 2, 194−200
33. Kushner, B.J. (1983) Adjustable sutures in strabismus surgery. J Ocular Ther Surg, 2, 11−15
34. Kushner, B.J. (1988) Exotropic deviations: a functional classification and approach to treatment. Am Orthoptic J, 38, 81−93
35. Kushner, B.J. (1992) Surgical pearls for the management of exotropia. Am Orthoptic J, 42, 65−71
36. Kushner, B.J. (1995) Partly accommodative esotropia. Should you overcorrect and cut the plus? Arch Ophthalmol, 113, 1530−4
37. Kushner, B.J. (1998) The distance angle to target in surgery for intermittent exotropia. Arch Ophthalmol, 116, 189−94
38. Kushner, B.J. (1998) Selective surgery for intermittent exotropia based on distance/near differences. Arch Ophthalmol, 116, 324−8
39. Kushner, B.J., Morton, G.V. (1998) Distance/near differences in intermittent exotropia. Arch Ophthalmol, 116, 478−86
40. Kushner, B.J. (1999) Does overcorrecting minus lens therapy for intermittent exotropia cause myopia? Arch Ophthalmol, 117, 638−42
41. Kushner, B.J. (1999) Diagnosis and treatment of exotropia with a high accommodation convergence−accommodation ratio. Arch Ophthalmol, 117, 221−4
42. Kushner, B.J., West, C. Monovision may be detrimental to patients with strabismus. In: R.J. Balkan, G.S. Ellis, H.S. Eustis, Eds. (2004) At the crossings. Pediatric ophthalmology and strabismus. Proc 52nd annual symposium of the New Orleans Academy of Ophthalmology., p. 77−86. Kugler Publications, The Hague
43. Lee, S.Y., Hyun Kim, J., Thacker, N.M. (2007) Augmented bilateral lateral rectus recessions in basic intermittent exotropia. J AAPOS, 11, 266−8
44. Moore, S. (1969) The prognostic value of lateral gaze measurements in intermittent exotropia. Am Orthoptic J, 19, 69−71
45. Niederker, O., Scott, W. (1975) The value of diagnostic occlusion for intermittent exotropia. Am Orthopt J, 38, 107−10
46. Nusz, K.J., Mohney, B.G., Diehl, N.N. (2006) The course of intermittent exotropia in a population-based cohort. Ophthalmology, 113, 1154−8
47. Oh, J.Y., Hwang, J.M. (2006) Survival analysis of 365 patients with exotropia after surgery. Eye, 20, 1268−72
48. Parks, M.M. (1969) The monofixation syndrome. Trans Am Ophthalmol Soc 67:609−57
49. Pratt-Johnson, J.A., Barlow, J.M., Tillson, G. (1977) Early surgery in intermittent exotropia. Am J Ophthalmol, 84, 689−94
50. Pratt-Johnson, J.A., Tillson, G., Pop, A. (1983) Suppression in strabismus and the hemiretinal trigger mechanism. Arch Ophthalmol, 101, 218−24

51. Pratt-Johnson, J.A., Tillson, G. (1984) Suppression in strabismus: an update. Br J Ophthalmol, 68, 174−8
52. Repka, M.X., Arnoldi, K.A. (1991) Lateral incommitance in exotropia: fact of artifact. J Pediatr Ophthalmol Strabismus, 28, 125−30
53. Richard, J.M., and Parks, M.M. (1983) Intermittent exotropia. Surgical results in different age groups. Ophthalmology, 90, 1172−7
54. Sanfilippo, S., Clahane, A.C. (1970) The effectiveness of orthoptics alone in selected cases of exodeviations: the immediate results and several years later. Am Orthopt J, 20, 104−17
55. Santiago, A.P., Ing, M.R., Kushner, B.J., Rosenbaum, A.L. Intermittent exotropia. In: A.L. Rosenbaum, A.P. Santiago, Eds. (1999) Clinical strabismus management, p. 163−175. Saunders, Philadelphia
56. Saunders, R.A., Trevedi, R.H. (2008) Sensory results after lateral rectus muscle recession for intermittent exotropia operated prior to two years of age. J AAPOS, 12, 132−5
57. Scobee, R.G. Exophoria. (1952) The oculorotary muscles, p. 171. Mosby, St. Louis
58. Stathacopoulos, R.A., Rosenbaum, A.L., Zanoni, D., Stager, D.R., McCall, L.C., Ziffer, A.J., Everett, M. (1993) Distance stereoacuity. Assessing control in intermittent exotropia. Ophthalmology, 100, 495−500
59. Noorden, G.K. von. Exodeviations. In: G.K. von Noorden, Ed. (1996) Binocular vision and ocular motility, p. 341−59. Mosby Year-Book, St. Louis
60. Wilson, M.E., McClatchey, S.K. (1991) Dissociated horizontal deviation. J Pediatr Ophthalmol Strabismus, 28, 90−5

Orthoptic Evaluation and Treatment

Kyle Arnoldi

10

Contents

Core Messages

- The sensorimotor examination clarifies the patient's symptoms and expectations, precisely quantifies the ocular deviation, and determines the potential for binocular single vision in a focused, efficient manner.
- The goals of orthoptic therapy are to minimize the risk of post-operative over- or under-correction, to improve comfortable control over a non-surgical deviation, and to alleviate symptoms of diplopia and visual confusion.

10.1 Overview

In the broadest sense, the purpose of the sensorimotor exam is to efficiently gather information on eye alignment, ocular motility, and binocular function in order to aid in diagnosis and formulation of an appropriate treatment plan. The orthoptic assessment will help establish whether the case is surgical or non-surgical. If surgical, the exam will assist in the determination of the target angle as well as predict the response to surgical over- or under-correction. The exam will also appraise the existing sensory state, ascertain the potential for binocular vision, and forecast the sensory outcome of strabismus surgery. Perhaps most importantly, the sensorimotor evaluation should clarify the patient's symptoms (or caregiver's complaints) and

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aid both the clinician and the patient in forming reasonable treatment goals and expectations.

A pre- and post-operative sensorimotor exam is recommended for all patients undergoing strabismus surgery. It is mandated for any patient with persistent binocular vision complaints (such as diplopia, visual confusion, or asthenopia) neither attributable to defects in the ocular media nor ameliorated with appropriate refractive correction. The sensorimotor exam can be worthwhile pre-operatively for patients scheduled for cataract or refractive surgery. But the orthoptic evaluation, particularly the sensory component, is invaluable in any surgical candidate beyond the age of visual maturity with a history of long-standing strabismus. It is this subgroup of patients that is most likely to suffer the consequences of pre-existing anomalous binocular vision, resulting in diplopia in spite of alignment of the visual axes.

This chapter is not intended to be a step-by-step comprehensive tutorial on how to perform the various steps and tests in an orthoptic exam, nor is it intended to present an exhaustive menu of all possible tests and methods used in the orthoptic evaluation. A familiarity with commonly used tests is assumed. Rather, while some new methods will be presented, the balance of the chapter covers the finer points of some universally used tests, avoiding common sources of error, presenting new ways to use standard tests, and alternative ways to interpret the results. The focus is on exam efficiency: learning the most from the exam in the least amount of time, utilizing a minimum number of well-known methods.

This chapter is organized in what is hoped the reader will find to be a logical fashion, covering the Motor Evaluation first, followed by the Sensory Evaluation, and concluding with Treatment. Some clinicians feel strongly that sensory testing should be done prior to any other exam component with the exception of the History. They argue, in spite of evidence to the contrary, that even testing vision has the potential to "break fusion," dissociate the eyes, and destroy any trace evidence of a fragile binocularity[29] . However, there are several sound reasons for, at minimum, quantifying visual acuity and eye alignment in primary position at distance and near before any sensory testing is done. Without some information on acuity and alignment, it is difficult to select the appropriate fixation target or sensory test, and even more so to interpret the result obtained. By doing the sensory evaluation first, the examiner works in an open-loop system, without appropriate input or feedback guiding clinical judgment. To avoid inadvertently omitting some critical test, one is forced to perform *every* test! This is an inefficient approach to the sensorimotor exam, which at best results in wasted time, at worst in lost cooperation from the patient. In short, the motor exam can direct and even predict the course of the sensory exam, but the converse is not true.

It is conceivably more important to find evidence of strong, but *anomalous* fusion in a pre-operative sensorimotor exam, than any vestige of a brittle binocularity in the post-operative evaluation. Deep-rooted fusion ability will not vanish irretrievably with brief occlusion during vision testing or even with alternate cover testing. Moreover, binocularity that is as tenuous as to be unrecoverable following vision testing may be of no consequence to the patient and should not impact any management decisions.

10.2 The Motor Evaluation

While most clinicians equate an orthoptic evaluation with the sensory exam alone, the motor exam is an equally important and necessary component, requiring expertise and attention to detail. The purpose of the motor evaluation is threefold: (1) to detect and quantify an eye misalignment; (2) to evaluate the function of each extraocular muscle; and (3) to assess control over the deviation. Results of the motor exam will determine if the patient is a candidate for surgical vs non-surgical therapy and, for the surgical candidate, which muscles should be targeted and how much should be done. There are many case-selective tests that may be used in the motor evaluation, some requiring special equipment, but the two basic methods used universally are the cover tests and version/duction testing.

10.2.1 Cover Tests

The cover tests in all their variations are the cornerstone of the motor exam. They are very familiar even to the dabbler in strabismus, yet they are deceptively

difficult and easily done incorrectly. Performed well, they may obviate the need for other motor tests. But under the right circumstances, small errors in execution may lead to large errors in measurement! A review of proper technique is therefore appropriate. There are three primary sources of error in cover testing: (1) errors in fixation target selection; (2) errors in prism placement; and (3) errors in occlusion.

An ideal fixation target is one that both stimulates and controls accommodation. For a patient with 20/20 vision in both eyes, this means a target no larger than 20/40 [39]. For those with reduced vision in one or both eyes, a target no larger than two Snellen lines above the visual threshold for the poorer-seeing eye must be used.

Once the target has been identified by the patient, it will lose much of its accommodative power. Staring at the same 20/30 letter for minutes at a time does not control accommodation! The ideal target is a computer screen with multiple, randomized lines of 20/30 letters that can be refreshed frequently as the patient reads aloud during the cover test. Modern computerized vision testing has made this easy to accomplish for distance fixation.

Near fixation is more problematic, as most reduced Snellen cards or sticks present optotypes over a wide scale from 20/400 to 20/20, with relatively few lines qualified to be in the "accommodative target" range. In answer to this, the Snow fixation stickers were developed (by J. Snow, C.O., Penn State Hershey Medical Center, Hershey, Pa.). These stickers feature near targets with multiple lines of 20/30 to 20/60 letters (Fig. 10.1). They can be applied to a tongue depressor, to the bridge of the examiner's glasses, or directly onto the examiner's nose for fixation. The latter two methods are favored because they do not require the patient to hold the fixation target, which can be difficult for both the very young and the very elderly, yet they free both of the examiner's hands for prism and cover testing.

When examining the very young it is even more important to have one's hands free! It is also more difficult to find a true accommodative target that will capture the child's attention long enough for testing. Finger puppets, small toys, and most reward stickers tend to be too large to be considered accommodative. Small, detailed stickers affixed to the examiner's nose are ideal for this purpose. These may be found in gift, card, or stationery stores (Fig. 10.2).

The second common error in cover testing is incorrect prism placement. These errors include inadvertent rotation of the prism around the *x*-, *y*-, or

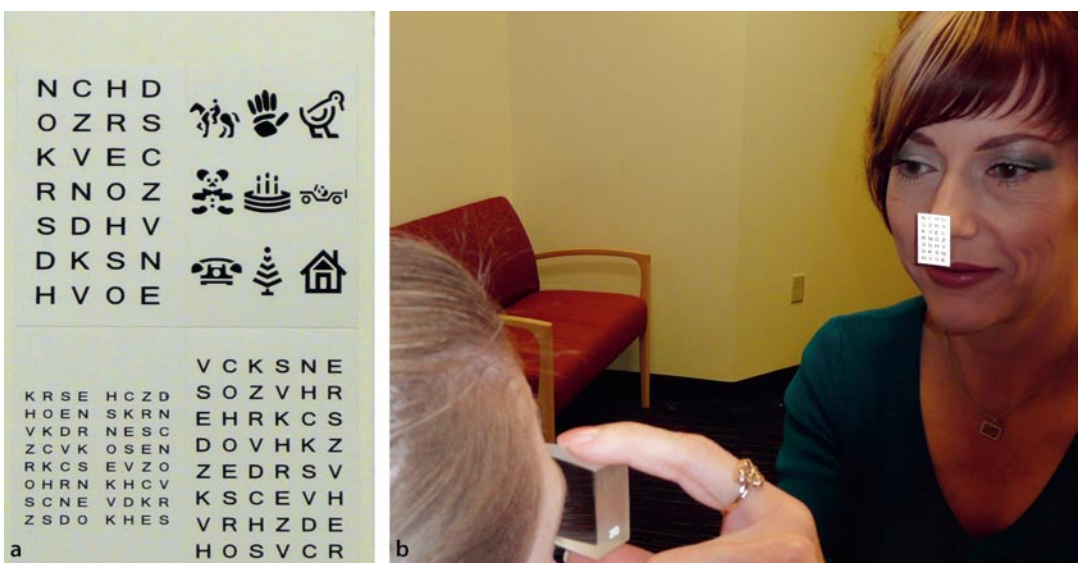

Fig. 10.1a,b Snow fixation stickers. Multiple lines of 20/30–20/60 letters in sticker form (**a**) may be affixed to the examiner's glasses or nose (**b**) to allow hands-free examination of the patient on an accommodative target

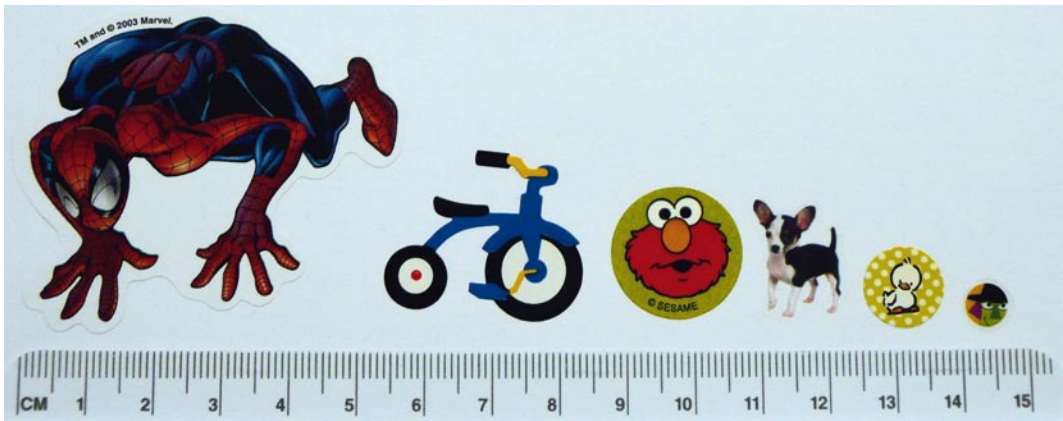

Fig. 10.2 Near fixation stickers. Most stickers are not small enough to stimulate and control accommodation during a prolonged cover test. Even the smallest sticker pictured is, at best, equivalent to a 20/60- to 20/80-sized target

z-axis, or errors in vertex distance in which the prism is held too far away from the eye.

The strength of any given prism is determined by the index of refraction of the optical medium and the angle formed at the apex of the prism. The labeled value on the prism is the minimum deviation of a light ray that can be produced by that particular prism; however, the prism diopter value stamped on the base is only accurate if the prism is held in the position for which it was calibrated. The effective power of a prism can be altered by rotating the prism before the eye to increase or decrease the angle at which light rays will strike the surface. The larger the angle at the apex of the prism, the greater the potential error in measurement with only slight alterations in prism position.

Most loose prisms in use today are plastic and calibrated for use in the position of minimum deviation (PMD; Fig. 10.3). This is the position in which the same amount of refraction will occur at both the anterior and posterior surfaces of the prism. When a plastic prism is rotated away from the PMD, the effective power of the prism is increased, and the deviation being measured will be underestimated. Rotation of a prism around the *z*-axis will cause measurement errors in eso- and exodeviations, and rotation around

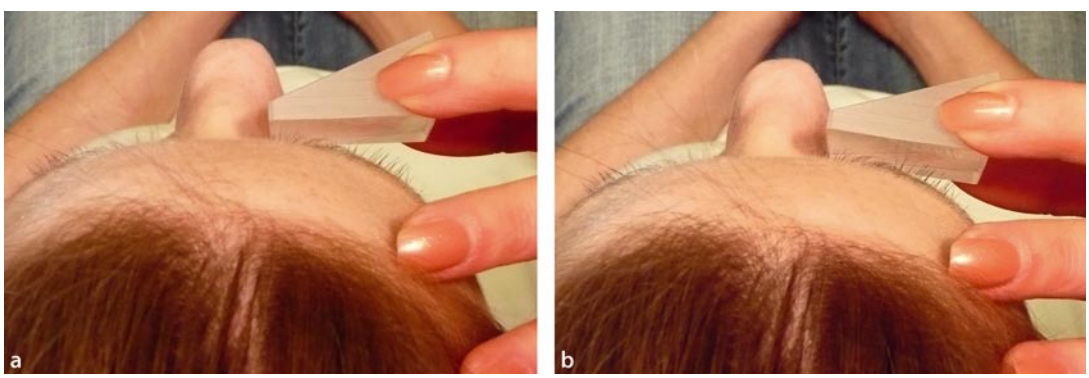

Fig. 10.3a,b The position of minimum deviation. Plastic prisms are calibrated for use in the position of minimum deviation (**a**) which is difficult to reproduce consistently. Positioning the prism in the frontal plane (**b**) is an acceptable alternative that minimizes measurement error

the *x*-axis causes errors in vertical strabismus measurement.

Unfortunately, the PMD is awkward as it requires the examiner to hold the prism in a slight rotation that is difficult to estimate quickly and repeat through frequent prism changes during cover testing. Holding the prism in the frontal plane position (FPP), in which the posterior face of the prism is parallel to the orbital rim, is easier to locate, more comfortable for the examiner, and is close enough to the PMD that it is used interchangeably. Errors in prism rotation may be minimized by using a prism bar or rotary prism.

Measurement errors due to accidental prism rotation are particularly common when horizontal deviations are measured in right or left gaze, or when vertical deviations are measured in up or down gaze. Care must be taken not to rotate the plastic prism with the head into these secondary positions of gaze, as this will move the prism out of the frontal plane (Fig. 10.4). This error occurs with particular frequency when measuring large exodeviations in side gazes, and may reveal a false lateral incomitance [34].

When measuring large deviations in the secondary positions of gaze, it is also important to remember that the globe does not have unlimited freedom of rotation due to the considerable elastic and stabilizing forces within the orbit. Underestimation of the deviation may occur if the prism is placed in such a way that it forces the eye to rotate beyond its capacity in order to take up fixation. The eye will stop shifting with repeated alternating cover because the eye has reached its limit of rotation, not because the deviation has been completely neutralized. The larger the deviation, the more of a problem this may cause. To avoid this testing artifact, place the prism over the eye with the greatest room to move. For example, base-in prism should be placed over the adducted eye when measuring large exodeviations in side gazes. The important exception to this rule

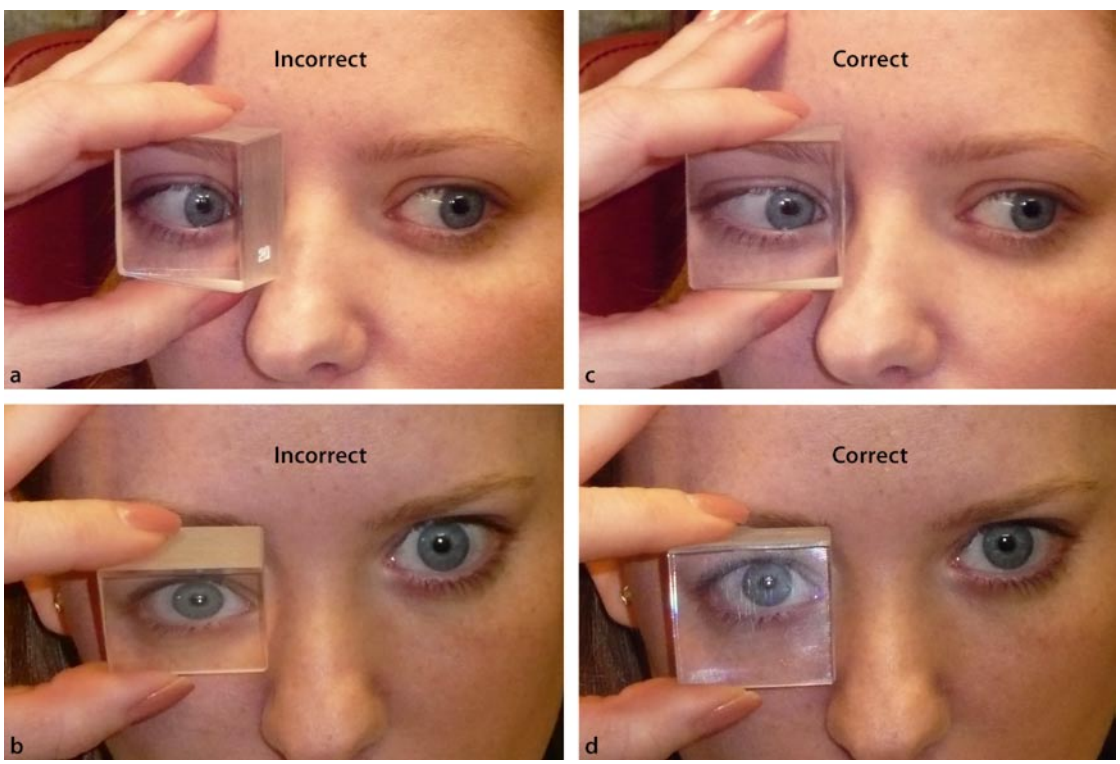

Fig. 10.4a–d Measurement error due to prism rotation I. Inadvertent rotation of a horizontal prism around the *z*-axis in side gazes (**a**) or rotation of a vertical prism around the *x*-axis in vertical gazes (**b**) can create the illusion of incomitance. Care must be taken not to rotate the prism with rotation of the eye (**c,d**)

is found in the case of restrictive or paralytic strabismus, in which the prism must be placed over the affected eye regardless of the gaze being measured. Again, the examiner may not observe a shift during cover testing because the affected eye simply cannot move into the position of gaze being tested. Putting the prism over the restricted eye moves the image to meet the eye, rather than forcing the eye to move to the image.

Inadvertent rotation of a horizontal or vertical prism around the *y*-axis will not only overestimate the deviation, but will also create the appearance of, or exacerbate, a multiplanar deviation. The examiner must be acutely mindful of *y*-axis rotation when measuring a deviation in head tilts, as only small changes in measurement of a vertical strabismus are often used to determine if the result is positive or negative. The prism base should remain parallel with the floor of the orbit, not the floor of the room, with head rotation to the shoulder (Fig. 10.5).

The effective power of a prism will also change with a change in the distance of the prism to the eye. Though obviously not possible, the ideal position for the prism would be the center of rotation of the eye. In lieu of this, the prism should be held as close as is reasonable to the eye: typically no more than 1−2 cm away from the cornea. The distance must be appropriate but also consistent throughout the cover test. It is helpful to brace the side of your middle finger against the patient's brow bone, while holding the prism between the index finger and thumb. If the patient wears spectacles, the prism can be held directly against the frame of the glasses.

Errors in prism position may also occur when measuring deviations that exceed the largest prism available. Two plastic prisms with the base in the same direction cannot be stacked back to back as this completely alters the angle of incidence and, consequently, the angle of refraction. To some extent, the errors induced by stacking can be minimized by splitting the power with one prism before each eye; however, angles measured in prism diopters are not additive, and so even this method is not entirely accurate. The deviation measured by the sum of two prisms will always be greater than the sum of the calibrated values. There are tables that display the total value for prisms held in this manner [38]. Alternatively, the true deviation in prism diopters can be calculated by multiplying the tangent of the total angle of deviation in degrees by 100.

In general, all measurement miscalculations due to inaccurate prism placement have the potential of being exaggerated at near fixation. Because of the shorter working distance, the often larger deviations, and the natural inward rotation of the visual axes, errors can be magnified.

Inadequate occlusion is the final, and possibly the most common, type of error leading to inaccurate measurement of strabismus. In order to reveal the entire deviation, the eyes must be maximally dissociated. To accomplish this, an opaque or translucent occluder held close to the eye is recommended. This is prefer-

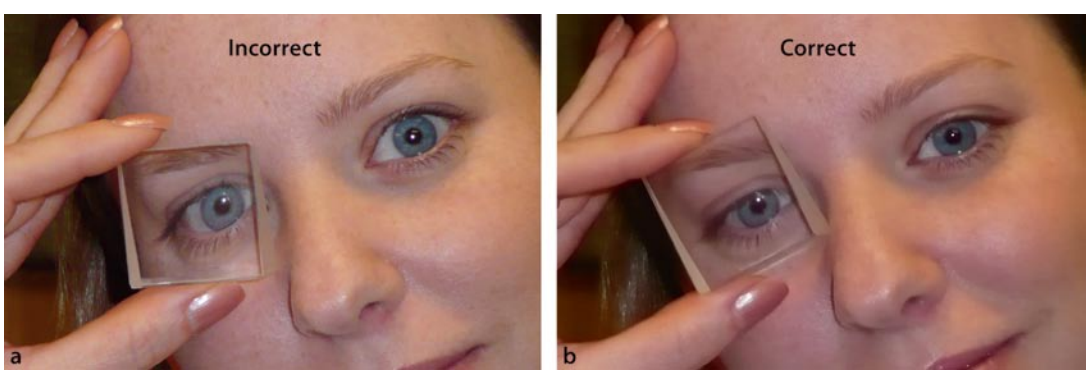

Fig. 10.5a,b Measurement error due to prism rotation II. Inadvertent rotation of a prism around the *y*-axis in head tilt will create the illusion of a multi-planar deviation as well as overestimate the vertical deviation (**a**). The base of the prism should be held parallel to the floor of the orbit (**b**), not the floor of the room

able to the popular "thumb" occluder (Fig. 10.6), or other variations held away from the face. Occlusion methods such as these may be adequate for vision testing, because they do successfully obstruct the fovea, but they do not sufficiently block the peripheral visual field. This is necessary in order to minimize peripheral motor fusion. Motor fusion (also known as fusional or disparity vergence), the ability to align the eyes in such a manner as to image the object of regard on corresponding retinal points to allow sensory fusion, is driven primarily by matching input from the overlapping areas of our visual fields. Non-foveal input from the central and peripheral retina has the most powerful influence on vergence, simply because there are more retinal elements to match [18]. Foveal input has comparatively little influence on motor fusion. This can be easily demonstrated by occluding the fovea of one eye using a remote thumb, and introducing a 14−16 Δ base-out prism over one eye. Even in the absence of foveal input, fusional convergence will be observed in the subject with average fusional vergence ability as long as adequate peripheral input remains. In contrast, if the subject now fixates through a single pinhole mounted in a trial frame as base-out prism is introduced, convergence is not induced and diplopia results.

A good cover test requires patience and repetition, particularly in the case of intermittent or latent deviations, or in cases with decreased acuity. The occluder should be held in place for a few seconds to ensure that the patient is able to achieve fixation before it is rapidly transferred to the other eye without allowing a period of binocularity. It must be kept in mind that high-powered prisms will degrade the vision of the eye viewing through it. The occluder may have to be left in place over each eye a bit longer to allow the patient time to fixate through a high-powered prism. Measuring to reversal, meaning the prism and alternate cover test is continued, adding prism past the point where no shift in the visual axes is observed, is also recommended. The full deviation is then the last prism value that produced no shift in fixation.

Variations of the cover test used in certain specific situations include the cover−uncover test, the simultaneous prism and cover test, and diagnostic occlusion. The cover−uncover test is often used not only to detect a manifest deviation, but to assess control over an intermittent deviation by estimating how easily fusion is disrupted and how quickly it is regained once the cover is removed (see Sect. 10.2.4).

The simultaneous prism and cover test is used to quantify the manifest deviation when a latent deviation is also present. As the name of the test suggests, it is important to *simultaneously* place the prism over the deviating eye as the cover is introduced over the fixating eye. In other words, it is not equivalent to holding a prism over the deviating eye during a cover−uncover of the fixating eye. By definition, those who have both a manifest and a latent component to their deviation have motor fusion (fusional vergence). By maintaining a prism over the deviating eye while the patient is binocular, motor fusion is re-

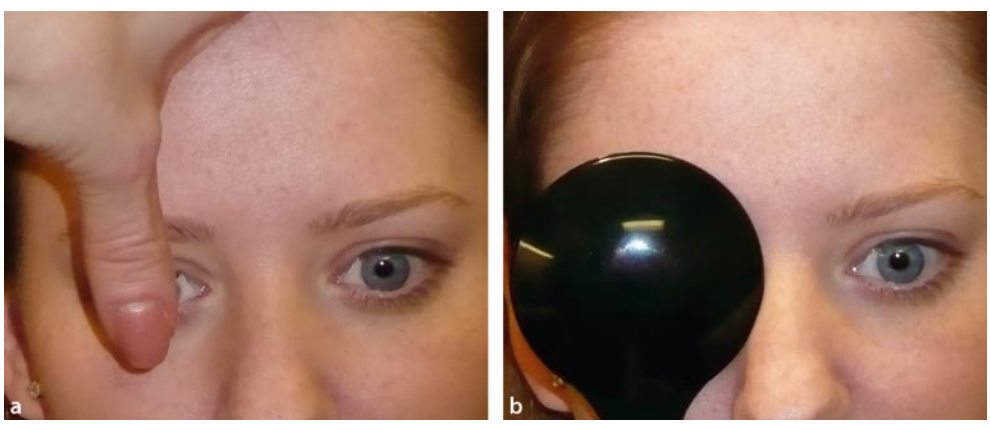

Fig.10.6a,b Proper occlusion. In order to uncover the full deviation, particularly in cases of phoria or intermittent tropia, all peripheral visual input must be blocked from view. Occlusion with a thumb (**a**) is not as effective in achieving maximal dissociation as an opaque or translucent occluder (**b**) held close to the eye

cruited in order to maintain the image of the fixation target on the preferred perifoveal retinal point. If performed in this way, the test results will over-estimate the manifest deviation.

Diagnostic occlusion (Marlow occlusion [29] or the Patch Test), is prolonged monocular occlusion and is, essentially, a protracted cover test. The patch is kept in place over a period of 30−60 minutes, but it may be continued over 24−48 hours. The better the patient's control over the deviation, the longer the period of diagnostic occlusion necessary in order to fully appreciate the deviation. Diagnostic occlusion is most commonly used pre-operatively in cases of exotropia suspected to be of the pseudo-divergence excess type. It is also valuable in the symptomatic patient with a phoria, or the child whose parent sees a deviation that is not apparent with standard cover testing. Rules of fixation targets, prism placement, and adequate occlusion apply to these cover-test modifications.

10.2.2 Ocular Rotations

The motor exam includes the evaluation of the function of each individual extraocular muscle by observing version and duction movements. The standard method of grading function compares muscle action relative to its yoke and is based on a -4 to +4 scale. If mobility is restricted such that the eye is not even able to move into primary position, negative numbers larger than -4 may be used. Investigating ocular rotations in this manner may be technically easy to do, though the results are sometimes difficult to interpret. Variations in soft tissue or orbital anatomy may result in the strong illusion of muscle imbalance, particularly in the secondary and tertiary positions of gaze. In addition, this system assesses comparative muscle function. Limitation of movement may be underestimated if it is bilateral (whether symmetric or asymmetric), except in the case of obvious and severe under-action. Though there is little inter-observer reproducibility with this method, it is the one most commonly used and is probably adequate for most cases. Certainly in the case of muscle "over-action," this method is clinically useful.

Another method of quantifying ocular rotations estimates function in degrees based on the same scale used for the Hirschberg test (1 mm ≈ 7º). As the examiner holds a transilluminator or penlight held at the midline of the face, the patient follows a fixation target as it moves into the diagnostic positions of gaze. The corneal light reflex should remain in approximately the same location in each eye if there is no over- or under-action present. If a limitation is present, the reflex in the affected eye will become displaced. The amount of limitation in degrees can be estimated based on the amount of displacement of the light reflex in millimeters. This method may be a bit more precise but suffers from the same drawbacks as the conventional method, though perhaps to a lesser degree.

For the purposes of measuring change over time, more meticulous and reproducible techniques are preferred. One of these methods uses the cervical range of motion (CROM) device, an instrument originally designed for the purpose of measuring the range of motion of the cervical spine. The apparatus consists of three meters representing position with respect to the *x*- (chin elevation or depression), *y*- (head tilt), and *z*- (face turn) axes, mounted in a spectacle frame and secured to the patient's face with Velcro straps. Rather than comparing function to the yoke muscle, the CROM quantifies the degrees of excursion or range of movement with the fellow eye occluded. The head is rotated into the primary field of action of each of the extraocular muscles as the patient fixates an accommodative target. When the limits of rotation are reached, the image will slip off the fovea, causing blur. The degree of excursion into that field can then be read directly off of the dials on the apparatus. This method has proven to be reliable and repeatable [24].

10.2.3 Other Tests of Motor Function

While the motor evaluation typically starts with cover testing and observation of versions, results of these tests may indicate the need for further motor evaluation in some cases. Additional tests may include prism adaptation, diagnostic occlusion, calculation of the AC/A ratio, tests for torsion, and Lancaster red-green or Hess/Lees screen testing.

Prism adaptation is accomplished by offsetting the manifest deviation with temporary prisms. After a period of hours to days, the alignment and binocular

vision is re-assessed through the prism. If the deviation has increased, the prism is increased accordingly and the process repeated until the deviation either stabilizes, exceeds the amount available in a temporary prism, or over-corrects the strabismus. The goal of prism adaptation is to determine the target angle for surgery, and to predict the sensory and motor outcome with realignment of the eyes.

Both diagnostic occlusion (described in Sect. 10.2.1) and prism adaptation can be used to confirm the full angle of strabismus measured with the cover test. One method may be better than the other, depending on the case. For example, patients with some control over the deviation, particularly if the deviation was observed to build up gradually with prism and alternate cover testing, are best evaluated with diagnostic occlusion. Prism adaptation should be used with caution in these cases, as those with good motor fusion, including patients with strabismus and anomalous correspondence (see Sect. 10.3.2) may undergo phoria adaptation in which the tonic vergence system adapts to the prism, temporarily resetting the baseline eye alignment and resulting in an "eating up" of the prism [27]. In these cases, prism adaptation is less a test to determine the full angle than a test of the limits of tonic and fusional vergence amplitudes. These patients will be at increased risk for over-correction if surgery is done for the prism-adapted angle.

Cases of distance-near disparity, where the magnitude of the deviation changes by 10 prism diopters or more with a change in fixation distance, may be investigated using diagnostic occlusion or prism adaptation. Diagnostic occlusion is typically used more for the *exo*deviation that is greater at *distance*, and often reveals a larger near deviation approaching or even exceeding the distance angle. Prism adaptation, on the other hand, is advised for surgical *eso*deviations that are greater at *near*. When prism adapted for the larger near angle, the distance esodeviation may build or the prism may over-correct [2, 25]. This method is very useful in predicting the likelihood of over-correction if surgery is done for the larger angle.

In cases of horizontal strabismus in which the distance and near deviations differ by more than 10 prism diopters, it is often necessary to calculate the AC/A ratio. Just as one would never assume that all exodeviations greater at distance are caused by a high AC/A, one should never take for granted that the ratio is high in all cases of near esotropia exceeding the distance amount. Accommodative convergence is only one type of convergence contributing to the near alignment. Abnormalities of proximal, fusional, and tonic convergence are also possible, and it is important to distinguish between them, as this will impact management options.

There are three methods that have been used to assess the AC/A ratio. The first is the Clinical Method, which simply entails a comparison of the distance and near measurements in primary position. Though quick and easy, it is the least accurate of all the methods and is not recommended. It does not control for the effect of proximal or fusional convergence, does not quantify the ratio, and should not be used to predict if bifocals would be effective.

The Heterophoria Method is based on the distance-near disparity in measurement, and the geometry of convergence using the interpupillary distance as the base of a triangle whose apex is at the fixation point. Like the Clinical Method, this method neither accounts for nor controls proximal or fusional convergence. It is based on the faulty assumption that accommodative convergence contributes 100% of the convergence necessary to maintain bi-foveal fixation at near, and therefore results in an artificially high AC/A ratio. The Heterophoria Method predicts a normal AC/A would be equal to the interpupillary distance. It further predicts that a normal AC/A will increase over time with growth and increased separation of the orbits. Both of these predictions have been shown to be false [7].

The Gradient Method is the only direct measure of the amount of convergence generated per unit of accommodative effort, which is the very definition of the AC/A ratio. The Gradient is also the most accurate method, as it is the only one that controls for both proximal and fusional convergence because measurements are taken at a fixed testing distance. The Gradient Method not only yields a precise measure of the ratio but can be used to predict whether optical methods may be used successfully to manage the strabismus, and how much the spectacles must be altered to achieve the desired effect. The Gradient AC/A can be calculated by repeating measurements through plus lenses at near or minus lenses at distance [4], subtracting the difference in alignment and dividing by the change in accommodative demand.

A test for torsion should always be included in the motor evaluation of a patient with any acquired vertical strabismus. Expected in cases of superior oblique palsy, it should be remembered that a cyclotropia can also occur in other paretic or restrictive vertical strabismus. Torsion testing is also advisable in any patient with diplopia not resolved with offset of the deviation.

For diagnostic purposes, the double Maddox rod test is the recognized standard. Because this test is very disruptive to fusion, it is excellent for revealing and quantifying the full measure of even small cyclotropic deviations. It is also ideal for quantifying large degrees of torsion. The Awaya cyclo-deviation near test (S. Awaya, M.D., New Cyclo Tests, Handaya Co., Sendai, Miyagi, Japan) though not quite as dissociating as the double Maddox rod, has the advantage of ease of interpretation. Small degrees of torsion can be difficult for the examiner to read on a trial frame but are easily identified on the Awaya. There are two main disadvantages to this test. Firstly, the maximum amount of torsion detectable is 12º, and secondly, it can only record net torsion. If a cyclotropia is present in both eyes, this test will report the sum of the two.

Patients with measurable cyclodeviations are not always symptomatic, however. It is therefore necessary to determine to what extent the cyclodeviation is interfering with fusion. For this, a less dissociating test should be done in addition to the Maddox rod or Awaya test. The simplest way to do this is to mount individual loose Bagolini striated glasses in a trial frame in the same manner as is done with the Maddox rods [36]. For this test, unlike the Maddox rods, the room should remain illuminated and feature contoured peripheral cues to stimulate and assist fusion (see Sect. 10.3 for more information on preferred visual environments for fusion). If significant torsion is detected in this way, it may have to be addressed surgically in order to restore fusion.

Cyclodeviations can also be detected and investigated using the amblyoscope. The amblyoscope is less dissociating than the Double Maddox rod or Awaya test but is more so than the Bagolini glasses. There are two principle advantages of the amblyoscope over the other tests for torsion. Firstly, the cyclodeviation can be offset, leaving no doubt that the patient is capable of fusion. Secondly, the amblyoscope is the only tool with the ability to quantify torsional fusional amplitudes.

Tests such as the Lancaster red-green, the Hess screen, or the Lees screen yield a graphic representation of strabismus in multiple fields of gaze, facilitating quick comparisons over sequential visits in cases of evolving strabismus. These types of tests use foveal projection to map out the strabismus, so that the position of the resulting fields corresponds to the position of the eyes. (This is in contrast to diplopia, in which the double image is located in the field opposite to that which the eye is directed.) Primary and secondary deviations, incomitance, patterns, over- and under-actions, paresis, and restriction can all be diagnosed at a glance with these types of tests; however, prerequisites for testing include normal retinal correspondence, the absence of suppression, foveal fixation in both eyes, and the ability to comprehend and comply with the test instructions, all of which preclude the use of these tests in a large percentage of the pediatric population. These tests offer the advantage of controlled and repeatable fixation distance and positions of gaze, and in the hands of an experienced practitioner, they are much faster to complete and record than prism and cover testing in multiple fields.

10.2.4 Assessment of Control

Though quantifying the magnitude of eye misalignment is important, it is often the assessment of control that determines whether treatment is needed at all, and if so, when it should be done. Control can be evaluated in several ways: the cover/uncover test, the use of control scales, and measurement of fusional amplitudes are the most widely used. Stereoacuity may also correspond to control, but as it is not a direct measure of control, it is covered in the Sect. on sensory testing (see Sect. 10.3.1).

A qualitative measure of control can be made using the cover/uncover test. Though highly subjective, this method is simple and practical. Control is typically graded as good, fair, or poor as the patient maintains fixation in the position of greatest concern. Momentary occlusion of the non-dominant eye is used to ascertain how easily control is disrupted. Once dissociated, the patient is observed to determine how readily fusion is regained. This may be quantified to some extent by estimating the time interval between the

loss and recovery of fusion. The examiner should also look for assists such as blinking, saccades, change in fixation distance, or head movement that the patient may recruit in order to regain control.

Several scoring systems have been described specifically for use in evaluating control in intermittent exotropia, though presumably they could be used in any type of strabismus. These systems typically feature varying combinations of two or more of the following: input from the parent or caregiver; observation during the exam; and results of a dissociating test such as a cover test. Results are combined to reveal a score indicating level of control, with higher numbers representing poorer control, and zero representing excellent control. Studies have shown these systems to be sensitive, reliable, and repeatable [14, 30].

Measurement of motor fusion amplitudes can be used to quantify control [5]. Diminished control is evidenced by a low "break point" (point at which vergence demand exceeds fusional reserves, resulting in a manifest deviation), or a remote "recovery point" (point at which fusion can be recovered as vergence demand is lessened). These values are determined by introducing a rotary prism or prism bar at the lowest value, held with the base in the direction opposite to that which was used to measure the strabismus (i.e., base-*in* for an *eso*deviation). This simulates an increase in the strabismic angle. The prism is slowly increased until fusion cannot be maintained (break point), then slowly reduced until fusion is regained (recovery point). The break point may be marked by appreciation of diplopia. While this should never be used as the sole indicator of the break point by the examiner, the absence of diplopia at the break is significant. Breaking fusion with suppression is another indication of poor control.

What would be considered a normal break point varies with the magnitude and direction of the underlying strabismus but ideally should be at least equal to the degree of misalignment to ensure comfortable control. A recovery point more than 5 prism diopters away from the break point would be considered remote [40]. With the exception of monofixation syndrome, constant deviations are so because they far exceed their fusional reserves. A phoria is such because fusional vergence far exceeds the degree of latent misalignment. But those with intermittent deviations are likely near their motor fusion threshold and have the most to gain by vergence amplitude testing.

Poor control is one of the defining features of tropic deviations so it is often erroneously assumed that control does not need to be evaluated in these situations; however, the presence of a manifest deviation does not preclude fusional vergence ability, and it is useful to identify it, no matter how limited or fragile. The cover/uncover test and the control scales are generally not useful for constant strabismus; therefore, the fusional vergence amplitudes method should be used. This is done by offsetting the deviation with a prism bar, rotary prism, or on the amblyoscope. The prism amount is then gradually reduced until the patient breaks fusion and becomes tropic. The process is then repeated by increasing the prism until fusion is once again broken, with or without diplopia. This method defines the alignment range over which the patient's fusional ability may be sufficient to maintain orthotropia.

10.3 The Sensory Evaluation

The sensory exam is the oracle of the orthoptic evaluation: it can clarify the current sensory state, give the examiner a glimpse into the past, and predict possible sensory and motor futures. However, the ultimate purpose of the sensory exam is to determine if the patient has fusion, or the potential for fusion. The answer may change or refine treatment goals, and may figure prominently in the decision whether to treat at all.

There is more than one type of fusion, and it is possible to demonstrate one type without others. Tests are available to detect and measure motor fusion (retinal image disparity-driven vergence), sensory fusion (two-dimensional, flat fusion), and stereopsis (retinal disparity sensitivity resulting in three-dimensional fusion); however, it is not always possible or even necessary to test for all of these forms of fusion on every exam. The sensory exam can be done very efficiently if the right tests are chosen, and most sensory tests can be used to answer more than one diagnostic question. The direction of the sensory exam will depend on (1) the patient's history, symptoms, and capabilities, (2) the results of the motor examination, and (3) the examiner's own experience and expectations for the case.

A thorough sensory evaluation can be done with a modest collection of tools: a set of prisms (may be in

the form of a box of prisms, a prism bar, or a rotary prism); a red filter; a stereotest; and the Worth 4-dot or Bagolini glasses. An after-image test is helpful in some cases but not absolutely necessary. A complete exam can also be done − and in some instances done better and faster − with a single piece of equipment: a haploscopic device such as an amblyoscope or synoptophore.

10.3.1 The History

The sensory exam begins with the often difficult task of deciphering the patient's description of symptoms. It is an important step because the patient's account may provide significant clues to sensory status. Along with the results of the motor evaluation, the history will help the examiner select the appropriate sensory tests to employ. A careful interview is also imperative in order to assist the patient or caregiver in generating realistic expectations so as to maximize satisfaction with treatment.

One of the most frequent complaints associated with strabismus is diplopia. Though it is not the only unpleasant and debilitating consequence of strabismus, it is currently the only one assigned its own diagnostic code in the International Classification of Diseases, 9th edn. (ICD-9). When investigating a complaint of diplopia, in addition to the obvious questions (e.g., "Is it constant or intermittent?", "Does it disappear when you close one eye?", "Are the images side by side or up and down?") there are a few less obvious questions that will clarify much.

"*What do you mean by 'double vision'?*" Many − particularly older children − use this phrase because they have been told they have double vision, or because they lack the vocabulary to describe what they are really experiencing. The phrase "double vision" is also occasionally used erroneously to describe the eye misalignment, and not necessarily the sensory consequences of that misalignment.

Some patients will deny double vision, but when asked to elucidate their symptoms they describe classic diplopia. For example, torsional diplopia is particularly difficult for the patient to describe, because the fixation point may be single while images in the periphery are twisted or tilted. These patients may actually complain of disorientation or dizziness when in motion. Some patients complain of blurry vision, ghosting, or glare. There are also those who deny diplopia yet unwittingly engage in diplopia-avoidance behavior, such as head posturing or closing one eye.

The most challenging cases of diplopia are those in which the patient appreciates a double image but is unable to locate the object in space relative to the fixation point. This is sometimes referred to as lost localization [19]. Taking a history from these patients is as frustrating for the patient as it is for the examiner. These patients are often looked upon with suspicion and told that their visual experience is not possible. In fact, not only is this type of diplopia genuine, it is a sign of early-onset strabismus with anomalous correspondence and loss of suppression in the nondominant eye.

Diplopia is not the only symptom of strabismus. When asked, many patients will describe difficulties resulting from a loss of stereopsis or fusion. For example, some report difficulty walking down stairs, up a curb, or even across a level surface if it features a boundary created by a change in color, texture, or pattern that might suggest or create the illusion of depth. Some patients express their symptoms as the inability to locate things where they should be or expect them to be. Other patients report stationary objects in their peripheral visual field suddenly and unexpectedly moving. Still others have problems reading due to moving print.

Visual confusion, another consequence of strabismus, is the result of stimulation of corresponding retinal points with dissimilar images. It may be just as common as diplopia, but it is rarely reported because it can be so difficult for the patient to describe. As a result, clinicians rarely ask about it. Patients with visual confusion may recount a bizarre jumbling or confusion of images that resembles retinal rivalry.

Finally, those with alternating suppression or fixation switch diplopia may report images jumping suddenly in front of them from the peripheral field, or losing their place and skipping lines when reading.

"*Does the double vision change with alterations in the ambient illumination?*" Symptoms that change in different visual environments are an important clue to etiology. For example, it is natural for double vision secondary to strabismus to be more noticeable under mesopic (dim illumination) or scotopic (darkness) conditions, particularly when viewing a brightly il-

luminated stimulus. Double vision should be worse when driving at night, for example, because there are fewer peripheral visual cues that assist both fusion and suppression. Diplopia that worsens under photopic (bright illumination) conditions, on the other hand, is uncommon and may actually signify macular pathology, with or without an overlying strabismus (see also Sect. 10.3.5).

"*Is there any way you can hold your head to either make the images come together or make the double vision become less bothersome?*" It is surprising how many patients have never tried this. The answer to this one question goes a long way in establishing a diagnosis and determining fusion capability.

Finally, "*Does the double image appear to move?*" Images that are not only double, but appear to move or float, particularly when they are near the "real" image, signal poor fusion ability. This symptom is indicative of a central disruption of fusion. The patient should be questioned about head trauma or brainstem vascular event.

10.3.2 Sensory Fusion

One of the objectives of the sensory evaluation is to determine if the patient is capable of sensory fusion, the ability to integrate two separate, but similar, visual images into a single impression. Sensory fusion is more than the absence of diplopia, and it should not be assumed that because a patient claims to be diplopia-free or is orthophoric, images from the two eyes are necessarily being fused into one perception. The detection of sensory fusion is singularly important in two clinical situations: (1) the strabismic patient who does not complain of diplopia; and (2) the strabismic patient who has recently been re-aligned, whether by surgical or optical methods. In the former case, the lack of diplopia may be explained by the presence of anomalous correspondence; in the latter, evidence of developing sensory fusion at the new angle of alignment may provide some assurance that the eyes will remain aligned over the long term. Testing for sensory fusion is also worthwhile in the young, otherwise normal patient to document the presence of binocular vision.

Sensory fusion testing is a step in the sensorimotor exam that should not be overlooked in patients with strabismus secondary to very poor vision or large visual field defects. Though these patients are not likely to have good quality fusion post-operatively, they are actually at increased risk for bothersome diplopia. The more the visual field is missing or degraded, the harder it is for the visual system to match up the fields, and the more likely it is to result in bothersome diplopia once the eyes are aligned.

The Worth 4-dot test was originally designed to detect sensory fusion, but because it is so dissociating, it is actually a test that challenges the sensory fusion mechanism. It is, however, quite effective in detecting foveal suppression, estimating the depth and extent of the suppression scotoma (see Sect. 10.3.6), and detecting anomalous correspondence (Sect. 10.3.7). There are some weaknesses to the test that must be kept in mind, but if used judiciously, and performed and interpreted correctly, it can yield a wealth of sensory information.

One disadvantage of the test is that it is too easy for the patient to discover the "correct" answer with repeated use over consecutive examinations, peeking around the glasses, or an inopportune slip of the tongue on the part of the examiner (as the answer lies in the very name of the test). It will be most illuminating the first time it is employed. If the patient becomes too familiar with the test, the responses become less reliable. In giving the anticipated answer, whether that may be one indicating fusion, suppression, or diplopia, the child may receive positive feedback from the examiner. This positive reinforcement will increase the likelihood of that answer being given again at a future visit, even if it does not reflect the true sensory status at that time. Therefore, the Worth 4-dot must be used in moderation, particularly with children. The other major drawback is that the Worth 4-dot utilizes a color-based (anaglyphic) format. This can lead to false-positive or false-negative responses in patients with uncorrected refractive error [37]. Finally, the test may yield false or variable responses due to discrepancies in luminance and contrast between the red and green filter.

The Worth 4-dot test should be performed initially in normal room illumination. This test is slightly less dissociating under these conditions; it will therefore be easier for the patient to appreciate sensory fusion (or suppression). Begin at distance fixation using the same flashlight that is used for near testing. It is not recommended to use the wall-mounted light boxes or

computer-based Worth 4-dot stimuli for this purpose, as these targets form a retinal image large enough to project beyond the limits of a foveal suppression scotoma. The fovea measures about 1.5 mm in diameter, so to test for foveal fusion or suppression, the image should subtend an angle no larger than 1.5º. For example, the Worth flashlight held at distance subtends an angle of 1.25º [31]. The average wall-mounted or computer-based Worth tests feature light stimuli that are up to seven times larger than the flashlight stimuli. To subtend an angle of 1.5º, the light box would need to be mounted over 40 ft. away from the patient!

Figure 10.7 illustrates one useful strategy for utilizing the Worth 4-dot to obtain the maximum amount of sensory information. The appropriate first question to the patient should be, "How many lights do you see?" The answer to this question will determine the next step in the exam. If the patient gives a fusion response at distance, no further testing with this particular instrument may be necessary as foveal fusion with peripheral retinal suppression is unlikely. If the patient reports five lights, which suggests diplopia, he should be questioned carefully whether all five are illuminated simultaneously, or whether the lights alternate from two to three. Patients with alternating suppression do not always appreciate this difference. The patient should be asked to first concentrate on the lights presented to the dominant eye to determine if the other set of lights disappears. The patient should then be encouraged to switch fixation (either spontaneously or with the assistance of a cover–uncover) and the results under two test conditions compared. Those who habitually fixate with one eye may not demonstrate a measurable suppression scotoma in that dominant eye. Consequently, they will appreciate suppression when fixating with the dominant eye, and diplopia when fixating with the habitually deviating eye. These patients are at increased risk for fixation switch diplopia [23]. If true diplopia (rather than alternating suppression) is found, prism can be introduced to attempt to restore fusion; however, it is easier and less confusing for both patient and examiner if this step is done using a red filter and light source rather than the Worth 4-dot test.

The next step is to repeat the Worth 4-dot at near fixation in the same matter, and compare the distance and near responses. Strabismic patients who report suppression at distance and near fixation on the Worth tests have a very large suppression scotoma. Patients with suppression at distance but fusion at near may have anomalous correspondence. If diplopia secondary to macular pathology is suspected based on the patient's history, then the Worth 4-dot test should be repeated at 33 cm, and again at distance and near with the room lights extinguished. The diplopic patient with macular pathology may sometimes report diplopia at distance and fusion at near under photopic conditions, and the reverse under scotopic conditions. In contrast, the patient with diplopia secondary to strabismus will be more likely to appreciate diplopia under scotopic conditions whether tested at 6 m and 33 cm.

10.3.3 Detecting and Quantifying Motor Fusion

Of all the types of fusion, disparity vergence is arguably the most important because this is the type of fusion that maintains eye alignment. Without motor fusion, a patient cannot enjoy the benefits of sensory fusion or stereopsis. Without motor fusion, patients with accommodative strabismus have little hope of weaning out of their hyperopic spectacles or bifocals. It may also be true that without motor fusion, a successful surgical outcome may not remain so over time. Motor fusion is also the type most easily tested in a patient not capable of a subjective response. Yet, of the three major types of fusion, motor fusion is the one least likely to be tested and monitored on a regular basis. A test of motor fusion is most valuable in the following types of patients: (1) the infant who is incapable of demonstrating binocular vision in other, more subjective ways; (2) the strabismic patient who may have anomalous correspondence; (3) the patient with accommodative strabismus (eso- or exotropic) who is attempting to wean out of glasses; (4) the orthotropic patient with asthenopic symptoms; and (5) the adult with long-standing strabismus who is scheduled for surgery.

The basic procedure for detecting and measuring motor fusion using a prism bar or rotary prism is reviewed in Sect. 10.2.4. For a quick and simple method to detect motor fusion, introduce a 16–20Δ

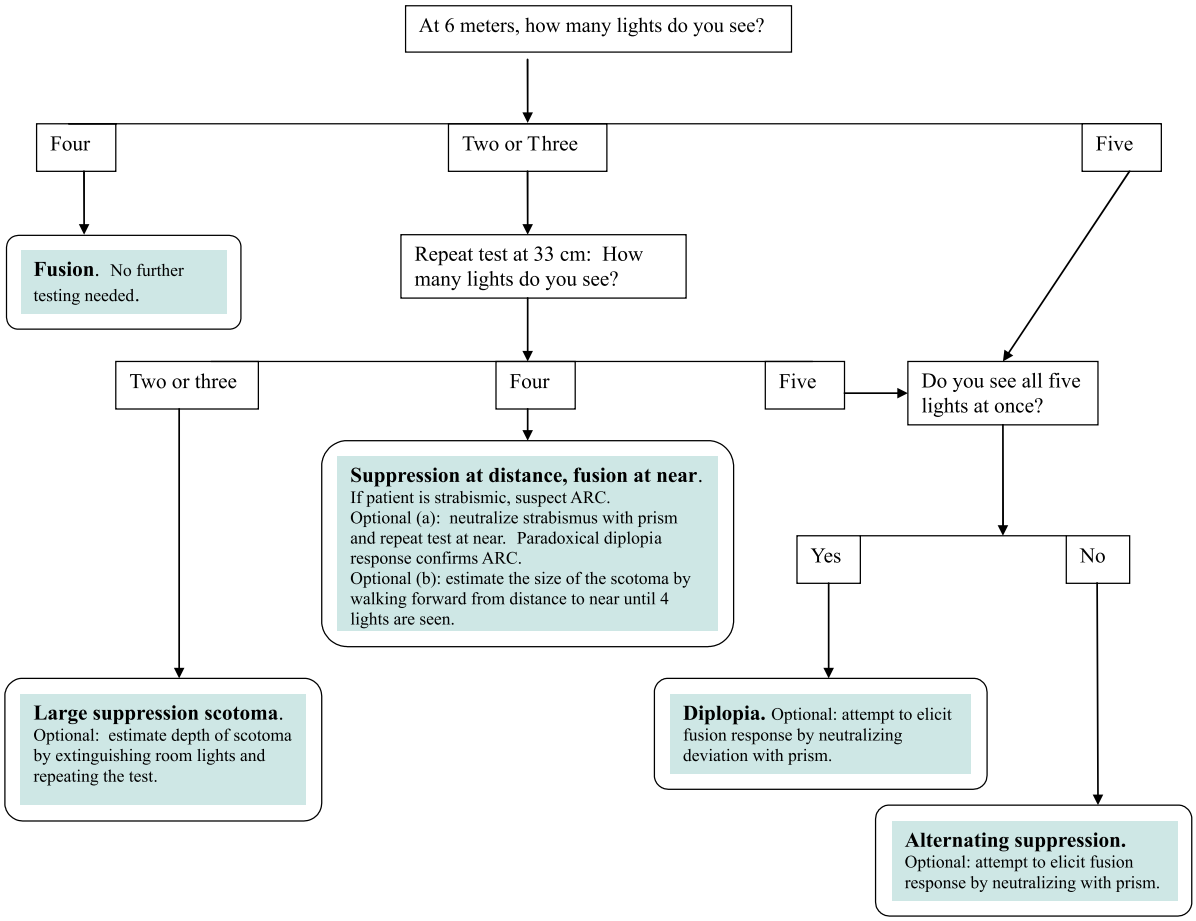

Fig. 10.7 The Worth 4-dot flow chart

base-out prism over the dominant eye while fixation is secured and maintained on a near target [22]. This is sometimes referred to as "jump convergence." A convergence response to re-acquire the target should be observed, followed by a divergence movement when the prism is removed. A 20Δ prism is used because smaller prisms may induce a convergence response that is too difficult to see, and larger prisms may exceed the patient's normal fusional convergence amplitudes, resulting in a false-negative finding. This simple test is the preferred method for detecting binocular vision in the infant and young child. Motor fusion amplitudes can also be measured on the amblyoscope, but this method is more difficult for children. In order to recognize the fusion break point, the patient must be able to appreciate and communicate subtle changes in the fixation target's appearance or position.

The jump convergence method is also useful in the strabismic patient who may have anomalous correspondence if the angle of strabismus is <20Δ. Those with larger deviations are best tested on a haploscope. The jump convergence test evaluates the retinomotor value of a peripheral retinal point relative to the "pseudo-fovea" of the deviating eye. ("Pseudo-fovea" is a term given to the non-foveal retinal element of the deviating eye that has acquired a correspondence with the fovea of the fixating eye under binocular conditions.) Anomalous motor fusion is an important feature of anomalous correspondence. Patients with anomalous correspondence and motor fusion are at elevated risk for an early surgical under-correction or

recurrence of the pre-operative angle as the fusional vergence mechanism seeks to restore correspondence between the fovea of the fixing eye and the pseudofovea of the non-dominant eye. These cases are also likely to "eat up" prism with prism adaptation, building to the limits of their convergence amplitudes (see Sect. 10.2.3). If surgery is then performed for this larger angle, an over-correction is highly likely.

Both the strabismic patient attempting to wean out of spectacles and the asthenopic patient should be tested with a prism bar or rotary prism, as their fusional vergence range may be too low to be detected with jump vergence. The base of the prism should be placed in the direction opposite to that used to measure the deviation so as to increase the vergence demand. For example, divergence amplitudes are necessary to control an esotropia. To measure divergence, the prism will be held base-*in* and gradually increased in power until fusion is broken. This will result in a manifest esotropia, with the patient reporting either diplopia or suppression. In this example, the base-in prism effectively simulates an increasing esodeviation, and the break point estimates just how much esodeviation the patient can manage before becoming esotropic.

The visual system, both sensory and motor components, operates on a "use it or lose it" principle. The brain is unlikely to expend the energy to maintain a pathway, network, or system that is not being utilized regularly. It is a waste of effort and resources, and the central nervous system is nothing if not efficient. Adults with long-standing strabismus illustrate this point well. Motor fusion amplitudes in the same direction as the strabismus (i.e., convergence in esotropic patients) are likely to be subnormal, and it is important to detect this prior to surgery if the goal is to achieve a small over-correction in the immediate post-operative period. While the child with a small surgical over-correction usually recovers, the adult with the same small over-correction may not. Measuring the fusional amplitudes pre-operatively will help to determine the risk of persistent post-operative diplopia secondary to a small over-correction. For example, a patient with a long-standing exotropia may demonstrate convergence amplitudes that are above the norm, even though they may be insufficient to control the deviation completely; however, this same patient will have poor or absent divergence amplitudes because there has been no need for the vergence system to maintain that ability. This patient will have difficulty overcoming even a small angle over-correction.

10.3.4 Detecting and Quantifying Stereopsis

Stereopsis is the ability of the visual cortex to utilize retinal image disparity to localize objects in space relative to the horopter. (The horopter is the curve described by the distribution of matching retinal elements.) It is the most complex and highly developed type of binocular vision, and the type most susceptible to insult to the visual system. Restoration of stereopsis in the formerly strabismic patient is typically considered the pinnacle of success, and is often the single criterion of binocularity included in final outcome measures in surgical studies. It is also the type of binocularity most often tested on a routine exam. Because it is so sensitive to decreased vision, suppression, and ocular misalignment, it has also been used as a vision screening tool. Stereopsis has also been used effectively to monitor control of an intermittent deviation, particularly intermittent exotropia, for the purpose of determining appropriate timing for surgery [15, 17]. As the patient spends more time in the tropic state, suppression gains a foothold and becomes deeper. Suppression is present under binocular conditions, even when the eyes are in the phoric state [32], so a suppression scotoma has the potential to reduce stereoacuity by blocking the disparity signal. Decreased stereopsis, therefore, may indicate an expanding or deepening suppression scotoma, which typically results from a loss of control over an intermittent deviation with an onset during childhood [42].

Stereopsis can be detected and measured a number of different ways. Each stereotest has its own strengths and weaknesses. Because there is no one ideal method, the choice of test will depend on the question the examiner is seeking to answer. Most of the methods require glasses (polarized or red-green) or a septum to control the image presented to each eye. The right- and left-eye images are typically identical in contour and size, but with one image displaced by a small amount horizontally. It is not necessary that

each eye be presented with an identifiable image [13]. The depth effect can be achieved with visual noise alone, though these types of tests are typically more challenging for the patient.

It is very difficult to isolate pure disparity sensitivity in a clinical setting. Most tests available today suffer from monocular clues to depth that may lead to false-positive results or artificially enhanced stereoacuity. The Titmus Stereotest is probably the most well-known example of a stereotest flawed by these artifacts. A stereoblind patient may demonstrate deceptively good stereoacuity due to the non-stereoscopic, image displacement cues. In spite of this, the Titmus test continues to be the most popular and accessible test of stereoacuity worldwide. Like the Worth 4-dot test, if used judiciously and meticulously by an examiner familiar with its limitations, this stereotest can be reasonably effective. The infamous Titmus Housefly, in particular, can actually be quite useful. Because it is designed with such a large degree of disparity (3000 s of arc at 40 cm), even those with the most insubstantial disparity sensitivity may be able to appreciate the image in depth. It is also effective as a qualitative test of stereoacuity in young children who may be incapable of understanding instructions. Without any coaching at all, the dramatic and unpleasant image provokes curiosity and occasionally fear in the young child. A strong reaction is often indicative of a positive response. In fact, it is often when the examiner must instruct the patient that the Titmus test loses some of its effectiveness! It is very difficult to explain the test without inadvertently leading the patient to the correct answer. Some children have a need to please, and may be better at reading the examiner than they are at reading the test! Moreover, those who have worn the polarized glasses and stared at the fly two or three times per year over a decade or more tend to respond affirmatively because they have learned the "correct" answer. Like the Worth 4-dot test, the Titmus fly will be most accurate the first time it is used, and with increasing exposure will come a higher false-positive rate. Those who have never enjoyed stereopsis do not understand what the sensation is like, so asking the patient if the stimulus is "three-dimensional" or "elevated" from the page is meaningless; however, these patients are sometimes able to tell that there is something different about the stimulus and may assume that this difference is what we mean by depth or "3D" effect.

Another point that must be emphasized is that this test is calibrated for use at 40 cm, not the customary 33 cm otherwise used for near fixation. Advancing the book to 33 cm will increase the retinal disparity produced, and overestimate the degree of stereopsis. For those patients with either very poor or very fine stereopsis, the effect on stereoacuity produced by the shorter test distance is probably negligible; however, for those in monofixation range, repositioning the test book by several centimeters could mean the difference between fine and gross stereopsis and possibly change the diagnosis.

If in doubt of a patient's positive response, the examiner can rotate the book 90º and repeat the test. This changes the disparity from horizontal to vertical, and collapses the 3D effect. Those with true disparity sensitivity will notice a dramatic flattening of the image occasionally accompanied by the sensation of vertical diplopia; those without disparity sensitivity will report no change in the image.

The only stereotest of true depth available for use in the clinic is the Frisby Stereoacuity Test, a series of clear plastic plates divided into four square segments with random blue shapes printed on one side. One of the square segments features a hidden circle pattern that is printed on the back side of the plate, thereby displacing it off of the plane of fixation (horopter). This test has several advantages. Firstly, it does not require dissociation by glasses or septum to create the illusion of an image positioned off of the plane of fixation. Such dissociation could potentially break fusion and result in artificially poorer stereoacuity. Secondly, because the plates can be rotated to change the location of the circle and turned over to change the disparity from crossed to uncrossed, it is not possible for the patient to memorize the correct answer. Finally, the Frisby test can measure over a wide range of disparities simply by changing test distance, and is one of the few tests available that has been modified to test distance stereoacuity (Frisby-Davis 2).

Like the Titmus test, there are monocular clues to depth on the Frisby test. Both the plates and the patient's head must be kept steady to avoid the motion parallax cue to depth. The plate should not be placed on a flat surface. In addition, recent comparison studies have found that while the Frisby test may be very good at detecting stereopsis, other types of random dot stereotests may be better at quantifying and monitoring changes over time [28].

10.3.5 Investigating Diplopia

Examination of the diplopic patient has several goals: (1) to determine if the diplopia corresponds to, and can be explained by the strabismus; (2) to estimate the impact of the diplopia on the patient's quality of life; and (3) to determine if the diplopic patient is capable of single binocular vision. The pattern and type of diplopia should fit with the pattern and type of strabismus revealed by the motor exam. Placing a red filter over the dominant eye will assist the patient in determining the precise location of most types of diplopic images. Exceptions include torsional diplopia, monocular diplopia, or diplopia secondary to lost localization (see Sect. 10.3.1). If there is a discrepancy between the motor exam and the type of diplopia found on sensory exam, the diplopia may be paradoxical. Paradoxical diplopia typically occurs with a change in alignment in the patient with anomalous correspondence. Post-operative paradoxical diplopia is a common but temporary complication of strabismus surgery in adults with a history of childhood-onset strabismus, good visual acuity, and anomalous correspondence on pre-operative sensory testing[9]. Anomalous correspondence may persist in the early post-operative period and produce a double image that corresponds to the pre-operative position of the fovea of the deviating eye.

Documenting the impact of diplopia on quality of life can be important for several reasons. For example, the examiner will inquire about any restriction of activities or deterioration in performance of activities that require depth perception. The answer to these questions may play a role in the decision to intervene with treatment. There are also situations where documentation of the impairment must be provided to a third party prior to treatment. This is one reason why plotting the field of binocular single vision can be useful. In the past this was most commonly accomplished using the Goldmann perimeter, but these manual perimeters have all but been replaced by automated models that are difficult to adapt for use in recording diplopia. Moreover, the Goldmann perimeter charts diplopia on a concave surface steeper than the curve of the horopter, which may not be as authentic a representation of visual space as a flat surface. Finally, the Goldmann apparatus cannot detect or plot torsional diplopia without special adaptations to the stimulus, which may be costly or cumbersome. To address these concerns, the Matta map was developed (N. Matta, C.O., Family Eye Associates, Lancaster, Pa.). This method of diagramming diplopia is a modification of the Lancaster red-green test utilizing the screen and one torch without the red-green glasses. While keeping the head in primary position seated 1 m from the screen, the patient views the examiner's red line image as it is projected to each of the markers on the Lancaster screen that represent the nine positions of gaze. The patient indicates whether a single or double image is seen at each location, and the examiner maps out the field of single vision on graph paper. Like the Goldmann method, the Matta map can be used as a static test (as described) or as a kinetic test to precisely define the boundaries of single vision.

The cervical range of motion (CROM) method has also been described as an alternative to Goldmann diplopia fields (see also Sect. 10.2.2) [16, 24]. When using the CROM to map a diplopia field, the patient is asked to binocularly fixate an accommodative target with the head held in whatever position allows single vision. The head is then rotated away from this position as fixation is maintained until diplopia is noted. The head position in degrees can be read from the dials. One of the advantages of the CROM is that it can be used with real targets in free space as a stimulus, rather than lights projected onto the inside of a bowl (Goldmann) or a screen (Matta Map). The targets and backgrounds used for both the Goldmann and Matta methods impart more of a challenge for both fusion and suppression, and therefore may overestimate the diplopia experienced on a day-to-day basis. In addition, the CROM can be used to measure the field of single vision at distance fixation and is more precise in its quantification of the range of motion. On the other hand, the CROM device is more cumbersome and less comfortable for the patient than the other two methods, and it does not produce the simple graphic representation of the field of single vision. It is also a more expensive piece of equipment than the Matta map.

Just as one should not assume that the diplopia-free patient is fusing, neither should it be assumed that all diplopic patients are capable of sensory fusion. The most common method used to determine if the diplopic patient is capable of fusion is to offset the deviation with prism in "free space" (natural viewing conditions). The problem with this technique

is that it cannot distinguish between fusion, suppression, and simple inattentiveness to the second image. If the deviation is large, the neutralizing prism may simply blur or distort the diplopic image, making it easier to ignore and resulting in elimination of diplopia without necessarily restoring fusion. An offsetting prism may also move the diplopic image into a suppression scotoma. The ideal way to distinguish between these three very different diplopia-free conditions is to examine the patient on a haploscope using fusion slides. Although still artificial, the stimuli are closer to natural viewing conditions than those in some other tests, and the slides feature fusion controls enabling the examiner to detect suppression. If an amblyoscope is not available, the patient can be given a test for sensory fusion or stereopsis through an offsetting prism.

To investigate diplopia in the patient complaining of intermittent double vision, testing is begun in a "fusion-friendly" environment. This means as close to natural viewing conditions as possible: normal room illumination; a visually busy surround featuring multiple contours; and similar images presented to each eye. If diplopia is not present under these conditions, binocular vision can be put under pressure to estimate the vigor of the fusion ability. The first step is to make the images dissimilar by introducing a red filter over the dominant eye. The filter reduces both luminance and contrast, and thus, if placed over the non-dominant eye, it will be more likely to result in suppression. If fusion can be maintained despite the dissimilar images, the next step is to extinguish the room lights, thus eliminating peripheral cues for fusion. This method of gradually increasing dissociation to put the fusion ability under stress can be modified for use with almost any of the sensory tests.

There exist two subsets of diplopic patients who will prove incapable of sensory fusion using the techniques described above. They are those with central retinal pathology and those with central disruption of fusion. In these situations, determining if the patient is capable of sensory fusion is necessary not only for management, but for diagnosis.

A small number of diplopic patients have a macular wrinkle, neovascular membrane, or central serous retinopathy with or without a true overlying strabismus [8, 10]. These conditions may cause a spreading or bunching of retinal elements in the fovea resulting in a shift in foveal localization relative to the periphery. Under normal photopic conditions, this creates a sort of disconnection between foveal and peripheral fusion as though the two were out of phase. When the foveal images are fused, the peripheral elements are diplopic, and vice versa. Rather than a true myogenic or neurogenic strabismus, the misalignment that results is caused by inappropriate activation of the disparity-driven vergence system in its attempt to reconcile peripheral and foveal fusion.

These patients can be identified clinically by their atypical symptoms and response to prism. For example, they may report that their diplopia becomes worse under photopic conditions. The "lights on/lights off" test illustrates this well [10]. The diplopia is present with the room lights on, but when extinguished, minimizing peripheral visual cues to fusion, the second image disappears.

Patients with diplopia secondary to macular pathology also tend to "eat up" prism. Prism offset may initially relieve symptoms, only to return at the original magnitude over a period of minutes to hours as the vergence system adjusts the eye alignment to restore peripheral fusion.

As with macular diplopia, double vision secondary to central disruption of fusion typically cannot be alleviated with prism, amblyoscope, or strabismus surgery. These patients can be identified by their medical history, which may feature severe closed-head trauma with or without loss of consciousness, brain-stem stroke, or long-term monocular occlusion due to media opacity. They are recognized on exam by the constant movement of the diplopic image, particularly noticeable when the diplopic image is in close proximity to the image from the dominant eye. When the strabismus is neutralized with prism under natural viewing conditions, the diplopia not only persists but may become more bothersome as the second image floats around the true image. A cyclotropia may also result in persistence of diplopia with prism offset, but can be differentiated from central disruption of fusion based on this movement of the diplopic image. Central disruption of fusion is best diagnosed on a haploscopic device for several reasons. Firstly, cyclotropia can be offset ruling out torsion as the cause of the persistent diplopia. Secondly, central disruption of fusion displays a characteristic binocular behavior best described as a lack of correspondence between the two eyes. In some cases,

the images may be manipulated to be perceived in the same approximate location but are never truly fused into one visual perception.

10.3.6 Suppression

Detecting suppression, particularly in the adult, is valuable for several reasons. The presence of suppression frames the onset of strabismus within the early childhood years. Quantifying the depth of suppression may further refine that timeframe, as deep suppression takes longer to develop. In addition, measuring the boundaries of the suppression scotoma will provide clues to changes that have occurred in alignment over time. Delineating a suppression scotoma will also assist in defining the diplopia-free zone of alignment, which will assist in planning the management strategy.

Once the ability to suppress is learned, it is retained throughout life, barring any anti-suppression intervention (see Sect. 10.4.2). The depth and dimensions of the suppression scotoma may also remain stable in spite of treatment of the strabismus. Only the most superficial suppression is cured by realignment of the visual axes. The suppression scotoma can enlarge, however, should the angle of strabismus change. The suppression mechanism is designed to eliminate only that input that is in direct competition with the dominant eye. This includes the fovea and the deviation point of the deviating eye (the deviation point is the peripheral retinal element of the deviating eye on which the image of the target being fixated by the dominant eye falls), as well as all points in between; therefore, the size and shape of the suppression scotoma is directly related to the magnitude and direction of the strabismus. When the location and size of the scotoma is compared with the current angle of strabismus, it can provide a clue to eye alignment earlier in life. If the deviation changes, either spontaneously or secondary to intervention, the suppression scotoma will adapt. How quickly it adapts likely depends on the age of the patient, with younger patients responding faster.

It is important to remember that if a patient complains of diplopia, a suppression scotoma may still be present. The presence of diplopia only means that the images are now falling on non-suppressed retinal elements. Locating a suppression scotoma will aid in diagnosis and may save the patient money, time, and the needless anxiety that often accompanies a systemic work-up for new onset diplopia. Similarly, a strabismic patient who denies diplopia does not necessarily have suppression. If the image from the deviating eye is far enough away from the true image, it can often be ignored. It remains necessary to detect any suppression ability, even in these cases, as suppression may either assist or interfere with the management of the strabismus.

Evidence of suppression can be found with use of almost any sensory test, but certain tests are intended specifically for this purpose. The 4Δ base-out test is one example. It was originally designed as a screening tool [20] to detect small angle strabismus by revealing foveal suppression, and has two principle advantages over other sensory tests. Firstly, it is more objective than most. Secondly, it requires minimal cooperation on the part of the patient. This test is of little value in asymptomatic patients with moderate- to large-angle manifest strabismus. It is very useful, however, in patients who appear orthophoric on cover testing but have decreased stereopsis, decreased vision, or other finding that suggests lack of bi-foveal fixation. Although it cannot be used to diagnose amblyopia, a positive test may confirm the examiner's suspicions as to the nature of the decreased vision, as suppression is often found in an eye with amblyopia. The 4Δ base-out test can also confirm bi-foveal fixation in a patient too young to participate in optotype vision testing or perform a stereotest. It can be difficult to distinguish a small-angle tropia from a phoria or intermittent tropia, and the 4Δ may assist in this as well.

In general, it is easier for the examiner to appreciate the combination version and vergence movement induced by this test if the patient fixates at distance, but it can be performed at near fixation as well. It is important to use a 4Δ prism for this test, as larger prisms will shift the image outside a foveal suppression scotoma, and a smaller prism may induce eye movements that are too small for the examiner to see. The prism may be held base-out even in the presence of an exo- or hyperdeviation, as foveal suppression scotomas will often encompass and extend slightly beyond the fovea into nasal retina even in exodeviations. Rarely, a patient with small-angle strabismus will alternate fixation. In these cases, the 4Δ may yield a false-negative response.

As previously noted, suppression is present under binocular conditions, whether or not the patient is currently manifesting a strabismus. Though a suppression scotoma may be virtually undetectable during the phoric phase of an intermittent deviation, it should never be assumed that the suppression scotoma has disappeared entirely as long as the patient is binocular. In fact, identifying a suppression scotoma coexisting with a latent strabismus may be significant to prognosis. This can be done indirectly by monitoring stereoacuity (see Sect. 10.3.4), or directly by using a haploscopic device. Haploscopic instruments are ideal for investigating suppression, and in fact, are designed to do so using the fusion (Worth's Grade II) slides. These slides feature similar images to encourage fusion, with monocular controls that are seen only by the left or right eye on each slide. The size of the suppression targets on the slides varies so that even small scotomas can be detected.

Detecting suppression during the phoric phase of an intermittent deviation is problematic without an amblyoscope; however, if the suppression scotoma is large and dense, it can be exposed using a simple physiologic diplopia exercise. Have the patient hold one index finger at arm's length, and the other index finger 18−20 cm. from the midline of the face. While wearing the red-green glasses, the patient should fixate on the distant finger. If no temporal retinal suppression is present, the patient should observe the closer finger as double: one red and one green. If suppression is present, only one near finger will be seen at a time: one red or one green. To detect nasal retinal suppression, the patient should be instructed to fixate on the near finger and attempt to appreciate the distant finger as double. If only one finger is seen at distance, nasal suppression is present. The red/green glasses will allow the examiner to determine which eye is being suppressed.

When it is necessary to perform a thorough dissection. of the suppression scotoma, a great deal of information can be learned using only filters and lights. For example, the depth of the suppression scotoma may be estimated by repeating the Worth 4-dot test with the room lights extinguished and comparing the results with those obtained under photopic conditions. In a dark room, those whose suppression is fragile may report diplopia. Similarly, those whose fusion is tenuous may report suppression or diplopia. If the depth of the suppression must be more precisely quantified, the patient should fixate a light source as the examiner gradually increases the density of either the red or the neutral density filter over the dominant eye until diplopia is appreciated. Alternatively, an amblyoscope may be used. Using the rheostat feature, the illumination of the target over the dominant eye is gradually reduced until the image from the non-dominant eye is appreciated.

The size of the scotoma can also be calculated using the Worth 4-dot test, based on the distance from the patient at which fusion is first noted [12]. The examiner should begin with the flashlight at distance, and gradually move closer to the patient until four lights are appreciated. If greater precision is desired, the examiner can use a red filter and prism bar. Place a red filter over the dominant eye as the patient views a target at a fixed distance. Gradually increase the prism power until the patient reports diplopia, and repeat this procedure with the prism base in the opposite direction. If using the amblyoscope, begin with the arms of the device set at the angle of strabismus, so that the images are being projected onto both foveas. From there, the arms are moved slowly out of this position until the non-dominant eye appreciates the image.

10.3.7 Determining Retinal Correspondence

Retinal correspondence refers to the cortical matching of similar input from compatible retinal areas and the concomitant anatomical linkage of their sensory neurons in the visual cortex. For example, if correspondence is normal, then both foveas will have identical visual directions and retinomotor values under binocular conditions. The sets of neurons in the primary visual cortex that receive input from the fovea of the right and the left eye will be physically linked as well. Correspondence is what defines the horopter and retinal image disparity, and is the foundation for all binocular interaction, both normal and anomalous. Both human and animal studies have demonstrated that stereopsis, the most sophisticated corollary of correspondence, has an abrupt onset in the first months of life, regardless of the position of the eyes [6]. This implies that normal correspondence

is a default state that is programmed to commence functioning once the eye-of-origin information is available with the formation of ocular dominance columns early in the critical period. (The critical period is a two-phase period of rapid growth and development from birth to age 9–10 years during which the visual system is extremely susceptible to insult but also highly responsive to treatment.) Normal correspondence can be lost, however, if eye misalignment, and the resulting incompatible input, is allowed to persist [11].

It is generally believed that anomalous retinal correspondence (ARC) is an adaptation to this mismatched input that allows the strabismic individual to enjoy sensory and motor fusion and occasionally stereopsis. The ARC is a shift in subjective visual directions of the retinal elements of the deviating eye, relative to those of the fixating eye, that occurs only under binocular conditions. This creates a new, anomalous horopter and Panum's area, allowing binocular vision. (Panum's area is the zone surrounding the horopter in which binocular single vision is possible, though similar images are stimulating non-corresponding retinal elements.)

A lack of correspondence, though certainly abnormal, is not typically categorized as ARC. A lack of correspondence results in the absence of normal or abnormal sensory fusion, motor fusion, and stereopsis, and the presence of intractable diplopia (see Sect. 10.3.5) These signs and symptoms are reported in cases of central loss of fusion, horror fusionis, and following aggressive anti-suppression therapy in a patient with poor fusion ability. (Horror fusionis is described as active rejection of bifoveal stimulation. As the stimuli are manipulated to approach projection onto both foveas, the diplopic images appear to move further apart.)

Discerning the state of retinal correspondence is valuable for several reasons. Firstly, like suppression, the presence of anomalous correspondence fixes the age of onset during the critical period. In order for the brain to "rewire" in this way, a patient must have a relatively long-standing, constant, and stable deviation with onset early in childhood. Secondly, the presence of ARC, by definition, confirms that the patient has the capability for some type of fusion in spite of an ocular misalignment. This ability may increase the likelihood of long-term stable eye alignment in a formerly strabismic patient. Finally, strabismic patients with ARC are at increased risk for postoperative paradoxical diplopia. Though the pattern of retinal correspondence will eventually adapt to the new post-operative angle of strabismus, the retinal elements of the non-dominant eye will retain their abnormal visual directions and anomalous correspondence for a time. In this situation, an object located at the fixation point will fall on points that are not yet corresponding, and paradoxical diplopia will result.

Though the rewiring that occurs in ARC is not necessarily limited to the fovea and the deviation point of the non-dominant eye [41], the subjective visual direction of these two points are the most conveniently tested in the clinic. If the examiner is seeking evidence of fusion, the subjective visual direction of the deviation point should be compared with that of the fovea of the dominant eye. These types of tests are sometimes referred to as fovea-to-periphery tests. If the examiner is seeking to estimate the probability of post-operative paradoxical diplopia, the subjective visual direction of the fovea of the deviating eye should be compared with that of the fovea of the dominant eye [9]. These tests are known as fovea-to-fovea tests. It is entirely possible − and in fact common − to demonstrate ARC with one type of test and not the other, indicating that not all retinal elements are rewired simultaneously in all types of ARC. There is some evidence to suggest that the visual system selectively chooses certain points to rewire, presumably based on a maximum visual benefit for minimum effort strategy. It has been shown that patients with small to moderate angle strabismus (up to 20Δ), particularly esotropic patients, are more likely to show anomalous correspondence on fovea-to-periphery tests. Those with larger deviations, particularly exotropia, are more likely to show anomalous correspondence on fovea-to-fovea tests (Fig. 10.8) [3].

Anomalous correspondence in the form of acquisition of a pseudo-fovea accompanied by fusion is most commonly associated with esotropia ≤20Δ; however, retinal correspondence should also be evaluated in those with deviations outside of this narrow range, particularly if the patient is an adult scheduled for strabismus surgery. Though it may be both easier and more beneficial for the visual cortex to adapt to moderate angles of esotropia, ARC does occur in larger deviations, in exodeviations, and even in small hy-

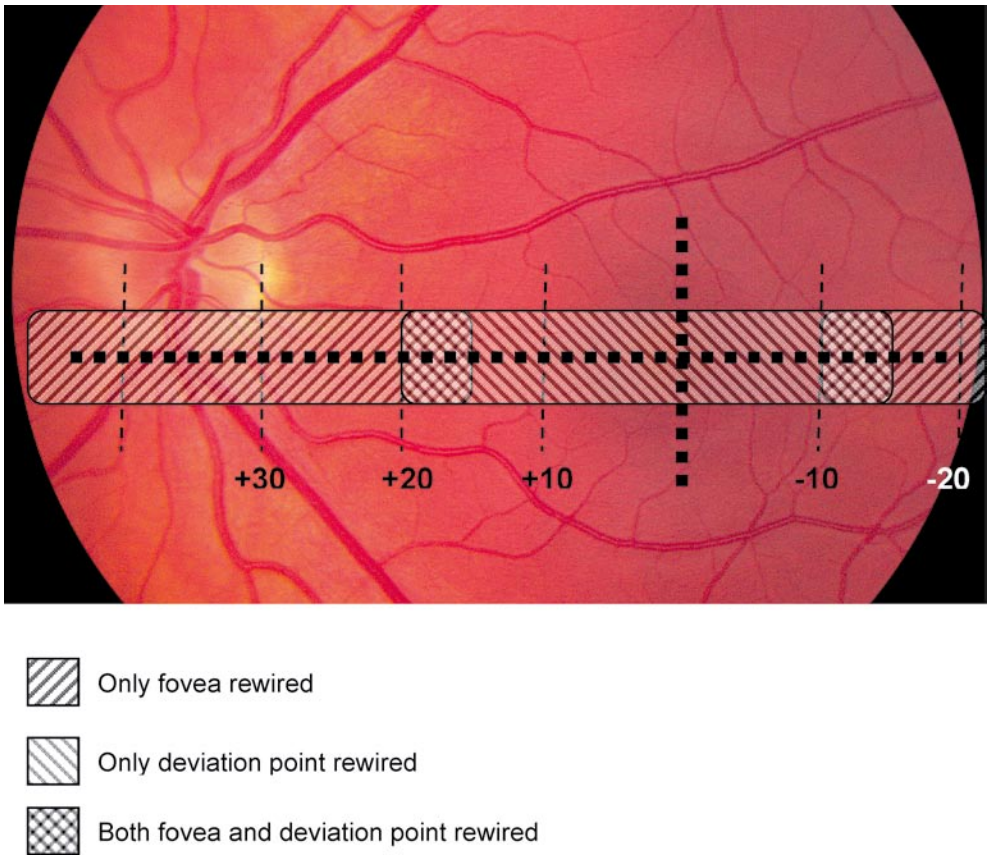

Fig. 10.8 Patterns of ARC in horizontal strabismus. In anomalous retinal correspondence (ARC), not all retinal elements of the deviating eye "rewire" to acquire a new visual direction. Only those deviations between XT 15 and ET 20 are compatible with the formation of a "pseudo-fovea," while the deviating fovea is more likely to rewire in larger angles of strabismus. Deviations between ET 15−20Δ, and XT 10−15Δ may show ARC on *both* fovea-to-fovea and fovea-to-periphery tests, indicating that the deviation point and the fovea of the misaligned eye have both been rewired

perdeviations. The binocularity that results may not be as rich or robust as that found in small-angle esotropia, but it may be more likely to cause problems following realignment of the visual axes. Those with large-angle horizontal deviations and ARC are at increased risk for post-operative paradoxical diplopia because they tend to have the type of ARC that results in a modification of the subjective visual direction of the deviating fovea under binocular conditions. This subgroup of patients should be tested specifically with a fovea-to-fovea test prior to surgery.

All that is needed to prove the presence of ARC is a fusion response on any sensory test in the presence of a manifest deviation. Though almost any sensory test can be used to determine retinal correspondence, the two discussed here were designed specifically for this purpose. The choice of test should be made on a case-by-case basis, based on the type and magnitude of the deviation, the duration of the current eye alignment, and the rationale for testing, whether to detect evidence of fusion or to predict the likelihood of post-operative paradoxical diplopia. The first is the Bagolini glasses test, a fovea-to-periphery test. This test evaluates correspondence by testing for the presence of sensory fusion. Unlike other tests of sensory fusion, this one is favored because the level of dissociation is very mild. As noted previously, it is much easier for a patient to achieve sensory fusion under viewing conditions that are as close to natural as possible. Those patients with brittle fusion may test

positive with the Bagolini glasses, when other tests of sensory fusion produce suppression or diplopia. The Bagolini glasses test can be converted to a fovea-to-fovea test by neutralizing the deviation with prism.

The second test is the after-image test. This fovea-to-fovea test is highly dissociating. It is advised to use this test pre-operatively in any adult with a history of childhood onset strabismus, even if the patient does not show ARC on any other test. Those who display ARC on this test have a very deep-seated anomalous correspondence and are likely to experience post-operative paradoxical diplopia. The after-image test is ideal for determining the visual−spatial localization of the deviating fovea, particularly in deviations that are long-standing, of larger magnitude, and in exotropia. When performing this test, it is important to flash the dominant eye first, orienting the line stimulus parallel to the direction of the strabismus (i.e., a horizontal light stimulus for patients with eso- or exotropia). If ARC is present, the habitually deviated eye will often have a suppression scotoma dense enough to lose the after-image by the time the dominant eye is stimulated, if the deviating eye is exposed first.

10.4 Orthoptic Treatment

The non-surgical treatment of binocular vision and ocular motility disorders has a long history, beginning with ophthalmologists in the late nineteenth century, then orthoptists in the early twentieth century, and more recently, with some branches of optometry. The history is predominantly one of trial and error, anecdote, and hearsay, as most of it predates the modern age of evidence-based medicine. Through personal experience, teaching passed down from mentor to student over generations, and case reports, we have learned that several common sensory and motor conditions can be addressed with non-surgical therapies. We have also learned − the hard way − that many of them that *can* be treated should *not* be treated. The urge to repair something that is anomalous, regardless of whether it is causing symptoms, is sometimes overwhelming. Giving in to this temptation may create a problem where none existed.

There are two major risks to non-surgical therapy. The first major risk is insuperable diplopia, the inevitable result of aggressive treatment of suppression or ARC in a patient incapable of normal binocular vision. The second major risk of non-surgical therapy is a delay in appropriate diagnosis and medical care. There is little risk if the therapy is supervised by a pediatric ophthalmologist; however, if undertaken without an initial medical evaluation to rule out causative or coexisting systemic or ocular disease, at best the therapy may cost the patient money and time, and at worst it may cost binocularity, vision, or worse.

One of the surprising areas of controversy regarding non-surgical therapy is where the treatment should take place. Some doctors believe that the exercises should be done under supervision in the practitioner's office, with or without supplemental home exercises; others believe that home-based therapy with proper instruction is just as effective. To date, most studies comparing home- vs office-based therapies suffer from a design flaw that compares a rigorous and multi-faceted in-office program with unsophisticated and monotonous "pencil push-ups" done at home. These two regimens are not equivalent and should not be compared.

Most office-based exercises can be effectively adapted for home use. Assuming that the therapist then puts the same amount of effort into instruction, the essential difference between these two treatment regimens is simply a matter of compliance. If the treatment is done in the office, the clinician is assured of compliance for at least that amount of time per week. If done at home, the patient or parent must take responsibility for doing the exercises, and the clinician must accept the patient's or the parent's word that the prescribed regimen is being followed.

10.4.1 Criteria for Patient Selection

The most important aspect of orthoptic therapy is not *where* it is done, or perhaps even *what* specific exercises are prescribed, but rather *who* is chosen to receive this type of treatment. This is another important area of disagreement regarding orthoptic therapy. Some clinicians believe that non-surgical therapy is never appropriate for any condition, just as there are those who believe it is just as effective as, or more so, than surgery for almost anything, including con-

ditions not directly related to vision or ocular motility. The reality is somewhere in between these two extremes. Orthoptic therapy is effective, but only in carefully selected cases.

Candidates for orthoptic therapy include those with modest angles of misalignment, good to fair control of the deviation, and good binocular vision ability or potential. Candidates must also be in good health, have sufficient intelligence to understand the instructions, and possess a long enough attention span to complete the exercises. The candidate must also possess stamina and determination, because significant improvement in symptoms may take weeks to months to realize.

Non-surgical treatment is contraindicated in those with onset of strabismus in early childhood, with no history or sign of fusion ability, or with a history of a long-standing constant deviation even if they once had good fusion. This group is at significant risk for intractable diplopia with orthoptic therapy.

These restrictions and stipulations realistically limit orthoptic therapy to healthy patients, between the ages of 5 and 70 years (with exceptions), with symptomatic phorias, small-angle intermittent esotropia, intermittent exotropia $\leq 20\Delta$, and accommodative esotropia that has been well controlled with plus lenses. Taken all together, these criteria markedly restrict the number of patients who might be successfully managed with non-surgical treatment alone.

Convergence insufficiency is a vergence disorder that deserves special mention. This is the one condition for which there is sufficient proof of efficacy of orthoptic therapy [33]. In spite of this, treatment of convergence insufficiency is not without controversy. One of the major areas of disagreement, surprisingly, is the criteria used to diagnosis the condition. Some eye care practitioners will make this diagnosis based solely on the presence of symptoms (such as headache) no matter how vague or non-specific, even if the eye examination is entirely normal [35]; others require some clinical sign of pathology such as a remote near point of convergence, weak convergence amplitudes, low AC/A ratio, or exodeviation at near fixation. Yet even those who rely on the presence of clinical signs cannot agree on what defines a remote near point, or low fusional convergence amplitudes, for example. Consequently, convergence insufficiency is considered uncommon in some practices, while it approaches epidemic proportions in others!

10.4.2 Anti-Suppression

Suppression is curable, but in almost all cases, suppression is beneficial and its treatment contraindicated. There are some specific cases in which suppression can be counterproductive and treatment might be considered if conditions specified in Sect. 10.4.1 are met. One such case would be a patient with an intermittent deviation whose control may be improved by reducing a large suppression scotoma. The vergence system, which functions to keep similar images on corresponding retinal points, initiates a vergence response only if it receives a retinal image disparity error signal within the patient's motor fusion range [26]. In this way, the vergence system maintains eye alignment. If the signal is suppressed due to cortical inhibition of the disparity input, the closed-loop disparity-driven vergence system remains inactive, even if the patient has more than adequate motor fusion amplitudes to make the adjustment. This initiates a cycle whereby the lack of vergence adjustment allows the non-corresponding points to continue to be stimulated, which only deepens the suppression scotoma, making it easier for the eyes to deviate. By reducing suppression, the visual system has access once again to the normal vergence feedback loop which may improve control.

The second type of patient who may benefit from anti-suppression exercises is one who has recently undergone successful strabismus surgery. The persistence and adaptable nature of suppression may lead to a recurrence of some types of strabismus. Realignment of the eyes does not automatically eradicate moderate to dense suppression in most cases. Because of the vicious cycle of suppression followed by loss of the disparity signal leading to inactivation of vergence, over time the original strabismus may recur. Anti-suppression therapy, by breaking this cycle, may increase the probability of long-term correction following surgery.

Anti-suppression therapy may be passive or active. While the risk of diplopia is not zero with passive anti-suppression, it is certainly lower than with the active variety. Passive therapy is easier to do than active therapy, is minimally disruptive to daily activity, and can be done even in very young children. It does not require a prescribed daily interval of exercise. On the other hand, because it is not direct or aggressive, it may require months of use for maximum

effect. In addition, passive anti-suppression is not recommended for the post-operative patient as these methods typically deny the patient the binocular experience necessary to develop or maintain fusion.

The best example of passive anti-suppression would be alternate patching. This can be done full or part-time, depending on the patient's diplopia risk and whether or not surgery is planned. The principle is simple: alternate patching eliminates the binocular competition resulting from eye misalignment in order to avoid reinforcing sensory adaptations such as suppression. A similar passive anti-suppression method entails penalizing the preferred eye with the application of a blurring film or filter over the lens worn by the dominant eye.

Active anti-suppression typically involves a regimen of specific exercises done for a prescribed time interval on a daily basis. Unlike alternate patching, most active anti-suppression exercises require that both eyes be used simultaneously and asks the patient to actively seek the second image. The patient must be binocular during the therapy, and one of several methods is used to present a slightly different image to each eye. The risk of diplopia is higher with active treatment, and for this reason it is used less frequently. This type of anti-suppression treatment can be used both pre- and post-operatively, if necessary.

An inclusive review of anti-suppression exercises would fill an entire volume. Potential techniques are limited only by the imagination of the examiner. There are some classic models, however, that illustrate the principles well. For example, suppression is easiest to maintain under the same conditions that are conducive to fusion (see Sect. 10.3.5); therefore, the easiest way to break through a suppression scotoma is to dim the ambient illumination and present dissimilar images to each eye. For those with dense suppression, this can be accomplished in the office using a haploscopic device, as the rheostat feature will allow the examiner to preferentially dim the illumination of the image over the dominant eye. At home, the patient may use a red filter over the dominant eye, with or without a prism to separate the images, and a flashlight. In a dimly lit room, the patient must attempt to see both the red and white flashlights simultaneously.

For those with mild suppression, one example of active anti-suppression for use at home requires that the patient wear red and/or green filters while drawing or coloring with red and green markers or crayons. Other anti-suppression methods employ physiologic diplopia to present a different view to each eye. Stereograms and bar reading are two examples of this technique. More sophisticated, though not necessarily more effective, methods using computers and polarized glasses have also been developed.

10.4.3 Vergence Training

Probably the most common non-surgical therapy prescribed by orthoptists is fusional vergence training. Vergence training can be used to manage a symptomatic phoria, to eliminate the need for strabismus surgery in an intermittent deviation (or postpone it indefinitely), or to improve the ability to control slight surgical over- or under-corrections. Regardless of the case, however, the patient must have some vergence ability at baseline upon which the exercises will build. As with anti-suppression, vergence training should only be done on patients with fusion potential. In addition, the patient should have equal or near-equal vision in both eyes, and no significant suppression. In order for vergence training to be successful, the patient must be able to discern when fusion has broken, typically by the appreciation of diplopia.

Vergence exercises can be divided into three types: sustained vergence; pursuit vergence; and saccade vergence. Regardless of the method, the patient must maintain fusion throughout the exercise in order for it to be effective. Sustained vergence exercises, such as reading with prism, necessitate prolonged fixation through increased vergence demand at a fixed distance. Pursuit vergence techniques, such as pencil push-ups or stereograms, involve tracking of a target moving in depth. Saccade vergence methods require quick changes in vergence, either with changes in fixation distance (dot cards or Brock string) or with a change in vergence demand at a fixed distance (prism rock or jump vergence). All three types are highly effective and may be prescribed in combination, or individually, to address a very specific symptom or clinical sign.

Over-exuberant pre-operative convergence training for intermittent exotropia can result in convergence spasm with a large, variable over-correction

Take Home Pearls

- Special attention must be given to prism placement when measuring a deviation in the secondary, tertiary, and head-tilt positions to avoid significant measurement errors due to inadvertent prism rotation.
- To reveal the full deviation on a cover test, motor fusion must be suspended through adequate occlusion. To do this, the entire peripheral visual field must be occluded for a few seconds before the cover is switched to the opposite eye.
- The only accurate way to determine the AC/A ratio is by calculation with the Gradient Method, using either plus lenses at near fixation, or minus lenses at distance fixation. The presence of a distance to near disparity in measurement is insufficient evidence of a high AC/A.
- A pre-operative sensory examination should not be overlooked in patients with strabismus secondary to vision loss, unless the deviating eye has light perception vision or worse.
- The sensory component of the exam should be carried out in a visual environment as close to natural viewing conditions as possible: normal room illumination; visually busy surroundings featuring multiple contours; and similar images presented to each eye.
- Almost any sensory test can be used to determine retinal correspondence. One need only look for the evidence of fusion in a patient with a manifest strabismus.
- Though most often overlooked, of all types of fusion, motor fusion may be the most important because it functions to maintain eye alignment.
- Determining if a patient is capable of fusion is necessary for both diagnosis and management, as there are two types of diplopic patients largely incapable of binocular single vision: those with central retinal pathology and those with central disruption of fusion.
- Orthoptic therapy should only be attempted on patients with good fusion potential. This includes evidence of bi-foveal fixation ability and some degree of vergence ability.

[1]. The secondary esotropia may occur even if the vergence training had been discontinued months or years prior to surgery. In some cases, the esotropia and diplopia may eventually resolve on their own, but many require cycloplegia to break the spasm. In rare cases, repeat surgery may be necessary. To avoid this complication, it is wise to avoid vergence training altogether in larger exodeviations or in any patient who is destined for strabismus surgery.

References

1. Ansons AM, Davis H (2001) Diagnosis and management of ocular motility disorders, 3rd edn. Blackwell, Oxford, p 3212.
2. Arnoldi KA (1999) Convergence excess characteristics and treatment. Am Orthopt J 49:37–47
3. Arnoldi K (2004) The VII Burian memorial lecture: factors contributing to the outcome of sensory testing in patients with anomalous binocular correspondence. In: Verlohr

D, Georgievski Z, Rydberg A (eds) Global perspectives converge downunder. Trans Xth Int Orthoptic Congress. International Orthoptic Association, Melbourne, Australia p 73–80
4. Arnoldi K, Reynolds JD (2006) Diagnosis of pseudo-divergence excess exotropia secondary to high accommodative convergence to accommodation ratio. Am Orthopt J 86:133–137
5. Arnoldi KA, Reynolds JD (2008) Assessment of amplitude and control of distance deviation in intermittent exotropia. J Pediatr Ophthalmol Strabismus 45:150–153
6. Birch EE (1993) Stereopsis in infants and its developmental relation to visual acuity. In: Simons K (ed) Early visual development, normal and abnormal. Oxford University Press, New York
7. Breinin GM, Chin NB (1973) Accommodation, convergence, and aging. Doc Ophthalmol 34:109–121
8. Burgess D, Roper-Hall G, Burde RM (1980) Binocular diplopia associated with subretinal neovascular membranes. Arch Ophthalmol 98:311–317
9. Castleberry C, Arnoldi K (2003) Predicting post-operative paradoxical diplopia. Am Orthopt J 53:88–97
10. DePool ME, Campbell JP, Broome SO et al. (2005) The dragged-fovea diplopia syndrome: clinical characteristics, diagnosis, and treatment. Ophthalmology 112:1455–1462
11. Fawcett SL, Wang Y, Birch EE (2005) The critical period for susceptibility of human stereopsis. Invest Ophthalmol Vis Sci 46:521–525
12. Frank J, France T, Harrington J (1981) The Worth four dot test: Is it really "worthless"? Am Orthopt J 31:68–72
13. Frisby JP, Mein J, Saye A et al. (1975) Use of random-dot stereograms in the clinical assessment of strabismic patients. Br J Ophthalmol 59:545–552
14. Haggerty H, Richardson S, Hrisos S et al. (2004) The Newcastle Control Score: a new method of grading the severity of intermittent distance exotropia. Br J Ophthalmol 88:233–235
15. Hatt SR, Haggerty H, Buck D et al. (2007) Distance stereoacuity in intermittent exotropia. Br J Ophthalmol 91:219–221
16. Hatt SR, Leske DA, Holmes JM (2007) Comparing methods of quantifying diplopia. Ophthalmology 114:2316–2322
17. Holmes JM, Birch EE, Leske DA et al. (2007) New tests of distance stereoacuity and their role in evaluating intermittent exotropia. Ophthalmology 114:1215–1220
18. Howard IP, Fang X, Allison RS et al. (2000) Effects of stimulus size and eccentricity on horizontal and vertical vergence. Exp Brain Res 130:124–132
19. Jampolsky A (1955) Characteristics of suppression in strabismus. Arch Ophthalmol 54:683–696
20. Jampolsky A (1964) The prism test for strabismus screening. J Pediatr Ophthalmol Strabismus 1:30–33
21. Jenkins PF (2002) The effect of dissociation on the sensory status. Am Orthopt J 52:85–88
22. Kaban T, Smith K, Beldavs R et al. (1995) The 20-prism-dioptre base-out test: an indicator of peripheral binocularity. Can J Ophthalmol 30:247–250
23. Kushner BJ (1995) Fixation switch diplopia. Arch Ophthamol 113:896–899
24. Kushner BJ (2000) The usefulness of the cervical range of motion device in the ocular motility examination. Arch Ophthalmol 118:946–950
25. Kutschke PJ, Keech RV (2001) Surgical outcome after prism adaptation for esotropia with a distance-near disparity. J AAPOS 5:189–192
26. Leigh RJ, Zee DS (1991) The neurology of eye movements, 2nd edn. Davis, Philadelphia, pp 266–277
27. Leigh RJ, Zee DS (2006) The neurology of eye movements, 4th edn. Oxford University Press, New York, pp 361–363
28. Leske DA, Birch EE, Holmes JM (2006) Real depth vs randot stereotests. Am J Ophthalmol 142:699–701
29. Marlow FW (1920) Prolonged monocular occlusion as a test for muscle balance. Trans Am Ophthalmol Soc 18:275–290
30. Mohney BG, Holmes JM (2006) An office-based scale for assessing control in intermittent exotropia. Strabismus 14:147–150
31. Moody EA (1983) Ophthalmic examination of infants and children. In: Harley RD (ed) (1983) Pediatric ophthalmology, 2nd edn. Saunders, Philadelphia, pp 108–133
32. Pritchard C, Flynn JT (1981) Suppression of physiologic diplopia in intermittent exotropia. Am Orthopt J 31:72–79
33. Rawstron JA, Burley CD, Elder MJ (2005) A systematic review of the applicability and efficacy of eye exercises. J Pediatr Ophthalmol Strabismus 42:82–88
34. Repka MX, Arnoldi KA (1991) Lateral incomitance in exotropia: Fact or artifact? J Pediatr Ophthalmol Strabismus 28:125–128
35. Rouse MW, Borsting E, DeLand PN (2002) Reliability of binocular vision measurements used in the classification of convergence insufficiency. Optom Vis Sci 79:254–264
36. Ruttum M, Noorden GK von (1984) The Bagolini striated lens test for cyclotropia. Doc Ophthalmol 58:131–139
37. Simons K, Elhatton K (1994) Artifacts in fusion and stereopsis testing based on red/green dichoptic image separation. J Pediatr Ophthalmol Strabismus 31:290–297
38. Thompson JT, Guyton DL (1983) Ophthalmic prisms: measurement errors and how to minimize them. Ophthalmology 90:204–210
39. Noorden GK von, Campos EC (2002) Binocular vision and ocular motility, 6th edn. Mosby, St. Louis, p. 178
40. Noorden GK von, Campos EC (2002) Binocular vision and ocular motility, 6th edn. Mosby, St. Louis, pp 202
41. Noorden GK von, Campos EC (2002) Binocular vision and ocular motility, 6th edn. Mosby, St. Louis, pp 223–225
42. Yildirim C, Altinsov HI (2000) Distance alternate-letter suppression test for objective assessment of sensorial status in intermittent exotropia. Eur J Ophthalmol 10:4–10

Principles and Management of Complex Strabismus

11

Irene H. Ludwig

Contents

Core Messages

- Perform a thorough history. Most of the information needed to manage complex strabismus is obtained by the history.
- Keep an open mind until the diagnosis is certain. Do not try to fit the patient into your first diagnostic impression.
- Allow time for thorough evaluation, and measure ocular motility yourself. Schedule a return office visit, if necessary.
- Additional diagnostic tests are selectively chosen as needed; orbital CT scan to rule out fracture, chronic sinusitis and view extraocular muscles, MRI scan of brain, tensilon test, laboratory tests for thyroid function, and rheumatologic disease.
- Final diagnosis may await the intraoperative assessment, including forced ductions to rule out fibrosis, restrictions, or weakness, and direct visualization of the extraocular muscles to rule out trauma, malposition, or healing abnormality following prior strabismus surgery.
- During surgery, be flexible in approach to allow for unexpected findings. After repair, use spring-back test to assure centration of the eye, and reposition muscle(s) if necessary. Use non-absorbable sutures when poor healing is suspected or tendons are under high tension.
- Postoperatively tailor steroid use to the condition, and use adjunctive procedures such as motility exercise and in-office forced duction to expand range of motion.

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11.1 Introduction

All strabismus cases require a thorough diagnostic approach, but some cases are unusually complex and those are the focus of this chapter. Some diagnoses may seem straightforward on initial impression, but due to incomplete information, complexities are overlooked, and outcomes are unsuccessful. Methodical acquisition of information combined with careful observation is the key to success. Complex cases are less daunting if they are approached methodically, and enough time is allotted to obtain an adequate history and complete exam. It may not be possible to achieve the full range of ocular motion in every patient, but just about every eye can be centered and many can have restoration of functional motility.

11.2 History

The patient's history is the most important factor in diagnosis (footnote), yet we often allow little time for the history and proceed directly to the exam. In most cases the history will suggest the diagnosis provided that the correct questions are asked. Was the onset abrupt or gradual? Was there any trauma proceeding onset of symptoms? Patients usually need to be prodded on these questions, as they often forget seemingly minor, but significant, blunt trauma. When strabismus occurred due to trauma, was there loss of consciousness? How long? Was there facial trauma, skull or facial fracture, or ecchymosis? Did the face hit an air bag?

Is there a history of smoking, chronic disease, recurrent sinusitis, hyperflexibility, poor wound healing, or poor nutrition? Is the strabismus worse with fatigue or upper respiratory infection? Is there associated pain or eyestrain? Is there a family history of strabismus?

Acute onset of strabismus will occur with a vascular event, and the patient should be able to recall exactly when he or she first noticed symptoms. The entire motility deficit develops in one event, followed by stable alignment or gradual improvement, with vascular or traumatic cranial nerve paresis.

Subacute onset followed by stability of alignment is the usual time course of strabismus due to partial avulsion of an extraocular muscle by blunt trauma (flap tear) [7, 8]. The motility deficit usually develops as the muscle fibroses to surrounding connective tissue. Subacute onset followed by progression of alignment abnormality would be the pattern usually seen with accommodative esotropia, intracranial compressive lesion, raised intracranial pressure, acute sinusitis, orbital myositis, orbital floor collapse, or some cases of thyroid ophthalmopathy.

Chronic, gradually progressive onset of strabismus is the most common form of acquired strabismus and the patient's history of onset is usually vague. There may be years of prism wear with gradual increase until the prism requirement becomes too great and the patient is referred for surgery. Increasing head tilt or head turn may cause neck pain, prompting the patient to seek treatment. Old photographs may be needed to document the time of onset of head tilt or turn. Some patients notice periods of stability, with bouts of exacerbation, which they associate temporally with upper respiratory illness. Patients who have had successful alignment after prior strabismus repair may develop gradual consecutive strabismus from stretching of the scar between the sclera and muscle tendon, which may accelerate during bouts of illness, malnutrition, and pregnancy [6, 9]. Conditions that usually present with chronic onset include presumed sinus-related strabismus [10], myasthenia gravis, and slow-growing intracranial lesion. Some congenital syndromes, such as Duane's syndrome and congenital fourth cranial nerve palsy, may deteriorate gradually. Consecutive exotropia in monofixation syndrome without prior strabismus surgery, and stretched scar due to prior strabismus repair [6, 9], usually have a slowly progressive time course. Extraocular muscle fibrosis syndromes, such as thyroid ophthalmopathy and chronic orbital myositis, may be gradually progressive.

Variable onset and variable expression of strabismus is seen in some patients with chronic strabismus and good fusional vergence ability. These patients may have symptoms that seem out of line with the minimal or no strabismus manifest in the office. For example, a child's parent sees esotropia in the evening, but the office exam shows minimal esophoria. An adult complains of severe diplopia but has minimal phoria on exam. The history can alert you to the possibility that strong fusional vergence is masking

the true deviation, and suggest the need to perform prism adaptation. Myasthenia gravis should always be considered in the differential diagnosis of acquired strabismus, especially when symptoms and alignment measurements show variability.

11.3 Examination

Measure motility carefully, including alignment in all directions of gaze, cover–uncover and alternate cover test and version testing. Stereopsis is measured as well as subjective torsion (double Maddox, Bagolini lens, or Lancaster red-green test), and objective torsion (dilated fundus exam).

The Parks' three-step test [11] is a tool to identify a single paretic muscle. It does not apply to muscle fibrosis or direct muscle trauma. Fibrosis of an inferior rectus of one eye may produce the identical pattern on the three-step test result as superior oblique palsy in the contralateral eye. It is important to discriminate this for each patient. Mild extorsion in the lower eye, rather than marked extorsion in the higher eye, may be a clue that a fibrotic, rather than paretic, etiology is present. Forced duction may be needed to distinguish between the two. Large fusional vergence has traditionally been considered as diagnostic of a congenital paretic etiology but may also be present with vertical deviations of gradual onset.

In office prism adaptation is a useful tool to uncover the full deviation in patients with suspected large fusional vergence, and reduce the frequency of surgical undercorrection. The measured deviation is placed into trial frames with loose prisms and best correction (with near add if necessary). The patient reads for 20 min, the deviation is remeasured, and prism increased accordingly. This process is continued until a small deviation in the opposite direction is produced. The trial frames are then removed, and alignment testing is performed in all gaze directions both distance and near. This "adapted alignment" is used to calculate the surgical correction.

Repeat evaluation on a different date and preferably at a different time of day is useful when variability or active progression or regression is suspected, as with myasthenia gravis, evolving thyroid ophthalmopathy, or improving cranial nerve palsy.

11.4 Diagnostic Testing

If orbital disorder or thyroid ophthalmopathy are suspected by exam, imaging of the orbits may be needed. A CT scan best demonstrates the bony orbits and sinuses, but intrinsic orbital lesion is better seen with MRI. Select the technique that corresponds to your leading differential diagnoses [2]. Laboratory tests may be performed to rule out thyroid dysfunction or rheumatologic disorder. Tensilon test should be performed if myasthenia gravis is suspected. Negative antiacetylcholine receptor antibody test is frequently negative in ocular myasthenia and is only helpful in diagnosis if positive.

Presumed sinus-related strabismus is a form of atypical acquired strabismus that may mimic cranial nerve palsy, high AC/A ratio, or thyroid ophthalmopathy [10]. Acute or chronic sinusitis may lead to adjacent fibrosis of the extraocular muscles and surrounding orbital tissues as well as secondary strabismus. Warning features include atypical age of onset, no family history of strabismus, normal refraction, and evidence for normal development of binocularity. Some patients relate the onset of strabismus to an upper respiratory infection, but others are unaware of sinus symptoms. If ongoing sinusitis is the cause of strabismus and is not treated, recurrence may occur despite good initial surgical correction. Sinus CT scan is the most accurate method to rule out sinus disease (Fig. 11.1). Sinus and nasopharyngeal carcinoma, mucoceles, and other sinus lesions are rare causes of gradually progressive strabismus, which will also be detectable by imaging.

Malposition of extraocular muscles may be congenital (orbital malformation, pulley abnormalities) or acquired (high myopia with lateral rectus displacement). Coronal sections on orbital CT or MRI scan will demonstrate these abnormalities [2].

11.5 Preoperative Discussion

Prior to undertaking surgery, discussion with the patient needs to stress that you are undertaking a reconstructive process, which may require multiple procedures to achieve final success. Most patients are relieved to learn that you are committed and will not

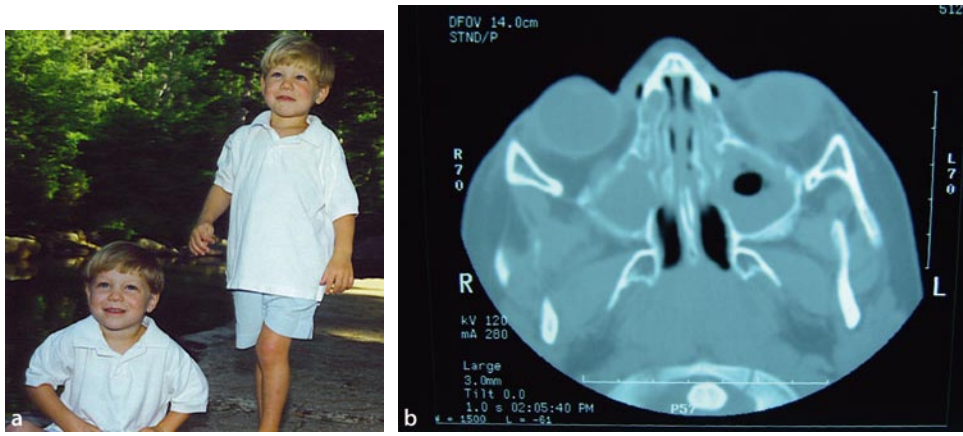

Fig. 11.1 **a** Child with esotropia acquired at age 2 years (*right*) with his identical twin brother (*left*). **b** Cause of esotropia ultimately assumed to be severe chronic sinusitis, as seen on CT scan. (Reproduced with permission from the Trans Am Ophthalmol Soc in Ludwig IH, Smith JF (2004). Presumed sinus-related strabismus. Tr Am Ophth Soc 102:159–167)

abandon their case if the first procedure is not fully satisfactory.

Patients may have systemic disease, which will influence surgical decision making, and they should be involved in any related discussion. Systemic anticoagulation will increase the risk of bleeding from local anesthetic injection, but that may be preferred rather than the increased risk of embolic event if anticoagulants are discontinued. Strabismus surgery under general anesthesia is usually possible with moderate anticoagulation, and this route may be preferred for some. Systemic disease may preclude general anesthesia in some patients, who may safely receive local anesthetic. Eyes with substantial deviations and increased fibrosis, such as post-retinal detachment or glaucoma surgery, are very difficult to operate with local anesthetic.

11.6 Intraoperative Assessment

Forced ductions are tested in all directions, including intorsion and extorsion, as well as exaggerated forced duction of the oblique muscles. The torsional forced duction test is performed with two forceps grasping the eye at the three o'clock and 9 o'clock positions. The eye is then extorted and intorted while being gently proptosed. Normal rotation is 60–70º of extorsion and intorsion before resistance is met. Decreased rotation may signify tightness of the anterior fibers of the oblique muscles, or abnormal adhesions between extra- and intraconal tissues. The exaggerated forced duction test of the oblique muscles is performed with the eye gently retropulsed and provides information about the posterior fibers of the oblique muscles.

The next step is direct observation of the extraocular muscles by surgical exploration. If prior eye muscle surgery had been performed, the density of overlying scar tissue is assessed. Unusually light, non-adherent scar, with unusually easy dissection, suggests poor wound healing [6]. Measure the distance from the scleral point of attachment of each muscle to its original insertions. Compare that to previous operative reports to rule out scar migration (see later) [6]. Inspect the muscle for evidence of scar stretch [6, 9], slipped muscle [13], missing muscle tissue [7, 8], or erosion by retinal band. Dense scar tissue may indicate excessive inflammation or adhesive syndrome [12] due to posterior disruption of Tenon's capsule by prior surgery or trauma.

11.7 Surgical Repair

In general, the best initial approach is to directly repair the original cause of strabismus, such as reattaching a lost muscle or repairing a torn muscle. Other muscles are then operated as necessary to cor-

rect residual deviation. Examples include recessing a contractured antagonist muscle, or using a Faden suture in one eye to balance motility restriction in the other eye. Sometimes several procedures are performed simultaneously, if the need is obvious, but frequently the additional muscles are operated later, after the response to the initial procedure is gauged.

11.8 Management of Scar Tissue

Scar tissue is obviously necessary to heal the operated extraocular muscle in its new position, but when scarring is excessive due to heavy-handed prior strabismus surgery, trauma, RD repair, etc., the scar tissue needs to be managed along with the muscles. Steroids will delay scar formation, but scarring will always eventually recur. It is better to control the position and direction of restriction generated by the scar rather than attempt to prevent scar from forming. Scar is first dissected free from the globe in order to operate on the muscle. If scar is neglected at this point, it will reform and often change an initially good alignment result. Instead, scar needs to be sutured directly to sclera using a fine-gauge absorbable suture, in a position where it will not interfere with the alignment outcome. This is a handy technique, and with practice, it can even be used to enhance the effect of the muscle surgery.

Tenon's capsule and intermuscular septum allow normal sliding of orbital tissues and capsule disruption increases fibrosis and can restrict motility. Dissecting the minimal amount necessary to expose the muscle insertion and repair strabismus is a principle which will reduce restrictive strabismus complications. Conversely, when capsule disruption has occurred, direct repair is advisable.

11.8.1 Stretched Scar

Consecutive strabismus following prior strabismus surgery is a common complication occurring in 2–8% of cases in which good initial alignment was achieved [6]. In many of these cases, gradual lengthening of the scar between the sclera and muscle tendon has developed, causing the surgical over correction [6, 9]. Some limitation of motility in the direction of action of the involved muscle(s) may be seen, but this may be mild and is not always present, especially if the stretch is 3 mm or less. During initial dissection to isolate the muscle, scar tissue is surprisingly mild and easily stretched in these patients. Once hooked, the muscle can usually be lifted away from sclera with ease (Fig. 11.2). Recognition of the transition between scar and normal tendon may be difficult, as the scar assumes a striated appearance, which mimics tendon (Fig. 11.3). Knowledge of the normal tendon length for the muscle will help to guide the surgeon to the transition between normal tendon and scar. Non-absorbable suture is placed through secure tendon (Fig. 11.4), scar tissue anterior to the suture is excised, and the muscle securely sutured to sclera, using standard surgical tables as a guide to the best

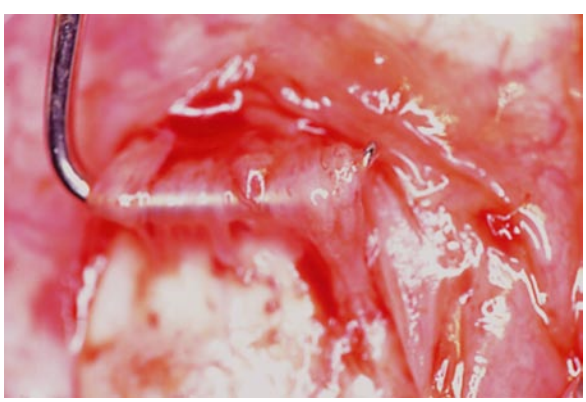

Fig. 11.2 As muscle hook is pulled away from sclera, medial rectus stretched scar lifts upward

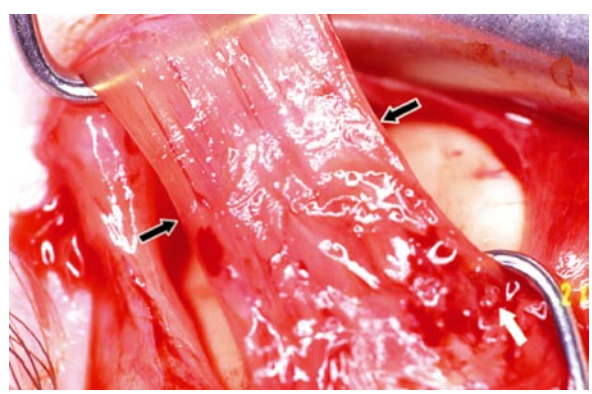

Fig. 11.3 Stretched scar of medial rectus. *Arrows* indicate transition between scar and tendon. Lower hook indicates scleral attachment site

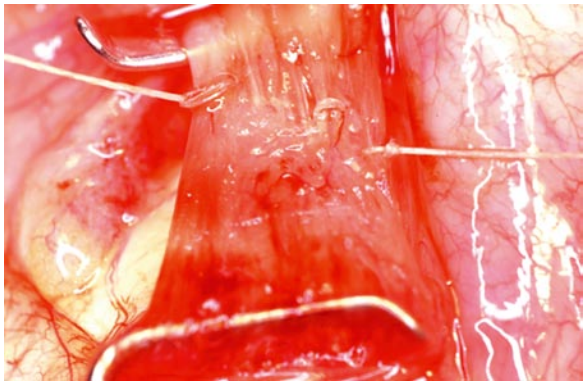

Fig. 11.4 Stretched scar of inferior rectus. Braided polyester suture is placed through tendon, prior to excision of scar r. (Reproduced with permission from the Trans Am Ophthalmol Soc in Ludwig IH (1999) Scar remodeling after strabismus surgery. Tr Am Ophth Soc 92:583–651)

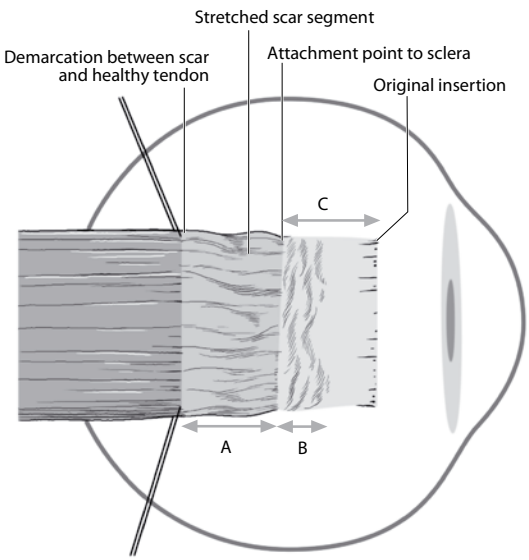

Fig. 11.5 Illustration of stretched scar repair calculation. Planned millimeters of resection/advancement from surgical tables = A+B. C–B = mm behind original insertion where sutures are placed

location to reattach the muscle (Fig. 11.5). Adjustable suture use increases the risk of stretched scar and is not recommended for these patients. Steroid use should be avoided, as it impedes wound healing. Patients are asked to avoid stretching the eyes into extremes of gaze for several months, and daily vitamin C supplementation is recommended.

Stretched scar cases were frequently confused with classic slipped muscles (see later) but have been documented to occur despite proper surgical technique, and to restretch frequently if absorbable sutures are used [6].

11.8.2 Scar Migration

When the operative report from prior strabismus surgery is available, it is sometimes observed that the extraocular muscle is attached at a position other than where it had been attached. Muscle scars under tension can migrate during the healing period. Migration of attachment position is commonly seen after Jensen, Hummelsheim, and traditional Faden procedures [6]. This problem can usually be prevented by the use of non-absorbable sutures.

11.9 Other Complex Strabismus

Paralytic strabismus, Duane's syndrome, and dissociated deviations may be complex. These are discussed in other chapters and will be omitted here. The slipped muscle, as described by Parks and Bloom [13], is similar in concept to stretched scar in that the tendon is not attached directly to sclera but is separated by a segment of other tissue − in this case a long segment of muscle capsule. This is defined as due to improper surgical technique, incorporating only capsule in the suture, which causes the muscle to retract posteriorly. The resultant deviation is large, occurs quickly in the postoperative period, and usually responds well to prompt repair with standard sutures.

Regarding partial avulsion of a rectus muscle (flap tear).

11.9.1 Partial Avulsion of a Rectus Muscle (Flap Tear)

With blunt trauma to the face, partial avulsion of one or more rectus muscles may occur [7, 8]. Traction from the bending or fracturing orbital wall may pull

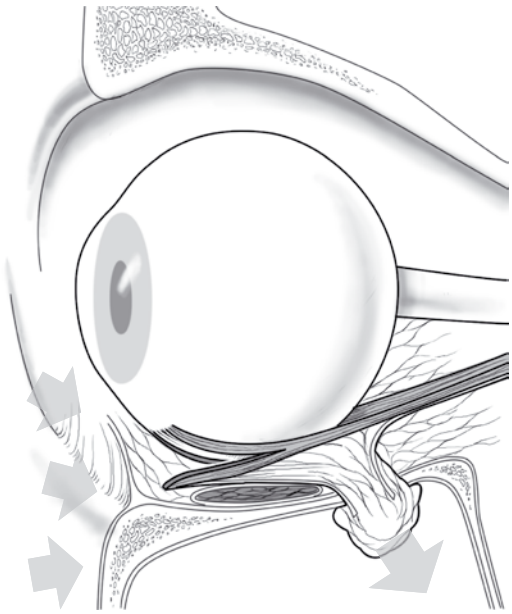

Fig. 11.6 Proposed mechanism of flap tear, showing traction on inferior rectus (*arrows*) during orbital fracture

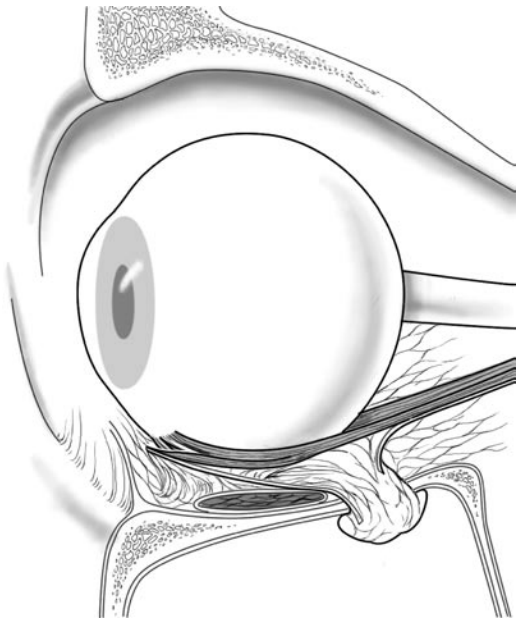

Fig. 11.7 After tear has occurred, the flap heals to surrounding orbital connective tissue, restricting motion

on the orbital septae and tear the outer or orbital layer of the rectus muscle from the inner or global layer [3]. In other cases, perhaps due to sudden muscle contracture, a portion of the tendon is disinserted from the sclera (Fig. 11.6). This avulsed "flap" of muscle may then heal to surrounding orbital soft connective tissue leading to restrictive strabismus (Fig. 11.7). The motility defect may simulate muscle paresis, usually with decreased action of the involved muscle, due to a tether effect created by the scarred portion of avulsed muscle. Orbital fracture is frequently, but not always, present. Partial avulsions are also seen following retinal detachment repair and direct trauma to the muscle insertion.

The most common partially avulsed extraocular muscles are the inferior and medial recti, but superior and lateral rectus flap tears have been seen. The size of the avulsed flap is variable.

History is critical to flap-tear diagnosis. A patient with blunt head or facial trauma with no loss of consciousness may be more likely to have suffered direct muscle trauma rather than cranial nerve palsy. History of ecchymosis or periorbital edema is suggestive. Diplopia may be immediate, but usually does not develop until several weeks after injury, when scar tissue begins to create restriction of gaze. Cranial nerve palsy due to head trauma from a motor vehicle accident is sometimes combined with flap tear caused by facial impact with an air bag.

Flap tears produce incomitant strabismus. The most common form is hyperdeviation greatest on downgaze due to partial avulsion of the ipsilateral inferior rectus. This may be confused with fourth cranial nerve palsy, which is ruled out by the lack of extorsion in the hyperdeviated eye. Inferior rectus paresis is ruled out by a normal inferior rectus force generation test. Bilateral inferior rectus flap tear may produce "A" pattern exotropia, convergence insufficiency, and vertical strabismus. Exotropia with convergence insufficiency has also been seen with medial rectus flap tears.

Orbital CT scans are useful to rule out orbital fracture, but traditional MRI scans are usually not helpful. Newer, high-resolution MRI scans, which produce images of the extraocular muscles in multiple-gaze positions, may eventually prove more useful to pinpoint the flap-tear abnormality [2].

To repair a partially avulsed rectus muscle, first review the anatomy and repair literature [7, 8]. Forced duction will usually demonstrate restriction toward

the field of action of the involved muscle movement of the eye, and torsional forced duction usually shows marked restriction to intorsion and extorsion, presumably due to the abnormal adhesion between the intra- and extraconal spaces.

A standard inferonasal fornix incision allows inspection of both the inferior and medial recti. Disruption of the normal muscle capsule is an important clue to the presence of a flap tear; therefore, only the minimum dissection necessary to see the muscle should be performed. The attached portion of inferior rectus is placed on the muscle hook, and the Desmarres retractor is used to expose the muscle, capsule, and intermuscular septum. The partial avulsion appears as either a narrowing of muscle width or muscle thinning. Both types show capsule disruption (Fig. 11.8). When in doubt, compare the anatomy by viewing the same muscle of the contralateral eye. The avulsed "flap" of muscle is found external to the Desmarres retractor and adherent to orbital connective tissue. The flap edge is freed from adhesions to surrounding tissue, attempting to preserve the avulsed capsule with the muscle flap. Tissue layers should be handled gently. Non-absorbable suture (braided 6-0 polyester) is placed through the distal end of the flap, with locking bites (Fig. 11.9). The flap is sutured to its normal anatomic position, directly to sclera. Capsule is repaired with running 8-0 polyglactin suture (Fig. 11.10). If an external rent in Tenon's capsule is present, with prolapsed orbital fat, the fat is reposited and the rent closed with 8-0 polyglactin.

If orbital fracture coexists with partial muscle avulsion, it may be repaired through a separate incision and on the same day, if possible. Best results have been obtained with muscle repair alone or simultaneous fracture and muscle repair. Patients with a significant delay between orbital fracture repair and muscle repair have worse results, perhaps due to orbital tissue fibrosis or secondary changes in antagonist muscles.

If flap tear is suspected by history and forced ductions, but cannot be located during surgery, it is best to resect the remaining attached portion of the involved muscle. This will reduce the flap's tether effect. Recession of the antagonist muscle does not improve tether restriction but may be needed as a secondary procedure.

Postoperatively, exercise of motility in the involved gaze directions is critical to reduce the risk of restriction from to adhesions. The use of steroids could reduce adhesion formation, but as they inhibit healing of tendon to sclera, they are usually avoided.

11.9.2 Lost Muscle

A lost extraocular muscle has lost all direct or indirect connection to the sclera [14]. Most lost muscles occur during ophthalmic surgery while the muscle is under traction. Sometimes, in patients with weak connective tissue, the muscle may rupture at the musculo-tendinous junction. This is known as the "pulled-in-two syndrome" (PITS) [4]. The proximal portion of the muscle retracts posteriorly, and becomes "lost." During strabismus surgery, the suture may pull through

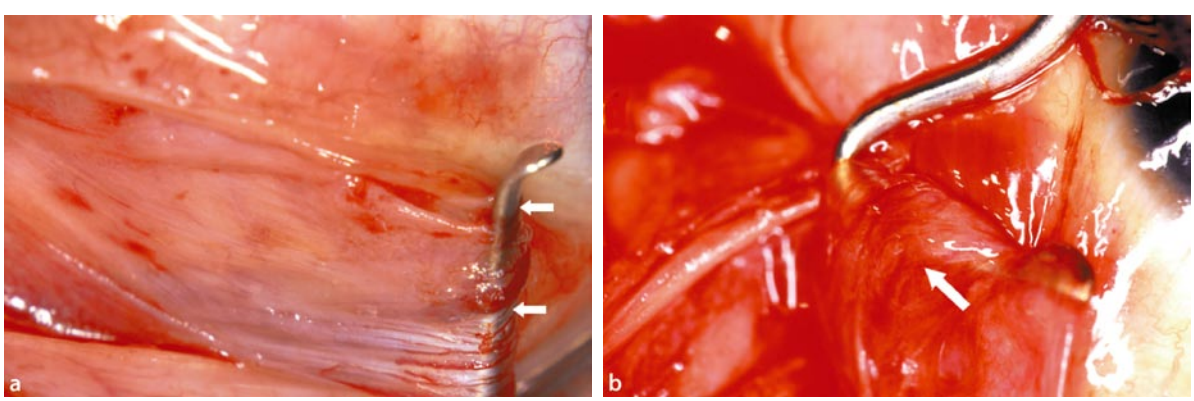

Fig. 11.8 Flap tear of medial rectus (**a**) and inferior rectus (**b**). *Arrows* indicate missing tissue. (Reproduced with permission from the Trans Am Ophthalmol Soc in Ludwig IH, Brown MS (2001). Strabismus due to flap tear of a rectus muscle. Tr Am Ophth Soc 99:53–63)

the tendon after muscle disinsertion, thereby creating a lost muscle. Sinus surgery may lead to lost muscle, by eating away a portion of the muscle, and creating a lost proximal end as well as a length defect. In blunt trauma, the muscle may completely avulse from its insertion, without losing its attachments to intermuscular septum, and lost muscle may occur with direct penetrating trauma.

If the lost muscle retains its septal attachments to the oblique muscles, these can be traced back to the lost rectus muscle. This technique is useful for the inferior, superior, and lateral recti. The medial rectus lacks these indirect attachments and is therefore the most difficult muscle to recover when lost. It is sometimes possible to follow Tenon's capsule posteriorly to the point where the medial rectus originally penetrated Tenon's capsule to locate the lost muscle. Avulsed lost muscles are usually found near the globe and adherent to orbital soft connective tissue. When dehiscence at the musculotendinous junction has occurred, the torn tissue is fragile and lacks strength to support sutures. Repair is to the surrounding muscle capsule, which allows better support due to connective tissue in the capsule. It also reduces tension and vascular strangulation in the damaged muscle tissue. Orthopedists use this principle in tendon repair [5]. Lost muscle following sinus surgery usually involves significant tissue loss, which prevents direct repair. Non-absorbable sutures to bridge the gap may be used. If the lost muscle cannot be repaired, the antagonist muscle is weakened, and transposition of adjacent muscles is performed.

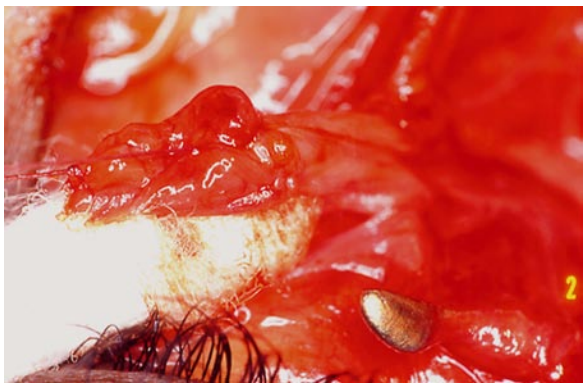

Fig. 11.9 Flap tear from muscle in Fig. 11.8 (*right*). Flap has been dissected free, and braided polyester suture has been placed through its distal end d. (Reproduced with permission from the Trans Am Ophthalmol Soc, in Ludwig IH, Brown MS (2001). Strabismus due to flap tear of a rectus muscle. Tr Am Ophth Soc 99:53–63)

Thyroid ophthalmopathy patients are complex strabismus cases due to their frequently severe extraocular muscle fibrosis. Most patients will achieve almost full functionality if surgery is planned and executed carefully. The goal is always to obtain the best balance of alignment with as wide a field of single vision as possible while operating the least number of muscles possible. When there is a large vertical deviation, it is best to avoid a large recession of a single inferior rectus, which will restrict downgaze. Smaller recession of the inferior rectus combined with recession of the superior rectus of the contralateral eye (if it is intorted), or recession/anterior transposition of the inferior oblique of the contralateral eye (if it is extorted), will usually allow more functional range

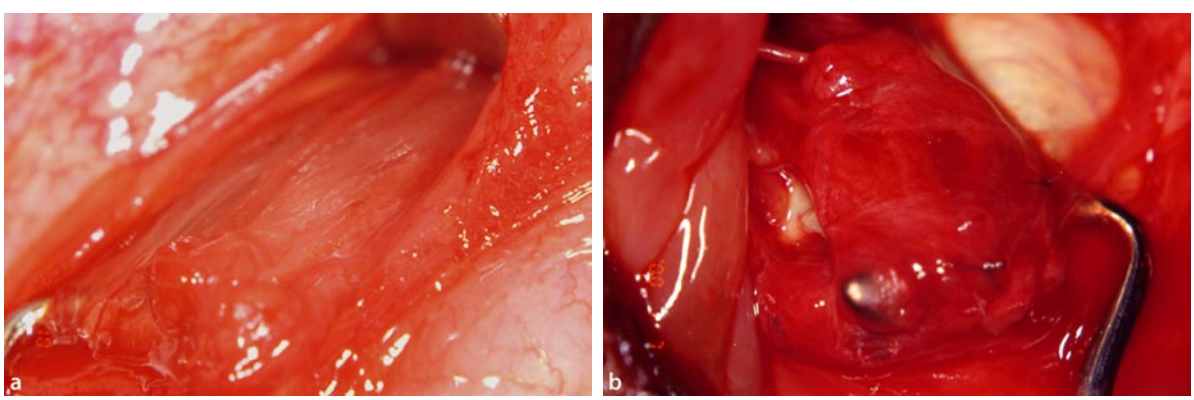

Fig. 11.10a,b Flap tears after repair. Medial rectus from Fig. 11.8 (**a**), and inferior rectus from Fig. 11.8 (**b**)). (Reproduced with permission from the Trans Am Ophthalmol Soc in Ludwig IH, Brown MS (2001). Strabismus due to flap tear of a rectus muscle. Tr Am Ophth Soc 99:53–63)

of single binocular vision in up and downgaze. Care should be taken to not disturb Tenon's capsule and intermuscular septum beyond the bare minimum necessary to isolate the muscle, thus minimizing the inflammatory response. Powerful muscles, such as the inferior and medial recti, should be operated with non-absorbable suture to reduce the high risk of stretched scar. Oblique dysfunction is commonly overlooked − especially intorsion due to fibrosis of the superior oblique(s). Simple, graded, hang-back recessions of the superior oblique(s) at their insertions are highly effective in relieving torsional diplopia due to SO overaction.

Prior retinal detachment (RD) repair patients may experience diplopia due to visual distortion as well as strabismus. Strabismus may result from muscle fibrosis due to surgical trauma and foreign body reaction and encapsulation of the encircling hardware. Flap tears have been observed in post-RD patients, presumably due to aggressive stripping of Tenon's capsule from the muscle during RD repair [7, 8]; these create a deviation away from the field of action of the torn muscle. Erosion of a rectus muscle by an encircling band which has migrated anteriorly is also seen. The eroded muscle is usually found to have reattached itself posterior to the band, but with reduced function due to its recessed position. Repair of an eroded muscle or flap tear is best performed with non-absorbable suture. Bulky exoplant material may mechanically interfere with muscle function and may need to be debulked. The superior oblique tendon is frequently caught in, or scarred to, the retinal band, altering its function, and may need to be released. Each case is evaluated individually and any repair should attempt to correct the pathology with minimal dissection. Excessive scar tissue should be addressed with the scar principles outlined previously.

Glaucoma valve procedures may cause complex strabismus due to muscle fibrosis. Usually exotropia is seen as the implants are placed in the superotemporal quadrant, causing lateral rectus fibrosis. Hypertropia is also frequent due to superior rectus fibrosis. A large recession of the lateral rectus combined with anterior transposition of the inferior oblique through an inferotemporal fornix incision will improve exotropia and hypertropia, and reduce the risk of interfering with the bleb and valve. Bleb rupture may occur, leading to decompression of the eye. To prevent this, combined surgery with the glaucoma surgeon allows temporary tying off of the valve stem before strabismus repair.

11.10 Helpful Hints

Torsion is under-evaluated and underappreciated in strabismus management. Torsion may be symptomatic and may also contribute to vertical misalignment. In planning the surgical approach to vertical strabismus, torsional correction may require no additional surgery other than selecting the appropriate muscle (such as recessing an inferior rectus in a hypotropic, extorted eye), or transposing a muscle as it is being recessed or resected to adjust the torsion. Advancing the tendon of the superior oblique at its insertion 3−4 mm will correct large extorsion with little vertical effect.

Balance restrictions to obtain the widest possible field of single vision. Upgaze restrictions are the easiest to deal with through the handy antielevation effect possible with the inferior oblique. When no further improvement of upgaze can be achieved in one eye, graded anterior transpositioning of the inferior oblique [15] of the other eye will often correct diplopia by creating a balanced restriction. Downgaze restrictions are more difficult to correct and sometimes it is better to convert a downgaze restriction to an upgaze restriction with an inferior rectus resection, sufficient to correct downgaze diplopia. Contralateral inferior oblique surgery can later be performed to balance upgaze. Faden sutures are also helpful to balance restrictions. A new method of Faden suture, which creates restriction through restricting muscle pulley movement, has been described [1]. This seems to be a useful approach to achieve the restrictive result without the risk of scleral perforation or excessive muscle fibrosis.

Balance incomitance in motility measurements by choosing muscles, which will produce the most effect in the field(s) of action where deviation is the greatest.

Use scar tissue to help align the eye. Scar tissue layers may be sutured directly to sclera to redirect the restrictive pull and enhance surgical outcome.

Stabilize shifted muscles in myopes with pulley-type Faden sutures [1].

Take Home Pearls

- Obtain a thorough and well-targeted history. The patient usually supplies most of the information needed to manage complex strabismus, provided that you listen.
- Methodically examine motility yourself.
- Keep an open mind about diagnosis and surgical approach until all information has been received and considered. Information gathering also occurs under direct visualization in the OR and surgical plans should remain flexible to allow for unexpected findings.
- Allow extra time for surgery should the unexpected arise. If the complex case is last on the schedule, there will be less time pressure and less chance of having to stop before the job is complete.
- Critical observation and thinking will lead to success in managing complex strabismus. Nomograms and tables will not help if the diagnosis is incorrect. If an attempted surgical procedure does not produce the expected effect, reconsider the diagnosis.
- There is no greater reward than seeing the disabled patient, wearing a black patch, previously turned away by other specialists, returned to full function with carefully designed and executed strabismus surgery.
- The importance of good history taking cannot be overstressed. This author had the good fortune to learn under a master of diagnosis in clinical neurology. That "genius" could seemingly pull diagnoses out of thin air after other experts had exhausted all available diagnostic tests and had long since given up. His secret was a patiently extracted and artfully directed patient history. He was such a keen observer and listener that in most cases his diagnosis was suspected even before the exam. Ancillary testing was usually just a confirmation of what he already knew he would find.

11.10.1 Absorbable vs Non-Absorbable Sutures

As described previously, non-absorbable sutures are advised to prevent recurrence of stretched scars and in flap-tear repairs [6–9]. They should also be considered in other situations where the muscle tendon will be under great tension, such as any inferior rectus recession or resection, especially since the inferior rectus has the highest incidence of stretched scar. If the suture will be well covered, such as an inferior rectus, braided polyester is excellent. If the suture may be exposed, such as with an anteriorly positioned lateral rectus, clear polypropylene suture (used in tandem with braided absorbable suture for stability) is needed, as braided polyester can produce an inflammatory response if it is not well covered. Clear polypropylene is well tolerated and non-reactive, but the knots must be tied underneath the muscle to prevent discomfort from cut suture ends. The 6-0 braided polyester and 6-0 clear polypropylene sutures are commercially available with standard strabismus needles.

11.10.2 Intraoperative "Adjustments"

The springback test is useful to estimate balance of forces at the end of a repair [16]. The eye is rotated

into one extreme of gaze and then allowed to spring back. It is then rotated into the opposite direction and that springback is compared with the first. If they appear equally deviated from the midline, the forces are about equal. If there is an obvious imbalance, the muscles and/or tissues may need to be repositioned.

Classic adjustable sutures are not useable with some scar tissue techniques described previously, and are not advised for stretched scar repair, flap tears, or high-tension muscles. In some cases, awakening the patient in the OR allows measurement of alignment. If the deviation is not satisfactory, the patient is then reanesthetized and the muscle repositioned directly to sclera.

11.11 Postoperative Management

Postoperatively, the use of steroids should be carefully considered and not automatic. Patients with scar migration, or stretched scar, should not have their wound healing further retarded by steroids. Overcorrected strabismus after muscle resection may warrant topical steroids to try to induce stretch.

Vitamin C deficiency causes powerful weakening of scar tissue [6]. Stretched scar patients should be advised to maintain good nutrition with special attention to vitamin C.

When motility restriction is corrected with surgery, the patient should exercise motility into extremes of gaze regularly; however, if motility restriction is created deliberately (inferior oblique anterior transposition, Faden), or if stretched scar has been repaired, the patient should avoid rotating the eyes sharply for several months.

Severe motility restriction after trauma may improve with in-office forced duction manipulation of the eye several times weekly in addition to the at-home stretching.

When the repair has not fully corrected the alignment, be honest with the patient by saying that more may need to be done.

References

1. Clark RA, Ariyasu R, Demer JL (2004) Medial rectus pulley posterior fixation: a novel technique to augment recession. J AAPOS 8:451–456
2. Demer JL, Clark RA, Kono R et al. (2002) A 12-year, prospective study of extraocular muscle imaging in complex strabismus. J AAPOS 6:337–347
3. Demer JL, Oh SY, Poukens V (2000) Evidence for active control of rectus extraocular muscle pulleys. Invest Ophthalmol Vis Sci 41:1280–1290
4. Greenwald M (1990) Intraoperative muscle loss due to muscle-tendon dehiscence. Proceedings of the 16th annual meeting of the Association for Pediatric Ophthalmology and Strabismus, Bolton Landing, New York
5. Ketchum LD, Martin NL, Kappel DA (1977) Experimental evaluation of factors affecting the strength of tendon repairs. Plast Reconstr Surg 59:708–719
6. Ludwig IH (1999) Scar remodeling after strabismus surgery. Trans Am Ophth Soc 92:583–651
7. Ludwig IH, Brown MS (2001) Strabismus due to flap tear of a rectus muscle. Trans Am Ophth Soc 99:53–63
8. Ludwig IH, Brown MS (2002) Flap tear of rectus muscles. An underlying cause of strabismus after orbital trauma. Ophthalmic Plast Reconstr Surg 18:443–450
9. Ludwig IH, Chow AY(2000) Scar remodeling after strabismus surgery. J AAPOS 4:326–333
10. Ludwig IH, Smith JF (2004) Presumed sinus-related strabismus. Trans Am Ophth Soc 102:159–167
11. Parks MM (1958) Isolated cyclovertical muscle palsy. Arch Ophthalmol 60:1027
12. Parks MM (1972) A study of the weakening surgical procedure for eliminating overaction of the inferior obliques. Am J Ophthalmol 73:107
13. Parks MM, Bloom JN (1979) The “slipped” muscle. Ophthalmology 86:1389–1396
14. Plager DA, Parks MM (1990) Recognition and repair of the “lost” rectus muscle. Ophthalmology 97:131–137
15. Stager DR (2001) Anatomy and surgery of the inferior oblique muscle: recent findings. J AAPOS 5:203–208
16. Noorden GK von (1996) Binocular vision and motility. Theory and management of strabismus, 5th edn. Mosby, St. Louis, pp 526–583

Dissociated Deviations

M. Edward Wilson

12

Contents

Core Messages

- The dissociated strabismus complex (DSC) includes dissociated vertical deviation (DVD), dissociated horizontal deviation (DHD), dissociated torsional deviation (DTD), latent nystagmus, and sub-normal binocularity.
- DSC may represent an atavistic resurgence of the dorsal light reflex that emerges when bifixation and high-grade binocularity are absent.
- Although DVD is usually the most clinically significant component of DSC, some patients will manifest a prominent DHD with less noticeable DVD and DTD.
- DVD, when manifest frequently, can be treated surgically by several different approaches including superior rectus muscle recession, inferior oblique muscle anterior transposition, and inferior rectus muscle resection.
- DHD is not treated effectively by DVD surgery alone. When prominent, DHD requires a specific surgical strategy that usually involves recession of the lateral rectus muscle on the side of the manifest DHD.

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12.1 Introduction

Dissociated deviations in strabismus have been observed and reported for more than a century [30]. The most often quoted early descriptions are from Bielschowsky [2]. E.L. Raab (Mount Sinai School of Medicine, New York University, New York, N.Y.) is credited with popularizing dissociative vertical deviation (or more commonly, dissociated vertical deviation, DVD) as a descriptive label for this intriguing type of strabismus. Many other names, such as alternating sursumduction and dissociated double hypertropia, have faded from use. More recently, dissociated movements and misalignments have been grouped into what is now known as the dissociated strabismus complex (DSC) [15, 34, 36, 38]. It is well known that these dissociated deviations can be vertical, horizontal, or torsional. DSC obviates the semantic confusion that occurs when referring to a dissociated deviation as a DVD when the most prominent movement, in some patients, is horizontal or torsional. Latent nystagmus and sub-normal binocularity should also be included as parts of DSC.

Within the DCS grouping, vertical movements are recorded using the familiar term, dissociated vertical deviation (DVD). Horizontal movements are recorded as dissociated horizontal deviation (DHD) and torsional movements are known as dissociated torsional deviation (DTD). Examiners are encouraged to use a 1+ to 4+ scale to rate each of the DCS components separately. DVD and DHD can be measured or estimated in prism diopters, but variability exists based on the attentiveness of the patient. Often the DVD and DHD are larger at times than can be quantitated using alternate prism and cover measurements.

The classic DSC pattern is of a nonfixating eye slowly elevating, extorting, and abducting upon the spontaneous loss of binocular function or with cover testing (Fig. 12.1). A reversal of these movements is seen with recovery and refixation. Vertical movements usually predominate, but horizontal or torsional movements may be the most noticeable manifestation of the complex in some patients. Latent nystagmus is also usually seen during the exam, but macular binocular vision with high-grade stereopsis is never present.

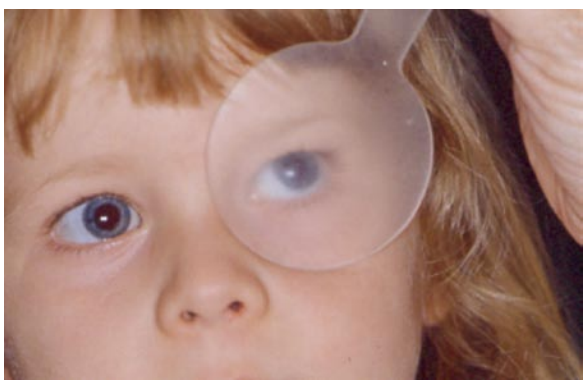

Fig. 12.1 Dissociated strabismus complex. The left eye is shown, elevated, abducted, and extorted behind cover

12.2 Etiology

The exact cause of DSC remains unknown, but two recent theories have been published. Guyton has proposed that DSC [13] movements serve to damp latent nystagmus by stabilizing the fixating eye. This "nystagmus blockage" function, according to Guyton, is a learned response, which helps to prevent a decrease in visual acuity that would otherwise occur with manifest-latent nystagmus. Using eye movement recordings of patients with DCS, Guyton observed a comitant drift of both eyes with the fixating eye adducting, depressing, and intorting, while the nonfixating eye abducts, extorts, and elevates. The horizontal muscles were shown to produce the horizontal component of the drift, while the oblique muscles produced the cyclovertical drift. According to Guyton, these movements produce what we see clinically as the slow phase of latent nystagmus. Comitant saccades then occur that compensate for the drift of the fixating eye. This produces the fast phase of latent nystagmus. In conjunction with the vertical and cyclovertical vergence movements, there is an upward vertical version that is necessary to compensate for the depression of the fixating eye caused by the vergence movement. This version is produced mostly by the inferior oblique muscle of the fixating eye and the superior rectus muscle of the nonfixating eye. Also, the eye movement recordings documented a horizontal version, away from the fixating eye, presumably to compensate for the collective abduction effects of both oblique muscles as they become ac-

tive in the fixating eye. The combined effect of these movements is that the fixating eye stabilizes, but the nonfixating eye is driven into a variable state of elevation, extorsion, and abduction.

Brodsky [6], in contrast, has stated that any horizontal damping of latent nystagmus is likely an epiphenomenon of dissociated esotonus that helps to explain the horizontal portion (DHD) of DSC, rather than the result of a compensatory adaptation to improve visual acuity. The remaining DSC movements, according to Brodsky [4], are the result of an atavistic resurgence of the dorsal light reflex that emerges when macular binocular vision and high-grade stereopsis are absent. In evolution, primitive responses to external stimuli are suppressed by newer reflexes. When newer systems fail, these retained primitive reflexes can reappear. Nathan [22] believes that in humans the eyes have phylogenetically retained some of their primitive organ-balance functions. When there is absence of macular binocular vision, unequal visual input can induce a central vestibular imbalance in which the internal sense of vertical no longer corresponds to the gravitational vertical. In further support of this theory, Brodsky [5] has shown evidence that, in DSC, a subjective sensation of visual tilt under monocular conditions produces two compensatory eye movements: a vertical divergence movement to realign the eyes relative to an altered internal representation of vertical, and a cycloversion (torsion) movement that rotates the eyes to neutralize a perceived visual tilt. In contrast, the horizontal component of DSC, known as DHD, is more likely related to a dissociation of the esotonus that is needed in humans to overcome the anatomical tendency for the eyes to be divergent [6].

12.3 Incidence and Associations

The DSC is commonly associated with congenital esotropia, but it may also be seen in association with other forms of strabismus [14, 35]. In addition, it can be seen to develop whenever a child suffers from a permanent unilateral vision loss. DVD, the most prominent component of DSC, is one of the most common types of hyperdeviation seen in a strabismus practice. Helveston [14] found DVD in 11.1% of 1000 consecutive patients with strabismus or nystagmus. Among esotropia patients, the incidence was 14%. In exotropia, DVD was found in 8.7%, and in hypertropia, DVD co-existed in 7.2%. Wilson and Parks [35] found DVD in 62% of 98 patients with congenital esotropia who were followed up to, or beyond, 6 years of age. Other investigators have reported the association of DVD and congenital esotropia in up to 92% of patients [23]. Surgery at an earlier age does not decrease the incidence of DVD [23, 35]. Incidence figures for DSC may depend on how carefully subtle findings are sought when examining patients at high risk for DSC, such as those who have a history of congenital esotropia. In addition, some components of DSC may appear to be present during some examinations and absent during others. DHD is often less prominent than DVD; however, DHD prominent enough to require horizontal muscle surgery occurs in 5% or more of patients with congenital esotropia [10]. In addition, Brodsky [6] found evidence of DHD in 50% of a cohort of patients with consecutive exotropia after surgery for congenital esotropia. DSC also can occur in association with acquired deviations, whether they are esotropia, exotropia, or hypertropia. All conditions have in common an absence of macular binocular vision. DSC is not seen when high-grade stereopsis (bifixation or macular binocular vision) is preserved.

Since both inferior oblique muscle overaction and DSC occur commonly in congenital esotropia patients, the two conditions often coexist. At times, however, DVD can simulate inferior oblique muscle overaction by becoming manifest in adduction as the nose interrupts fixation. Equally confusing is the association of a true hypertropia with DVD or a true esotropia or exotropia with DHD. As stated previously, latent or manifest-latent nystagmus occurs frequently in association with the other components of DSC. Latent nystagmus is rarely seen in the absence of DSC.

12.4 Ocular Manifestations

The DSC is nearly always bilateral but asymmetric [32]. When a unilateral dissociated deviation is detected initially, careful observation over several examinations usually reveals an asymmetric, bilateral DSC, rather than a truly unilateral finding. Dissociated deviations may be controlled by binocular fusion

mechanisms and remain latent, or the deviations may manifest spontaneously. When DSC becomes manifest, it does so intermittently, changing as the state of attention of the individual changes. Visual inattention often produces a larger deviation than can be measured by even prolonged alternate cover testing and variability is the rule. Deviations can appear small and well controlled on one visit only to be large and manifest spontaneously a brief time later. Although dissociated horizontal and torsional movements are being recognized with greater frequency, DVD remains the predominant manifestation in most cases of DSC.

Placing base-down prisms before the higher eye or base-up prisms before the lower eye until all refixation movements are neutralized can quantitate a true hypertropia. The alternate cover test reveals these refixation movements to be upward in one eye and downward in the other eye. The absence of upward refixation movements in either eye on alternate cover testing usually distinguishes DVD from true vertical tropia. In addition, the upward deviation is very slow (2−40°/s) in DVD compared with true hypertropia (200−400°/s) [14]. Movements in DSC do not resemble a saccade or pursuit movement but rather a slow divergence of a non-fixating eye. In addition, one or more of the other components of DSC (DTD, DHD, or latent nystagmus) almost invariably can be detected in patients with prominent DVD.

When one is attempting to quantify DVD or DHD, each eye must be measured separately. Prisms are placed before the eye to be measured until it no longer drifts behind cover. A true neutralization is not reached. The endpoint is when the eye measured becomes still. Both eyes will not "neutralize" simultaneously. Measurements of DSC vary day to day − even moment to moment − and tend to increase with prolonged occlusion. For these reasons, a subjective 1+ to 4+ scale is sometimes used instead of an exact prism diopters measurement to describe each component of DSC and the largest deviation seen during the exam is usually the one graded. For a DVD estimated or measured <10 prism diopters (PD), a 1+ designation is often used. Deviations between 10 and 15 PD are labeled as 2+ , 15−20 as 3+ , and >20 PD as 4+. If a true hypertropia and DVD coexist, prism and alternate cover test neutralization of the hypertropia should be made first. The overlying DVD can then be estimated or measured. Use a rapid alternate cover test to measure the true hypertropia, not allowing the hypotropic eye time to dissociate behind the cover. The true hypertropia and the more marked DVD usually are present on the same side.

The DSC can exist as a prominent DHD with very little DVD, or as a prominent DVD in one eye and a prominent DHD in the other (Fig. 12.2). The DHD is distinguished from intermittent exotropia by the slow speed of the abducting movement, the association of DTD, and the absence of true neutralization with prisms. Close inspection also reveals that the DHD does not begin to drift until the formally covered eye has returned to the primary position and picked up fixation. In contrast, exotropia produces simultaneous movement of one eye (as it is uncovered) toward fixation and the other eye (as it is covered) away from fixation. In addition, many patients with DHD will reveal a micro-esotropia on rapid alternate cover testing, but slow alternate cover testing (allowing the eye with DHD to fully dissociate) reveals the exodeviated posture behind cover.

As stated previously, DSC can coexist with oblique muscle dysfunction. Wilson and Parks [35] found DVD and inferior oblique muscle overaction (IOOA) occurring together in 45% of patients with congenital esotropia who were observed to at least 6 years of

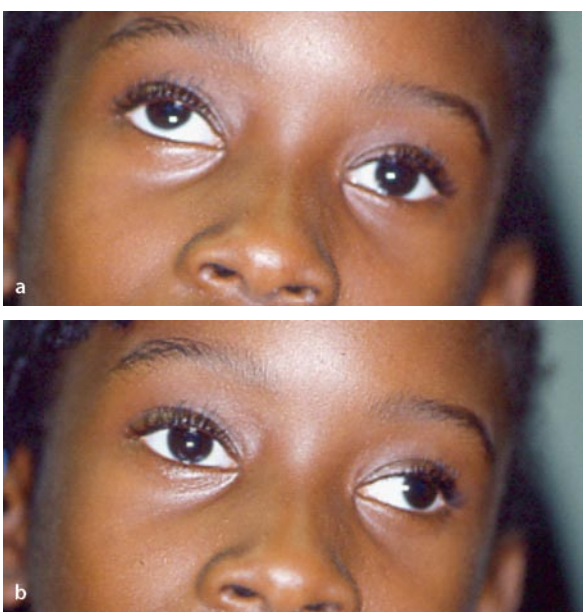

Fig. 12.2a,b Dissociated strabismus complex. **a** DVD most prominent in the right eye. **b** DHD most prominent in the left eye

age. In addition, it is well known that in adduction the nose may act as an occluder, allowing DVD to simulate IOOA. A true hypertropia present in side gaze but absent in primary gaze is evidence that oblique muscle dysfunction exists. The adducted eye would manifest a hypotropia when superior oblique muscle overaction (SOOA) is present and a hypertropia when IOOA exists. The absence of a true hypertropia in adduction does not, however, exclude IOOA from occurring in conjunction with SOOA. With coexistence of DVD and IOOA, the adducted eye may elevate under cover from either disorder. The abducted eye, when covered, has opposing forces at work. The DVD causes the eye to float upward while the IOOA drives the abducted eye downward. A true hypertropia is seen only if the IOOA-stimulated hypotropia of the abducting eye overcomes the DVD-stimulated hyperdeviation. This reasoning also can be used to help verify the coexistence of DVD and either IOOA or SOOA. Oblique muscle dysfunction causes the DVD to appear incomitant. The IOOA reduces DVD in abduction, and SOOA reduces DVD in adduction. In other words, if DVD is evident in primary gaze but much less elevation is present behind cover when either eye is in abduction, bilateral IOOA should be suspected and a V pattern sought to confirm the diagnosis. If elevation behind cover is much less in adduction, SOOA should be suspected and an A pattern sought to verify the diagnosis. Care must be taken to anticipate the effect on DVD when coexisting oblique muscle dysfunction is treated surgically.

Torticollis has been documented in up to 35% of patients with DVD when an ocular fixation preference is present [1]. Patients with alternating fixation are much less likely to manifest a head tilt secondary to DVD. When present, the head tilt usually is toward the side of the nonfixating eye with the larger, more often manifest, DVD; thus, the DVD usually increases with forced tilt away from the eye with the more severe DVD and decreases on tilt toward the eye with more severe DVD. This tilting pattern is opposite from that seen in superior oblique muscle palsy, in which the hypertropia increases on ipsilateral tilt and decreases on contralateral tilt. Exceptions to this pattern occur when patients with DVD maintain a head posture opposite from that predicted and show forced-tilt changes more like those of superior oblique muscle palsy (Fig. 12.3). Brodsky and coworkers [7] report that patients in their series who tilted toward the side of the nonfixating eye with the larger DVD had earlier strabismus surgery and better stereopsis than those with a head tilt toward the side of the fixating eye. These patients could calibrate their head position to modulate DVD in the two eyes and stabilize binocular fusion, thus keeping the DVD latent. When patients tilt toward the fixating eye, it is likely a compensatory postural adaptation at the central vestibular level to realign the head to a tilted internal representation of vertical. This does not serve to stabilize binocular fusion, and when seen, it is present despite continuing manifest DVD.

Asymmetrical DVD presents the patient with conflicting needs. The head tilted to one side helps the binocular fusion and to the other side helps the central vertical orientation error. In patients with better fusion and stereopsis, the drive to tilt toward the nonfixating eye with the larger DVD wins out. At times, when fusion is poor, the central drive wins out even at the cost of more manifest DVD.

The Bielschowsky phenomenon [2] is unique to DSC. It can be demonstrated most easily when DVD and amblyopia are present. Downward movement of the elevated occluded nonfixating eye occurs when

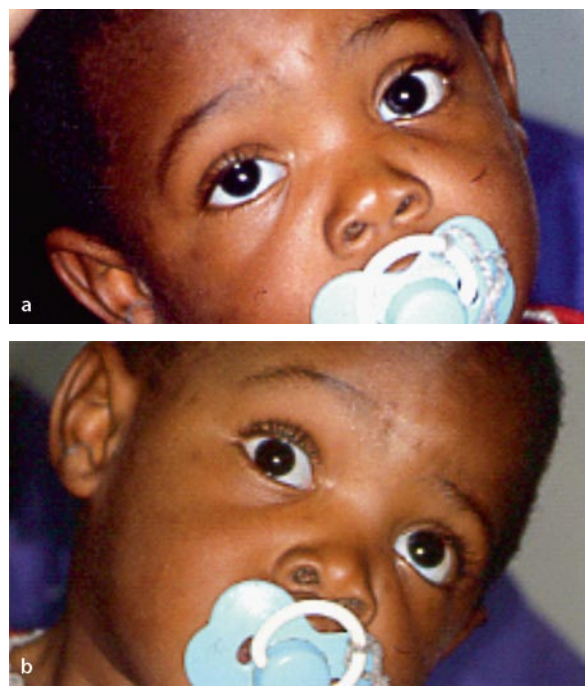

Fig. 12.3 **a** Right head tilt shows manifest DVD in the right eye. **b** Left head tilt shows manifest DVD in the left eye

filters of increasing density are placed before the fixating eye. The eye behind cover may even come to rest below primary position. A Bagolini graded red filter bar helps elicit the Bielschowsky phenomenon. Alternatively, illumination to the fixating eye can be progressively reduced by rotating two polarized filters on one another to create a darkening filter. Increasing illumination to the fixating eye also can produce the Bielschowsky phenomenon. The phenomenon has also been demonstrated in the horizontal plane when prominent DHD is present [36].

12.5 Treatment

Although DSC does not cause symptomatic diplopia, it does disrupt binocular vision when it is manifest and it can be disfiguring. Even a small DVD can appear prominent as the eye elevates and sclera begins to be visible at the lower eyelid margin. Also, the exodeviation produced by DHD rarely avoids detection and often prompts complaints from parents of affected patients, even when the deviation manifests infrequently. A prominent abnormal head posture also can be an indication for treatment. In some patients who experience alternating fixation, manifest DVD predominates when one eye deviates and DHD predominates when fixation switches and the fellow eye drifts.

Despite its ability to be disfiguring, most patients with DSC do not need treatment. The condition is often small in magnitude and well controlled. If a DSC drift is seen only rarely, with fatigue, reassurance and observation is the best course of therapy. Available treatments are imperfect and none of them can eliminate DSC totally. Successful treatment merely reduces the frequency and magnitude of spontaneously manifest DSC so that it is rarely seen at home. Despite treatment, dissociated strabismus can almost always still be detected in the office during alternate cover testing. No patient is cured of DSC, and recurrence of manifest deviations is common even after aggressive treatment.

Nonsurgical treatment options to reduce the frequency of manifest DSC have met with only limited success. Because DSC is usually asymmetric, switching the fixation preference to the eye that deviates most often may improve the patient's control of DSC and reduce how often the eyes are seen to drift. Optical and pharmacologic penalization techniques designed to blur the eye that has less DSC and switch fixation to the eye with more DSC have been reported [27, 32]. These treatments are used only when the DSC is markedly asymmetric and they depend on a fixation switch to the previously nonpreferred eye. The Worth four-dot test and a variety of vectographic tests can be used to verify this fixation switch.

Most cases of symptomatic DVD or DHD are managed surgically. Standard surgical treatments for DVD have no effect on DHD [33]; therefore, DHD requires specific surgical strategies. The DTD is not treated surgically. Latent nystagmus is often also present and can become manifest in patients with poorly controlled DSC. Treatment that restores DSC control and gross binocularity may also result in a manifest-latent nystagmus converting back to its latent status.

Recession of the superior rectus muscles is the most common treatment for DVD. Surgery is usually performed bilaterally unless the DVD is strictly unilateral or dense amblyopia is present. When performed unilaterally, a moderate superior rectus muscle recession of 5−9 mm is typical [3]. A hypotropia often is produced that lasts days, weeks, or longer. Fewer undercorrections occur when unilateral surgery is performed for DVD; however, manifest DVD in the previously asymptomatic eye is commonly seen after unilateral surgery, even in patients where a switch in fixation preference does not occur. Reports advocating bilateral surgery either symmetrically or asymmetrically for all patients with DVD have appeared in the literature since at least the early 1980s [18].

When performing bilateral superior rectus muscle recessions for DVD, I prefer large (7−10 mm) symmetric recessions, regardless of the asymmetry in DVD severity between the eyes. If a true hypertropia coexists with DVD, however, I perform more superior rectus muscle recession on the hypertropic eye. The hypertropia usually is found in the eye with the larger DVD, further justifying asymmetric recessions for these patients. For surgeons who prefer asymmetric bilateral surgery for DVD, the quantity of surgery is determined by the severity of DVD in each eye.

In the past, posterior fixation sutures on the superior rectus muscles, either alone or in combination with a superior rectus muscle recession, were advocated as an effective treatment for DVD [28]. Esswein and coworkers [11], however, reported that

although the effectiveness of 3- to 5-mm superior rectus muscle recessions combined with posterior fixation sutures was excellent at 6 months postoperatively (87% corrected or improved), a failure rate of 55% was documented 3 years after surgery. In contrast, the success rate of 7- to 9-mm superior rectus muscle recessions diminished only slightly over time, with 86% corrected or improved at 6 months, 80% after 1 year, 77% after 2 years, and 72% after 3 years. Posterior fixation sutures for the treatment of DVD are not recommended.

Residual or recurrent DVD may still become frequently manifest after superior rectus muscle recession has been performed bilaterally. Re-recession of these muscles is possible if the initial surgery placed the muscle <8−10 mm from the insertion; however, recession beyond 8−10 mm it is not recommended and, in fact, is difficult to accomplish safely. I prefer to secure the recessed muscle directly onto the sclera rather than using the hang-back technique. Even when the frenulum between the superior rectus muscle and the superior oblique muscle is completely severed, hang-back recessions are unlikely to result in >10 mm of retro-placement from the insertion. To achieve easy exposure of the superior sclera 8−10 mm posterior to the superior rectus insertion, remove the lid speculum and place a Desmarres retractor in its place. Instead of lifting up on the upper eye lid and conjunctival tissues, press them down toward the orbital roof and keep the retractor in contact with the sclera.

Inferior rectus muscle resection is an alternative to re-recession of the superior rectus muscle for residual or recurrent DVD. Although rarely done, inferior rectus muscle resections have been shown to be effective in the treatment of residual DVD after superior rectus muscle recessions [24]. My experience has been the same. When needed, this operation is very effective at dosages of 4−6 mm bilaterally. Some surgeons advocate inferior rectus muscle resections as a primary treatment for DVD [28]; however, the lower eyelid elevation, flattening, and fullness that often result after this procedure has limited its popularity as a first-line surgery.

A modified recession procedure of the inferior oblique muscle, known as inferior oblique anterior transposition (IOAT), was developed to treat severe inferior oblique muscle overaction [9]. This procedure is now also used to treat DVD, especially when inferior oblique muscle overaction and DVD co-exist (as they often do) [8, 16, 20, 21]. The IOAT procedure has been shown to be effective for DVD up to about 15 PD [8]. Larger DVDs, of 20 PD or more, are not well treated by IOAT. The operation works by weakening the inferior oblique muscle and also converting it into an antielevator [17]. The term “antielevation” implies that the muscle still contracts on attempted supra-duction, but in its new location, the contraction limits elevation rather than assisting it. The muscle is not converted into an active depressor.

Stager et al. [29] studied the inferior oblique muscle’s neurovascular bundle as a new functional origin after IOAT. Both the new origin and the new insertion of the inferior oblique muscle parallel the inferior rectus muscle. This altered anatomy produces a co-contraction of sorts with the superior rectus muscle. The inferior oblique contracts on attempted elevation and still has a functional origin and insertion parallel to the inferior rectus muscle.

The IOAT procedure is not without its own unique set of possible complications. The altered anatomy mentioned above helps to explain the frequent occurrence of an upgaze deficit when IOAT is used. If the muscle is spread too widely and/or re-attached too far anteriorly, a characteristic Y or T pattern is produced, characterized by elevation deficiency and divergence in upgaze and the false appearance of residual inferior oblique muscle overaction [17]. A trade-off appears to exist in which further anterior placement of the inferior oblique muscle corrects more DVD but also is more likely to cause an up-gaze deficit and a T pattern. Limiting the new anterior insertion of the inferior oblique to the level of the inferior rectus insertion reduces the incidence of marked upgaze deficit; however, Gonzalez and Klein [12] have reported using inferior oblique muscle resection combined with transposition anterior to the inferior rectus insertion with good control of larger DVD. Severe upgaze deficit is a risk with this procedure, however.

When marked DVD (>15 PD) coexists with inferior oblique muscle overaction, simultaneous recession surgery on the four vertical muscles is often very effective. This approach is controversial because of the uncertain risk of marked upgaze deficiency and resulting upper eyelid retraction. Limiting the superior rectus muscle recessions to 8 mm and the inferior oblique recessions to 10 mm reduces, in my hands, the likelihood that this combined surgery will pro-

duce a functionally important upgaze deficit; however, IOAT has been combined with superior rectus muscle recessions of up to 10 mm without producing severe upgaze deficits in a limited number of patients [26, 31].

The IOAT also has been suggested as a prophylactic surgery for DVD in patients a history of congenital esotropia who have inferior oblique muscle overaction and are at high risk for developing DVD. (The incidence of DVD in congenital esotropia is 60−90%.) Mims and Wood [21] performed IOAT in 61 patients with congenital esotropia with bilateral inferior oblique muscle overaction. They placed the inferior oblique muscle 2 mm anterior to the temporal border of the inferior rectus muscle insertion. With an average follow-up of 27 months, only 1 patient needed surgery for DVD compared with nine in a control group of patients with congenital esotropia who had not undergone inferior oblique muscle surgery. The IOAT procedure has been recommended whenever inferior oblique muscle overaction is present in a patient with mild coexisting DVD or when the patient is at high risk for DVD.

Other procedures have been reported for the treatment of DVD, but they are not in common use today. These procedures include superior oblique tendon tuck or resection [25], which can result in Brown syndrome, and botulinum toxin injection to the superior rectus muscles [19], which invariably leads to ptosis lasting several weeks.

Surgical treatment for symptomatic DHD usually involves unilateral or bilateral lateral rectus muscle recession [36, 37]. For patients with unilateral or asymmetric DHD measured or estimated at >15 PD, an ipsilateral lateral rectus recession of 7 mm is recommended. The recession is reduced to 5 mm if the DHD measures 15 PD or less. The lateral rectus recession is reduced if the lateral rectus muscle has been previously resected. This last reduction is based on forced duction testing performed at the time of DHD surgery. More reduction is indicated when the resected lateral muscle is tight. Bilateral lateral rectus muscle recessions carry a higher risk of postoperative esotropia unless a true exotropia is also present along with the DHD.

When esotropia >10 PD coexists with DHD, the lateral rectus recession is limited to 5 mm, or the esotropia may be treated concomitantly with the DHD. This may entail bilateral medial rectus muscle recession along with unilateral lateral rectus muscle recession or bilateral medial rectus muscle posterior fixation sutures, in cases of high accommodative con-

Take Home Pearls

- DVD can co-exist with hypertropia or hypotropia. Careful examination can distinguish these components and help determine the appropriate surgical plan.
- DVD is usually treated with bilateral surgery even if the deviation is seen most often in only one eye.
- Large 7- to 10-mm superior rectus muscle recessions are most often utilized for the surgical treatment of DVD. The IOAT is used for small to moderate DVD when IOOA is present. Inferior rectus muscle resections are less frequently utilized but are often effective for residual manifest DVD.
- DHD can co-exist with esotropia or exotropia. Most often, DHD and a micro-esotropia associated with monofixation syndrome co-exist. In these patients, unilateral lateral rectus muscle recession usually improves the DHD without worsening the esotropia.
- DHD with exotropia usually requires bilateral surgery as opposed to DHD alone, which is usually treated with unilateral surgery.
- DSC does not occur in patients with macular binocular vision and high-grade stereopsis.

vergence to accommodation ratio, along with unilateral lateral rectus muscle recession.

When exotropia and DHD coexist or when DHD is frequently manifest in either eye as a result of alternate fixation, bilateral lateral rectus muscle recession is recommended.

In conclusion, dissociated deviations include movements in the vertical, horizontal, and torsional axes. The DVD should not be used to refer to the entire complex. To avoid semantic confusion, DSC should be subdivided into its vertical (DVD), horizontal (DHD), and torsional (DTD) components when patient examination data are recorded. Latent nystagmus should be included as part of the complex. The DVD and DHD require separate surgical strategies but often are treated surgically together. True hypertropia, hypotropia, esotropia, or exotropia can coexist with DSC. Treatment must be individualized for these patients, addressing both the dissociated and associated portions of the strabismus.

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References

1. Bechtel RT, Kushner BJ, Morton GV (1996) The relationship between dissociated vertical divergence (DVD) and head tilts. J Pediatr Ophthalmol Strabismus 33: 303−306
2. Bielschowsky A (1940) Lectures on motor anomalies. Dartmouth College Publications, Hanover, p. 17
3. Braverman DE, Scott WE (1977) Surgical correction of dissociated vertical deviations. J Pediatr Ophthalmol 14: 337−342
4. Brodsky MC (1999) Dissociated vertical divergence: a righting reflex gone wrong. Arch Ophthalmol 117: 1216−1222
5. Brodsky MC (2002) Dissociated vertical divergence: perceptual correlates of the human dorsal light reflex. Arch Ophthalmol 120: 1174−1178
6. Brodsky MC (2007) Dissociated horizontal deviation: clinical spectrum, pathogenesis, evolutionary underpinnings, diagnosis, treatment, and potential role in the development of infantile esotropia (an American Ophthalmological Society thesis). Trans Am Ophthalmol Soc 105: 272−293
7. Brodsky MC, Jenkins R, Nucci P (2004) Unexplained head tilt following surgical treatment of congenital esotropia: a postural manifestation of dissociated vertical divergence. Br J Ophthalmol 88: 268−272
8. Burke JP, Scott WE, Kutshke PJ (1993) Anterior transposition of the inferior oblique muscle for dissociated vertical deviation. Ophthalmology 100: 245−250
9. Elliott RL, Nankin SJ (1981) Anterior transposition of the inferior oblique. J Pediatr Ophthalmol Strabismus 18: 35−38
10. Enke ES, Stewart SA, Scott WE (1994) The prevalence of dissociated horizontal deviations in congenital esotropia. Am Orthoptic J 44: 109
11. Esswein MB, von Noorden GK, Coburn A (1992) Comparison of surgical methods in the treatment of dissociated vertical deviation. Am J Ophthalmol 113: 287−290
12. Gonzalez C, Klein B (1993) Myectomy and anterior transposition of the inferior oblique muscle: a new surgical procedure and its results in 49 operations. Binocul Vis Eye Muscle Q 8:249
13. Guyton DL (2000) Dissociated vertical deviation: etiology, mechanism, and associated phenomena. Costenbader Lecture. J AAPOS 4: 131−144
14. Helveston EM (1980) Dissociated vertical deviation: a clinical and laboratory study. Trans Am Ophthalmol Soc 78: 734−779
15. Helveston EM (2005) Surgical management of strabismus: a practical and updated approach, 5th edn. Wayenborgh Publishing, Oostende, Belgium, pp 88−89
16. Kratz RE, Rogers GL, Bremer DL, Leguire LE (1989) Anterior tendon displacement of the inferior oblique for DVD. J Pediatr Ophthalmol Strabismus 26: 212−217
17. Kushner BJ (1997) Restriction of elevation in abduction after inferior oblique anteriorization. J AAPOS 1: 55−62
18. Magoon E, Cruciger M, Jampolsky A (1982) Dissociated vertical deviation: an asymmetric condition treated with large bilateral superior rectus recession. J Pediatr Ophthalmol Strabismus 19: 152−156
19. McNeer KW (1989) Botulinum toxin injection into the superior rectus muscle of the non-dominant eye for dissociated vertical deviation. J Pediatr Ophthalmol Strabismus 26: 162−164
20. Milot J, Tremblay OCC, Quellette C (1994) Anterior transposition of the inferior oblique for dissociated vertical deviation with inferior oblique overaction. Can J Ophthalmol 29: 284
21. Mims JL III, Wood RC (1989) Bilateral anterior transposition of the inferior obliques. Arch Ophthalmol 107: 41−44
22. Nathan P (1982) The nervous system, 2nd edn. Oxford University Press, Oxford, p. 103
23. Neely DE, Helveston EM, Thuente DD, Plager DA (2001) Relationship of dissociated vertical deviation and the timing of initial surgery for congenital esotropia. Ophthalmology 108: 487−490
24. Noel LP, Parks MM (1982) Dissociated vertical deviation: associated finding and results of surgical treatment. Can J Ophthalmol 17: 10
25. Richard JM (1987) Combined superior oblique muscle tendon resection and inferior oblique muscle recession for dissociated vertical deviation: 25 cases. Binocul Vis 2: 137

26. Roberts EL, Saunders RA, Wilson ME (1996) Surgery for vertical head position in null point nystagmus. J Pediatr Ophthalmol Strabismus 33: 219–224
27. Simon JW, Bayramler H, Kamath S (1996) Atropine penalization therapy of dissociated vertical deviations. Binocul Vis Strabismus Q 11: 263
28. Sprague JB, Moore S, Eggers H, Knapp P (1980) Dissociated vertical deviation. Treatment with the faden operation of Cuuppers. Arch Ophthalmol 98: 465–468
29. Stager DR, Weakley DR Jr, Stager D (1992) Anterior transposition of the inferior oblique. Anatomic assessment of the neurovascular bundle. Arch Ophthalmol 110: 360–362
30. Stevens GT (1895) On double vertical strabismus. Ann Ocularist 113: 225
31. Varn MM, Saunders RA, Wilson ME (1997) Combined bilateral superior rectus muscle recession and inferior oblique muscle weakening for dissociated vertical deviation. J AAPOS 1: 134–137
32. Noorden GK von (ed) (1990) Binocular vision and ocular motility: theory and management of strabismus, 4th edn. Mosby, St. Louis, p. 341
33. Wheeler DT, Enke ES, Scott WE (1996) Surgical management of dissociated horizontal deviation associated with congenital esotropia. Binocul Vis Strabismus Q 11: 256
34. Wilson ME (1993) The dissociated strabismus complex. Binocul Vis 8: 45
35. Wilson ME, Parks MM (1989) Primary inferior oblique overaction in congenital esotropia, accommodative esotropia, and intermittent exotropia. Ophthalmology 96: 950–957
36. Wilson ME, McClatchey SK (1991) Dissociated horizontal deviation. J Pediatr Ophthalmol Strabismus 28: 90–95
37. Wilson ME, Saunders RA, Berland JE (1995) Dissociated horizontal deviation and accommodative esotropia: treatment options when an eso- and an exodeviation co-exist. J Pediatr Ophthalmol Strabismus 32: 228–230
38. Wilson ME, Hutchinson AK, Saunders RA (2000) Outcomes from surgical treatment for dissociated horizontal deviation. J AAPOS 4: 94–101

A and V Patterns

David A. Plager

13

Contents

Core Messages

- A and V Patterns can be found in association with: (a) "overacting" oblique muscles; (b) orbital abnormality; (c) adduction deficiency, such as in large-angle exotropia or with a slipped muscle; (d) muscle anomaly, such as lax or missing muscle(s); and (e) no apparent oblique dysfunction or orbital abnormality.
- Optimal treatment of the A/V pattern should account for the etiology causing it.
- In general, if there is oblique muscle dysfunction, surgical correction should be directed at the offending oblique muscles.
- If there is no oblique muscle dysfunction, surgery usually involves vertical shifts of horizontal recti.

13.1 Introduction

Pattern or alphabet strabismus can present in many forms including A, V, X, Y, or lambda pattern; of these, A and V patterns are the most common. An A pattern describes a motility picture where the horizontal strabismus is smallest in upgaze and progressively increases as the eyes move into downgaze. A V pattern is the inverse – the horizontal deviation is smallest in downgaze and increases as the eyes elevate toward upgaze (Figs. 13.1, 13.2) [1–3, 12–15].

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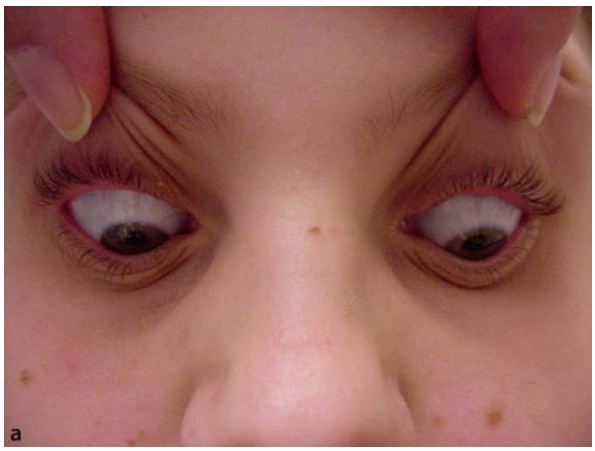
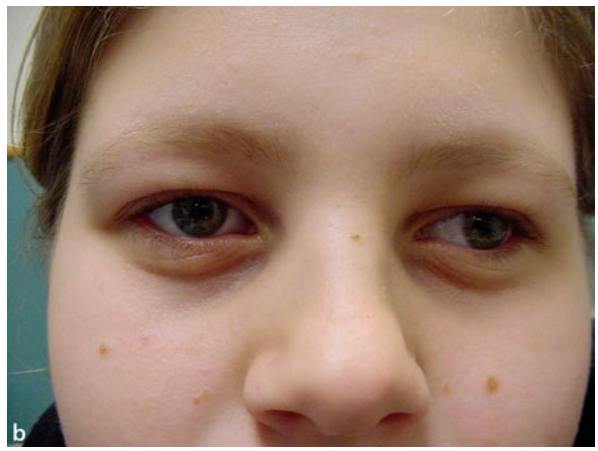




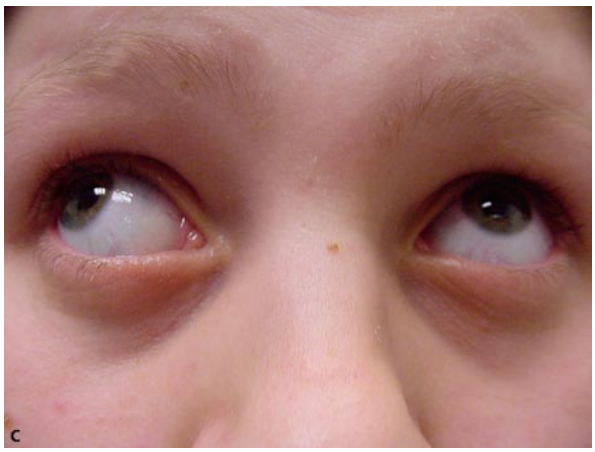


Fig. 13.1a–c The V pattern with increasing exotropia in upgaze: **a** downgaze; **b** primary gaze; **c** upgaze

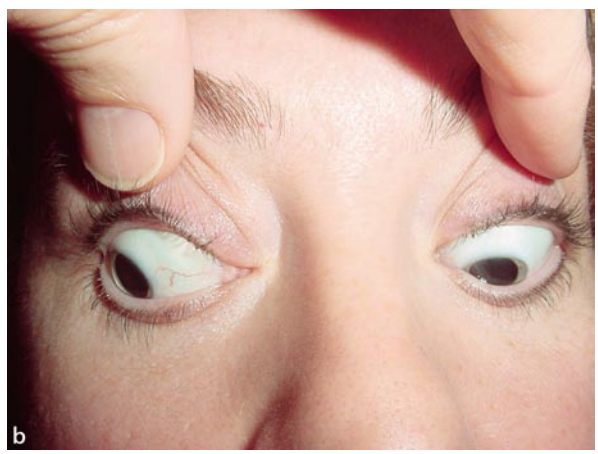


Fig. 13.2a–d The A pattern with increasing exotropia in downgaze: **a** downgaze left; **b** downgaze right; **c,d** *see next page*

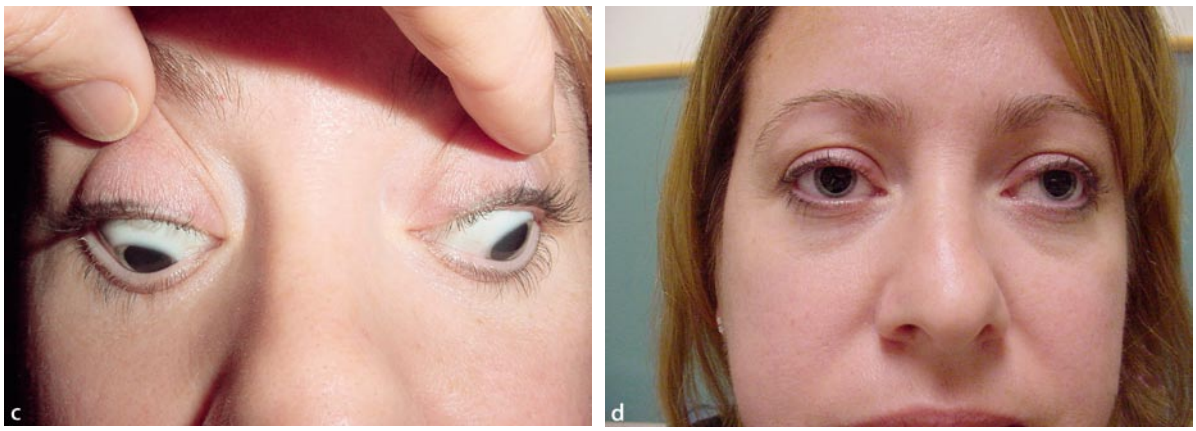


Fig. 13.2a–d *(continued)* The A pattern with increasing exotropia in downgaze: **c** downgaze; **d** primary gaze

The X-pattern describes eyes where the horizontal deviation is smallest in primary and increases in both upgaze and downgaze. The Y-pattern is present when the horizontal deviation is smaller in primary and downgaze but increases in up gaze. Lambda pattern is the inverse of a Y pattern where the deviation remains similar in primary and upgaze and increases in downgaze.

Optimal correction of alphabet pattern strabismus is influenced by the etiology of the pattern. Several etiologies exist, sometimes in combination, to produce the observed vertical incomitance.

13.2 Causes of A or V pattern

13.2.1 Oblique Muscle Dysfunction (Overaction)

The terms inferior oblique overaction (IOOA) or superior oblique overaction (SOOA) are ingrained in strabismus language, but they are more descriptive of the clinical appearance than the etiology. The terms overelevation in adduction or over depression in adduction are more accurately descriptive but also more unwieldy to use. We will use inferior oblique overaction or superior oblique overaction to describe this clinical appearance when it is not due to other orbital or muscle factors (Fig. 13.3) [8].

Bilateral overelevation in adduction will cause a V pattern and can be found in association with either a primary position esotropia or exotropia. Conversely, over depression in adduction will cause an A pattern esotropia or exotropia.

Why does this apparent "overaction" occur? There is no evidence or even logic to suggest that these muscles are somehow "over innervated" or excessively strong. So why do we see the clinical picture commonly described as inferior or superior oblique overaction?

Production of a V pattern secondary to IOOA (and associated SO underaction) can be caused by innervation anomaly alone as in bilateral acquired superior oblique palsy resulting from neurotrauma. It is noteworthy that the degree of inferior oblique overaction in these clearly acquired cases is usually mild, if present at all. The underaction of the SOs and V pattern with esotropia in downgaze may be more apparent than the IOOA.

Congenital superior oblique palsies usually have more pronounced IOOA and these are frequently found in association with lax SO tendons [10]. This suggests the possibility that the apparent IOOA is really an "under checking" phenomenon caused by the SO tendon abnormality. Clearly, the ultimate SO tendon abnormality – absence – is associated with marked inferior oblique overaction.

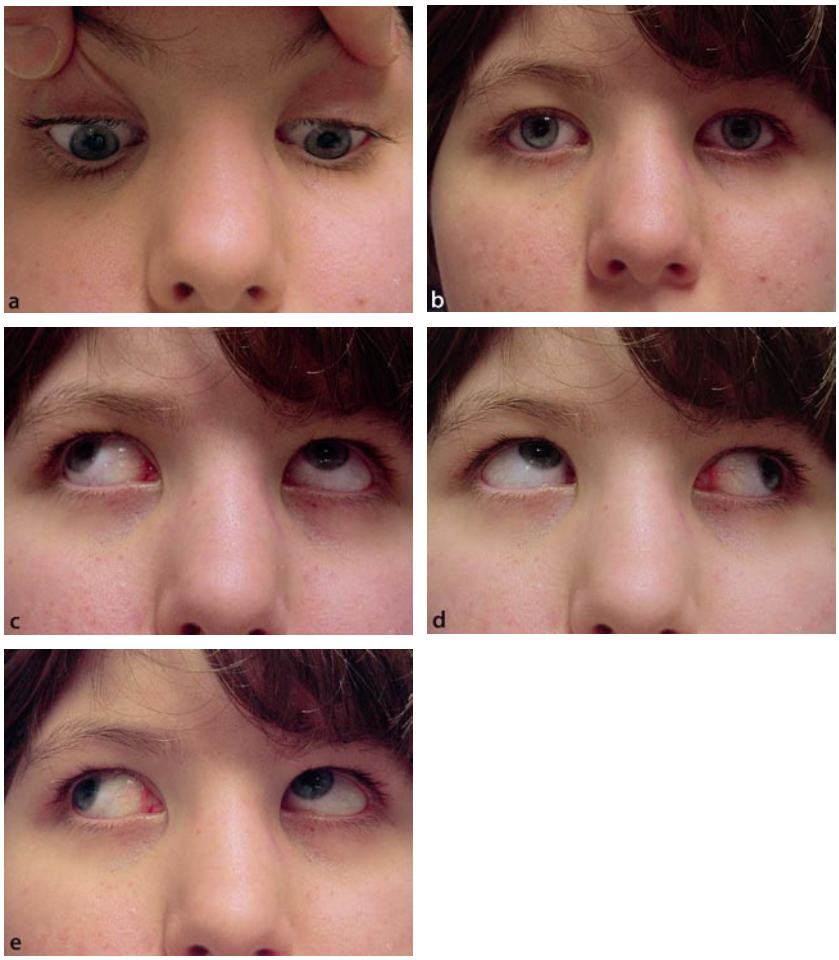


Fig. 13.3a–e Patient with large V pattern associated with overelevation in adduction (inferior oblique overaction) in each eye: **a** downgaze; **b** primary gaze; **c** upgaze; **d** upgaze left; **e** upgaze right

It is also interesting to note that the patients with bilateral IOOA associated with the congenital esotropia complex frequently have marked bilateral SO tendon laxity (unpublished data). This, however, is not always the case, which raises the question about both the etiology and importance of this finding. Whatever the cause of this clinical association, it is the most common scenario for bilateral inferior oblique overaction and resultant V pattern.

The oblique dysfunction and V pattern can be apparent in early infancy concurrent with the initial onset of esotropia, but more frequently is first noted at age 3−4 years, or later. It can develop in the years following horizontal surgery for the esotropia or can become manifest before the horizontal misalignment is addressed.

13.2.2 Orbital Abnormality

The prototype anomalies causing usually a V pattern with overelevation in adduction are the cranial facial syndromes such as Crouzon syndrome (Fig. 13.4) [17]. Imaging of orbits in such patients frequently shows excyclorotation of the entire orbit including all muscles (Fig. 13.5). One can hypothesize that adduction of a medial rectus that is displaced superiorly will impart a vertical force vector on attempted adduction. Less dramatic muscle position abnormalities are found in patients with displaced muscle pulleys without a cranial facial syndrome (Fig. 13.6) [18]. For instance, in patients with downward displacement of the lateral rectus muscles, it has been hypothesized by Clark et al. [18] that the downward vector of a

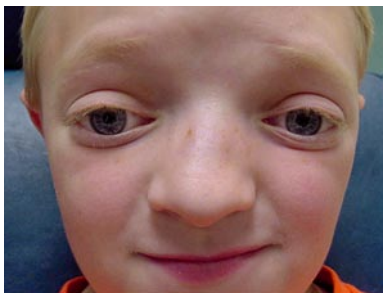
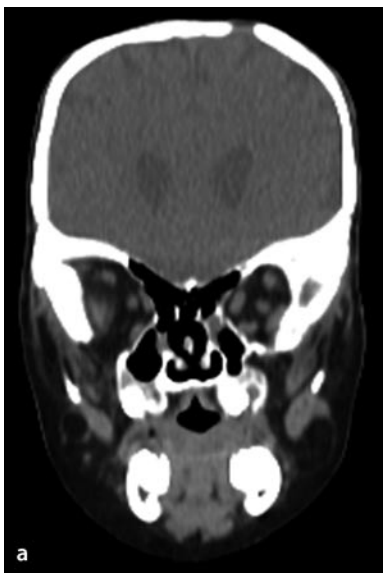


Fig. 13.4 Child with craniosynostosis (Crouzon syndrome)



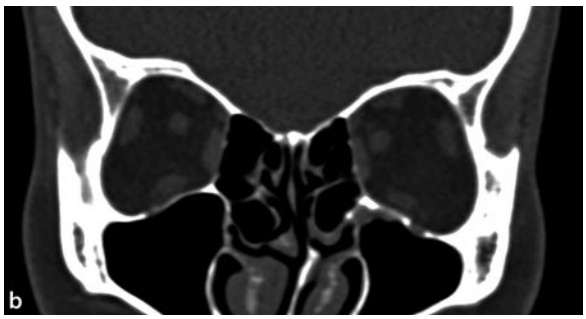


Fig. 13.5 **a** An MR scan of a craniosynostosis patient. Note that the orbits are both excyclorotated. **b** An MR scan of a patient with incyclorotated orbits and large A pattern. (Courtesy of J. Demer)

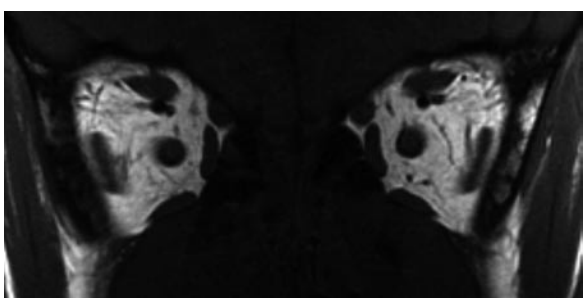


Fig. 13.6 An MR scan of a patient with pulley displacement. Note vertical displacement of horizontal rectus muscles. (Courtesy of J. Demer)

fixating abducting eye with an inferiorly displaced lateral rectus will cause a compensatory firing of the elevators of the same eye to maintain fixation which, in turn (by Hering's law), causes a firing of the elevators of the opposite eye, giving an apparent overelevation in adduction.

13.2.3 Adduction Deficiency with Large Exodeviation

Pattern strabismus which can be an A, a V, or most commonly an X pattern can occur in cases of large-angle exotropia. This is particularly evident when there is an associated adduction deficiency as is

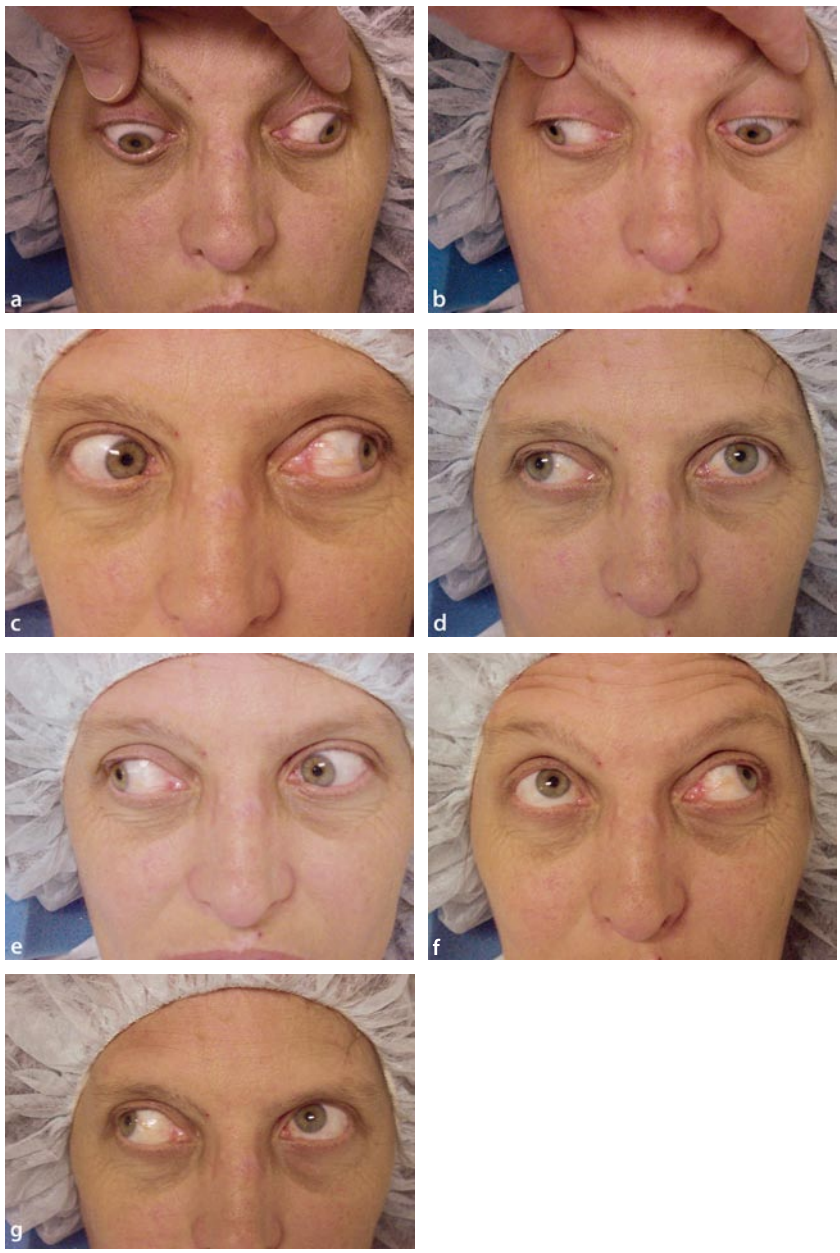
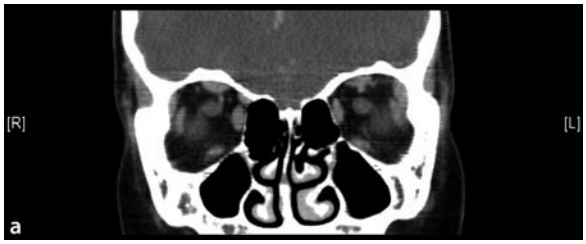


Fig. 13.7a–g The X pattern exotropia secondary to adduction deficiencies. Patient found to have slipped medial rectus muscles in each eye: **a** downgaze left; **b** downgaze right; **c** left gaze; **d** primary gaze; **e** right gaze; **f** upgaze left; **g** upgaze right

found with slipped medial rectus muscles. In such cases, when the patient is asked to look up or down with the eye in maximal adduction, a pseudooveraction of the inferior oblique is seen on upgaze and of the superior oblique on downgaze (Fig. 13.7) This apparent overaction is due to the orbital connective tissue anatomy that allows an eye to move further up or down when it is not maximally adducted. In these cases, the pseudooveraction and X pattern decrease when the exodeviation and adduction deficiency are corrected.

13.2.4 Muscle Laxity or Anomaly

Overelevation in adduction can be found in association with laxity of the superior oblique tendon, as



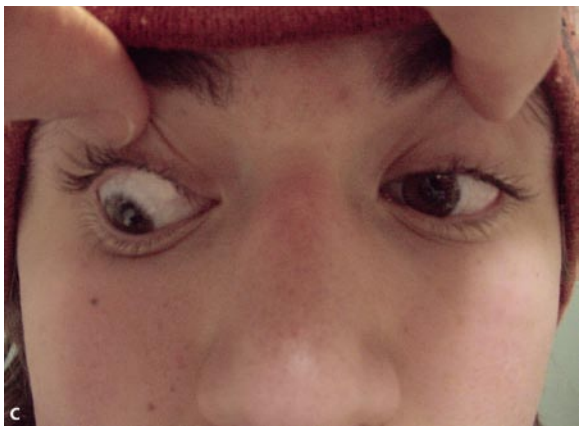


Fig. 13.8a–c Typical appearance of marked inferior oblique overaction and superior oblique underaction in a patient with clinical picture of superior oblique palsy. **a** The MR shows similar patient with absent left superior oblique muscle. **b** Upgaze right; **c** downgaze right

is frequently found in cases of congenital superior oblique palsy. Although usually unilateral, this finding can be present bilaterally. The ultimate tendon abnormality, absent tendon/muscle, is always accompanied by overaction of the antagonist muscle. This is usually found in cases of absent superior oblique tendon or muscle (Fig. 13.8). Theoretically, the inverse of this − over depression in adduction − would be found in cases of absent inferior oblique muscle, but this is not a common naturally occurring phenomenon; however, iatrogenic causes of superior oblique "overaction" and resultant A pattern can be found following excessive or inappropriate weakening of the inferior oblique(s).

13.2.5 Primary A or V pattern

Some patients can exhibit an A or V pattern without evidence of oblique muscle overaction, large exodeviation, or craniofacial anomaly. Presumably, most of these patients have subtle abnormalities of the course or insertion of the rectus muscles or their associated pulleys.

13.3 Clinical Examination Findings

13.3.1 Presentation

Young children may present with abnormal head posture, e.g., chin up for an A-pattern esotropia, if the assumed posture promotes fusion. Older patients may also assume a compensatory head position but will frequently complain of asthenopia or even diplopia. Misalignment evident only in upgaze is usually not functionally significant. Strabismus in the functionally important primary and reading (downgaze) positions will promote symptoms.

13.3.2 Examination

Diagnosis of A- or V-pattern strabismus requires prism cover measurements in primary gaze, upgaze, and downgaze. Fixation should be for distance when the measurements are made. Up- and downgaze should be approximately 30º from primary gaze. Von Noorden and Olson have further specified that optimum measurements should be made at 35º in downgaze and 25º in upgaze [16].

Inexperienced examiners will sometimes misdiagnose increased esotropia deviation for near viewing obtained in downgaze as a high AC/A ratio, when in fact they have encountered a V pattern. This mistake

can be avoided by ensuring that near deviations are measured with the eyes in level (primary) gaze, not in the more natural downgaze reading position.

13.3.3 When Is an A or V Pattern Clinically Important?

Any deviation that causes symptoms or a compensatory head posture is clinically relevant, but in general and by convention, V patterns greater than 15 prism diopters (PD) from up to downgaze and A patterns greater than 10 PD are considered significant. Again it must be stressed that the threshold for functional significance is far more likely to be crossed if the largest deviation is present in downgaze rather than upgaze.

13.4 Surgical Options

In general, surgery directed at collapse of the A or V pattern involves either weakening of oblique muscles or vertical transpositions of horizontal rectus muscles. The choice must be made with knowledge of the etiology of the pattern for each individual patient. A basic tenet of surgery for pattern strabismus is that surgery should be directed at the oblique muscles when significant oblique "overaction" is present and surgery aimed at displacement of the rectus muscles perpendicular to their direction of action should be used when oblique overaction is not the cause of the pattern. This treatment algorithm is basic, crucial, sometimes overlooked, and not new − it was suggested by Knapp nearly 50 years ago [5−7, 9, 16].

13.4.1 Oblique Muscle Weakening

13.4.1.1 V-pattern Esotropia

In V-pattern esotropia with over elevation in adduction with no muscle or orbital anomaly, bilateral weakening of the inferior obliques is highly effective for collapsing the pattern. Weakening can be accomplished with myectomy or recession at the surgeon's preference. The amount of deviation decreased seems relative to the amount of inferior oblique overaction, but 20−25 PD can be expected.

A special circumstance arises when IOOA and V pattern is found in association with dissociated vertical deviation (DVD). This is usually in the setting of congenital esotropia (ET) complex. Anterior transposition of the IO is as effective for decreasing IOOA and collapsing the V pattern as myectomy or recession procedures, but has the added effect of decreasing the DVD. In patients with congenital ET, IOOA, and V pattern, our practice is to perform the anterior transposition even without manifest DVD as a "prophylactic" procedure for the presently inapparent DVD. Since the oblique surgery will have a negligible effect on primary position deviation, appropriate rectus muscle surgery to eliminate the primary position deviation should be carried out at the same time.

13.4.1.2 V-pattern XT

Intermittent or constant XT with overelevation on adduction and a larger deviation in upgaze is common. Weakening of the IOs along with horizontal rectus surgery for the primary position deviation is very effective. These patients frequently maintain excellent binocular vision and stereoacuity despite their deviation. A dissociated strabismus complex component is rare. Fundus excyclotorsion is usually apparent with ophthalmoscopy. Weakening the inferior obliques in such cases does not cause problems with subjective torsion post-operatively.

13.4.1.3 A-Pattern ET

A-pattern ET is relatively uncommon compared with V-pattern ET or XT. When accompanied by significant degrees of SOOA and a larger A pattern (>25 PD) bilateral SO weakening is effective at collapsing the A pattern. Several weakening strategies can work including free tenotomy or guarded tenotomy with insertion of a spacer. Concomitant hori-

zontal rectus surgery should be done for the primary position deviation.

Special caution should be exercised when bilateral superior oblique weakening surgery is considered for a patient with high-grade stereopsis, specifically bifixating patients with normal (40 s/arc or better) stereoacuity. These patients will likely be sensitive to excyclotorsion induced by the superior oblique weakening. This can result in debilitating torsional diplopia and a very unhappy patient. Fortunately, large A patterns and SOOA are rarely found in bifixating patients.

13.4.1.4 A-pattern XT

A-pattern XT with evidence of SOOA will also respond to weakening of the SOs. This will usually be found with large amounts of vertical incomitance. Appropriate horizontal rectus muscle surgery for the primary position deviation should be carried out. The same caution regarding SO weakening in bifixating patients applies here as described in Sect. 13.4.1.3.

13.4.1.5 A-XT with SOOA and DVD

A special form of strabismus, A-XT with SOOA and DVD, is well known and can occur either secondarily (e.g., consecutive XT following BMR for esotropia) or as a primary strabismus triad. Treatment is similar as with A XT without DVD except that surgery aimed specifically at the DVD should be added. Most commonly this would involve large recessions of the superior rectus in each eye. In patients where the A pattern and SOOA are small, large recessions of the SRs alone will help the DVD and decrease the A pattern.

13.4.2 Effect of Oblique Muscle Weakening on Primary Position Alignment

The tertiary action of the superior obliques is abduction of the eyes; therefore, bilateral SO weakening may cause some eso shift in the primary position. This effect is small enough that it is ignored by many surgeons, though anticipating a small eso shift of 0−8 PD may help in determining amounts of concomitant horizontal rectus muscle surgery.

There is concensus that inferior oblique weakening will collapse a V pattern by decreasing the deviation in upgaze and increasing it in downgaze. Although the IO has some abducting function, the effect of IO weakening on primary position deviation is minimal; therefore, any horizontal primary position deviation should be addressed by appropriate horizontal rectus surgery.

13.4.3 Grading of Oblique Muscle Surgery

Grading of oblique muscle overaction is an inexact science. Most surgeons use a grading scale of 1+ to 4+ overaction. For inferior oblique grading, 1+ overaction means only slight overaction or over elevation in adduction. Grade 4+ means the most overelevation possible. Grades 2+ and 3+ overaction are the two gradations between those extremes. Other authors suggest that 1+, 2+, 3+, and 4+ overaction roughly translates to 5, 10, 15, and 20 PD of hypertropia on far-side gaze, respectively. In terms of how often the various grades of IOOA require surgery, Parks professed that 1+ was operated rarely, 2+ sometimes, 3+ frequently, and 4+ almost always. This scheme referred to primary IO overaction in absence of other more compelling surgical indications such as diplopia, asthenopia, or torticollis.

13.4.4 Inferior Oblique Muscle Weakening Procedures

Inferior oblique weakening is most commonly performed via recession or myectomy. Recessions can be graded: Parks' scheme included 10-mm recession for mild-to-moderate overaction and 1-4mm recession for what he termed 3+ overaction. Other prac-

titioners prefer myectomy for most degrees of IO overaction on the theory that myectomy tends to be self-adjusting, i.e., greater effects are produced when the IO overaction is greater and lesser effects when overaction is less. Inferior oblique weakening of any sort to decrease a V pattern is discouraged when IO overaction is not present.

Most procedures for weakening the inferior oblique can be performed unilaterally if indicated or different procedures can be chosen for each side in asymmetric cases. The exception is that anterior transposition of the IO should not normally be performed on only one side because of the relative restriction to elevation it produces. This will frequently result in a secondary hypertropia of the opposite eye. Occasionally, this feature can be used to advantage when the hyperdeviating eye has a DVD component and has poor vision such as from dense amblyopia. In such a case, the deviating eye is likely to never be preferred for fixation and the secondary deviation is less likely to be manifest.

13.4.5 Superior Oblique Muscle Weakening Procedures

There is more variety in methods proposed for superior oblique weakening, as shown below.

13.4.5.1 Tenotomy or Tenectomy

The strongest weakening procedure of the SO tendon is a full-thickness tenotomy nasal to the superior rectus. Some practitioners like to excise a section of tendon (tenectomy) in addition to transecting it on the theory that this will decrease the likelihood of recurrent overaction; however, a properly performed tenotomy nasal to the SR, completeness of which is confirmed with traction testing immediately post-tenotomy, is a very effective weakening procedure.

Modifications to the standard tenotomy/tenectomy procedure are designed to lessen the weakening effect on the SO. Potential modifications are given below.

13.4.5.2 Spacer

A foreign element, e.g., silicone segment or a so-called chicken suture made of non-absorbable synthetic material can be used to provide a permanent connection between the two severed ends of the SO tendon. Although the weakening effect of these adjuncts should be complete, they can theoretically decrease the tendency toward long-term overcorrection which can turn the A pattern into a V pattern. In cases where the A pattern and SO overactions are large and the patient has sub-normal binocular vision, these modifications to standard tenotomy may not offer compelling benefit.

13.4.5.3 Partial Tenotomy

If a lesser weakening effect is desired, this can be accomplished by a partial tenotomy, e.g., seven-eighths (or three-quarter) tenotomy. This is performed by identifying and disinserting the thin spread out fibers of the SO tendon at their scleral attachment on the temporal side under the superior rectus. Theoretically, lysis of these posterior-most fibers should decrease the vertical effect of the SO without decreasing much of the torsional effect of the anterior most fibers. This can be a useful procedure in cases where only mild SO overaction is present or when it is used unilaterally to balance a mild asymmetry in SO overaction, but it is not effective enough for most cases of significant A-pattern strabismus.

13.4.6 Horizontal Rectus Surgery

Patients with A or V pattern and no significant overelevation or depression in adduction are best treated with vertical shifts of the horizontal rectus muscles [16, 19]. Whether the primary position deviation is ET or XT, the direction of shift for the horizontal recti is the same. Specifically, medial recti are shifted toward the apex of the pattern (up for A pattern, down for V pattern) and lateral recti are shifted toward the open or empty direction of the pattern (up for V pattern and down for A pattern). Some practitioners find the pneumonic MALE (medial-apex, laterals-empty) helpful to remember the proper direction of shift.

Typically surgery for pattern strabismus is done bilaterally, e.g., a V-pattern ET would be treated with bimedial rectus recession with downshift; however, the same deviation can be treated with unilateral surgery by recession with downshift of one MR and resection with upshift of the ipsilateral LR [4].

The amount of vertical shift is typically half to one full tendon width depending on the magnitude of the pattern. The recession effect of horizontal rectus surgery is not significantly impacted by up- or downshifting the muscle.

13.4.7 Vertical Rectus Surgery

The A and V patterns can be diminished by horizontal offsets of the vertical rectus muscles. For instance, temporal transposition of the superior recti will expand the closed end of the A pattern. Similarly, temporal transposition of the inferior recti will expand the closed end of the V pattern by weakening the adduction vector of the inferior recti in downgaze. Transposing the SRs nasally will help close the open end of the V pattern in an exotropic patient and transposing the IRs nasally will help close an A-pattern exotropia.

Most patients requiring correction of A or V pattern will have a primary position deviation that would benefit from horizontal rectus recession or resection. Offsetting the horizontal recti vertically at the same time makes more sense, is technically easier, and obviates potential complications with eyelid position changes and anterior-segment ischemia compared with operating on all four rectus muscles concurrently. For these reasons, correction of A or V patterns with surgery on the vertical rectus muscles is of more theoretical interest than practical utility.

13.4.8 X-Pattern Strabismus

The strabismus pattern marked by increase in the deviation of the eye as the eyes move from primary gaze toward upgaze and also by increase from primary gaze toward downgaze is termed an X pattern. It occurs almost exclusively in exodeviations and can be primary or secondary, the latter usually following medial rectus recessions for esotropia.

In these secondary cases of consecutive XT, the pattern occurs because of deficiency of adduction from either excessive medial rectus recession or in the presence of slipped medial rectus muscles. Because the eyes do not adduct fully, they appear to overelevate and overdepress when the patient is called on to elevate or depress the eye while adducted.

Correction of the pattern does not require weakening of all four obliques; instead, addressing the adduction deficiency and straightening the eyes in primary position by advancing the medial recti, fixing slipped muscles, and/or recessing restricted lateral rectus muscles will diminish the pattern (Fig. 13.9).

13.4.9 Complications of Surgery for A and V Patterns

13.4.9.1 Consecutive Pattern

Conversion of an A pattern to a V pattern, and vice versa, can occur. This is more likely to occur when a strong oblique muscle weakening procedure is performed in a patient with mild oblique dysfunction pre-operatively. Trying to strengthen an iatrogenically weakened oblique is not a satisfying procedure to attempt; correction of a symptomatic consecutive pattern is more likely to respond to weakening of the newly overacting oblique muscles or shifts of the horizontal rectus muscles.

It would be unusual to convert a pattern with vertical shifts of the horizontal recti alone.

13.4.9.2 Asymmetric Result

Inducing a hyperdeviation with perhaps diplopia and/or a compensatory head posture in a patient when none was present pre-operatively can occur when asymmetric surgery is performed (whether intentionally or not). One source of this problem is incompletely performed weakening of the oblique on one side. In the case of SO tenotomy or IO myectomy, completeness of the weakening procedure can be most assured at the time of surgery by performing the procedure under direct observation followed by confirmation of completeness with oblique traction testing.

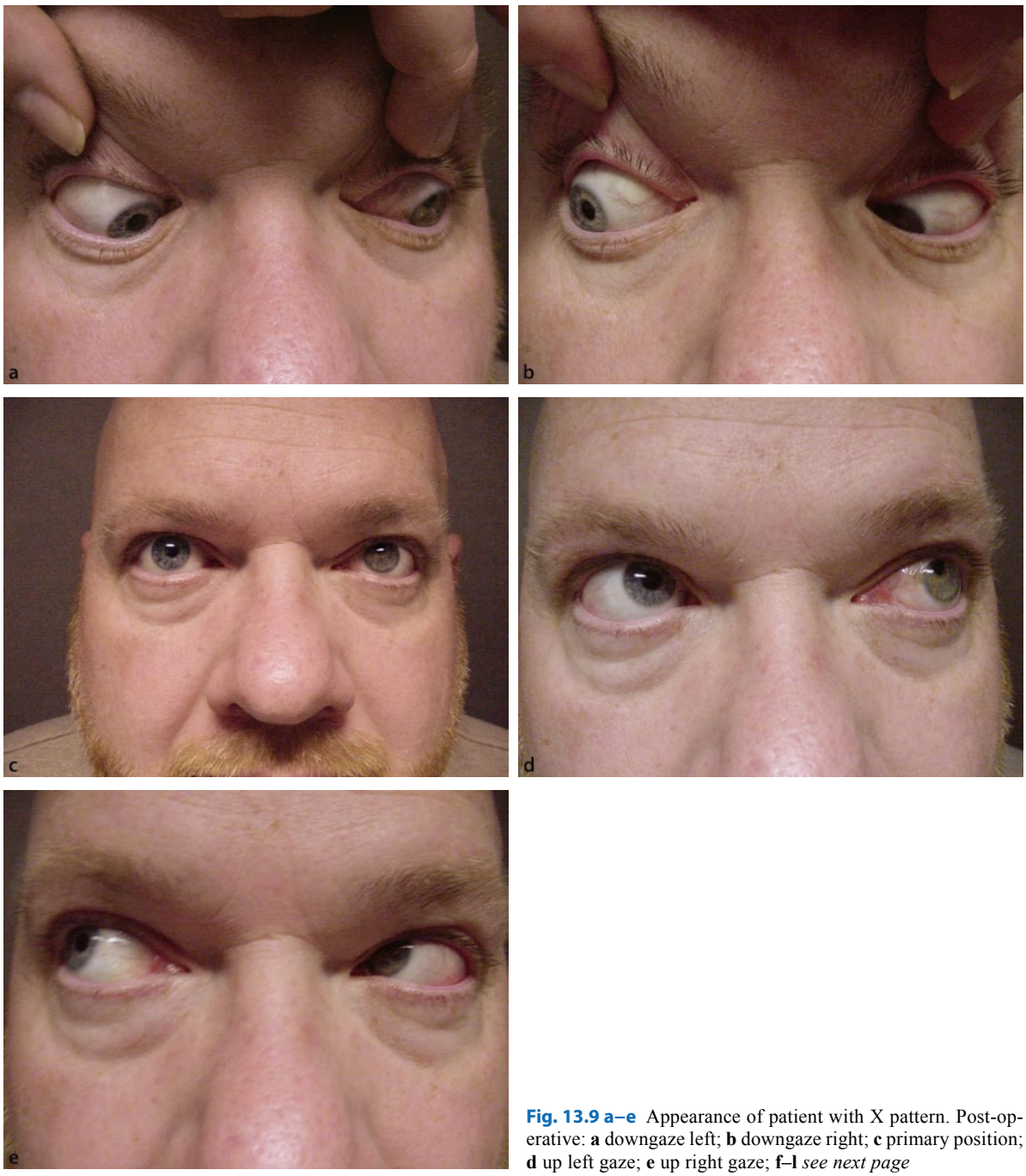


Fig. 13.9 a–e Appearance of patient with X pattern. Post-operative: **a** downgaze left; **b** downgaze right; **c** primary position; **d** up left gaze; **e** up right gaze; **f–l** *see next page*

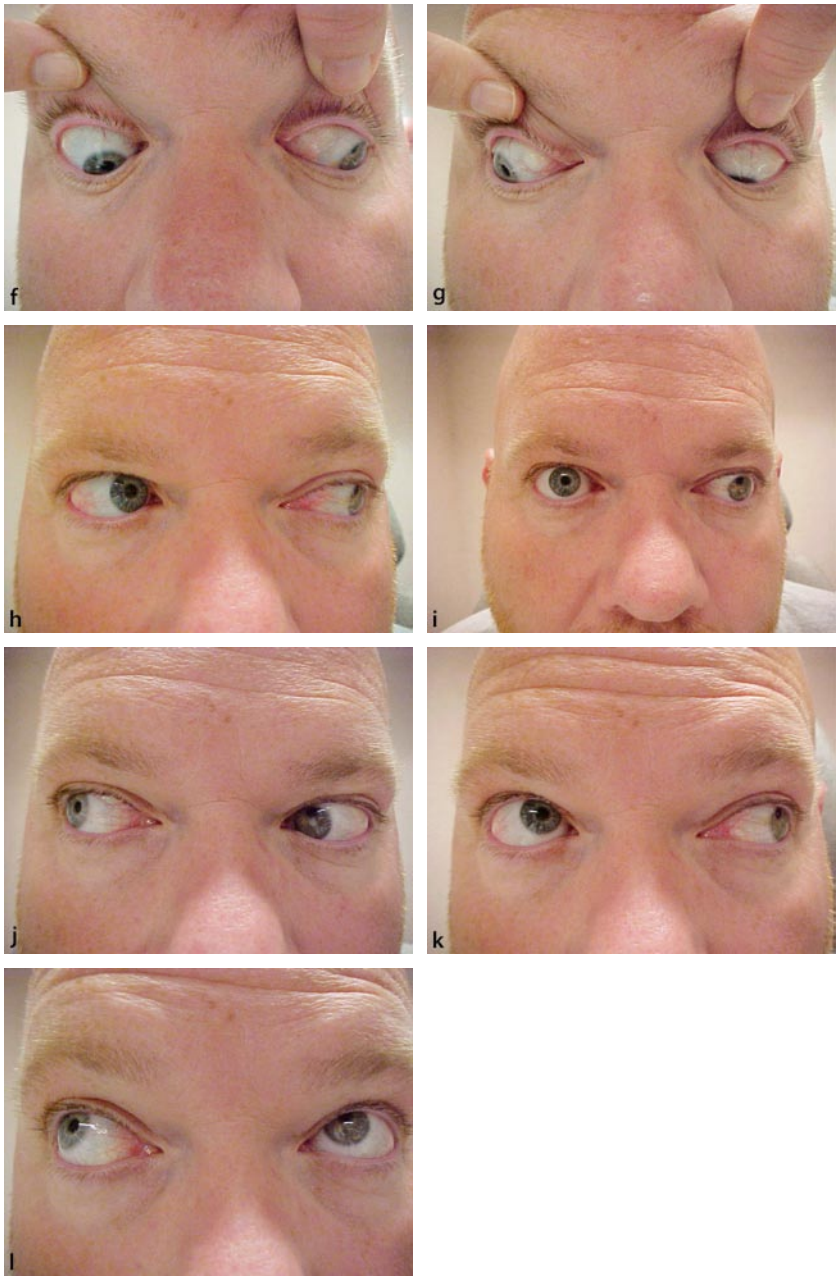


Fig. 13.9 f–l *(continued)* **f** down left; **g** down right. Pre-operative: **h** left; **i** primary; **j** right; **k** up left; **l** up right. Note that the pattern is diminished with advancement of medial rectus muscles only

Take Home Pearls

- In general, if the A or V pattern is caused by SO or IO "overaction," surgery should be directed at the obliques.
- If there is no significant oblique overaction, surgery should involve vertical shift of the horizontal rectus muscles in the appropriate direction.
- Bilateral inferior oblique weakening can collapse large V patterns when significant IO overaction is present.
- In patients with V pattern and IOOA in association with congenital esotropia complex, consideration should be given to performing IO anterior transposition, even if DVD is not obvious.
- Correction of X pattern with apparent overaction of all four oblique muscles in association with large-angle exotropia can be accomplished with correction of the horizontal deviation alone without surgery on the oblique muscles.
- Bilateral superior oblique weakening can collapse large A patterns up 30–40 PD or more. Bilateral IO weakening is not expected to collapse as large a pattern.
- Bilateral SO weakening should not be done in patients with normal binocular vision, i.e., bifixators with high-grade stereopsis (40 s/arc stereo or better).

Correction of this asymmetric result usually involves return to the operating room where oblique traction testing should help pinpoint the problem [11]. If there is no asymmetric residual oblique dysfunction, then standard vertical rectus recession may be needed.

13.4.9.3 Surgical Misadventure

As with any strabismus surgery, careful attention to surgical planes, fat pads, and basic strabismus principles must be observed. This is particularly true when operating on the oblique muscles. The inferior oblique is encased in fat pads that must not be violated and the superior oblique has tenuous connections to the underside of the superior rectus that must be identified. Even the levator complex can be violated with indiscriminate dissection around the superior oblique tendon.

References

1. Breinin GM (1961) Vertically incomitant horizontal strabismus. The A-V syndromes. NY State J Med 61:2243
2. Breinin G (1964) The physiopathology of the A and V patterns. In: Symposium: the A and V patterns in strabismus. Trans Am Acad Ophthalmol Otolaryngol 68:363
3. Folk ER (1997) Costenbader Lecture. A and V syndrome: a historical perspective. J Pediatr Ophthalmol Strabismus 34:154
4. Goldstein JH (1967) Monocular vertical displacement of the horizontal rectus muscles in the A and V patterns. Am J Ophthalmol 64:265
5. Jampolsky A (1965) Oblique muscle surgery of the A and V pattern. J Pediatr Ophthalmol 2:31
6. Knapp P (1959) Vertically incomitant horizontal strabismus: the so-called A and V syndrome. Trans Am Ophthalmol Soc57:666
7. Knapp P (1971) A and V patterns. In: Symposium on strabismus. Trans New Orleans Acad Ophthalmol St. Louis, Mosby Year-Book, p 242
8. Kushner BJ (2006) Multiple mechanisms of extraocular muscle "overaction." Arch Ophthalmol 124:680–688
9. Parks MM (1972) The weakening surgical procedures for eliminating overaction of the inferior oblique muscles. Am J Ophthalmol 73:107
10. Plager DA (1992) Tendon laxity in superior oblique palsy. Ophthalmology 99(7):1032–1038

11. Plager DA (2004) Reoperation strategies. In: Plager DA (ed) Strabismus surgery: basic and advanced strategies. Oxford University Press, Oxford
12. Scott AB (1968) A and V patterns in exotropia. An electromyographic study of horizontal rectus muscles. Am J Ophthalmol 65:12
13. Urist MJ (1951) Horizontal squint with secondary vertical deviations. Arch Ophthalmol 46:245
14. Urist MJ (1958) The etiology of the so-called A and V syndromes. Am J Ophthalmol 46:835
15. Urist MJ (1968) Recession and upward displacement of the medial rectus muscles in A-pattern esotropia. Am J Ophthalmol 65:769
16. Noorden GK von, Olson CL (1965) Diagnosis and surgical management of vertically incomitant horizontal strabismus. Am J Ophthalmol 60:434
17. Robb RM, Boger WP (1983) Vertical strabismus associated with plagiocephaly. J Pediatr Ophthalmol Strabismus 20:58
18. Clark RA, Miller JM, Rosenbaum AL, Demer JL (1998) Heterotopic muscle pulleys or oblique muscle dysfunction? J AAPOS 2:17
19. Scott WE, Drummond GT, Keech RV (1989) Vertical offsets of horizontal recti muscles in the management of A and V pattern strabismus. Aust NZ J Ophthalmol 17:281

General Principles in the Surgical Treatment of Paralytic Strabismus

14

Edward G. Buckley

Contents

Core Messages

- Improve ocular movement into the field of the paretic muscles either by increasing the action of the involved muscle through a resection or tuck-type procedure, or by creating an alternate force vector (often necessary in complete paralysis) by an extraocular muscle transposition procedure.
- Create matching weaknesses of movement in the yoke muscles of the other eye. Since it is generally impossible to restore normal function to the paralytic muscle, the "normal" eye needs to be matched to whatever resulting function can be achieved in the involved eye.
- Minimize the creation of new deviations by selecting appropriated surgical options.
- The direction of greatest deviation determines *which* muscles are operated and the quality of the remaining duction (good, fair, poor) helps select *what* operation to perform.

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14.1 Introduction

Paralytic strabismus is challenging to treat because the amount of ocular misalignment varies depending on the direction of gaze [1−3]. This incomitance makes it impossible to manage these situations successfully with prisms or standard strabismus techniques that work best when the size of the deviation is the same in the major gaze positions. The problem becomes more complicated if multiple muscles are affected. This is especially true with third cranial nerve palsies where both horizontal and vertical muscles are paretic. In such circumstances, both types of deviations need to be addressed to get a satisfactory result. In patients with fourth cranial nerve palsies there may also be a torsional issue that can be an extremely bothersome, and failure to eliminate the torsion can result in an unsatisfactory outcome. Finally, in patients who have had a long-standing paralysis, the ocular motility defect may have a restrictive component. The most common type of restriction is a contracture of the antagonist muscle. The more profound the muscle weakness, the more likely a restriction will result. Recognition of this phenomenon is paramount in designing a successful surgical procedure.

The incomitance of paralytic strabismus must be treated with surgical procedures which produce an incomitant result [4−19]. What is necessary to restore useable binocular function is an operation which has a greater effect in one field of gaze than in another. Developing the appropriate "incomitant" strabismus surgery can be achieved by taking three fundamental principles into consideration:

1. Improve ocular movement of the involved eye.
2. Balance yoke muscles (create matching weaknesses in the other eye).
3. Minimize the creation of new incomitant deviations.

While the first two principles may seem obvious, avoiding or anticipating the "creation" of a new incomitant deviation is not always appreciated until it unexpectedly occurs. The "unexpected" part is relative because almost always it was predictable. It is important to consider the gaze positions where this new deviation may be created by the proposed surgical intervention and to use another approach or use the creation of a new deviation to assist in the overall surgical plan.

In most cases the one gaze position where the eyes are aligned prior to any surgical intervention is located in the *opposite* direction to the field of action of the paralytic muscle. (A patient with right sixth cranial nerve palsy often sees singly in left gaze.) Strengthening or tightening the paralytic muscle will limit ocular rotation in the opposite direction creating a deviation where none existed before the surgery. The choice of surgical options should take into account what new deviations may be *created.* A recession may result in a new deviation since the muscle is now weaker or a resection may restrict the ocular movement in the opposite direction. Planning for, and dealing with, these predictable outcomes will help in obtaining the widest field of useable vision. This is an extremely important point. Often patients are extremely distressed when the previous area of single binocular vision is eliminated in an attempt to improve the diplopia in other fields of gaze. This becomes especially disconcerting if the resultant field of single binocular vision is extremely narrow, or if the diplopia changes direction with small gaze changes (i.e., esotropia in one field and exotropia in another).

14.2 Surgical Planning

In addition to the foregoing principles, when planning the actual surgical procedure it is important to take into consideration two additional factors: (a) the amount of residual muscle function that is present in the paretic muscle(s); and (b) the direction of gaze where the deviation is the greatest.

The amount of residual muscle function helps in determining *how* the muscle should be modified. Good to moderate function responds best to simple strengthening procedures such as resection, weakening the antagonist muscle, or the opposite yoke muscle. Poor or absent function requires some alternative force or very large resections. The direction of gaze where the deviation is the greatest helps in selecting *which* muscles should be modified. If the deviation is greatest in the field of the antagonist, then this muscle needs to be weakened as opposed to the opposite yoke. By combining these factors with the three general principles listed above, a surgical approach can be proposed to achieve the optimum result (Table 14.1).

Table 14.1 Isolated muscle paresis surgical strategy. *MR* medial rectus muscle, *LR* lateral rectus muscle, *SR* superior rectus muscle, *IR* inferior rectus muscle, *IO* inferior oblique muscle, *SO* Superior oblique muscle

Muscle	Mild	Moderate	Severe
Medial rectus	Recession-yoke LR ± resection MR	Resection MR plus recession LR	Resection MR (transposition IR/SR with small resection) Recession-yoke LR
Lateral rectus	Recession-yoke MR	Resection LR plus recession-yoke MR	Transposition IR/SR Recession-yoke MR
Superior rectus	Resection SR or recession-yoke IO	Resection SR plus recession IR	Transposition MR/LR Recession contralateral SR
Inferior rectus	Resection IR or recession-yoke SO	Resection IR plus recession SR	Transposition MR/LR Recession/faden contralateral IR
Superior oblique	Recession IO or recession-yoke IR	Recession IO plus recession-yoke IR	Tuck SO plus recession-yoke IR
Inferior oblique	Recession-yoke SR	Recession SO plus recession-yoke SR	Recession SO Recession-yoke SR

14.3 Good Muscle Function (Mild Duction Limitation)

The most important factor to consider when designing a surgical procedure to correct paralytic strabismus is the amount of residual muscle function present in the paretic muscle(s). In patients with a mild duction limitation (slightly decreased movement in the muscle's field of greatest action), the deviation can be improved equally by either strengthening the function of the paralytic muscle (resection), weakening the overacting yoke muscle (recession), or weakening the antagonist muscle (recession). Mild duction defects can be associated with fairly large deviations in the primary position; therefore, it is not the size of the deviation in primary position, but the ocular rotation that the muscle can achieve, that is important to assess. The actual choice of procedure depends on the second factor, the gaze position where the deviation is the greatest (Fig. 14.1). If the deviation is greatest in the field of the paralytic muscle, then strengthen the muscle and/or weaken the yoke. If it is greatest in the direction of the paretic muscle's antagonist (i.e., the antagonist is overacting such as an overacting inferior oblique in superior oblique muscle palsy), weaken the antagonist.

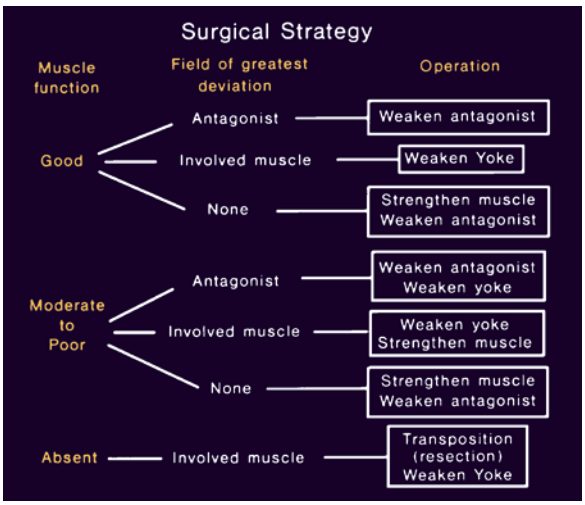


Fig. 14.1 Strategy for designing a surgical procedure for patients with a paralytic muscle taking into account the muscle's residual function and the field of greatest misalignment

14.3.1 *Fourth-Nerve Palsy*

A patient with a right fourth cranial nerve palsy has a right hypertropia worse on left gaze. If the deviation is worse up and left, then a right inferior oblique recession is performed (weaken the antagonist). If the deviation is worse down and left, then either strengthen the right superior oblique muscle (tuck)

or weaken the contralateral yoke (left inferior rectus muscle recession; Fig. 14.2).

In patients whose paretic muscle function is still good, it is often better to weaken the yoke muscle since this minimizes the chances of creating a new deviation in the opposite direction.

14.3.2 Sixth Cranial Nerve Palsy

A patient has a mild esotropia due to right sixth cranial nerve palsy (Fig. 14.3a). The deviation is greatest in right gaze. Surgical treatments could include resection of the right lateral rectus muscle, recession of the left medial rectus muscle, or recession of the right medial rectus muscle. If the field of greatest deviation is in right gaze, then resection of the right lateral and/or recession of the left medial rectus muscle are necessary (Fig. 14.3b). In some circumstances, the preferred approach is to weaken the action of the other eye.

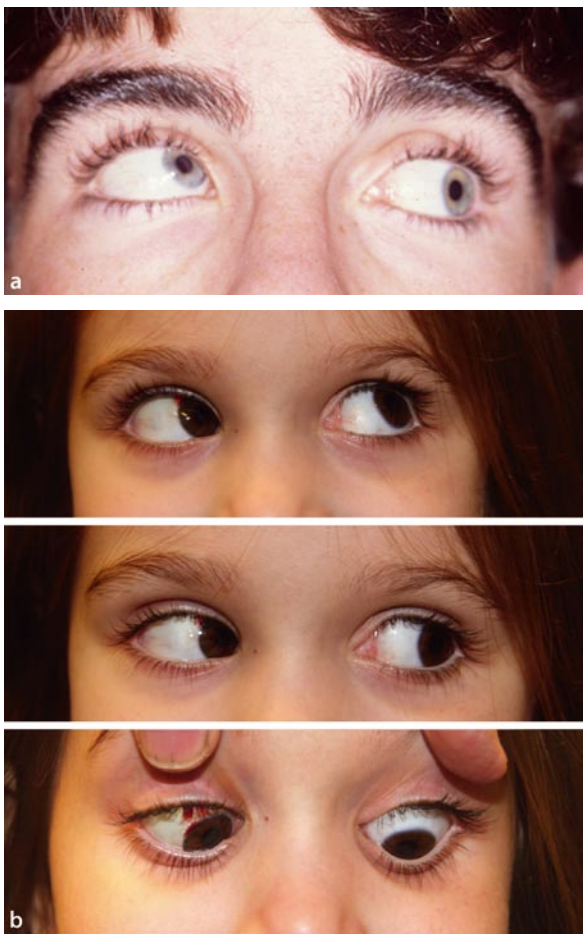


Fig. 14.2a,b Patients with a right fourth nerve palsy. **a** Note marked over action of the right inferior oblique on left gaze. Treatment should include a right inferior oblique weakening procedure. **b** Patient has marked under action of the right superior oblique muscle. Treatment should include either a tuck of the right superior oblique or a recession of the "yoke" left inferior rectus

14.3.3 Partial Third-Nerve Palsy

A patient has a mild inferior rectus muscle weakness of the right eye (Fig. 14.4a). There is a hypertropia on down gaze, but none in the primary position. Strengthening the involved muscle or weakening its antagonist (superior rectus muscle) will create a deviation in primary gaze. The preferred option is to weaken the contralateral yoke (left inferior rectus muscle) using the fadenoperation (posterior fixation suture; Fig. 14.4b).

The concept of *creating a matching weakness in the uninvolved eye* (Principle 2: Balance the yoke muscles) is fundamental to achieving a wide range of single binocular vision in patients with paralytic strabismus.

14.4 Moderate Decreased Duction

A moderate decrease in duction implies that the ocular rotation is reduced as much as 50−75%, but function is definitely still present. The treatment of a moderate paresis *requires* a strengthening procedure on the paretic muscle (Principle 1: Improve ocular rotation) *in combination* with either a weakening procedure of the ipsilateral antagonist, a weakening procedure of the contralateral yoke, and/or a weakening of the contralateral yoke's antagonist. Weakening the antagonist muscle alone will result in improvement in the primary position alignment but a very limited range of binocular field since both muscles are now poorly functioning. In most circumstances it is better to weaken the contralateral yoke as opposed to the ipsilateral antagonist (Principle 2: Balance the yoke muscles).

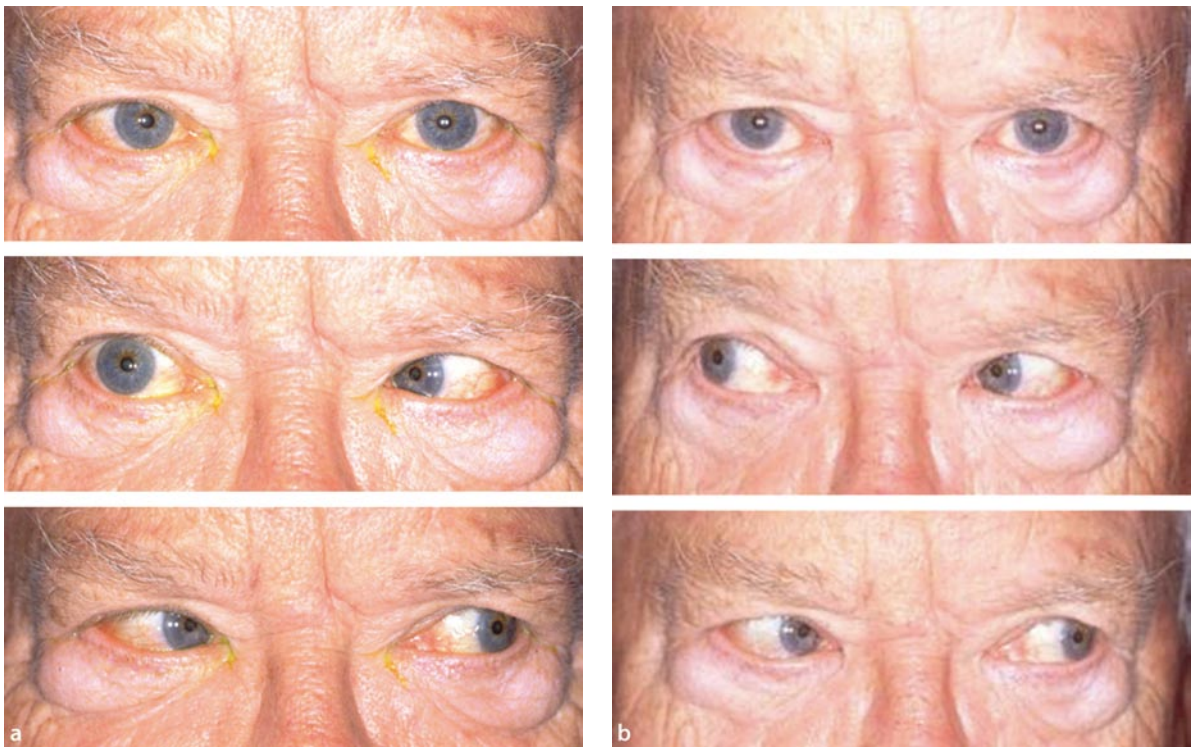


Fig. 14.3a,b Patient with a right sixth nerve palsy. **a** Preoperative appearance with good right lateral rectus function. **b** After recessing the yoke left medial rectus. This approach takes advantage of Hering's Law. Note there is no exotropia created on left gaze.

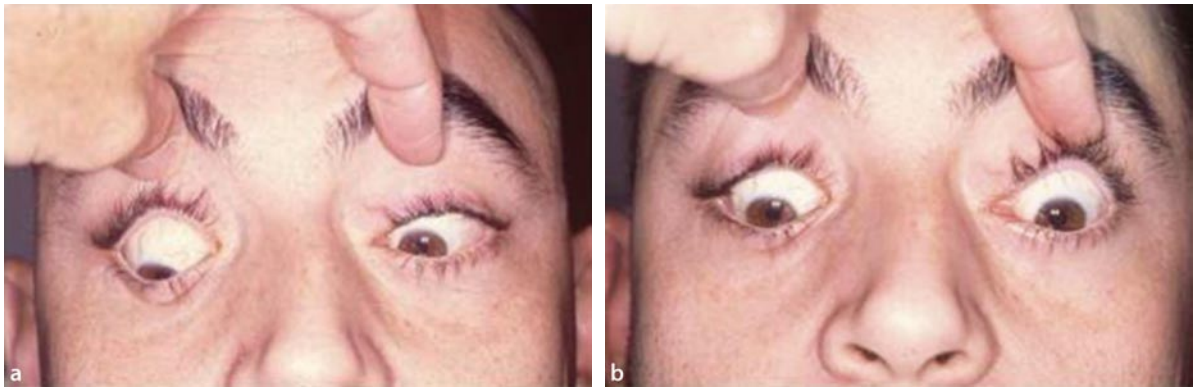


Fig. 14.4a,b Patient with vertical diplopia on downgaze but no deviation in primary gaze. **a** Note limitation of downward movement of the left eye. **b** After right inferior rectus fadenoperation, the down gaze diplopia is eliminated

14.4.1 Fourth-Nerve Palsy

A patient with a right fourth-nerve palsy has a hypertropia worse in down and left gaze (Fig. 14.2b). Since the deviation is greatest in the field of the involved right superior oblique muscle, a strengthening procedure (tuck) is appropriate. To minimize the creation of an iatrogenic Brown syndrome, weakening the contralateral yoke (left inferior rectus muscle), alone or in combination with the tuck, is also an option.

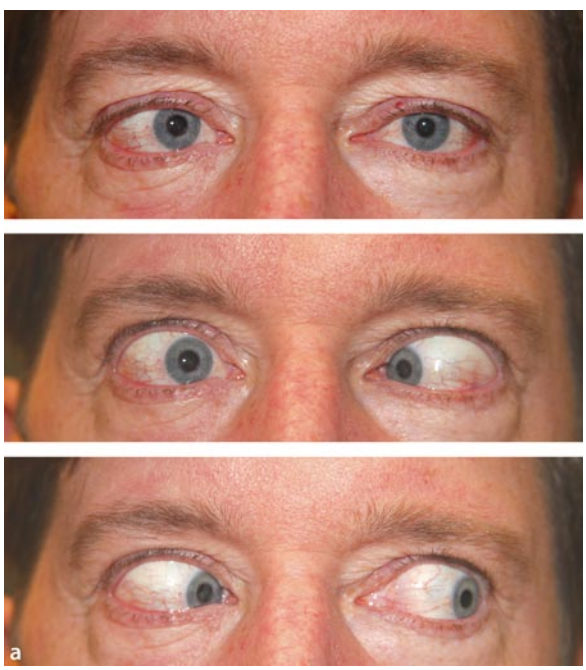
A recession of the right inferior oblique muscle will usually be the least helpful since there is almost no deviation up and to the left in its field of action.

If the antagonist muscle is contracted, then the restriction should be addressed necessitating a loosening procedure of that muscle. This will create a new deviation in opposite gaze for which treatment will be required (Principle 3: Anticipate problems).

14.4.2 Sixth-Nerve Palsy

A patient has large right sixth-nerve palsy with a tight right medial rectus muscle on forced duction (Fig. 14.5a) which will require a recession of the tight right medial rectus muscle along with a resection of the paralytic right lateral rectus muscle. If the deviation preoperatively was comitant and there is a moderate esotropia in left gaze, then this will yield a satisfactory result; however, if the field of greatest deviation is in right gaze and there was little or no esotropia in left gaze, an exotropia will occur postoperatively in that direction (Fig. 14.5b). To address this problem, a left lateral rectus muscle recession (on adjustable suture) can be entertained, either at the time of the original surgery or as a second procedure. When performed at the time of the original surgery, it allows for the placement of the right medial rectus muscle in the best position to achieve as much movement on right gaze as possible, without worrying about an exodeviation being created in left gaze since that can be adjusted for by recessing the left lateral rectus muscle.

The importance of *minimizing the creation of a new deviation* in the one field of gaze where the patient previously had single vision cannot be emphasized enough.



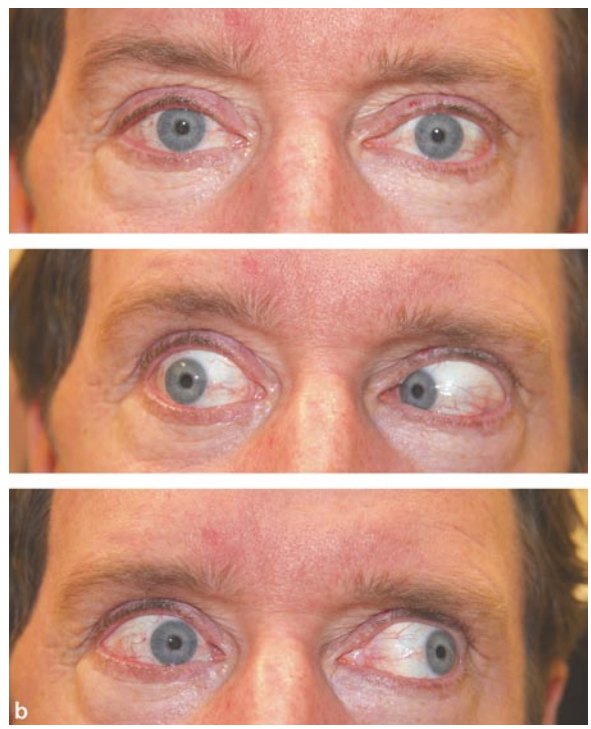


Fig. 14.5a,b Patient with a right sixth nerve palsy and a tight right medial rectus muscle. **a** Note marked limitation of abduction of the right eye. There is no deviation on left gaze. **b** Motility after a recession of the right medial and resection of the right lateral rectus muscles. Note that the patient now has an intermittent exotropia in the primary position and an exotropia on left gaze. This will require a left lateral rectus recession

14.5 Absent Muscle function

A severe duction limitation usually indicates no function of the muscle, except if significant restriction is also present, and on ocular rotations the eye cannot be moved into the field of action of the muscle. An example of a severe limitation is a sixth nerve palsy with no abduction of the eye past midline, negative forced duction testing, and sluggish response to an OKN drum rotated temporal to nasal with the viewing eye in adduction. The OKN drum elicits an abducting saccade which, if weak or absent, provides indirect evidence of severe muscle function impairment. If there is no muscle function then some form of alternative force needs to be created. There are basically two options for this: a large resection (or tightening of the involved rectus muscle) or a transposition procedure.

In an example of sixth-nerve palsy, a patient has complete right sixth-nerve palsy (Fig. 14.6, top). Since there is no abduction of the right eye a transposition procedure was performed, moving the right superior and inferior rectus muscle to the right lateral rectus muscle. A residual esotropia persists in right gaze (Fig. 14.6, middle). Transpositions or resections will not normally result in full movement and a weakening procedure of the contralateral yoke will be necessary to enhance the effect (Principle 2: Balance the yoke muscles; Fig. 14.6, bottom).

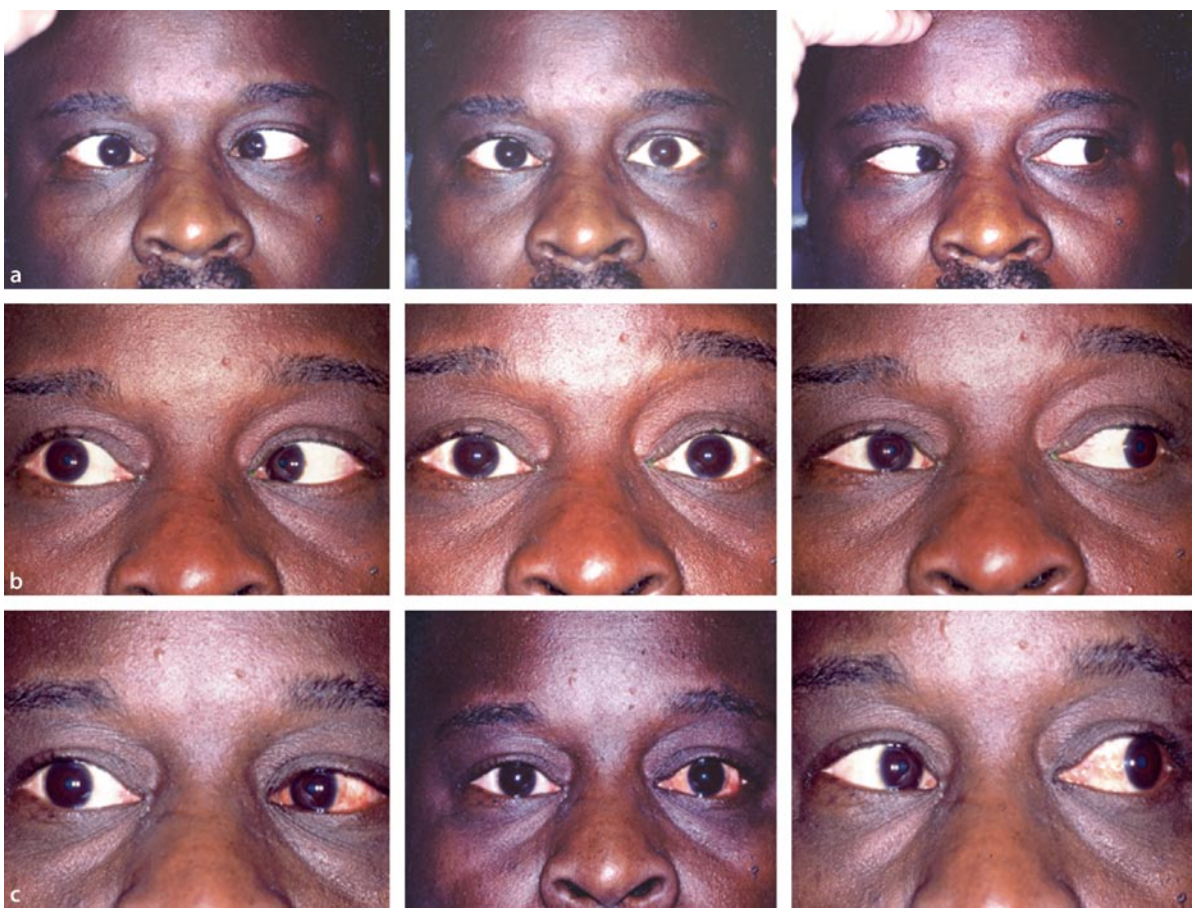


Fig. 14.6 Patient with a right sixth nerve palsy. **a** Right gaze shows severe limitation of ocular movement to the right. **b** Post-transposition procedure with improved movement but still esotropic on right gaze and now exotropic on left gaze. **c** After a left medial and lateral rectus muscle fadenoperation

While recession is generally used to weaken the yoke muscle, another effective way is the use of the fadenoperation (Fig. 14.6). This procedure is especially effective in lateral rectus muscle paresis and can provide an additional enhancement [1]. In patients with mild limitation and a small deviation in the primary position it can be combined with a recession. In more severe limitations it can be used to expand the field of single binocular vision in the direction of the paralytic muscle since its major advantage is that it does not increase the risk of an unwanted deviation on opposite gaze (Principle 3: Anticipate problems).

If the ipsilateral antagonist muscle is contracted or tight, then a recession of this muscle will be necessary and can be assessed at the time of the original transposition procedure. If anterior segment ischemia is a concern, Botulinum toxin can be injected into the antagonist muscle to achieve a temporary weakening and can be performed at the time of or before the transposition surgery. If injected prior to the surgical procedure, it can assist in assessing residual muscle function of the paralytic muscle.

Patients usually develop a deviation on opposite gaze after transposition procedures combined with recession of the antagonist muscle or after large resections of the paralytic muscle (Figs. 14.5, 14.6). This deviation can be proved or eliminated by a recession of the contralateral antagonist of the yoke. Often this requires a fairly large recession to control. If the eyes are straight in the primary position and the deviation is only present in one direction, then a fadenoperation on the muscle can be used (Fig. 14.6).

Large resections can be substituted for a transposition procedure if the muscles to be transposed are also poorly functioning. This is typically the case in partial third cranial nerve palsies where multiple muscles are involved. Transposing an already weakened muscle usually accomplishes little and limits further surgical options because of anterior segment vascular supply considerations. In such situations very large resections can be used with good results (Fig. 14.7). These resections may need to be repeated as they tend to "loosen" with time since the muscle has no real function.

14.6 Multiple Muscle Paresis

In patients who have more than one paretic muscle, the outcome goals need to be altered, as it is usually impossible to return the patient to full function. Emphasis should be placed on aligning the eyes centrally and in the down-gaze position. Alternative forces are usually necessary and will require either a transposition or a large resection. Each muscle is assessed independently with the results combined to design a unified surgical approach.

In an example of third cranial nerve palsy, a 65-year-old patient has a right third nerve palsy. The patient is unable to elevate and adduct the right eye (Fig. 14.8). He shows an exotropia that appears relatively similar in all horizontal gaze positions and a marked right hypotropia. He will need an alternate force for the right superior rectus muscle because there is no function, and a resection of the right medial rectus muscle with either a right lateral rectus muscle recession or a left lateral rectus muscle recession. Since a transposition can be combined with a resect/recess procedure, the entire surgery can be performed on his right eye, involving only two of the rectus muscles. The medial rectus muscle is resected and transposed superiorly to the medial border of the superior rectus muscle, and the lateral muscle is transposed to the lateral border of the superior rectus muscle and then recessed with reference to the spiral of Tillaux. A fadenoperation on the left inferior rectus muscle was performed in anticipation of a greater vertical problem on downgaze after the above surgery. Post-operation he had an improved field of single vision (Fig. 14.8b).

Other combinations of partially functioning muscles can be approached in the same manner. The underlying general principles are *to improve ocular rotation whenever possible and to weaken overacting yoke muscles*. Surgery on antagonist muscles can be used to enhance the resection effect but runs the risk of creating a deviation in a field where one did not previously exist. If this is necessary, then surgery on the contralateral antagonist will also be needed.

In another example, A 40-year-old man has left third cranial nerve palsy. The patient is unable to elevate, depress, and adduct the left eye (Fig. 14.9a). He will need either a large resection of the left medial rectus muscle or an alternate force (transposition) for the left medial rectus muscle because there

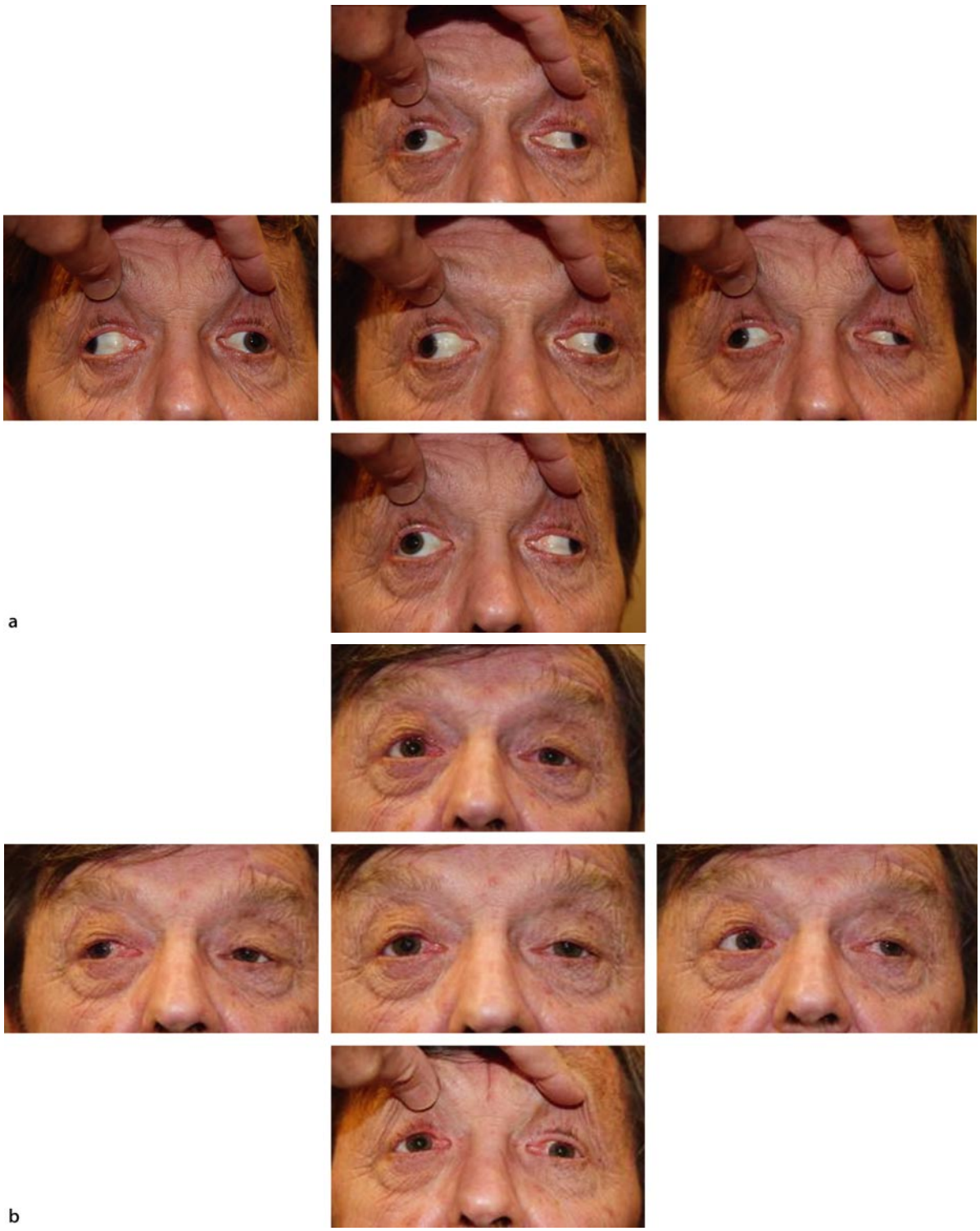


Fig. 14.7a,b Patient with bilateral third-nerve palsy. **a** Preoperative motility. Since there is no elevation and depression, transposing the superior and inferior muscles medially will not help with adduction. Large resections of the medial rectus muscles are the only possibility and can be performed without also weakening the lateral rectus muscles. **b** Post-operative motility. Note excellent alignment in the primary position with some horizontal movement. Excessive weakening of the lateral rectus muscles would have resulted in marked limitation of movement in all directions

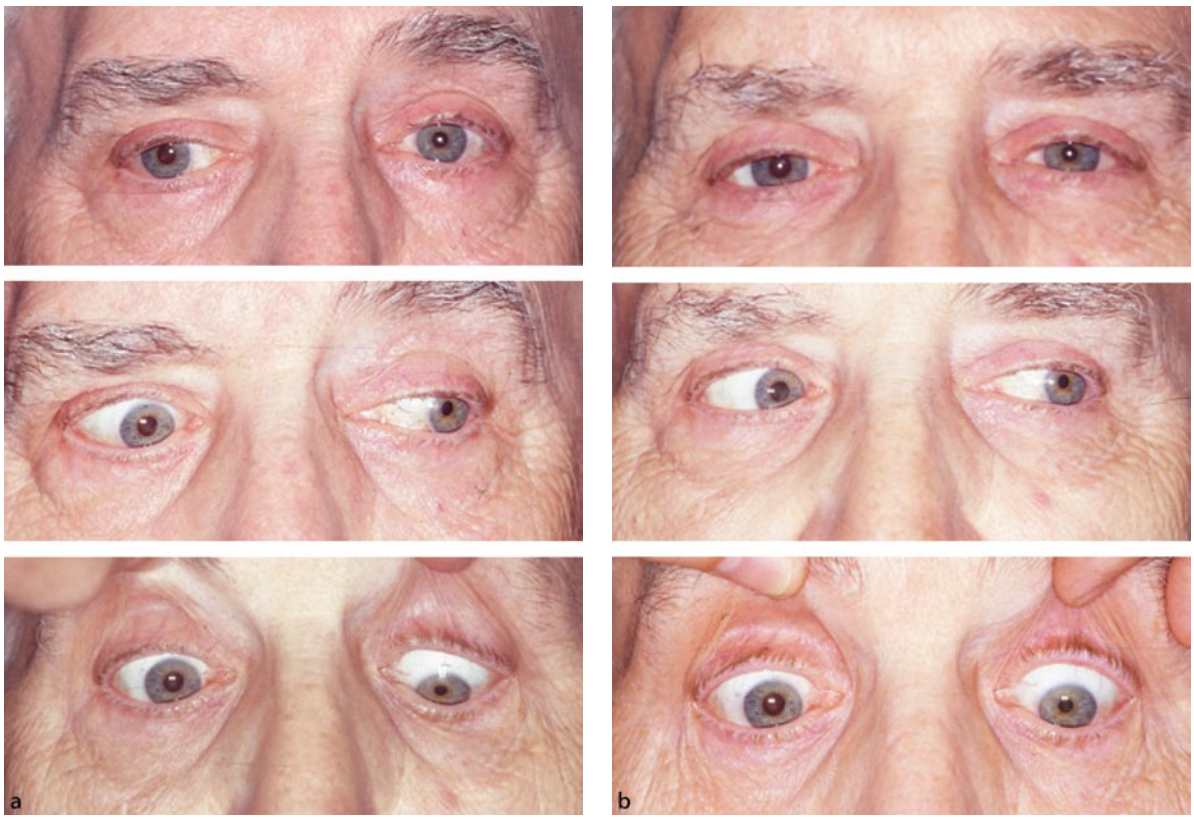
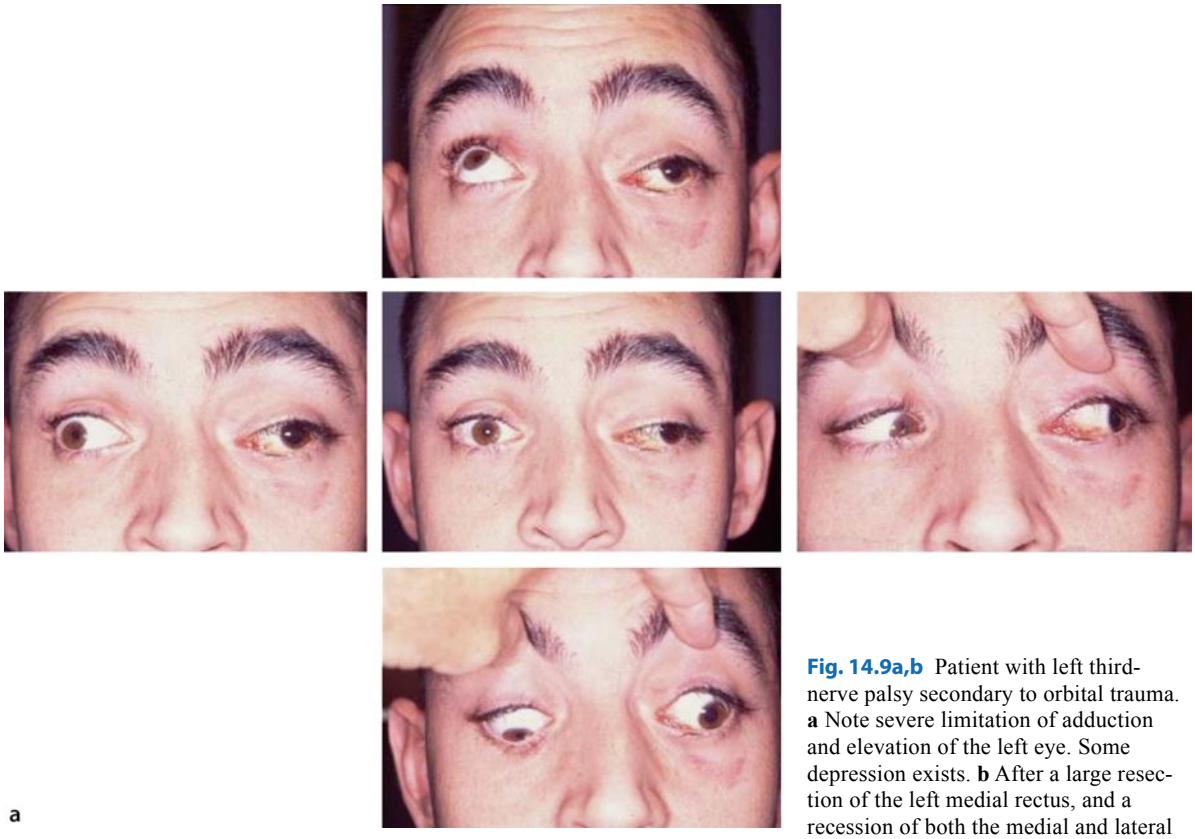


Fig. 14.8a,b Patient with right partial third-nerve palsy. **a** Note marked inability to elevate and adduct the right eye. There is a very mild limitation of depression. **b** After transposition of the right medial and lateral rectus superiorly. The medial rectus was also resected for the exotropia. Note that the depression weakness would be exaggerated due to the elevation effect of the transposition. This was treated with a fadenoperation on the left inferior rectus

is no function. Since the superior and inferior are also not functioning well, a resection of the left medial rectus muscle was performed (Principle 1: Improve function). In addition, a large recession of the yoke right lateral rectus muscle (Principle 2: Balance the yoke muscles) and a recession of the right medial rectus muscle plus a fadenoperation on the right inferior rectus muscle was performed (Principle 3: Anticipate problems) (Fig. 14.9b).

Care should be exercised in recessing the antagonist muscle, especially in vertical deviations in third-nerve palsies which appear to have only an isolated muscle involved. Sometimes there is asymmetric involvement with one of the vertical muscles more paretic than the other. A recession of the "normal functioning" vertical muscle may result postoperatively in a more than anticipating underaction of this muscle. If at all possible, recessing the contralateral yoke muscle will obviate this complication.



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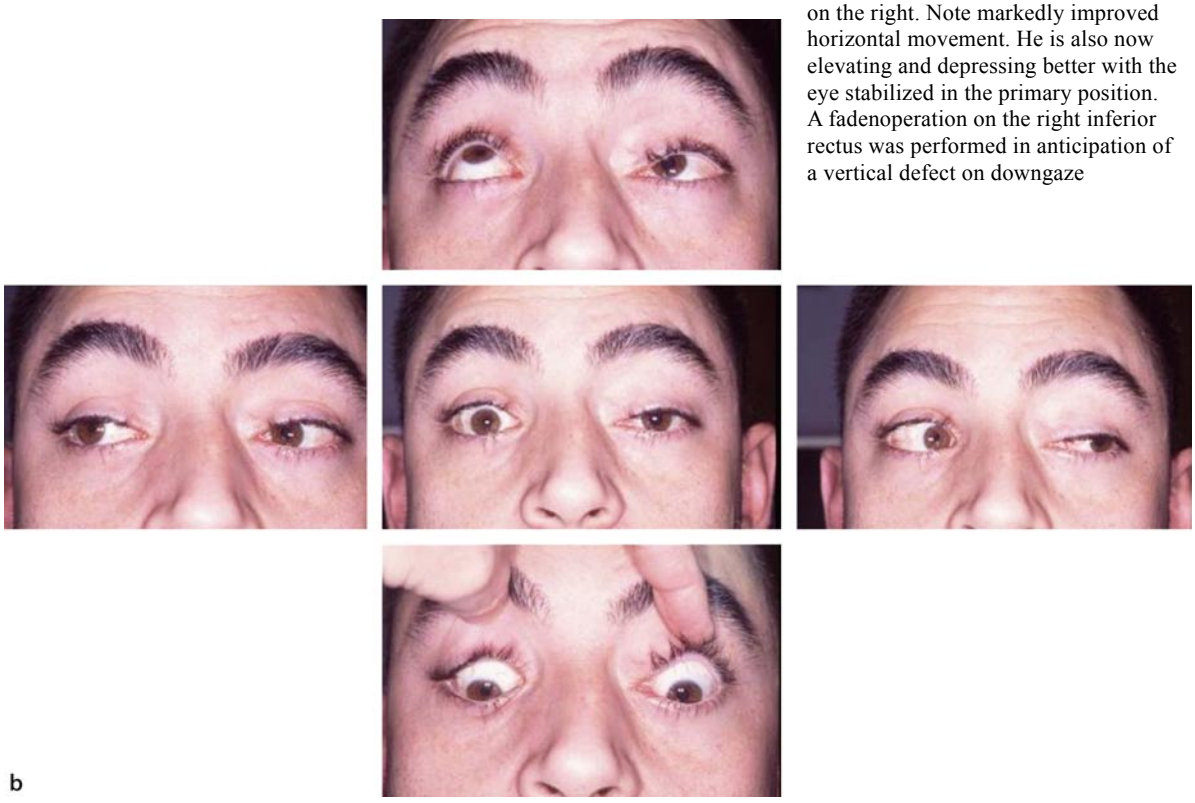

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Fig. 14.9a,b Patient with left third-nerve palsy secondary to orbital trauma. **a** Note severe limitation of adduction and elevation of the left eye. Some depression exists. **b** After a large resection of the left medial rectus, and a recession of both the medial and lateral on the right. Note markedly improved horizontal movement. He is also now elevating and depressing better with the eye stabilized in the primary position. A fadenoperation on the right inferior rectus was performed in anticipation of a vertical defect on downgaze

Take Home Pearls

- A successful surgical procedure for paralytic strabismus must give the patient a sufficiently large area of single binocular vision to allow them to function without diplopia over a range of at least 20°.
- A careful analysis of the ocular motility deficit with particular attention to the *amount of residual ocular rotation* is extremely important in selecting a procedure which will yield the maximum benefit.
- Whenever possible, improve the eye movement in the field of action of the paretic muscle(s) (Principle 1).
- Always consider weakening the partner yoke muscle (Principle 2).
- Anticipate creating new deviations with your surgery and use that to help correct the incomitant strabismus or plan to add additional procedures to address it (Principle 3).
- Assessing residual muscle function determines *how* the muscles should be modified.
  - Good function: strengthen the muscle (resection or weaken the antagonist) or weaken the yoke.
  - Poor Function: alternative force.
- The field of greatest deviation helps determine *which* muscles should be modified.
  - Opposite gaze: weaken the antagonist and/or weaken the yoke.
  - Same gaze: strengthen the muscle and weaken the yoke.
  - No difference: strengthen the muscle and weaken the antagonist.
- Avoid just weakening the antagonist muscle in patients with paretic muscles which are poorly functioning. This will create a very small binocular field since the eye will not move well in either direction.
- Very large resections can be very useful in situations where there is poor or no muscle function; these may have to be repeated to achieve long-term success.
- The OKN drum can be helpful in differentiating paresis from restriction. Have the eye gaze in the direction opposite the paresis and rotate the drum toward that direction. This will elicit a saccade in the direction of the paretic muscle which, if brisk, indicates that the ocular rotation limitation has a restrictive component.

References

1. Buckley E (1999) Fadenoperation (posterior fixation suture). In: Rosenbaum AL (ed) Clinical strabismus management. Saunders, Philadelphia
2. Buckley E, Meekins B (1988) Fadenoperation for incomitant vertical strabismus. Am J Ophthalmol 105:304−310
3. Buckley E, Townshend L (1991) A simple transposition procedure for complicated strabismus. Am J Ophthalmol 111:302−306
4. Fitzsimons R, Lee J, Elston J (1988) Treatment of sixth nerve palsy in adults with combined botulinum toxin chemodenervation and surgery. Ophthalmology 95:1535
5. Foster R (1997) Vertical muscle transposition augmented with lateral fixation. J Am Assoc Pediatr Opthalmol Strabismus 1:20
6. Gottlob I, Catalano R, Reinecke R (1991) Surgical management of oculomotor nerve palsy. Am J Ophthalmol 111:71
7. Helveston E (1993) Muscle transposition procedures. In: Surgical management of strabismus: an atlas of strabismus surgery, 4th edn. Mosby, St. Louis, p. 291

8. Jensen C (1964) Rectus muscle union: a new operation for paralysis of the rectus muscles. Trans Pac Coast Ophthalmol Soc 45:359
9. Kattleman B, Flanders M, Wise J (1986) Supramaximal horizontal rectus surgery in the management of third and sixth nerve palsy. Can J Ophthalmol 21:227
10. Knapp P (1969) The surgical treatment of double elevator paralysis. Trans Am Ophthalmol Soc 67:304
11. Kodsi S, Younge B (1992) Acquired oculomotor, trochlear, and abducent cranial nerve palsies in pediatric patients. Am J Ophthalmol 114:568
12. Kushner B (1995) Management of diplopia limited to downgaze. Arch Ophthalmol 113:1426
13. McManaway J, Buckley E, Brodsky M (1990) Vertical rectus muscle transposition with intraoperative botulinum toxin injection for the treatment of sixth nerve palsy. Graefe Arch Ohthalmol 228:401−406
14. Metz H (1988) The use of vertical offsets with horizontal strabismus surgery. Ophthalmology 95:1094
15. Metz H (1993) 20th annual Frank Costenbader Lecture-muscle transposition surgery. J Pediatr Ophthalmol Strabismus 30:346
16. Repka M, Lam G, Morrison N (1994) The efficacy of botulinum neuro toxin A for the treatment of complete and partially recovered chronic sixth nerve palsy. J Pediatr Ophthalmol Strabismus 31:79
17. Rosenbaum, A., Adjustable vertical rectus muscle transposition surgery. Arch Ophthalmol, 1991. 109: p. 1346.
18. Rosenbaum A, Kushner B, Kirschen D (1989) Vertical rectus muscle transposition and botulinum toxin (Oculinum) to medial rectus for abducens palsy. Arch Ophthalmol 107:820
19. Saunders R (1984) Incomitant vertical strabismus: treatment with posterior fixation of the inferior rectus muscle. Arch Ophthalmol 102:1174

Diagnosis and Surgical Management of Ocular Motility Syndromes

15

Ronald G.W. Teed and Richard A. Saunders

Contents

Core Messages

- Children with duction deficits and abnormal head posture are likely to have an identifiable ocular motility syndrome.
- Most defined motility syndromes present with a spectrum of clinical appearance and severity.
- Clinical history, along with careful evaluation of versions and ductions, will usually reveal the correct diagnosis. Ancillary testing, such as forced ductions or estimates of generated muscle force, will sometimes be required in planning treatment.
- Surgical intervention can usually improve the strabismus and eliminate the abnormal head posture, but ocular motility is rarely restored to normal.

15.1 Syndromes Primarily Associated with Horizontal Duction Deficits

15.1.1 Duane Retraction Syndrome

Duane retraction syndrome (DRS) is a usually unilateral, and almost always congenital, disorder of ocular motility that usually occurs on a sporadic basis. Its signature features are the presence of abnormal

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horizontal eye movements, usually a deficiency of abduction, and some degree of globe retraction in adduction. This is most easily identified by a narrowing of the palpebral fissure, which develops or worsens in adduction. Abnormal head posture is common, as are up-shoots and down-shoots of the globe. If the fellow eye has normal ocular motility, patients will almost invariably assume a head position to allow binocular vision.

The etiology of most cases of DRS is believed to be maldevelopment of the sixth cranial nerve nucleus, fascicle and nerve, with subsequent misinnervation of the lateral rectus muscle by a branch (or branches) of the third cranial nerve [25, 42]. The underlying pathology is hypoplasia of the motor neurons in the six cranial nerve nucleus, with sparing of the internuclear neurons [42]. This finding helps explain why DRS manifests as unilateral duction abnormalities, rather than as a horizontal gaze palsy, as seen in internuclear ophthalmoplegia. Rare acquired cases suggest that a supranuclear basis is also possible [1].

DRS can be associated with other ocular and non-ocular abnormalities; however, it most often presents as an isolated disorder. Rather than a single entity, DRS should be viewed as a spectrum of ocular dysmotility, with precise clinical findings determined by the degree of lateral rectus muscle paresis and patterns of dysinnervation of the lateral rectus and sometimes other extraocular muscles. Although binocular vision is frequently maintained in DRS, about one half of cases require a compensatory face turn to maintain orthotropia. Most reports demonstrate diplopia outside a relatively small field of single binocular vision [50]. Surgical treatment is most often performed to correct a strabismus in primary gaze (and associated compensatory face turn), but it is occasionally indicated to treat cosmetically objectionable globe retraction, diplopia, up-shoot and/or down-shoot, or ocular discomfort.

15.1.1.1 History and Epidemiology

While first described by Heuck in 1879 [24], and later by Stilling and Turk [66, 69], Alexander Duane is usually credited for describing the characteristic constellation of impaired horizontal eye movements based on a review of 54 patients with this disorder which bears his name [14]. These findings consisted of globe retraction, narrowing of the palpebral fissure, and oblique eye movements in attempted adduction. Duane retraction syndrome, or Stilling–Turk–Duane syndrome, is now a commonly recognized abnormality of ocular motility. It is usually sporadic in occurrence, but inherited cases have been reported [8]. Familial DRS is inherited in an autosomal-dominant pattern [49]. Several phenotypes have been described, with genetic loci identified on chromosomes 2, 8, and 20 [2, 3, 7]. Occasionally, associated findings in DRS include ocular anomalies, such as iris dysplasia, cataract, and other dysinnervation disorders including Marcus Gunn jaw wink and "crocodile tears" syndrome [63]. Non-ocular findings, including radial dysplasia and auricular abnormalities, occur in about 30% of cases [49]. DRS is specifically known to occur in association with Goldenhar syndrome and Klippel–Feil syndrome, and has been described following fetal exposure to thalidomide [40]. For this reason, and the high prevalence of associated systemic malformations in the DRS patient, it has been proposed that normal innervation of the extraocular muscles is susceptible to disruption between the fourth and fifth weeks of embryogenesis [11, 21].

DRS represents approximately 1% of all strabismus cases [13]. Multiple published series of DRS have confirmed that its occurrence is greater in females (nearly 60%) and in the left eye (58–72%) [13, 50, 62,]. Approximately 20% are bilateral [13]. Curiously, there may be a male preponderance in bilateral cases [30]. As a practical matter, over one-third of all DRS cases seen in clinical practice occur in the left eye of females. This may alert the physician to suspect the diagnosis of DRS in uncooperative children or cases where the motility findings are not perfectly clear.

15.1.1.2 Clinical Findings and Classification

While the clinical manifestations of DRS may vary, reflecting the continuum of extra-ocular muscle dysinnervation, classification is still probably a worthwhile endeavor. The basic findings tend to be stereotyped, with some variability in severity of individual features, such as the horizontal duction deficit and up-shoot or down-shoot of the globe. While not intuitively obvious, most vertical phenomena can be explained by aberrant innervation of the lateral rectus muscle.

Several classification schemes have been proposed, but the one described by Huber in 1974 is still commonly used (Table 15.1) [26]. It is based on original data from medial and lateral rectus muscle electromyography in DRS patients; however, other studies have shown variability in the patterns of dysinnervation across DRS types [60]. It may therefore be equally useful for surgical planning to classify patients based on primary-gaze alignment (esotropic, exotropic, etc.), combined with the magnitude of the primary-gaze deviation and severity of associated findings, such as globe retraction [33, 34].

In addition to the three Huber types, other patterns of DRS-like motility disorders have been described, including a vertical variant that may reflect dysinnervation of the superior rectus and/or inferior oblique muscles [74]. DRS should be distinguished from other forms of extraocular muscle dysinnervation, which occasionally occur on a congenital or acquired basis but do not involve co-contraction or narrowing of the palpebral fissure in adduction.

15.1.1.2.1 The Huber Classification of DRS

Huber described three types of DRS based on clinical findings and electromyographic data recorded from the extraocular muscles in different positions of gaze; however, these types may blend together and the distinctions may sometimes appear arbitrary (Table 15.1). For this and other reasons, the Huber classification is not necessarily helpful with regard to planning treatment – its use is mostly limited to a convenient clinical shorthand.

Type-I DRS

Type-I DRS is the most common clinical presentation and includes approximately 85% of cases. It is characterized by limited abduction, sometimes mimicking sixth cranial nerve palsy (Fig. 15.1). Adduction is normal or only modestly reduced and associated with globe retraction and narrowing of the palpebral fissure (Fig. 15.2). Electromyography shows little or no electrical activity of the lateral rectus muscle in abduction, but paradoxical activity in adduction. This is thought to result from anomalous innervation by the third cranial nerve [4, 26].

Approximately one-half of patients with type-I DRS are orthotropic in primary-gaze position in childhood [50], and virtually all of the remainder is esotropic. The deviation is usually less at near viewing. A compensatory face turn towards the involved eye is often present and permits sensory fusion. Amblyopia or loss of binocularity is therefore uncommon [68].

Table 15.1 Classification of Duane syndrome

Type	Essential clinical features	Pathophysiology	Ocular alignment	Frequency
Huber I	Limited abduction Co-contraction in adduction Up- and down-shoots may occur	Abducens nerve paresis; abnormal lateral rectus muscle innervation	Usually esotropic	Common (85%)
Huber II	Limited adduction Co-contraction in adduction Limited abduction (variable) Up- and down-shoots common	Abducens nerve may be intact or hypoplastic; abnormal lateral rectus muscle innervation	Usually exotropic	Uncommon (15%)
Huber III	Limited abduction and adduction Co-contraction in adduction (often severe) Up- and down-shoots common	Abducens nerve paresis; abnormal lateral rectus muscle innervation	Usually orthotropic	Rare (1%)
"Splits"	Same as type II, except mild co-contraction in adduction and DRS eye abducts with lateral gaze of normal eye	Unknown, but likely similar to type II	Always exotropic	Rare
Vertical	Limited vertical gaze Co-contraction in opposite gaze	Unknown	Variable	Rare

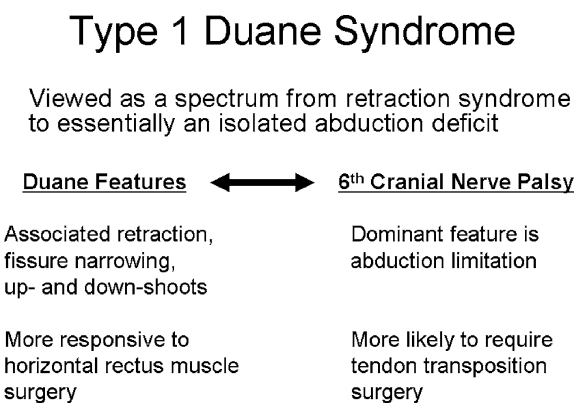

Fig. 15.1 Continuum in type-I DRS. This disorder may resemble congenital sixth cranial nerve palsy when aberrant innervation is limited

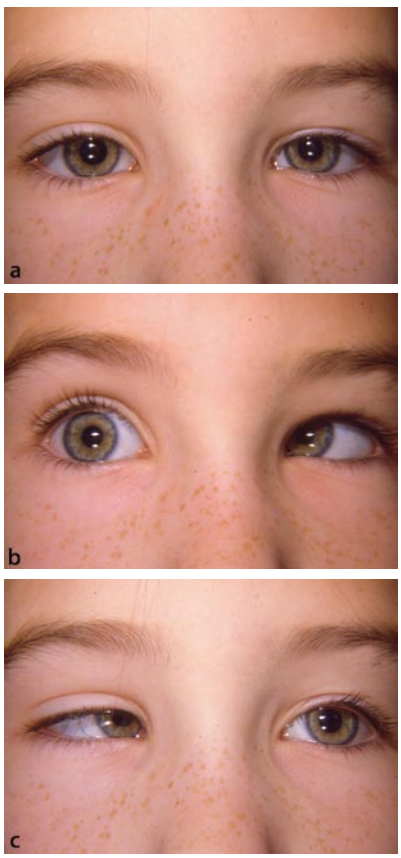

Fig. 15.2a–c Boy with typical bilateral type-I Duane retraction syndrome (DRS). There is marked limitation of abduction in both eyes, narrowing of the palpebral fissures in adduction, and a small-angle esotropia in primary gaze position. The esotropia usually decreases at near viewing. Surgical treatment was not recommended. (From [79])

Type-I DRS may need to be distinguished from both congenital sixth cranial nerve palsy and congenital esotropia. In sixth cranial nerve palsy, globe retraction and eyelid findings are absent; in congenital esotropia, abduction is normal or near normal and the deviation in primary-gaze position is generally large. Furthermore, the deviation in type-I DRS is rarely greater than 30 prism diopters, even when the abduction deficit is severe or both eyes are affected [13, 27]. This discrepancy between primary-gaze deviation and the abduction deficit allows a virtually certain diagnosis (and obviates the need for intracranial imaging) in infants where co-contraction may not be clinically apparent. Finally, in type-I DRS, the limitation in abduction typically improves with elevation or depression (Fig. 15.3), which is not true of other "look-alike" diagnoses.

Type-II DRS

Type-II DRS is a far less common presentation, occurring in about 10% of cases. It is characterized by limited adduction with normal or slightly limited abduction. Globe retraction and palpebral fissure narrowing on attempted adduction are common, and may be severe. Up- and down-shoots of the involved eye in adduction are frequently present (Fig. 15.4). This pattern is thought to arise when the lateral rectus muscle receives innervation from the sixth cranial nerve in addition to anomalous branches of the third cranial nerve. Originally thought to be characterized by an intact sixth cranial nerve, a recent imaging study showed that type-II DRS may also be associated with sixth cranial nerve hypoplasia [12].

Nearly all patients with type-II DRS are exotropic in primary position [50]. A compensatory face turn away from the DRS eye will normally permit sensory fusion. As might be expected, the exotropia is typically greater at near than distance viewing.

Type-III DRS

Type-III DRS is a rare presentation that may be viewed as a combination of the preceding two types. There is marked limitation of both abduction and adduction. It occurs in approximately 1% of cases, but the distinction from type-I DRS may be arbitrary in cases where the limitation of adduction and abduc-

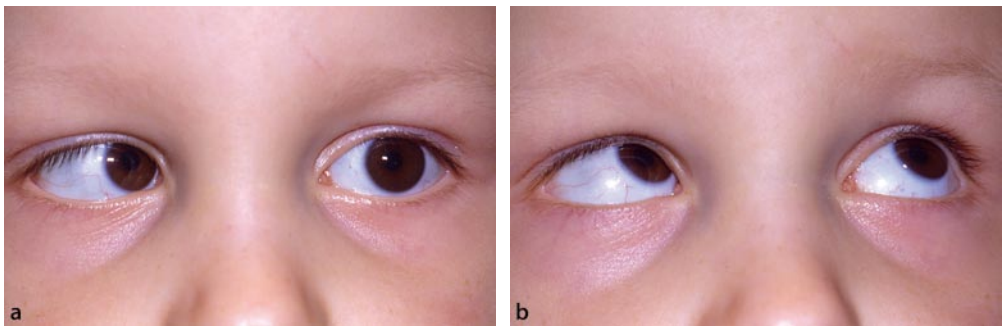

Fig. 15.3a,b Patient with type-I DRS in the left eye shown in attempted left lateral gaze. Note the improved abduction in elevation (also present in depression)

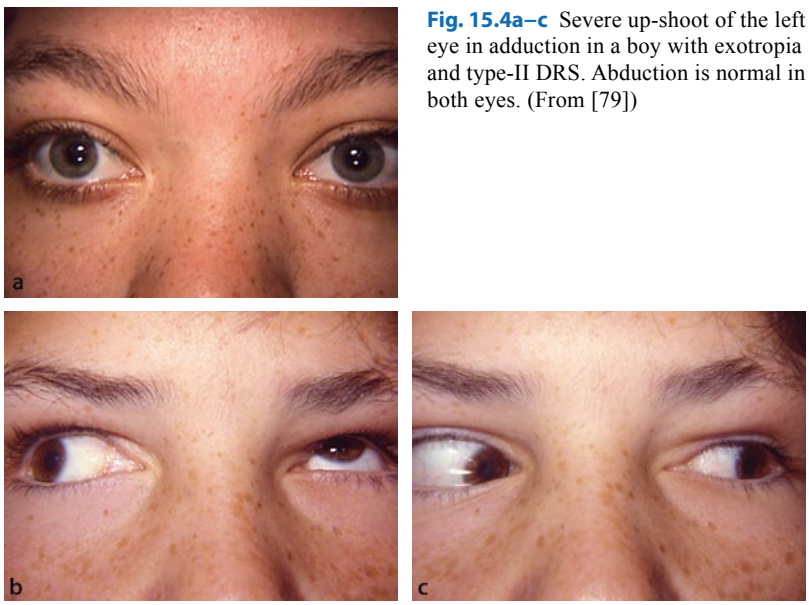

Fig. 15.4a–c Severe up-shoot of the left eye in adduction in a boy with exotropia and type-II DRS. Abduction is normal in both eyes. (From [79])

tion is symmetrical and not severe. This pattern is thought to arise when there is little or no sixth cranial nerve activity, and the lateral rectus muscle is largely innervated by anomalous branches of the third cranial nerve. Since the involved eye moves poorly, these patients are usually well aligned in primary position and fuse without (or with minimal) head posture; however, globe retraction and palpebral fissure narrowing in attempted adduction are often severe and usually the reason patients seek ophthalmologic treatment.

Synergistic Divergence

Often colorfully termed "the splits," this is a rare but well-recognized variant of type-II DRS, where there is sufficient anomalous innervation of the lateral rectus muscle to cause an *ab*duction movement on attempted opposite gaze, resulting in a startling "wrong way" duction. For example, with left eye involvement, when the patient attempts left gaze, the left eye moves left; but when right gaze is attempted, the eye again moves left. These patients are always exotropic in primary gaze, which is their position of least strabismus.

Vertical DRS

Occasionally, a retraction-like syndrome will occur with a reduced *vertical* duction and globe retraction in the opposite position of gaze. If congenital in ori-

gin, this may properly be considered a DRS variant, however rare. It is not known whether vertical DRS results from infranuclear cranial nerve misdirection, a supranuclear disorder, or even structural abnormalities within the orbit or extraocular muscles [37]. Acquired vertical (or horizontal) motility disorders due to trauma (such as blowout fracture of the orbit), which may have a similar clinical picture, are not properly considered DRS, since they are not associated with dysinnervation of the extraocular muscles.

15.1.1.3 Management of DRS

The DRS rarely is associated with amblyopia [68], although clinically important anisometropia does occur in approximately one-fourth of cases [13, 31]. This should generally be treated with glasses and/or patching prior to consideration of surgical intervention. Hyperopic glasses occasionally produce enough ocular realignment to avoid surgery. Many cases of DRS cannot be improved or do not need to be treated surgically, which is generally the preferred management in young children; however, surgical intervention is warranted in cases with a chronic face turn, manifest deviation in primary-gaze position, large up- or down-shoots, and painful or cosmetically unacceptable globe retraction. Forced ductions are almost always restricted, often severely so, making strabismus surgery technically challenging.

While some general principles apply, surgical treatment is always tailored to a specific patient (Tables 15.2, 15.3). The expectations of surgical correction must be tempered with the fact that DRS can never be entirely corrected, and the risk of adverse surgical outcomes is real. Rectus muscle resection in customary dosages can worsen the globe retraction. It is therefore not commonly performed in an attempt to restore primary-gaze alignment or improve ductions.

Most cases of type-I DRS with esotropia and ipsilateral face turn respond well to unilateral or bilateral medial rectus muscle recession. Generally, an esotropia of up to 15 prism diopters can be managed with a single medial rectus muscle recession of 6 mm or less. Larger recessions typically worsen the adduction deficit, often dramatically so, especially in the context of marked co-contraction. Large recessions also risk producing a consecutive exotropia, essentially converting a type-I into a type-II DRS, particularly if the patient has reduced saccadic velocity in adduction [46]. Selected patients with unilateral DRS will benefit from bilateral surgery, allowing a smaller medial rectus muscle recession in the DRS eye. If there is a mild limitation to abduction, the use of a posterior fixation suture on the contralateral medial rectus muscle may help to equalize ductions [58]. Bilateral DRS should be approached with caution and the surgical dose reduced; the measured strabismus in primary gaze may actually represent a secondary deviation because of bilaterally restricted abduction. Alternating up- and down-shoots in adduction are caused by lateral rectus muscle co-contraction and are treated with recession or "Y-split" of the lateral rectus muscle, depending on clinical circumstances [52].

The preferred treatment for type-II DRS is unilateral or bilateral lateral rectus muscle recessions, sometimes accompanied by recession of the medial rectus muscle if the co-contraction is severe. Surgical dosing typically needs to be greater than in type-I DRS. The A and V patterns, if present, may result from aberrant innervation of the lateral rectus muscle and therefore are improved with lateral rectus muscle recession.

Transposition surgery has been effective in managing DRS, particularly type-I cases. Full or partial tendon transposition of the vertical rectus muscles to the lateral rectus muscle insertion, with or without augmentation with posterior fixation sutures, can improve abduction by approximately 10–15° and relieve the compensatory face turn in over half of cases [18, 44, 70]; however, transposition procedures can be unpredictable. In particular, they can restrict adduction and worsen globe retraction, and cause postoperative vertical strabismus in up to 15% of cases [44]. For this reason, horizontal rectus muscle recessions are generally preferred as the initial treatment (Table 15.4).

15.1.2 Moebius Syndrome

First described by Moebius in 1888 [43], Moebius syndrome, a congenital sequence, refers to the constellation of horizontal ocular motility disorders and seventh (facial) nerve palsy [41]. Most commonly,

Table 15.2 Principles of surgical management of Duane retraction syndrome

Rectus muscle recession is the simplest and most predictable method of correcting primary gaze alignment and eliminating abnormal head posture
Avoid rectus muscle resections, unless co-contraction is negligible
Large MR recessions tend to cause adduction deficits when performed on the DRS eye and potentially convert a type-I pattern with esotropia into a type-II pattern with exotropia
Bilateral surgery is often preferred to unilateral surgery, and may improve the field of single binocular vision if used to create a balancing duction deficit in the normal eye; however, the creation of "fixation duress" can potentially worsen co-contraction and other dysinnervation symptoms
Aberrant vertical movements, including up- and down-shoots and A or V patterns, usually result from co-contraction of the lateral rectus muscle, rather than oblique muscle "overaction" or anomalous innervation of vertical rectus muscles. Oblique muscle weakening is generally not effective as an isolated treatment
More aggressive surgical management aimed at improving the field of single binocular vision has greater risk of producing unwanted and unacceptable outcomes. "Minimalist" interventions are usually preferred in children who are at risk for developing suppression and amblyopia

MR medial rectus muscle

Table 15.3 Basic surgical approach for Duane retraction syndrome

Type	Most common problems	Primary intervention	Secondary intervention
Huber I	**ET with face turn**		
	≤15 PD	Ipsilateral MR recession (up to 6 mm)	VRT with or without posterior fixation
	>15 PD	Bilateral MR recession (up to 9 mm of contralateral MR)	
	Co-contraction in adduction		
	Mild to moderate	Ipsilateral MR recession (up to 6 mm)	Ipsilateral LR recession
	Severe	Ipsilateral MR and LR recession (up to 6 mm MR, 10 mm LR)	
	Pseudo-IOOA	Ipsilateral LR recession	Ipsilateral IO weakening
	Up- or down-shoot	Ipsilateral LR recession, at least to the equator	Ipsilateral LR Y-split (recession not required)
Huber II	**XT with face turn**		
	≤15 PD	Ipsilateral LR recession (6–9 mm)	Contralateral LR recession
	>15 PD	Bilateral LR recession	
	Co-contraction in adduction		
	Mild to moderate	Ipsilateral LR recession	Ipsilateral LR recession
	Severe	Ipsilateral small MR recession and large LR recession	
	Pseudo-IOOA	Ipsilateral LR recession	Ipsilateral IO weakening
	Up- or down-shoot	Ipsilateral LR recession at least to the equator	Ipsilateral LR "Y-split" (recession not generally required)
Huber III	**Co-contraction, pseudo-IOOA, and up- or down-shoot**	Ipsilateral MR and LR recession	Ipsilateral LR Y-split
"Splits"	**Large XT with paradoxical movements**	Inactivation of ipsilateral LR	Nasal transposition and resection of vertical recti

ET esotropia, *PD* prism diopters, *MR* medial rectus muscle, *VRT* vertical rectus muscle transposition, *LR* lateral rectus muscle, *IO* inferior oblique muscle, *IOOA* inferior oblique muscle over action, *XT* exotropia

Table 15.4 Transposition surgery for type-I Duane retraction syndrome

Feature	Horizontal rectus muscle recession preferred	VRT preferred
Younger child	Yes	–
Improving binocular visual field of paramount importance	–	Yes
Previous rectus muscle recession(s) with residual face turn	–	Yes
Forced ductions positive in abduction	Yes	–
Forced ductions negative in abduction	–	Yes
Prominent co-contraction	Yes	–
Prominent up- or down-shoots	Yes	–

VRT vertical rectus muscle transposition

the presentation includes bilateral sixth cranial nerve palsy; however, the spectrum of clinical presentation can include unilateral abducens nerve palsy or a horizontal gaze palsy [23]. Most cases are sporadic; however, autosomal-dominant inheritance has been reported [76]. It is commonly associated with systemic abnormalities, including other cranial nerve palsies, limb malformations, mental retardation, and orofacial defects [19, 53].

15.1.2.1 Clinical Findings

The Moebius patient presents early in infancy with difficulty feeding, incomplete eyelid closure, and mask-like facies. Tongue hypoplasia will often secure the clinical diagnosis. In contrast to DRS, the esotropia may be large angle; however, relatively straight eyes with deficit horizontal movement is also a frequent finding. In infants with early-onset esotropia, the deviation is often 50 prism diopters or greater. Although it is important to differentiate this presentation from congenital esotropia, the associated orofacial abnormalities make the diagnosis fairly straightforward.

15.1.2.2 Management of Moebius Syndrome

The management of Moebius syndrome primarily requires careful monitoring for exposure keratitis. In addition to the facial nerve palsy, these patients can also present with fifth cranial nerve dysfunction with resultant corneal hypoesthesia or anesthesia. In some cases, tarsorrhapy is required to protect the cornea. The esotropia is generally responsive to large bilateral medial rectus muscle recessions, though this approach may further limit horizontal ductions. Lateral rectus muscle resection or transposition procedures may be required in some cases [64].

15.2 Syndromes Primarily Associated with Vertical Duction Deficits

The evaluation and management of patients with cyclovertical strabismus presents a unique challenge for the clinician. Vertical duction deficits associated with hyper- or hypotropia may be associated with a variety of unrelated conditions, including supranuclear pathology, cranial nerve palsy, extraocular muscle restriction, or periocular scarring. Clinical examination, however, will almost always yield the correct diagnosis. It is usually evident when paying close attention to duction deficits, presence and degree of vertical strabismus in different positions of gaze, assessment of restriction or extraocular muscle weakness, and occasionally other ancillary findings (Table 15.5). It is critically important to distinguish abnormalities of ocular *versions* (e.g., inferior oblique muscle "underaction"), which are assessment of relative (binocular) eye movements, from abnormalities of ocular *ductions*, which are assessment of monocular eye movements. Ductions are best assessed with the fellow eye occluded.

Table 15.5 Differential diagnosis of non-traumatic monocular upgaze deficiency

Dysthyroid orbitopathy
Brown syndrome
Superior rectus muscle palsy
Inferior rectus muscle fibrosis
Orbital adherence syndrome
Monocular elevation deficiency (both infra- and supra-nuclear)
Orbital space-occupying mass

15.2.1 Brown Syndrome

Originally described by Harold Brown, Brown's "superior oblique tendon sheath syndrome" is now known to be associated with failure of normal movement of the superior oblique tendon through the trochlea [5]. Because of the tethering of the globe's normal movement in the orbit, a characteristic constellation of findings occurs which normally makes the diagnosis straightforward. Forced ductions, which are typically performed in the operating room under general anesthesia, are unequivocally positive. The restricting superior oblique tendon causes a characteristic and usually unyielding limitation of elevation in adduction.

Brown syndrome is almost always congenital in etiology but can be inflammatory, post-traumatic, or even the presenting sign of sinus infection [6, 9, 20, 38, 54, 57, 65]. Superior oblique tendon tuck can also produce a virtually identical clinical picture, although usually not as severe and mostly self-limited [20, 22]. There is no known laterality or gender predilection, but it can occasionally be familial [48, 77]. Approximately 10% of congenital cases are bilateral [75]. Brown syndrome can be intermittent (so-called click syndrome), and approximately 10% of cases undergo spontaneous resolution [10, 73, 75].

15.2.1.1 Clinical Findings

The signature clinical finding of Brown syndrome is monocular limitation of elevation, worse in adduction and better in abduction. When versions are tested, there is a straight-line descent of the involved eye as it moves from an elevated/abducted position to an adducted position (Fig. 15.5). If elevation is compromised near primary position, there will be a compensatory chin-up head posture, often with a face turn to position the involved eye in abduction (away from the restriction). Upgaze saccades will be normal outside the restricted gaze positions.

Children with congenital Brown syndrome often present for management of torticollis, and occasionally with the complaint that the fellow eye makes excessive upward movements in abduction. It is rarely associated with ocular torsion or "overaction" of the ipsilateral superior oblique muscle (i.e., the eyes are straight in all downgaze positions). This allows easy distinction of Brown syndrome from other entities, such as inferior oblique muscle palsy, adherence syndrome, or primary over action of the superior oblique muscle, which may also be associated with some elevation deficiency in adduction. A particularly useful clinical finding is the presence of *globe proptosis* in attempted elevation (Fig. 15.6), which tends to relax the restricting superior oblique tendon [59]. This finding is often striking, and partially accounts for the widening of the palpebral fissure seen when these patients attempt to look up. Pseudo-Brown syndrome

Fig. 15.5a–c Girl with severe Brown syndrome in the right eye. Note the characteristic "straight line" descent of the right eye as the patient looks from up right gaze to up left gaze

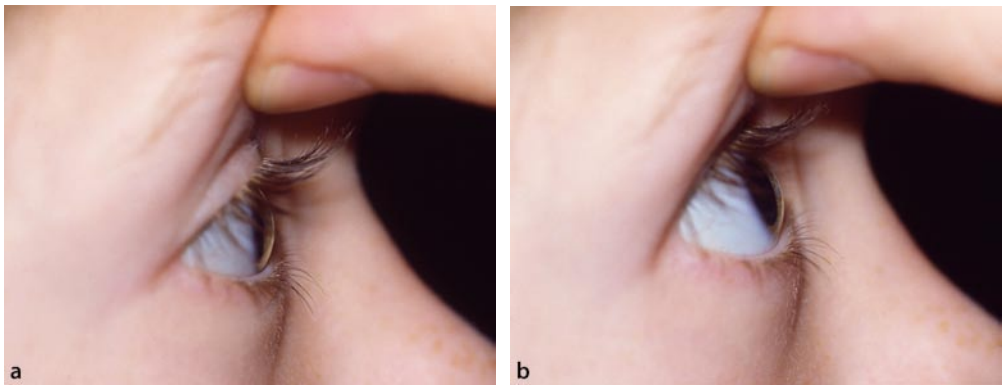

Fig. 15.6a,b Globe proptosis in attempted up gaze is common in Brown syndrome and virtually diagnostic of this condition. It is caused by the location of the trochlea anterior to the superior oblique tendon insertion. This allows greater elevation of the eye when the globe moves forward in the orbit. Similar findings were found on forced duction testing

Table 15.6 Diagnosis of Brown syndrome

Always present	Usually present	Rarely present
Limitation of elevation, worse in adduction	Primary gaze hypotropia with compensatory chin-up head posture	Superior oblique muscle "overaction"
Normal upgaze saccades away from restriction	Widening of palpebral fissure with globe proptosis on attempted elevation	Associated horizontal strabismus (except V pattern)
Positive forced ductions referable to superior oblique tendon tether	Down-shoot of globe in adduction	Pain in restricted gaze positions
Resolution of restriction with superior oblique tenotomy	V-pattern strabismus	
	Normal sensory status	

from inferior rectus muscle restriction, ocular adherence after multiple strabismus procedures, or blowout fracture of the orbit, will not exhibit this positional globe proptosis (Table 15.6).

15.2.1.2 Management of Brown Syndrome

Patients with Brown syndrome may be candidates for surgical treatment if there are important symptoms or cosmetic issues interfering with daily life and there is little prospect for spontaneous improvement. Most often, the reason for surgery is a primary-gaze hypotropia with a compensatory chin-up head posture and/or face turn. The elevation deficit, particularly in adduction, can be cosmetically objectionable and associated with diplopia; however, weakening the superior oblique muscle always carries the risk of producing an iatrogenic superior oblique muscle palsy, which can occur in up to one half of operated cases [17, 72]. In some cases, the iatrogenic postoperative strabismus can be more debilitating than the Brown Syndrome [56]. For this reason, patients without spontaneous torticollis and preserved elevation above the horizontal meridian are best left unoperated. Prophylactic weakening of the ipsilateral inferior oblique muscle at the time of superior oblique tendon tenotomy has been proposed [17, 48], but has unpredictable results. This should be reserved as a secondary procedure if symptomatic superior oblique muscle palsy develops.

Except for rare cases of acquired inflammatory Brown syndrome, which can be treated with locally injected steroids or systemic non-steroidal anti-in-

flammatory agents, the preferred treatment is surgical. This almost invariably involves lengthening of the superior oblique tendon between the trochlea and the scleral insertion. The most useful surgical procedures are tenotomy, spacer (silicone band or suture), and for some borderline cases, posterior tenectomy [71]. Alternative procedures, designed to shorten the path of the superior oblique muscle and tendon by avulsing the trochlea from the orbital wall, have also been described; however, these involve anterior orbitotomy and are not commonly performed [45].

Prior to surgery, forced ductions need to be performed carefully to confirm the clinical diagnosis. The restriction to elevation is not subtle. The tight superior oblique tendon is easily appreciated like a "knife edge" as the globe is passively moved from adduction into elevation, and then abduction. Once the superior oblique tendon is transected, forced ductions are immediately improved or normalized, which is a useful method of confirming successful tenotomy; however, repeated manipulation of the globe, forcefully moving the tendon through the trochlea, may temporarily improve ductions until after the patient is awakened from anesthesia and the Brown syndrome reappears, largely unchanged.

Most long-term successes occur in patients with some residual duction deficit post-operatively. This tends to improve with time, as does the residual "underaction" of the inferior oblique muscle. The presence of *any* post-operative hypertropia in the operated eye is a bad omen. It usually predicts the development of symptomatic superior oblique muscle palsy with inferior oblique muscle over action, positive Bielschowsky head tilt test, and compensatory torticollis. In most cases, ipsilateral inferior oblique muscle recession will resolve the problem but obviously requires a second surgery.

15.2.2 Monocular Elevation Deficiency

Monocular elevation deficiency is an uncommon strabismus disorder, which is almost always congenital, but may have a number of pathophysiologically distinct etiologies [39]. It has been described in the past as "double elevator palsy," implying that the severe elevation deficiency was necessarily caused by weakness in both the superior rectus and inferior oblique muscles. This name is actually a misnomer, since the inferior oblique muscle accounts for little of the elevation observed in normal patients, even in adduction [51]. Furthermore, inferior rectus muscle restriction, either primary or secondary, can appear clinically similar to superior rectus muscle weakness, making a more nosologically neutral term preferable. Monocular elevation deficiency should therefore be considered a clinical presentation, rather than a unique diagnosis.

15.2.2.1 Clinical Findings

Monocular elevation deficiency is typically noted during infancy, when the child is noted to adopt a chin-up head posture. In forced primary gaze, a hypotropia is present, with variable degrees of elevation deficit in attempted upgaze (Fig. 15.7). Unlike Brown syndrome, the elevation deficit is usually worse in abduction. Nonetheless, the distinction can occasionally be difficult in young children (Table 15.7).

Most, but not all, cases of monocular elevation deficiency can be explained by unilateral superior rectus muscle weakness, which can be an isolated finding or combined with ipsilateral ptosis (50%). Such cases may result from congenital abnormalities in the third cranial nerve nucleus [55]. Inferior rectus muscle restriction is usually present (70%) [61] and may suggest the alternate diagnosis of primary congenital fibrosis (see Sect. 15.2.3). While ptosis is common in both, there is not usually diagnostic confusion, since the latter diagnosis is typically bilateral, familial (autosomal dominant), and may involve multiple extraocular muscles. In addition, forced ductions tend to be less restricted in monocular elevation deficiency, and a modest elevation limitation is the rule in secondary inferior rectus muscle contracture. Occasionally, monocular elevation deficiency will be supranuclear in etiology [28], in which case a Bell's reflex may be present and clearly establishes that diagnosis.

15.2.2.2 Management of Monocular Elevation Deficiency

Treatment is often undertaken during early childhood to relieve a chin-up head posture. This almost always involves recession of the inferior rec-

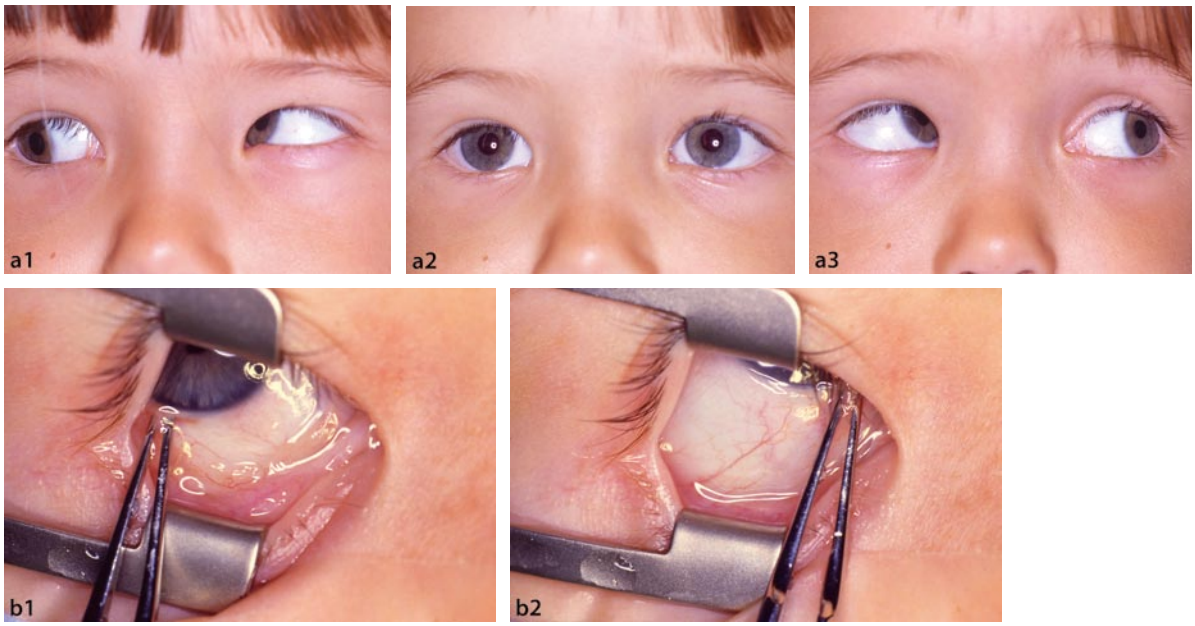

Fig. 15.7a,b A 3-year-old girl with persisting monocular elevation deficiency in the right eye after right inferior rectus muscle recession. **a** The right superior rectus muscle is paretic and the elevation deficiency is worse in right gaze. **b** At the time of repeat surgery, forced ductions revealed secondary contracture of the right inferior rectus muscle. The globe is restricted to elevation in abduction (*left*), but not in adduction (*right*)

Table 15.7 Distinguishing Brown syndrome from monocular elevation deficiency

Clinical feature	Brown syndrome	Monocular elevation deficiency
Limitation of elevation	Worse in adduction	Often worse in abduction
Primary gaze hypotropia	Usually small or absent	Small to large
V pattern with positional globe proptosis	Usually present	Absent
Slowed upgaze saccades	Absent	Usually present
Inferior rectus muscle restriction	Absent	Usually present
Ptosis	Absent	Often present

tus muscle. Even in children with evidence of slow upgaze saccades, it is usually preferable to perform inferior rectus muscle recession (typically 5–7 mm) first and reevaluate primary-gaze alignment and head posture post-operatively. Larger recessions, or even free tenotomy, will be necessary in cases of primary congenital fibrosis but may cripple downgaze or produce severe lower eyelid retraction. Vertical transposition of the medial and lateral rectus muscles can be considered as secondary procedures, if required (Fig. 15.8) [32]. When upgaze is only moderately limited, a large recession of the contralateral superior rectus muscle can cure a residual hypotropia and help symmetrize upgaze.

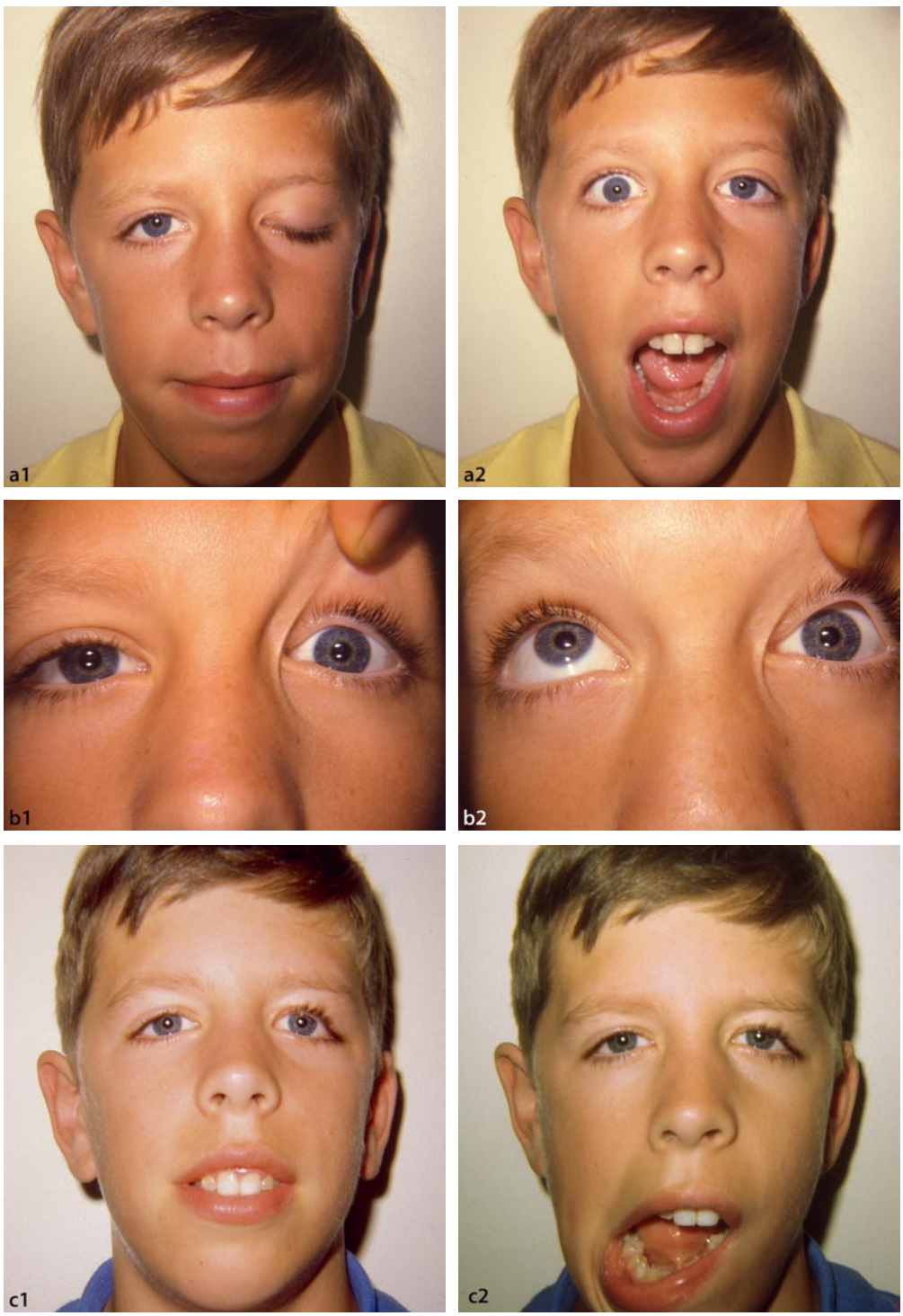

Fig. 15.8 **a** A 12-year-old boy with congenital monocular elevation deficiency, left hypotropia, left upper eyelid ptosis, and Marcus Gunn jaw wink. **b** There is marked limitation of elevation of the left eye. **c** Same patient shown 6 months after treatment with autogenous fascia lata brow suspension, inferior rectus muscle recession, and vertical transposition of the horizontal rectus muscles in the left eye (Knapp procedure)

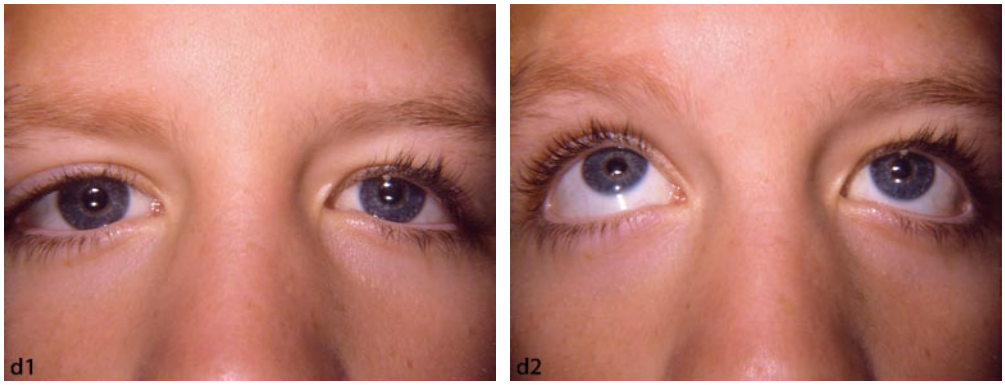

Fig. 15.8 *(continued)* **d** There is good primary gaze alignment, and elevation of the left eye is improved. Follow-up has been 25 years without recurrence of the ptosis or hypotropia

15.2.3 Congenital Fibrosis Syndrome

Considered to be a primary dysinnervation syndrome, congenital fibrosis of the extraocular muscles (CFEOM) is characterized by fibrous replacement of extraocular muscle and Tenon's capsule resulting in moderate-to-severe limitation of ductions. There is almost always associated strabismus. The clinical presentation depends on the specific muscle involvement. The underlying disorder in CFEOM is believed to be primary dysinnervation of the oculomotor and/or trochlear nerves [16]. The histopathological finding of fibrous replacement of the extraocular muscles is thought to be a secondary effect. It has been suggested that the different phenotypes are manifestations of different congenital anomalies of innervation.

15.2.3.1 Clinical Findings

The syndrome has been previously described as the congenital presentation of limitation in elevation or depression, limitation in horizontal movement, eyes fixed in a depressed position, and associated ptosis and chin elevation (Fig. 15.9) [36]. The CFEOM may present sporadically, but three phenotypes have been described [15, 67]. The CFEOM 1 is the most common and presents with bilateral ptosis, eyes fixed in a depressed position, and variable horizontal duction deficits. This phenotype follows an autosomal-dominant inheritance pattern. The CFEOM 2 is inherited in an autosomal-recessive pattern and presents with bilateral ptosis and a large-angle exotropia, with associated vertical duction deficits. The CFEOM 3 has a more variable presentation and can present with unilateral disease. It is inherited in an autosomal-dominant pattern.

15.2.3.2 Management of Congenital Fibrosis

The primary goal in these patients is to correct chin-up head posture, manage any associated amblyopia, and keep the visual axes clear. There is little hope of curing the strabismus. Extraocular muscle surgery is technically difficult and can challenge the abilities of even a seasoned strabismus surgeon. Very large recessions or even free tenotomy of the inferior rectus muscles can be required [78]; however, realigning the eyes behind ptotic eyelids may actually worsen the patient's disability. Ptosis repair is usually required, but is potentially hazardous due to corneal exposure, since ocular motility is limited and there is no Bell's reflex. For this reason, the upper eyelid should be elevated only to the upper pupillary border. Overall, these patients are quite difficult to manage, and careful discussion with the parents of the inherent limitations of surgical treatment is essential.

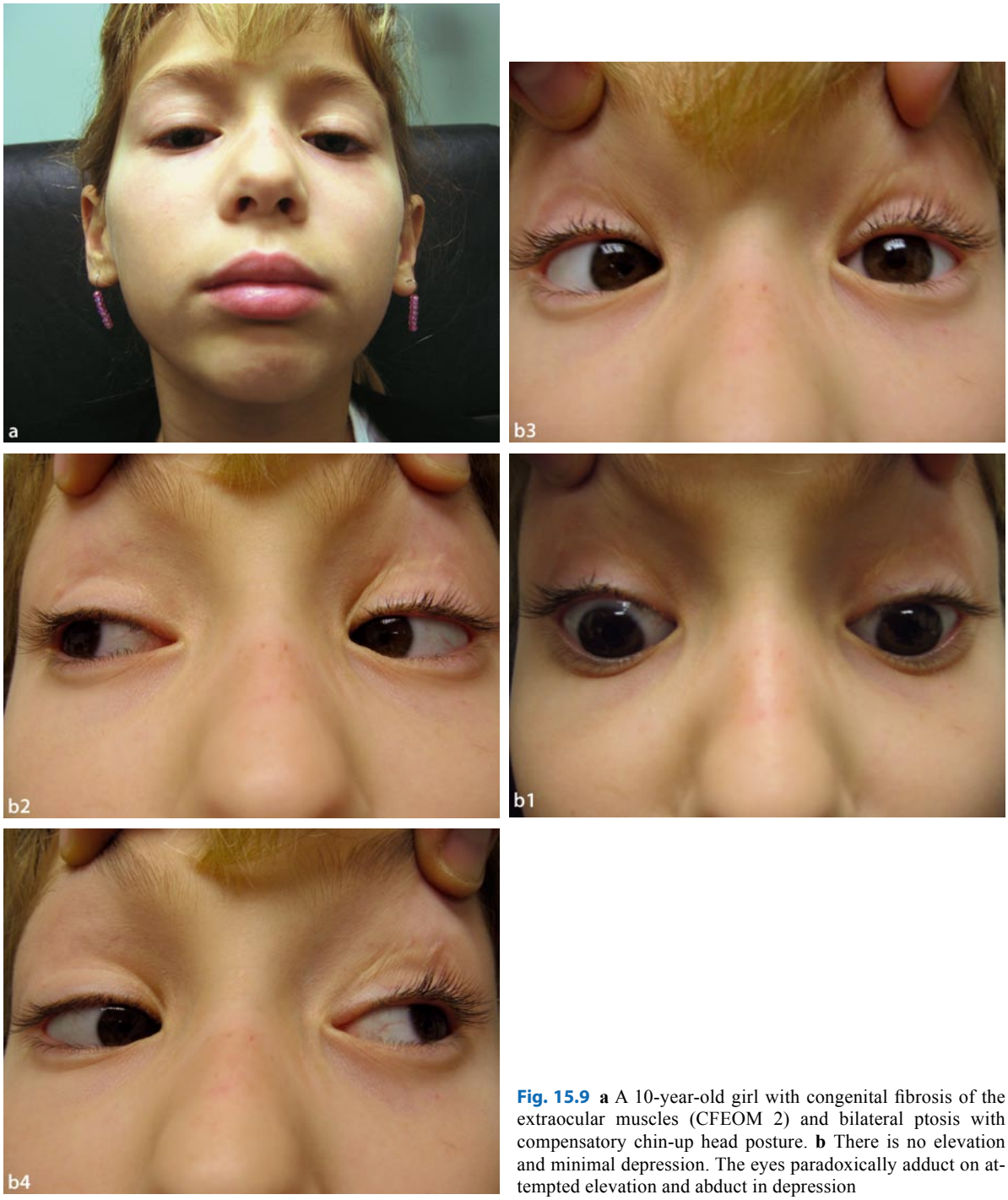

Fig. 15.9 **a** A 10-year-old girl with congenital fibrosis of the extraocular muscles (CFEOM 2) and bilateral ptosis with compensatory chin-up head posture. **b** There is no elevation and minimal depression. The eyes paradoxically adduct on attempted elevation and abduct in depression

15.2.4 Ocular Adherence Syndrome

First described by Johnson [29], the diagnosis of ocular adherence syndrome encompasses a range of restrictive strabismus entities related to abnormal connections among and between the extraocular muscles and the surrounding orbital tissue.

15.2.4.1 Clinical Findings

The classic *fat adherence syndrome*, described by Parks as a complication of inferior oblique muscle myectomy, is an acquired restriction following violation of posterior Tenon's capsule [47]. Prolapsed orbital fat induces inflammation and fibrosis, and causes adhesions to the sclera and extraocular muscles. This results in a restrictive hypotropia, typically worse in adduction, and positive forced duction testing (Fig. 15.10); however, manipulation of the

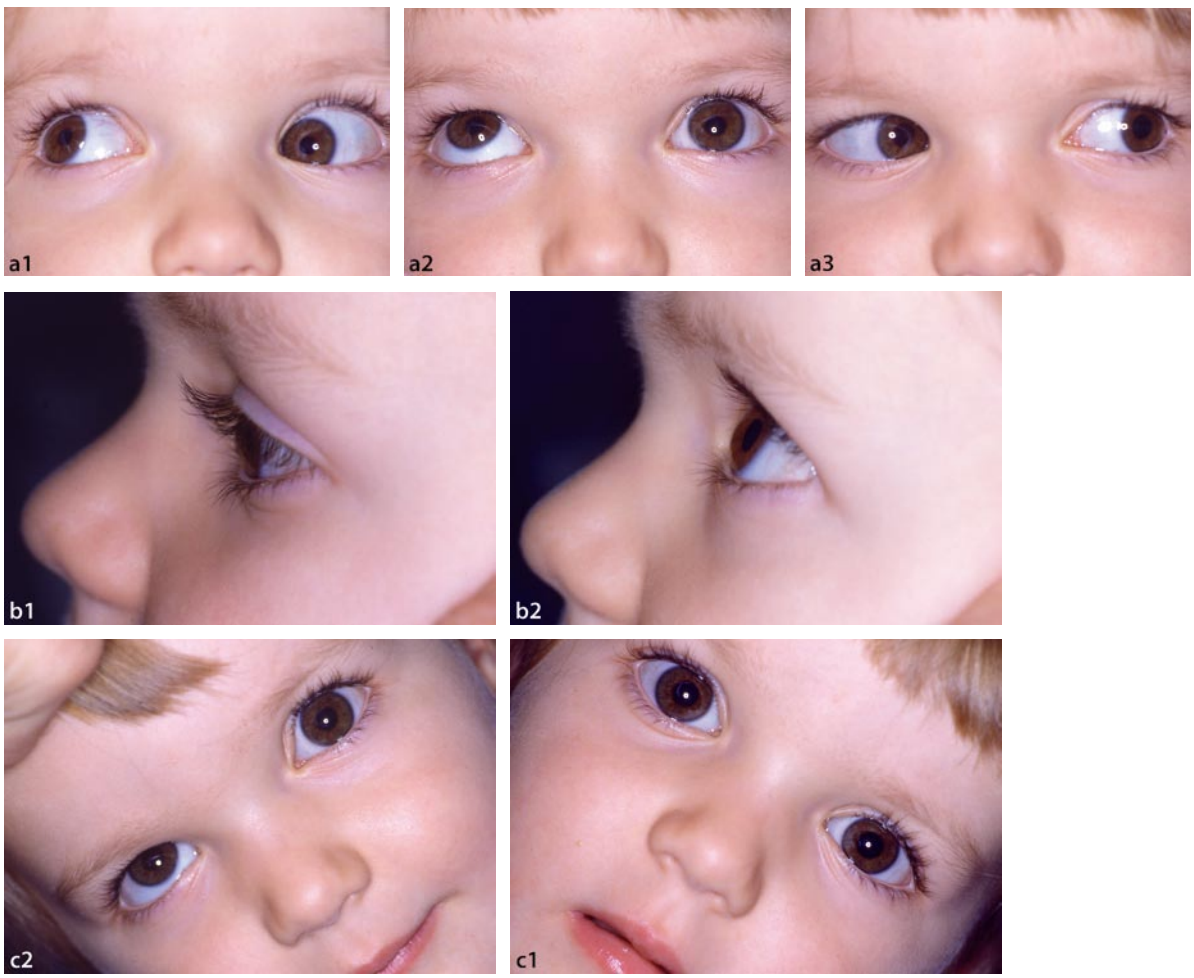

Fig. 15.10 **a** A 2-year-old girl with an unanticipated right hypertropia following inferior oblique myectomy in the left eye for congenital left superior oblique muscle palsy. There is now a 30-prism-diopter left hypotropia in primary gaze and a larger secondary deviation (right hypertropia) when fixating with the left eye. Note the marked limitation of elevation of the left eye, worse in adduction (pseudo-Brown syndrome). **b** There is no globe proptosis on attempted elevation of the left eye. **c** The Bielschowsky head tilt test shows increased right hypertropia on right head tilt, which is an artifact of surgical overcorrection (i.e., does not indicate the presence of a right superior oblique muscle palsy [80])

globe does not reveal the unyielding superior oblique tendon found in Brown syndrome, nor does one see proptosis in attempted elevation.

Adherence syndrome has been observed following strabismus surgery on other extraocular muscles, as well as following retinal surgery and periorbital trauma. Kushner has described specific characteristics of the *inferior oblique muscle adherence syndrome*, which typically presents with a restrictive hypotropia similar to fat adherence syndrome; however, the abnormalities of ocular motility can be traced to incarceration or scarring of the inferior oblique muscle to, or near, the inferior rectus muscle following inferior rectus surgery or scleral buckling [35].

15.2.4.2 Management of Ocular Adherence Syndrome

The best management of adherence syndrome is prevention. Careful surgical technique to limit the posterior dissection of the muscle sleeve and avoid penetration into Tenon's capsule will significantly reduce the incidence of adherence syndrome. When it does occur, surgical management primarily involves meticulous removal of the fat adherence and, if possible, closure and reinforcement of the defect in Tenon's capsule. In addition to release of adherent tissues, successful treatment of the strabismus almost always requires surgery on additional extraocular muscles (Fig. 15.11).

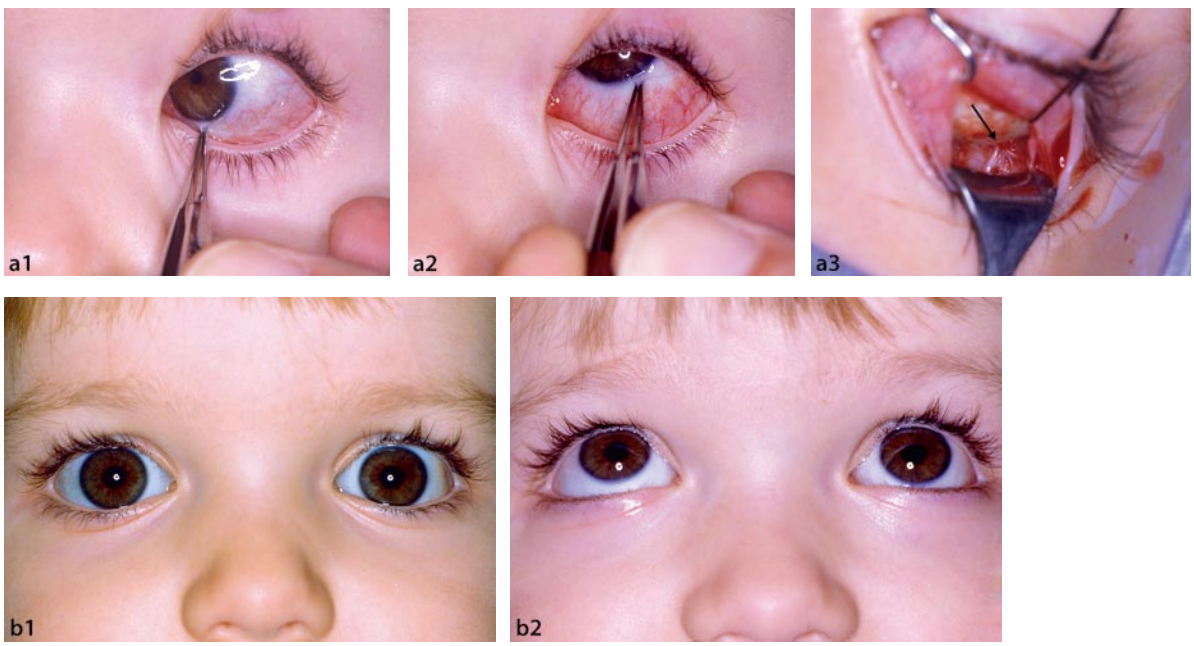

Fig. 15.11 Same patient as Fig. 15.10 **a** At the time of surgery, forced ductions localized the restriction to the inferior orbit. Surgical exploration revealed adherence of Tenon's fascia to the globe at the site of the previous myectomy (*arrow*). **b** Seven months post-operatively, freeing of adhesion in the left eye and a large recession of the right superior rectus muscle has resulted in good primary gaze alignment and improved elevation of the left eye

Take Home Pearls for Horizontal Strabismus Syndromes

- Congenital strabismus in which limitations of adduction or abduction are substantial, but the primary gaze deviation small, suggests the diagnosis of DRS.
- Globe retraction in adduction may or may not be observable in infancy.
- In type-I DRS abduction is usually better when the eye is elevated or depressed.
- Surgical treatment is most often indicated to correct primary-gaze strabismus, which causes the abnormal head posture in DRS.
- Most DRS patients can successfully be treated with recession of one or two horizontal rectus muscles.
- Transposition surgery can yield improved ductions and field of single binocular vision in DRS, but increases the complexity, morbidity, and surgical risk.
- Bilateral type-I DRS should be managed with reduced surgical dosage.
- Moebius syndrome is easily recognized by the associated facial palsy.

Take Home Pearls for Vertical Strabismus Syndromes

- Brown syndrome is almost always caused by abnormal movement of the superior oblique tendon through the trochlea.
- Clinical examination for Brown syndrome is usually diagnostic, with an elevation deficiency that worsens from abduction to adduction. Because the condition is restrictive, upgaze saccades will be normal when tested where the globe can move freely.
- Positional globe proptosis is a common associated finding in Brown syndrome and does not occur in superior rectus muscle palsy or inferior rectus muscle restriction.
- Many patients with acquired Brown syndrome and a few with congenital Brown syndrome will spontaneously improve.
- Monocular elevation deficiency can often be managed initially with inferior rectus muscle recession.
- Congenital fibrosis syndrome is difficult to treat surgically. Because of limited globe motility, ptosis repair creates a risk of exposure keratopathy.
- The surgical management of ocular adherence syndrome usually requires release of the adherence *and* intervention on non-involved muscles.

References

1. Akman A, Dayanir V, Sener EC, Sanac AS (1996) Acquired Duane's retraction syndrome. J Pediatr Ophthalmol Strabismus 33:267–269
2. Al-Baradie R, Yamada K, St. Hillaire C et al. (2002) Duane radial ray syndrome (Okihiro syndrome) maps to 20q13 and results from mutations in SALL4, a new member of the SAL family. Am J Hum Genet 71:1195–1199
3. Appukuttan B, Gillanders E, Juo SH et al. (1999) Localization of a gene for Duane retraction syndrome to chromosome 2q31. Am J Hum Genet 65:1639–1646
4. Breinin GM (1957) Electromyography: a tool in ocular and neurologic diagnosis. II. Muscle palsies. Arch Ophthalmol 57:165–167

5. Brown HW (1950) Congenital structural muscle anomalies. In Allen JH (ed) Symposium on strabismus. Trans New Orleans Acad Ophthalmol Mosby Year-Book, St. Louis, pp 205–236
6. Brown HW (1973) True and simulated superior oblique tendon sheath syndrome. Doc Ophthalmol 34:123–136
7. Calabrese G, Telvi L, Capodiferro F et al. (2000) Narrowing the Duane syndrome critical region at chromosome 8q13 down to 40kb. Eur J Hum Genet 8:319–324
8. Chung M, Stout JT, Borchet MS (2000) Clinical diversity of hereditary abnormalities in Duane's retraction syndrome. Ophthalmology 107(3):500–503
9. Clark E (1966) A Case of apparent intermittent overaction of the left superior oblique. Br Orthopt J 23:116–117
10. Costenbader FD, Albert DG (1958) Spontaneous regression of pseudoparalysis of the inferior oblique muscle. Arch Ophthalmol 59:607–608
11. Cross HE, Pfaffenbach DD (1972) Duane retraction syndrome and associated congenital malformations. Am J Ophthalmol 73:442–450
12. Denis D, Dauletbekov D, Girard N (2008) Duane retraction syndrome: type II with severe abducens nerve hypoplasia on magnetic resonance imaging. J AAPOS 12:91–93
13. DeRespinis PA, Caputo AR, Wagner RS et al. (1993) Duane's retraction syndrome. Surv Ophthalmol 38:257–288
14. Duane A (1905) Congenital deficiency of abduction, associated with impairment of adduction, retraction movements, contraction of the palpebral fissure and oblique movements of the eye. Arch Ophthalmol 34:133–159
15. Engle EC (2002) The molecular basis of the congenital fibrosis syndromes. Strabismus 10:125–128
16. Engle EC, Goumnerov BC, McKeown CA et al. (1997) Oculomotor nerve and muscle abnormalities in congenital fibrosis of the extraocular muscles. Ann Neurol 41:314–325
17. Eustis HS, O'Reilly C, Crawford JS (1987) Management of superior oblique palsy after surgery for true Brown's syndrome. J Pediatr Ophthalmol Strabismus 24:10–17
18. Foster RS (1997) Vertical muscle transposition augmented with lateral fixation. J AAPOS 1:20–30
19. Ghabrial R, Versace P, Kourt G et al. (1998) Mobius' syndrome: features and etiology. J Pediatr Ophthalmol Strabismus 35:304–311
20. Girard LJ (1956) Pseudoparalysis of the inferior oblique muscle. South Med J 49:342–349
21. Hedera P, Friedland RP (1993) Duane syndrome with giant aneurysm of the vertebral basilar arterial junction. J Clin Neuro Ophthalmol 13:271–274
22. Helveston EM, Ellis FD (1983) Superior oblique tuck for superior oblique palsy. Aust J Ophthalmol 11:215–220
23. Henderson JL (1939) The congenital facial diplegia syndrome: clinical features, pathology, and aetiology. Brain 62:381–403
24. Heuck G (1879) Uber angeborenen vererbten Beweglichkeitsdefect der Augen. Klin Monatsbl Augenheilkd 17:253
25. Hotchkiss MG, Muller NR, Clark AW et al. (1980) Bilateral Duane's retraction syndrome. A clinical–pathologic case report. Arch Ophthalmol 98:870–874
26. Huber A (1974) Electrophysiology of the retraction syndromes. Br J Ophthalmol 58:293–300
27. Isenberg S, Urist MJ (1977) Clinical observations in 101 consecutive patients with Duane's retraction syndrome. Am J Ophthalmol 84:419–425
28. Jampel RS, Fells P (1968) Monocular elevation paresis caused by a central nervous system lesion. Arch Ophthalmol 80:45–57
29. Johnson LV (1950) Adherence syndrome: pseudoparalysis of the lateral or superior rectus muscle. Arch Ophthalmol 44:870–878
30. Khan AO, Oystreck D (2006) Clinical Characteristics of Bilateral Duane Syndrome. J AAPOS 10:198–201
31. Kirkham TH (1970) Anisometropia and amblyopia in Duane's syndrome. Am J Ophthalmol 69:774–777
32. Knapp P (1969) The surgical treatment of double elevator paralysis. Trans Am Ophthalmol Soc 67:304–323
33. Kraft SP (1988) A surgical approach for Duane syndrome. J Pediatr Ophthalmol Strabismus 25:119–129
34. Kraft SP (1993) Surgery for Duane syndrome. Am Orthop J 43:18–26
35. Kushner BJ (2007) The Inferior oblique muscle adherence syndrome. Arch Ophthalmol 125:1510–1514
36. Laughlin RC (1956) Congenital fibrosis of the extraocular muscles: a report of six cases. Am J Ophthalmol 41:432–438
37. Lueder GT (2002) Anomalous orbital structures resulting in unusual strabismus. Surv Ophthalmol 47(1):27–35
38. Mein J (1971) Superior oblique tendon sheath syndrome. Br Orthopt J 28:70–76
39. Metz HS (1979) Double elevator palsy. Arch Ophthalmol 97:901–903
40. Miller M, Stromland K (1991) Ocular motility in thalidomide embryopathy. J Pediatr Ophthalmol Strabismus 28:47–51
41. Miller MT, Stromland K (1999) The Mobius sequence: a relook. J AAPOS 3:199–208
42. Miller NR, Kiel SM, Green WR et al. (1982) Unilateral Duane's retraction syndrome type 1. Arch Ophthalmol 100:1468–1472
43. Moebius PJ (1888) Über angeborene doppelseitige Abducens–Facialis–Lähmung. Münch Med Wochenschr 35:91–94
44. Molarte AB, Rosenbaum AL (1990) Vertical rectus muscle transposition surgery for Duane syndrome. J Pediatr Ophthalmol Strabismus 27:171–177
45. Mombaerts I, Koornneef L, Everhard-Halm YS et al. (1995) Superior oblique luxation and trochlear luxation as new concepts in superior oblique muscle weakening surgery. Am J Ophthalmol 120:83–91
46. Nelson LB (1986) Severe adduction deficiency following a large medial rectus recession in Duane's retraction syndrome. Arch Ophthalmol 104:859–862
47. Parks MM (1972) The weakening surgical procedures for eliminating overaction of the inferior oblique muscle. Am J Ophthalmol 73:107–122
48. Parks MM, Eustis HS (1987) Simultaneous superior oblique tenectomy and inferior oblique recession in Brown's syndrome. Ophthalmology 94:1043–1048

49. Pfaffenbach DD, Cross HE, Kerans TP (1972) Congenital anomalies in Duane's retraction syndrome. Arch Ophthalmol 88:635–639
50. Raab EL (1986) Clinical features of Duane's syndrome. J Pediatr Ophthalmol 23(2):64–68
51. Robinson DA (1975) A quantitative analysis of extraocular muscle cooperation and squint. Invest Ophthalmol 14:801–825
52. Rogers GL, Bremer DL (1984) Surgical treatment of the upshoot and downshoot in Duane's retraction syndrome. Ophthalmology 91(11):1380–1383
53. Rogers GL, Hatch GF, Gray I (1977) Mobius syndrome and limb abnormalities. J Pediatr Ophthalmol Strabismus 14:134–138
54. Roper-Hall MJ, Roper-Hall G (1971) The superior oblique "click" syndrome in Orthoptics. Proc Second International Orthoptic Congress, Amsterdam 11–13 May 1971. Excerpta Medica, Amsterdam, pp 360–366
55. Rosner S (1963) Double elevator paralysis. Am J Ophthalmol 55:87–93
56. Santiago AP, Rosenbaum AL (1997) Grave complications after superior oblique tenotomy or tenectomy for Brown syndrome. JAAPOS 1:8–15
57. Saunders RA, Stratas BA, Gordon RA et al. (1990) Acute-onset Brown's syndrome associated with pansinusitis. Arch Ophthalmol 108:58–60
58. Saunders RA, Wilson ME, Bluestein EC et al. (1994) Surgery on the normal eye in Duane retraction syndrome. J Pediatr Ophthalmol Strabismus 31:162–169
59. Scott AB (1976) The superior oblique tendon sheath syndrome: differential diagnosis of deficient elevation in adduction. In: Moore S, Nein J, Stockbridge L (eds) Orthoptics: past, present, and future. Statton, New York, pp 463–485
60. Scott AB, Wong GY (1972) Duane's syndrome. An electromyographic study. Arch Ophthalmol 87:140–142
61. Scott WE, Jackson OB (1977) Double elevator palsy: the significance of inferior rectus restriction. Am Orthopt J 27:5–10
62. Shainberg MJ (2000) Duane syndrome. Am Orthop J 50:30–35
63. Shauley Y, Weissman A, Meyer E (1993) Ocular and systemic characteristics of Duane syndrome. J Pediatr Ophthalmol Strabismus 30:178–183
64. Spierer A, Barak A (2000) Strabismus surgery in children with Mobius syndrome. J AAPOS 4:58–59
65. Stein R (1965) Posttraumatic intermittent pseudoparesis of the inferior oblique: remarks to the superior oblique tendon sheath syndrome. Klin Monatsbl Augenheilkd 147:712–720
66. Stilling J (1887) Untersuchungen über die Entstehung der Kurzsichtigkeit. Bergman, Wiesbaden, Germany, 1887:13
67. Traboulsi EL (2004) Congenital abnormalities of cranial nerve development: overview, molecular mechanisms, and further evidence of heterogeneity and complexity of syndromes with congenital limitation of eye movements. Trans Am Ophthalmol Soc 102:373–389
68. Tredici TD, Noorden GK von (1985) Are anisometropia and amblyopia common in Duane's syndrome? J Pediatr Ophthalmol Strabismus 22:23–25
69. Turk S (1899) Bemerkungen zu einem Falle von Retraction des Auges. Centralbl Pract Augenheilkd 23:14
70. Velez FG, Foster RS, Rosenbaum AL (2001) Vertical rectus muscle augmented transposition in Duane syndrome. J AAPOS 5:105–113
71. Velez FG, Velez G, Thacker N (2006) Superior oblique posterior tenectomy in patients with Brown syndrome with small deviations in the primary position. JAAPOS 10:214–219
72. Noorden GK von, Olivier P (1982) Superior oblique tenectomy in Brown's syndrome. Ophthalmology 89:303–309
73. Waddell E (1982) Brown's syndrome revisited. Br Orthopt J 39:17–21
74. Weinacht S, Huber A, Gottlob I (1996) Vertical Duane's retraction syndrome. Am J Ophthalmol 122:447–449
75. Wilson ME, Eustis HS, Parks MM (1989) Brown's syndrome. Surv Ophthalmol 34:153–172
76. Wishnick MM, Nelson LB, Huppert L et al. (1983) Moebius syndrome and limb abnormalities with dominant inheritance. Ophthalmic Pediatr Gen 2:77–81
77. Wortham E, Crawford JS (1988) Brown's syndrome in twins. Am J Ophthalmol 105:562–563
78. Yazdani A, Traboulsi EL (2004) Classification and management of patients with congenital fibrosis of the extraocular muscles. Ophthalmology 111:1035–1042
79. Alexandrakis G, Saunders RA (2001) Duane retraction syndrome. Ophthalmol Clin North Am 14(3):407–417
80. Saunders RA, Roberts EL (1995) Abnormal head posture in patients with fourth cranial nerve palsy. Am Orthop J 45:24–33

Adjustable Sutures in Strabismus Surgery

16

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Contents

Core Messages

- Adjustable sutures provide a second chance to improve the outcome of first surgery.
- Adjustable sutures may reduce the need for reoperations but add to the time and complexity of surgery.
- Ideal candidates are patients in whom the standard strabismus dosages may not apply.
- Adjustable sutures make intellectual sense, but solid data of the advantage are lacking.

16.1 Introduction

Strabismus surgery is by no means an exact science. The outcome of surgery depends partly on measurements, partly on the experience and intuition of the surgeon, and very much on the healing capacity and fusion status of the patient. The goal of surgery is to align the eyes with fewest procedures; however, the surgeon may encounter surprises when the patient recovers from surgery. The same amount of surgery for the same angle of deviation will yield different results in different patients, often for no obvious reason. This is especially true for long-standing complicated strabismus, reoperations, innervational abnor-

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malities, restrictive myopathies, or following injuries to the eye.

A search for improved accuracy in strabismus surgery led to an approach which allowed adjustment during the early postoperative period. Adjustable suture strabismus surgery was first described by Claude Worth in 1908 [8]; however, the first modern account of adjustable suture surgery was presented by Jampolsky in 1975 [13, 14]. He described a two-stage adjustable suture technique with surgery under general anesthesia and adjustment of the ocular position under local anesthesia on the morning after surgery or on the same day after 4–8 h, when the patient was fully alert.

The basic principle of the adjustable suture technique is to secure the extraocular muscle to the sclera using a temporary or sliding knot. After the patient has recovered from anesthesia, the alignment of the eyes is checked. The length of suture between the attachment site and muscle may be shortened or lengthened to fine-tune the alignment in an awake patient. The adjustments are usually performed within 24 h of the primary surgery. The goal of this extra step is to decrease the need for reoperation.

A number of surgeons have used adjustable sutures in adults to improve immediate postoperative alignment. They have described their experiences with adjustable sutures [3, 17, 22, 26, 30, 31, 32,], but there have been no prospective randomized controlled trials that directly compare non-adjustable with adjustable sutures for strabismus surgery in adults [29]. There are very few reports on the use of adjustable suture surgery in children [5, 6, 10, 27]. This is most likely because of the difficulty obtaining the cooperation of a child for postsurgical manipulations.

In this chapter, we describe current approaches to adjustable suture surgery, with an emphasis on our preferred techniques.

16.2 Indications

The ideal candidates for adjustable suture strabismus surgery are patients in whom the standard strabismus surgical dosages may not apply (Table 16.1). Patients with combined horizontal, vertical, and torsional deviations are also thought to benefit from the adjustable suture technique. Adjustable sutures are particularly useful when the aim of surgery is to regain binocular single vision and when the patient has a risk of postoperative diplopia. In these cases the ability to adjust after surgery provides reassurance to the patient.

Table 16.1 Standard indications for adjustable suture strabismus surgery

Restrictive strabismus (thyroid ophthalmopathy, scleral buckle, or anesthetic myotoxicity)
Previous trauma or surgery
Slipped, lost, or disinserted muscles
Incomitant deviations (Duane syndrome, myasthenia gravis, or paralytic strabismus)
Any long-standing complex strabismus

It is our practice to use adjustable sutures on all muscles of all adults, even those with comitant strabismus and no prior surgery. We also use adjustable sutures in selected children who meet the standard indications mentioned in Table 16.1.

16.3 Patient Selection

The adjustment procedure can cause some discomfort and can evoke substantial anxiety in patients; therefore, patient selection is crucial if the suture adjustment is to be performed without sedation. Most surgeons recommend the technique in children older than 12 years; however, we have found that it can be performed in cooperative children as young as 5 years. Dawson and co-authors found that the supervised, active participation of a parent or caretaker was a key feature in the success of completing the adjustment [5].

Many surgeons perform the "Q-tip" test to identify patients who will be suitable for the adjustment procedure. This test consists of touching a cotton swab or twirled tissue end to the medial and/or lateral aspect of the unanesthetized bulbar conjunctiva. If the patient is able to tolerate manipulation of the bulbar conjunctiva, then he or she should do well with the adjustment procedure. If the patient fails the Q-tip test, then it may be best to either perform non-adjustable surgery or to arrange for backup sedation.

In young children, the use of the adjustable suture technique may require two stages of anesthesia. The surgery is carried out, the child is assessed when fully awake, and then more sedation is given, if required, to allow the suture to be adjusted.

The adjustable suture technique can be used with either a recessed or a resected rectus muscle. Adjustable suture surgery has also been successfully performed on the superior oblique tendon [9].

16.4 Anesthetic and Analgesic Considerations

The choice of anesthesia is important if the suture adjustment is to be performed on the day of strabismus surgery. There are three key anesthetic considerations in adjustable suture surgery: (1) recovery of extraocular muscle function in time for assessment and adjustment; (2) patient comfort, alertness, and cooperation for postoperative motility assessment; and (3) sedation protocol for suture adjustment in patients unable to cooperate for adjustment.

16.4.1 Recovery of Extraocular Muscle Function

For general anesthesia patients, extraocular muscle function recovers to normal by the time the patient has recovered sufficient alertness for postoperative assessment. When local anesthesia is used, long-acting local anesthetics, such as bupivacaine, should also be avoided due to the lasting effect on extraocular muscle function. When shorter-acting local anesthetics, such as lidocaine, are used, a minimum of 5 h is required for motility to recover.

16.4.2 Patient Comfort, Alertness, and Cooperation for Postoperative Motility Assessment

16.4.2.1 Premedication

One of the most commonly reported side effects of strabismus surgery is postoperative nausea and vomiting (PONV). Some studies have reported the incidence to be two times greater in children than adults, ranging from 48 to 85% [11, 23]. It is imperative that the anesthesiologist attempt to minimize this risk to facilitate the postoperative eye examination and suture adjustment and to reduce the risk of aspiration and patient discomfort. Factors that influence PONV include the preoperative anxiety of the patient, anesthetic agents administered, and the use of opioids. Anesthesiologists can reduce the risk of PONV by avoiding emetogenic agents such as volatile anesthetics, nitrous oxide, opioids, etomidate, ketamine, and acetylcholinesterase inhibitors, and by administering anticholinergics, anxiolytics, and antiemetics.

16.4.2.2 Induction and Maintenance

Induction with intravenous propofol is recommended [4, 33]. Maintenance of anesthesia should preferably be maintained with short-acting intravenous agents, such as propofol or dexmedetomidine, because volatile anesthetics, such as halothane, isoflurane, and sevoflurane, may prolong emergence and/or cause emergence agitation and delirium [4, 33].

Muscle relaxants are not necessary during surgery, but they may facilitate the strabismus correction itself by making it easier for the surgeon to manipulate the extraocular muscles. If a muscle relaxant is used, a short-acting agent, such as mivacurium, which is rapidly metabolized by endogenous plasma cholinesterases and therefore does not require reversal agents, is recommended [33]. Longer-acting muscle relaxants may have residual neuromuscular blockade effects on the patient without the administration of reversal agents thereby delaying postoperative examination. The use of longer-acting muscle relaxants require reversal with acetylcholinesterase inhibitors and anticholinergics, which may also increase the incidence of PONV [11].

16.4.2.3 Analgesia

Analgesia for strabismus surgery has presented anesthesiologists and ophthalmologists with several dilemmas. These patients clearly require analgesia both intraoperatively and postoperatively, but many opioid analgesics cause sedation, which makes accurate postoperative examination nearly impossible. In addition, narcotics such as morphine increase the

incidence of PONV [11, 19, 24]. The administration of short-acting local anesthetics, such as topical tetracaine prior to emergence from anesthesia, may provide adequate analgesia without any associated side effects of narcotics [1]. Long-acting local anesthetics should be avoided, as noted above. If a parenteral opioid must be used, we recommend remifentanil, alfentanil, or fentanyl, which have a rapid onset and are short-acting. In patients with normal renal function, our preference is to use intraoperative ketorolac, which minimizes postoperative pain without concomitant sedation or PONV [19]. Ketorolac is probably most effective if given at the start of the procedure, but if there is concern about increased intraoperative bleeding, it may be given 30 min prior to the end of the surgery. For patients who will not require additional anesthesia for the suture adjustment, oral or rectal analgesics, such as acetaminophen in conjunction with an enteral opioid such as oxycodone, improve pain with less sedation and/or PONV than intravenous opioids [24].

Some anesthesiologists recommend using 65% nitrous oxide, although it can contribute to PONV, along with other intravenous anesthetics for maintenance of anesthesia during strabismus correction to reduce the use of other anesthetic agents that may prolong emergence [4, 11]. Anticholinergics administered preoperatively or at the time of induction, such as scopolamine, glycopyrrolate, or atropine, may provide several benefits both intraoperatively and postoperatively [12, 23]. They delay gastric discharge minimizing secretions, and may prevent the oculocardiac reflex. More importantly, administration of anticholinergics may decrease the incidence of PONV due to their antimuscarinic actions. High doses of anticholinergic agents may cause undesirable side effects, such as blurred vision, restlessness, and hallucinations. Benzodiazepines, such as diazepam, lorazepam, and midazolam also have many beneficial effects on the patient undergoing strabismus correction [4, 23]. They may not only decrease anxiety helping to facilitate either the insertion of peripheral venous catheters or the mask induction of anesthesia, but they may reduce the incidence of PONV as well. Benzodiazepines should be administered judiciously, because high doses may also cause undesirable sedation postoperatively.

16.4.2.4 Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) is a major problem in some patients. Ondansetron, a 5-HT3 antagonist, is a very effective antiemetic with very few side effects, and therefore it should be given prophylactically to prevent PONV [25]. Additional antiemetics should also be considered for use both prophylactically and for symptomatic treatment of PONV [11]. For example, dexamethasone, a potent synthetic glucocorticoid, may augment the antiemetic effects of ondansetron. Metoclopramide, a dopamine agonist and prokinetic, can also be used as an antiemetic after strabismus surgery, but in high doses it may cause extrapyramidal side effects including oculogyric crisis. Hydroxyzine, an antihistamine, may also provide relief of both perioperative anxiety and PONV, and therefore may also be considered during the perioperative period.

16.4.3 Sedation Protocol for Suture Adjustment

For patients, mainly children, who will be unable to remain still during the suture adjustment, the anesthesiologist should be notified in advance of the possible need to provide additional anesthesia. These patients should be in a monitored setting such as the postanesthesia care unit or operating room. A quiet location, such as an isolation room or procedure room, away from the noise and bustle of a recovery room may help calm the patient and provide needed privacy. The recommended ASA standards for basic anesthetic monitoring and airway management should be strictly adhered to for patient safety regardless of the adjustment location.

Short-acting intravenous anesthetics that facilitate rapid emergence with minimal side effects, such as propofol, should be used. Often a full induction dose of propofol (1−3 mg/kg) is required to allow insertion of the eyelid speculum and manipulation of the adjustable sutures. Topical anesthesia with proparacaine or tetracaine is an important adjunct [1].

As with any general anesthetic administration, the anesthesiologist should remain at the bedside until emergence.

16.5 Surgical Technique

The surgery is performed under general or local anesthesia per surgeon preference. The adjustment is performed when the patient is fully awake or after the local anesthetic has worn off and the function of the muscle has returned to normal.

16.5.1 Limbal vs Fornix Approach

The limbal approach provides broad exposure during the surgery and suture adjustment. This approach requires conjunctival closure, as it is difficult to cover the suture knot with the conjunctiva after the adjustment.

The fornix approach includes a hidden incision underneath the eyelid with less scarring, thus producing excellent cosmetic results in most cases. Exposure is limited, which may increase the technical difficulty of surgery and suture adjustment. The fornix approach is more comfortable for the patient, as the sutures are covered. In some cases, no conjunctival closure is required.

16.5.2 Technique

There are two main methods for muscle reattachment:

1. Bow-tie technique (Fig. 16.1a). The sutures are passed through scleral tunnels and they are tied together in a single loop bow tie as with a shoelace. At adjustment, the bow is untied, the muscle position adjusted, and the bow retied. Once the desired alignment is obtained, the bow is cut and converted to a square knot.
2. Cinch or sliding-noose technique (Fig. 16.1b). The sutures are passed through scleral tunnels emerging less than 1 mm apart. A noose is created by tying a separate piece of suture around the scleral sutures. The ends of the noose suture are tied together to provide a bucket handle for manipulation of the noose during adjustment.

The surgeon has the option of adjusting the sutures intraoperatively, or postoperatively from 1 h to 1 week after surgery. Intraoperative adjustment allows for immediate correction of a major postoperative misalignment but is less likely to allow for more refined adjustment, which requires an alert patient. Adjustment is generally performed within 24 h because of

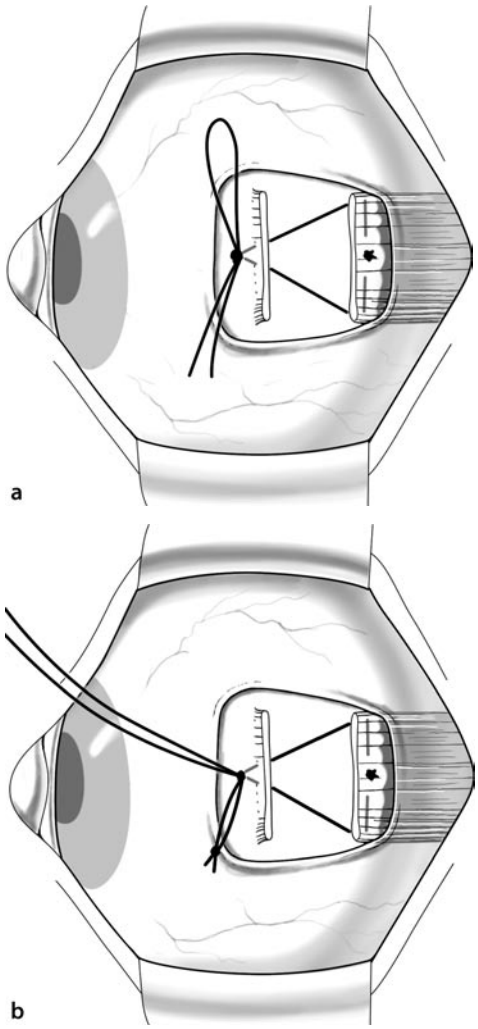

Fig. 16.1 **a** Bow-tie technique: The sutures are tied together in a single-loop bow tie like a shoelace. **b** Sliding-noose technique: A noose is created by tying a separate piece of suture around the scleral sutures

irritation caused by the untied sutures protruding from conjunctiva. The exact timing of adjustment between 1 and 24 h is a matter of local logistics and surgeon preference. When the surgeon is satisfied with the adjustment, the sutures are firmly tied together to permanently secure the muscle. Surgeons who use larger conjunctival incisions often preplace the conjunctival sutures during the primary surgery and tie them off after the final adjustment [21].

16.5.3 Adjustable Sutures in Children

A variety of adaptations of the adjustable suture technique for use in children have been described. The sutures can be adjusted under topical anesthesia on the morning following surgery [3] or in the afternoon on the same day of surgery [5]. The "Releasable adjustable" suture technique allows the suture adjustment on the next day as an office procedure, using intranasal Midazolam and topical lidocaine 2% jelly [10]. The modified adjustable suture technique eliminates the necessity of further manipulation in children who do not require adjustment [6].

16.5.4 Semi-Adjustable Sutures

Muscle slippage is more likely when surgery is performed on the inferior rectus muscle, with an incidence of between 7 and 41%. This has been observed both in adjustable and non-adjustable cases [35]. Kushner described a "semi-adjustable" technique in an effort to secure the muscle more firmly to the globe, thus reducing the incidence of muscle slippage while preserving the potential for adjustment [16]. The process involves suturing the corners of the muscle firmly to the sclera and placing the center of the muscle on an adjustable suture (Fig. 16.2). A trade-off of this procedure is that it limits the potential to increase the amount of recession at the time of adjustment. By targeting an initial overcorrection with placement of the corner sutures, this downside is limited.

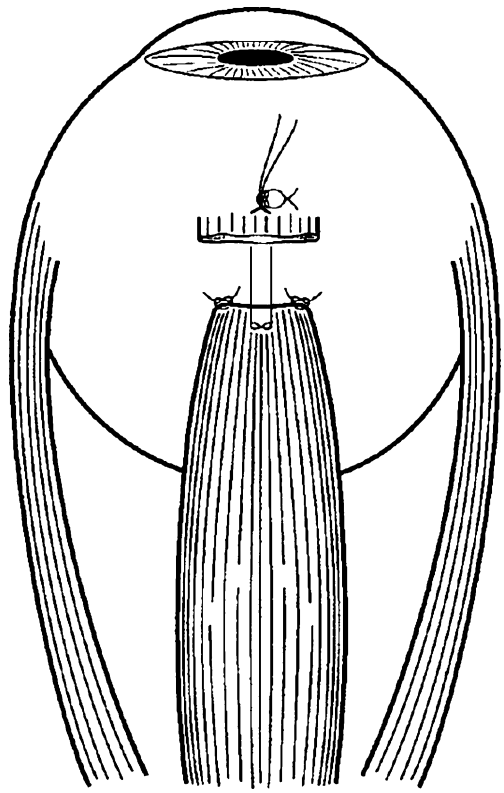

Fig. 16.2 Semi-adjustable sutures showing that the corners of the inferior rectus muscle are sutured firmly to the sclera and the center of the muscle is placed on an adjustable suture. (From [16])

16.5.5 Adjustable Superior Oblique Suture Spacer

The "superior oblique suture spacer" is a modification of Knapp's [15] and Wright's [34] technique which allows partial, reversible, and intraoperatively adjustable superior oblique weakening [28]. The technique uses a non-absorbable suture to separate the cut ends of the superior oblique tendon with precision. This allows the separation to be adjusted in a graded manner intraoperatively according to the exaggerated traction test and fundus torsion.

16.6 Advantages and Disadvantages

The major advantage of adjustable suture strabismus surgery is that it is believed to reduce the rate of re-operations by providing a chance to refine alignment in an alert patient; however, the surgery is complex, involving greater operating time plus the logistics of scheduling the adjustment. The procedure increases the amount of suture material left in the eye after the adjustment. There is increased patient anxiety, though the discomfort is generally minimal. Some patients are unable to cooperate for adjustment. To the great disappointment of patient and surgeon, despite all of the care taken to perfectly align the eyes at adjustment, there may still be a change in alignment as the eye heals, giving an unsatisfactory result.

16.7 Complications

Complications following the adjustable suture technique are rare. Intra-adjustment complications include nausea, vomiting, and ocular pain. An oculocardiac reflex and possible bradycardia may be associated with muscle manipulations; thus, some patients may experience syncope, lightheadedness, diaphoresis, or sense of temperature change. The risk can be reduced with reassurance, topical anesthesia, supine positioning, and avoiding an eyelid speculum. Cardiac monitoring during adjustment is not needed except in cases of heart disease and heart block.

Suture breakage and inability to adjust the muscle can occur. There may be persistence and irritation of the suture knot after adjustment, which cannot be safely removed until around 3 weeks after the surgery. Mocan and Azar [20] have reported four patients who developed severe conjunctival dehiscence, requiring amniotic membrane transplantation, after strabismus surgery with adjustable sutures. Eustis and colleagues [7] found a more robust tissue response to surgery in patients with adjustable sutures, with 4 of 30 (13%) patients developing suture granuloma and 2 (7%) patients with a sub-conjunctival infection.

16.8 Our Preferred Surgical Technique

In this section, the senior author's preferred techniques for adjustable suture surgery, including the "short tag noose" suture, will be detailed. There are not necessarily any studies to support these preferences, but these are the approaches that have evolved through experience with mentors, colleagues, students, and, of course, patients.

The adjustable suture recession or resection surgery is performed under general anesthesia in all patients, if medically permissible. Despite excellent retrobulbar anesthesia, many patients are still quite uncomfortable with the sensation of pulling on the muscle. General anesthesia allows for assessment of the position of the eyes under anesthesia, a valuable tool in surgical planning in some cases [2]. It also allows for forced duction testing without concern for causing discomfort. Finally, general anesthesia obviates the need to wait for local anesthetic to wear off, allowing for earlier suture adjustment on the day of surgery, thus simplifying the logistics of the procedure.

In patients not medically appropriate for general anesthesia, subtenon's irrigation of lidocaine is used. With this approach, the eye is anesthetized with proparacaine and prepped and draped. Four percent lidocaine hydrochloride (Xylocaine, Astra Zanaca, North Ryde, NW Australia) is drawn up into a 3-cc syringe capped with an irrigating (Randolph) cannula. The patient is sedated and a lid speculum is placed. A sharp Westcott scissors is then used to open the conjunctiva in the quadrant near the muscle. The cannula is advanced deep into the quadrant and 2 cc of anesthetic is injected.

Care is taken during surgery to maximize patient comfort in the postoperative period. Hydroxypropyl methylcellulose (Goniosol, Ciba Vision Ophthalmics, Duluth, Ga.) is placed over the cornea at intervals during the surgery to prevent the cornea from drying without need for frequent applications of normal saline. A fornix incision is preferred, keeping the incision size as small as possible. A Guyton muscle hook allows the muscle to be manipulated through a conjunctival incision as small as 1 cm. At each step, a minimum of tension is placed on the incision.

We prefer the sliding noose adjustable suture approach. The muscle is secured with a double-armed 6-0 polyglactin 910 (Vicryl, Ethicon, Somerville, N.J.) suture and disinserted from the sclera. The mus-

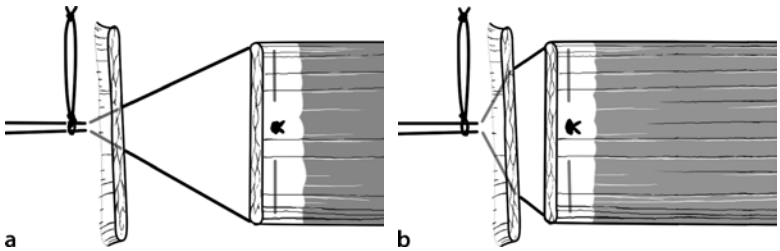

Fig. 16.3 **a** Hang-back recession needs lesser "V" separation. **b** Resection with an exaggerated "V" separation

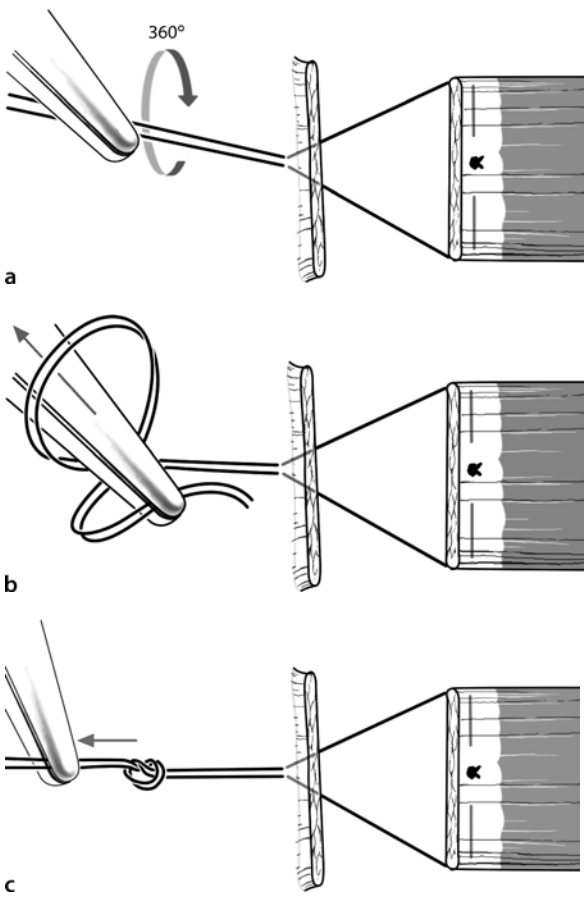

Fig. 16.4a–c Tying an overhand knot. The *straight arrows* show the direction in which the sutures are passed/pulled in a sequential manner. **a** The empty needle holder is looped 360° in a clockwise direction around the sutures. **b** The suture ends are then grasped with the same needle holder and pulled through the loop. **c** The knot is tightened by pulling the suture taut

cle insertion is identified and grasped with 0.5 Castroveijo forceps. Spatulated needles from the sutures are passed one after the other, through the original insertion, at half-thickness depth. The needles are passed in a "V" configuration (Fig. 16.3). For recessions, the scleral passes are separated by 1−2 mm when they enter sclera, but are nearly touching where they exit (Fig. 16.3a). For resections, where the muscle may be pulled up to the insertion at adjustment, this "V" separation is exaggerated to 3−5 mm at the entry site, but the sutures still nearly touch at the exit site (Fig. 16.3b).

For an adjustable recession, the standard hang-back approach and surgical dosages are used. For an adjustable resection, an extra 1−3 mm of muscle is resected. The muscle is then allowed to hang back by the same amount. This allows for either advancement or recession of the resected muscle at adjustment. It also avoids the sometimes unsightly appearance of muscle tissue (rather than tendon) at the insertion site (Fig. 16.3b).

After the sutures are passed, they are pulled up so that the muscle is drawn up to the original insertion. These sutures are then secured to each other using an overhand knot (Fig. 16.4), with care being taken not to allow either pole of the muscle to fall back asymmetrically. The extra suture is cut just above the overhand knot. These joined sutures are called pole sutures. To apply the adjustable noose, the 5-cm fragment of polyglactin 910 suture is used. This piece of suture is placed underneath the pole sutures and wrapped around a second time (Fig. 16.5). A square knot is then tied to ensure a tight noose, which prevents inadvertent slippage. This is critical – the noose should be as tight as possible. The ends of this noose are tied together in an overhand knot as described above, using two needle holders to obtain a noose length distinctly shorter than the pole sutures. The extra suture above the overhand knot is trimmed. The noose is slid forward or back to the desired location. If the pole sutures are nearly touching where they exit, the noose is placed at the exact desired recession (e.g., 5 mm from the exit site for a 5-mm recession).

If the pole sutures are separated where they exit, an additional "fudge factor" is added (e.g., 5.5 mm for a 5-mm recession if the pole sutures exit 1 mm apart). The new muscle position is confirmed by measuring its distance from the scleral insertion.

A 5-0 polyester (Mersilene, Ethicon, Somerville, N.J.) traction suture is often placed, as it helps in manipulating the globe and retracting conjunctiva during suture adjustment. The first pass of the traction suture is perpendicular to the muscle insertion above the quadrant where the incision was made (Fig. 16.6a, pass 1), while the second pass is parallel and anterior to the insertion (Fig. 16.6a, pass 2). The two loose suture ends are then gathered into the left hand, along with the loop between the two passes, and a needle holder, held in the right hand, is positioned over the sutures (Fig. 16.6b).The loose ends are secured to each other with two overhand knots (Fig. 16.6c).

The sutures are tucked under the conjunctiva at the end of the surgery. The conjunctiva is not routinely sutured as the small incision self-seals under the eyelid; however, excess Tenon's tissue should be excised to prevent the formation of conjunctival cyst or pyogenic granuloma. This can most easily be accomplished by copiously irrigating the incision with saline, then grasping and excising protruding tissue (taking care to avoid any suture material). If the conjunctival incision has enlarged inadvertently during surgery, it is partly closed with a 6-0 fast-absorbing gut suture or 8-0 polyglactin 910 suture (Vicryl, Ethicon, Somerville, N.J.), burying the knots for comfort. The incision must be left large enough to allow for suture adjustment even if it is partially closed with sutures. An eye patch is not necessary unless there is an epithelial defect. Antibiotic/steroid drops are preferred over ointment to avoid blurring the vision during the adjustment. The long suture ends are folded and taped over the medial surface of the nose or just lateral to the lateral canthus with a half-inch steristrip.

For pediatric adjustable sutures where sedation will be required for adjustment, two steps are taken to avoid the need for sedation in case adjustment is not needed. Firstly, no polyester traction suture is placed. Secondly, the pole sutures and noose are trimmed and tucked under conjunctiva. An overhand knot is placed just 2−3 mm away from the suture exit site, allowing for an additional 2- to 3-mm recession while not leaving excessive suture material. The noose sutures are also trimmed, but no overhand knot is placed so that they can be distinguished from the pole sutures. This has been described as the "short tag noose" technique (Fig. 16.7) [18].

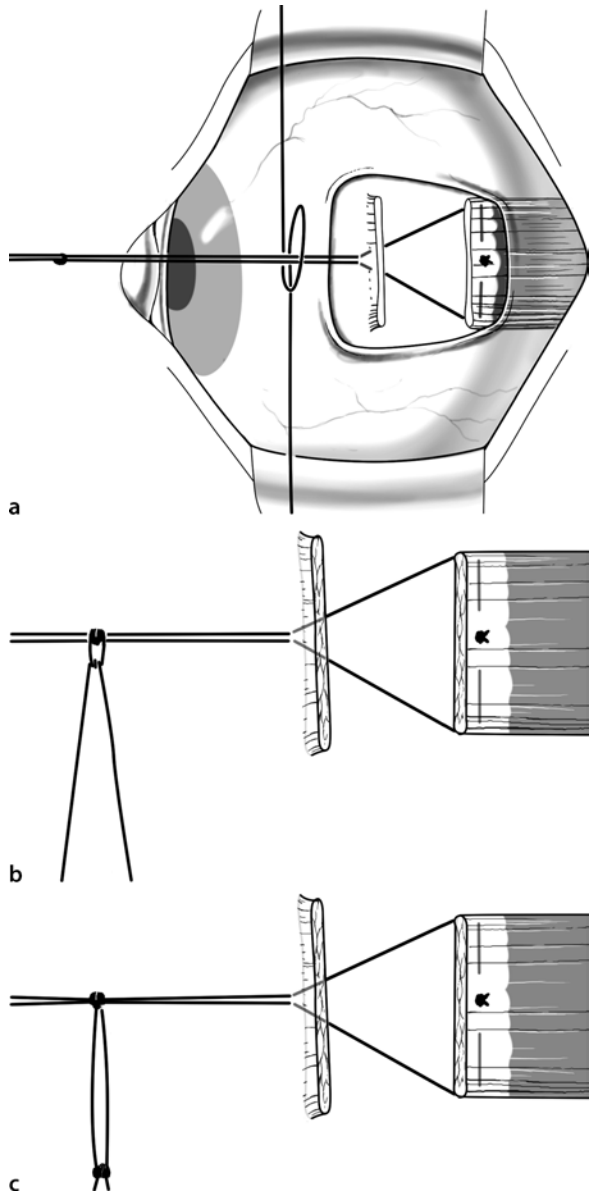

Fig. 16.5a–c Application of the noose. **a** A piece of suture is placed underneath the pole sutures and wrapped around a second time. The suture noose is tied using a square knot. **c** The ends of the noose are tied together in an overhand knot

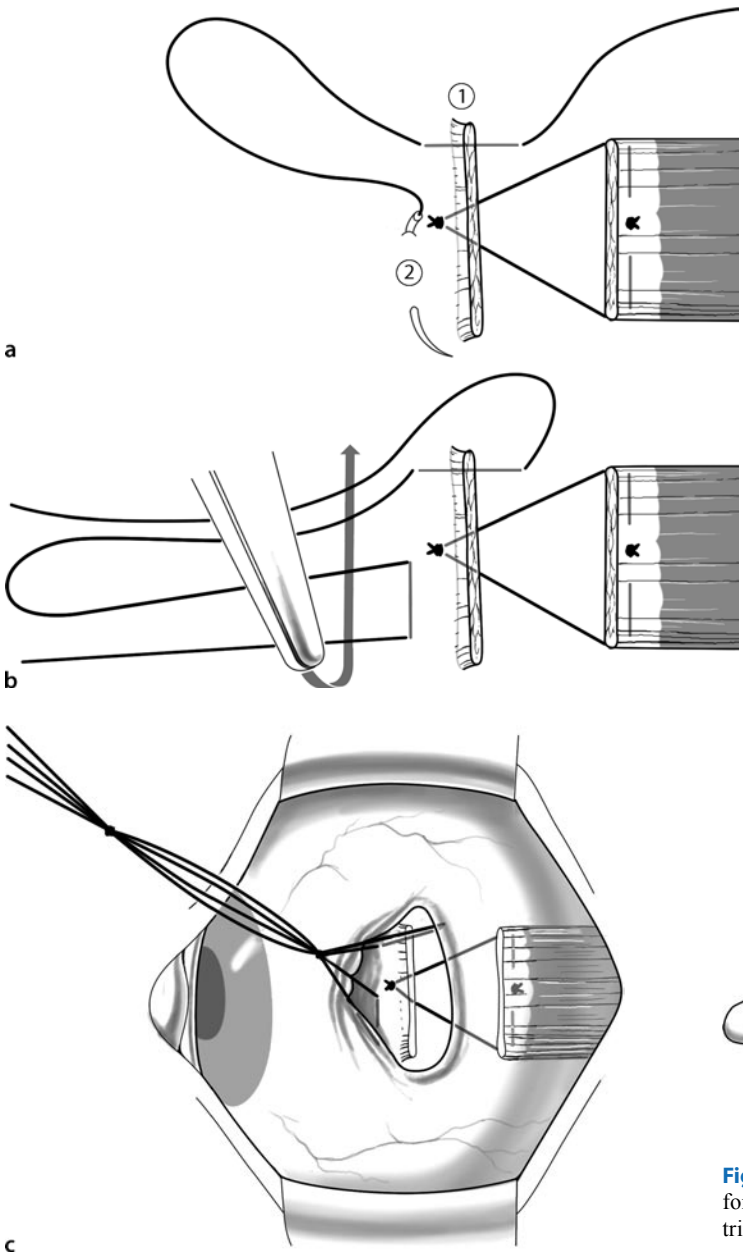

Fig. 16.6a–c Traction suture. **a** The first pass (*1*) is perpendicular to the muscle insertion on the side opposite the conjunctival incision, while the second (*2*) is parallel and anterior to the insertion. **b** The two loose suture ends are gathered along with the loop into the left hand (not shown) and the ends are secured to each other using the needle holder to create an overhand knot close to the muscle. **c** A second overhand knot further secures the distal end of the sutures

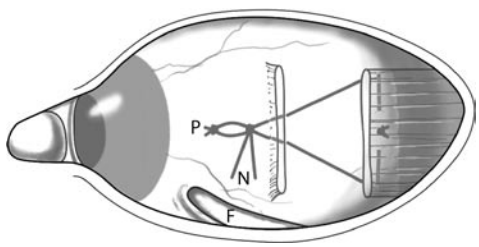

Fig. 16.7 Short tag-noose technique shows the fornix incision (*F*), trimmed pole sutures (*P*), and trimmed noose (*N*) buried under the conjunctiva

16.9 Timing of Adjustment

The adjustment is performed 1−2 h after surgery in the recovery room when the surgery is performed under general anesthesia. If local anesthesia is used, the adjustment should not be performed until at least 5 h have passed to give time for the local anesthetic effect to wear off. We also perform late adjustments up to 1 week after surgery in some cases.

16.10 Adjustment Technique

To initiate the suture adjustment session, the steristrips are removed, and debris is cleaned from the eyelid. Topical anesthetic drops are instilled at least thrice at 2- to 3-min intervals. We prefer proparacaine over tetracaine, which causes severe stinging when first instilled. To assure that the patient is sufficiently alert, we ask the patient to sit without back support

Fig. 16.8a,b Straight-edge test to assess for prism in spectacle lenses. **a** No prism present. Note that the table edge forms a single, continuous line through and between both lenses. **b** Vertical prism present. Note the presence of base-up prism in the left lens, causing the table edge to appear discontinuous

on the edge of the bed with legs dangling. The alignment is assessed with corrective lenses in place, if indicated. If the patient had required prisms preoperatively, care should be taken to assure that the glasses used during adjustment do not have prism! This can be verified by viewing a straight edge passing across the centers of the lenses (Fig. 16.8). For patients with high refractive error and prism glasses, we will prescribe prism-free glasses at the time surgery is scheduled. Those glasses may be used at the preoperative visit as well as during and after the adjustment. For patients with high refractive error who wear contact lenses, the alignment can be assessed by applying topical anesthesia and inserting the contact lenses for the adjustment session. The lenses are then removed and cleaned after the suture adjustment is complete.

Once the patient is positioned, ductions and versions are carefully assessed. Cover testing is performed at distance and near. Often, a transilluminator light must be used as a target if vision is blurred. The goal of adjustment in cases of esotropia and hypertropia is to achieve orthotropia. An exception is to undercorrect the superior oblique palsy patient who has had an inferior oblique weakening procedure in combination with a vertical rectus muscle recession. The goal of adjustment for exotropia cases is to overcorrect so that the patient is diplopic at distance (ET 10−15 PD) with no shift at 0.33 m. The surgeon should take extra time adjusting patients with large fusional amplitudes (>50 PD), who have a tendency to show a larger early overcorrection due to persistent fusional efforts. Non-fusing exotropia patients may be overcorrected more, especially cases of sensory exotropia. For vertical misalignments, it is harder to predict which way the muscle will drift. In our experience, recessions tend to increase as they heal, while resections tend to decrease in effect. Non-absorbable (e.g., polyester) sutures may be considered for large vertical rectus recessions, especially on the inferior rectus muscle if not using the "semi-adjustable" technique. When non-absorbable sutures are used, the patient should be counseled that the knot may eventually erode through conjunctiva and have to be removed.

In very young, less cooperative children we maintain NPO status in the recovery room with the IV left in place. We advise the anesthesiologist in advance about the possible need for sedation in the recovery room. Many children are initially fearful, but given enough time, reassurance, and proparacaine, they will eventually cooperate for adjustment. If not, the anesthesia team generally administers IV Propofol (see Section 16.4.3, Sedation Protocol for Suture Adjustment, p. 216).

To access the noose for an adjustment, the pole sutures are grasped first to avoid inadvertent sliding of the noose. To tighten or decrease the recession, the pole sutures are pulled up to draw the muscle anteriorly while the patient is asked to look toward the muscle (or, if the patient is sedated, the globe is rotated toward the muscle using a traction suture or forceps). This traction on the pole suture pulls the noose suture up and away from the sclera. The pole sutures are stabilized with a needle holder clamped in front of the noose and the noose is slid posteriorly to the sclera with another needle holder (Fig. 16.9a). To loosen or increase the recession, the pole sutures are again pulled forward with a needle holder, this time stabilizing the pole sutures by clamping behind the noose. With the second needle holder, the noose is grasped and moved away from the muscle (Fig. 16.9b). Once the noose is adjusted, the sutures are released and the patient is asked to look toward the adjusted muscle while the eye held in place (or rotated away from the muscle if the patient is sedated). This will retract the muscle posteriorly and force the noose firmly against the sclera.

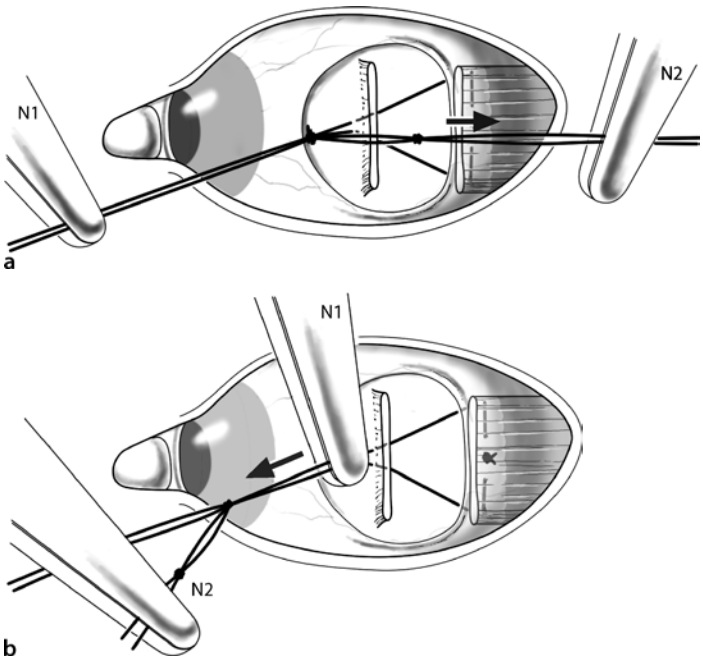

Fig. 16.9a,b Adjustment technique. **a** To tighten or decrease the recession, the pole sutures are stabilized with a needle holder (*N1*) clamped in front of the noose and the noose is slid posteriorly to the sclera (*arrow*) with another needle holder (*N2*). **b** To loosen or increase the recession, the pole sutures are stabilized by clamping behind the noose (*N1*). The noose is grasped and moved away from the muscle (*arrow*) with the second needle holder (*N2*)

We use two approaches to complete the adjustment. To permanently secure the suture, the distal overhand knot is cut to separate the pole sutures. The sutures are then firmly tied to each other. Care is taken not to pull up on the pole sutures while tying the sutures, as this may change the position of the muscle. Both pairs of polyglactin 910 sutures (pole and noose) are trimmed and the polyester traction suture is removed. The conjunctiva generally covers the suture ends without the need for closure.

A different completion step is used on the day of surgery to allow for readjustment up to 7 days later. A second overhand knot is tied on the pole suture to reduce its length to 2−3 mm. The noose sutures are then trimmed to a 5-mm length (we refer to this as the "short tag noose") with no overhand knot (Fig. 16.7). The polyester suture is removed and the suture ends tucked under conjunctiva. In our experience, the sliding noose will not move during the healing period as long as it has been tied securely with a good square knot.

In most cases, we use the short tag noose to allow for later suture readjustment. If a non-absorbable pole suture is used, or if there is a desire to minimize the amount of suture material in the wound, then the suture is permanently secured and trimmed.

When suture adjustment is performed more than 24 h after surgery, it is slightly more uncomfortable for the patient than same-day or next-day adjustment. The conjunctiva should be anesthesized with a proparacaine-soaked cotton-tipped applicator or subconjunctival infusion of a small amount of 2% lidocaine. The conjunctival incision will have self-sealed by the time of the adjustment, so that it will be necessary to tease it open with forceps. If the muscle is firmly adherent to sclera, a muscle hook may be needed to gently separate the muscle from sclera and allow the muscle to be pulled forward or recessed. This is important to verify, as otherwise the noose may slide but the muscle will not move. The younger the patient, the sooner the muscle becomes firmly adherent to the globe. We have not been able to adjust children more than 2 days after surgery without sedation. Elderly patients will tolerate adjustment up to 1 week later. We have performed very late adjustments up to 2 weeks after surgery, but only in the OR with sedation. After 2 weeks, we do not recommend attempting an adjustment out of concerned that that the now-dissolving polyglactin 910 suture will break before the muscle has re-adhered to the globe.

Some surgeons find it easier to advance the muscle when it is over recessed rather than to further recess

Take Home Pearls

- The Q-tip test helps identify patients who are suitable for adjustable sutures.
- Keep the incision size as small as possible for maximum comfort and minimum scarring.
- Ensure a tight noose to prevent inadvertent slippage.
- Assure the patient is sufficiently alert for adjustment.
- The goal is not always straight eyes. Aim for orthophoria in esotropia and hypertropia. Overcorrect exotropia.
- Do not ignore your original numbers – it is possible to over-adjust back to no effect.
- There is no need to tie off a well-done cinch knot.
- For pediatric adjustable strabismus suture surgery, use the short tag noose approach to avoid the need for sedation when postoperative alignment is good.

the muscle when it is under recessed; however, using our preferred technique, we have found no difference in recession vs advancement.

When deciding whether to perform an adjustment, do not ignore our original numbers. It is important to recognize when to stop adjusting. Adjustments >2 mm should be avoided except in unusual cases such as severe restrictive strabismus. If there is no change in alignment after an adjustment, then other factors, such as orbital restriction or transient muscle weakness, are at play and there is no point in trying to adjust further.

We recently reviewed the results of our short tag noose adjustable technique [18] in 95 patients aged 2−83 years; of them, 81% had complex strabismus (reoperation, muscle restriction, nerve palsy). The reoperation rate was 14% for horizontal and 20% for vertical strabismus. Eighteen percent of patients were adjusted >1 day after surgery, with an overall success rate of 85% for both horizontal and vertical strabismus and a reoperation rate of 0% for horizontal and 7% for vertical strabismus in that group.

16.11 Conclusion

Adjustable suture strabismus surgery makes sense intellectually, but validation studies to date are not uniformly compelling. Some studies suggest that the reoperation rate is as low as 10%. The target of the suture adjustment is not always straight eyes – the exact goal for postoperative alignment varies, and must be developed with time and experience. Our recent results indicate a reoperation rate of 14–20% in a referral practice of patients with complex strabismus; however, statistics may not be able to account for the "safety net" effect of being able to adjust when there is a big postoperative surprise. Adjustable sutures provide practical benefits to both the patient and the surgeon and have become preferable for adults and many young children. Adjustable sutures do not guarantee excellent results, but they can be useful when more than usual uncertainty exists about the expected degree of the correction.

References

1. Anninger W, Forbes B, Quinn G et al. (2007) The effect of topical tetracaine eye drops on emergence behavior and pain relief after strabismus surgery. J AAPOS 11:273–276
2. Castelbuono AC, White JE, Guyton DL (1999) The use of (a)symmetry of the rest position of the eyes under general anesthesia or sedation-hypnosis in the design of strabismus surgery: a favorable pilot study in 51 exotropia cases. Binocul Vis Strabismus Q 14:285–290
3. Chan TK, Rosenbaum AL, Hall L (1999) The results of adjustable suture technique in paediatric strabismus surgery. Eye 13:567–570
4. Cogen MS, Guthrie ME, Vinik HR (2002) The immediate postoperative adjustment of sutures in strabismus surgery with comaintenance of anesthesia using propofol and midazolam. J AAPOS 6:241–245
5. Dawson E, Bentley C, Lee J (2001) Adjustable squint surgery in children. Strabismus 9:221–224
6. Engel JM, Rousta ST (2004) Adjustable sutures in children using a modified technique. J AAPOS 8:243–248
7. Eustis HS, Elmer TR Jr, Ellis G Jr (2004) Postoperative results of absorbable, subconjunctival adjustable sutures. J AAPOS 8:240–242
8. George ND (2003) Adjustable sutures: Who needs them? Eye 17:683–684
9. Goldenberg-Cohen N, Tarczy-Hornoch K, Klink DF et al. (2005) Postoperative adjustable surgery of the superior oblique tendon. Strabismus 13:5–10
10. Hakim OM, El-Hag YG, Haikal MA (2005) Releasable adjustable suture technique for children. J AAPOS 9:386–390
11. Haynes GR, Bailey MK (1996) Postoperative nausea and vomiting: review and clinical approaches. South Med J 89:940–949
12. Honkavaara P, Pyykko I (1999) Effects of atropine and scopolamine on bradycardia and emetic symptoms in otoplasty. Laryngoscope109:108–112
13. Jampolsky A (1975) Strabismus reoperation techniques. Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol 79:704–717
14. Jampolsky A (1979) Current techniques of adjustable strabismus surgery. Am J Ophthalmol 88:406–418
15. Jampolsky A (1998) The Philip Knapp Lectureship. J AAPOS 2:131–132
16. Kushner BJ (2004) An evaluation of the semiadjustable suture strabismus surgical procedure. J AAPOS 8:481–487
17. Kipioti A, George ND, Taylor RH (2004) Tied and tidy: closing the conjunctiva over adjustable sutures. J Pediatr Ophthalmol Strabismus 41:226–229
18. Liang S, Loudon S, Salgado C et al. (2008) Short tag noose for optional, late suture adjustment in strabismus surgery (Abstract), J AAPOS 2008;12:102
19. Mendel HG, Guarnieri KM, Sundt LM et al. (1995) The effects of ketorolac and fentanyl on postoperative vomiting and analgesic requirements in children undergoing strabismus surgery. Anesthesia & Analgesia 80:1129–33
20. Mocan MC, Azar NF (2005) Amniotic membrane transplantation for the repair of severe conjunctival dehiscence after strabismus surgery with adjustable sutures. Am J Ophthalmol 140:533–534
21. Nguyen DQ, Hale J, Lany H von et al. (2007) Releasable conjunctival suture for adjustable suture surgery. J Pediatr Ophthalmol Strabismus 44:35–38
22. Ogut MS, Onal S, Demirtas S (2007) Adjustable suture surgery for correction of various types of strabismus. Ophthalmic Surg Lasers Imaging 38:196–202
23. Ozcan AA, Gunes Y, Haciyakupoglu G (2003) Using diazepam and atropine before strabismus surgery to prevent postoperative nausea and vomiting: a randomized, controlled study. J AAPOS 7:210–212
24. Pradda GS, Cruz OA, Krock JL (1997) Comparison of postoperative emesis, recovery profile, and analgesia in pediatric strabismus repair. Rectal acetaminophen versus intravenous fentanyl-droperidol. Ophthalmology 104:419–424
25. Rose JB, Martin TM, Corddry DH et al. (1994) Ondansetron reduces the incidence and severity of post-strabismus repair vomiting in children. Anesth Analg 79:486–489
26. Spierer A (2000) Adjustment of sutures 8 hours vs 24 hours after strabismus surgery. Am J Ophthalmol 129:521–524
27. Strominger MB, Richards R (1999) Adjustable sutures in pediatric ophthalmology and strabismus. J Pediatr Ophthalmol Strabismus 36:112–117
28. Suh DW, Guyton DL, Hunter DG (2001) An adjustable superior oblique tendon spacer with the use of nonabsorbable suture. J AAPOS 5:164–171
29. Sundaram V, Haridas A (2005) Adjustable versus non-adjustable sutures for strabismus. Cochrane Database Syst Rev: CD004240
30. Thacker NM, Velez FG, Rosenbaum AL (2005) Combined adjustable rectus muscle resection–recession for incomitant strabismus. J AAPOS 9:137–140
31. Tripathi A, Haslett R, Marsh IB (2003) Strabismus surgery: adjustable sutures-good for all? Eye 17:739–742
32. Velez FG, Chan TK, Vives T et al. (2001) Timing of postoperative adjustment in adjustable suture strabismus surgery. J AAPOS 5:178–183
33. Ward JB, Niffenegger AS, Lavin CW et al. (1995) The use of propofol and mivacurium anesthetic technique for the immediate postoperative adjustment of sutures in strabismus surgery. Ophthalmology 102:122–128
34. Wright KW (1991) Superior oblique silicone expander for Brown syndrome and superior oblique overaction. J Pediatr Ophthalmol Strabismus 28:101–107
35. Wright KW (1996) Late overcorrection after inferior rectus recession. Ophthalmology 103:1503–1507

Complications of Strabismus Surgery

Rudolph S. Wagner

17

Contents

Core Messages

- Surgical complications are defined as a deviation from the normal postoperative course. Failure to cure is not necessarily a complication and may result from variability or inaccuracy of preoperative measurements.
- Scleral penetration or perforation is more likely to occur in smaller eyes with thin sclera. Highly myopic eyes or eyes that have undergone cryotherapy also have thin sclera.
- A lost muscle is most likely to occur during a resection of the medial rectus muscle.

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- Findings of endophthalmitis include lethargy, asymmetric conjunctival injection, eyelid swelling, and possibly fever within 4 days of surgery. The diagnosis is made when leukocoria secondary to vitritis is recognized.
- Anterior segment ischemia is a rare but potentially serious complication of strabismus surgery, which occurs almost exclusively in adults who have undergone surgery on multiple rectus muscles.

17.1 Introduction

Complications following strabismus surgery have become less frequent with improvements in surgical techniques and instrumentation. Spatula needles, synthetic absorbable sutures, and direct visualization of the muscles with excellent lighting in the operating room all contribute to successful surgery. As with all surgery, the strabismus surgeon must be able to recognize and manage intraoperative and postoperative problems. Strabismus surgery is not an exact science and should not be described as such to patients and parents. Unsatisfactory postoperative alignment can usually be corrected or improved with intervention by refractive error correction, prism therapy, or additional surgery [1].

A surgical complication is defined as a deviation from the normal postoperative course. Surgery may be well executed without any complications but still fail. If the original purpose of surgery has not been achieved, under correction, overcorrection, or other unsatisfactory alignment may result. This is not a complication but a "failure to cure" [2]. Failure to cure in strabismus may result from variability or inaccuracy of preoperative measurements leading to the performance of inadequate or excessive amounts of surgical recession or resection. Other factors may predispose to surgical unpredictability, such as poor fusion, poor vision, and diplopia. In addition, secondary contracture of an operated muscle may result in postoperative changes in alignment. Complications of strabismus surgery may occur during surgery or at a later date, as a result of some intraoperative event. Complications can occur after a properly planned and well-executed procedure and do not necessarily imply a deviation in the standard of care.

17.2 Intraoperative Complications

The prompt recognition and appropriate management of complications that occur during strabismus surgery may obviate an untoward postoperative result.

17.2.1 Perforation of the Sclera

During strabismus surgery a needle may penetrate the sclera and enter the suprachoroidal space and choroid, or perforate the retina and enter the vitreous cavity. A partial- or full-thickness laceration of the sclera proximal to the muscle insertion may occur as the tendon is disinserted using scissors. Rarely, vitreous humor may be encountered following a full-thickness perforation.

A transient hyphema may be produced with deep passage of a needle attached to a fixation suture at the limbus. Fortunately, most scleral perforations do not result in serious injury to the eye and many are unrecognized both at the time of surgery and in the immediate postoperative period. Consequences of scleral perforation, however, may include reduced vision secondary to vitreous hemorrhage, retinal detachment, and endophthalmitis.

The true incidence of penetration of the globe beyond the sclera or perforation during strabismus surgery is difficult to ascertain. Estimates range from 10 to 2% [3, 4]. Many deep penetrations and perforations are not recognized when they occur and the low rate of serious consequences results in the under-reporting of these surgical events. In a recent prospective study of 217 eyes undergoing strabismus surgery by residents and fellows the incidence of scleral penetration was 5.1% and the incidence of perforation 2.8% [5]. The surgeon's experience was not related to the frequency of these complications. Penetrations beyond the sclera or perforations were more likely to occur with rectus muscle recessions than resections,

and horizontal rectus muscles were most frequently associated with penetrations and perforations when compared with vertical rectus and oblique muscles. The authors found that the S-24 needle was more frequently involved in the penetrations and perforations than other needles [5]. The S-14 or S-29 spatula needles are preferable because they are smaller and more suitable for surgery on children's eyes.

Scleral penetration or perforation is more likely to occur in smaller eyes with thin sclera, so younger patients are more at risk. The mean age at surgery for patients who experienced perforations was 4.8 years in one study [5]. Children who have been treated with cryotherapy or laser photocoagulation for retinopathy of prematurity often have very thin sclera near the muscle insertions. The sclera is thinnest in the area behind the rectus muscle insertions in all eyes. This may be obvious at the time of surgery since retinal pigment epithelium may be visible as a blue area through the thin sclera. Highly myopic eyes may have extremely thin sclera and such eyes are at higher risk of perforation. Sudden rupture of a localized area of very thin sclera near the insertion in a myopic patient during a recession of the superior rectus muscle has been reported [7].

Previous extraocular muscle surgery also creates a higher risk for perforation [6]. A tight adherent muscle insertion is often found in patients with congenital fibrosis of the extraocular muscles, Duane retraction syndrome, and thyroid-related ophthalmopathy. In these cases it may be very difficult to pass a muscle hook beneath the insertion to separate the tendon and muscle from the globe. Furthermore, the muscle hook elevates the sclera into the path of the scissors and may result in a partial- or full-thickness laceration of the sclera during tenotomy. Disinserting the muscle without using a muscle hook may actually be safer in such situations. Passage of a needle beneath the conjunctiva and lateral rectus muscle to place a traction suture may also result in scleral perforation.

17.2.2 Management of Penetration or Perforation of the Sclera

Deep penetration through the sclera into the choroid or retinal pigment epithelium should be suspected if the needle accelerates during passage. At times, the thin sclera posterior to the limbus will become darker blue in color following passage of the needle, indicating suprachoroidal hemorrhage. Perforation is detected when a visible gap in the sclera at the surgical site occurs. This may be associated with a strip of pigment or blood, and occasionally the extrusion of vitreous humor. Many cases of penetration and perforation are not recognized at the time of surgery and have no sequelae. A future indirect ophthalmoscopic retinal examination may reveal pigment accumulation within the retina or a chorioretinal scar, adjacent to the site where the muscle was attached to the sclera (Fig. 17.1).

Deep passage of sutures can best be avoided by having optimal visualization of the surgical field with good lighting and with the use of surgical loupes. Some surgeons prefer to grasp the spatula needle about one-third of the distance from the tip to allow control of the needle during passage through the sclera. This requires a release of the needle prior to advancement in cases where a long tunnel is preferred. Other surgeons prefer to grasp the needle two-thirds or three-quarters back from the tip for a single passage. The needle can usually be visualized within the scleral tunnel. Positioning of the surgeon's hands in cases of shallow orbits with small palpebral fissures may be difficult. A second muscle hook used to spread the muscle insertion is useful when suturing a tightly adherent muscle tendon prior to disinsertion. Some strabismus surgeons instill 2.5% phenylephrine at the beginning of the case both for hemostasis and

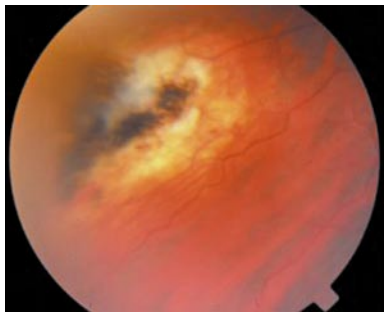

Fig. 17.1 Chorioretinal scar and localized granuloma 10 years following placement of posterior fixation suture using 5-0 braided Dacron. (Courtesy of R. Saunders)

dilation of the pupil in case indirect ophthalmoscopy is required during strabismus surgery.

If perforation is suspected, visualization of the retina is important. Recognition of penetration or perforation on indirect ophthalmoscopy warrants careful follow-up with repeat retinal examinations. Retinal consultation is helpful, particularly if elevation of the retina with fluid surrounding the surgical site is found [8]. Children have a formed vitreous and are unlikely to develop a retinal detachment following retinal injury during strabismus surgery. Larger lacerations of the sclera are more likely to result in a detached retina and require immediate intervention to close the wound. In some cases with uveal tissue prolapse, a scleral patch graph may be necessary [6]. In cases in which scleral perforation is recognized, local (topical and subconjunctival) and systemic antibiotics or even a drop of dilute povidone iodine may be administered to re-sterilize the wound.

17.2.3 Lost Muscle

During or following strabismus surgery a detached muscle may slip back and be "lost" posteriorly in the orbit. Plager and Parks reported that 67% of lost superior, inferior, and lateral rectus muscles were retrievable, while only about 10% of lost medial rectus muscles were located [11]. This complication can occur when the muscle or tendon is disinserted from the globe or during a resection when the muscle is transected. The preplaced sutures may not have incorporated sufficient tendon or muscle tissue and may release spontaneously or be cut inadvertently. A thin tendon or muscle may be released or cut with a muscle hook or may rupture spontaneously anywhere along its course. This most often occurs at the muscle tendon−junction. Rupture with mild traction is referred to as the "Pulled-in-Two" syndrome (PITS) [12]. The PITS is more likely to occur in a patient with a tenuous attachment from previous surgery or in an elderly individual where there is atrophy of the tissue.

A lost muscle is most likely to occur during a resection procedure, particularly on the medial rectus muscle. Although any muscle may be lost, the inferior oblique muscle usually does not retract when it is disinserted and remains in the proximal Tenon's capsule. It can usually be distinguished by its fleshy appearance. The superior rectus muscle may be transected during a planned superior oblique tenectomy procedure when direct visualization is not achieved. A muscle may also be lost following surgery if it detaches from the sclera because of inadequate suture attachment or unrecognized suture weakness or placement of the suture within the muscle capsule without securing the tendon or tissue with a locking knot.

17.2.4 Management of a Lost Muscle

Once this complication is recognized intraoperatively, planned steps must be taken to attempt to recover the muscle. This is the time for the surgeon to collect his thoughts, draw on his experience and overcome the anxiety or panic inherent in this situation. The medial rectus muscle in particular will most likely retract through Tenon's capsule, particularly if dissection of the intermusclar membrane, check ligaments, and capsule have been extended posteriorly during preparation for muscle resection or detachment. Enlarging a limbal incision or converting a fornix incision to a limbal incision will aid in visualization. It is important to understand that the muscle will often retract into Tenon's capsule along the orbital wall, and not "hug" the globe posterior to the equator. The rectus muscle pulley system and orbital check ligaments account for this. The conjunctiva is reflected and the Tenon's capsule grasped and advanced carefully with forceps. Using good overhead lighting and perhaps a head light, the global surface is visually inspected and the connective tissue carefully manipulated in an attempt to locate the potential space where the muscle capsule penetrated Tenon's capsule. It is wise to avoid excessive dissection posteriorly, as violation of the orbital fat pad will result in excessive posterior scarring and adherence. Evoking bradycardia (oculocardiac reflex) following grasping and tugging on suspected muscle tissue may indicate that the muscle has been found [13]. Although immediate retrieval is desirable, a less experienced surgeon might decide to close the conjunctival incision and refer the patient to a strabismus surgeon experienced in the retrieval of lost muscles. During the postoperative period, the severed muscle may attach to the sclera posteriorly,

particularly if there was minimal dissection to isolate the muscle prior to it being "lost." The absence of hemorrhage and edema may make the tissue planes more distinct when reoperation takes place approximately 1 week after the initial surgery.

If the retracted muscle is reattached to the sclera, it should be secured proximal to the original insertion. If it cannot be found, a transposition procedure is an option. A partial tendon transposition, such as an augmented Hummelsheim procedure or a modified Jensen procedure, will preserve anterior segment circulation [14]. Botulinum toxin injection to the antagonist of the lost muscle can further obviate operating on another rectus muscle. Surgical weakening of the antagonist is usually not necessary if the transposition procedure is done at the time the muscle is lost or shortly thereafter, since contracture has not yet occurred. Anterior transposition of the inferior oblique muscle has been used successfully to replace a lost or damaged inferior rectus muscle [15].

A lost muscle may be recognized in the postoperative period if there is a large deviation with limited or absent ductions in the field of action of a recently operated muscle. The sutures used for attachment to the sclera may detach spontaneously or rarely following trauma. Patients may also present with clinical findings suggestive of a lost muscle and a history of strabismus surgery. In these circumstances, a surgical plan including preoperative orbital imaging may be of some benefit [16].

Demer and co-workers devised a strategy to improve the retrieval of a lost or transected muscle utilizing orbital imaging to visualize the anatomy and function of the extraocular muscles [17]. Multipositional magnetic resonance imaging (MRI) demonstrates contraction and relaxation by comparison of the muscle's cross-sectional area in various positions. If contractility can be demonstrated, the authors suggest performing an orbitotomy along the adjacent wall if the muscle is located posteriorly, or a direct conjunctival approach if the imaging localizes the muscle anteriorly. If there is no contractility demonstrated, a transposition procedure may be a better option [18]. Alternatively, computed tomography (CT) images obtained with 2-mm-thick coronal and axial cuts using a spiral scanner may help to localize a lost muscle.

A technique to locate a lost muscle using a 3-dimensional image guidance system (LandmarkX System, Xomed, Jacksonville, Fla.) originally designed for neurosurgical procedures has been described. The CT images are loaded into the image guidance system. Using a transnasal endoscopic approach, the guidance probe is used to locate the muscle. The muscle can be secured with sutures and reattached to the globe [19]. It is important to understand that this type of surgical manipulation may disturb the retroorbital fat and connective tissue, resulting in postoperative scarring with limitation of muscle function even when the muscle is found and reattached.

17.2.5 Slipped Muscle

A previously operated muscle may slip posteriorly from its intended attachment site during the postoperative period. The muscle retracts within its capsule, while the muscle capsule remains attached to the new insertion site. This complication may result if the sutures do not adequately secure the tendon or muscle prior to tenotomy. The suture may only include muscle capsule if the full-thickness locking passes do not include muscle tissue. Postoperative trauma to the surgical site may also result in a slipped muscle [20].

A typical patient will present with muscle weakness and an unexpected postoperative strabismus. There is a duction deficit with limited rotations and reduced saccades in the field of action of the involved muscle. The duction limitation is not as pronounced as in a case of a lost muscle (Fig. 17.2). The resulting over-correction of the strabismus is usually not anticipated by the surgeon. Reoperation is usually necessary to correct the problem, and to prevent additional retraction and contracture of the antagonist muscle. It is difficult to confirm the location of the muscle with imaging. Intraoperatively the translucent muscle capsule may be identified as being attached to the sclera at the intended insertion site. There may be partial slippage of the muscle tissue within the capsule resulting in an asymmetric attachment. During surgical exploration the capsule should be followed posteriorly since muscle tissue or tendon may be contained within it.

Jampolsky described a "see-through test," in which a muscle hook is easily visible behind a muscle capsule from which muscle tissue has detached [21]. The capsule may present as a pseudotendon and only with gentle posterior placement of an additional muscle

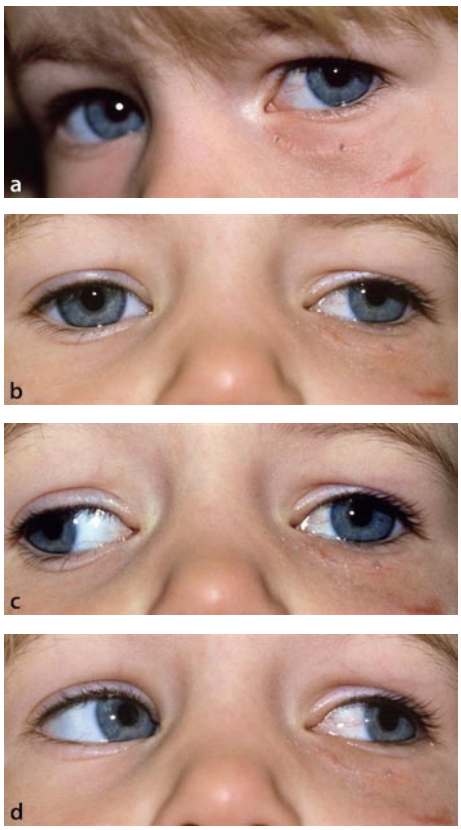

Fig. 17.2 **a** Child with slipped muscle postoperatively showing a right face turn following recession of left medial rectus muscle. **b** The same patient with a left exotropia present in primary-gaze position. **c** Poor adduction of the left eye in right gaze indicating a slipped left medial rectus muscle. **d** Normal horizontal versions in right gaze

hook will the true insertion of the slipped muscle be localized. Sutures may be passed and locked through the capsule while the true tendon is searched for if there is difficulty identifying the muscle. Sliding a muscle hook posteriorly between the capsule and the sclera is another useful technique to locate muscle tissue. Using this "step test" a bump or step is found at the junction of the muscle capsule and true tendon [21]. Once found, the slipped muscle is secured and advanced. The actual reattachment site may vary according to the surgeon's preference and the measured deviation. Additional strabismus surgery may be required in the future as there is less predictability of results following repair of a slipped or lost muscle.

17.2.6 Operating on the Wrong Muscle or Performing the Incorrect Procedure on an Extraocular Muscle

Strabismus surgery may be performed on a muscle not included in the original surgical plan. There may be an anomalous extraocular muscle insertions or agenesis as is found in some patients with craniosynostosis [22, 23]. Improper placement or lack of a traction suture may result in rotation of the globe such that the anatomic muscle insertions are rotated. In such a case the surgeon may incorrectly believe that he or she is operating on the intended muscle. The superior oblique tendon may be confused with the superior rectus tendon and the wrong muscle operated on especially with poor visualization of the operative field.

Lack of attention to detail may result in a muscle being resected when the intention is to perform a recession, or vice versa. These events are all less likely to occur if the surgeon confirms the planned procedure during the preoperative "time out" which is being utilized in most operating rooms to avoid operating on the wrong eye or perhaps the wrong patient.

The surgeon should analyze the causes for an unexpected result and explain to the patient that in many cases, reoperation can correct an untoward result.

17.3 Immediate Postoperative Occurrences

In the immediate postoperative period a corneal abrasion can produce severe pain and should be treated with patching. A retained foreign body (suture, cotton fiber, eyelash) can cause postoperative pain and a foreign body sensation.

Hemorrhaging into a muscle may produce a temporary underaction or spasm with a resultant limitation in the field of action of the involved muscle. This may mimic a slipped or lost muscle, but local hemorrhagic edema will help in recognizing this occurrence. Normal ductions will usually return in a few days once the edema and hemorrhage subside.

17.4 Postoperative Infections and Inflammation

Signs of mild conjunctivitis may develop within the postoperative period. The etiology may be bacterial, viral, or allergic. Sensitivity to topical medications or suture material may produce conjunctival vascular injection and a serous or mucoid discharge. Appropriate topical medications will help to alleviate the signs and symptoms in these cases. In 1991 Ing surveyed 63 strabismus surgeons regarding the incidence of infection they found following strabismus surgery and their use of preoperative and postoperative antibiotics to prevent or treat infections. Cellulitis was reported in 1 of 1900 cases and endophthalmitis at a rate of 1 per 30,000 cases. Infection was not entirely prevented by either preoperative or postoperative topical antibiotics. Twelve surgeons reported using no antibiotics but did not report higher rates of infection than those who did use them [24].

17.4.1 Orbital Cellulitis

Infections following strabismus surgery occur infrequently. Orbital cellulitis may develop on the second or third postoperative day and may be preseptal or postseptal. Clinical signs include proptosis, edema of the eyelids, chemosis, and restriction of ocular motility in a febrile patient. The infection usually responds well to systemic antibiotics [25, 26]. Signs of postseptal involvement necessitate parenteral antibiotic therapy. Indirect ophthalmoscopy should be performed to rule out endophthalmitis. A single case of visual loss from orbital cellulitis in a 56-year-old patient following strabismus surgery has been reported. Loss of vision occurred despite orbital surgery including orbital decompression [27].

17.4.2 Myositis

Orbital myositis is an idiopathic inflammatory condition that rarely occurs following strabismus surgery. Clinical findings include orbital pain, eyelid swelling, focal hyperemia, and chemosis over the affected muscle. There is a limitation of extraocular motility in the field of action of the affected muscle or in the opposite field. Computed tomography scanning demonstrates enlargement of the involved muscle. Symptoms of myositis may develop from 4 days to 4 weeks following strabismus surgery, and are more likely in a previously operated muscle. A rapid resolution after treatment with systemic corticosteroids can be considered pathognomonic for this condition. In their series of 4 cases, Wolf et al. postulated that painful postoperative inflammation involving a quadrant following muscle surgery may be falsely attributed to a "suture reaction" when it is indeed myositis in many cases [28].

17.4.3 Necrotizing Scleritis

Necrotizing scleritis belongs to the same spectrum of idiopathic orbital inflammatory disease as extraocular muscle myositis. This may occasionally occur after strabismus surgery and presents with diffuse conjunctival injection, ocular or orbital pain, headache, and acute change in refractive error. Absence of muscle thickening on CT scanning differentiates necrotizing scleritis from myositis. Bilateral anterior necrotizing scleritis has been recently reported in a 19-month-old girl following a postoperative infection after strabismus surgery (Fig. 17.3) [29].

A granulomatous inflammation of the sclera following strabismus surgery may occur months or even years later. This condition has been termed primary surgically induced necrotizing scleritis (SINS) and is often associated with autoimmunity in adults [30].

17.4.4 Endophthalmitis

Endophthalmitis following strabismus surgery is a very unlikely occurrence but is associated with loss of vision in most reported cases. The incidence is estimated to be between 1:30,000 and 1:185,000 [10, 24]. The typical findings include lethargy, asymmetric conjunctival injection, eyelid swelling, and possibly fever within 4 days of surgery [30]. The diagnosis

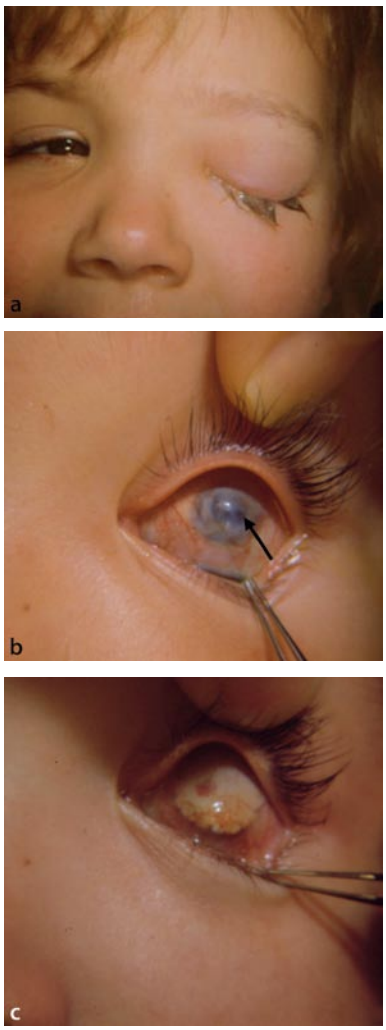

Fig. 17.3 **a** Child 1 week after bilateral superior rectus muscle recession for dissociated vertical deviation with cellulitis of her left upper eyelid. **b** Subsequent examination under anesthesia revealed scleral necrosis with large retinocele behind the original superior rectus muscle insertion (*arrow*). The globe is positioned in down gaze with a forceps, and the corneal limbus is visible near the lower eyelid. **c** Same patient 3 months after scleral patch graft. She retained good vision in the operated eye. (Courtesy of R. Saunders)

is made when leukocoria secondary to vitritis is recognized. Hypopyon may be present. The importance of viewing a normal red reflex sometime during the 7-day period following strabismus surgery in a child with fever, lethargy, and excessive postoperative ocular inflammation cannot be overemphasized.

The issue arises whether scleral perforation precedes endophthalmitis following strabismus surgery. Recchia and co-authors reported six cases of endophthalmitis after pediatric strabismus surgery. The ages of the patients ranged from 8 months to 6 years. The authors state that in none of their cases were scleral perforations reported. They conclude that "the development of endophthalmitis neither requires nor implies that perforation of the globe occurred" [30]. Cases have been reported where endophthalmitis occurred in association with both recognized and suspected scleral perforation [31]. Various organisms have been implicated as causing endophthalmitis following strabismus surgery. Reported organisms include *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, and *Hemophilus aegyptius* [32−34].

Regardless of the etiology, the outcomes pertaining to vision following endophthalmitis are generally poor in spite of heroic efforts to save these eyes. Most eyes that undergo vitrectomy are lost. There are case reports where eyes were saved following intravitreal antibiotic and steroid injections. The author has treated a case of delayed endophthalmitis (presentation 10 days following strabismus surgery) with peribulbar injections of antibiotics and corticosteroids coupled with systemic antibiotic therapy. Useful vision was maintained in this patient.

Risk factors for endophthalmitis might include surgery on small eyes with thin sclera as in very young children. In spite of its infrequency, this remains the most serious complication following strabismus surgery since it usually results in loss of vision.

17.5 Anterior Segment Ischemia

Anterior segment ischemia may occur following strabismus surgery on three, or at times two, rectus muscles. The seven anterior ciliary arteries traversing within the rectus muscles and the two long posterior ciliary arteries provide the blood supply to the anterior segment. Two anterior ciliary arteries run forward within each rectus muscle, except in the lateral rectus muscle where there is only one, although anatomic variations are common. It is important to note that the vessels do not always lie along the muscle borders,

particularly when performing surgery to split a rectus muscle for transposition [35].

The relative contributions of these vessels have been elucidated by the iris fluorescein angiography studies by Hayreh and Scott [36]. Tenotomy of one or both of the horizontal rectus muscles produced no appreciable circulatory disturbance in the iris, but tenotomy of the superior or inferior rectus muscle produced circulatory delay in the superotemporal or inferotemporal sectors. Tenotomies of a horizontal and one or two vertical rectus muscles combined produced a delay in filling in the iris in the vertical rectus muscle region only. Blood supply of the nasal half of the iris was usually not disturbed by tenotomy of the vertical and/or medial rectus muscle. Their findings indicate that the blood supply of the iris is segmental and suggest that operating on the two vertical rectus muscles along with the lateral rectus muscle increase the risk of developing anterior segment ischemia. The implication is that the long posterior ciliary arteries provide most of the blood supply to the medial and nasal areas of the iris, while the vertical rectus muscles assume the major role in supplying the superior temporal and inferior temporal regions of the iris.

The clinical findings of anterior segment ischemia may vary but usually include postoperative pain developing a few days after strabismus surgery. The pain may be moderate but can be severe in cases of impending necrosis. The affected eye may develop microcystic edema and corneal stromal thickening and corectopia (Fig. 17.4). Aqueous flare and cell and nonpigmented keratic precipitates are seen on slit lamp examination. The early changes may resolve spontaneously or rarely, progress to sector iris atrophy, corneal neovascularization, cataracts, or phthisis bulbi. There is do definitive treatment for anterior segment ischemia. The finding of anterior chamber flare and cell often results in the clinician administering systemic and topical corticosteroids, and topical atropine 1% drops. deSmet and co-workers successfully used oxygen administered in a hyperbaric chamber to treat ischemia in a 62-year-old dysthroid patient following a two vertical rectus muscle procedure [37].

Patients have been reported to develop anterior segment ischemia following full tendon transposition of the superior and inferior rectus muscles 9 and 20 years after they underwent horizontal rectus muscle surgery. Ipsilateral carotid artery ligation and hyperlipoproteinemia may have been contributory factors [38]. A 62-year-old woman with thyroid ophthalmopathy after simultaneous surgery on both vertical rectus muscles was reported to develop anterior segment ischemia [39]. Simon and colleagues reviewed the records of 34 eyes in 26 patients who underwent surgery on three or four rectus muscles. Only one patient, with thyroid disease, developed mild signs of anterior segment ischemia. They concluded that surgery on three or four rectus muscles in healthy patients is probably safe when performed in a staged fashion [40]. Full tendon transfer procedures combined with recession of another rectus muscle have been reported to produce anterior segment ischemia [43].

An attempt may be made to preserve the anterior ciliary arteries by dissecting them from the muscle and tendon. The muscle and tendon are recessed or resected while the vessels are left undisturbed. This meticulous surgery, usually performed using a microscope, may help to avoid the development of anterior segment ischemia [41, 42].

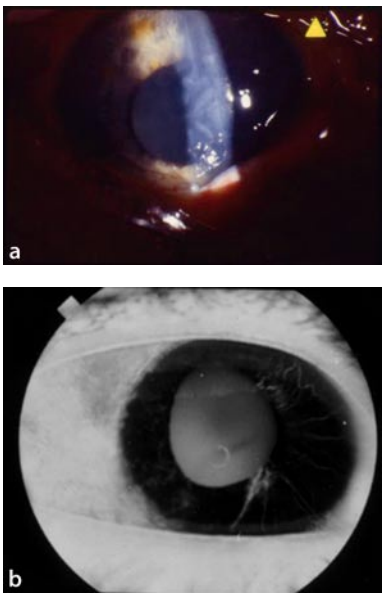

Fig. 17.4 **a** Striate keratopathy, corectopia, and anterior chamber cell and flare following full tendon transposition of the vertical recti and medial rectus muscle recession in 30-year-old man with Duane's syndrome. **b** Iris fluorescein angiography 10 days postoperatively shows delayed iris filling with leakage inferiorly. (Courtesy of R. Saunders)

17.6 Delayed Postoperative Reactions

Chronic inflammation and delayed healing following strabismus surgery may compromise an otherwise satisfactory result in alignment. Recognition of the etiology and appropriate treatment produces an optimal final surgical result in most cases.

Fig. 17.5 A hyperemic, pedunculated granuloma has formed 2 weeks following strabismus surgery

17.6.1 Foreign Body Granuloma

A foreign body granuloma may develop on the surface of the conjunctiva or sclera near the site where the sutures were placed to attach the muscle to the sclera. These probably represent a granulomatous reaction to suture material, retained eyelashes, cotton fiber or glove powder. A hyperemic pedunculated tender mass may become evident within a few weeks following strabismus surgery (Fig. 17.5); these may respond to topical steroids but often require surgical excision. The mass can be removed by placing a small scissor below the granuloma which is usually attached by a thin single strand to the conjunctiva or sclera. A single snip, following topical anesthesia, will usually suffice in a cooperative patient. Local pressure on a closed eyelid for 2 min is often necessary for hemostasis.

17.6.2 Prolapse of Tenon's Capsule

Leaving Tenon's capsule exposed near the limbus may produce an inflammatory reaction and ultimately a granuloma. It can also serve as a nidus for infection. Upon completion of conjunctival closure, irrigation of the operative field with balanced salt solution will cause any exposed Tenon's capsule to "fluff up." This can easily be distinguished from conjunctival tissue and can be resected or reposited.

17.6.3 Allergic Reactions

Suture material may produce an acute allergic reaction within 24 h of surgery. The patient may complain of ocular discomfort and itching and signs include conjunctival hyperemia, chemosis, and eyelid edema. Treatment of an acute allergic reaction consists of topical corticosteroids and cold compresses. Such reactions were far more common when cat-gut sutures were used. The near exclusive use of synthetic absorbable sutures has greatly decreased the likelihood of this occurrence. Topical medications that contain neomycin are associated with a high rate of sensitivity and may prolong the healing period.

17.6.4 Conjunctival Inclusion Cysts

Inadvertent enclosure of conjunctival epithelium into the wound may result in the production of a conjunctival inclusion cyst. These cysts appear as noninflamed translucent masses several days to weeks after surgery (Fig. 17.6). Attempts to drain these cysts with a needle puncture are usually unsuccessful as they refill with serous fluid. Cure usually requires surgical excision of the entire cyst down to bare sclera.

17.6.5 Subconjunctival Cysts

Kushner reported six patients operated on for large subconjunctival cysts that developed up to 35 years after strabismus surgery. In four of these patients the cyst was located between the anterior edge of the muscle and the site to which the muscle had been sutured during previous surgery. The muscle was found to be attached to the posterior wall of the cyst and not to the sclera. In two patients a sudoriferous cyst was found that had originally been mistaken for an abscess when excision was attempted [44].

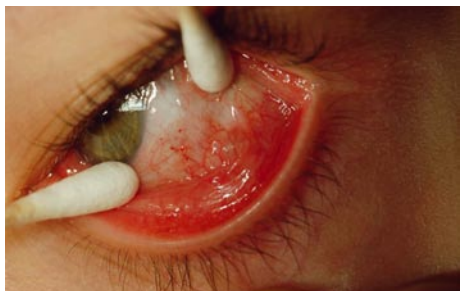

Fig. 17.6 A conjunctival inclusion cyst at the inferior temporal fornix incision site, 10 days following inferior oblique muscle recession

17.6.6 Dellen Formation

Dellen are small areas of corneal thinning with a shallow depression near the limbus. They result from perilimbal elevated tissue, such as heaped-up bulbar conjunctiva, which prevents the eyelid from resurfacing the cornea with tears during blinking. Fluorescein dye may pool in the corneal depression. This painful complication is more likely to occur following a limbal approach and when excessive tissue is advanced during a resection of a muscle. Artificial tears or other ocular lubricants may help to control the signs and symptoms. Patching may be necessary during the postoperative period. Once the conjunctival elevation lessens, the dellen will resolve. Rarely, surgery will be required to reduce the amount of perilimbal tissue.

17.6.7 Adipose Tissue Adherence Syndrome

Surgical penetration of Tenon's capsule near the fat pad where the extraocular muscles penetrate may result in the anterior prolapse of orbital adipose tissue. This can result in a scar composed of fat and fibrous tissue which becomes evident in the postoperative period. The resulting adherence syndrome will limit motility and produce incomitance. Future attempts to remove the scar may produce further restriction of motility. Recognized rents in Tenon's capsule should be closed with an absorbable suture after the orbital fat is reposited during initial strabismus surgery. This complication is more likely to occur during surgery on the inferior oblique muscle, because of its posterior location and proximity to Tenon's capsule. Isolation of the inferior oblique muscle under direct visualization helps to avoid this complication.

17.7 Restrictive Strabismus

A major problem following strabismus surgery, particularly in reoperations, is the development of postoperative adhesions. Scar tissue may involve the conjunctiva, Tenon's capsule, intermuscular membrane, orbital fat, sclera, and extraocular muscles. The scar tissue may result in a restrictive strabismus which can negate the effects of the strabismus procedure. Various materials and therapeutics have been used in an attempt to prevent the development of surgical adhesions. Sodium hyaluronate [45], and antimetabolites including mitomycin C [46] and 5-fluorouracil [47], have been used with mixed results. A bioabsorbable membrane composed of sodium hyaluronate and carboxymethylcellulose has been used experimentally as a sleeve or barrier to prevent surgical adhesions in strabismus surgery [48]. This material holds promise when placed between the muscle and conjunctiva in preventing scar formation.

17.7.1 Eyelid Position Changes

Surgery on the vertical rectus muscles may produce an unacceptable narrowing or widening of the palpebral fissure. Eyelid displacement occurs in the same direction as the shift in the insertion of the muscle. This results from inadequate dissection of the fascial connections between the inferior rectus muscle and the lower eyelid retractors, or between the superior rectus muscle and levator muscle complex. Eyelid changes are most likely to occur following recession of the inferior rectus muscle, because posterior dissection is limited by the attachment of the inferior oblique to the inferior rectus muscle (Lockwood's ligament; Fig. 17.7) [10]. As little as 4–5 mm of surgery can alter the lid position unless the inelastic cords that extend between the muscle capsule, lower eyelid tarsal skin, and inferior orbital septum are completely severed. As a general rule, all inter-

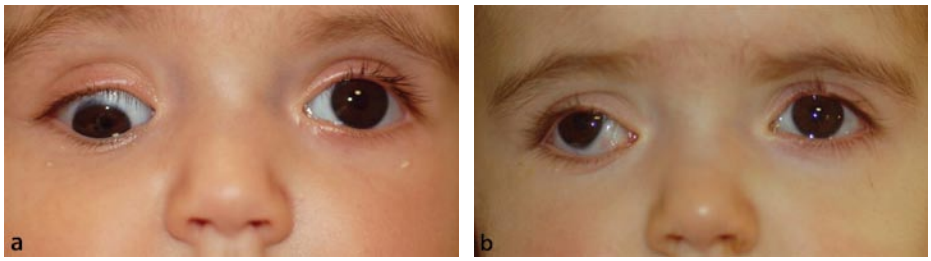

Fig. 17.7 **a** Right hypotropia in child with congenital fibrosis of the inferior rectus muscle. **b** Retraction of the right lower eyelid shows widening of the palpebral fissure of the conjunctiva of the right eye, following recession of the right inferior rectus muscle in patient in Fig. 17.8a

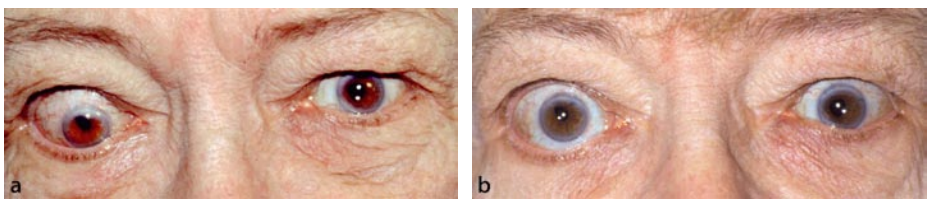

Fig .17.8 **a** A preoperative right hypotropia is shown in adult thyroid patient with Grave's ophthalmopathy. **b** A postoperative right lower eyelid retraction with conjunctival exposure following a recession of right inferior rectus muscle in the patient illustrated in **a**

muscular and fascial connections should be severed back to at least 12 mm when operating on the vertical rectus muscles. Retractor lysis and advancement and reattachment of the capsulopalpebral head may prevent eyelid retraction after inferior rectus muscle recession. Patients with thyroid ophthalmopathy are particularly prone to lower eyelid retraction following inferior rectus muscle surgery (Fig. 17.8) [49]. Proptosis may become more pronounced following extraocular muscle recessions particularly in patients with thyroid ophthalmopathy [9].

17.7.2 Advancement of the Plica Semilunaris and Conjunctiva

The plica semilunaris may be advanced inadvertently during strabismus surgery. The edge of the semilunar fold may be mistaken for the edge of the conjunctiva and may be advanced and sutured to the sclera. Advancement may also occur following a large medial rectus resection. This will produce protuberant chronically inflamed tissue and sometimes corneal dellen formation (Fig. 17.9). Additional surgery may be necessary to recess the plica and conjunctiva.

17.7.3 Adjustable Suture Issues

Complications can occur during or following an adjustable suture strabismus procedure. The sutures may detach from the sclera during postoperative adjustment. If recognized, the patient may need to be brought back to the operating room for reattachment.

A common problem following adjustable suture procedures is exposure of a large suture knot (Fig. 17.10). Every attempt should be made to cover the knot with the conjunctiva. An exposed knot may produce a painful foreign body sensation and interfere with postoperative healing. Topical corticosteroids may be useful, although excision of the knot may be necessary once the muscle has attached to the

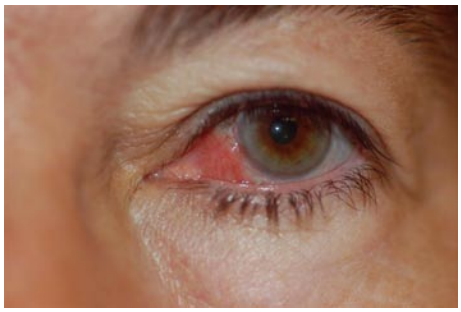

Fig. 17.9 Protuberant chronically inflamed conjunctiva following resection and advancement of the left medial rectus muscle in a patient who underwent a reoperation

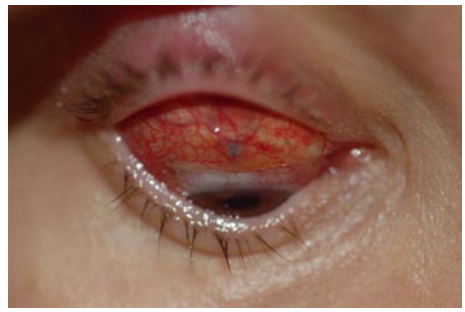

Fig. 17.10 Visible knot and sutures following an adjustable recession of the superior rectus muscle

sclera. Occasionally a patient may not tolerate the adjustment and experience syncope from a vaso-vagal nerve response. The administration of an intravenous nonsteroidal anti-inflammatory agent, such as ketorolac tromethamine, prior to adjustment works well in most cases.

17.7.4 Changes in Refractive Error

Surgery on two horizontal rectus muscles in one eye may produce a temporary change in the refractive error. Newly induced with-the-rule astigmatism following strabismus surgery usually resolves in a few months [50].

17.7.5 Complications Related to Anesthesia

During strabismus surgery, hooking and traction on an extraocular muscle may cause bradycardia. This oculocardiac reflex can produce asystole. Frequently, the anesthesiologist will ask the surgeon to release the traction on the muscle as he monitors the heart rate. Intravenous atropine may need to be administered during the procedure. This reflex is unpredictable and can occur following traction on any rectus muscle.

Malignant hyperthermia is a disease characterized by extreme heat production which may be triggered by inhalational anesthetic agents, muscle relaxants, and some local amide anesthetics. A hypermetabolic state occurs as intracellular calcium stimulates muscle contracture. A shift toward anaerobic metabolism results in lactate production and acidosis.

The earliest signs of malignant hyperthermia include tachycardia and elevated carbon dioxide. Temperature rise and respiratory and metabolic acidosis follow. This condition can be fatal due to cardiac arrest if diagnosis and treatment are delayed. Early treatment includes hyperventilation with oxygen and intravenous dantrolene which prevents the release of calcium from the muscle cells. The surgical procedure should be terminated as the anesthetic agent is discontinued.

The incidence of malignant hyperthermia is greater in children with strabismus, ptosis, and other musculoskeletal abnormalities. This extremely rare condition can occur as an isolated case or as a dominantly inherited condition with incomplete penetrance. The mortality rate from this condition is about 10%. Malignant hyperthermia susceptibility testing is available to screen for this condition [51].

Take Home Pearls

- The S-24 needle is more frequently involved in the penetrations and perforations than other needles [5]. A smaller S-14 or S-29 spatula needle might be a better choice.
- Instillation of 2.5% phenylephrine in each eye at the beginning of surgery will provide hemostasis and dilate the pupil well enough to allow indirect ophthalmoscopy, if necessary, upon completion of surgery.
- In cases of restricted strabismus a second hook under the insertion can help to create sufficient space to pass the sutures in the tendon.
- Preoperative MRI may be helpful in planning surgery to retrieve a lost rectus muscle.
- Review the patient's chart in the operating room prior to the first incision to confirm the correct muscle and planned procedure.
- Avoid penetrating Tenon's capsule and advancing the conjunctiva too anteriorly in resection procedures.

References

1. Wagner RS (2005) Surgical management of strabismus. In: Nelson LB, Olitsky SE (eds) Harley's pediatric ophthalmology, 5th edn. Lippincott Williams and Wilkins, Philadelphia, pp 193–200
2. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
3. Simon JW, Lininger LL, Scheraga JL (1992) Recognized scleral perforation during eye muscle surgery: incidence and sequelae. J Pediatr Ophthalmol Strabismus 29:273–275
4. McLean JM, Galin MA, Baras I (1960) Retinal perforation during strabismus surgery. Am J Ophthalmol 50:1167–1171
5. Dang Y, Racu C, Isenberg SJ (2004) Scleral penetrations and perforations during strabismus surgery and associated risk factors. J AAPOS 8:325–332
6. Awad AH, Mullaney PB, Al-Hazmi A et al. (2000) Recognized globe perforations during strabismus surgery: incidence, risk factors, and sequelae J AAPOS 4:150–153
7. Haugen OH, Kjeka O (2005) Localized extreme scleral thinning causing globe rupture during strabismus surgery. J AAPOS 9:595–596
8. Taherian K, Sharma P, Prakash P et al. (2004) Scleral perforations in strabismus surgery: incidence and role of prophylactic cryotherapy: a clinical and experimental study. Strabismus 12:17–25
9. Gomi CF, Yang S, Granet DB et al. (2007) Change in proptosis following extraocular muscle surgery: effects of muscle recession in thyroid-associated orbitopathy. J AAPOS 11:377–380
10. Wagner RS, Nelson LB (1985) Complications following strabismus surgery. Int Ophthal Clin 25:171–177
11. Plager DA, Parks MM (1990) Recognition and repair of the "lost" rectus muscle. A report of 25 cases. Ophthalmology 97:131–137
12. Paysse EA, Saunders RA, Coats DK (2000) Surgical management of strabismus after rupture of the inferior rectus muscle. J AAPOS 4:164–167
13. Apt L, Isenberg S (1980) The oculocardiac reflex as a surgical aid in identifying a slipped or lost extraocular muscle. Br J Ophthalmol 64:362–365
14. Brooks SE, Olitsky SE, Ribiero G (2000) Augmented Hummelsheim procedure for paralytic strabismus. J Pediatr Ophthalmol Strabismus 37:189–195
15. Olitsky SE, Notaro S (2000) Anterior transposition of the inferior oblique for the treatment of a lost inferior rectus muscle. J Pediatr Ophthalmol Strabismus 37:50–51
16. Coats DK, Olitsky SE (2007) Strabismus surgery and its complications. Springer, Berlin Heidelberg New York
17. Shin GS, Demer JL, Rosenbaum AL (1996) High resolution, dynamic, magnetic resonance imaging in complicated strabismus. J Pediatr Ophthalmol Strabismus 33:225–229
18. Underdahl JP, Demer JL, Goldberg RL et al. (2001) Orbital wall approach with preoperative orbital imaging for identification and retrieval of lost or transected extraocular muscles. J AAPOS 5:230–237
19. Srivastava SK, Reichman OS, Lambert SR (2002) The use of an image guidance system in retrieving lost medial rectus muscles. J AAPOS 6:309–314

20. Plager DA, Parks MM (1988) Recognition and repair of the slipped rectus muscle. J Pediatr Ophthalmol Strabismus 25:270–274
21. Raz J, Bernheim J, Pras E et al. (2002) Diagnosis and management of the surgical complication of postoperative "slipped" medial rectus muscle: a new "tendon step test" and outcome/results in 11 cases. Binocul Vis Strabismus Q 17:25–33
22. Velez FG, Thacker N, Britt MT et al. (2004) Cause of V pattern strabismus in craniosynostosis: a case report. Br J Ophthalmol 88:1598–1599
23. Bustos DE, Donahue SP (2007) Absence of all cyclovertical extraocular muscles in a child who has Apert syndrome. J AAPOS 11:408–409
24. Ing MR (1991) Infection following strabismus surgery. Ophthalmic Surg 22:41–43
25. Kivlin JD, Wilson ME (2000) Periocular infection after strabismus surgery. Periocular Infection Study Group. J Pediatr Ophthalmol Strabismus 32:42–49
26. Wilson ME, Paul TO (1987) Orbital cellulitis following strabismus surgery. Ophthalmic Surg 18:92–94
27. Hoyama E, Limawararut V, Pater J et al. (2006) Blinding orbital cellulitis: a complication of strabismus surgery. Ophthal Plast Reconstr Surg 22:472–473
28. Wolf AB, Yang MB, Archer SM (2007) Postoperative myositis in reoperated extraocular muscles. J AAPOS 11:373–376
29. Kearney FM, Blaikie AJ, Gole GA (2007) Anterior necrotizing scleritis after strabismus surgery in a child. J AAPOS 11:197–198
30. Recchia FM, Baumal CR, Sivalingam A (2000) Endophthalmitis after pediatric strabismus surgery. Arch Ophthalmol 118:939–944
31. Salmon SM, Friberg TR, Luxenberg MN (1982) Endophthalmitis after strabismus surgery. Am J Ophthalmol 93:39–41
32. Walton RC, Cohen AS (2004) *Staphylococcus epidermidis* endophthalmitis following strabismus surgery. J AAPOS 8:592–593
33. Thomas JW, Hamill MB, Lambert HM (1993) *Streptococcus pneumoniae* endophthalmitis following strabismus surgery. Arch Ophthalmol 111:1170–1171
34. Thorne JE, Maguire AM (2000) Hemophilus aegyptius endophthalmitis following strabismus surgery. J Pediatr Ophthalmol Strabismus 37:52–53
35. Caputo AR, Wagner RS (1983) Anterior segment ischemia following strabismus surgery. In: Harley RD (ed) Pediatric ophthalmology, 2nd edn, vol 1. Lippincott, Williams and Wilkins, Philadelphia, pp 272–275
36. Hayreh SS, Scott WE (1978) Fluorescein iris angiography. II. Disturbances in iris circulation following strabismus operation on the various recti. Arch Ophthalmol 96:1390–1400
37. deSmet MD, Carruthers J, Lepawsky M (1987) Anterior segment ischemia treated with hyperbaric oxygen. Can J Ophthalmol 22:381–383
38. Saunders RA, Sandall GS (1982) Anterior segment ischemia syndrome following rectus muscle transposition. Am J Ophthalmol 93:34–38
39. Wolf E, Wagner RS, Zarbin MA (2000) Anterior segment ischemia and retinal detachment after vertical rectus muscle surgery. Eur J Ophthalmol 10:82–87
40. Simon JW, Price EC, Krohel GB et al. (1984) Anterior segment ischemia following strabismus surgery. J pediatr Ophthalmol Strabismus 21:179–185
41. Murdock TJ, Mills MD (2000) Anterior segment ischemia after strabismus surgery with microvascular dissection. J AAPOS 4:56–57
42. McKeown CA, Lambert HM, Shore JW (1989) Preservation of the anterior ciliary vessels during extraocular muscle surgery. Ophthalmology 4:498–506
43. Simon JW, Grajny A (2004) Anterior segment ischemia following augmented 2-muscle transposition surgery. J AAPOS 8:586–587
44. Kushner BJ (1992) Subconjunctival cysts as a complication of strabismus surgery. Arch Ophthalmol 110:1243–1245
45. Searl SS, Metz HS, Lindahl KJ (1987) The use of sodium hyalorunate as a biologic sleeve in strabismus surgery. Ann Ophthalmol 19:259–268
46. Urban RC, Kaufman LM (1994) Mitomycin in the treatment of hypertrophic conjunctival scars after strabismus surgery. J Pediatr Ophthalmol Strabismus 31:96–98
47. Mora JS, Sprunger DT, Helveston EM et al. (1997) Intraoperative sponge 5-fluorouracil to reduce postoperative scarring in strabismus surgery. J AAPOS 1:92–97
48. Ozkan SB, Kir E, Culhaci N et al. (2004) The effect of seprafilm on adhesions in strabismus surgery: an experimental study. J AAPOS 8:46–49
49. Kim DB, Meyer DR, Simon JW (2002) Retractor lysis as prophylaxis for lower lid retraction following inferior rectus recession. J Pediatr Ophthalmol Strabismus 39:198–202
50. Thompson WE, Reinecke RD (1980) The changes in refractive status following routine strabismus surgery. J Pediatr Ophthalmol Strabismus 17:372–374
51. American Academy of Ophthalmology (2006) Surgery of the extraocular muscles. In: Pediatric ophthalmology and strabismus, section 6. Basic and Clinical Science Course, American Academy of Ophthalmology, San Francisco, pp 173–191

Nystagmus in Infancy and Childhood

Richard W. Hertle

18

Contents

Core Messages

- The three most common forms of nystagmus in childhood begin early in infancy and are not congenital, and include infantile nystagmus syndrome (old "congenital nystagmus"), fusion maldevelopment nystagmus syndrome (old "latent" nystagmus), and spasmus nutans syndrome.
- Nystagmus associated with neurological or vestibular disease can usually be suspected due to associated neurological signs and symptoms.
- Eye movement recordings now provide the clinician with a way to diagnose, classify, and understand the pathophysiology of nystagmus in infancy and childhood.
- Medical and surgical treatments aimed directly at decreasing or improving the ocular oscillation of nystagmus is now available.

18.1 Introduction

Eye care professionals are among the most common to evaluate infants and children with involuntary ocular movements, producing anxiety in the medical care provider as well as the family. This is due to the frequent association of nystagmus with strabismus. Ny-

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stagmus comes from the Greek word *nystagmos* (to nod), *drowsiness*, and from *nystazein* (to doze); *probably* akin to Lithuanian *snusti* (also to doze). It is a rhythmic, involuntary oscillation of one or both eyes. Using the information obtained from a complete history, physical examination, as well as radiographic and oculographic evaluations, over two dozen types of nystagmus were organized and classified according to a National Eye Institute supported collaborative effort by interdisciplinary national experts and is called the Classification of Eye Movement Abnormalities and Strabismus (CEMAS; Table 18.1) [1]. Some forms of nystagmus are physiological, whereas others are pathological. Although the nystagmus is typically described by its more easily observable fast (jerk) phase, the salient clinical and pathological feature is the presence of a slow phase in one or both directions. Thus, clinical descriptions of nystagmus are usually based on the direction of the fast phase and termed horizontal, vertical, or rotary, or any combination of these. The nystagmus may be conjugate or dysconjugate or predominantly pendular or jerky, the former referring to equal velocity to-and-fro movement of the eyes, and the latter referring to the eyes moving faster in one direction and slower in the other. Involuntary ocular oscillations containing only fast phases are "saccadic oscillations and intrusions" and *not* nystagmus (see CEMAS classification). It is well documented that these differences may be difficult, if not impossible, to differentiate clinically. Recent advances in eye movement recording technology have increased its application in infants and children who have clinical disturbances of the ocular motor system [2, 3]. Estimates of its incidence range from 1 in 350 to 1 in 6,550 [4−6]. It is difficult, if not impossible, to give accurate prevalence/incidence on all types of nystagmus combined, but it is known that up to 50% of the infantile strabismic population will either have infantile nystagmus syndrome (INS) or fusion maldevelopment nystagmus syndrome (FMNS). This could increase the prevalence of nystagmus up to 0.5% of the population.

Table 18.1 Classification of eye movement abnormalities and strabismus (CEMAS) classification of nystagmus types. (From [1])

Classification of eye movement abnormalities and strabismus involuntary ocular oscillations
Peripheral vestibular imbalance Menière, drug toxicity
Central vestibular imbalance Downbeat, upbeat, drug toxicity
Instability of vestibular mechanisms Periodic alternating nystagmus
Disorders of visual fixation Vision loss, See-saw nystagmus, drug toxicity
Disorders of gaze holding Gaze evoked, acquired pendular, drug toxicity
Acquired pendular nystagmus Central myelin, oculopalatal, Whipple, drug toxicity
Saccadic Intrusions and Oscillations Square wave jerks, macro-saccadic oscillations, opsoclonus, flutter, pulses
Miscellaneous eye movements Superior oblique myokymia, ocular motor neuromyotonia
Infantile nystagmus syndrome "Congenital," "motor," "sensory," idiopathic, nystagmus blockage
Fusion maldevelopment nystagmus syndrome Old "latent, manifest latent," nystagmus blockage
Spasmus nutans syndrome Without optic pathway glioma With optic pathway glioma

18.2 Etiology

Although the theoretical neuronal mechanisms of nystagmus are constantly evolving and beyond the scope of this chapter, it is important to state that central ocular motor control areas are either primarily or secondarily responsible for generation of the anomalous ocular motor signal(s). These signals include the pursuit system, vestibular system, and a part of the vestibular nuclei responsible for gaze holding called the "neural integrator."

The pursuit system, previously thought to have only a dynamic function, provides a major input for fixation stability (e.g., pursuit at "0 velocity" is stable fixation) [7]. The vestibular system maintains a constant resting firing rate that tends to drive the eyes contralaterally. This tendency is counterbalanced by the vestibular system on the opposite side unless the balance is changed by head rotation. The counterbal-

ance is lost with unilateral vestibular damage and the eyes tend to drift toward the affected side. Most forms of acquired nystagmus are due to disease of the vestibular system (centrally or peripherally). Eye movement recordings show various combinations of uniplanar or multiplanar, simple pendular, linear, or decelerating velocity slow phases [8].

The neural integrator is a theoretical neuronal system that changes the resting firing rate of the extraocular muscles in order to overcome the viscoelastic forces of the orbit and maintain a position of eccentric gaze. The exact location of the neural integrator is unknown, but much of its function resides in the nucleus prepositus hypoglossi located just caudal to the abducens nucleus [8]. With integrator leak, the firing rate of the extraocular muscles is inadequate to overcome the viscoelastic forces of the orbit and maintain the desired eccentric position of gaze. This results in a slow drift of the eyes toward the primary position of gaze and a corrective saccade back toward the desired eccentric position. "High gain" instability is an engineering term used to describe the theoretical neurophysiology explaining the slow-phase velocity observed in ocular motor recordings of infantile nystagmus syndrome ("gain" is the ratio of output to input) [3, 9]. In this form of nystagmus the slow phase accelerates away from the desired position of gaze. These patients' ocular motor systems' "output" is unstable due to improper calibration with "input" from the afferent system (vision). This calibration normally occurs in the first few weeks to months of life. The pathophysiology of FMNS (old latent/manifest latent nystagmus) is different from and less well understood than INS [10]. Since it commonly is associated with the infantile strabismus syndrome (infantile esotropia), it may be related to the documented persistence of naso-temporal motion processing asymmetry that is also characteristic of the syndrome [11].

18.3 Clinical Features

Distinguishing the "acquired" from the "benign" neonatal/infantile forms of nystagmus is important because of the implication for underlying neurological disease in acquired nystagmus. The term "congenital nystagmus" has become synonymous with the most common form of neonatal nystagmus characterized by an accelerating slow phase on eye movement recordings [12]. We replace that term with infantile nystagmus syndrome (INS) as defined by the National Classification of Eye Movement Abnormalities and Strabismus (CEMAS) [1].

In general, a clearly documented history of onset of any form of nystagmus in the first months of life should put the examiner at ease. Such history is not usually available since neonatal-onset nystagmus is frequently not noticed until later in life; however, two forms of neonatal nystagmus, INS and latent/FMNS, are so typical that they can be assumed to have begun in the neonatal period. A summary algorithm is presented in Fig. 18.1 to help the clinician in distinguishing the more "benign" forms of nystagmus in infancy and childhood.

18.4 Infantile Nystagmus Syndrome

Familiarity with the clinical features of infantile nystagmus syndrome (INS; previously congenital "motor" nystagmus or "CN") is essential. The INS is an ocular motor disorder of unknown etiology that presents at birth or early infancy and is clinically characterized by involuntary oscillations of the eyes (see Table 18.2 for distinguishing features). The INS can occur in association with congenital or acquired defects in the visual sensory system (e.g., albinism, achromatopsia, and congenital cataracts) [4, 13]. The cause and precise mechanism of INS has not been elucidated. Children with this condition frequently present with a head turn, which is used to maintain the eyes in the position of gaze of the null point (point of minimum nystagmus). Head oscillations are common in INS but are not used as the strategy to improve vision, except in those rare patients with abnormal gain of their vestibulo-ocular reflex. Oscillopsia is almost never present in INS. Accurate and repeatable classification and diagnosis of nystagmus in infancy as INS is best accomplished by a combination of clinical and motility findings; in some cases, the latter are indispensable for diagnosis (Fig. 18.2).

In an infant diagnosed with INS ocular motility analysis can also be helpful in determining visual status. Analysis of binocular or monocular differences in waveforms and foveation periods reflect development of the afferent visual system. The INS

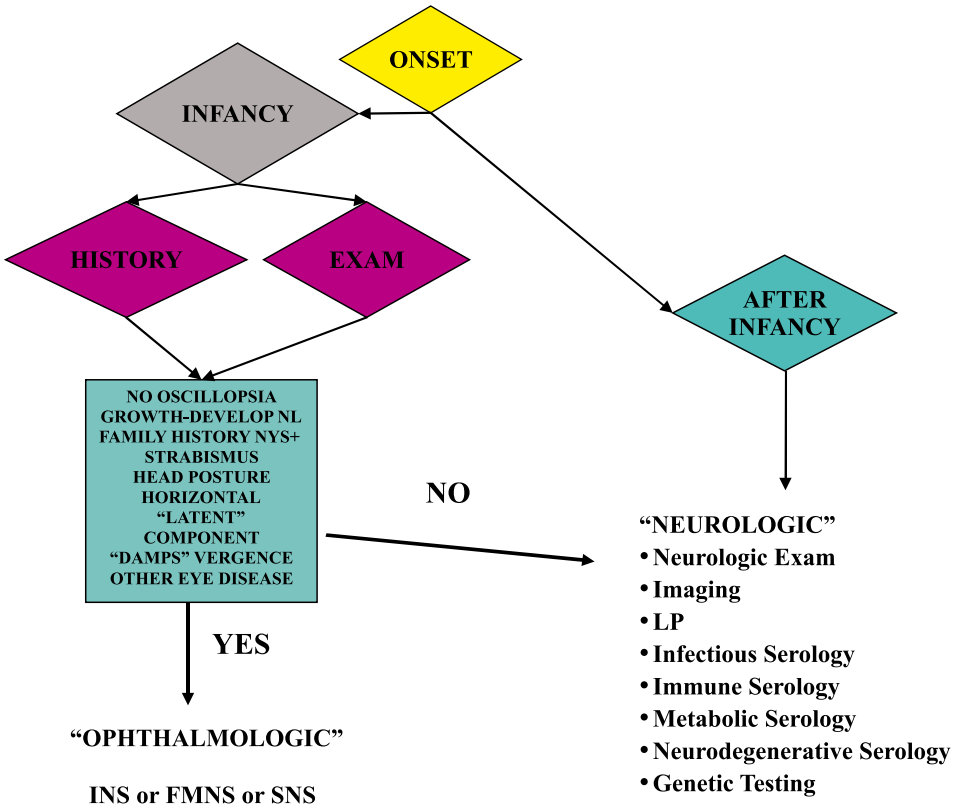

Fig. 18.1 Clinical algorithm to assist with clinical differentiation of nystagmus associated with visual system disease from neurological disease and additional work-up if neurological disease is suspected

Table 18.2 CEMAS criteria for infantile nystagmus syndrome. (From [1])

Disease name	Infantile nystagmus syndrome[a]
Criteria	Infantile onset, ocular motor recordings show diagnostic (accelerating) slow phases
Common associated findings	Conjugate, horizontal–torsional, increases with fixation attempt, progression from pendular to jerk, family history often positive, constant, conjugate, with or without associated sensory system deficits (e.g., albinism, achromatopsia), associated strabismus or refractive error, decreases with convergence, null and neutral zones present, associated head posture or head shaking, may exhibit a "latent" component, "reversal" with OKN stimulus or (a)periodicity to the oscillation. Candidates on chromosome X and 6. May decrease with induced convergence, increased fusion, extraocular muscle surgery, contact lenses, and sedation
General comments	Waveforms may change in early infancy, head posture usually evident by 4 years of age. Vision prognosis dependent on integrity of sensory system

[a] Old congenital nystagmus and "motor and sensory" nystagmus

may result from a primary defect (e.g., familial X-linked), ocular motor calibration, or from abnormal cross-talk from a defective sensory system to the developing motor system at any time during the motor system's sensitive period. The primary ocular motor instability underlying INS is the same, but its clinical and oculographic expression are modified by both initial and final developmental integrity of all parallel afferent visual system processes. Visual loss should be highly suspected in any infant or toddler

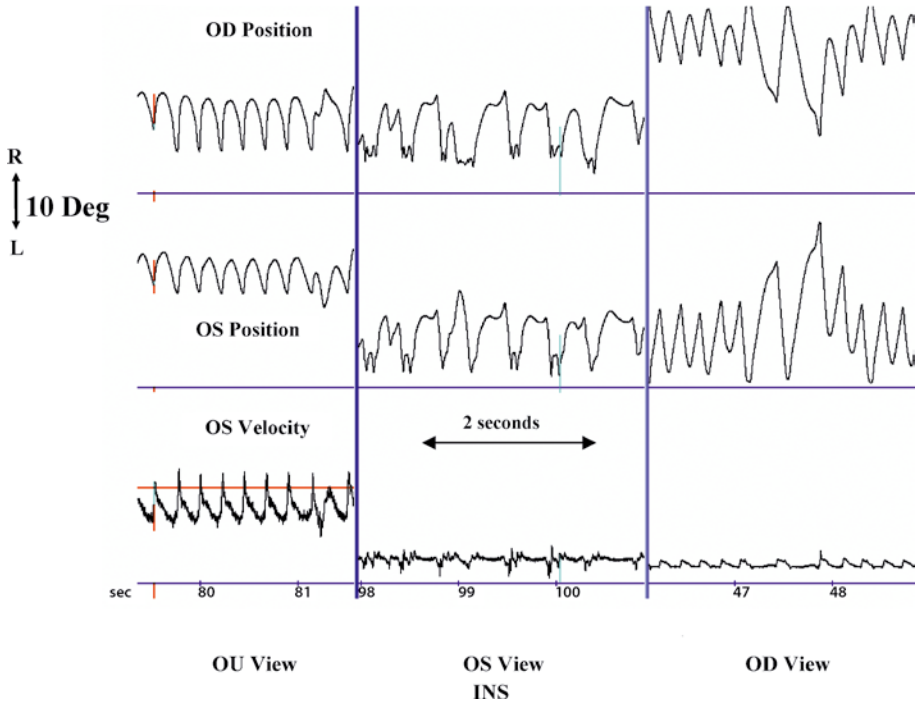

Fig. 18.2 Eye movement recording of infantile nystagmus syndrome (*INS*) with "latent component." With both eyes open there is right-beating nystagmus with increasing velocity slow phases (jerk with extended foveation). With the left eye viewing only there is a change in direction to left beating with a less stable jerk wave form and with right eye viewing the direction changes to right beating again, using the preferred eye. This patient would be clinically indistinguishable from one with fusion maldevelopment nystagmus syndrome. *R* right, *L* left, *OD* right eye, *OS* left eye, *OU* both eyes, *Deg* degrees, *Position* eye position trace, *Velocity* differentiated eye position trace giving eye velocity signal showing direction of fast phase

with onset of nystagmus after early infancy, since mild-to-moderate visual loss may not be readily apparent in the preverbal years. If a child with nystagmus has suspected visual loss, but a normal ocular examination, an afferent and neurological system work-up is necessary since retinal dysfunction may be detected even in the absence of pigmentary degeneration.

18.5 Fusion Maldevelopment Nystagmus Syndrome

Fusion maldevelopment nystagmus syndrome (FMNS; previously "latent" nystagmus) is a benign, jerk nystagmus that begins in early infancy and is easily observed under monocular viewing conditions. It is bilateral and conjugate, with the slow phase toward the covered eye and the fast phase toward the viewing or suppressed eye. Strabismus, usually in the form of esotropia, is almost always present (Table 18.3). It may be difficult to distinguish from INS since patients with INS, esotropia, and a "latent" component appear clinically identical to patients with FMNS. The only sure way to diagnose FMNS is by ocular motor recordings [4, 5, 10−12, 14]. The FMNS can appear to be converted to "pure" latent nystagmus if the strabismus is repaired (Figs. 18.2, 18.3).

With eye movement recordings, mild FMNS can usually be detected in those patients who appear to have only latent nystagmus clinically. The nystagmus simply becomes more prominent when one eye is occluded. True latent nystagmus is uncommon.

Table 18.3 CEMAS criteria for fusion maldevelopment nystagmus syndrome. (From [1])

Disease name	Fusion maldevelopment nystagmus syndrome[a]
Criteria	Infantile onset, associated strabismus, ocular motor recordings show two types of slow phases (linear and decelerating) plus high-frequency, low-amplitude pendular nystagmus (dual-jerk waveform), jerk in direction of fixing eye
Common associated findings	Conjugate, horizontal, uniplanar; usually no associated sensory system deficits (e.g., albinism, achromatopsia), may change with exaggerated convergence ("blockage"), head posture associated with fixing eye in adduction, no head shaking, may exhibit "reversal" with OKN stimulus, no (a)periodicity to the oscillation. Dissociated strabismus may be present. Decreases with increased fusion (binocular function)
General comments	Intensity decreases with age

[a] Old latent/manifest latent nystagmus

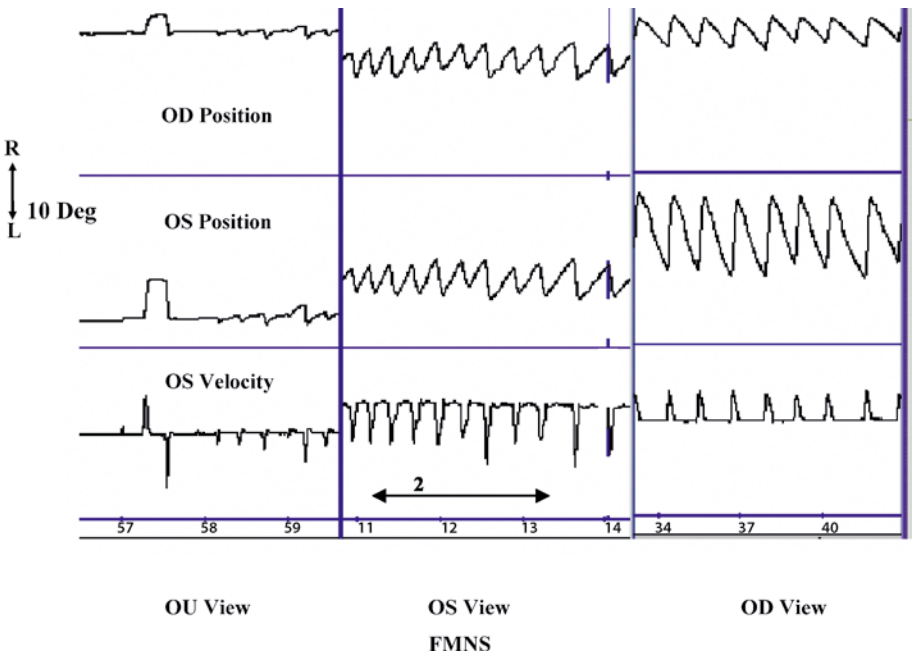

Fig. 18.3 Eye movement recording of fusion maldevelopment nystagmus syndrome (*FMNS*). With both eyes open there is are small-amplitude left-beating movements with linear and decreasing velocity slow phases. With the left eye viewing only there is a change in intensity to clinically obvious left-beating nystagmus; with the right eye viewing the direction changes to more intense right-beating nystagmus because this is the non-preferred eye. This patient would be clinically indistinguishable from one with infantile nystagmus syndrome and a "latent" component. *R* right, *L* left, *OD* right eye, *OS* left eye, *OU* both eyes, *Deg* degrees, *Position* eye position trace, *Velocity* differentiated eye position trace giving eye velocity signal showing direction of fast phase

The FMNS tends to dampen on adduction, so patients with this condition may present with a head turn toward the side of the fixating eye. These patients have an "adduction" null with the fixing eye and not a true "gaze" null position. In addition to causing the head posture, FMNS can cause the patient to have much worse monocular than binocular visual acuity.

Table 18.4 CEMAS criteria for spasmus nutans nystagmus syndrome. (From [1])

Disease name	Spasmus nutans syndrome
Criteria	Infantile onset, variable conjugacy, small-frequency, low-amplitude oscillation, abnormal head posture and head oscillation, improves ("disappears") during childhood, normal MRI/CT Scan of visual pathways; ocular motility recordings – high-frequency (>10 Hz), asymmetric, variable conjugacy, pendular oscillations
Common associated findings	Dysconjugate, asymmetric, multiplanar, family history of strabismus, may be greater in one (abducting) eye, constant, head posture/oscillation (horizontal or vertical), usually no associated sensory system deficits may have associated strabismus and amblyopia, may increase with convergence, head bobbing, head posture may be compensatory; normal fundus exam; decreases with increased fusion (binocular function)
General comments	Usually spontaneously remits clinically in 2−8 years, remains present with eye movement recordings

18.6 Spasmus Nutans Syndrome

Spasmus nutans syndrome (SNS) is the third most common "nonacquired" oscillation beginning in infancy and consisting of the association of pendular, high frequency, small amplitude, dysconjugate oscillations, a head nodding oscillation, and a head tilt. This usually becomes less noticeable as the infant becomes a toddler. Unlike in INS, the head nodding may result in improvement of vision and decrease in the nystagmus. The characteristic clinical feature of spasmus nutans is the very fine, rapid pendular nature of the nystagmus [15]. It may be horizontal, vertical, or torsional. Tremendous asymmetry is associated with amblyopia of the more involved eye. Spasmus nutans may be a completely benign condition that may clinically, but not oculographically, resolve within 2 years (Table 18.4); however, tumors of the diencephalon can cause a condition indistinguishable from spasmus nutans. Consequently, neuroimaging or careful monitoring for visual, neurological, or endocrinological decline is essential.

18.7 Clinical Evaluation

The goal of the history and physical examination is to determine whether the nystagmus has been present from "birth" (the first few months of life) or acquired later (Tables 18.5, 18.6). Information regarding a family history of neonatal eye disease, the pregnancy, labor, delivery, and growth and development since birth should be sought. Vision testing procedures assume special importance. The patient's "*binocular acuity*" should be tested first. Binocular acuity is the "person's" acuity and monocular acuity is the "eye's" acuity; these two are often very different in patients with nystagmus. If present, the patient must be allowed to assume their anomalous head posture (AHP; which is often impossible if a phoropter is being used). During the examination of visual acuity in nystagmus patients with an AHP it is imperative to observe the direction of the posture over a 5- to 7-min period. Up to 17% patients with INS (and up to 33% with albinism) have a periodicity to the direction of their fast phase [16]. This manifests clinically as a changing head posture in the direction of this fast phase.

In older children a subjective refraction is the foundation for any type of refractive therapy. The best way to do this is to fog the eye not being refracted with only enough extra plus to decrease the vision in that eye one to three lines. In many patients with coincidental strabismus (about 50% of the childhood nystagmus population) they can often fix well enough with one eye at a time, and be subjectively aware of this, that no fogging is necessary. Now your usual routine for subjective refraction can be accomplished. In those patients in whom there is a different refraction under cycloplegia, record *both* subjective and objective refraction for decision making regarding spectacle prescription.

Complete clinical evaluation of the ocular oscillation also includes fast-phase direction, movement intensity, conjugacy, gaze effects, convergence effects, and effect of monocular cover. The amplitude, frequency, and direction of the nystagmus in all di-

Table 18.5 Criteria for neurological work-up

History
Onset of nystagmus after 6–9 months of age
History of severe prematurely or developmental or genetic diseases
Abnormal pregnancy, labor, or delivery
Abnormal and/or delayed growth
Exposure to toxins or drugs
Ophthalmic examination
Abnormal vision of the eye(s) (e.g., photophobia, delayed visual behavior)
Abnormal structural examination of the eye(s) (e.g., foveal or optic nerve dysplasia)
Nystagmus pattern vertical, asymmetric, dysconjugate, or associated with other ocular motor disorders, e.g., decreased pursuit, abnormal saccades, and paretic gaze
General pediatric examination
Pediatrician is concerned with growth, development, or patient has manifest "hard" or "soft" focal or diffuse neurologic signs

Table 18.6 Extended nystagmus work-up

Ophthalmologic
Electroretinogram
Visual evoked response
Ocular motility recordings
Neurologic
Pediatric neurologic examination
Neuroimaging (e.g., CAT scan or MRI)
±Brainstem auditory evoked potential
±Electroencephalography
Developmental/genetic
Genetic specialist evaluation (e.g., pedigree, specialized physical exam, chromosome analysis, etc.)
Pediatric developmental specialist evaluation (e.g., psychometric, fine and gross motor and cognitive evaluations)
Serum and/or urine for metabolic diseases
Storage diseases (Neiman Pick C, Gaucher, sialidosis types I and II, Pelizaeus-Merzbacher disease, GM2 type III
Amino acidurias
Leukodystrophies and other degenerative neurologic conditions
Lipid metabolism disorders
Amyloidosis

rections of gaze can be documented with a simple diagram. The clinician can also observe the nystagmus while moving the patient's head. Evaluation of associated motility systems (e.g., strabismus, pursuit, saccades, and vestibulo-ocular reflex) can be clinically evaluated and recorded separately from observations of the oscillation. In older children fusional and accommodative amplitudes can be measured using prisms and a gradient technique, respectively. Changes in the character of the nystagmus with convergence or monocular viewing should be noted.

18.8 Ocular Motility Recordings

Electrophysiological analysis using precise eye movement recordings have provided a new basis for eye movement abnormality classification, etiology, and treatment. These electrophysiological investigations have impacted eye movement systems research in much the same way as electrocardiography did in the study of cardiac rhythms. The most common methods used in clinical practice in order of increasing sensitivity and precision includes "contact" electrooculography, infrared reflectance oculography, video oculography, and scleral contact lens/magnetic search coils. Practical applications of eye movement recording technology in clinical medicine include diagnosis/differentiation of eye movement disorders and utility as an "outcome measure" in clinical research. Eye movement recordings, by convention, display the data during continuous periods of time. Position and velocity traces are clearly marked with up being rightward or upward eye movements, and down being leftward or downward eye movements.

18.9 Treatment

There are a number of signs and symptoms due to nystagmus that are amenable to treatment (Tables 18.7, 18.8). The first and most obvious is *decreased vision* (central visual acuity, gaze-angle acuity, near acuity). Correction of significant refractive errors with spectacles and importantly contact lenses in children with nystagmus is the single most powerful therapeutic intervention for improving vision and visual

Table 18.7 Medical treatment of nystagmus

Nystagmus type	Treatment
Infantile nystagmus syndrome	Fresnell prisms, orthoptics, gabapentin, Baclofen, biofeedback, acupuncture
Acquired pendular nystagmus	Fresnell prisms, orthoptics, gabapentin, Baclofen, clonazepam, cannabis, alcohol, carbamazepine, 5-hydroxytryptophan, scopolamine, memantine, Botox
Peripheral vestibular	Positional exercises, betahistine, cinnarizine, acetazolamide
Downbeat	3,4 Diaminopyridine, clonazepam, gabapentin
Upbeat	Baclofen, clonazepam, gabapentin
Periodic alternating	Baclofen, Botox
See-saw	Baclofen
Saccadic intrusions/oscillations	Baclofen, propranolol, clonazepam
Superior oblique myokymia	Carbamazepine, propranolol, timolol
Opsoclonus	Corticosteroids, propranolol, clonazepam, Baclofen
Ocular motor neuromyotonia	Carbamazepine
Voluntary ocular flutter	Prism, orthoptics
Chronic internuclear ophthalmoplegia	Prism, orthoptics

Table 18.8 Nystagmus surgical procedures

Operation 1: Induced convergence (artificial divergence)
Indication: Binocular function (stereopsis) with observable convergence damping
Preparation: Prism adapt with 7 BO each eye, not Fresnell
Technique: Bilateral medial rectus recess 3.0 and bilateral lateral rectus tenotomy with reattachment
Operation 2: Eccentric horizontal null position alone
Indication: Clinically observable eccentric gaze null with head posture in opposite direction
Preparation: Rule out aperiodic or periodic infantile subtype, no changing posture over 10 min of observation
Technique:
Recess lateral rectus 10.0 in the abducted eye and medial rectus 7.0 in the adducted eye with tenotomies and reattachment of the other horizontal recti for turns up to 20°
Recess lateral rectus 10.0 in the abducted eye and medial rectus 7.0 in the adducted eye 10.0 and resect the medial rectus 7.0 in the abducted eye and resect the lateral rectus 11.0 in the adducted eye for turns >20°
Operation 3: Torsional head posture
Indication: Torsional head posture alone
Preparation: Rule out aperiodic or periodic infantile subtype, no changing posture over 10 min of observation
Technique: Horizontal transposition of vertical recti one full tendon width (hint: take the vertical recti off, move the eyes in the direction of the head posture, reattach the vertical recti), i.e., right head tilt, RSREC nasal, RIREC temporal, LSREC temporal, LIREC nasal

Table 18.8 *(continued)*

Operation 4: Chin-up head posture
Indication: Chin-up head posture alone, nystagmus changes intensity in upgaze
Preparation: Rule out aperiodic or periodic infantile subtype, no changing posture over 10 min of observation
Technique: Bilateral superior oblique 5.0 mm tenectomy nasal to the superior rectus plus bilateral inferior rectus 4.0 recessions
Operation 5: Chin-down head posture
Indication: Chin-down head posture alone, nystagmus changes intensity in downgaze
Preparation: Rule out aperiodic or periodic infantile subtype, no changing posture over 10 min of observation
Technique: Bilateral inferior oblique myectomy plus bilateral superior rectus 4.0 recessions
Operation 6: Head posture for Nystagmus and Strabismus
Indication: Head posture plus strabismus
Preparation:
Rule out aperiodic or periodic infantile subtype or esotropia with fusion maldevelopment and adduction Null, i.e., no changing posture over 10 min of observation
Determine fixing eye (eye driving the head posture)
Technique: Straighten the head with prism correction over the preferred eye, neutralize the resulting strabismic deviation with prism over the non-preferred eye. Perform bilateral recess/resect on each eye's respective measured prism correction
Operation 7: Multiplanar head posture
Indication: Combination chin up/down and face turn
Preparation: Rule out aperiodic or periodic infantile subtype or esotropia with fusion maldevelopment and adduction null, i.e., no changing posture over 10 min of observation
Technique: Three muscles each eye. Combine respective oblique plus vertical recti (above) for chin up/down with 10.0 recess of lateral rectus of abducting eye and 7.0 recess of medial rectus of adducting eye
Operation 8: Nystagmus and Strabismus
Indication: Nystagmus and horizontal strabismus with no head posture
Preparation: Treat refractive errors
Technique: Recess/resect of all four horizontal recti for the total deviation or bilateral recess for the total deviation plus tenotomy with reattachment on the remaining two horizontal recti
Operation 9: Nystagmus alone (about 15% of INS population)
Indication: INS with or without periodicity and *no* strabismus, static anomalous head posture or fusion with convergence damping
Preparation: Rule out strabismus, static head posture or convergence damping
Technique: Bilateral horizontal recti tenotomy with reattachment or bilateral horizontal rectus recession (lateral recti recess 10.0−12.0 and bilateral medial recess 8.0−10.0)

function in these patients. Refractive etiologies of decreased "vision" include either one or a combination of conditions, e.g., myopia, hyperopia, astigmatism, and anisometropia. These refractive conditions can contribute significantly to already impaired vision. The second is *an eccentric gaze, convergence null*, *or adduction null* [17−20]. The eccentric gaze-null is due to INS or acquired nystagmus (e.g., chin-down in down-beat nystagmus), the adduction null due to FMNS (manifest strabismus with the preferred eye fixing in adduction), convergence damping due to INS ("nystagmus blockage"), and a periodically

Take Home Pearls

- Eye care professionals who care for infants and children are among the most common to care for patients with nystagmus.
- Nystagmus in infancy and childhood is often associated with, but not caused by, other diseases in the visual system.
- The terms "motor" and "sensory" nystagmus are no longer correct terms, as the motor oscillation of infantile nystagmus with or without associated afferent system disease is due to the same abnormality in the pursuit system.
- Early diagnosis and treatment of the various types of nystagmus and associated visual system abnormalities improves the prognosis for vision and visual function.

changing head posture due to (a)periodic alternating nystagmus. The third is *oscillopsia*, which is usually due to either acquired nystagmus or a change in the sensory/motor status of patient with INS. Other less common associated signs and symptoms include hypoaccommodation and photophobia. General medical and eye muscle surgical treatment guidelines are outlined in Tables 18.7 and 18.8. The data collected from many surgical studies on these patients support the hypothesis that surgical manipulation of the extraocular muscles in patients with oculographically diagnosed INS "improves" the oscillation and visual functions [21−24]. Although patients will have absolute improvement in visual acuity, this is in the range of one to three Snellen lines. Other "measures" of visual function are improved after surgery, and probably contribute to the visual "well-being." These "measures" include vision in eccentric gaze (gaze-dependent visual acuity), absolute recognition time, and improved depth and breadth of the null zone and binocular field [21−24]. The clinical and electrophysiological consequences of extraocular muscle surgery in patients with INS may be due to interruption of the afferent proprioceptive loop, producing a damped peripheral ocular−motor response to the nystagmus signal [25].

The prognosis of all these ocular oscillations depends on the type of underlying ocular and systemic disease. In general, infantile forms improve with time unless they are associated with a degenerative ocular or systemic disease. Acquired forms are more visually disturbing and follow the course of the underlying neurological disease.

References

1. CEMAS Working Group (2001) A National Eye Institute Sponsored Workshop and Publication on the Classification of Eye Movement Abnormalities and Strabismus (CEMAS). In: Hertle RW (ed) The National Eye Institute Publications, www.nei.nih.gov. The National Eye Institute, The National Institutes of Health, Bethesda, Maryland
2. Hertle RW, Dell'Osso LF. Clinical and ocular motor analysis of congenital nystagmus in infancy [see comments]. J AAPOS 1999; 3(2):70−79
3. Dell'Osso LF, van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus. I: Fixation. Doc Ophthalmol 1992; 79(1):1−23
4. Abel LA. Infantile nystagmus: current concepts in diagnosis and management. Clin Exp Optom 2006; 89(2):57−65
5. Gottlob I. Nystagmus. Curr Opin Ophthalmol 1998; 9(5):32−38

6. Stang HJ. Developmental disabilities associated with congenital nystagmus. J Dev Behav Pediatr 1991; 12(5):322−323
7. Dell'Osso LF, van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus. II: Smooth pursuit. Doc Ophthalmol 1992; 79(1):25−49
8. Leigh RJ, Das VE, Seidman SH. A neurobiological approach to acquired nystagmus. Ann N Y Acad Sci 2002; 956:380−390
9. Dell'Osso LF. Biologically relevant models of infantile nystagmus syndrome: the requirement for behavioral ocular motor system models. Semin Ophthalmol 2006; 21(2):71−77
10. Abadi RV, Scallan CJ. Waveform characteristics of manifest latent nystagmus. Invest Ophthalmol Vis Sci 2000; 41(12):3805−3017
11. Norcia AM. Abnormal motion processing and binocularity: infantile esotropia as a model system for effects of early interruptions of binocularity. Eye 1996; 10 (Pt 2):259−265
12. Dell'Osso LF. Congenital, latent and manifest latent nystagmus: similarities, differences and relation to strabismus. Jpn J Ophthalmol 1985; 29(4):351−368
13. Reinecke RD. Costenbader Lecture. Idiopathic infantile nystagmus: diagnosis and treatment. J AAPOS 1997; 1(2):67−82
14. Abadi RV, Bjerre A. Motor and sensory characteristics of infantile nystagmus. Br J Ophthalmol 2002; 86(10):1152−1160
15. Weissman BM, Dell'Osso LF, Abel LA, Leigh RJ. Spasmus nutans. A quantitative prospective study. Arch Ophthalmol 1987; 105(4):525−528
16. Shallo-Hoffmann J, Riordan-Eva P. Recognizing periodic alternating nystagmus. Strabismus 2001; 9(4):203−215
17. Weiss AH, Kelly JP. Acuity development in infantile nystagmus. Invest Ophthalmol Vis Sci 2007; 48(9):4093−4099
18. Wang ZI, Dell'Osso LF. Being "slow to see" is a dynamic visual function consequence of infantile nystagmus syndrome: model predictions and patient data identify stimulus timing as its cause. Vision Res 2007; 47(11):1550−1560
19. Hertle RW, Reese M. Clinical contrast sensitivity testing in patients with infantile nystagmus syndrome compared with age-matched controls. Am J Ophthalmol 2007; 143(6):1063−1065
20. Yang D, Hertle RW, Hill VM, Stevens DJ. Gaze-dependent and time-restricted visual acuity measures in patients with infantile nystagmus syndrome (INS). Am J Ophthalmol 2005; 139(4):716−718
21. Hertle RW, Yang D. Clinical and electrophysiological effects of extraocular muscle surgery on patients with infantile nystagmus syndrome (INS). Semin Ophthalmol 2006; 21(2):103−110
22. Hertle RW, Dell'Osso LF, FitzGibbon EJ, et al. Horizontal rectus muscle tenotomy in children with infantile nystagmus syndrome: a pilot study. J AAPOS 2004; 8(6):539−548
23. Hertle RW, Anninger W, Yang D, et al. Effects of extraocular muscle surgery on 15 patients with oculo-cutaneous albinism (OCA) and infantile nystagmus syndrome (INS). Am J Ophthalmol 2004; 138(6):978−987
24. Dell'Osso L, Hertle RW, Williams, RW, Jacobs JB. A new study for congenital nystagmus: effects of tenotomy on an achiasmatic canine. J Am Assoc Pediatr Ophthalmol Strabismus 1998; In Press:xxx
25. Hertle RW, Chan CC, Galita DA, et al. Neuroanatomy of the extraocular muscle tendon enthesis in macaque, normal human, and patients with congenital nystagmus. J AAPOS 2002; 6(5):319−327

Pediatric Eyelid Disorders

Forrest J. Ellis

19

Contents

Core Messages

- Congenital ptosis typically involves reduced function of the levator palpebrae superioris muscle.
- In children with congenital ptosis, amblyopia is common.
- When present, amblyopia is usually refractive and caused by "induced-with-the-rule" astigmatism. Occlusion amblyopia is much less common.
- Surgical repair of congenital ptosis and other pediatric eyelid abnormalities involves procedures that require special considerations and techniques that may differ from oculoplastic surgical procedures performed on adults.

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19.1 Congenital Ptosis

19.1.1 Anatomic Considerations

The normal upper eyelid margin forms a curved arch and overlies the superior 1−2 mm of the cornea. The peak of this curve is approximately 1 mm nasal to the center of the cornea. Strands from the external levator aponeurosis attach to the skin and form the upper eyelid crease [1]. In conditions with abnormal levator development, such as congenital ptosis, the upper eyelid crease is reduced or absent. The orbital septum defines the anterior boundary of the orbit and overlies orbital fat. The orbital septum is important in eyelid anatomy. In Caucasians' upper eyelids the orbital septum and levator aponeurosis fuse at approximately the superior tarsal border 10 mm above the lid margin; however, in Asian eyelids the septum inserts much lower into the levator aponeurosis resulting in inferior displacement of orbital fat and a lower eyelid crease [2]. Posterior to the levator aponeurosis is the underlying Muller's muscle.

The upper eyelid tarsus is approximately 10 mm in its vertical height in the adult and proportionately shorter in children. The medial canthal tendon attaches to the anterior and posterior lacrimal crest and the fascia of the lacrimal sac. The lateral canthal tendon attaches to the lateral border of the tarsus and to Whitnall's tubercle inside the lateral orbital rim. The normal lateral canthus is slightly above the medial canthal tendon in the horizontal plane.

The levator muscle originates from the lesser wing of the sphenoid. It runs posterior to anterior along the superior orbit. Just inside the superior orbital rim the levator muscle crosses and fuses with Whitnall's ligament, which provides support to the levator muscle and its aponeurosis. Turning inferiorly at Whitnall's ligament, the levator aponeurosis spreads out horizontally to form a fan-shaped structure. This structure attaches to the periosteum medially and laterally forming the medial and lateral horns. The levator aponeurosis also inserts broadly across the anterior surface of the upper eyelid tarsus with fine strands of the levator aponeurosis inserting into the eyelid skin and forming the eyelid crease.

Muller's muscle complex arises from the posterior aspect of the levator muscle, lies along the posterior surface of the levator aponeurosis, and inserts into the superior border of the tarsus. The superior division of cranial nerve III innervates the levator palpebrae superioris muscle, while Muller's muscle is innervated by the sympathetic nervous system.

19.1.2 Developmental Considerations

Congenital ptosis of the upper eyelid is typically seen in association with an abnormal development of the levator muscle complex. Although typically sporadic, familial ptosis is linked to chromosome 1p [3]. It is now believed that the primary defect in congenital ptosis is an abnormality in the development of a part of cranial nerve III responsible for innervation of the levator palpebrae superioris. Because the extraocular muscles require innervation to develop properly, a developmental abnormality of innervation results in a muscle with reduced muscle fibers and a variable degree of reduced levator muscle function. This is a more limited presentation of what occurs in congenital fibrosis syndrome [4, 5], where ptosis of the upper eyelid is a common component. Congenital ptosis occurs either unilaterally or bilaterally. Superior rectus muscle weakness can occur in association with congenital ptosis.

Dysfunction or interruption of the ocular sympathetic nerve causes ptosis, miosis, and anhydrosis. This triad of signs is known as Horner syndrome [6].

Ptosis of the child's upper eyelid is most often present from birth. Ptosis in the child is occasionally due to congenital myasthenia, muscular dystrophy, syndromic associations, or to acquired abnormalities such as trauma or loss of innervation to Muller's muscle. It is usually due to an isolated abnormality in the neuromuscular development of the levator palpebrae superioris; however, mechanical factors can contribute to ptosis such as relative enophthalmos following an orbital fracture. Congenital ptosis that occurs in the Marcus Gunn jaw-winking phenomenon is a result of aberrant innervation of the levator muscle with nerves normally directed to the muscles of mastication. Typically, with contralateral jaw movement the ptotic eyelid elevates. This is often noticed in infancy when the child seems to "wink" while nursing or taking a bottle (Fig. 19.1).

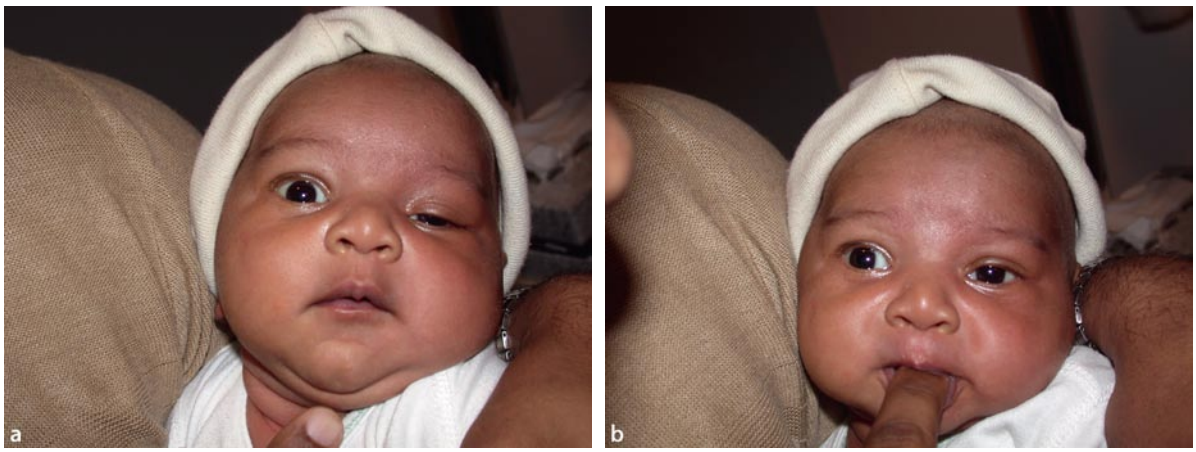

Fig. 19.1 **a** Left Marcus Gunn jaw wink ptosis. **b** Sucking results in elevation of the ptotic eyelid

19.1.3 Evaluation

Careful history should be taken as to the variability of the ptosis. While most patients with congenital ptosis report slight worsening with fatigue, this variability is typically minor and the ptosis is always present. A history of a normal eyelid position after sleep followed by significant ptosis when the patient is fatigued should raise a concern for myasthenia gravis. In the young child, sufficient cooperation to assess fatigability may not be possible. Tests, which can be performed to establish the diagnosis of myasthenia gravis, include the ice test, rest test, and the tensilon test and neostigmine tests. Tests for acetylcholine receptor antibodies are rarely positive in isolated ocular myasthenia gravis, especially in childhood. If present, acetylcholine receptor antibodies are strongly indicative of the presence of myasthenia gravis [7]. A positive tensilon test, abnormal single-fiber EMG recordings, and therapeutic responses to anticholinesterase medicines or corticosteroids establish this diagnosis. If myasthenia is strongly suspected, then a trial of mestinon or corticosteroids is indicated. All cases of acquired Horner syndrome and selected cases of congenital Horner syndrome should be evaluated for an underlying neurologic etiology, such as a neuroblastoma involving the ocular sympathetic pathway. Other causes of congenital and acquired ptosis should be considered, including third cranial nerve paresis, Kearns-Sayre syndrome (Fig. 19.2), orbital tumors and trauma.

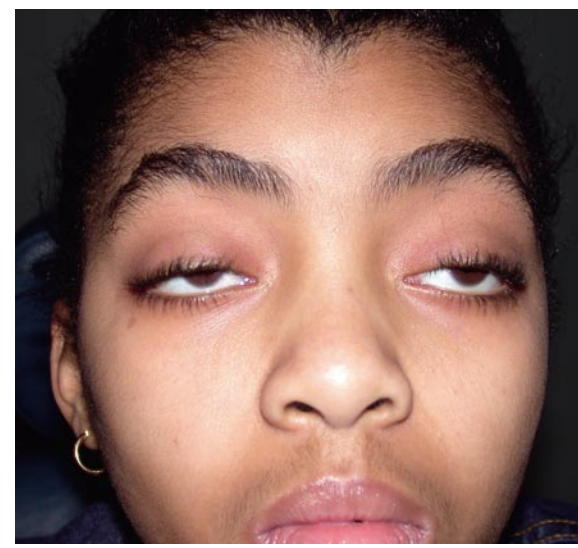

Fig. 19.2 Kearns-Sayre syndrome. Patient with severe ptosis and nearly complete external ophthalmoplegia

All patients with congenital ptosis require repeated visual acuity testing and determinations of refractive error. Frequently, amblyopia occurs due to induced astigmatism, and less commonly due to occlusion of the line of sight [8]. The presence of a chin elevation may allow for peripheral fusion but does not exclude the presence of amblyopia [9].

Treatment of uncomplicated congenital ptosis is dependent on the amount of ptosis present in the pri-

mary position, as well as the amount of levator muscle function. Patients with unilateral or bilateral ptosis often use their frontalis muscle to elevate the eyelids; therefore, it is important to position the brow in the normal position prior to measuring the amount of ptosis. The lid margin-reflex distance (MRD) should be measured. The MRD is the distance from a corneal light reflex to the upper eyelid margin with the patient's eyes in primary gaze. The amount of levator function also should be measured. This can be difficult in younger children and infants. In congenital ptosis the amount of ptosis inversely correlates with the amount of levator function. Repeated examinations help the surgeon obtain reliable measurements of the amount of ptosis and levator function. Levator function is measured by firmly fixing the brow to immobilize the frontalis muscle. The millimeters of eyelid margin movement from full downgaze to full upgaze is then determined. A full examination of the extraocular muscles should be performed. In addition to a determination of the superior rectus muscle function, one should check the Bell phenomenon (upward deviation of the eye during forced lid closure). A normal (present) Bell phenomenon is important because lagophthalmos is common following repair of congenital ptosis [10]. When superior rectus muscle function is reduced, a surgeon should be more conservative in the amount of surgery performed to correct the ptosis. Because reliable Schirmer testing is difficult in the child, examination of the tear film and careful evaluation of the cornea for any signs of exposure both pre- and postoperatively is necessary. In addition, one should determine the corneal sensitivity. Patients with diminished corneal sensitivity due to innervation abnormalities are at increased risk of exposure keratopathy following surgical correction of congenital ptosis. The surgeon should be cautious and avoid surgery or reduce the amount of ptosis correction if abnormal corneal sensitivity exists.

In addition to measuring levator function, the eyelid should be assessed with its response to phenylephrine. One drop of 2.5% phenylephrine is instilled into the lower cul-de-sac in younger children and infants. Re-measure the MRD after approximately 5 min. If the eyelid elevates to a near-normal position, tightening or resection of Muller's muscle is considered for ptosis repair.

In patients with Marcus Gunn jaw-winking ptosis, the amount of eyelid retraction with movement of the jaw should be evaluated. If significant retraction is present, extirpation of the involved levator muscle combined with a frontalis suspension should be performed. Failure to extirpate the involved levator muscle will result in persistent wink. If only mild retraction occurs, ptosis repair should be undertaken using standard amounts of surgery. An external levator resection is the usual procedure.

19.1.4 Timing of Surgical Intervention

In most situations congenital ptosis is repaired between the ages of 4 and 5 years. Occlusion amblyopia from severe ptosis is rare. When recognized, surgical repaired should be performed. Most ptosis-associated amblyopia is caused by induced astigmatism. If a significant astigmatism develops, spectacle correction and amblyopia therapy should be instituted.

19.1.5 Surgical Procedures

There are several options for the surgical management of congenital ptosis. The two main surgical procedures are the external levator resection and the frontalis suspension procedure. The Muller's muscle procedures (Fasanella Servat and Mullerectomy) may be used for the correction in mild ptosis, and works especially well in neurogenic ptosis associated with Horner syndrome.

19.1.5.1 Levator Muscle Procedures

Levator aponeurosis/muscle shortening procedures are performed in cases of mild to moderate ptosis (Fig. 19.3). Although classic levator aponeurosis dehiscence can be encountered in the pediatric population, more commonly decreased levator function and levator muscle dysgenesis is encountered. A more generous resection of the levator muscle aponeurosis is required in children than in the adult. The amount of resection is dependent on the amount of levator function measured (Table 19.1). In cases of severe congenital ptosis, supramaximal levator muscle resection can produce satisfactory eyelid height in pri-

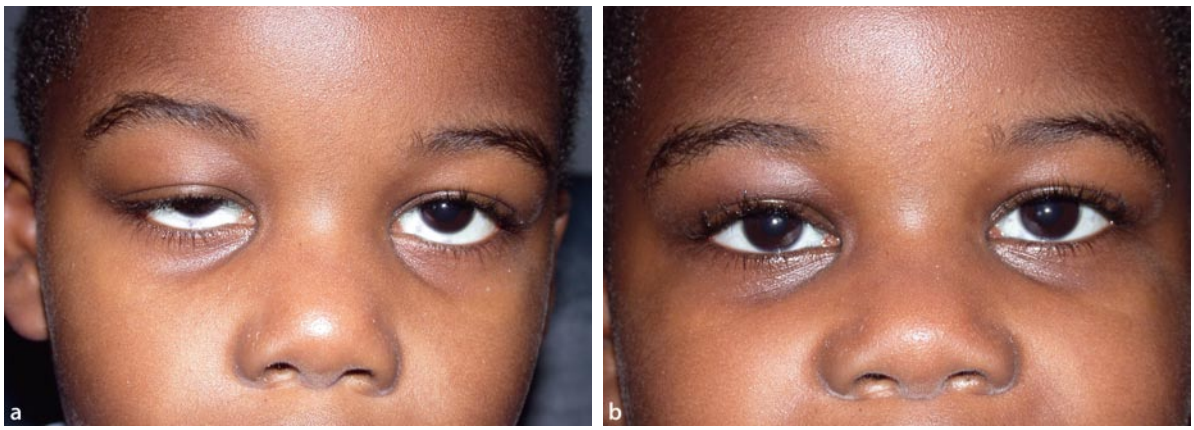

Fig. 19.3 **a** Moderate congenital ptosis of the right upper eyelid with moderate levator muscle function. **b** Improved eyelid height following 10-mm external levator muscle resection

Table 19.1 Assessment of levator function

Levator function	4-mm ptosis	3-mm ptosis	2-mm ptosis	1- to 2-mm ptosis + phenylephrine test
Poor (<4 mm)	Frontalis suspension	–	–	–
Moderate (5–7 mm)	–	ELR 17–22 mm	ELR 12–15 mm	–
Moderate (8–10 mm)	–	ELR 15–17 mm	ELR 10–12 mm	–
Good (10–13 mm)	–	–	ELR 6–9 mm	–
Excellent (>14 mm)	–	–	–	Mullerectomy

mary position; however, the lagophthalmos created by this procedure is usually much greater than that created with the frontalis suspension procedure.

The surgical approach is through the eyelid crease, dissecting through skin and then through orbital septum. The underlying levator aponeurosis is exposed beneath the preaponeurotic fat. The levator aponeurosis is separated from the tarsal plate and dissection in the plane between Muller's muscle and levator aponeurosis is carried superiorly to expose and separate the levator tendon (Fig. 19.4). In cases where a large resection is anticipated the lateral and medial horns of the aponeurosis are cut. Three partial thickness sutures are placed in the anterior tarsal surface 3–4 mm below the superior border of the tarsus. These sutures are then placed through the levator aponeurosis. Because the patient is usually under general anesthesia, the amount of resection needs to be determined prior to surgery. Sutures are tied with a single throw knot on the anterior surface of the aponeurosis and are replaced and retied until the surgeon is satisfied with the eyelid height and contour. Square knots are then tied and the levator tendon distal to the sutures is resected. The eyelid crease may be formed with separate sutures between the levator tendon and the eyelid skin, or by incorporating bites of the levator tendon into the skin closure.

19.1.5.2 Frontalis Suspension

Frontalis suspension procedures are used in unilateral or bilateral cases of severe ptosis with very poor levator function (Fig. 19.5) [11]. Autogenous fascia lata can be obtained from the leg of the child. Typically, children are 3–4 years of age before an adequate length of fascia lata is obtainable. Banked irradiated fascia lata is available; however, autogenous fascia

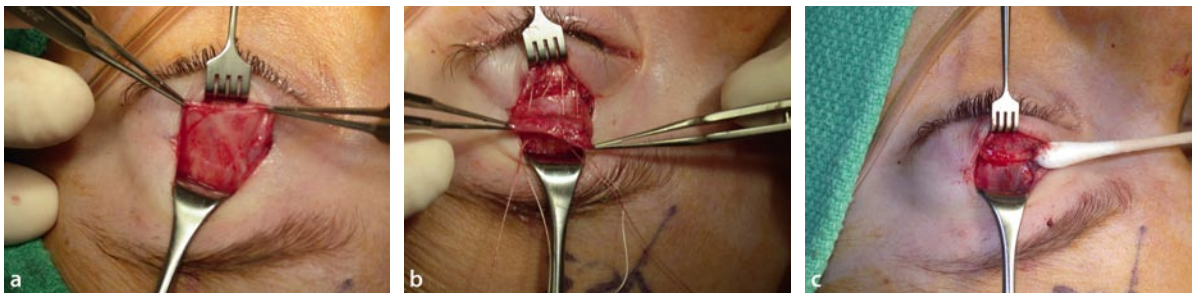

Fig. 19.4 **a** The aponeurosis of the levator muscle has been dissected off of the tarsus and underlying Muller's muscle and conjunctiva. **b** Sutures placed in the Tarsus and passed through the levator aponeurosis; Muller's muscle is seen at the superior border of the tarsus. **c** The sutures have been securely tied and distal portion of the levator aponeurosis resected

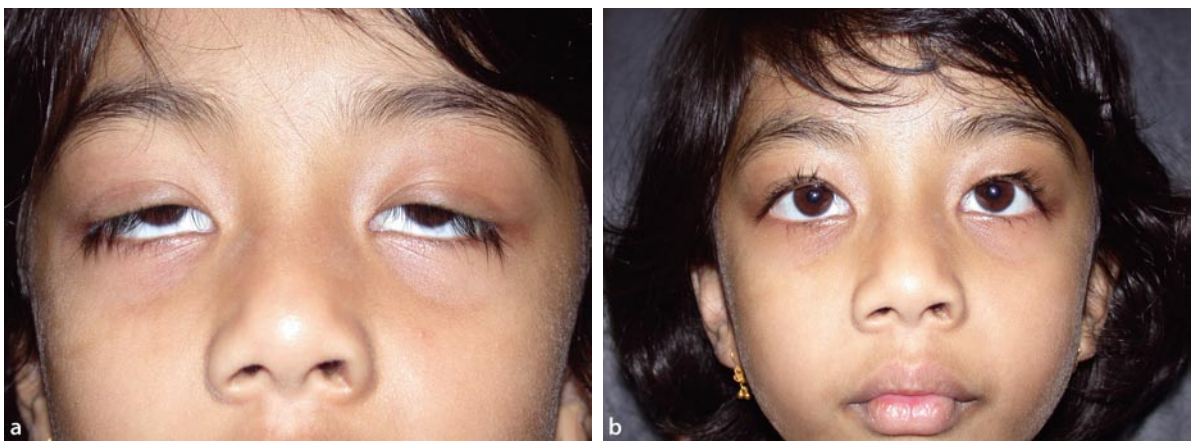

Fig. 19.5 **a** Severe bilateral congenital ptosis. **b** Improved eyelid height following bilateral frontalis suspension using the double rhomboid technique

lata has a lower rate of recurrent ptosis. Newer non-resorbing materials are available such as mersilene mesh, supramid suture, and expanded polytetrafluoroethylene (ePTFE). Synthetic supramid suture can be used for temporary elevation of the eyelid but may result in recurrent ptosis within 18 months [12]. Expanded polytetrafluoroethylene (ePTFE) is now available in strips specifically designed for use in ptosis repair (ptose-up, FCI Ophthalmics, Marshfield Hills, Mass.).

In cases of severe unilateral ptosis, bilateral frontalis suspensions have been performed in order to provide a symmetric eyelid appearance, particularly in downgaze where lagophthalmos is most notable; however, if unilateral frontalis suspension is performed and postoperative asymmetry is an issue, the fellow normal eyelid can be operated subsequently. In instances of asymmetric bilateral ptosis, requiring a frontalis suspension procedure on the more severely affected side, bilateral frontalis suspension typically results in the best cosmetic result.

The double rhomboid technique provides excellent results (Fig. 19.6). The brow of the child is the most mobile section of the forehead and allows for both adequate elevation of the eyelid as well as good closure of the eyelid. Some surgeons prefer a central knot higher on the forehead. While this provides excellent contour and suspension to the upper lid, the more fixed superior forehead does not allow as much dynamic eyelid movement.

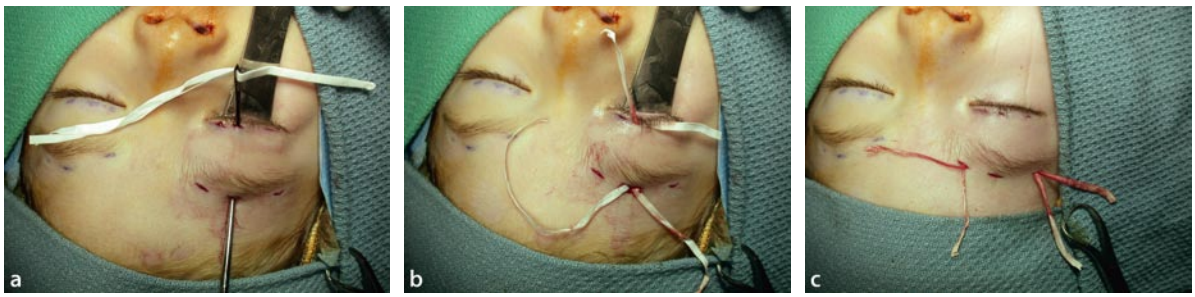

Fig. 19.6a–c Frontalis suspension using the double rhomboid technique. **a** Three brow incisions and three eyelid incisions are made. Two strips of ptose-up (FCI Ophthalmics, Marshfield Hills, Mass.) are passed using the Wright fascia needle. **b** Each strip is used to make a rhomboid. **c** Each strip of ptose-up is tied to itself, secured with a permanent suture, and then buried in the medial and temporal brow incisions

19.1.5.3 Tarsal Muller's Muscle Procedures

Tarsal Muller's muscle procedures are excellent procedures in those patients with excellent levator function and mild ptosis, especially for those patients who have a congenital or acquired Horner syndrome.

19.1.6 Complications of Ptosis Surgery

The primary complications of ptosis surgery are undercorrections, overcorrections, and lagophthalmos with exposure keratopathy. Other complications include abnormal eyelid crease, ectropion, entropion, conjunctival prolapse, infection, and bleeding. Blindness is a rare but devastating complication. Undercorrection is common in congenital ptosis, while overcorrection is unusual. Evaluation for exposure keratopathy should be performed for at all postoperative examinations. Lubrication with ointments and artificial tears is used postoperatively until the corneal examination is stable.

19.2 Other Eyelid Disorders

19.2.1 Blepharophimosis Syndrome

Blepharophimosis syndrome is an autosomal-dominant syndrome whose characteristic features include ptosis, epicanthus inversus, telecanthus, blepharophimosis (a short horizontal palpebral fissure length), and variable lower eyelid ectropion. Each of the individual abnormalities is addressed surgically, either simultaneously or at separate sessions.

19.2.2 Anophthalmos and Microphthalmos

True anophthalmos is extremely rare, and most cases of clinical anophthalmos likely represent severe microphthalmos. Microphthalmos represents a range of ocular developmental abnormalities from nearly complete absence of identifiable ocular structures to a small normally formed eye, a condition referred to as nanophthalmos. Microphthalmos often is associated with abnormal or reduced orbital bony size because the eyelid and orbital development are dependent on ocular development. Eyelid deformities also result and include a shortened horizontal palpebral fissure length. Treatment involves serial prosthetic conformers to enlarge the cul-de-sacs. In more severe cases the orbital volume can be expanded using dermis fat grafts, orbital implants, and orbital expanders [13]. Soft tissue growth parallels bone growth. Using these various techniques an acceptable cosmetic appearance is often achieved.

19.2.3 Cryptophthalmos

Cryptophthalmos is an extremely rare condition in which there is complete failure of development of the eyelid folds. A distinct feature of cryptophthalmos is failure of the brow to develop normally, resulting in fusion of the hairline and brow. This is distinct from an abnormal separation of the eyelid folds. Without development of the normal eyelid folds, the underlying cornea and conjunctiva do not normally form usually resulting in a severely malformed anterior segment of the eye. The posterior segment of the eye is sometimes disorganized. If an attempts is made to separate the eyelids, corneal transplantation to close the anterior segment defect and mucous membrane grafting to form conjunctival cul-de-sacs will usually be required. Preoperative evaluation with an electroretinogram, visual evoked potentials, imaging studies, and ultrasound provides insight into the structure and function of the underlying eye. Despite reconstructive surgery useful vision is rarely achieved. Fraser syndrome should be considered when cryptophthalmos is associated with cutaneous syndactyly, malformations of the larynx and genitourinary tract, craniofacial dysmorphism, orofacial clefting, mental retardation, and musculoskeletal anomalies [14].

19.2.4 Congenital Eyelid Coloboma

An eyelid coloboma is a congenital defect involving absence of a portion of the eyelid margin. This may occur in the upper or lower eyelid and may vary in size from a small eyelid marginal defect to a near complete absence of the eyelid. Colobomas are more common in the nasal aspect of the upper eyelid. Large colobomas can result in corneal exposure and ulceration.

Eyelid colobomas may result from abnormal migration of ectoderm and mesoderm causing an abnormal development of the eyelid margin. Colobomas may also result from a mechanical disruption of eyelid development such as seen with amniotic bands or facial clefts. Eyelid colobomas can be seen in association with other abnormalities including Goldenhar syndrome, dermoids, cleft lip, microphthalmia, and ocular coloboma.

Treatment of upper-eyelid coloboma is initially directed at maintaining lubrication and protection of the ocular surface (Fig. 19.7). Surgical correction is not emergent if adequate protection of the corneal surface is achieved. Larger coloboma may require more aggressive lubrication and perhaps occlusive dressing prior to surgical closure. For smaller colobomas surgical repair during the latter half of the first year of life is preferable to allow for tissue growth. Defects less than 25% of the horizontal width of eyelid may be directly closed after excision of the defect. The edges of the defect are excised to form a pentagonal defect and then the tarsus is closed with three interrupted absorbable sutures. The eyelid margin is closed with sutures anterior to the gray line, through the gray line, and posterior to the gray line. The skin is approximated with interrupted sutures. Larger defects up to 40% of the eyelid margin can be closed by adding a lateral canthotomy and cantholysis with medial rotation of the lid. Even larger eyelid defects require a free tarsal conjunctival graft. Eyelid-sharing procedures (Hughes procedure), which temporarily occlude the eye, are contraindicated in children because of the induced amblyopia.

19.2.5 Pseudo-Coloboma

More commonly, pseudo-colobomas of the lower lid are seen in craniofacial synostosis (Treacher–Collins syndrome). With these pseudo-colobomas the eyelid margin is intact, but there is a facial cleft laterally which results in an inferior and lateral displacement of the lower eyelid. Simple soft tissue tightening and elevation of the lateral canthal tendon is often ineffective in correcting the lateral dystopia of the eyelid because there is often an absence of vertical and horizontal eyelid tissue. For this reason transposition flaps from the upper to lower eyelids are useful in addition to re-suspension of the lateral canthal tendon.

19.2.6 Ankyloblepharon

Ankyloblepharon is a condition of failure of eyelid separation or may result from an abnormality

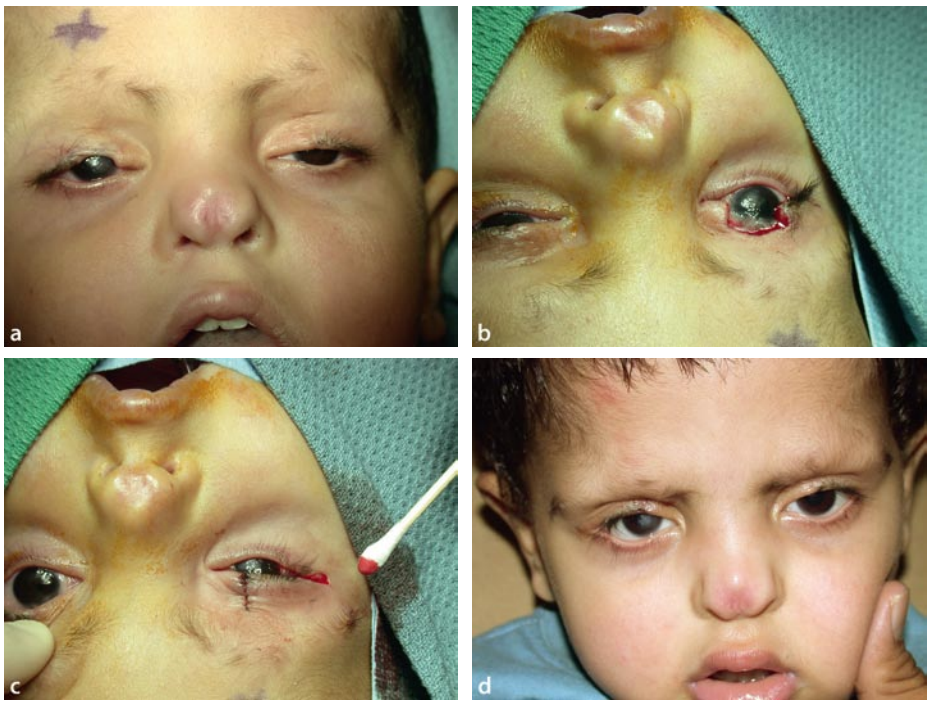

Fig. 19.7 **a** Congenital coloboma of the left upper lid with severe corneal scarring and visual loss from exposure. **b** The defect is excised to expose edges of the tarsus. **c** The tarsus and skin are re-approximated. A lateral canthotomy is required to facilitate closure of the defect. **d** Postoperative appearance

in the migration of the mesodermal elements of the eyelid. Ankyloblepharon filiforme adnatum may be isolated, demonstrating fine bands of tissue between the upper and lower eyelids, or it may be seen with trisomy 18 [15], Hay-Wells syndrome [16], or other chromosomal abnormalities [17]. The treatment of ankyloblepharon is entirely surgical. The bands of the eyelid are separated and the eyelid margins are reformed as necessary.

19.2.7 Distichiasis/Trichiasis

Distichiasis occurs when a developmental abnormality results in cilia formation in association with metaplastic meibomian glands. Although often asymptomatic, these lashes may cause superficial corneal irritation and abrasion. When acquired, distichiasis can be seen with chronic eyelid inflammations such as blepharitis, trachoma, and Stevens-Johnson syndrome.

Trichiasis refers to an acquired eyelash abnormality resulting from normally located but misdirected directed cilia. Chronic eyelid inflammation is the most common cause for trichiasis.

Treatment of eyelash abnormalities is not required in the absence of any abnormality of the corneal surface. Electrolysis or split thickness eyelid resections can be used to remove the lash follicles [18]. In addition, direct excision of the lash follicles is possible.

19.2.8 Congenital Ectropion

Congenital ectropion is rarely found in isolation. When involving the lower eyelid, it is often part of the blepharophimosis syndrome or Treacher–Collins syndrome. Also, congenital eyelid ectropion may be seen in patients with neonatal erythroderma (collodian baby) [19]. When secondary to an insufficiency in the vertical extent of the skin and orbicularis lay-

ers, a full-thickness skin graft or transfer flap is usually required in addition to a lateral tightening of the eyelid. When ectropion is associated with a shortened horizontal fissure (blepharophimosis), tightening of the lower-lid tarsus alone usually results in recurrent ectropion (Fig. 19.8).

Congenital eversion of the upper eyelid is rare and usually responds to repositioning of the eyelid and a brief course of pressure patching (Fig. 19.9) [20].

19.2.9 Congenital Entropion and Epiblepharon

Epiblepharon results from an extra fold of pretarsal lower lid skin and orbicularis, which rotates the lower eyelid cilia and margin inward. Epiblepharon is more common in Asian eyelids. Downward pressure over the excess skin allows the eyelid margin to assume a normal appearance. This condition is typically self-limiting and resolves with facial growth. Although most children are relatively asymptomatic, a small ellipse of subciliary skin and orbicularis can be removed if more significant corneal surface changes occur. Lower-lid retraction is avoided by removing only a minimal amount of skin.

Congenital lower-eyelid entropion is caused when preseptal orbicularis muscle overrides the pretarsal orbicularis muscle (Fig. 19.10). In addition, there may be laxity of the lower-lid retractors, allowing a true inward rotation of the lower eyelid. Correction requires reattachment of the lower eyelid retractors to the lower border of the tarsus, elimination of horizontal eyelid laxity when present, and resection of overriding skin and orbicularis.

Congenital horizontal tarsal kink results in entropion of the upper eyelid and may be associated with congenital levator aponeurotic disinsertion. More importantly, corneal ulceration occurs in 50% of cases [21].

19.2.10 Congenital Eyelid Retraction

Congenital eyelid retraction, especially of the lower eyelid, may occur in isolation or secondary to structural anomalies resulting in very shallow orbits and proptosis. Upper-eyelid retraction occurs transiently in some infants; however, persistent superior sclera seen in the absence of a structural cause warrants a medical evaluation for thyroid disease or neurological disease. Options to correct eyelid retraction are Mullerectomy, levator recession, and occasionally spacer grafts.

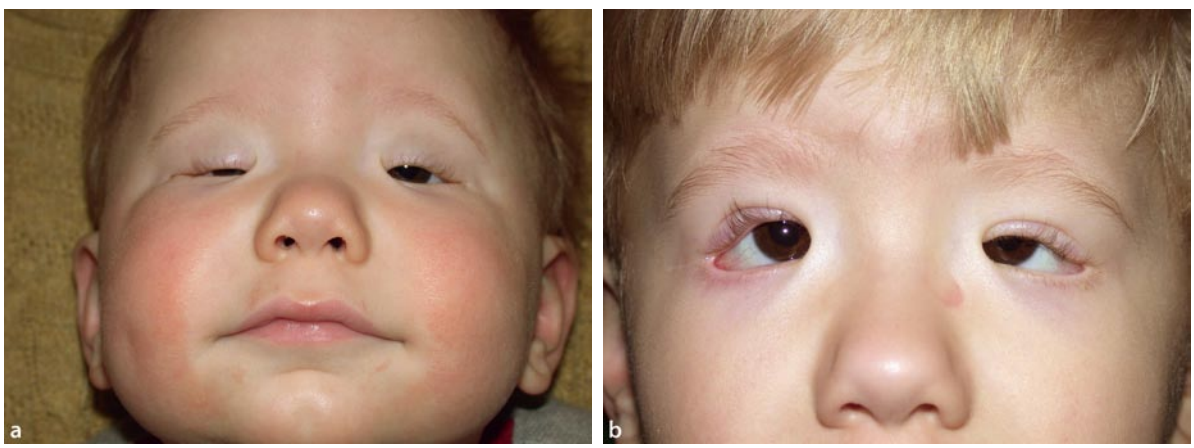

Fig. 19.8 **a** Blepharophimosis syndrome. The patient subsequently underwent bilateral frontalis suspension with supramid suture and bilateral lateral tarsal strip ectropion repair all at another institution. **b** Appearance at age 2 years. Note the more severe lower eyelid ectropion and retraction as well as the recurrent ptosis. Surgical correction will require skin grafting or tissue transfer to correct the vertical insufficiency of the lower eyelid as well as repeat frontalis suspension to correct the ptosis

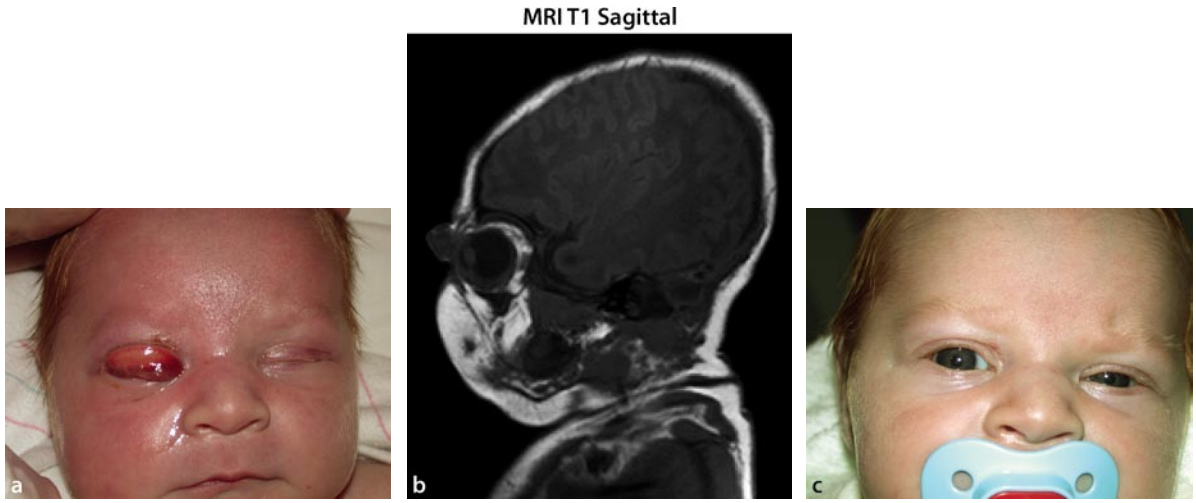

Fig. 19.9 **a** Congenital eversion of the upper eyelid associated with edema, erythema, and prolapsed supratarsal conjunctiva. The eyelid eversion persisted despite treatment with topical antibiotic/steroid and taping of the eyelid. **b** An MRI sagittal view of the affected eye, the radiologic interpretation was for a capillary hemangioma of the superior conjunctiva. **c** Appearance 2 days after intralesional steroid injection; the "lesion" and eyelid eversion did not recur

19.2.11 Euryblepharon

Euryblepharon is a condition characterized by increased vertical separation of the temporal aspect of the palpebral opening such that the palpebral conjunctiva is not in apposition with the eye. The lateral canthus is usually displaced inferiorly. Treatment requires a lateral canthoplasty as well as a skin graft into the lower lid to provide additional vertical height.

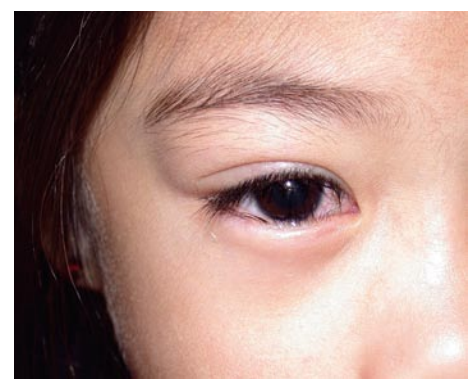

Fig. 19.10 Lower eyelid entropion with inward rotation of the eyelid margin. Note that the preseptal orbicularis muscle overrides the pretarsal orbicularis muscle

19.2.12 Epicanthus

Epicanthus consists of a fold of skin in the medial canthal region overlying the medial canthal tendon. This condition can occur in isolation or it can be associated with multiple genetic disorders such as trisomy 21 and the blepharophimosis syndrome. Epicanthal folds are generally classified as being one of four types: epicanthus supraciliaris; epicanthus inversus; epicanthus palpebralis; and epicanthus tarsalis. When severe, epicanthal folds can be corrected with a variety of techniques, including a Y−V plasty, the Mustarde [22], and Roveda procedures, all of which have been described.

19.2.13 Telecanthus

Telecanthus refers to a wide intercanthal distance. This is to be differentiated from hypertelorism, which describes an increased interorbital bony separation. Telecanthus is often associated with epicanthus and blepharophimosis. When associated with epicanthal folds, telecanthus may be corrected utilizing the same

procedures that are used to treat epicanthus; however, medial canthoplasty and/or transnasal wiring may be necessary in more severe cases.

19.3 Eyelid Neoplasia

19.3.1 Benign Lesions

19.3.1.1 Capillary Hemangioma

Capillary hemangioma is the most common eyelid and orbital tumor in the infant. It is composed of abnormal capillaries with proliferation of endothelial cells. Clinically, capillary hemangiomas present as superficial or deep lesions, and are soft and compressible. Superficial lesions have a bright-red appearance during the rapid growth phase and will blanch with compression. Deeper hemangioma may give a reddish or purple hue to the overlying skin. (Fig. 19.11). These neoplasms rapidly enlarge during the first several months of life and may continue to enlarge until 18 months of age. Rapid enlargement may lead to areas of necrosis or ulceration as the lesion outgrows its blood supply (Fig. 19.12). Most hemangiomas regress completely without residua. Involution typically occurs slowly and is complete by 3−7 years of age. During the involution the tumor color slowly changes to gray and the surface epithelium changes to a more normal skin appearance; however, residual skin thinning and wrinkles may occur.

Hemangiomas of the cervicofacial region may be a part of the PHACES syndrome. This includes hemangiomas in association with posterior fossa malformations, arterial anomalies, cardiac anomalies, eye anomalies, and sternal and abdominal clefting.

While larger tumors can cause occlusion amblyopia, refractive amblyopia from induced astigmatism is more common. As little as 1.5 diopters of astigmatism increases the risk of amblyopia [23]. Spectacle correction is frequently required along with amblyopia therapy.

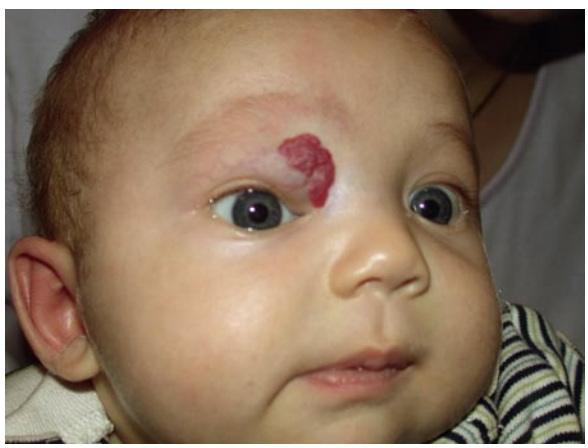

Fig. 19.11 Periocular capillary hemangioma. The most superficial components are bright red. The deeper portions of the tumor (inferior and temporal) impart a gray hue to the overlying eyelid skin

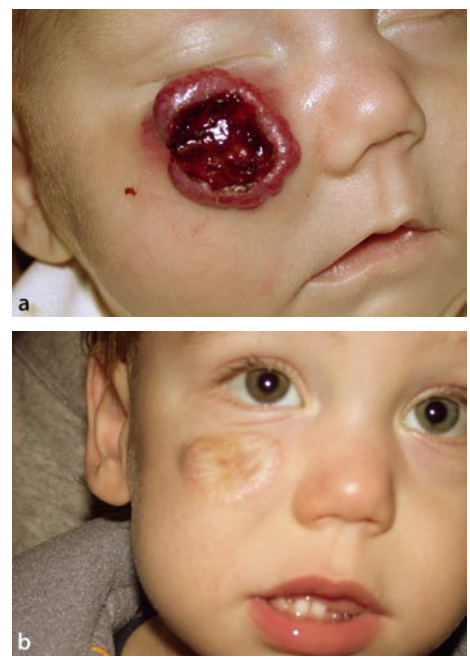

Fig. 19.12 **a** Extremely rapid growth of this capillary hemangioma resulted in central necrosis. **b** The same patient 2 years later. Treatment modalities included oral and topical steroids as well as superficial laser ablation

19.3.1.1.1 Evaluation

For larger lesions and lesions involving the orbit, or when the hemangioma appearance is not typical, CT or MRI are valuable imaging techniques. The CT scanning demonstrates an enhancing soft tissue lesion with irregular borders. The MRI is often better at differentiating capillary hemangioma from lymphangiomas. The MRI scanning may show the "chocolate" cyst of lymphangiomas that are not typical of capillary hemangiomas.

19.3.1.1.2 Management

Most commonly, observation alone is all that is required as these lesions typically involute spontaneously. Periocular capillary hemangiomas are more problematic, as they have a higher incidence of amblyopia and eyelid deformities. In cases of occlusion amblyopia from large periocular hemangiomas, more aggressive intervention needs to be considered. Options to slow the growth or decrease the size of a periocular capillary hemangioma include intralesional corticosteroids, oral corticosteroids, topical corticosteroids, superficial laser ablation, surgical excision, and systemic alpha interferon. Pulsed tunable dye laser (PDL) is effective for bleeding or ulcerated hemangiomas; however, a randomized trial showed no benefit to early PDL treatment in preproliferative or early proliferative capillary hemangiomas [24]. If fact, patients treated with laser showed greater skin atrophy and depigmentation. In general, corticosteroid therapy is the primary modality used in the medical treatment of hemangiomas. Intralesional corticosteroid injections for periocular capillary hemangiomas were described by Kushner [25]. Typically, a combination of long-acting and short-acting corticosteroids is injected in one or multiple sites into the lesion. The total steroid dosage per injection should be in the range of 3−5 mm/kg [26]. Following injection with both long-acting and short-acting steroid agents, a repeat injection may be required in 4−6 weeks. If short-acting agents are used in isolation, then subsequent injections, if necessary, may be repeated at 2- to 4-week intervals. Complications of steroid injection include eyelid necrosis, subcutaneous fat atrophy, and very rarely, central retinal artery occlusion [26, 27]. The potential complication of retinal artery occlusion is extremely rare and might be minimized by injecting under low pressure, reducing the chance of retrograde flow of particulate steroid material. In addition, direct intravascular injection should be avoided. Additional complications that have been described include adrenal suppression [28]. The pediatricians and the parents should be warned of this potential complication. Consideration should be given to measurement of circulating glucocorticoids. Despite these concerns, Addisonian crisis has not been reported following steroid injection for capillary hemangioma. Oral corticoid steroids are used as either a primary modality by many practitioners or a secondary modality when intralesional steroid injections have produced little benefit. Oral corticosteroids are administered at 1−4 mg/kg every 1 or 2 days. The length of treatment depends on the size and response of the tumor. In general, this may last for 6−12 weeks with a tapering of the steroid dosage.

Alternatives therapies include topical clobetasol propeniate [29]. In more systemic life-threatening hemangiomas alpha interferon has been used; however, significant side effects, including neutropenia and neurological toxicity, have been reported.

Finally, surgical excision of hemangiomas has been advocated for select cases [30]. This may be better for small isolated lesions rather than large diffuse lesions. Excision is particularly useful for those lesions that are very anterior and well circumscribed. Since hemangiomas interdigitate with normal eyelid structures surgical excision must be done with particular attention to the anatomy in order to avoid the creation of secondary problems such as ptosis. More commonly, surgery involving correction of eyelid crease abnormalities, ptosis, eyelid contour abnormalities, or removal of excessive skin is utilized once regression of the hemangioma has occurred.

19.3.1.2 Lymphangioma

Lymphangioma is a tumor that presents in a fashion similar to that of capillary hemangioma but does not undergo spontaneous involution. While more commonly involving the orbit, it can present as a mass of the eyelid or conjunctiva. Lymphangioma are composed of endothelial-lined channels, collections of lymphocytes, and occasional blood-filled cysts. These lesions may increase in size with upper respi-

ratory tract infections. More dramatic enlargement occurs with hemorrhage into a cyst. Management is challenging, as complete surgical resection is rarely possible. Use of the CO_2 laser facilitates the surgical excision of these lesions. Unlike capillary hemangiomas, corticosteroids are ineffective in the management of lymphangiomas.

19.3.1.3 Nevus Flammeus/Port-wine stain/Sturge-Weber syndrome

This congenital, non-progressive vascular lesion is present from birth and does not spontaneously involute. This cavernous hemangioma is typically unilateral and most commonly occurs in the distribution of the fifth cranial nerve. When the upper eyelid is involved, ipsilateral glaucoma and diffuse choroidal hemangiomas should be suspected. Likewise, ipsilateral leptomeningeal hemangiomas may occur. The cutaneous component may be treated with laser or with cosmetics.

19.3.1.4 Periocular Dermoid Cysts

Dermoid cysts occur most commonly in the periocular region overlying the fronto-zygomatic suture, fronto-lacrimal, or fronto-maxillary sutures. These cysts are firm, smooth, non-tender masses present from birth. The skin overlying the cysts is freely mobile and the cyst is usually affixed to bone. Enlargement is typically slow. Rupture secondary to trauma can expose the cystic contents to the subcutaneous tissue and result in significant inflammation and permanent scarring. A CT scan demonstrates the dermoid cyst to be a characteristically well-demarcated lesion. The surrounding bone frequently shows some molding around the cyst. Occasionally, a lateral dermoid cyst may have a barbell appearance with an intraorbital and extraorbital component. A CT scan is not necessary unless an internal cystic component is suspected.

Treatment of dermoid cysts involves surgical excision performed at about 1 year of age (Fig. 19.13). With increasing mobility the risk of traumatic rupture increases. Care should be taken to avoid rupture of the dermoid cyst during surgery. If rupture occurs, attempt to completely remove the contents of the cyst and the cyst capsule. Remnants of the dermoid can cause significant inflammatory reaction with fibrosis and scarring. Excision may be approached through either the eyelid crease incision or a sub or supra-brow incision.

19.3.1.5 Plexiform Neuroma

Plexiform neuroma is most often seen in the setting of neurofibromatosis type 1, causing an S-shaped deformity of the upper eyelid. The lid may have a bag-of-worms sensation to palpation. Plexiform neuroma interdigitate with normal tissues and enlarge with age. Surrounding bone may show absence or hypoplasia of the greater wing of the sphenoid. This tumor frequently causes mechanical ptosis, astigmatism, and amblyopia. If significant ptosis or induced astigmatism is present, surgical debunking of the tumor may be necessary; however, gradual recurrence is expected.

19.3.1.6 Nevi

The nevus develops as a benign proliferation of the epidermal melanocytes and can be congenital or acquired. Due to the fusion of the eyelids during fetal development, a nevus may be present on corresponding areas of both the upper and lower lids (kissing nevus). Surgical excision for improved cosmesis or due to concern for malignant transformation may be considered.

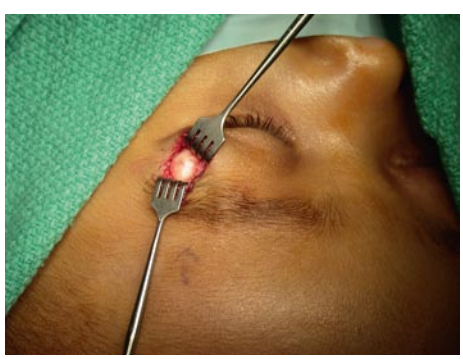

Fig. 19.13 Surgical excision of a periocular dermoid cyst

One form of congenital pigmentation is that of oculodermal melanocytosis (nevus of Ota). The skin as well as the ocular surface and conjunctiva have a slate-gray pigmentation. The uvea of the affected eye may also have increased pigmentation. While more common in Asians, when seen in Caucasians there is an increased risk of uveal melanoma.

A type of nevus that is of greater concern is the giant hairy nevi. Prophylactic excision of these nevi is recommended because of the 5% risk of malignant transformation [31].

19.3.1.7 Pilomatrixoma

Pilomatrixoma is a benign proliferation of hair matrix cells. These lesions tend to occur in children and have the appearance of a solid subcutaneous nodule.

19.3.1.8 Juvenile Xanthogranuloma

Juvenile xanthogranuloma is a proliferation of non-Langerhans' cell histiocytes. These lesions in the skin are yellow-red rounded papules and nodules. When they occur on the iris they may be associated with spontaneous (non-traumatic) hyphema. Since spontaneous resolution does occur, surgical excision of skin lesions is rarely necessary.

19.3.1.9 Chalazia

Chalazia are common lesions of the pediatric eyelid. A chalazion results when obstruction of a meibomian gland occurs, resulting in rupture of the oil gland into the surrounding soft tissue forming a pseudocyst. The inflammatory reaction creates an erythematous nodule in the eyelid. Typical treatment includes warm compresses and eyelid hygiene. Topical antibiotic ointment may be used in combination with topical corticosteroids to reduce the inflammatory component of the chalazion. Intralesional corticosteroids are sometimes used. Care should be taken to avoid steroid injection into darkly pigmented skin, as this may cause a focal area of hypopigmentation. For persistent chalazia, where the inflammatory process is quiescent, incision and drainage may be necessary. For younger children this is usually done under general anesthesia.

19.3.1.10 Milia

Mlia are cystic accumulations of keratin within the pilosebaceous units. These are extremely common in neonates and usually regress in the first 3–4 weeks of life. No treatment is required.

19.3.1.11 Pyogenic Granuloma

Pyogenic granuloma are bright red friable papules or nodules that and may occur on any cutaneous or mucosal surface. Periocular pyogenic granuloma is usually associated with prior ocular injury, surgery, and trauma, or in association with a chalazion. Larger lesions are simply excised and the base cauterized. Smaller lesions may respond to topical corticosteroids.

19.3.1.12 Syringoma

Syringomas are benign tumors of the eccrine duct structures. They are 1- to 3-mm translucent papules most commonly seen on the lower eyelid. The incidence is increased in Down's syndrome.

19.3.1.13 Xantholasma

Xantholasma are typically yellow-colored papules and plaques seen on the upper eyelids near the medial canthus. While rare in children, any child with xantholasma deserves an evaluation for disorders of lipid metabolism.

19.3.2 Malignant Lesions

19.3.2.1 Basal Cell Carcinoma

Malignant eyelid lesions are rare in the childhood. Basal cell carcinoma has been reported on the eyelids of children, but usually in association with nevus sebaceous, xeroderma pigmentosa, or basal cell nevus syndrome.

Basal cell nevus syndrome is an autosomal-dominant disorder with features that include jaw cysts, rib and vertebral abnormalities, calcification of the

falx cerebri, agenesis of corpus callosum, palmer and plantar pits, ovarian fibromas, cardiac fibromas, and medulloblastomas. Ocular features may include cataracts, glaucoma, coloboma, microphthalmia, and strabismus.

19.3.2.2 Squamous Cell Carcinoma

Squamous cell carcinoma is rare is children and is most typically seen in patients with xeroderma pigmentosa. Xeroderma pigmentosa is an autosomal-recessive disorder characterized by defective DNA repair under conditions of UV exposure.

19.4 Infectious Eyelid Disorders

19.4.1 Preseptal Cellulitis

A common infectious eyelid disorder in children is preseptal cellulitis. Preseptal cellulitis is limited to the skin and subcutaneous tissues anterior to the orbital septum. While the outcome is typically good in preseptal cellulitis, systemic sepsis and meningitis can occur. Preseptal cellulitis may be secondary to sinus infection, upper respiratory tract infections, or trauma. Occasionally, preseptal cellulitis can result from an infection of a chalazion or spread from dacryocystitis. Patients with proptosis, pupillary changes, and limited extraocular motility should be evaluated for orbital cellulitis. Treatment of preseptal cellulitis includes antibiotics and surgical drainage of abscesses. If a foreign body is suspected, then surgical removal of the foreign body is necessary for the infection to clear.

Necrotizing fasciitis is an infection caused by aerobic or anaerobic microorganisms, which spread rapidly through soft tissues. This condition has a high mortality rate. In the setting of necrotizing fasciitis aggressive surgical debridement and broad-spectrum antibiotics are necessary.

19.4.2 Blepharitis

Chronic blepharitis is common in children. Inflammation of the glands of the eyelid margin occurs with collarettes and crusting on the cilia. Secondary corneal vascularization and scarring can result. Treatment consists of warm compresses, lid hygiene with baby shampoo scrubs, and topical antibiotics. Treatment is continued for several weeks. Blepharitis may be chronic in children, despite treatment. Oral erythromycin has been effective in children with severe blepharokeratitis [32]. Oral tetracycline, minocyline, and doxycyline, while effective in adult blepharitis, are avoided in children due to the risk of dental enamel discoloration.

19.4.3 Herpes Simplex

When primary herpes simplex occurs in children it is usually asymptomatic. Periocular involvement in primary herpes simplex usually manifests as vesicles on the eyelid margin. This infection is self-limiting, but topical antibiotics may be used to prevent secondary bacterial infection. Latent herpetic infection may persist throughout life and be activated by many nonspecific stimuli. The most common ocular manifestation involves the cornea, but the lids may be involved in a recurrent infection. Herpetic blepharitis is characterized by the formation of yellow-crusted skin vesicles. Treatment involves the systemic administration of antiviral agents.

19.4.4 Herpes Zoster

Herpes zoster ophthalmia is unusual in childhood, but the upper or lower lids may be involved if the first or second division of the trigeminal nerve is affected. Vesicles along the side and tip of the nose should alert the clinician to the possibility of keratitis and uveitis. Systemic treatment with antiviral agents is used along with topical antibiotics to prevent secondary bacterial skin infections.

19.4.5 Molluscum Contagiosum

Molluscum contagiosum is a disorder caused by a poxvirus. The lesions are 2- to 4-mm papules and may be isolated or multiple. When present on the eyelids

they can be associated with a chronic follicular conjunctivitis. Infection with this agent is self-limiting and resolves in 6−18 months. When conjunctivitis is associated with molluscum contagiosum, the molluscum lesions near the lid margins should be excised or curetted. Asymptomatic children do not necessarily need treatment.

19.4.6 Pediculosis

Louse infections of the lids cause severe itching and irritation. The pubic louse has an affinity for the eyelids. Diagnosis is made easily on slit lamp examination when the ova and adult crab louse is observed. Treatment consists of improving the patient's personal hygiene and application of bland antibiotic ointment that suffocates the louse. Head and body antilouse shampoos are used along with home hygiene measures.

19.4.7 Contact Dermatitis

The skin of the eyelids may resemble crepe paper but becomes markedly erythematous and swollen after contact with inciting agents. Common irritants include topical medications (e.g., atropine), cosmetics, nail polish, soaps, poison ivy, and sumac. Treatment consists of removal of the inciting substance. Symptomatic relief may be obtained by using systemic antihistamines and local corticosteroid preparations.

19.5 Eyelid Trauma

In any child who has sustained a periocular injury the nature and history of the trauma should be elicited to the fullest extent possible. Blunt trauma with periocular ecchymosis will require careful evaluation of the eye and orbital structures. Apparently minor periocular trauma may be associated with orbital fractures and muscle entrapment in children [33, 34]; therefore, ocular motility testing should assessed and appropriate imaging studies performed when necessary. A thorough eye examination including a retinal examination should be included in the evaluation, as the history of the injury may be inconsistent with the physical findings.

19.5.1 Eyelid Lacerations

Simple eyelid skin lacerations where a foreign body is not present and which do not involve the eyelid margin should be closed directly. Only the skin is closed and care is taken to avoid vertical eyelid skin tension that can create eyelid retraction and abnormal eyelid contour. The orbital septum need not be closed for the same reason. Even in severe injuries, such as seen with dog bites, it is rare to have missing eyelid skin.

In cases where the lid margin has been violated the tarsus is closed primarily and followed by skin closure. In full-thickness eyelid lacerations, the tarsus is closed with interrupted 6-0 absorbable sutures. These are preplaced and positioned such that a slight eversion of the lid margin occurs when these sutures are securely tied. In the younger child, closure of the lid margin is performed with absorbable interrupted sutures.

Medial canthal reconstruction with canalicular reconstruction can be managed with a silastic intubation of the canalicular system (Fig. 19.14). Careful inspection utilizing cotton-tipped applicators to retract the injured tissues will typically reveal the medial portion of the lacerated canaliculus that is recognized by the glistening epithelium. Avoid grasping the lacerated medial canthal area with toothed forceps when searching for the torn edge of the canaliculus. Once located, silastic intubation of the torn canaliculus is performed. Once the tube is in place the epithelium of the canaliculus is closed with at least two 6-0 vicryl sutures. Monocanalicular tubes self-seat in the punctum and do not require intranasal suture fixation. Similarly, a bicanalicular tube can be secured to itself within the lacrimal sac, thus avoiding intranasal fixation. Usually these tubes are removed in the office after 4−6 months.

19.5.2 Burn Injuries

Burns may result from caustic chemical exposure or from thermal injuries. Lye burns are more serious than acid burns. While base (alkali) penetrates deeply

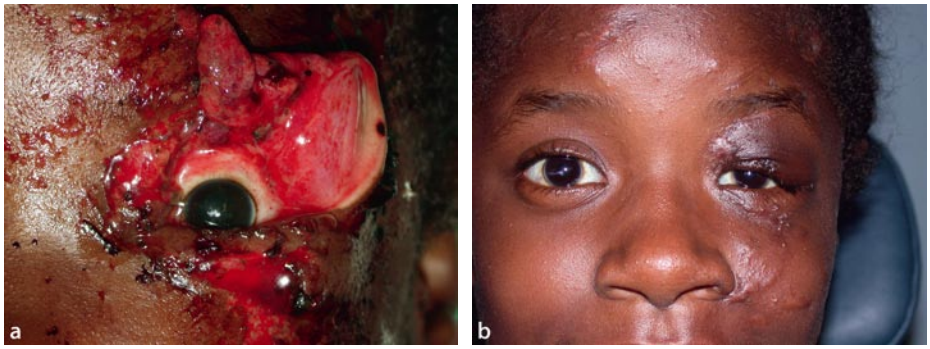

Fig. 19.14 **a** Severe upper eyelid avulsion and lower eyelid laceration. Child was thrown from a moving vehicle. **b** Appearance following medical canthal reconstruction, upper and lower eyelid canalicular repair, and repair of multiple skin lacerations. Residual ptosis was present and required further surgery. The corneal scarring on the right eye is due to the trauma

by causing protein dissolution, acid burns cause protein coagulation, which limits the depth of acid penetration. The immediate treatment of chemical burns is thorough lavage with water or saline. The cul-de-sacs should be included in the irrigation and all particulate matter should be removed. Scarring may lead to lagophthalmos, entropion, or ectropion. If scarring and contracture are severe, surgical lysis of the adhesions, excision of the scar tissue, and full-thickness skin grafting may be necessary.

Take Home Pearls

- When levator muscle function is less than 4 mm, frontalis muscle suspension procedures are usually preferred.
- Lagophthalmos is often more severe following large levator muscle resections compared with frontalis muscle suspensions.
- Congenital ptosis may be associated with reduced superior rectus muscle function. Testing the Bell's reflex (superior deviation of the eye with forced eyelid closure) is easily observed when instilling dilating eye drops.
- The more ptotic eyelid usually does not close as much as the normal eyelid. The ptotic eyelid often appears more open under general anesthesia. Marking the affected eyelid in the preoperative area avoids wrong-site surgery.
- Eyelid sharing procedures are avoided in children with eyelid defects (colobomas) because of the risk of occlusion amblyopia.

References

1. Dortzbach RK, Sutula FC. Involutional blepharoptosis. A histopathological study. Arch Ophthalmol 1980; 98(11):2045–9
2. Jeong S, Lemke BN, Dortzbach RK, Park YG, Kang HK. The Asian upper eyelid: an anatomical study with comparison to the Caucasian eyelid. Arch Ophthalmol 1999; 117(7):907–12
3. Engle EC, Castro AE, Macy ME, Knoll JH, Beggs AH. A gene for isolated congenital ptosis maps to a 3-cM region within 1p32-p34.1. Am J Hum Genet 1997;60(5):1150–7
4. Engle EC. The molecular basis of the congenital fibrosis syndromes. Strabismus 2002; 10(2):125–8
5. Heidary G, Engle EC, Hunter DG. Congenital fibrosis 5of the extraocular muscles. Semin Ophthalmol 2008; 23(1):3–8
6. Jeffery AR, Ellis FJ, Repka MX, Buncic JR. Pediatric Horner syndrome. J AAPOS 1998; 2(3):159–67
7. Anlar B. Juvenile myasthenia: diagnosis and treatment. Paediatr Drugs 2000; 2(3):161–9
8. Harrad RA, Graham CM, Collin JR. Amblyopia and strabismus in congenital ptosis. Eye 1988; 2 (Pt 6):625–7
9. McCulloch DL, Wright KW. Unilateral congenital ptosis: compensatory head posturing and amblyopia. Ophthal Plast Reconstr Surg 1993; 9(3):196–200
10. Carter SR, Meecham WJ, Seiff SR. Silicone frontalis slings for the correction of blepharoptosis: indications and efficacy. Ophthalmology 1996; 103(4):623–30
11. Crawford JS. Repair of ptosis using frontalis muscle and fascia lata. Trans Am Acad Ophthalmol Otolaryngol 1956; 60:672
12. Liu D. Blepharoptosis correction with frontalis suspension using a supramid sling: duration of effect. Am J Ophthalmol 1999; 128 (6):772–3
13. Gossman MD, Mohay J, Roberts DM. Expansion of the human microphthalmic orbit. Ophthalmology 1999; 106(10):2005–9
14. Slavotinek AM, Tifft CJ. Fraser syndrome and cryptophthalmos: review of the diagnostic criteria and evidence for phenotypic modules in complex malformation syndromes. J Med Genet 2002; 39(9):623–33
15. Tuysuz B, Ilikkan B, Vural M, Perk Y. Ankyloblepharon filiforme adnatum (AFA) associated with trisomy 18. Turk J Pediatr 2002; 44(4):360–2
16. McGrath JA, Duijf PH, Doetsch V, et al. Hay-Wells syndrome is caused by heterozygous missense mutations in the SAM domain of p63. Hum Mol Genet 2001; 10(3):221–9
17. Weiss AH, Riscile G, Kousseff BG Ankyloblepharon filiforme adnatum. Am J Med Genet 1992; 42(3):369–73
18. Vaughn GL, Dortzbach RK, Sires BS, Lemke BN. Eyelid splitting with excision or microhyfrecation for distichiasis. Arch Ophthalmol 1997; 115(2):282–4
19. Niemi KM, Kanerva L, Kuokkanen K, Ignatius J. Clinical, light and electron microscopic features of recessive congenital ichthyosis type I. Br J Dermatol 1994; 130(5):626–33
20. Watts MT, Dapling RB. Congenital eversion of the upper eyelid: a case report. Ophthal Plast Reconstr Surg 1995; 11(4):293–5
21. Sires BS. Congenital horizontal tarsal kink: clinical characteristics from a large series. Ophthal Plast Reconstr Surg 1999; 15(5):355–9
22. Mustarde JC. The treatment of ptosis and epicanthal folds. Br J Plast Surg 1959; 12:252
23. Weakley DR Jr. The association between nonstrabismic anisometropia, amblyopia, and subnormal binocularity. Ophthalmology 2001; 108(1):163–71
24. Batta K, Goodyear HM, Moss C, Williams HC, Hiller L, Waters R. Randomised controlled study of early pulsed dye laser treatment of uncomplicated childhood haemangiomas: results of a 1-year analysis. Lancet 2002; 360(9332):521–7
25. Kushner BJ. The treatment of periorbital infantile hemangioma with intralesional corticosteroid. Plast Reconstr Surg 1985; 76(4):517–26
26. Drolet BA, Esterly NB, Frieden IJ. Hemangiomas in children. N Engl J Med 1999; 341(3):173–81
27. Kushner BJ. Hemangiomas in children. N Engl J Med 1999; 341(26):2018
28. Goyal G, Watts P, Lane CM, et al. Adrenal suppression and failure to thrive after steroid injections for periocular hemangioma. Ophthalmology 2004; 111:389–95
29. Cruz OA, Zarnegar SR, Myers SE. Treatment of periocular capillary hemangioma with topical clobetasol propionate. Ophthalmology 1995; 102(12):2012–5
30. Plager DA, Snyder SK. Resolution of astigmatism after surgical resection of capillary hemangiomas in infants. Ophthalmology 1997; 104(7):1102–6
31. Lorentzen M, Pers M, Bretteville-Jensen G. The incidence of malignant transformation in giant pigmented nevi. Scand J Plast Reconstr Surg 1977; 11(2):163–7
32. Meisler DM, Raizman MB, Traboulsi EI. Oral erythromycin treatment for childhood blepharokeratitis. J AAPOS 2000; 4(6):379–80
33. Jordan DR, Allen LH, White J, Harvey J, Pashby R, Esmaeli B. Intervention within days for some orbital floor fractures: the white-eyed blowout. Ophthal Plast Reconstr Surg 1998; 14(6):379–90
34. Criden MR, Ellis FJ. Linear nondisplaced orbital fractures with muscle entrapment. J AAPOS 2007; 11(2):142–7

Pediatric Lacrimal Disorders

Gregg T. Lueder

20

Contents

Core Messages

- Nasolacrimal duct obstruction (NLDO) is one of the most common abnormalities in pediatric ophthalmology.
- NLD often resolves spontaneously.
- The symptom that is most useful in distinguishing NLDO from other causes of epiphora is the lack of photophobia.
- In-office probing of younger patients with NLDO and operating room probing of older patients are acceptable treatments.
- Recognition of different types of NLDO is useful in guiding management:
  - Most NLDO is due to membranous obstruction of the distal NLD and is relieved with simple NLD probing.
  - Some children with NLDO have diffuse stenosis of the distal NLD, which may require more than simple probing to treat effectively (either balloon catheter dilation or stents).
  - A small number of children with NLDO (particularly infants with mucoceles) have cysts or other abnormalities of the distal NLDO.
- Nasal endoscopy is a useful adjunct to treatment of children with complicated NLDO.

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20.1 Epidemiology, Etiology, and Natural History

Nasolacrimal obstruction (NLDO) is one of the most common problems encountered in pediatric ophthalmology, affecting approximately 6% of newborns [10]. The tears are produced in the lacrimal gland, flow across the eye to the lacrimal puncta, travel through the lacrimal sac and duct, and empty into the nares beneath the inferior turbinate. Embryologically, the distal lacrimal system develops from a solid sheet of ectodermal tissue that projects into the nasolacrimal groove between the frontonasal and lacrimal prominences in the 42-day-old embryo [4, 33]. Canalization of this tissue, which begins on day 60, results in formation of the lacrimal sac and nasolacrimal duct. The most common site of obstruction in NLDO is at the valve of Hasner, where the nasolacrimal ducts enter the nares. It usually results from incomplete canalization, rather than acquired obstruction, of the distal duct.

Two primary signs result from NLDO. The first sign is epiphora. Because the tears are unable to pass through the duct, they back up (in similar fashion to a clogged pipe) through the lacrimal system to the tear lake on the eyelid. Marked blockage results in frank epiphora, with tears spilling spontaneously onto the cheeks. This may appear as if the infant is crying. Milder blockage may produce an increased tear lake (which gives the appearance that the infant is about to start crying) with intermittent epiphora. The epiphora is usually exacerbated by conditions that stimulate tear production, such as cold weather or brisk winds. The second sign is chronic discharge and periocular crusting. This results from bacterial infection of the lacrimal sac. Bacteria from normal flora are present in the tears, but they usually do not cause infection because they are rinsed through the lacrimal system into the nares. Patients with NLDO have stasis of tears in the lacrimal sac, producing an environment conducive to bacterial growth. The typical infection has the appearance of a low-grade, chronic dacryocystitis. Both epiphora and dacryocystitis are exacerbated by upper respiratory infections, due to swelling of the nasal mucosa that worsens the obstruction of the distal duct. Except for newborns with nasolacrimal duct cysts (see below), affected patients do not have swelling or erythema overlying the lacrimal sac. If the NLDO is marked, patients may develop erythema and maceration of the skin around the eyes.

Interestingly, most infants with NLDO do not appear to be particularly bothered by their disorder. With the exception of patients who have skin irritation due to marked obstruction, parents usually report that their affected infants only intermittently rub their eyes. The history is important, because if the parents describe significant photophobia, one should look for other etiologies of epiphora. Corneal abnormalities in particular may cause increased tear production. Glaucoma is the most important entity that may be mistaken as NLDO by primary care physicians, who may attribute the epiphora that occurs in glaucoma to NLDO. Glaucoma is usually easily ruled out by an ophthalmologic examination that includes evaluation of corneal size and clarity, measurement of intraocular pressure, and examination of the optic nerves. Another disorder in the differential diagnosis of NLDO, particularly in Asian children, is epiblepharon with corneal irritation due to misdirected eyelashes. Children with this condition often produce excess tears, and may also have a mucoid discharge; therefore, inspection of the lid margins should be included in the evaluation of children with suspected NLDO.

The natural history of NLDO is one of spontaneous resolution. The symptoms usually begin within the first few weeks of life, and most infants improve within the first few months. This continues during the first 9−12 months of life, with resolution of symptoms in approximately 90% of infants [29]. At around 9−12 months of age, however, most studies show that the rate of spontaneous improvement decreases [27].

20.2 Conservative Management

Because most infants with NLDO spontaneously improve, the initial treatment should be conservative. Most primary care physicians are familiar with NLDO, and the initial treatment is done under their direction. Infants with mild symptoms often require no treatment at all. If the symptoms are more significant, treatment options include nasolacrimal massage, topical antibiotics, or both.

If topical antibiotics are used, it is important that parents understand that the antibiotics will not cure the obstruction, and that it is common for symptoms

to recur when the antibiotics are stopped. Antibiotics may be used intermittently to decrease ocular crusting and discharge, until either the obstruction spontaneously resolves or the child undergoes surgery.

The concept behind lacrimal massage is that compression of the tear sac causes fluid to be forced through the lacrimal duct, which may cause the obstruction to open by hydraulic pressure [6]. Although commonly recommended, the effectiveness of lacrimal sac massage has never been proven. This is because the natural history of NLDO is one of spontaneous improvement, so that any intervention performed early in the course of disease could mistakenly be interpreted as being beneficial; however, there are some studies that strongly suggest that lacrimal massage is beneficial [16, 35].

If lacrimal massage is recommended, it is important to demonstrate the proper technique to the patient's caregivers. Because the lacrimal duct is mostly covered by bone, the only access to the system is at the site of the lacrimal sac beneath the medial canthus. One can demonstrate this to parents by having them place their fingers at the inside corner of the eyelid. The medial canthus can be palpated, and feels like a small BB beneath the skin. Gentle pressure with a finger at this site causes compression of the lacrimal sac, while simultaneously obstructing the canaliculi, giving the desired effect.

20.3 Surgical Management

20.3.1 Simple Probing

If NLDO does not spontaneously resolve, patients may require a surgical procedure to relieve the obstruction. There are two main approaches to this condition. Some ophthalmologists prefer to perform NLDP on awake infants in the office. This may be performed as early as 1 month of age, but usually at 4−6 months of age [34]. The main advantages of this approach are: (1) general anesthesia is avoided; and (2) the problem is resolved at a younger age. The primary disadvantages are: (1) the procedure is uncomfortable; (2) there is an increased risk of creating a false passage in an awake infant who is moving; and (3) the procedure is performed on some infants who would spontaneously improve with time.

The second approach is to wait until the children are older (9−12 months of age) and perform the procedure in the operating room under general anesthesia. The main advantages of this approach are: (1) a number of children will improve spontaneously by waiting until a older age, thus avoiding the need for surgery; (2) the operating room is a more controlled environment, the patient is not moving, and additional procedures (e.g., endoscopy, stent placement) can be performed if necessary; and (3) pain control. The primary disadvantages are: (1) the symptoms persist longer; and (2) the risk of general anesthesia. The overall success of NLDP is usually very high (>90% in my experience) for both in-office and operating room probing. Given the relative advantages and disadvantages discussed above, neither approach can clearly be considered superior to the other [14, 17].

As the debate between in-office and operating room probing demonstrates, the high success rate for infant lacrimal surgery in general makes it difficult to scientifically establish an optimal treatment paradigm. Statistically, when two different treatments are very effective, large numbers of patients are necessary to establish one as statistically better than the other. In practical terms, such studies are probably not necessary, because NLDO is usually successfully treated regardless of which procedure is used. Given that NLDO is not a sight-threatening problem, and the cost of a large-scale, multi-center, prospective trial of different treatments would likely be prohibitively expensive, it is unlikely that such studies will be performed. The Pediatric Eye Disease Investigator Group has utilized an alternative approach, which has some of the merits of a large-scale study but at considerably less expense. In these studies, a large number of individuals each contribute small numbers of patients to a common data collection center. This has proved very successful in the study of amblyopia [28, 37], and similar information may be obtained from this group by studying NLDO. For the present, individual decisions regarding which method of treatment to select will be based on factors such as personal experience, local practices, the availability and safety of pediatric anesthesia, and family preferences.

In addition to probing alone, some authors have advocated placement of stents in all children at the time of initial NLDP, reporting a success rate of 96%

with this procedure [8]. Although this success rate is very high, in the author's opinion it does not justify adopting routine stent placement in all children with NLDO. If one assumes that approximately 90% of patients are successfully treated with NLDP alone, then this practice would result in 90 children out of 100 receiving stents unnecessarily in order to successfully treat the six children who would have required stents. It is arguable as to whether the benefit outweighs the potential risks, and more intense follow-up is required for patients who have stents placed [30].

20.3.2 Older Children and Children with Persistent Symptoms After Initial Probing

In the past, there has been some debate regarding the efficacy of NLDP in children who present for treatment at an older age (most commonly defined as age 18 months and older). Some studies suggest that the success rate of probing decreases as patients grow older [15, 24, 27]. Other studies report success rates with simple probing in older children that are nearly equal to those performed at a younger age [18, 31]. The practical implication of this debate involved the treatment of older children. If the success rate of surgery was less, then most authors advocated additional treatment (typically stent placement) in order to increase the rate of successful outcomes. If there were no difference in success, then stents would be unnecessary.

The likely answer to this controversy involves the recognition that there is more than one type of nasolacrimal obstruction [11, 18, 19]. The most common type, simple membranous obstruction of the distal valve of Hasner (Fig. 20.1), is treated with a high success rate with simple nasolacrimal probing, regardless of whether the probing is performed at an early age or an older age. The second type involves diffuse stenosis that extends along the distal nasolacrimal duct (Fig. 20.2). Studies that recognize this distinction provide evidence that simple NLD probing has a lower success rate in this group [11, 13, 18, 19].

The different types of obstruction can be recognized intraoperatively based on palpation of the nasolacrimal system as the probe is passed into the distal

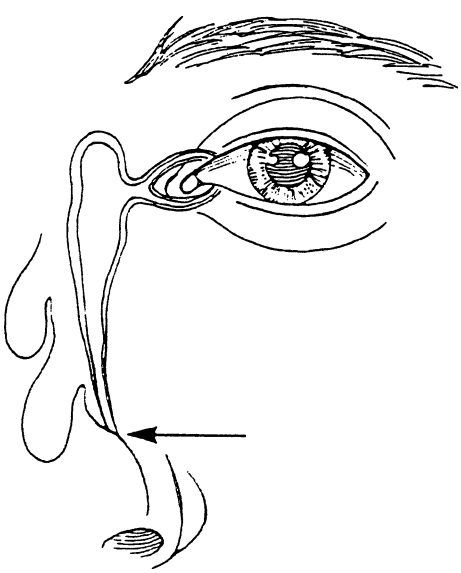

Fig. 20.1 Typical membranous obstruction at distal valve of Hasner (*arrow*). (From [19])

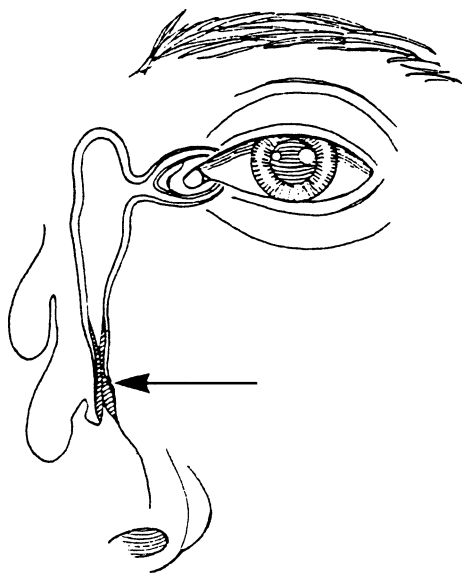

Fig. 20.2 Diffuse stenosis extending along distal nasal lacrimal duct (*arrow*). (From [19])

duct. Typical membranous obstruction is encountered near the end of the probe passage with a distinct popping sensation as the probe passes through the membrane. The probe can then be freely manipulated up and down in the distal duct with minimal resistance. Diffuse stenosis of the distal duct is distinctly different. The obstruction in this form of obstruction is encountered earlier, often just as the probe passes from the lacrimal sac into the duct. The obstruction produces a gritty, crunchy sensation as the probe moves through it, and this usually requires more force than that needed during a typical probing. The sensation feels similar to passing the probe through a vial of gritty sand. This palpable stenosis continues until the probe passes into the nares, and there is often a residual gritty sensation even after the probing is complete.

Based on this distinction, a rational approach to older children with NLDO is to perform a probing with the ability to add additional procedures based on the type of obstruction encountered [19]. If typical membranous obstruction is palpated and relieved with probing, no additional procedures need be performed. If diffuse stenosis is encountered, balloon catheter dilation (BCD) or stent placement should be considered. In BCD, a probe with a deflated catheter is passed into the distal duct and inflated to a pressure of 8 atm [1]. The balloon extends along the entire length of the distal duct and allows greater dilation than that of a probe alone. An alternative to BCD is stent placement, which also works well in these patients. The primary advantage of BCD is that stents, with their increased cost and morbidity, can be avoided. The primary disadvantage is the cost of the equipment.

The second group of children with NLDO who require additional treatment is the 5−10% who have persistent symptoms after their initial probing. Treatment options for this group of patients include repeat simple probing, BCD, and probing with stent placement. Similar to older children discussed above, the failure of initial probing in many of these patients may be due to diffuse stenosis of the distal duct, and the treatment considerations are the same as for the older group.

In addition to the distinction between simple and diffuse obstruction, another form of anatomic variation may be present in children with NLDO. In most patients, there is no visible abnormality of the distal NLD when it is viewed from the nares, because the obstruction is internal to the duct. In approximately 7% of older children and children with persistent symptoms after initial probing, an intranasal abnormality can be visualized endoscopically [20]. These abnormalities include relatively thick cysts (discussed below under mucoceles), translucent membranous obstructions, and enlarged, edematous nasal mucosa. The presence of such abnormalities may be suspected if metal-on-metal contact cannot be palpated during surgery between the probe in the NLD and a probe passed beneath the inferior turbinate in the nares. The use of endoscopy to recognize and remove such abnormalities is a useful adjunct to treatment [20].

The treatment of children with NLDO that persists despite the treatments discussed above usually required dacryocystorhinostomy. A discussion of this procedure is beyond the scope of this chapter.

20.4 Special Forms of NLDO

20.4.1 Neonates with Mucocele

Approximately 1−2% of children with NLDO will present in infancy in a manner that is distinctly different from typical NLDO [9, 29]. These children have a blue-tinged swelling overlying the lacrimal sac that is present at or shortly after birth, variously called mucocele, dacryocystocele, dacryocele, and amniotocele. The swelling results from distention of the lacrimal sac, presumably due to a one-way valve effect, in which fluid can enter, but not exit, the sac through the valves of Rosenmuller, combined with obstruction of the distal NLD. The primary differential diagnosis for this condition includes encephalocele and capillary hemangioma. The distinction from encephalocele is usually clear, as encephaloceles present above the medial canthus, while mucoceles present below the medial canthus. Hemangiomas typically have a blue-tinged appearance similar to a mucocele, but they also usually have visible vascular patterns that are not seen on mucoceles (Fig. 20.3). In addition, hemangiomas are not usually present immediately after birth, but appear after the first 1−2 weeks, and they feel spongy on palpation, rather

than fluctuant. If a mass is present in the expected location below the medial canthus, and particularly if there are symptoms of epiphora and/or dacryocystitis, imaging studies are usually not necessary to verify the diagnosis.

In addition to the swelling that is noted at or shortly after birth, another important distinction between mucoceles and typical NLDO is the presence of acute dacryocystitis. Typical NLDO is characterized by an indolent, recurrent, low-grade chronic dacryocystitis, not accompanied by visible swelling overlying the lacrimal sac. In contrast, if a mucocele becomes infected, the area becomes inflamed and erythematous (Fig. 20.4). Purulent material is often not spontaneously noted, due to the one-way valve effect of the valves of Rosenmuller, but frank pus may sometimes be expressed with pressure over the sac.

A third important distinction is the nearly universal presence of a nasolacrimal duct cyst in children with mucoceles (Fig. 20.5). The etiology of these cysts presents the "chicken-and-the-egg" question. Does the cyst, with its marked obstruction, cause the mucocele to develop, or does the presence of the mucocele cause the cyst to develop? A plausible etiology is that two conditions must be present for cysts to form: (1) Rosenmuller valves that have a strong one-way valve effect, creating increased pressure within the lacrimal sac; and (2) a more-resistant-than-normal membrane at the distal valve of Hasner, which expands to form a cyst.

In addition to the lacrimal symptoms, nasolacrimal cysts may cause breathing problems if they are large enough to obstruct the nasal passages [7, 22]. Subtle symptoms of this may be raspy breathing. More significant symptoms include difficulty feeding. This may occur because infants are obligatory nasal breathers. If their mouths are occluded with bottles or nipples and cysts obstruct their nares, they may be

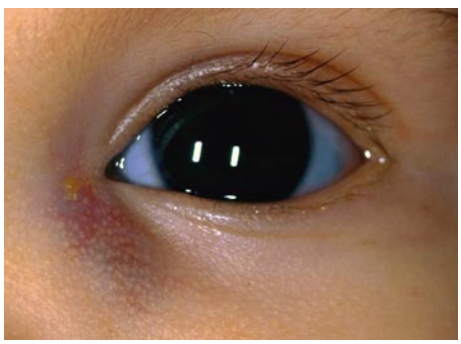

Fig. 20.3 Hemangioma with vascular markings. (From [40])

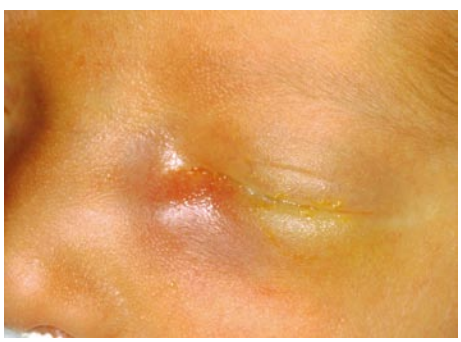

Fig. 20.4 Neonatal mucocele with swelling and erythema overlying lacrimal sac. (From [39])

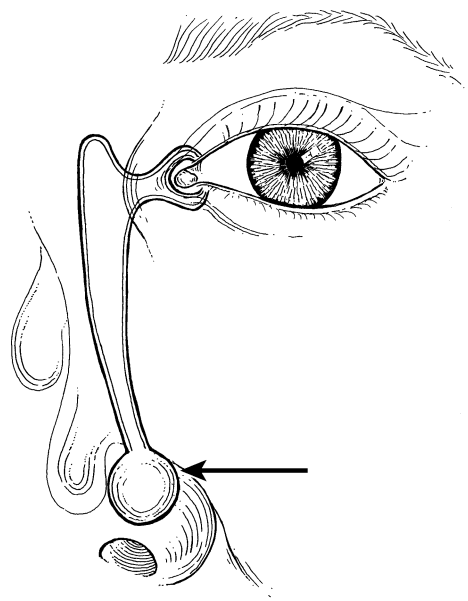

Fig. 20.5 Distal nasal lacrimal duct cyst (*arrow*). (From [20])

unable to breathe. The most severe symptom is frank respiratory distress, in which case urgent treatment is indicated.

The initial treatment of non-infected mucoceles is conservative, typically with warm compresses, gentle massage to the swollen area, and topical antibiotics. If the sac becomes infected, surgical treatment is indicated. These infants have more severe infections than those in typical NLDO. Because these infections occur within the first few weeks of life, when infants have relatively immature immune systems, there is an increased risk of systemic infection; therefore, systemic antibiotics should be used if acute dacryocystitis develops.

Because mucoceles are uncommon, it is not possible to discern an optimal treatment based on the literature. The author's approach is to treat non-infected mucoceles conservatively for the first 1−2 weeks of life [32]. If the mucocele does not resolve by this time, if the mucocele becomes infected and acute dacryocystitis develops, or if the patient has respiratory distress, then surgery is performed. Intravenous antibiotics are given intraoperatively due to the young age and more severe infections. The NLD probing is performed in the same manner performed in older children. Nasal endoscopy is performed routinely because of a relatively high rate of recurrence with probing alone [25], particularly if dacryocystitis is present [2]. A nasolacrimal cyst has been present in every case treated by the author (Fig. 20.6) [20]. The cyst is removed with an alligator forceps under endoscopic visualization. Frequently, frank pus comes out of the sac once it is penetrated (Fig. 20.7), and this is removed with suction. After the cyst is removed, the stent can be clearly visualized in its normal location. The success rate for this procedure has been 95% [20].

20.4.2 Trisomy 21

Children with trisomy 21 have a number of ocular problems that occur with increased frequency, one of

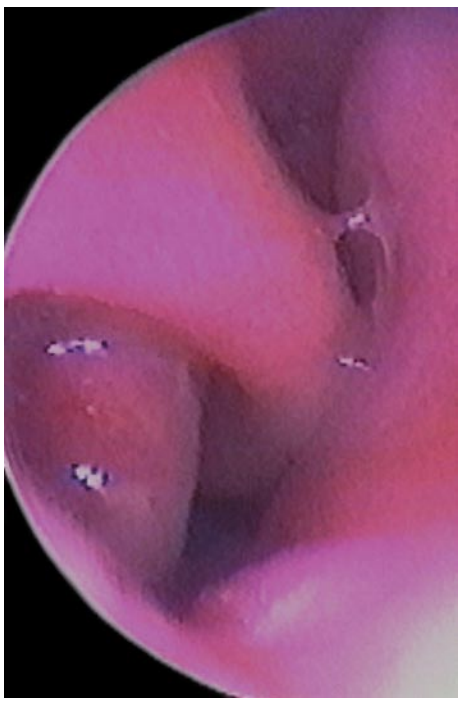

Fig. 20.6 Nasal lacrimal duct cyst beneath inferior turbinate in infant with mucocele. (From [39])

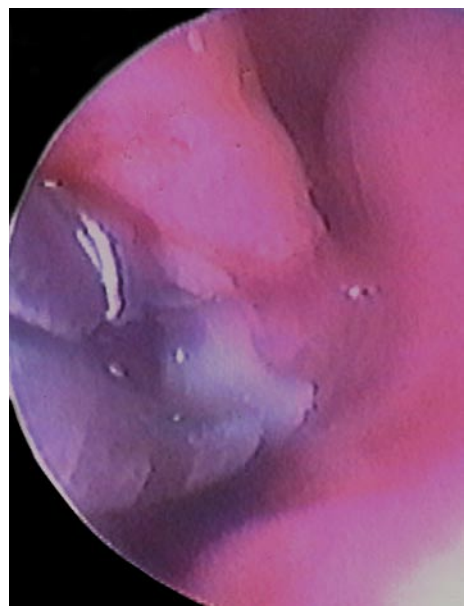

Fig. 20.7 Purulent material present within cyst opened with alligator forceps. (From [39])

which is NLDO. In general, the success rate for treating such patients is less than in other children [5, 21]. There are probably several reasons for this. Firstly, children with trisomy 21 have a higher incidence of blepharitis, which may be difficult to distinguish from NLDO due to the common symptoms of increased tearing and mucoid discharge. Secondly, one of the systemic features of trisomy 21 is midfacial hypoplasia, which includes the bony structures that surround the nasolacrimal system, making anatomic abnormalities more likely. The third reason is hypotonia, which is a systemic manifestation of trisomy 21. This is likely the most important reason for decreased success. Proper function of the lacrimal system relies on a pump mechanism generated by the orbicularis muscles [12, 26]. The hypotonia in trisomy 21 patients decreases the effectiveness of this pump, creating relative stasis of fluid within the lacrimal sac, which increases the likelihood of infection. Children with trisomy 21 may also have typical NLDO, which can be successfully treated with NLDP; however, NLDP does not improve the lacrimal stasis and, therefore, symptoms are more likely to persist.

Because of these factors, the author's approach to children with trisomy 21 and NDLO is now similar to that of older children with NLDO. A previous study was performed utilizing BCD in all such patients, [21] but this is no longer used routinely. A regular probing is performed, as well as endoscopy. BCD is performed if diffuse stenosis is present or if fluid irrigates poorly following the probing. There is a higher incidence of palpating minimal or no obstruction during probing in children with trisomy 21, which supports the contention that hypotonia contributes to the etiology of NLDO in these patients.

There is a higher rate of NLDP failure in patients with trisomy 21. Even when the condition improves following surgery, patients often have some residual symptoms. Despite repeated procedures, it is often difficult to completely eradicate all of these symptoms, due to the factors discussed above. Preoperative counseling regarding the prognosis for NLDP in children with trisomy 21 is important. If the symptoms improve after surgery, the author's usual practice is to accept minor residual symptoms, and not to perform repeat surgery with the often-elusive goal of achieving complete resolution of symptoms.

20.4.3 Punctal and Canalicular Abnormalities

Other anatomic abnormalities of the nasolacrimal system may produce symptoms that are similar to those of NLDO. One of these symptoms is absence or maldevelopment of the puncta or canaliculi. Children with this problem develop epiphora, because the tear lake does not have access to the lacrimal system. An important historical and examination finding in these patients is the absence of dacryocystitis. The lacrimal sac does not become infected in these patients, because bacteria cannot gain access to the sac itself.

When examining patients with symptoms of NLDO, it is important to inspect the lacrimal puncta for evidence of maldevelopment. It is relatively easy to inspect the lower puncta by gently everting the lower lid in the office. Evaluation of the upper puncta is more difficult and may not be possible in an uncooperative infant. Preoperative recognition of punctal abnormalities is helpful for parental counseling and operative planning. The type of abnormality ranges from a simple membranous obstruction overlying the puncta (in which case the puncta itself may look normal), to complete agenesis of the canaliculus (in which case the eyelid margin may be completely flat, without any discernible dimple in the area where the puncta is normally located (Fig. 20.8).

The true incidence of punctal and canalicular maldevelopment is unknown. This is because if only one of the upper or lower canaliculi is abnormal, the

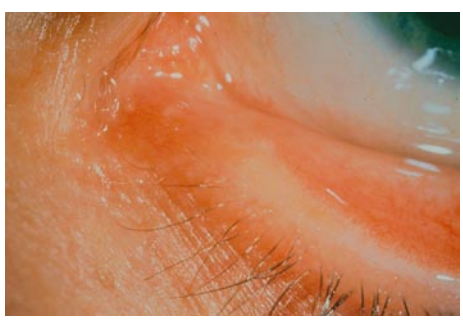

Fig. 20.8 Congenital absence of lacrimal puncta. (From [40])

other canaliculus may provide enough drainage that epiphora does not develop. This abnormality may therefore be more common than is realized, because patients have no symptoms and are therefore never examined.

Treatment of membranous punctal obstruction is straightforward, even if the membrane is not recognized until the patient is in the operating room. Puncturing the membrane with a punctal dilator usually successfully treats the problem. Treatment of true canalicular agenesis is more difficult. If there is no visible punctal tissue, a linear incision can be made through the lid margin between the site where the puncta normally is located and the medial canthus, looking for canalicular tissue. This is often unsuccessful [23]. Patients with canalicular agenesis and chronic epiphora may require Jones tube placement to improve their symptoms, and this is often deferred until an older age [23, 38].

Many patients who present with symptoms of NLDO and who are found to have punctal and canalicular abnormalities also have typical membranous obstruction of the distal NLD [23]. This is particularly true if the patients have dacryocystitis, because this indicates that there is a connection between the eyelid and the lacrimal sac. If punctal agenesis is present on only the upper or lower eyelid, a simple probing through the patent puncta has a high rate of success in such patients, and is recommended as an initial treatment before considering more extensive canalicular surgery.

20.4.4 Lacrimal Fistulae

Another unusual anatomic abnormality of the lacrimal system is a lacrimal fistula. In this disorder, an accessory tract develops between the lacrimal sac and the skin overlying the medial canthus. This may be recognized as a small dimple in the skin at this site (Fig. 20.9), but a fold of skin sometimes obscures this. The opening is so small that it may not be brought to medical attention in the absence of symptoms. If the fistula is patent, patients may develop epiphora from the site. Occasionally the fistula is not recognized until during surgery for NLDP, at which time fluid emerges from the tract during irrigation of the lacrimal system.

No treatment is necessary if patients are asymptomatic. Surgery is indicated if bothersome epiphora or an infected fistula tract is present. There is a high rate of recurrence with simple cauterization of the tract. Successful treatment usually requires excision of the tract and ligation of the fistula where it joins the lacrimal sac (Fig. 20.10) [3, 36].

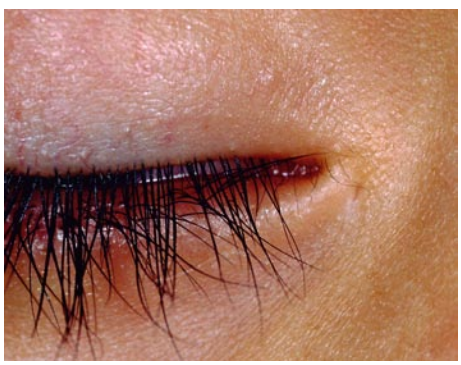

Fig. 20.9 Dimple at site of lacrimal fistula. (From [40])

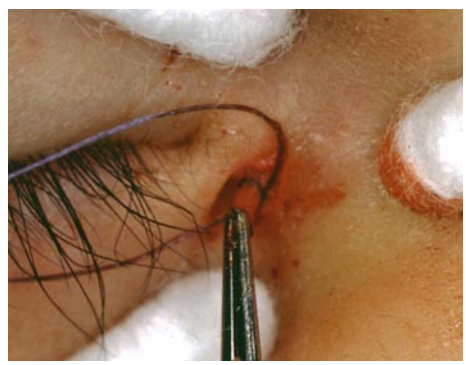

Fig. 20.10 Surgical excision of lacrimal fistula

Take Home Pearls

- Spending a few minutes explaining the etiology and management of NLDO to parents of infants is useful. They should understand that topical antibiotics will not cure the obstruction, and that it is normal for symptoms to recur when antibiotics are discontinued.
- Attention to palpation during probing may help guide surgical decisions:
  - The presence of diffuse stenosis of the distal duct may require more than simple probing to cure (either balloon catheter dilation or stent placement).
  - The failure to palpate metal-on-metal contact between a probe in the NLD and a probe in the nares may indicate the presence of a nasolacrimal duct cyst or other anatomic abnormality.
- It is often difficult to eradicate symptoms of NLDO in children with trisomy-21. A significant improvement in symptoms may be an acceptable outcome.
- Infants with mucoceles almost always have nasolacrimal duct cysts. Removal of these cysts may increase the success rate of surgery.
- Children with punctal agenesis of one eyelid and symptoms of NLDO often improve with simple NLDP through the eyelid with the patent canaliculus.

References

1. Becker B, Berry FD, Koller H (1996) Balloon catheter dilatation for treatment of congenital nasolacrimal duct obstruction. Am J Ophthalmol 121:304–309
2. Becker BB (2006) The treatment of congenital dacryocystocele. Am J Ophthalmol 142:835–838
3. Birchansky L, Nerad JA, Kersten RC, Kulwin DR (1990) Management of congenital lacrimal sac fistula. Arch Ophthalmol 108:388–390
4. Cassady JV (1952) Developmental anatomy of nasolacrimal duct. Arch Ophthalmol 47:141–158
5. Coats DK, McCreery KMB, Plager DA, Bohra L, Kim DS, Paysse EA (2003) Nasolacrimal outflow drainage anomalies in Down's syndrome. Ophthalmology 110:1437–1441
6. Crigler LW (1923) The treatment of congenital dacryocystitis. J Am Med Assoc 81:23–24
7. Edmond JC, Keech RV (1991) Congenital nasolacrimal sac mucocele associated with respiratory distress. J Pediatr Ophthalmol Strabismus 28:287–289
8. Engel JM, Hichie-Schmidt C, Khammar A, Ostfeld BM, Vyas A, Ticho BH (2007) Monocanalicular silastic intubation for the initial correction of congenital nasolacrimal duct obstruction. J AAPOS 11:183–186
9. Ffooks OO (1961) Lacrimal abscess in the newborn. Br J Ophthalmol 45:562–565
10. Guerry D III, Kendig EL Jr. (1948) Congenital impatency of the nasolacrimal duct. Arch Ophthalmol 39:193–201
11. Honavar SG, Prakash VE, Rao GN (2000) Outcome of probing for congenital nasolacrimal duct obstruction in older children. Am J Ophthalmol 130:42–48
12. Kakizaki H, Zako M, Miyaishi O, Nakano T, Asamoto K, Iwaki M (2005) The lacrimal canaliculus and sac bordered by the horner's muscle form the functional lacrimal drainage system. Ophthalmology 112:710–716
13. Kashkouli MB, Beigi B, Parvaresh MM, Tabatabaee Z (2003) Late and very late initial probing for congenital nasolacrimal duct obstruction: What is the cause of failure? Br J Ophthalmol 87:1151–1153
14. Kassoff J, Meyer DR (1995) Early office-based vs late hospital-based nasolacrimal duct probing. Arch Ophthalmol 113:1168–1171
15. Katowitz JA, Welsh MG (1987) Timing of initial probing and irrigation in congenital nasolacrimal duct obstruction. Ophthalmology 94:698–705
16. Kushner B (1982) Congenital nasolacrimal system obstruction. Arch Ophthalmol 100:597–600
17. Kushner BJ (1995) Early office-based vs late hospital-based nasolacrimal duct probing. Arch Ophthalmol 113:1103–1104
18. Kushner BJ (1998) The management of nasolacrimal duct obstruction in children between 18 months and 4 years old. J AAPOS 2:57–60
19. Lueder GT (2002) Balloon catheter dilation for treatment of older children with nasolacrimal duct obstruction. Arch Ophthalmol 120:1685–1688
20. Lueder GT (2004) Endoscopic treatment of intranasal abnormalities associated with nasolacrimal duct obstruction. J AAPOS 8:128–132
21. Lueder GT (2000) Treatment of nasolacrimal duct obstruction in children with trisomy 21. J AAPOS 4:230–232
22. Lusk RP, Muntz HM (1987) Nasal obstruction in the neonate secondary to nasolacrimal duct cysts. Int J Pediatr Otorhinolaryngol 13:315–322
23. Lyons CJ, Rosser PM, Welham RAN (1993) The management of punctal agenesis. Ophthalmology 100:1851–1855

24. Mannor GE, Rosen GE, Frimpong-Ansah K, Ezra E (1999) Factors affecting the success of nasolacrimal duct probing for congenital nasolacrimal duct obstruction. Am J Ophthalmol 127:616–617
25. Mansour AM, Cheng KP, Mumma JV, Stager DR, Harris GJ, Patrinely JR, Lavery MA, Wang FM, Steinkuller PG (1991) Congenital dacryocele. Ophthalmology 98:1744–1751
26. Milder B, Weil B (1983) The lacrimal system. Appleton-Century-Crofts, Norwalk, Connecticut
27. Paul TO, Shepherd R (1994) Congenital nasolacrimal duct obstruction: natural history and the timing of optimal intervention. J Pediatr Ophthalmol Strabismus 31:362–367
28. Pediatric Eye Disease Investigator Group (2005) Randomized trial of treatment of amblyopia in children aged 7 to 17 years. Arch Ophthalmol 123:437–447
29. Petersen RA, Robb RM (1978) The natural course of congenital obstruction of the nasolacrimal duct. J Pediatr Ophthalmol Strabismus 15:246–250
30. Robb RM (2007) Probing and intubation as primary treatment for nasolacrimal duct obstruction? J AAPOS 11:113
31. Robb RM (1998) Success rate of nasolacrimal duct probing at time intervals after 1 year of age. Ophthalmology 105:1307–1310
32. Schnall BM, Christian CJ (1996) Conservative treatment of congenital dacryocele. J Pediatr Ophthalmol Strabismus 33:219–221
33. Sevel D (1981) Development and congenital abnormalities of the nasolacrimal apparatus. J Pediatr Ophthalmol Strabismus 18:13–19
34. Stager D, Baker JD, Frey T (1992) Office probing of congenital nasolacrimal duct obstruction. Ophthalmic Surg 23:482–484
35. Stolovitch C, Michaeli A (2006) Hydrostatic pressure as an office procedure for congenital nasolacrimal duct obstruction. J AAPOS 10:269–272
36. Sullivan TJ, Clarke MP, Morin JD, Pashby RC (1992) The surgical management of congenital lacrimal fistulae. Aust N Z J Ophthalmol 20:109–114
37. The Pediatric Eye Disease Investigator Group (2004) A randomized trial of atropine regimens for treatment of moderate amblyopia in children. Ophthalmology 111:2076–2085
38. Yuen SJA, Oley C, Sullivan TJ (2004) Lacrimal outflow dysgenesis. Ophthalmology 111:1782–1790
39. Lueder GT (1995) Neonatal dacryocystitis associated with nasolacrimal duct cysts. J Pediatr Ophthalmol Strabismus 32:102–106
40. Lueder GT (1997) Neonatal lacrimal system anomalies. Semin Ophthalmol 12:109–116

Congenital Ocular Malformations

Aleksandra V. Rachitskaya and Elias I. Traboulsi

21

Contents

Core Messages

- The embryogenesis of the eye and ocular adnexa is complex and depends on the organized expression and interaction of a number of developmental genes. Mutations in such genes or the influence of certain environmental toxins and teratogens cause ocular malformations. A number of ocular developmental genes have been identified and clinical molecular testing is now available for some.

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- Ocular malformations can be isolated or part of complex multisystem syndromes. Certain ocular malformations are harbingers of serious "hidden" abnormalities in other organs such as the heart, brain, or vascular system.
- Ocular malformations cause vision loss directly by interfering with media clarity or integrity of ocular structures, or by causing diseases such as amblyopia, glaucoma, or retinal detachment that in turn result in loss of vision.
- The management of patients with ocular malformations includes making an accurate diagnosis, identifying any potentially associated syndromes or malformations in other organ systems, optimizing visual function, and anticipating the occurrence of other problems such as glaucoma and amblyopia.

21.1 Embryology of the Eye

As a group, congenital malformations of the eye constitute a significant source of visual morbidity and are often a sign of malformation syndromes and of hidden brain or other organ abnormalities. Malformations result from a variety of chromosomal or single gene defects, or they may be caused by in utero exposure to exogenous teratogens.

In order to evaluate congenital malformations, one needs to have an understanding of the embryology of the eye. Here we provide a brief overview of eye development. The reader is referred elsewhere for more detailed discussions [14, 129]. The three embryonic layers include ectoderm, mesoderm, and endoderm. Anterior ectoderm differentiates into neural ectoderm that gives rise to the eye and the brain. The first evidence of the developing eye is observed on day 21 of gestation when the optic sulci, also known as optic pits, appear. These invaginations can be found on the inner surface of anterior neural folds of neural ectoderm that will later form forebrain (prosencephalon). At the same time, the neural folds start the fusion process that results in neural tube formation. Neural crest cells are found at the junction of the neural ectoderm and overlying surface ectoderm. They play an important role in eye development. These cells migrate beneath the surface ectoderm to different areas of the embryo, and specifically to the area of optic sulci. There they serve as precursors to many eye structures including corneal stroma, iris stroma, ciliary muscle, choroid, sclera, and orbital cartilage and bone. It is worth mentioning that although throughout the rest of the body the connective tissue and bone structures are derived from mesoderm, the orbital bone and connective tissue are derived from neural crest cells. In the eye the mesoderm is responsible only for the striated muscle of the extraocular muscles and vascular endothelium.

As the neural tube closes anteriorly and the forebrain vesicles are formed, the optic sulci develop as bilateral evaginations of neural ectoderm on the forebrain vesicles. This expansion results in the formation of optic vesicles at gestation day 25. The optic vesicles are connected to the forebrain by the optic stalk, a precursor of the optic nerve. At day 27, the surface ectoderm overlying the evaginating optic vesicles thickens to form the lens placode. Subsequent to lens placode formation, the placode and underlying neural ectoderm start invaginating. The neural ectoderm invaginates on itself forming a double-layered optic cup, the inner layer of which will become the neurosensory retina and the outer the retinal pigment epithelium. The invagination process results in an inferiorly positioned optic fissure, also known as the embryonic or choroidal fissure. The tissue lining the fissure is of neural crest origin and gives rise to the hyaloid artery that courses from the optic stalk to the developing lens derived from the surface ectoderm. The hyaloid artery is a branch of the primitive ophthalmic artery. After the fissure closes at 6 weeks, primitive ciliary epithelium derived from neural ectoderm starts secreting aqueous fluid that creates intraocular pressure (IOP) and aids in expansion of the optic cup [22, 129]. Failure of the fissure to close results in microphthalmia and typical (in location) colobomas.

The lens is formed from the lens placode, which is derived from surface ectoderm. One important step in lens formation is the detachment of the lens vesicle from the surface ectoderm. Anterior lenticonus, anterior capsular cataracts, and anterior segment dysgenesis with keratolenticular adhesions in Peters' anomaly may result from faulty keratolenticular separation [129]. The hyaloid vessels form a network around the posterior lens capsule and then anastomose anteriorly with a network of vessels in the pupillary membrane anterior to the lens capsule that contains vessels and connective tissue. The vascular network that is formed around the lens is termed tunica vasculosa lentis and it regresses at 4 months of gestation along with the hyaloid artery. Mittendorf's dot is a 1- to 2-mm area of fibrosis on the posterior capsule and is likely to represent an incomplete regression of the hyaloid artery at its attachment site. An incompletely regressed pupillary membrane is called persistent pupillary membrane (Fig. 21.1).

The surface ectoderm forms the corneal epithelium, whereas both corneal stroma and endothelium are derived from neural crest cells. In addition, neural crest cells form anterior iris stroma, the ciliary muscle, and most structures of the iridocorneal angle. Aqueous draining is observed by 17–18 weeks of fetal life and gradually increases during development [67]. Increased IOP occurs in many disorders in which the anterior chamber angle structures do not develop properly and in which aqueous drainage is impaired; these conditions include Axenfeld-Rieger syndrome, iridogoniodysgenesis/iris hypoplasia, Peters' anomaly, primary congenital glaucoma along with cornea plana, sclerocornea, megalocornea, and congenital hereditary endothelial dystrophy [48].

The retina's cellular differentiation progresses in the form of a wave from inner to outer layers and from central retina to peripheral retina. Ganglion cells appear first. Amacrine, horizontal, and cone cells appear at approximately the same time, but none before the first ganglion cell [16]. Macular differentiation occurs relatively late [45], and it is only after birth that the ganglion and bipolar cells completely vacate the fovea centralis. The central retinal artery is derived from the portion of hyaloid artery within the optic stalk. A benign small tuft of glial cells that emanates from the center of the optic disk is termed Bergmeister's papilla (Fig. 21.2) and is a remnant of the hyaloid system of blood vessels and associated tissues. The central retinal artery forms temporal and nasal retinal arcades, with the latter reaching the periphery first. Thus, a newborn can have an immature partially avascular area in the temporal periphery [129].

The vitreous develops in three stages. The primary vitreous is a highly vascularized gel that is replaced by the avascular secondary vitreous. The tertiary vitreous serves as a precursor of the lens zonule. At birth, most of the posterior vitreous gel is secondary vitreous with the vitreous base and zonule representing tertiary vitreous. Cloquet's canal is an atrophied primary vitreous that persists as an optically clear zone emanating from the optic nerve to the posterior aspect of the lens [129].

The optic stalk that connects the optic vesicle to the forebrain serves as a precursor to the optic nerve. The ganglion cells of the developing retina send their axons through the optic stalk at week 6. The optic chiasm consists first of all crossed fibers and only later do the uncrossed fibers reach the optic chiasm. The first ganglion axons reach the dorsal nucleus of the lateral geniculate body at week 9. At month 5 of gestation, axons start becoming myelinated in the area of lateral geniculate body. It takes about 3 months for the wave of myelinization to reach the globe. Myelinization stops at the lamina cribrosa at 1 month after birth. Anomalous myelination of nerve fibers is clinically obvious as a flat, feathery, glossy sheen on the surface of the retina and has been associated with high myopia and amblyopia in some cases (Fig. 21.3) [32, 112].

Fig. 21.1 Few strands of remnants of the papillary membrane attach to a small fibrous piece of tissue on the anterior lens capsule

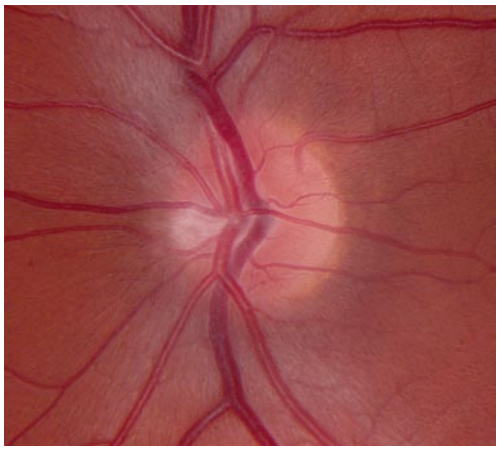

Fig. 21.2 Remnant of the hyaloid system on nasal aspect of optic disk, Bergmeister's papilla

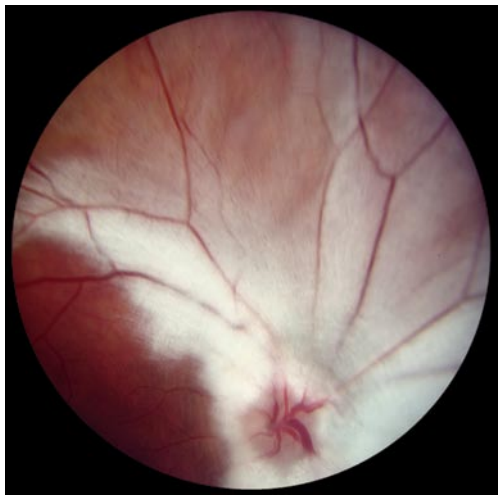

Fig. 21.3 Extensive myelination of the nerve fiber layer associated with high myopia and amblyopia in this patient

21.2 Anophthalmia and Colobomatous Microphthalmia

21.2.1 Anophthalmia

Anophthalmia refers to the unilateral or bilateral apparent absence of the globe in an orbit with normal adnexal elements. Rudiments of optic vesicle-derived structures and structures derived from mesoderm and/or neural crest may be found on histopathologic sectioning of the orbit in consecutive or degenerative anophthalmia (clinical anophthalmia), but not in primary or true anophthalmia. The orbit is shallow and orbital volume remains small with increasing age, presumably because of absence of the trophic action of the globe on the orbit. True or primary anophthalmia is extremely rare and results from failure of the optic vesicle to bud from the cerebral vesicle; the optic nerves and tract are usually absent. In secondary anophthalmia there usually are associated severe forebrain malformations, such as holoprosencephaly, and affected fetuses are usually aborted. Consecutive or degenerative anophthalmia results from regression or degeneration of the optic vesicle. Inherited isolated anophthalmia is usually autosomal recessive. Anophthalmia can be present in a number of syndromes such as the Lenz microphthalmia syndrome and with a variety of chromosomal rearrangements. More recently, mutations in the *SOX2* gene on chromosome 3 were found to account for a significant proportion of cases of anophthalmia [35]. Treatment of anophthalmia consists of maintenance of orbital volume and conjunctival forniceal depth by insertion of ocular prostheses of increasing sizes into the orbit.

21.2.2 Colobomatous Microphthalmia and Typical Uveal Coloboma

In microphthalmic eyes there is variable reduction in the volume of the eye. The corneal diameter is usually less than 10 mm and the anteroposterior globe diameter is less than 20 mm. The incidence of microphthalmia/clinical anophthalmia is 0.22 per 1,000 births; the incidence of coloboma is 0.26 per 1,000 births. The diagnosis of microphthalmia can generally be made by inspection of the eye. The cornea is small, but may be of normal size in posterior microphthalmos. Microcornea can occur in the absence of microphthalmia as a dominant or recessive trait. There may be a coloboma of the iris (Fig. 21.4), choroid, and/or optic nerve (Fig. 21.5). Cataracts may be present. Microphthalmic eyes usually have high hypermetropic refractive errors but may be myopic. The

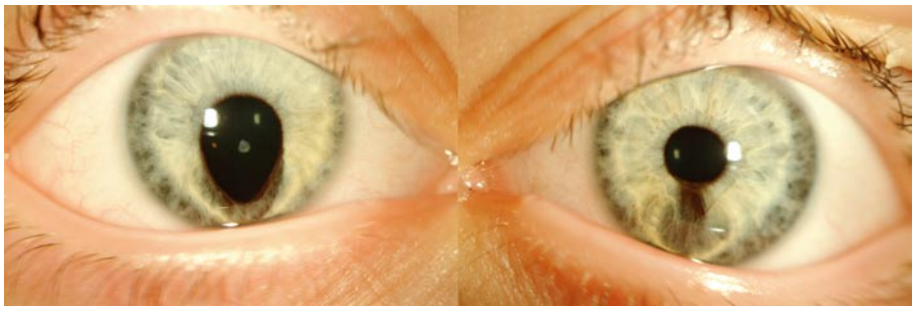

Fig. 21.4 Left and right eyes of a patient with typical uveal colobomas. The right iris shows a full thickness defect inferonasally and a keyhole pupil while the left eye has a round pupil and only thinning of the inferior iris

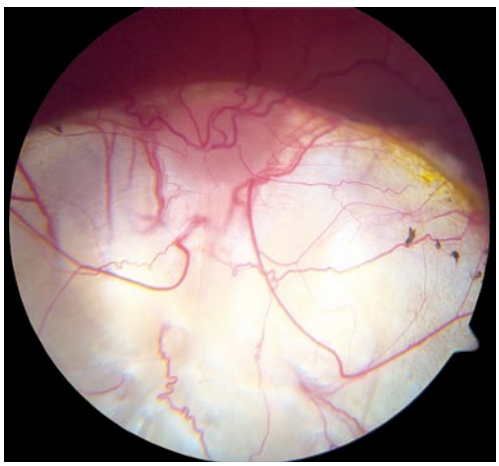

Fig. 21.5 Very large typical inferior chorioretinal coloboma that has involved the entirety of the optic nerve head. Note the yellow luteal pigment in the *upper right* of the figure; this area corresponds to the fovea

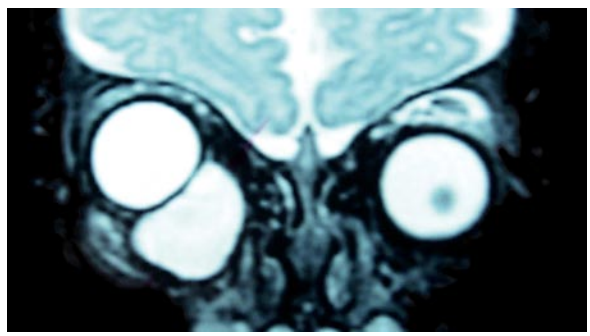

Fig. 21.6 Coronal MRI section demonstrating right microphthalmia with cyst. These are typically inferior to the globe and cause a bulge in the lower lid

diagnosis of borderline cases can be confirmed by measuring the diameter of the eye using ultrasonography. The normal adult eye measures between 21.50 and 27.00 mm.

Microphthalmia can be unilateral or bilateral and may or may not be associated with uveal coloboma, hence its general classification into colobomatous and non-colobomatous. Asymmetric reduction of the volume of the eyes is common in bilateral cases. Large colobomas may produce a white reflex from the pupil (leukocoria) and have been confused with retinoblastoma. Rare complications of colobomas include subretinal neovascularization and retinal detachment.

Colobomas result from failure of closure of the embryonic fissure in the invaginated optic vesicle, a process completed by week 6 of gestation. "Typical" colobomas are inferonasal and may involve iris, ciliary body, inferior choroid, and/or optic nerve head. Eyes with colobomas may be of normal size but are generally microphthalmic. A cyst may form in the area of defective closure, producing microphthalmia with cyst (Fig. 21.6). Patients with this condition usually present with a bulging of the inferior lid and superior displacement of the globe by the cyst.

The coordinated expression of a large number of developmental genes is necessary for normal ocular

and optic nerve development and the pathways and interactions between these genes are currently being elucidated. Mutations in any of these genes can theoretically result in microphthalmia and/or coloboma.

Microphthalmia can be isolated or familial, or can occur in a number of single gene, chromosomal, and embryopathic multisystem malformation syndromes. About a quarter of patients with microphthalmia/coloboma have the CHARGE association (Fig. 21.7) [10]. There is extreme variable expressivity in familial cases, with some family members exhibiting severe microphthalmia and others only small asymptomatic uveal colobomas in normal-sized eyes; hence the importance of ocular examination of all family members. *CHX10* on chromosome 14q24.3 is one of the genes associated with microphthalmia [36].

Errors of refraction should be corrected. Cataract extraction is performed if the retina is attached and the size of the eye is not extremely small. Prostheses are fit over very small blind eyes for cosmetic purposes. Genetic counseling should be provided after examination of all available family members to determine the possible mode of inheritance in familial cases. The empiric risk of recurrence in a sibling is 2% if both parents are unaffected and increases to 14% if one parent is affected. The yield of chromosomal studies is poor for isolated microphthalmia/coloboma but increases significantly if there is associated mental retardation and at least one other congenital malformation.

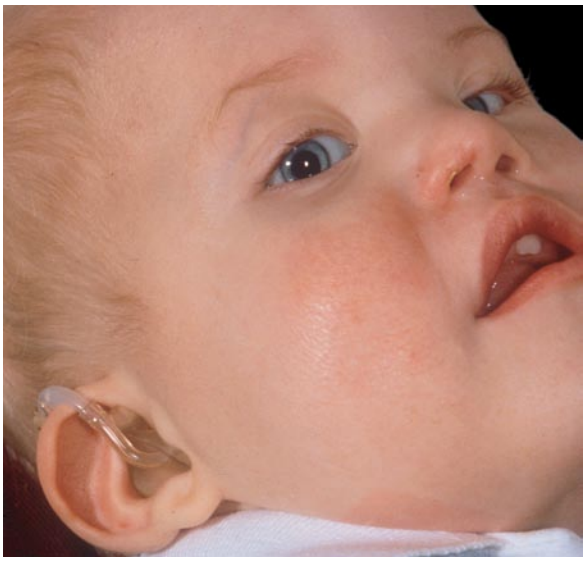

Fig. 21.7 Patient with CHARGE association. Left eye is microphthalmic. Note hearing aid and abnormally shaped ear

21.3 Congenital Disorders of the Anterior Segment

Anterior segment anomalies can result from disturbances of neural crest cell, ectoderm, or global ocular development. The anterior segment consists of the cornea, iris, anterior chamber angle, and lens. Research in *Drosophila melanogaster* and murine and other animal models has identified several transcription factor genes that play a vital role in normal development of the anterior segment. *PAX6* has the most panocular expression and has been implicated in aniridia [42], Peters' anomaly [42], Axenfeld's anomaly [5], keratitis [73], optic nerve malformations [6], and foveal hypoplasia [123]. *Foxc1* (*Fkhl7*), *Pitx2* (*Rieg1*), and *Lmx1b* are some of the developmental genes expressed in neural crest cells. The former two have been implicated in such forms of anterior segment dysgenesis as iridogoniodysgenesis anomaly, iris hypoplasia, Axenfeld-Rieger anomaly, Axenfeld-Rieger syndrome, and congenital glaucoma [56, 58, 69, 74, 80, 87, 103]. *Foxe3* and *Maf* are expressed within the developing lens and are involved in cataract formation and anterior segment ocular dysgenesis [49, 102, 120]. Additionally, the *CYP1B1* gene that is not a transcription factor but encodes an enzyme has been implemented in congenital glaucoma [110].

Abnormalities of neural crest cell development in the eye result in posterior embryotoxon, iris hypoplasia and iridogoniodysgenesis, the Axenfeld-Rieger anomaly and Axenfeld-Rieger syndrome, primary congenital glaucoma, and iridocorneal endothelial syndromes.

21.3.1 Posterior Embryotoxon

Isolated posterior embryotoxon denotes an anteriorly displaced and prominent Schwalbe's line. It is present in a small percentage of normal individuals and generally does not require treatment. However, it

should be recognized that posterior embryotoxon can be part of the Axenfeld-Rieger anomaly and hence eyes that display it are predisposed to glaucoma. Additionally, it has been associated with Alagille syndrome, a condition characterized by hepatic ductular hypoplasia, with neonatal jaundice, pulmonic valvular stenosis as well as peripheral arterial stenosis, abnormal "butterfly" vertebrae, decrease in interpediculate distance in the lumbar spine, absent deep tendon reflexes, poor school performance, and peculiar facies [1, 95, 127].

21.3.2 Iris Hypoplasia and Iridogoniodysgenesis

First described by Berg in 1932, hypoplastic irides have a gray/brown color that represents the pigmented iris epithelium showing through hypoplastic iris stroma that is derived from neural crest cells. The iris appears flat and lacks the normal crypts and variations in thickness. Iris vessels may be prominent. It may or may not be associated with a prominent Schwalbe's line. Iris hypoplasia can be associated with angle maldevelopment–iridogoniodysgenesis and thus be part of the autosomal dominant iridogoniodysgenesis anomaly (type I iridogoniodysgenesis) that is characterized by iris hypoplasia and goniodysgenesis with frequent juvenile glaucoma, and that maps to 6p25 [68]. A group of dominant disorders involving changes in the anterior segment of the eye associated with glaucoma (Axenfeld-Rieger anomaly, iris hypoplasia, and iridogoniodysgenesis) maps to 6p25 and results from mutations in the *FOXC1* gene [80].

Type II iridogoniodysgenesis is also an autosomal dominant disorder characterized by iris hypoplasia, goniodysgenesis, and increased IOP, but is caused by mutations in the *PITX2* gene on chromosome 4q-25-q26, the same gene that causes classic Axenfeld-Rieger syndrome indicating that iridogoniodysgenesis and Axenfeld-Rieger syndrome are allelic variants of the same disorder [3, 56].

An autosomal recessive form of iridogoniodysgenesis has been reported to be associated with congenital glaucoma, skeletal anomalies, and peculiar facial appearance [93].

Ophthalmologists caring for patients with iridogoniodysgenesis should be acutely aware of the glaucomatous component of the disorder, and IOP should be periodically checked in these patients.

21.3.3 Axenfeld-Rieger Anomaly and Axenfeld-Rieger Syndrome

Axenfeld-Rieger anomaly (ARA) clinically is characterized by posterior embryotoxon with iris strands, corectopia, iris hypoplasia, and abnormalities of the anterior chamber angle. Iridocorneal adhesions cause pupil displacement or corectopia and iris atrophy can be so severe that it results in pseudopolycoria (Fig. 21.8). The anterior angle abnormalities include high insertion of the iris root on the trabecular meshwork, resultant adhesions over the angle, and excessive connective tissue deposition [61]. The consequence of these ocular abnormalities is a 50% lifetime risk of glaucoma [61].

The systemic manifestations of Axenfeld-Rieger syndrome (ARS) are extremely variable. They include cranio-dento-facial findings such dental hypoplasia, anterior teeth crowding, and underdevel-

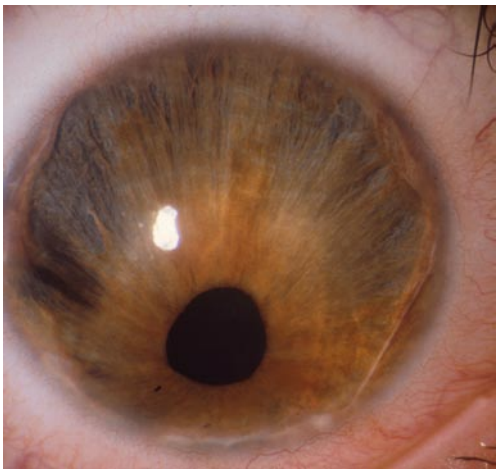

Fig. 21.8 Anterior segment of patient with Rieger's syndrome. The pupil is displaced inferiorly. The superior part of the iris is thin. There is an anteriorly displaced Schwalbe's line (mostly in the inferior part of the cornea in this patient) with strands of iris adherent to it in some locations

oped maxilla [50]. Patients often have failure of the periumbilical skin to involute, sensory hearing loss, congenital heart defects, skeletal abnormalities, and rarely anal stenosis [23, 52, 61].

Currently there are two genes associated with ARS and at least two more incompletely defined genetic loci [61]. *PITX2* (*RIEG1*) is located on chromosome 4q25 and *FOXC1* maps to 6p25. The genes for loci 13q14 and 16q24 have not been identified.

Treatment depends on the patient's presenting symptoms. Pupilloplasty might be required for patients with severe pupillary stenosis. Glaucoma should be treated medically first; surgery appears to have a lower success rate than that in primary congenital glaucoma. If medical treatment fail, enhanced filtering surgery is recommended [113]. It is important to remember that glaucoma drugs have a higher risk of systemic effects in pediatric patients. Parasympathomimetics and β-blockers can be used. Carbonic anhydrase inhibitors, prostaglandin agonists, and sympathomimetics are usually used as second-line pharmacologic interventions [113].

21.3.4 Primary Congenital Glaucoma

Glaucoma in an infant can be part of a syndrome. For instance, patients with ARS have greater chance of developing glaucoma [104], as do children with neurofibromatosis type 1, Sturge-Weber syndrome, Lowe syndrome, and Peters' anomaly [7, 65]. Primary congenital glaucoma (PCG) arises as an independent entity with evidence of isolated trabeculodysgenesis. It usually presents bilaterally with buphthalmos (ocular enlargement), photophobia, epiphora, and blepharospasm and can be associated with corneal edema [7]. Untreated or poorly responsive cases go on to develop significant corneal opacification (Fig. 21.9). Formerly believed to be caused by the persistence of a membrane (Barkan's membrane) over the angle structures, it is now considered to be due to developmental arrest of the trabecular meshwork. The trabecular meshwork has been shown to have thickened trabecular beams and uveal cords with narrow trabecular spaces [7]. An examination under sedation or general anesthesia is frequently required for establishment of definitive diagnosis. Since PCG responds poorly to medical treatment, surgical intervention is often required [7]. A technique combining trabeculotomy with trabeculectomy has been reported to be a successful for treatment of PCG with corneal opacity [64]. Goniotomy surgery can be attempted if corneal clarity is preserved, but often a repeat procedure is needed [96]. The use of adjunctive mitomycin C in trabeculectomy is controversial for, although it results in higher number of successful outcomes, it has been associated with increased incidence of late-onset endophthalmitis [8, 38, 106]. Aqueous shunt devices should be used with caution [20, 33] and cyclodestruction is generally reserved to be the last option [7].

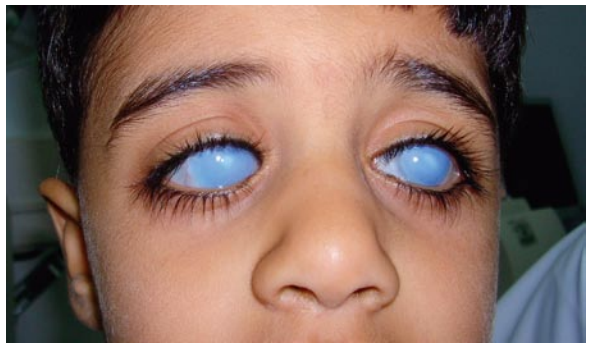

Fig. 21.9 Bilateral total opacification of enlarged corneas in a young boy with congenital glaucoma

Genetic studies have identified *CYP1B1* as the gene associated with the GLC3A locus on chromosome 2p22-p21, and the gene responsible for the majority of cases of primary infantile glaucoma. The CYP1B1 protein belongs to the cytochrome P450 superfamily of enzymes that have the ability to metabolize a variety of substrates. It has been hypothesized that this form of cytochrome P450 might be responsible for producing a compound necessary for normal development or for removing a substrate that might inhibit development of the trabecular meshwork [98].

21.3.5 Iridocorneal Endothelial Syndromes

Iridocorneal endothelial (ICE) syndromes include three clinical entities such as progressive iris atrophy, Chandler's syndrome, and iris-nevus syndrome

(Cogan-Reese syndrome). All three share the characteristic findings of the iridocorneal adhesions and the corneal endothelial abnormality. The iris findings differentiate the three syndromes for progressive iris atrophy presents with marked corectopia, ectropion uvea, iris atrophy, and hole formation [105]. On the other hand, Chandler's syndrome has normal iris or mild to moderate degrees of corectopia, ectropion uvea, and iris atrophy with no hole formation [17]. A Cogan-Reese syndrome iris can range from normal to severely affected. This syndrome is characterized by pigmented nodules on the iris stroma [18]. ICE syndromes are usually unilateral, affect women more commonly than men and present in early to middle adulthood. The corneal endothelium abnormality presents as a beaten silver appearance by slit-lamp biomicroscopy, and by specular microscopy the endothelial cells are pleomorphic in size and shape with virtually pathognomonic intracellular dark spots. On electron microscopy one sees areas of multilayered endothelium as well as areas of scant endothelium and abnormal accumulation of connective tissue under the intact Descemet's membrane [104].

Pediatric patients usually do not require corneal grafting, but might need it as adults. Complications of glaucoma are treated first medically and then surgically.

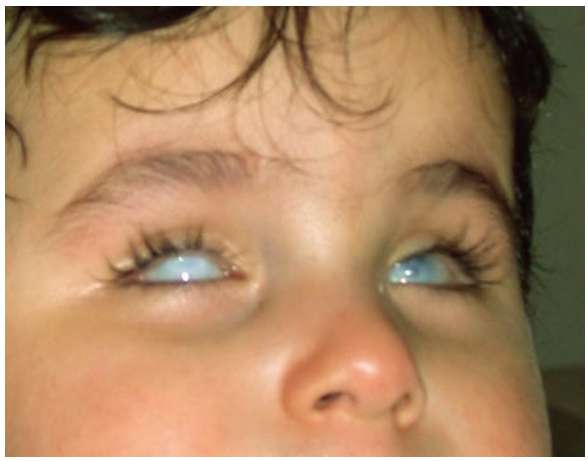

Fig. 21.10 Bilateral Peters' anomaly, more severe in the right than the left eye in this young girl with no other malformations

21.3.6 Peters' Anomaly and Peters' Plus Syndrome

Peters' anomaly is characterized by a central corneal leukoma (Fig. 21.10), lack of the posterior corneal stroma and Descemet's membrane, and a variable degree of iridocorneal and keratolenticular attachments, with the most severe being of a lens adherent to the corneal stroma. Eighty percent of cases are bilateral, 50–70% are associated with glaucoma, and 25–50% with microphthalmia [130]. Other ocular features include cataracts, colobomas, and aniridia [42, 117, 128].

A variety of genes have been associated with Peters' anomaly including *PAX6*, *FOXC1*, *PITX2*, and *CYP1B1* [30, 42, 47, 122]. However, the disease pathogenesis remains unclear. Recently, a study identified biallelic truncating mutations in the β1,3-galactosyltransferase-like gene (*B3GALTL*) in patients with Peters' plus syndrome. This would implicate glycosylation defects in the pathogenesis of the disorder [60]. Peters' plus syndrome is autosomal recessive and includes short stature, brachymorphism, cupid bow of the upper lip, broad hands and feet, round face, abnormal ears, and developmental delay in addition to ocular findings [63].

The management of patients with Peters' anomaly is focused on the provision of sufficient clear cornea to allow vision and the early detection and treatment of glaucoma. Depending on the size of the opacity, the treatment varies from observation to optical iridectomy to penetrating keratoplasty. Postoperatively refractive correction and occlusion therapy are almost always needed [130]. The rate of graft survival is the greatest among the initial grafts as compared to the second, third, or fourth grafts. The initial grafts are most likely to fail during the first two postoperative years, with more than half of all failures occurring within the first three postoperative months [131]. Glaucoma represents a major comorbidity of Peters' anomaly and its treatment is usually surgical. The commonly performed surgeries to lower IOP include cyclocryotherapy, trabeculectomy, goniotomy, and valve implantation [130]. Visual outcome is guarded.

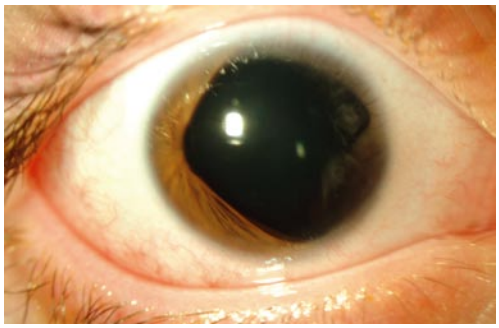

Fig. 21.11 Near-total absence of the iris in this patient with aniridia. Note indistinct limbus and superficial opacification superotemporally

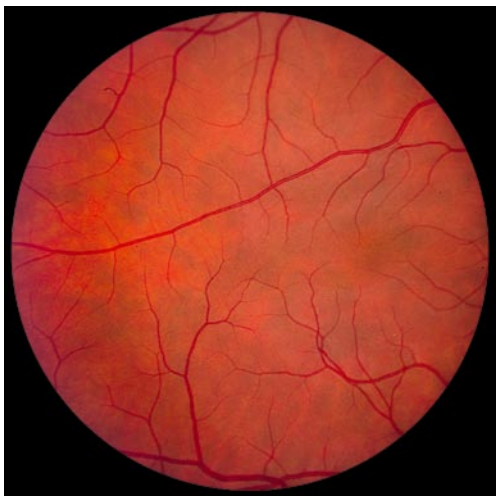

Fig. 21.12 Foveal hypoplasia in a patient with aniridia. Note flat foveal area with small vessels reaching the center of the fovea

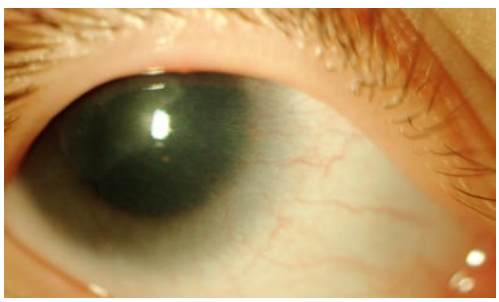

Fig. 21.13 Peripheral keratopathy ("pannus") in a patient with aniridia. This is caused by an absence of normal-functioning limbal stem cells that depend on a normal *PAX6* gene

21.3.7 Aniridia

Aniridia is a misnomer that refers to the congenital absence of some or most of the iris (Fig. 21.11). The extent of vision deficit varies similarly [51]. It is caused by a mutation in the *PAX6* gene on 11p13 and can be associated with other ocular malformations including cataract, lens subluxation, foveal hypoplasia (Fig. 21.12), optic nerve hypoplasia, and nystagmus [34]. If there is a chromosomal deletion of the 11p13 region that involves adjacent genes, patients have an increased risk of developing Wilms' tumor since the deletion might include the Wilms' tumor gene, *WT1* on 11p13. The WARG syndrome is a combination of Wilms' tumor, aniridia, mental retardation, and ambiguous genitalia, genitourinary abnormalities, or gonadoblastoma. The WARG syndrome is one of the best-studied "contiguous gene syndromes," since aniridia, Wilms' tumor, and probably mental retardation are determined by separate genes [91 101]. In the Gillespie syndrome, aniridia is associated with cerebellar ataxia and mental retardation [121].

Aniridia patients should undergo genetic testing and have repeated abdominal ultrasounds. If an intragenic *PAX6* mutation is identified, then the risk of Wilms' tumor becomes nil as there is no chromosomal deletion in such patients. The great majority of familial aniridia cases are due to intragenic mutations, hence Wilms' tumor is almost exclusively detected in isolated cases who have chromosomal deletions. Glaucoma occurs in 20–75% of patients and is treated with medications, goniotomy, or glaucoma drainage device placement [4, 118]. Aniridic keratopathy is the major cause of acquired vision loss in patients with aniridia. It is characterized by vascularization of the peripheral cornea, so-called pannus (Fig. 21.13), conjunctival invasion of the corneal surface, corneal epithelial erosions, and epithelial abnormalities, which eventually result in corneal opacity [88]. It has been shown that penetrating keratoplasty has a very low success rate in aniridia patients due to the lack of limbal stem cells that rely on a normal *PAX6* function for development and maintenance. Keratolimbal allograft is a stem cell transplantation technique that has been gaining popularity [46].

21.4 Congenital Disorders of the Cornea

21.4.1 Dermoids

Limbal and corneal dermoids are choristomas that typically occur on the temporal limbus. They consist predominantly of ectodermally derived elements (Fig. 21.14). They can be associated with Goldenhar's syndrome that is characterized by hemifacial microsomia with ipsilateral deformity of the external ear and vertebral anomalies [11]. Other associated anomalies include ipsilateral lid coloboma and Duane's syndrome.

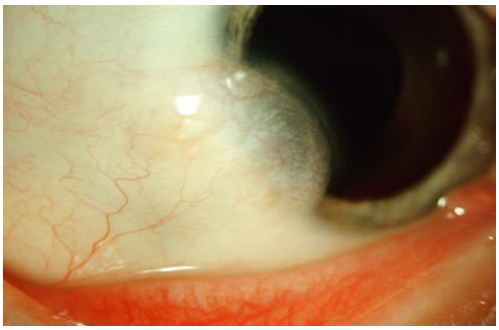

Fig. 21.14 Limbal dermoid in a typical inferotemporal location

21.4.2 Megalocornea

Megalocornea is defined as a cornea with a horizontal diameter greater than 13 mm. When it is present as an isolated defect, it is inherited in an X-linked manner and is mapped to Xq21.3-q22 [62]. Examples of systemic associations include Marfan syndrome and megalocornea–mental retardation syndrome [21, 79]. Patients with X-linked megalocornea have a posterior crocodile shagreen abnormality of the cornea and develop presenile cataracts [113].

21.4.3 Microcornea

Microcornea refers to a cornea with a horizontal diameter less than 10 mm. Microcornea can be associated with microphthalmos or with multiple systemic disorders including but not limited to Nance-Horan syndrome, Warburg Micro syndrome, and Ehlers-Danlos syndrome [44, 77, 126]. The presence of microcornea in patients with congenital cataracts indicates a small eye and may be a poor prognostic sign for visual outcome.

21.4.4 Cornea Plana

Cornea plana is a cornea with curvature less than 43D. When caused by a mutation in *KERA* gene on chromosome 12q, it is inherited as an autosomal recessive trait. Interestingly, autosomal recessive cornea plana is most prevalent in northern Finland likely due to the founder effect in the population that arrived in those regions approximately 400 years ago [37]. It has also been reported in a large number of patients from Saudi Arabia and other parts of the Middle East. Autosomal recessive and autosomal dominant forms are genetically and clinically distinct [85, 111]. Both can lead to hyperopia, hazy corneal limbus, and arcus lipoides at an early age. However, the recessive form is more severe. A round opaque central corneal thickening of about 5 mm is a common finding in recessive cornea plana, but is never present in the dominant form. Additionally, in the recessive form there are iris malformations as well as a slit-like pupil and adhesions between the iris and cornea (Fig. 21.15) [111].

21.4.5 Sclerocornea

Sclerocornea can be a part of the cornea plana syndrome. It is characterized by indistinct scleral and corneal limits. When inherited in a dominant form, it is milder than when inherited as a recessive trait. Sclerocornea totalis occurs when the whole cornea is involved. Microscopically, there is thinning of the peripheral cornea, lack of Bowman's layer, irregular stromal lamellae, stromal vascularization, markedly underdeveloped or absent Descemet's membrane, and marked attenuation of the endothelium [28]. Sclerocornea can occur as a part of a syndrome such as the MIDAS syndrome that stands for microphthalmia,

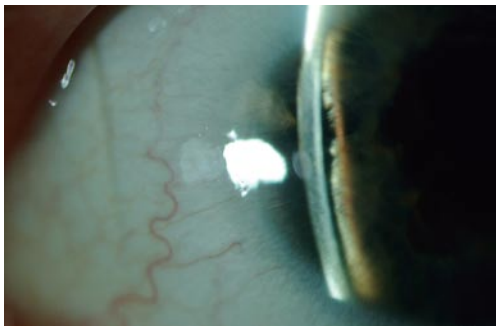

Fig. 21.15 Autosomal recessive cornea plana. Note very flat and small, rather than curved cornea. The anterior chamber is extremely flat and the iris is malformed. The limbus is indistinct

dermal aplasia, and sclerocornea [43]. Observation or keratoplasty are used for most patients, depending on the degree of opacification. The success rate of penetrating keratoplasty in these patients is less than 50% [72]. The cornea can clear substantially in the first weeks of life, hence it is not wise to rush into any surgical intervention before several weeks of age.

21.4.6 Corneal Dystrophies

Corneal dystrophies can affect any layer of the cornea with characteristic clinical presentation patterns that depend on the level of anatomic involvement and the underlying pathology. Thus, dystrophies of epithelium and Bowman's layer present with recurrent erosions of the cornea along with diminished visual acuity resultant from epithelial irregularity and scarring. The decreased visual acuity in stromal dystrophies is due to deposition of various substances in keratocytes and extracellular matrix. Corneal edema due to a malfunctioning endothelial pump is the cause of vision problems in Descemet's membrane and corneal endothelium dystrophies [2]. The main corneal dystrophies presenting at birth are congenital hereditary stromal dystrophy, Fleck corneal dystrophy, congenital hereditary endothelial dystrophy, and posterior polymorphous dystrophy.

Both congenital hereditary stromal corneal dystrophy and Fleck dystrophy affect the stroma. Only a few reports of a true congenital hereditary stromal corneal dystrophy (CHSD) have been published. CHSD is an autosomal dominant disorder characterized by opacities, which were equally pronounced in all areas of the cornea. There are no signs of vascularization and corneal sensitivity is normal or slightly reduced. The patients usually do not have other ocular symptoms, especially corneal erosions or photophobia. However, refractive errors, amblyopia, and strabismus are commonly observed in the affected individuals. Congenital stromal dystrophy of the cornea is caused by a mutation in the decorin gene [13, 81]. Fleck corneal dystrophy is characterized by tiny white flecks that can be found on all corneal levels; they present early and progress minimally. Congenital hereditary endothelial dystrophy and posterior polymorphous dystrophy are dystrophies of Descemet's membrane and the corneal endothelium. Congenital hereditary endothelial dystrophy (CHED) can be autosomal dominant or recessive with the recessive form being more severe and presenting with corneal clouding at birth and complicated by nystagmus. It has been reported that mutations in *SLC4A11* gene, a member of bicarbonate transporter proteins, are associated with the autosomal form [124]. Posterior polymorphous dystrophy (PPMD) is an autosomal dominant disorder with highly variable expressivity and mutation described in *VSX1*, *COL8A2*, and *TGF8* genes. It is rare and involves a metaplasia and overgrowth of corneal endothelial cells. Endothelial cells in PPMD manifest in an epithelial morphology and gene expression pattern and thus produce an aberrant basement membrane, and, sometimes, spread over the iris and nearby structures increasing the risk for glaucoma [54].

All three types of congenital corneal dystrophies can be confused with glaucoma. The differentiating features of CHED and PPMD are normal horizontal corneal diameter with increased corneal thickness, and normal IOP measurements. Treatment of corneal dystrophies has changed in recent years with the introduction of phototherapeutic keratectomy (PTK). In PTK an excimer laser, similar to the one used in photorefractive keratectomy, is utilized. PTK can be used only on anterior corneal dystrophies including Meesmann corneal dystrophy, Reis-Bücklers syndrome, Thiel-Behnke syndrome, granular dystrophy, lattice dystrophy, and central crystalline dystrophy of Schnyder. It has been previously shown that the rate of recurrence of corneal dystrophies after lamellar or penetrating keratoplasty is significant [70]. Excimer

laser can be used on grafted and non-grafted corneas and can be repeated more than once. Although PTK offers a less-aggressive, safer alternative with faster recovery, it is still not devoid of recurrences of corneal dystrophy [26]. Other treatment options for anterior corneal dystrophies include diamond burr polishing of Bowman's membrane [119]. Corneal dystrophies with involvement of endothelium and Descemet's membrane are usually treated by performing a penetrating keratoplasty or deep lamellar endothelial keratoplasty (DLEK) [83]. DLEK provides faster visual rehabilitation, with better spherical equivalents and less astigmatism [114]. Conservative management of patients and avoidance of penetrating keratoplasty except in cases of severe reduction of vision is advised.

21.5 Congenital Cataracts

The reader is referred to the other chapters in this text book that cover congenital cataracts in more detail (Chaps. 22, 23). Congenital cataracts can be unilateral or bilateral, inherited, idiopathic, or caused by intrauterine infections. Depending on the etiology, a cataract can be nuclear, posterior, or lamellar with nuclear cataract usually present at birth and non-progressive and lenticular cataracts developing later and progressing faster [133].

Bilateral cataracts are mostly idiopathic. When inherited, cataracts are inherited mainly as autosomal dominant, but also as autosomal recessive and X-linked traits [133]. Rarely cataracts can be caused by metabolic disorders such as galactosemia [9]. Cataracts can also arise from intrauterine infections such as toxoplasmosis, which is also associated with chorioretinal scars. Rubella virus affects lens development and results in cataract formation, usually in the form of a nuclear cataract, but possibly total. In congenital and neonatal herpes conjunctivitis, keratitis, iridocyclitis, iris atrophy, posterior synechiae, and cataract have been described. Congenital cataracts are also associated with varicella-zoster virus and syphilis and are rarely found with cytomegalovirus infection [71].

Cataracts can be one of the presenting signs of a syndrome such as trisomy 21 or Turner's syndrome and multiple other inherited entities [133]. Unilateral cataracts as a rule are idiopathic. They can be associated with lenticonus/lentiglobus and persistent fetal vasculature as part of the persistent hyperplastic primary vitreous spectrum [133]. In order to prevent the development of amblyopia, cataract surgery with or without intraocular lens (IOL) placement is recommended. Surgery should be performed within 2 months of birth. Optical correction and patching are required in postoperative follow-up. Opacification of the visual axis and secondary glaucoma are significant complications of infantile cataract surgery [133].

21.6 Persistent Hyperplastic Primary Vitreous/Persistence of the Fetal Vasculature

Persistent hyperplastic primary vitreous (PHPV) is a complex ocular malformation disorder in which the predominant abnormalities result from persistence of elements of the fetal vasculature mostly in the anterior segment of the eye (Fig. 21.16), but also in the vitreous and around the disk area. The persistence of these remnants leads to secondary complications such as retinal traction, ciliary process tractions, and abnormalities in the posterior capsule of the lens. In its most classic form there is a fibrovascular stalk/membrane extending from the optic nerve to the posterior lens capsule, with contraction of the posterior capsule/membrane and dragging of the ciliary processes toward the center of the posterior lens capsule. The eye in severe PHPV cases is smaller than average. In its mild forms, there may only be a posterior lenticonus or polar cataract, with a very thin remnant of the hyaloid vessels. Other forms are described elegantly in Goldberg's review on the subject [40].

21.7 Congenital Anomalies of the Optic Nerve

Congenital abnormalities of the optic nerve are probably some of the most commonly seen ocular malformations and can involve one or both eyes. Patients with poor vision due to optic nerve anomalies should

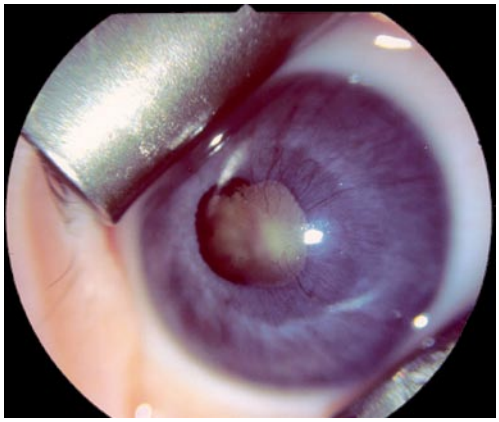

Fig. 21.16 Anterior segment of a patient with persistence of the fetal vessels and PHPV. There are numerous iridohyaloid vessels. A retrolental membrane is visible in the center. Elongated ciliary processes can be seen superonasally

be managed by treating refractive errors, occlusion therapy in selected cases, and screening patients for possible associated central nervous system malformations such as pituitary hypoplasia and moyamoya disease, that may jeopardize their lives in some instances. [31]

21.7.1 Aplasia of the Optic Nerve

Aplasia of the optic nerve is a very rare congenital, non-hereditary condition of unknown etiology. These patients lack optic disk, optic nerve, retinal ganglion cells, and retinal vessels. The electroretinogram (ERG) is usually flat, but if present shows diminished a and b waves. Optic nerve aplasia can be associated with other ocular abnormalities such as microphthalmia, enophthalmos, ptosis, smaller corneal diameter, and absent Descemet's membrane and endothelium. A small or absent chiasm is a common CNS abnormality [116].

21.7.2 Hypoplasia of the Optic Nerve

Optic nerve hypoplasia (ONH) is characterized by a reduced number of optic nerve axons from the time of birth, with otherwise normal glial and supportive mesodermal tissue. ONH is among the three leading causes of childhood blindness along with cortical visual impairment and retinopathy of prematurity [108].

Ophthalmoscopically and in its most classic form ONH is characterized by a peripapillary hypopigmented halo around a small optic disk (Fig. 21.17). The peripapillary double-ring might be absent. The retinal vessels are present, but tend to have a tortuous course. Magnetic resonance imaging (MRI) can show not only the reduced size of the optic nerve, but also associated brain abnormalities. It is useful to calculate the ratio of the distance from the center of the optic disk to the centre of the macula/optic disk diameter for diagnostic purposes (with a value of 4 or more giving a definite diagnosis) [31]. Visual acuity can be normal in mild cases. Abnormalities of the visual evoked potential are observed in approximately 35% of cases, with findings suggestive of transsynaptic degeneration. A normal ERG can be helpful in distinguishing ONH from Leber's congenital amaurosis.

Optic nerve hypoplasia is a non-progressive sporadic disorder and is associated with a number of possible underlying etiologies. It is believed that patients with ONH have excessive apoptosis of axons in utero, and not primary failure of axon differentiation [57]. ONH is more common in children of young first parity mothers with a positive history of smoking, history of type I diabetes, and preterm birth with complications. It is a feature of the fetal alcohol syndrome and of septo-optic dysplasia (ONH, pituitary gland hypoplasia, and midline abnormalities of the brain), a condition linked to the *HESX1* gene in some patients [25].

Patching can improve vision in patients with superimposed amblyopia, and refraction and spectacle prescription is beneficial. Children with ONH should undergo evaluation for possible associated CNS and endocrinologic abnormalities [39].

21.7.3 Optic Disk Coloboma

Optic disk coloboma should be differentiated from the morning glory disk anomaly and peripapillary staphyloma. Ophthalmoscopically, optic disk coloboma presents as an inferior bowl-shaped ex-

cavation with missing neuroretinal rim that has occurred due to faulty closure of the embryonic fissure. In coloboma, the only feature that relates to visual outcome is the degree of foveal involvement [82].

Colobomas can be complicated by optic nerve sheath-derived cysts that can communicate with subarachnoid space and rarely lead to compressive optic neuropathy [94]. Retinal detachments have also been observed as well as spontaneous reattachments [31].

Colobomas can be inherited in an autosomal dominant manner or occur sporadically [31]. They can also be a part of many syndromes, such as papillorenal syndrome characterized by optic nerve colobomas, vesicoureteral reflux, and renal anomalies, and are related to a mutation in the *PAX2* gene [97]. CHARGE syndrome includes coloboma of the eye, heart anomaly, choanal atresia, mental retardation, genitourinary abnormalities, ear abnormalities, and/or deafness [84]. Other syndromes with a retinochoroidal and/or optic nerve ocular colobomatous component include Walker-Warburg, Goltz focal dermal hypoplasia, Goldenhar's syndrome, and Aicardi's syndrome [116].

As in other congenital malformative ocular disorders, patching and optimal refractive correction are indicated in the appropriate patient.

21.7.4 Morning Glory Disk Anomaly

Morning glory anomaly is named so because its appearance is reminiscent of the flower with the same name; there is a conical excavation of the posterior fundus including the optic disk, filled with white glial tissue, and surrounded by a raised annulus of pigmentary chorioretinal changes (Fig. 21.18) [31, 116]. This usually unilateral anomaly is also associated with an increased number of retinal vessels that run in a straighter course from the papilla, and with occasional arteriovenous malformations near the optic disk. A unique phenomenon of contractile movements of the optic disk has been reported that can possibly be accounted for by a cuff of smooth muscle tissue identified within the terminal optic head [31].

Patients with morning glory anomaly can have substantial visual deficits. Complications commonly include retinal detachments and occasional subretinal neovascularization under the fovea and peripapillary retina [31].

Morning glory disk anomaly can be an isolated finding of unknown pathogenesis or it may be associated with transsphenoidal encephaloceles [53] or more commonly vascular abnormalities of the internal carotids such as moyamoya disease [59]. It has

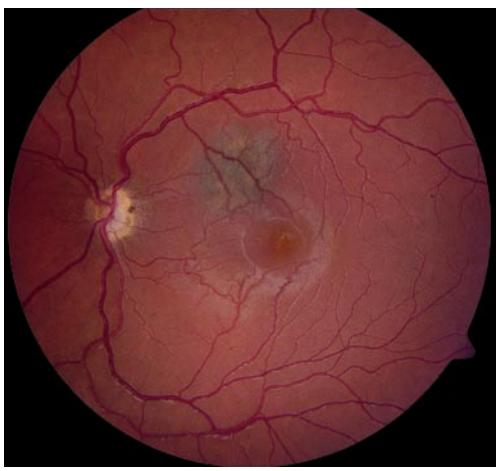

Fig. 21.17 Optic nerve hypoplasia. There is a double-ring sign, mild tortuosity of the retinal vessels, and an incidental choroidal nevus

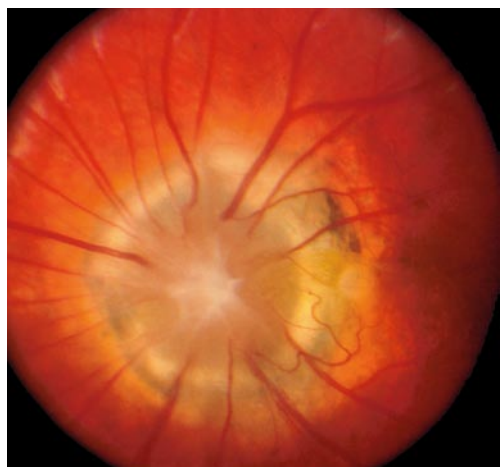

Fig. 21.18 Most typical morning glory disk anomaly. The scleral opening is large with radial vessels, a central tuft of glial tissue, and a peripapillary ring of variably pigmented tissue

been postulated that failure of the posterior sclera and the lamina cribrosa of the optic nerve head to form lead to herniation of the intraocular contents through the defect which results in the characteristic conical formation [116].

Careful refraction and treatment of associated strabismic or anisometropic amblyopia is indicated. Occlusion treatment should be continued only in patients with documented improvement in vision. Retinal detachments occur in 30% of cases and have poor visual outcome even in cases of successful surgical reattachment [116]. Magnetic resonance or computed tomographic angiography are indicated to rule out moyamoya or other intracranial vascular disease that occurs in up to 40% of cases.

21.7.5 Peripapillary Staphyloma

Peripapillary staphyloma is characterized by a normal or temporally pale optic nerve located within an excavated defect of the sclera lined by retina and choroid. The optic disk and retinal vessels are normal. There has been occasional observations of contractility [31]. The differentiation between peripapillary staphyloma and morning glory anomaly can be difficult. Peripapillary staphyloma has a deep cup-shaped excavation as opposed to the tapering funnel-shaped excavation of the morning glory anomaly. Additionally, the disk structure is normal in staphylomas, and there is no central glial tuft as observed in the morning glory anomaly [116].

Vision in patients with peripapillary staphyloma ranges from normal to markedly reduced and is accompanied by centrocecal scotoma, myopia, or emmetropia. Peripapillary scotoma is usually a rare unilateral isolated finding and is presumed to result from abnormal posterior scleral development.

21.7.6 Optic Pits

These are cavitary malformations of the optic nerve head that are characterized by an oval depression in the rim, most often located in the temporal aspect of the nerve head (Fig. 21.19). They are usually solitary, but up to three pits have been described in one nerve head. They are gray or greenish in hue and can be very small or occupy almost all of the nerve head. There may be a communication with the subarachnoid space that leads to the accumulation of subretinal fluid in the macular area, so-called macular schisis. Another possible source for the macular fluid is liquefied vitreous. Vision is normal, but can be reduced in cases with macular detachment [86].

21.8 Congenital Disorders of the Retina

21.8.1 Retinal Dysplasia

Retinal dysplasia is more of a pathologic than a clinical term and refers to maldevelopment of the retina

Fig. 21.19 Left optic pit. Note that left optic nerve head is larger than the right

with either poor differentiation of retinal cells such as photoreceptors or poor laminar organization of retinal layers. Retinal dysplasia may be localized to one area of the retina or may be generalized. One of the hallmarks of retinal dysplasia is the rosette formation that can also be seen in retinoblastoma. Retinal dysplasia is more commonly found in the context of syndromes such as Warburg's syndrome, Aicardi's syndrome in so-called lacunae, and in Norrie's disease. Dysplastic retina clinically appears as a non-transparent or whitish area of the fundus, or may take the form of a fold, scar-like formation, or lacuna.

21.8.2 Foveal Hypoplasia

In foveal hypoplasia there is absence of the normal umbo in the center of the macula, and this generally reflects an abnormality in the underlying retinal architecture and distribution of cones and rods. Histopathologic studies in albinism have shown no difference in the composition of the retina in the fovea from that in the adjacent area. This is also observed on optical coherence tomography. Foveal hypoplasia is most often encountered in albinism and in aniridia. Albinism is discussed elsewhere in this book, and aniridia is discussed earlier in this chapter. Oculocutaneous albinism is caused by abnormalities of melanin synthesis in skin, hair, and eyes. Patients usually present with hypopigmented uveal tract and retinal pigment epithelium, nystagmus, iris transillumination, foveal hypoplasia, and abnormal decussation of the optic nerve fibers at the optic chiasm [132]. Patients with oculocutaneous albinism often have hyperopia with oblique astigmatism. Four genetic loci for albinism have been mapped and three genes isolated: tyrosinase, an enzyme crucial in melanin production, the P gene encoding the tyrosine-transporting membrane protein, and the gene for X-lined albinism, *OA1* [99].

21.9 Congenital Disorders of the Lids and Orbits

Abnormal intercanthal and medial orbital wall distances as well as lid malformations can be isolated physical findings or may be associated with a large number of syndromes. For instance, hypotelorism occurs in more than 60 syndromes [29].

21.9.1 Hypotelorism

Hypotelorism is characterized by reduced distance between the medial walls of the orbits with decreased inner and outer canthal distances. Hypotelorism is commonly seen in disorders of brain development such as craniosynostosis with premature closure of metopic cranial sutures leading to trigonocephaly [92] and holoprosencephaly, failure to divide the forebrain into left and right hemispheres that is usually accompanied by defects in patterning of the midline of the face [55]. An extreme example of hypotelorism is cyclopia, a centrally located eye. Cyclopia has been linked to mutations in sonic hedgehog gene [78].

21.9.2 Hypertelorism

Hypertelorism is defined as an increased distance between the medial orbital walls, or interorbital distance, with increased inner and outer intercanthal distances. Clinically, the best way to assess hypertelorism is to measure interpupillary distance [29]. A flat nasal bridge, epicanthal folds, exotropia, widely spaced eyebrows, narrow palpebral fissures, and dystopia canthorum can all lead to the incorrect diagnosis of hypertelorism [19]. Hypertelorism is associated with more than 550 disorders. Three mechanisms of hypertelorism development have been proposed. First, hypertelorism can be caused by early ossification of the lesser wings of the sphenoid and fixation of the orbits in the fetal position preventing them from moving from 180° position in early development to 70° at birth, and to 68° in adults. Second, there could be a failure in nasal capsule development allowing the primitive brain vesicle, a frontal encephalocele, to protrude into the space normally occupied by the capsule resulting in morphokinetic arrest in the position of the eyes. Thirdly, hypertelorism can be a result of skull base developmental disturbance [19]. The examples of the latter include craniosynostosis syndromes such as Apert's and Crouzon's and midfacial abnormalities such as frontonasal dysplasia. Ap-

ert's syndrome is caused by mutation in the gene encoding fibroblast growth factor receptor 2 (FGFR2) and is characterized by midface hypoplasia, symphalangism (fusion between the phalanges of the digits), radiohumeral fusion, variable mental retardation, protrusion of the eyes, strabismus, and asymmetry of the orbits [24]. Crouzon's syndrome is characterized as coronal craniosynostosis that in addition to hypertelorism has variable involvement of other calvarial sutures, brachycephaly, frontal bossing, proptosis, strabismus, maxillary hypoplasia, mandibular prognathism, atresia of the external auditory canals, premature calcification of stylohyoid ligament, Chiari I malformation, hydrocephalus, mental retardation, and protrusion of the eyes [24]. Mutations in the FGFR2 cause Crouzon's syndrome as well [90].

21.9.3 Telecanthus and Dystopia Canthorum

Telecanthus refers to an increased distance between the inner canthi. Telecanthus can be associated with true hypertelorism or can occur in isolation. Dystopia canthorum is isolated telecanthus with lateral displacement of the lacrimal puncta [29].

Telecanthus also occurs in the context of many syndromes, but dystopia canthorum is characteristic of Waardenburg's syndrome type 1 that presents with a frontal white forelock of hair, heterochromia iridis, white eye lashes, leukoderma, and cochlear deafness [125]. It results from mutations in the *PAX3* gene that is involved in neural crest development.

21.9.4 Congenitally Sunken and Prominent Eyes

Sunken eyes result from hyperdevelopment of the orbital ridges and walls, microphthalmos, or decreased orbital fat tissue as observed with Cockayne's syndrome [29]. Patients with Cockayne's syndrome have poor growth and neurologic abnormalities, sensorineural hearing loss, cataracts, pigmentary retinopathy, cutaneous photosensitivity, and dental caries [76]. Cockayne's syndrome results from defective DNA nucleotide excision repair of actively transcribing genes [89].

Prominent eyes are observed in Apert's and Crouzon's syndromes due to reduced orbital volume. They are also observed in cases of midfacial hypoplasia found in infants of mothers who consumed such drugs as warfarin and retinoic acid and also in such disorders as Stickler's and Schinzel-Giedion syndromes [29]. Stickler's syndrome is an entity consisting of progressive myopia, premature degenerative changes in various joints, hearing deficit, and midfacial hypoplasia [109]. Schinzel-Giedion syndrome manifests as severe midface retraction, multiple skull anomalies, congenital heart defect, hydronephrosis, clubfeet, and hypertrichosis [100].

Pediatric craniofacial surgery is the main treatment modality for patients with malformations of the orbit and requires close collaborations between a multidisciplinary team of physicians that include craniofacial surgeons, ophthalmologists, and neurosurgeons.

21.9.5 Eyelid and Palpebral Fissure Malformations

Lid differentiation starts at week 6 of gestation with fusion at week 8 and complete separation at month 7. During the time that the lids are fused, the development of the orbicularis oculi muscles, tarsal plates, meibomian glands, lacrimal puncta, canaliculi, skin appendages, and conjunctiva occurs [29].

21.9.5.1 Epicanthal Folds

Epicanthal folds come in four varieties: epicanthus inversus, epicanthus tarsalis, epicanthus palpebralis, and epicanthus supraciliaris. Epicanthus inversus, a vertical cutaneous fold going from the lower lid toward the internal part of the upper lid, is the only epicanthal fold that has syndromic significance and is associated with blepharophimosis, a reduction in horizontal and vertical dimensions of the palpebral fissure. The other types of epicanthal folds represent normal variants [29, 41].

21.9.5.2 Upward Slanting oalpebral Fissures

An upward slanting palpebral fissure is an nonspecific but very common finding in trisomy 21 or Down syndrome [29]. Downward slanting palpebral fissure is seen in Treacher-Collins syndrome, an autosomal dominant disorder of craniofacial development which results from loss-of-function mutations in the gene *TCOF1* [27].

Fig. 21.20 Young child with blepharophimosis syndrome. Note blepharophimosis, telecanthus, ptosis, and epicanthus inversus

21.9.5.3 Cryptophthalmos

Cryptophthalmos is characterized by completely fused lids and is seen in Fraser's syndrome with cutaneous syndactyly, malformations of the larynx and genitourinary tract, craniofacial dysmorphism, orofacial clefting, mental retardation, and musculoskeletal anomalies [107].

21.9.5.4 Ablepharon-Macrostomia Syndrome

Ablepharon-macrostomia syndrome is characterized by absent eyelids, absent eyebrows, eyelashes and hair, fusion defects of the mouth, expressionless fa-

Take Home Pearls

- Visual acuity cannot be predicted in the infant with colobomatous microphthalmia or other malformations such as optic nerve hypoplasia or Peters' anomaly. One should in general be cautiously optimistic about visual function unless there is no evidence of light perception.
- It is important to differentiate typical optic nerve coloboma from the morning glory disk anomaly as their genetics and their associated anomalies are very different.
- Brain imaging is important in certain anomalies such as optic nerve hypoplasia, colobomas of the optic nerve head, and the morning glory disk anomaly. Vascular imaging of the internal carotid system is essential in patients with the morning glory disk anomaly who are at high risk of having moyamoya disease.
- Careful assessment for glaucoma and periodic life-long checking of intraocular pressure should be done in patients with anterior segment dysgenesis.
- Testing for *PAX6* mutations is essential in patients with aniridia. Those with intragenic mutations are not at risk for Wilms' tumor. Patients with deletions of 11p13 outside of the gene are at risk for the tumor.

cies, rudimentary external ears, ambiguous genitalia, absent or rudimentary nipples, coarse dry skin with redundant skin folds, and delayed expressive language development [66].

21.9.5.5 Ankyloblepharon

Ankyloblepharon is partial or complete adhesion of the ciliary edges of superior and inferior eyelids [29]. Hay-Wells or ankyloblepharon-ectodermal dysplasia-clefting syndrome is a rare autosomal dominant disorder characterized by ankyloblepharon, ectodermal dysplasia, and cleft lip and/or cleft palate [15].

21.9.5.6 Blepharophimosis

Blepharophimosis, as described above, is a reduction in horizontal and vertical dimensions of the palpebral fissure. It can be associated with various syndromes or can occur on its own. Blepharophimosis syndrome is characterized by blepharophimosis, telecanthus, and epicanthus inversus (Fig. 21.20) [115]. Syndromic associations include Ohdo blepharophimosis syndrome, Marden-Walker syndrome, and Schwartz-Jampel syndrome [75].

Congenital disorders of the eyelids require a thorough knowledge of syndromic associations and sometimes require surgical intervention [12].

References

1. Alagille D, Odievre M, Gautier M, Dommergues JP (1975) Hepatic ductular hypoplasia associated with characteristic facies, vertebral malformations, retarded physical, mental, and sexual development, and cardiac murmur. J Pediatr 86:63–71
2. Aldave AJ, Sonmez B (2007) Elucidating the molecular genetic basis of the corneal dystrophies: are we there yet? Arch Ophthalmol 125:177–186
3. Alward WL, Semina EV, Kalenak JW, Heon E, Sheth BP, Stone EM, Murray JC (1998) Autosomal dominant iris hypoplasia is caused by a mutation in the Rieger syndrome (RIEG/PITX2) gene. Am J Ophthalmol 125:98–100
4. Arroyave CP, Scott IU, Gedde SJ, Parrish RK II, Feuer WJ (2003) Use of glaucoma drainage devices in the management of glaucoma associated with aniridia. Am J Ophthalmol 135:155–159
5. Azuma N, Yamaguchi Y, Handa H, Hayakawa M, Kanai A, Yamada M (1999) Missense mutation in the alternative splice region of the PAX6 gene in eye anomalies. Am J Hum Genet 65:656–663
6. Azuma N, Yamaguchi Y, Handa H, Tadokoro K, Asaka A, Kawase E, Yamada M (2003) Mutations of the PAX6 gene detected in patients with a variety of optic-nerve malformations. Am J Hum Genet 72:1565–1570
7. Beck AD (2001) Diagnosis and management of pediatric glaucoma. Ophthalmol Clin North Am 14:501–512
8. Beck AD, Wilson WR, Lynch MG, Lynn MJ, Noe R (1998) Trabeculectomy with adjunctive mitomycin C in pediatric glaucoma. Am J Ophthalmol 126:648–657
9. Beigi B, O'Keefe M, Bowell R, Naughten E, Badawi N, Lanigan B (1993) Ophthalmic findings in classical galactosaemia: prospective study. Br J Ophthalmol 77:162–164
10. Blake KD, Prasad C (2006) CHARGE syndrome. Orphanet J Rare Dis 1:34
11. Boles DJ, Bodurtha J, Nance WE (1987) Goldenhar complex in discordant monozygotic twins: a case report and review of the literature. Am J Med Genet 28:103–109
12. Brady KM, Patrinely JR, Soparkar CN (1998) Surgery of the eyelids. Clin Plast Surg 25:579–586, ix
13. Bredrup C, Knappskog PM, Majewski J, Rodahl E, Boman H (2005) Congenital stromal dystrophy of the cornea caused by a mutation in the decorin gene. Invest Ophthalmol Vis Sci 46:420–426
14. Bron AJ, Tripathi RC, Tripathi BJ, Wolff E (1997) Wolff's anatomy of the eye and orbit. Chapman & Hall Medical, London
15. Cabiling DS, Yan AC, McDonald-McGinn DM, Zackai EH, Kirschner RE (2007) Cleft lip and palate repair in Hay-Wells/ankyloblepharon-ectodermal dysplasia-clefting syndrome. Cleft Palate Craniofac J 44:335–339
16. Cepko CL, Austin CP, Yang X, Alexiades M, Ezzeddine D (1996) Cell fate determination in the vertebrate retina. Proc Natl Acad Sci U S A 93:589–595
17. Chandler PA (1956) Atrophy of the stroma of the iris: endothelial dystrophy, corneal edema, and glaucoma. Am J Ophthalmol 41:607–615
18. Cogan DG, Reese AB (1969) A syndrome of iris nodules, ectopic Descemet's membrane, and unilateral glaucoma. Doc Ophthalmol 26:424–433
19. Cohen MM Jr, Richieri-Costa A, Guion-Almeida ML, Saavedra D (1995) Hypertelorism: interorbital growth, measurements, and pathogenetic considerations. Int J Oral Maxillofac Surg 24:387–395
20. Coleman AL, Smyth RJ, Wilson MR, Tam M (1997) Initial clinical experience with the Ahmed Glaucoma Valve implant in pediatric patients. Arch Ophthalmol 115:186–191
21. Consul BN, Mehrotra AS, Mathur GB (1966) Marfan's syndrome with bilateral megalocornea and subluxated cataractous lenses. J All India Ophthalmol Soc 14:262–263
22. Coulombre AJ (1957) The role of intraocular pressure in the development of the chick eye. II. Control of corneal size. AMA Arch Ophthalmol 57:250–253
23. Crawford RA (1967) Iris dysgenesis with other anomalies. Br J Ophthalmol 51:438–440

24. Cunningham ML, Seto ML, Ratisoontorn C, Heike CL, Hing AV (2007) Syndromic craniosynostosis: from history to hydrogen bonds. Orthod Craniofac Res 10:67–81
25. de la Mata I, Garcia JL, Gonzalez C, Menendez M, Canada J, Jimenez-Barbero J, Asensio JL (2002) The impact of R53C mutation on the three-dimensional structure, stability, and DNA-binding properties of the human Hesx-1 homeodomain. Chembiochem 3:726–740
26. Dinh R, Rapuano CJ, Cohen EJ, Laibson PR (1999) Recurrence of corneal dystrophy after excimer laser phototherapeutic keratectomy. Ophthalmology 106:1490–1497
27. Dixon J, Trainor P, Dixon MJ (2007) Treacher Collins syndrome. Orthod Craniofac Res 10:88–95
28. Doane JF, Sajjadi H, Richardson WP (1994) Bilateral penetrating keratoplasty for sclerocornea in an infant with monosomy 21. Case report and review of the literature. Cornea 13:454–458
29. Dollfus H, Verloes A (2004) Dysmorphology and the orbital region: a practical clinical approach. Surv Ophthalmol 49:547–561
30. Doward W, Perveen R, Lloyd IC, Ridgway AE, Wilson L, Black GC (1999) A mutation in the RIEG1 gene associated with Peters' anomaly. J Med Genet 36:152–155
31. Dutton GN (2004) Congenital disorders of the optic nerve: excavations and hypoplasia. Eye 18:1038–1048
32. Edward DP, Kaufman LM (2003) Anatomy, development, and physiology of the visual system. Pediatr Clin North Am 50:1–23
33. Eid TE, Katz LJ, Spaeth GL, Augsburger JJ (1997) Long-term effects of tube-shunt procedures on management of refractory childhood glaucoma. Ophthalmology 104:1011–1016
34. Elsas FJ, Maumenee IH, Kenyon KR, Yoder F (1977) Familial aniridia with preserved ocular function. Am J Ophthalmol 83:718–724
35. Fantes J, Ragge NK, Lynch SA, McGill NI, Collin JR, Howard-Peebles PN, Hayward C, Vivian AJ, Williamson K, van Heyningen V, FitzPatrick DR (2003) Mutations in SOX2 cause anophthalmia. Nat Genet 33:461–463
36. Ferda Percin E, Ploder LA, Yu JJ, Arici K, Horsford DJ, Rutherford A, Bapat B, Cox DW, Duncan AM, Kalnins VI, Kocak-Altintas A, Sowden JC, Traboulsi E, Sarfarazi M, McInnes RR (2000) Human microphthalmia associated with mutations in the retinal homeobox gene CHX10. Nat Genet 25:397–401
37. Forsius H, Damsten M, Eriksson AW, Fellman J, Lindh S, Tahvanainen E (1998) Autosomal recessive cornea plana. A clinical and genetic study of 78 cases in Finland. Acta Ophthalmol Scand 76:196–203
38. Freedman SF, McCormick K, Cox TA (1999) Mitomycin C-augmented trabeculectomy with postoperative wound modulation in pediatric glaucoma. J AAPOS 3:117–124
39. Garcia ML, Ty EB, Taban M, Rothner AD, Rogers D, Traboulsi EI (2006) Systemic and ocular findings in 100 patients with optic nerve hypoplasia. J Child Neurol 21:949–956
40. Goldberg M (1997) Persistent fetal vasculature (PFV): an integrated interpretation of signs and symptoms associated with persistent hyperplastic primary vitreous (PHPV). LIV Edward Jackson Memorial Lecture. Am J Ophthalmol 124:587–626
41. Guercio JR, Martyn LJ (2007) Congenital malformations of the eye and orbit. Otolaryngol Clin North Am 40:113–140, vii
42. Hanson IM, Fletcher JM, Jordan T, Brown A, Taylor D, Adams RJ, Punnett HH, van Heyningen V (1994) Mutations at the PAX6 locus are found in heterogeneous anterior segment malformations including Peters' anomaly. Nat Genet 6:168–173
43. Happle R, Daniels O, Koopman RJ (1993) MIDAS syndrome (microphthalmia, dermal aplasia, and sclerocornea): an X-linked phenotype distinct from Goltz syndrome. Am J Med Genet 47:710–713
44. Heim P, Raghunath M, Meiss L, Heise U, Myllyla R, Kohlschutter A, Steinmann B (1998) Ehlers-Danlos syndrome type VI (EDS VI): problems of diagnosis and management. Acta Paediatr 87:708–710
45. Hendrickson A, Kupfer C (1976) The histogenesis of the fovea in the macaque monkey. Invest Ophthalmol Vis Sci 15:746–756
46. Holland EJ, Djalilian AR, Schwartz GS (2003) Management of aniridic keratopathy with keratolimbal allograft: a limbal stem cell transplantation technique. Ophthalmology 110:125–130
47. Honkanen RA, Nishimura DY, Swiderski RE, Bennett SR, Hong S, Kwon YH, Stone EM, Sheffield VC, Alward WL (2003) A family with Axenfeld-Rieger syndrome and Peters' anomaly caused by a point mutation (Phe112Ser) in the FOXC1 gene. Am J Ophthalmol 135:368–375
48. Idrees F, Vaideanu D, Fraser SG, Sowden JC, Khaw PT (2006) A review of anterior segment dysgeneses. Surv Ophthalmol 51:213–231
49. Jamieson RV, Perveen R, Kerr B, Carette M, Yardley J, Heon E, Wirth MG, van Heyningen V, Donnai D, Munier F, Black GC (2002) Domain disruption and mutation of the bZIP transcription factor, MAF, associated with cataract, ocular anterior segment dysgenesis and coloboma. Hum Mol Genet 11:33–42
50. Jena AK, Kharbanda OP (2005) Axenfeld-Rieger syndrome: report on dental and craniofacial findings. J Clin Pediatr Dent 30:83–88
51. Jordan T, Hanson I, Zaletayev D, Hodgson S, Prosser J, Seawright A, Hastie N, van Heyningen V (1992) The human PAX6 gene is mutated in two patients with aniridia. Nat Genet 1:328–332
52. Jorgenson RJ, Levin LS, Cross HE, Yoder F, Kelly TE (1978) The Rieger syndrome. Am J Med Genet 2:307–318
53. Komiyama M, Yasui T, Sakamoto H, Fujita K, Sato T, Ota M, Sugita M (2000) Basal meningoencephalocele, anomaly of optic disc and panhypopituitarism in association with moyamoya disease. Pediatr Neurosurg 33:100–104
54. Krafchak CM, Pawar H, Moroi SE, Sugar A, Lichter PR, Mackey DA, Mian S, Nairus T, Elner V, Schteingart MT, Downs CA, Kijek TG, Johnson JM, Trager EH, Rozsa FW, Mandal MN, Epstein MP, Vollrath D, Ayyagari R, Boehnke M, Richards JE (2005) Mutations in TCF8 cause posterior polymorphous corneal dystrophy and ectopic expression of COL4A3 by corneal endothelial cells. Am J Hum Genet 77:694–708

55. Krauss RS (2007) Holoprosencephaly: new models, new insights. Expert Rev Mol Med 9:1–17
56. Kulak SC, Kozlowski K, Semina EV, Pearce WG, Walter MA (1998) Mutation in the RIEG1 gene in patients with iridogoniodysgenesis syndrome. Hum Mol Genet 7:1113–1117
57. Lambert SR, Hoyt CS, Narahara MH (1987) Optic nerve hypoplasia. Surv Ophthalmol 32:1–9
58. Lehmann OJ, Ebenezer ND, Jordan T, Fox M, Ocaka L, Payne A, Leroy BP, Clark BJ, Hitchings RA, Povey S, Khaw PT, Bhattacharya SS (2000) Chromosomal duplication involving the forkhead transcription factor gene FOXC1 causes iris hypoplasia and glaucoma. Am J Hum Genet 67:1129–1135
59. Lenhart PD, Lambert SR, Newman NJ, Biousse V, Atkinson DSJ, Traboulsi E, Hutchinson AK (2006) Intracranial vascular anomalies in patients with morning glory disk anomaly. Am J Ophthalmol 142:644–650
60. Lesnik Oberstein SA, Kriek M, White SJ, Kalf ME, Szuhai K, den Dunnen JT, Breuning MH, Hennekam RC (2006) Peters plus syndrome is caused by mutations in B3GALTL, a putative glycosyltransferase. Am J Hum Genet 79:562–566
61. Lines MA, Kozlowski K, Walter MA (2002) Molecular genetics of Axenfeld-Rieger malformations. Hum Mol Genet 11:1177–1184
62. Mackey DA, Buttery RG, Wise GM, Denton MJ (1991) Description of X-linked megalocornea with identification of the gene locus. Arch Ophthalmol 109:829–833
63. Maillette de Buy Wenniger-Prick LJ, Hennekam RC (2002) The Peters' plus syndrome: a review. Ann Genet 45:97–103
64. Mandal AK, Naduvilath TJ, Jayagandan A (1998) Surgical results of combined trabeculotomy-trabeculectomy for developmental glaucoma. Ophthalmology 105:974–982
65. Mattox C, Walton DS (1993) Hereditary primary childhood glaucomas. Int Ophthalmol Clin 33:121–134
66. McCarthy GT, West CM (1977) Ablepharon macrostomia syndrome. Dev Med Child Neurol 19:659–663
67. McMenamin PG (1989) Human fetal iridocorneal angle: a light and scanning electron microscopic study. Br J Ophthalmol 73:871–879
68. Mears AJ, Mirzayans F, Gould DB, Pearce WG, Walter MA (1996) Autosomal dominant iridogoniodysgenesis anomaly maps to 6p25. Am J Hum Genet 59:1321–1327
69. Mears AJ, Jordan T, Mirzayans F, Dubois S, Kume T, Parlee M, Ritch R, Koop B, Kuo WL, Collins C, Marshall J, Gould DB, Pearce W, Carlsson P, Enerback S, Morissette J, Bhattacharya S, Hogan B, Raymond V, Walter MA (1998) Mutations of the forkhead/winged-helix gene, FKHL7, in patients with Axenfeld-Rieger anomaly. Am J Hum Genet 63:1316–1328
70. Meisler DM, Fine M (1984) Recurrence of the clinical signs of lattice corneal dystrophy (type I) in corneal transplants. Am J Ophthalmol 97:210–214
71. Mets MB (2001) Eye manifestations of intrauterine infections. Ophthalmol Clin North Am 14:521–531
72. Michaeli A, Markovich A, Rootman DS (2005) Corneal transplants for the treatment of congenital corneal opacities. J Pediatr Ophthalmol Strabismus 42:34–44
73. Mirzayans F, Pearce WG, MacDonald IM, Walter MA (1995) Mutation of the PAX6 gene in patients with autosomal dominant keratitis. Am J Hum Genet 57:539–548
74. Mirzayans F, Gould DB, Heon E, Billingsley GD, Cheung JC, Mears AJ, Walter MA (2000) Axenfeld-Rieger syndrome resulting from mutation of the FKHL7 gene on chromosome 6p25. Eur J Hum Genet 8:71–74
75. Mustafa T, Ziahosseini K (2007) Atypical blepharophimosis syndrome. Ophthalmology 114:1027
76. Nance MA, Berry SA (1992) Cockayne syndrome: review of 140 cases. Am J Med Genet 42:68–84
77. Nance WE, Warburg M, Bixler D, Helveston EM (1974) Congenital X-linked cataract, dental anomalies and brachymetacarpalia. Birth Defects Orig Artic Ser 10:285–291
78. Nanni L, Ming JE, Bocian M, Steinhaus K, Bianchi DW, Die-Smulders C, Giannotti A, Imaizumi K, Jones KL, Campo MD, Martin RA, Meinecke P, Pierpont ME, Robin NH, Young ID, Roessler E, Muenke M (1999) The mutational spectrum of the sonic hedgehog gene in holoprosencephaly: SHH mutations cause a significant proportion of autosomal dominant holoprosencephaly. Hum Mol Genet 8:2479–2488
79. Neuhauser G, Kaveggia EG, France TD, Opitz JM (1975) Syndrome of mental retardation, seizures, hypotonic cerebral palsy and megalocorneae, recessively inherited. Z Kinderheilkd 120:1–18
80. Nishimura DY, Swiderski RE, Alward WL, Searby CC, Patil SR, Bennet SR, Kanis AB, Gastier JM, Stone EM, Sheffield VC (1998) The forkhead transcription factor gene FKHL7 is responsible for glaucoma phenotypes which map to 6p25. Nat Genet 19:140–147
81. Odland M (1968) Dystrophia corneae parenchymatosa congenita. A clinical, morphological and histochemical examination. Acta Ophthalmol (Copenh) 46:477–485
82. Olsen TW, Summers CG, Knobloch WH (1996) Predicting visual acuity in children with colobomas involving the optic nerve. J Pediatr Ophthalmol Strabismus 33:47–51
83. Ousley PJ, Terry MA (2005) Stability of vision, topography, and endothelial cell density from 1 year to 2 years after deep lamellar endothelial keratoplasty surgery. Ophthalmology 112:50–57
84. Pagon RA, Graham JM Jr, Zonana J, Yong SL (1981) Coloboma, congenital heart disease, and choanal atresia with multiple anomalies: CHARGE association. J Pediatr 99:223–227
85. Pellegata NS, Dieguez-Lucena JL, Joensuu T, Lau S, Montgomery KT, Krahe R, Kivela T, Kucherlapati R, Forsius H, de la Chapelle A (2000) Mutations in KERA, encoding keratocan, cause cornea plana. Nat Genet 25:91–95
86. Postel EI, Pulido JS, McNamara JA, Johnson MW (1998) The etiology and treatment of macular detachment associated with optic nerve pits and related anomalies. Trans Am Ophthalmol Soc 96:73–88; discussion 88–93
87. Priston M, Kozlowski K, Gill D, Letwin K, Buys Y, Levin AV, Walter MA, Heon E (2001) Functional analyses of two newly identified PITX2 mutants reveal a novel molecular mechanism for Axenfeld-Rieger syndrome. Hum Mol Genet 10:1631–1638

88. Ramaesh K, Ramaesh T, Dutton GN, Dhillon B (2005) Evolving concepts on the pathogenic mechanisms of aniridia related keratopathy. Int J Biochem Cell Biol 37:547–557
89. Rapin I, Weidenheim K, Lindenbaum Y, Rosenbaum P, Merchant SN, Krishna S, Dickson DW (2006) Cockayne syndrome in adults: review with clinical and pathologic study of a new case. J Child Neurol 21:991–1006
90. Reardon W, Winter RM, Rutland P, Pulleyn LJ, Jones BM, Malcolm S (1994) Mutations in the fibroblast growth factor receptor 2 gene cause Crouzon syndrome. Nat Genet 8:98–103
91. Riccardi VM, Sujansky E, Smith AC, Francke U (1978) Chromosomal imbalance in the Aniridia-Wilms' tumor association: 11p interstitial deletion. Pediatrics 61:604–610
92. Richardson D, Thiruchelvam JK (2006) Craniofacial surgery for orbital malformations. Eye 20:1224–1227
93. Rodriguez-Rojas LX, Garcia-Cruz D, Mendoza-Topete R, Barba LB, Barrios MT, Patino-Garcia B, Lopez-Cardona MG, Nuno-Arana I, Garcia-Ortiz JE, Cantu JM (2004) Familial iridogoniodysgenesis and skeletal anomalies: a probable new autosomal recessive disorder. Clin Genet 66:23–29
94. Rosenberg LF, Burde RM (1988) Progressive visual loss caused by an arachnoidal brain cyst in a patient with an optic nerve coloboma. Am J Ophthalmol 106:322–325
95. Rosenfield NS, Kelley MJ, Jensen PS, Cotlier E, Rosenfield AT, Riely CA (1980) Arteriohepatic dysplasia: radiologic features of a new syndrome. AJR Am J Roentgenol 135:1217–1223
96. Russell-Eggitt IM, Rice NS, Jay B, Wyse RK (1992) Relapse following goniotomy for congenital glaucoma due to trabecular dysgenesis. Eye 6:197–200
97. Sanyanusin P, Schimmenti LA, McNoe LA, Ward TA, Pierpont ME, Sullivan MJ, Dobyns WB, Eccles MR (1995) Mutation of the PAX2 gene in a family with optic nerve colobomas, renal anomalies and vesicoureteral reflux. Nat Genet 9:358–364
98. Sarfarazi M, Stoilov I, Schenkman JB (2003) Genetics and biochemistry of primary congenital glaucoma. Ophthalmol Clin North Am 16:543–554, vi
99. Schiaffino MV, Baschirotto C, Pellegrini G, Montalti S, Tacchetti C, De Luca M, Ballabio A (1996) The ocular albinism type 1 gene product is a membrane glycoprotein localized to melanosomes. Proc Natl Acad Sci U S A 93:9055–9060
100. Schinzel A, Giedion A (1978) A syndrome of severe midface retraction, multiple skull anomalies, clubfeet, and cardiac and renal malformations in sibs. Am J Med Genet 1:361–375
101. Scott DA, Cooper ML, Stankiewicz P, Patel A, Potocki L, Cheung SW (2005) Congenital diaphragmatic hernia in WAGR syndrome. Am J Med Genet A 134:430–433
102. Semina EV, Brownell I, Mintz-Hittner HA, Murray JC, Jamrich M (2001) Mutations in the human forkhead transcription factor FOXE3 associated with anterior segment ocular dysgenesis and cataracts. Hum Mol Genet 10:231–236
103. Semina EV, Reiter R, Leysens NJ, Alward WL, Small KW, Datson NA, Siegel-Bartelt J, Bierke-Nelson D, Bitoun P, Zabel BU, Carey JC, Murray JC (1996) Cloning and characterization of a novel bicoid-related homeobox transcription factor gene, RIEG, involved in Rieger syndrome. Nat Genet 14:392–399
104. Shields MB (2001) Axenfeld-Rieger and iridocorneal endothelial syndromes: two spectra of disease with striking similarities and differences. J Glaucoma 10:S36–S38
105. Shields MB, Campbell DG, Simmons RJ (1978) The essential iris atrophies. Am J Ophthalmol 85:749–759
106. Sidoti PA, Belmonte SJ, Liebmann JM, Ritch R (2000) Trabeculectomy with mitomycin-C in the treatment of pediatric glaucomas. Ophthalmology 107:422–429
107. Slavotinek AM, Tifft CJ (2002) Fraser syndrome and cryptophthalmos: review of the diagnostic criteria and evidence for phenotypic modules in complex malformation syndromes. J Med Genet 39:623–633
108. Steinkuller PG, Du L, Gilbert C, Foster A, Collins ML, Coats DK (1999) Childhood blindness. J AAPOS 3:26–32
109. Stickler GB, Belau PG, Farrell FJ, Jones JD, Pugh DG, Steinberg AG, Ward LE (1965) Hereditary progressive arthro-ophthalmopathy. Mayo Clin Proc 40:433–455
110. Stoilov I, Akarsu AN, Sarfarazi M (1997) Identification of three different truncating mutations in cytochrome P4501B1 (CYP1B1) as the principal cause of primary congenital glaucoma (buphthalmos) in families linked to the GLC3A locus on chromosome 2p21. Hum Mol Genet 6:641–647
111. Tahvanainen E, Forsius H, Kolehmainen J, Damsten M, Fellman J, de la Chapelle A (1996) The genetics of cornea plana congenita. J Med Genet 33:116–119
112. Tarabishy AB, Alexandrou TJ, Traboulsi EI (2007) Syndrome of myelinated retinal nerve fibers, myopia, and amblyopia: a review. Surv Amblyopia 52:588–596
113. Taylor D, Hoyt CS (2005) Pediatric ophthalmology and strabismus. Elsevier Saunders, London
114. Terry MA, Ousley PJ (2004) Rapid visual rehabilitation after endothelial transplants with deep lamellar endothelial keratoplasty (DLEK). Cornea 23:143–153
115. Townes PL, Muechler EK (1979) Blepharophimosis, ptosis, epicanthus inversus, and primary amenorrhea. A dominant trait. Arch Ophthalmol 97:1664–1666
116. Traboulsi EI (1998) Genetic diseases of the eye. Oxford University Press, New York
117. Traboulsi EI, Maumenee IH (1992) Peters' anomaly and associated congenital malformations. Arch Ophthalmol 110:1739–1742
118. Tsai JH, Derby E, Holland EJ, Khatana AK (2006) Incidence and prevalence of glaucoma in severe ocular surface disease. Cornea 25:530–532
119. Tzelikis PF, Rapuano CJ, Hammersmith KM, Laibson PR, Cohen EJ (2005) Diamond burr treatment of poor vision from anterior basement membrane dystrophy. Am J Ophthalmol 140:308–310
120. Vanita V, Singh D, Robinson PN, Sperling K, Singh JR (2006) A novel mutation in the DNA-binding domain of MAF at 16q23.1 associated with autosomal dominant "cerulean cataract" in an Indian family. Am J Med Genet A 140:558–566
121. Verhulst S, Smet H, Ceulemans B, Geerts Y, Tassignon MJ (1993) Gillespie syndrome, partial aniridia, cerebellar

ataxia and mental retardation in mother and daughter. Bull Soc Belge Ophtalmol 250:37–42
122. Vincent A, Billingsley G, Priston M, Glaser T, Oliver E, Walter M, Ritch R, Levin A, Heon E (2006) Further support of the role of CYP1B1 in patients with Peters anomaly. Mol Vis 12:506–510
123. Vincent MC, Gallai R, Olivier D, Speeg-Schatz C, Flament J, Calvas P, Dollfus H (2004) Variable phenotype related to a novel PAX6 mutation (IVS4+5G>C) in a family presenting congenital nystagmus and foveal hypoplasia. Am J Ophthalmol 138:1016–1021
124. Vithana EN, Morgan P, Sundaresan P, Ebenezer ND, Tan DT, Mohamed MD, Anand S, Khine KO, Venkataraman D, Yong VH, Salto-Tellez M, Venkatraman A, Guo K, Hemadevi B, Srinivasan M, Prajna V, Khine M, Casey JR, Inglehearn CF, Aung T (2006) Mutations in sodium-borate cotransporter SLC4A11 cause recessive congenital hereditary endothelial dystrophy (CHED2). Nat Genet 38:755–757
125. Waardenburg PJ (1951) A new syndrome combining developmental anomalies of the eyelids, eyebrows and nose root with pigmentary defects of the iris and head hair and with congenital deafness. Am J Hum Genet 3:195–253
126. Warburg M, Sjo O, Fledelius HC, Pedersen SA (1993) Autosomal recessive microcephaly, microcornea, congenital cataract, mental retardation, optic atrophy, and hypogenitalism. Micro syndrome. Am J Dis Child 147:1309–1312
127. Watson GH, Miller V (1973) Arteriohepatic dysplasia: familial pulmonary arterial stenosis with neonatal liver disease. Arch Dis Child 48:459–466
128. Withers SJ, Gole GA, Summers KM (1999) Autosomal dominant cataracts and Peters anomaly in a large Australian family. Clin Genet 55:240–247
129. Wright KW, Spiegel PH, Wright KW (2003) Pediatric ophthalmology and strabismus. Springer, New York
130. Yang LL, Lambert SR (2001) Peters' anomaly. A synopsis of surgical management and visual outcome. Ophthalmol Clin North Am 14:467–477
131. Yang LL, Lambert SR, Lynn MJ, Stulting RD (1999) Long-term results of corneal graft survival in infants and children with Peters anomaly. Ophthalmology 106:833–848
132. Young TL (2003) Ophthalmic genetics/inherited eye disease. Curr Opin Ophthalmol 14:296–303
133. Zetterstrom C, Lundvall A, Kugelberg M (2005) Cataracts in children. J Cataract Refract Surg 31:824–840

Pediatric Cataract: Preoperative Issues and Considerations

22

Rupal H. Trivedi and M. Edward Wilson[1]

Contents

Core Messages

- Pediatric cataract care is complex. The surgery itself is but one step among many aimed at achieving normal visual function over a long life span.
- A comprehensive history and an ocular and systemic examination are important for preoperative decision-making in children with cataracts.
- Lengthy discussions between the parents/caregivers and the surgeon are common. The outcome is often better when the parents/caregivers are informed and committed partners with the ophthalmic team.
- Preoperative examination under anesthesia (EUA) is necessary for most children at the time of cataract surgery.

22.1 Introduction

Cataracts remain one of the most important causes of treatable blindness in children. Management of children with cataracts is time consuming, but rewarding. A thorough preoperative evaluation sets the stage for

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the decision-making that precedes surgery. A comprehensive history, and an ocular and systemic examination help to address several issues and concerns (Table 22.1). It is important to make decisions in partnership with the parents. Taking the extra time to help parents understand the implications of the cataracts their child has and the options for treatment will save time later and will promote better compliance with medications, glasses, contact lenses, and occlusion therapy. An informed parent is usually a willing participant in the treatment of their child. The more they understand and accept the necessary steps, the better partner they will become in the battle for good visual function. Herein, we present our step-by-step approach to the assessment of children with cataracts who are being evaluated for surgery.

22.2 History

A cataract evaluation begins with a chief complaint (Table 22.2) from the parents that may be a white spot in the pupil (Fig. 22.1a–c), visual inattentiveness, nystagmus, strabismus, asymmetry of one eye relative to the other (e.g., microphthalmos), photophobia, ocular injury, or simply because of referral from other physician who has identified a possible lens opacity. At times, the evaluation is scheduled because of a family history of childhood cataracts or because the child has one of a growing number of systemic conditions or syndromes that can be associated with cataracts. A detailed history includes de-

Table 22.1 Preoperative assessment: major goals

- Need for surgery
- Timing of surgery
- Cause of cataract
- Association of any ocular or systemic anomaly
- Need for further genetic or laboratory investigations
- Assumed compliance of child and family to postoperative correction of residual refractive error and to amblyopia therapy [which helps in deciding whether to implant an intraocular lens (IOL) or not and, if implanting, how much residual refraction should be aimed for while selecting an IOL power]
- Estimated postoperative visual prognosis (see Table 22.7)
- Making partnership with parents

Table 22.2 History

Identification and demographics:

- Name
- Age
- Gender
- Race
- Date of birth
- Weight

Chief complaint:

- White spot in the pupil
- Visual inattentiveness
- Nystagmus (e.g., eye wiggles)
- Strabismus (e.g., crossed eyes or abnormal position of eyes)
- Asymmetric size of one eye relative to the other
- Photophobia
- Ocular injury
- Referral from other physician
- Family history of childhood cataract

Detail history of present illness:

- Age at onset of symptoms or age at cataract diagnosis
- Birth weight
- Evidence of maternal infection (especially the TORCH infections)
- Rash or febrile illness during pregnancy
- Any other prenatal and perinatal history that may be pertinent (e.g., alcohol, tobacco, drug use, ionizing radiation during pregnancy)
- History of ocular trauma (unless cataract appears to be purely non-traumatic)
- Ocular status on previous eye examinations
- History of corticosteroid therapy (especially in posterior subcapsular cataract)

Direct questioning:

- Does your child appear to see well?
- Do your child's eyes look straight or do they seem to cross or drift or seem lazy?
- How long have you noticed a change in your child's vision?
- How well does your child function in a new environment?

Family history:

- Any family history of childhood cataract (especially in bilateral cataract)
- If parents are operated on for cataract, outcome of surgery should be asked
- In the absence of family history in a case of bilateral cataract without any other known reason, slit-lamp examination of parents can be requested

mographic data. Specific information is gathered on gender, ethnicity, and date of birth, birth weight, evidence of maternal infection (especially the TORCH infections), rash or febrile illness during pregnancy (may be suggestive of intrauterine infection), any other prenatal and perinatal history that may be pertinent (e.g., alcohol, tobacco, drug use, ionizing radiation during pregnancy), history of ocular trauma (unless cataract appears to be purely non-traumatic), age at onset of visual symptoms, ocular status on previous eye examinations (can be helpful in assessing visual prognosis after treatment), and history of corticosteroid therapy (especially in posterior subcapsular cataract). Simple questions can help in determining the surgical need, the timing or urgency of surgery, and the visual prognosis after cataract removal (e.g., Does your child appear to see well? Do your child's eyes look straight or do they seem to cross or drift or seem lazy? How long have you noticed a change in your child's visual function?). Frequently, even with poor vision, a child may be functioning reasonably well in a familiar environment. The child will be reluctant, however, to explore an unfamiliar area. Ask parents how well their child functions in a new environment as a useful indicator of vision. Infants with complete bilateral congenital cataracts usually demonstrate decreased visual interest and experience delayed milestones. Approximately one third of cataracts are inherited, so family history of cataract should be evaluated (especially in bilateral cataract). Mention to the parents that you may want to look at their eyes (Fig. 22.2). Explain that a finding in the eyes of the parents may help streamline the evaluation and workup of the child, thus preventing unnecessary tests.

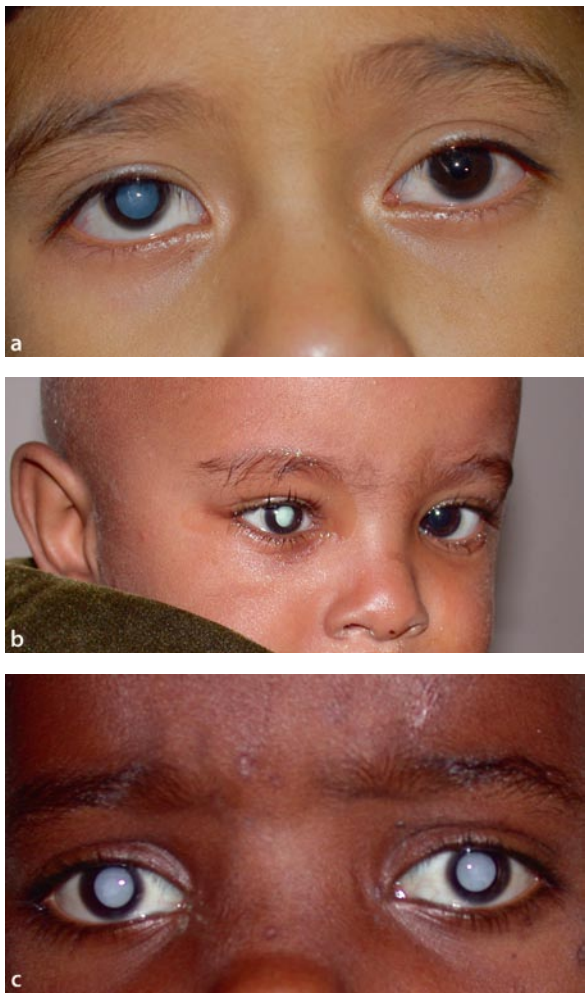

Fig. 22.1a–c Cataract presented as white reflex

Fig. 22.2 Unoperated cataract observed in mother's eye. Child was operated on for cataract

22.3 Examination

22.3.1 Assessment of Visual Function

The method of evaluating visual function will vary according to the age of the child and the level of cooperation. A communication barrier exists between the ophthalmologist and very young preverbal or preliterate patients. Parents and caregivers can help to break this communication barrier by working together to encourage the child to perform functional testing in the office that can help quantify the visual acuity (VA) of the child with cataract as precisely as possible. Documentation of the child's level of cooperation with the examination can be useful in interpreting the results and in making comparisons among the examinations over time. When results are equivocal, repeated office visits may be needed.

22.3.1.1 Infant and Preverbal Child

The assessment strategy is to determine whether each eye can fixate on an object, maintain fixation, and then follow the object into all directions (Table 22.3). The assessment should be performed binocularly and then monocularly. This can be done by drawing the child's attention to the examiner's or family member's face (infants under 3 months) or a toy either handheld or at 20 feet. The force with which the child objects to alternate occlusion of the eyes is useful to judge the relative vision in each eye. Fixation behavior is recorded for each eye as "fixates, follows, maintains." Some prefer the equivalent terms "central, steady, and maintained" to describe the fixation observed. In an awake and alert child, if poor fixation and following are noted binocularly after 3–4 months of age, a significant visual loss is suspected and searched for.

For strabismic children, an assessment of binocular fixation pattern is performed in which the examiner determines the length of time that the non-preferred eye can hold fixation. It can be reported as, will not hold fixation with non-preferred eye, holds fixation briefly with non-preferred eye, or no fixation preference. With a straight-eyed child and those with

Table 22.3 Examination

A. Assessment of visual function[a]
   - Fixate (or not) on an object, maintain (or not) fixation, and then follow (or not) the object into all directions
   - The force with which the child objects to alternate occlusion of the eyes
   - For strabismic children, the length of time that the non-preferred eye can hold fixation
   - With a straight-eyed child and those with small angle deviation, the base-down prism induced-tropia fixation test
   - Preferential looking techniques (Teller acuity cards) or Cardiff cards
   - A sweep visual-evoked response
   - ETDRS visual acuity for verbal child
   - Fusion and stereoacuity testing at distance as well as near
   - Glare testing (in children with posterior subcapsular cataracts who complain of intolerable glare, but have good Snellen VA)

B. Red reflex test

C. Ocular alignment and motility

D. External examination and anterior segment (preferably for both eyes)
   - Penlight evaluation: eyelids, eyelashes, conjunctiva, sclera, cornea, and iris
   - Pupil: size, shape, symmetry, and reaction to light should be noted
   - A slit-lamp evaluation should be carried out if the child is old enough to be cooperative: type and location of cataract, lens subluxation, iridodonesis, aniridia
   - In cases of unilateral cataract, examination of the fellow eye after pupil dilation is essential to rule out asymmetric bilateral findings

E. Examination under anesthesia (preferable for both eyes)[b]
   - Intraocular pressure
   - Keratometry measurements
   - Examine the eye using the operating microscope
   - Immersion A-scan ultrasound for globe axial length
   - Horizontal corneal diameter
   - Fundus examination
   - B-scan ultrasound examination (when no view on fundus examination)
   - Preoperative cycloplegic refraction

[a] Child's cooperation level should be noted
[b] At the end of EUA and before start of surgery, we visit with the parents to explain the findings of the EUA in brief

small angle deviation, the base-down prism induced-tropia fixation test can be used to optically separate the two eyes (see Chap. 4). A 20 prism-diopter base-down prism is our preferred instrument since it displaces the pupillary reflex and the image sufficiently to detect which eye is being used for fixation at any time during testing (Fig. 22.3a–c). The prism is placed before one eye at a time for approximately two seconds and the fixation response is described. A scoring system can be used where the responses to the base-down prism are noted using a −2 to +2 scale. In this system, the right eye receives the prism first. A score of −2 means that the child fixates with left eye only, −1 is when the child alternates at times but prefers OS, 0 indicates alternate fixation without preference, +1 means that the child alternates at times but prefers OD, and +2 indicates that the child fixates with the right eye only. The prism is then placed over the left eye and it is scored using the same scale. The total induced-tropia test (ITT) score is the sum of the grades of the right eye and the left eye. Scores of ±3 or ±4 indicate a strong fixation preference and probable poor vision, whereas scores of 0 or ±1 indicate little or no fixation preference and probably better vision. The results of the induced-tropia test can be recorded simply as alternates or the preferred eye is the right/left and non-preferred eye holds well, holds briefly, or shows no hold. However, the quantitative scoring system is helpful to monitor early postoperative surgical outcome and in subsequent amblyopia management (see Chap. 4).

In preverbal children with partial cataracts or lamellar cataracts, we also use foot-pedal operated "barking dogs" or other noise-making and moving toys at the distance within the examination room (see Chap. 1). Each toy needs to be mounted on a shelf and displaced vertically from one another. As the examiner activates one toy and then another using the foot-pedal switch, the quality of the saccade from the child is noted. At 20 feet, a brisk saccade to the activated toy from the one simultaneously inactivated represents sufficient visual function in that eye to place into question the need for surgery on a partial cataract.

Other quantitative methods such as preferential looking techniques (Teller acuity cards) or Cardiff cards can be used. A sweep visual-evoked response can also quantify VA, but it may not always be readily available.

22.3.1.2 Verbal Child

Quantitative VA assessment in cooperative verbal children can be assessed using optotype VA testing (identifying or matching symbols or letters), allowing quantification of VA on a Snellen or preferably, a logMAR scale. Distance VA should be de-

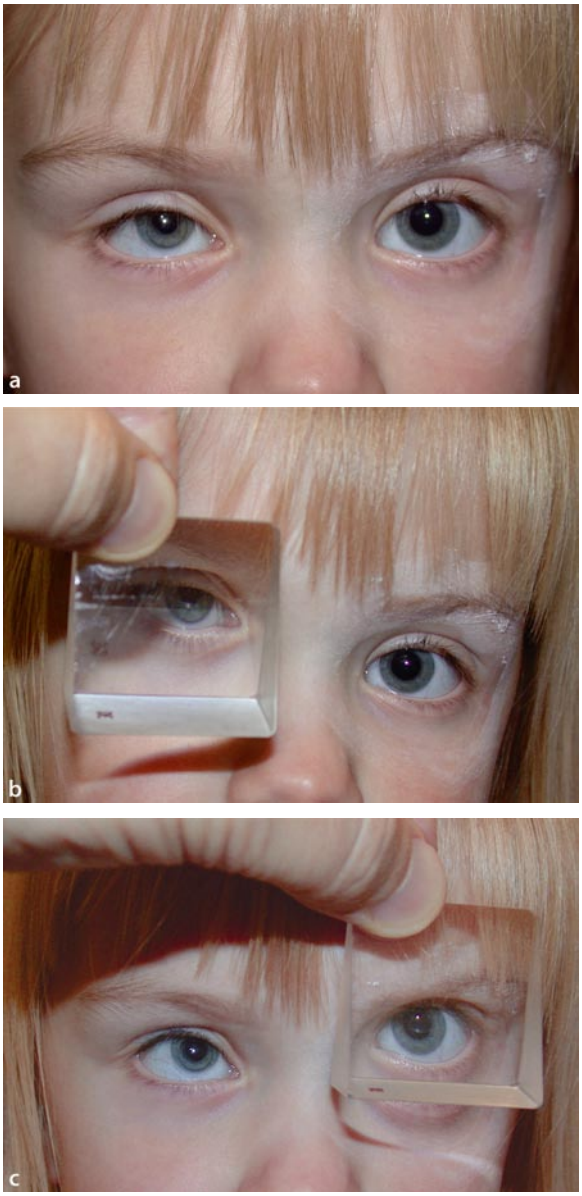

Fig. 22.3a–c Base-down prism test

termined monocularly whenever possible (http://one.aao.org/CE/PracticeGuidelines/PPP_Content.aspx?cid=761ac199-5cfe-42f4-b40b-33f9d5f0d364 – appendix). The fellow eye should be completely covered (with adhesive occluder to prevent peeking). The test should be performed at a distance of 15–20 feet with the eye chart calibrated to the exact measured distance from the examination chair to the chart. Children should be tested using a linear display of letters if possible. Young children may be easier to test if isolated optotypes with crowding bars are used. We like the HOTV matching game since the letters can be called by name or identified by pointing to the matching letter on the lap card. The letters HOTV are chosen because they avoid right to left confusion by being mirror-image letters. In addition to VA, the testing distance, type of optotype, whether the optotype is presented a line at a time or isolated, and cooperation level of the child should be documented in the medical record.

Fusion and stereoacuity testing at distance as well as near may also be helpful when deciding how much visual dysfunction is present in a cataract patient. In children with posterior subcapsular cataracts who complain of intolerable glare, but have good Snellen VA, glare testing should be performed to evaluate the need for surgery.

22.3.2 Red Reflex Test

The red reflex test can be used to detect the density and extent of the opacity in the visual axis. The retinoscope is a very useful instrument for viewing the red reflex within the pupillary space to see how much of the reflex is blackened by the cataract. In addition, the direct ophthalmoscope can be used to perform the Bruchner red reflex test where both eyes are viewed together and the red reflexes compared. When both eyes are viewed simultaneously, potentially amblyogenic conditions, such as anisometropia, strabismus, and asymmetric cataracts can be identified. The direct ophthalmoscope is focused on both eyes simultaneously at approximately 3 feet away.

22.3.3 Ocular Alignment and Motility

Details on strabismus and nystagmus mainly help when explaining prognosis to the parents and to prepare them for patching or further surgeries. Ocular alignment is assessed by using the corneal light reflection, the binocular red reflex test (see Sect. 22.3.2), and the cover test (http://one.aao.org/CE/PracticeGuidelines/PPP_Content.aspx?cid=761ac199-5cfe-42f4-b40b-33f9d5f0d364 – appendix). Cover/uncover and alternate cover tests are performed in primary gaze at distance and at near. Accommodative targets are utilized when feasible. These tests require the patient's cooperation and interaction with the examiner in addition to sufficient vision to fixate on the target. Earlier-onset unilateral cataracts have the highest risk for strabismus and late-onset bilateral cataracts have the least risk. Also, as a general rule, patients with partial cataracts and relatively good preoperative VA have less strabismus. Strabismus at presentation is often an indication that the cataract is long-standing and that significant amblyopia is likely to be present. Infants with profound bilateral dense cataracts develop nystagmus at approximately 3 months of age because the fixation reflex normally develops by that time. Once nystagmus has developed, it is likely to persist even if the cataracts are subsequently removed. If manifest nystagmus does develop, the visual prognosis is worse. Visual acuity in eyes with nystagmus and infantile cataracts is rarely better than 20/100 after cataract surgery.

22.3.4 External Examination and Anterior Segment Evaluation

External examination of the eye with a suspected cataract usually consists of a penlight evaluation of eyelids, eyelashes, conjunctiva, sclera, cornea, and iris. Evidence of blepharitis or any discharge or tearing should be evaluated and, if applicable, treatment should be advised prior to the proposed surgery date. For pupil, size, shape, symmetry, and reaction to light should be noted. Microphthalmia and poorly dilating pupils are indicators of arrested developed and in-

crease the risk of a poor anatomical and functional outcome after cataract surgery.

After dilation, a slit-lamp evaluation should be carried out if the child is old enough to be cooperative. The slit-lamp examination findings can help with the search for a cause of the cataract, help establish a prognosis, and help plan the surgical strategy. The morphology of the cataract may affect prognosis and give a clue to the etiology. Unilateral posterior subcapsular cataract (PSC) should prompt a careful search for evidence of trauma. Bilateral PSC may result from chronic uveitis, prolonged corticosteroid treatment for chronic disease, radiation treatment for malignancy, or non-accidental injury (child abuse). Children with juvenile idiopathic arthritis may have associated band-shaped keratopathy and posterior synechiae. Lens subluxation, iridodonesis, and aniridia should be looked for. Total cataract involving the whole lens can occur in Down syndrome, type 1 diabetes mellitus, in congenital rubella (where shaggy nuclear cataracts are more common), and posterior lentiglobus. In cases of unilateral cataract, examination of the fellow eye after pupil dilation is essential to rule out asymmetric bilateral findings. Anterior lenticonus is most often associated with Alport's syndrome and should be investigated accordingly. A sudden onset of total cataract may be an indication of unsuspected trauma, diabetic cataract, or preexisting ruptured anterior (reported in anterior lenticonus) or posterior capsule (reported in posterior lentiglobus).

For children approximately above 5–6 years of age, the ability of a child to cooperate for slit-lamp examination is also an indirect indicator that the child will cooperate for YAG-laser capsulotomy if needed. In children above 5–6 years of age with an intact posterior capsule and AcrySof intraocular lens (IOL) implantation, visually significant posterior capsule opacification (PCO) is known to develop 18–24 months after surgery. If a child in this age range seems to be cooperative for slit-lamp examination during preoperative evaluation, the surgeon may decide to leave behind an intact posterior capsule (assuming high odds of getting the child's cooperation for YAG if needed).

Finally, a slit-lamp examination of both parents, if possible, helps to establish the presence of familial cataracts and cataract-associated conditions. These findings can be subtle and the parents may not have been told that they have any pathology at all.

22.4 Important Decisions

22.4.1 Indication for Surgery

Indications for cataract surgery include cataracts obstructing the examiner's view for fundus examination in the non-dilated pupil or a blackened retinoscopic reflex preventing refraction of the patient. Deciding when to remove a partial cataract can be difficult. Non-verbal children add more difficulties to this decision. Individual judgment needs to be made for partial cataract. The loss of accommodation after the cataract is removed may negatively affect visual functioning more than the partial cataract itself. Visual function evaluation was discussed earlier in this chapter (Sect. 22.3.1). For verbal children, cataract surgery is contemplated if Snellen VA is 20/50 or worse, or if the child is intolerant to glare or resistant to amblyopia therapy with gradually deteriorating visual function. Since a subjective VA cannot be obtained in infants with cataracts, greater reliance is placed on the morphology of the cataract, other associated ocular findings, and the visual behavior of the child in order to ascertain whether the cataract is visually significant or not. The degree of visual impairment induced by lens opacity differs markedly depending on the location of the opacity. Generally, a more posterior and more central location of the opacity is more amblyogenic. Generally speaking, a cataract that blackens the retinoscopic reflex for 3 mm or more in the center of the pupil is considered visually significant.

If a partial cataract is being treated conservatively, it is important to carefully follow these children. Conservative treatment using mydriatic drops necessitates the patient wearing glasses for reading if any cycloplegic effect is induced. This has not found widespread acceptance. Associated glare and loss of accommodation are the most common obstacles. Visual outcome has also been unimpressive. Despite these limitations, the use of mydriatic drops may be kept in reserve in eyes with slowly progressive cataracts or paracentral cataracts less than 3 mm and, es-

pecially, in patients for whom cataract surgery needs to be deferred for any reason, be it medical (high risk for anesthesia), social, or economic.

22.4.2 Timing of Surgery

Deciding on the appropriate timing of surgery is most critical during early infancy (Table 22.4). In the case of a unilateral dense cataract diagnosed at birth, the surgeon can wait until 4–6 weeks of age. Waiting until this age decreases anesthesia-related complications and facilitates the surgical procedure. Waiting beyond this time, however, adversely affects visual outcome [1, 14]. In the case of a bilateral cataract diagnosed at birth, a good visual outcome can be achieved if the child is operated on before 10 weeks of age [6]. The first eye surgery can be offered at 4–6 weeks of age, and the second eye surgery after another 1–2 weeks. It is important to keep the time interval to a minimum between the two eye surgeries. Lloyd and colleagues note that they advise patching the first operated eye until the second has had surgery, to prevent amblyopia in the second operated eye [8]. This type of occlusion is not commonly done but undue delays between surgeries should be avoided. For older children, timing of surgery is not as crucial. In children beyond the amblyopic age, surgery can often be decided based on convenience and other logistic issues.

Sequential cataract surgery, more popularly known as simultaneous bilateral cataract surgery (SBCS), remains controversial. Almost every discussion on SBCS either starts or ends with a comment on the disagreement surrounding its use. The important question is not "can it be done?" but, more properly, "should it be done?" Even conservative surgeons, who vote against routine use of SBCS in children, are more likely to use this approach when anesthesia poses more than average risks or the patient lives far away and a visit for surgery on the second eye would be difficult.

In eyes with penetrating trauma and cataract, primary repair of the corneal or scleral wound is usually preferred as the initial step. Cataract surgery with IOL implantation should be performed 1–4 weeks after a complete evaluation of damage to intraocular structures (e.g., posterior capsule rupture, vitreous hemorrhage, and retinal detachment) with ancillary methods such as B-scan ultrasonography.

22.4.3 Aphakic Rehabilitation

Intraocular lens implantation in children has the benefit of reducing dependency on compliance with other external optical devices (aphakic glasses and contact lenses) and providing at least a partial optical correction. These are important advantages to the visual development in amblyopia-prone eyes. However, concerns about primary IOL implantation are the technical difficulties of implanting an IOL in the eyes of children, selecting an appropriate IOL power, and the risk of visual axis opacification (VAO) after implantation. Despite performing primary posterior capsulectomy and vitrectomy, the rate of VAO is higher in pseudophakic infantile eyes as compared with aphakic infantile eyes [7]. On the other hand, although it is possible for an eye with a unilateral infantile cataract to achieve good visual outcome following contact lens correction, it has continued to be the exception rather than the rule. Both IOLs and aphakic contact lenses may support similar VA after surgery for unilateral cataract in the presence of good compliance with contact lens wear. However, IOLs support better VA when compliance with contact lens wear is moderate or poor [2]. For bilateral cataracts, aphakic

Table 22.4 Timing of surgery

– Unilateral dense cataract diagnosed at birth: The surgeon can wait until 4–6 weeks of age
– Bilateral cataract diagnosed at birth: The first eye surgery can be offered at 4–6 weeks of age, and the second eye surgery after another 1–2 weeks. It is important to keep the time interval to a minimum between the two eye surgeries
– For older children, timing of surgery is not as crucial. Depending on age, laterality, and density of cataract, surgery can often be decided based on convenience and other logistic issues
– In eyes with penetrating trauma and cataract, primary repair of the corneal or scleral wound is usually preferred as the initial step. Cataract surgery with IOL implantation should be performed 1–4 weeks after repair

glasses (Fig. 22.4) and/or contact lens use may be a reasonable option. However, for unilateral cataracts in infancy, the issue of when to implant an IOL is unresolved. We await the results of ongoing multicenter clinical trial research to help guide us. For children beyond infancy, IOL implantation is less controversial.

Fig. 22.4 Aphakic glasses in a child with bilateral aphakia

22.5 Parental Counseling

In this electronic age, with many having access to internet information, families often arrive in the office with much more knowledge about their child's condition than would have been true only a few years ago. Parents may come with list of questions (Table 22.5). Surgeons who perform pediatric cataract surgery should be prepared for sometimes a quite lengthy discussion with this new breed of parent/patient. A coordinated plan of action can best be developed when the parents understand the reasons for, goals of, and the advantages and potential complications of cataract surgery. When properly informed preoperatively, the parents and the physician become partners with the common goal of doing what is best for the child. Time spent establishing this partnership is not wasted, because a better-informed family is much more likely to comply with the frequent follow-ups, medications, patching, glasses wear, etc., that are so essential to the eventual visual outcome (Table 22.6). The parents/caregivers play a critical role in the postoperative care of the eye and treatment of amblyopia. They must understand that a successful visual outcome depends on more than the surgical procedure; it also depends on their ability to maintain adequate aphakic correction and follow through with amblyopia therapy. The lion's share of the discussion in regards to pediatric cataract surgery will be with issues related to the IOL. Before moving forward with IOL implantation, it is important to discuss the major pros and cons of the available options with the parents/legal guardian. In the USA, parents should be made aware that while IOL implantation has become the most common method used to correct aphakia in children overall, it is still considered "off label" by the Food and Drug Administration (FDA). This designation means that the IOLs implanted in children were tested as part of their FDA market approval process, but only in adults. It does not mean that the FDA has disallowed their use in children. It only implies that the device is being used for a purpose or in a patient population that is different from the one in which it was tested as part of the market approval process [13].

Table 22.5 Parents' questions

- What causes cataract in my child?
- How frequent is it?
- Is this cataract ready for removal?
- What will my child see after surgery?
- How often will my child need to visit the hospital after cataract surgery?
- Would you consider implanting an IOL for my child?
- Would you implant an IOL if this was your child?

Table 22.6 Parental counseling

- Reason for surgery
- Goal of surgery
- Advantages of surgery
- Explain visual prognosis
- Potential complications and consequences of surgery
- Prepared for frequent postoperative follow-up visits and serial EUA (if needed)
- FDA status (for surgery in USA)
- Importance of refractive error correction and amblyopia treatment postoperatively

Parents should be made aware that surgery is only one component of the treatment. A child operated on for cataract requires regular scheduled care for the first

decade of life, and then every 1–2 years throughout life. However, to achieve the best visual outcome for the child, a long-term commitment from the parents is required. Visual prognosis can be explained to the parent based on preoperative evaluation (Table 22.7). The changing refraction will require frequent follow-up examinations. Glaucoma is known to develop even years after cataract surgery. Parents need to understand that their child may need serial examinations under anesthesia until the child is cooperative enough to be examined in the office. The parents should also be informed about treatment of VAO, strabismus, glaucoma, and rarely, decentered IOL, synechiolysis, or removal of a loose stitch. For eyes operated during early infancy, parents should be made aware that the first 6-month follow-up is crucial. Despite performing primary posterior capsulectomy and vitrectomy, many infant eyes develop VAO, and most eyes that develop VAO, develop it in the first six postoperative months. Earlier detection (and treatment if needed) can help to achieve a better visual outcome. For eyes operated on with an intact posterior capsule, parents should be made aware that the child would require a secondary procedure for PCO. Parents of children with lens implants are also made aware that glasses will likely still be needed postoperatively even when an IOL is implanted. In addition, glasses power may need to be changed frequently after surgery, because of changing refraction. Useful web resources for parents are http://www.pgcfa.org/cataract.htm and http://www.ich.ucl.ac.uk/factsheets/families/F020023/ (information for families with cataract).

Table 22.7 Preoperative factors indicating poor prognosis following surgery

1. Longer duration between onset of cataract and surgery
2. Unilateral cataract
3. If bilateral: asymmetrical cataract
4. Any manifest strabismus
5. Presence of nystagmus
6. Severe preoperative visual impairment as per age appropriate standards (e.g., in an awake and alert child, poor fix and following noted binocularly after 3 months of age is an indicator of poor vision)
7. Longer preoperative interocular axial length difference
8. Juvenile idiopathic arthritis-induced cataract, cataract associated with pars planitis, cataract associated with severe ocular anomalies or systemic problems

22.6 Next Steps

The surgeon may elect to prepare for surgery but delay the final decision on surgery until the time of the EUA. We routinely perform an EUA during the same session as the cataract surgery. However, to do an EUA as a separate session is also an acceptable approach. As preoperative preparation for surgery we prescribe topical medications: on check-in (approximately 1 h before surgery), the antibiotic drop (fourth-generation fluoroquinolone) is given every 5 min (4 times) and the dilating drops (peds combo, 2 mL 2% cyclopentolate, 0.5 mL 10% phenylephrine, 0.5 mL 1% tropicamide) are also given every 5 min (3 times). Dilating drops should be given for both eyes. We also advise for any laboratory investigation to detect the cause of cataract (see Sect. 22.7) and refer the child for preoperative anesthetic workup.

22.7 Laboratory Investigations to Detect the Cause of Cataract

As compared to unilateral cataract, laboratory investigation of bilateral cases is more rewarding. Exhaustive lists of possible laboratory investigations for a child with cataract can be found in several text books, however, in an otherwise healthy child, most physicians do not advise extensive laboratory and genetic investigations. After detailed evaluation, 86% of unilateral and 68% of bilateral cataract have no discernible cause [4]. Based on history and examination, customized laboratory investigations can be advised. Deciding the list of laboratory investigations to detect the cause can be occasionally based on logistic issues, financial considerations, and parents' enthusiasm and willingness to spend time and effort to do so. While recommending laboratory investigation, it is important to keep in mind that the common causes of cataract in children include intrauterine infections, metabolic disorders, and genetically transmitted syndromes. Since cataracts can be the presenting sign of diabetes, children with acquired cataracts of unknown etiology should be questioned about classic symptoms of diabetes and evaluation for hyperglycemia should be performed. Children with Lowe syndrome have hypotonia, mental retardation, aminoaciduria, and an abnormal facial appearance with frontal bossing, and

chubby cheeks. The lens typically has a reduced anterior-posterior diameter [11]. In addition, these eyes have frequent association with glaucoma. If Lowe syndrome is suspected, the urine should be screened for amino acids. If there is a history of maternal rash, fever, flu-like symptoms, or neonatal physical signs of intrauterine infection, then acute and convalescent TORCH titers should be obtained. Developmental pediatricians and clinical geneticist are experts in selective investigation based on the characteristics of the child. These specialists are invaluable and should be consulted when appropriate.

22.8 Examination Under Anesthesia

Intraocular pressure (IOP) should be checked as soon as possible after induction of anesthesia (Table 22.3). Although we routinely use the Tono-Pen, if in doubt, we recheck IOP using the Perkins tonometer. In addition to high IOP, a difference of IOP between the two eyes is alarming. Cataracts and glaucoma are associated with congenital rubella and Lowe syndrome. The next step for us is to take keratometry measurements. We use the Nidek handheld keratometer (Fig. 22.5). However, many other centers uses an autorefractokeratometer for this purpose. The remaining examinations listed below can be performed in any chronology: examine the eye using the operating microscope, immersion A-scan ultrasound for globe axial length (Fig. 22.6), horizontal corneal diameter, retinoscopy (if possible), and a retinal fundus examination. Some physicians use a slit-lamp attachment to the operating microscope for evaluating location of the cataract. Immersion A-scan performed by a skilled ultrasonographer helps to reduce the incidence of postoperative refractive surprises. A shorter or longer axial length in the eye with the cataract can be a sign of poor prognosis. When possible, at least the posterior pole of the fundus should be assessed by indirect ophthalmoscopy, looking particularly for underdevelopment or malformation of the disc or macula and the presence of abnormal pigmentation. In the case of no view on fundus examination, we perform a B-scan ultrasound examination. Although it is often not possible to do a preoperative cycloplegic refraction of an eye with a dense cataract, an uninvolved or less involved fellow eye should be refracted. The presence of refractive error in the fellow eye may help when deciding on an IOL power. In case of congenital anterior lens opacity (CALO), anisometropia has been reported to be more amblyogenic than the size of lens opacity [3]. Patients with CALOs who have anisometropia of 1 diopter D or more are 6.5 times more likely to develop amblyopia. At the end of the EUA and before the start of surgery, we visit with the parents to explain the findings of the EUA in brief. We explain what findings were expected and any that were not expected. We discuss any changes in the surgical plan that might be appropriate given the findings at EUA. This also gives the parents a good sense of how long the examination took and how long the surgery will take.

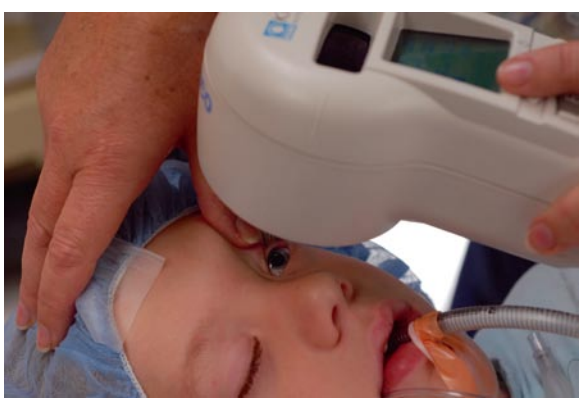

Fig. 22.5 Handheld keratometry in operating room during examination under anesthesia

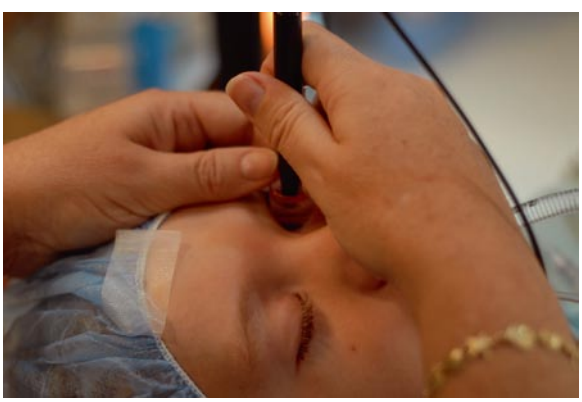

Fig. 22.6 Immersion A-scan during examination under anesthesia

22.9 Selection of Intraocular Lens Power

Implantation of a fixed-power IOL into an eye that is still growing makes it difficult to choose the IOL power to implant. IOL implantation at the calculated emmetropic power helps to fight amblyopia during childhood, but risks significant myopia at ocular maturity. Ideal IOL power should balance the best help to amblyopia management in childhood with the least possible refractive error in adulthood (Fig. 22.7). With a growing eye prone to develop a myopic shift of refraction after cataract removal, the surgeon faces the decision of what refraction should be the immediate postoperative aim [5, 9, 10, 12]. Several nomograms have been published in the literature. However, we do not recommend the use of any published table alone for deciding IOL power. These tables are only meant to help as a starting point toward appropriate IOL power selection, which is a multifactorial decision customized for each child based on many variables [age, laterality (one eye or both), amblyopia status (dense or mild), likely compliance with glasses, and family history of myopia]. Our recom-

Table 22.8 Expected postoperative residual refraction based on patient age at cataract surgery[a]

Age at surgery	Residual refraction to minimize late myopia	Median residual refraction in our series
First month	+ 12	+ 8.3
2 – 3 months	+ 9	+ 8.5
4 – 6 months	+ 8	+ 6.0
6 – 12 months	+ 7	+ 4.5
1 – 2 years	+ 6	+ 3.0
2 – 4 years	+ 5	+ 0.9
4 – 5 years	+ 4	+ 0.5
5 – 6 years	+ 3	+ 0.5
6 – 7 years	+ 2	+ 0.1
7 – 8 years	+ 1.5	+ 0.2
8 – 10 years	+ 1	+ 0.1
10 – 14 years	+ 0.5	0
> 14 years	Plano	− 0.1

[a] We do not recommend the use of any published table alone for deciding IOL power. These tables are only meant to help as a starting point toward appropriate IOL power selection, which is a multifactorial decision customized for each child based on many variables [especially, age, laterality (one eye or both), amblyopia status (dense or mild), likely compliance with glasses, and family history of myopia]

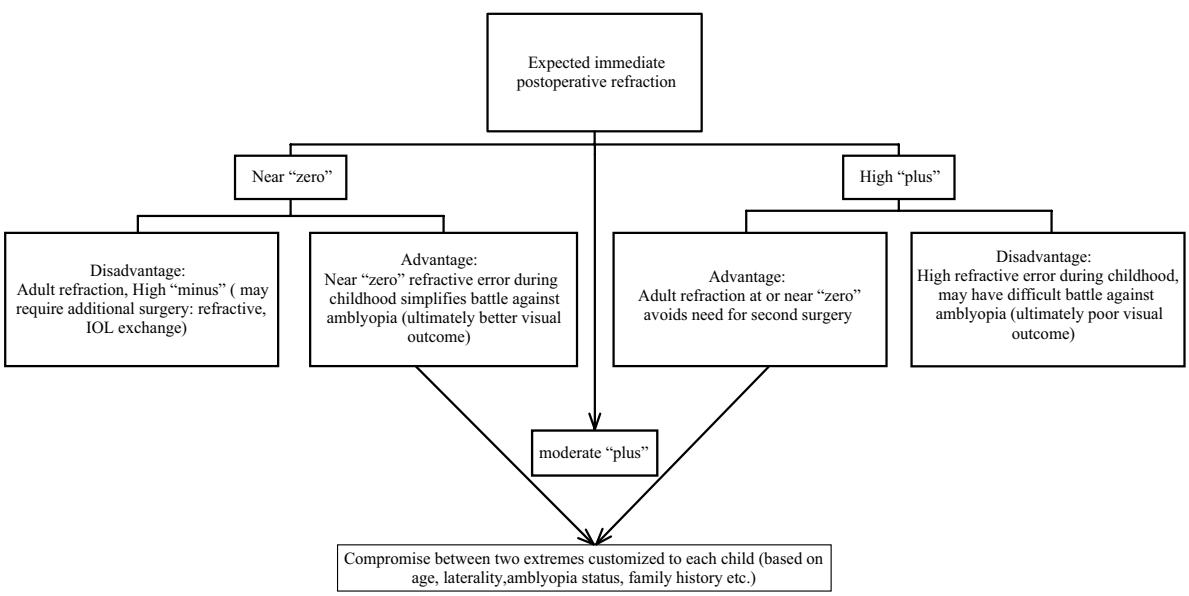

Fig. 22.7 Postoperative refractive aim while selecting IOL power

mendations to lessen long-term myopia are shown in Table 22.8. It is noteworthy that while analyzing 471 eyes in our database, we noted that we had selected less undercorrection than is typically advised to lessen late myopia (unpublished data). The median residual refractions we aimed for are also listed in Table 22.8. When implanting IOLs in children with bilateral cataracts and no amblyopia, leaving mild, moderate, or even a marked amount of hypermetropia is reasonable. However, in unilateral cataracts with dense amblyopia, less early dependence on glasses may help the amblyopia treatment. The late myopia, even if marked, may be an acceptable trade for better visual outcome from amblyopia treatment. Refractive surgery or IOL exchange may be needed in these eyes at ocular maturity.

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Take Home Pearls

- A cataract that reduces the VA to worse than or equal to 20/50, or blackens the retinoscopic reflex for 3 mm or more in the center of the pupil is likely visually significant enough to consider surgery.
- Bilateral cataracts may be associated with metabolic conditions, congenital infections, or genetic syndromes. A customized investigation is recommended based on the evaluation by experts in development pediatrics and clinical genetics.
- A thorough examination of an eye with a cataract, the fellow eye, and the eyes of the parents will help define the associated findings, the etiology, and the prognosis.
- For IOL power selection, several nomograms based on age at surgery have been published. However, we do not recommend the use of any published table alone for deciding IOL power. Selection of an optimum power of IOL is a multifactorial decision, customized to each child.
- Cataract surgery in children is but one step on the long road to visual rehabilitation, not the end of the journey.

References

1. Birch EE, Stager DR (1996) The critical period for surgical treatment of dense congenital unilateral cataract. Invest Ophthalmol Vis Sci 37:1532–1538
2. Birch EE, Cheng C, Stager DR Jr, Felius J (2005) Visual acuity development after the implantation of unilateral intraocular lenses in infants and young children. J AAPOS 9:527–532
3. Ceyhan D, Schnall BM, Breckenridge A, Fontanarosa J, Lehman SS, Calhoun JC (2005) Risk factors for amblyopia in congenital anterior lens opacities. J AAPOS 9:537–541
4. Johar SR, Savalia NK, Vasavada AR, Gupta PD (2004) Epidemiology based etiological study of pediatric cataract in western India. Indian J Med Sci 58:115–121
5. Lambert SR (1998) Ocular growth in early childhood: implications for pediatric cataract surgery. Op Tech Cataract Refract Surg 1:159–164
6. Lambert SR, Lynn MJ, Reeves R, Plager DA, Buckley EG, Wilson ME (2006) Is there a latent period for the surgical treatment of children with dense bilateral congenital cataracts? J AAPOS 10:30–36
7. Lambert SR, Lynn M, Drews-Botsch C, Loupe D, Plager DA, Medow NB, Wilson ME, Buckley EG, Drack AV, Fawcett SL (2001) A comparison of grating visual acuity, strabismus, and reoperation outcomes among children with aphakia and pseudophakia after unilateral cataract surgery during the first six months of life. J AAPOS 5:70–75
8. Lloyd IC, Goss-Sampson M, Jeffrey BG, Kriss A, Russell-Eggitt I, Taylor D (1992) Neonatal cataract: aetiology, pathogenesis and management. Eye 6:184–196
9. Plager DA, Kipfer H, Sprunger DT, Sondhi N, Neely DE (2002) Refractive change in pediatric pseudophakia: 6-year follow-up. J Cataract Refract Surg 28:810–815
10. Plager DA, Lipsky SN, Snyder SK, Sprunger DT, Ellis FD, Sondhi N (1997) Capsular management and refractive error in pediatric intraocular lenses. Ophthalmology 104:600–607

11. Tripathi RC, Cibis GW, Tripathi BJ (1986) Pathogenesis of cataracts in patients with Lowe's syndrome. Ophthalmology 93:1046–1051
12. Trivedi RH, Wilson ME (eds) (2007) Intraocular lens power calculation for children. Jaypee Brothers Medical, New Delhi
13. Wilson ME (2000) Intraocular lenses for children in the year 2000: when is oversight by the institutional review board or Food and Drug Administration required? J AAPOS 4:325
14. Wilson ME Jr, Trivedi RH, Hoxie JP, Bartholomew LR (2003) Treatment outcomes of congenital monocular cataracts: the effects of surgical timing and patching compliance. J Pediatr Ophthalmol Strabismus 40:323–329

Pediatric Cataract Surgery: Operative and Postoperative Issues

23

M. Edward Wilson and Rupal H. Trivedi[1]

Contents

Core Messages

- Surgical management of cataracts in children is markedly different from adults. Children have reduced scleral and corneal rigidity, more inflammation after surgery, and a propensity to develop reopacification of the visual axis.
- For proper management of the anterior and posterior capsule in children, technique changes have been made that are unique to pediatric surgery. Vitrectomy instrumentation is used extensively in childhood cataract surgery.
- The best surgical techniques for children will evolve most efficiently with optimal cooperation and collaboration between pediatric ophthalmologists and adult cataract surgeons. This way, new adult-tested techniques can be selectively utilized for pediatric surgery.
- The approach chosen to correct aphakia plays an important role in the outcome of pediatric cataract surgery. Intraocular lens power selection is a complex decision based on eye growth projections and the management of amblyopia.
- When cataract surgery is required in the early years of life, complications such as glaucoma and visual axis opacification are frequent. These patients must be monitored and may need examinations under anesthesia during the higher risk years.

[1] The authors have no financial or proprietary interest in any product mentioned herein.

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23.1 Introduction

The aim of pediatric cataract surgery is to provide and maintain a clear visual axis and a focused retinal image. The long-term visual outcome is often negatively affected by the development of amblyopia secondary to the cataract itself, or due to postoperative reopacification of the ocular media. Cataract surgery in children remains complex and challenging. One of the major challenges for pediatric cataract surgery has been the adaptation of techniques used for adult cataract surgery. However, pediatric cataract surgery is quite different from surgery for cataracts in the elderly (Figs. 23.1–23.3). A propensity for increased postoperative inflammation and capsular opacification, a refractive state that is constantly changing due to growth of the eye, difficulty in documenting anatomical and refractive changes due to poor compliance, and a tendency to develop amblyopia are among the factors that make cataract surgery in the child different from that in the adult. In addition, the lack of a hard nucleus, vastly reduced scleral and corneal rigidity, and enhanced posterior vitreous pressure demand a surgical approach that differs in many ways from the adult procedure.

23.2 Preoperative and Intraoperative Medications

It is important to apply antibiotic drops to the eye prior to beginning surgery. We begin topical application of a fourth-generation fluoroquinolone on check-in approximately 1 h prior to surgery. The drop is given every 5 min for a total of 4 times. While it may be ideal to start the antibiotic earlier than 1 h before surgery, we have found it logistically difficult and have settled for the plan as outlined above.

Dilating drops are also given preoperatively on check-in every 5 min for 3 times. We make up a peds combination drop that consists of 2 mL 2% cyclopentolate, 0.5 mL 10% phenylephrine, and 0.5 mL

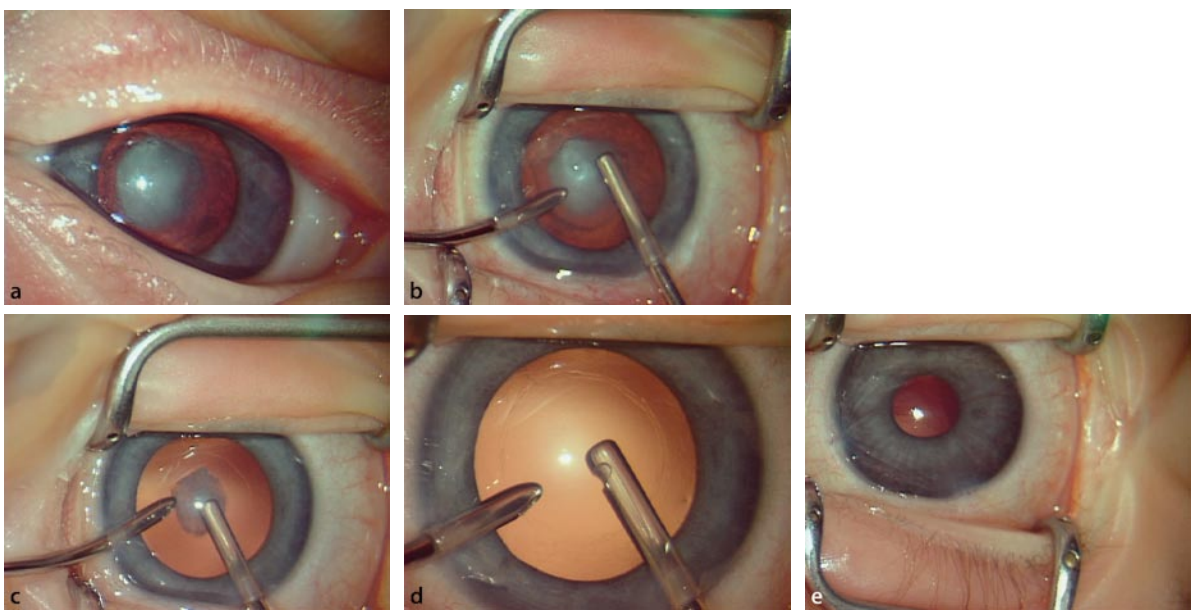

Fig. 23.1a–e Sequence showing cataract surgery without IOL implantation. **a** Preoperative view of cataract in an infant eye. **b** Vitrectorhexis. **c** Dense posterior capsule plaque noticed after removal of lens substance. **d** Both anterior and posterior capsulorhexis. Leave behind adequate size of anterior and posterior capsulorhexis to facilitate secondary IOL implantation some years later. **e** Postoperative appearance of the aphakic eye

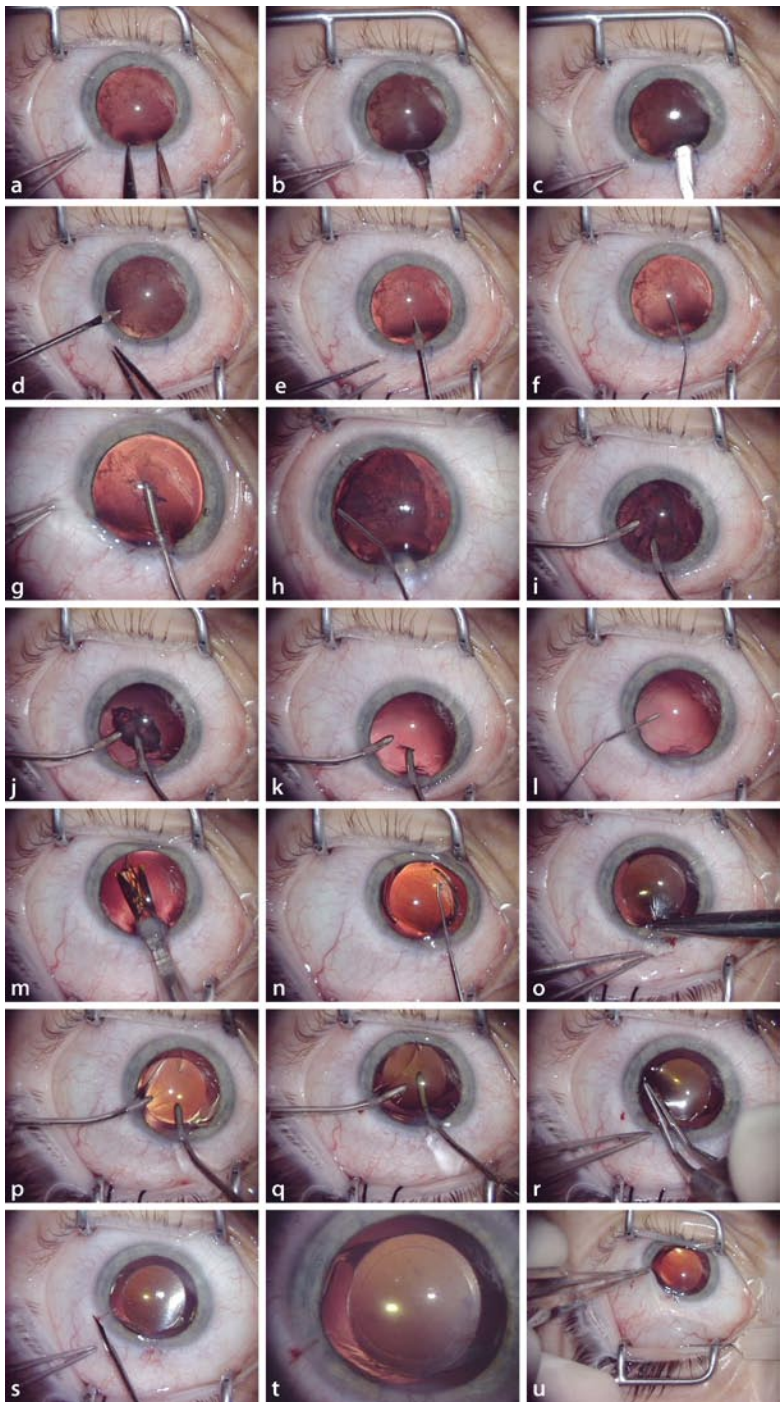

Fig. 23.2a–u Sequence showing surgery of a posterior subcapsular cataract in a 9-year-old child. **a** Marked caliper (3.0 mm or less) to outline the dimensions of the tunnel. **b** Angled crescent knife to make initial groove. **c** Same crescent knife (as in **b**) was used with bevel-up position to make the tunnel. **d** Paracentesis incision was made at approximately 2 o'clock from lateral edge of the main incision. We use an MVR 20-gauge blade for this purpose. **e** Same MVR blade was used to enter the anterior chamber through the corneal tunnel. Using same size blade as the instruments helps avoid leaking of the incision. **f** Healon GV injected into anterior chamber. This helps flattening the anterior capsule and maintains the anterior chamber during intraoperative maneuvering. **g** Small incision capsulorhexis forceps for making CCC. This fits easily through a paracentesis and will allow conversion to vitrector instruments when needed without leakage around the vitrector handpiece during use. **h** Hydrodissection. **i** Bimanual irrigation/aspiration allows thorough removal of lens substance and avoids anterior chamber fluctuations. **j** Bimanual irrigation/aspiration. **k** Bimanual irrigation/aspiration. **l** Injection of ophthalmic viscosurgical devices (OVD) in anterior chamber through paracentesis incision. This helps protect corneal endothelium while implanting an IOL and also helps maintain anterior chamber depth. **m** In-the-bag implantation of single-piece AcrySof IOL. **n** Push-pull device is used to position the IOL. **o** Main incision or corneal tunnel is sutured with 10-0 nylon. **p** OVD removal is accomplished before suturing the paracentesis incision. **q** Thorough removal of cohesive OVD is very essential to avoid IOP spike during early postoperative period. Here OVD is removed by going behind the IOL optic. **r** Paracentesis incision is sutured with 10-0 absorbable suture. **s** Trimming of suture ends using the MVR blade. **t** In-the-bag fixation of the IOL (SN60WF). Notice well-centered IOL. **u** Subconjunctival injection of antibiotic and steroid (dexamethasone 4 mg). Notice that we used upper quadrant for subconjunctival injection

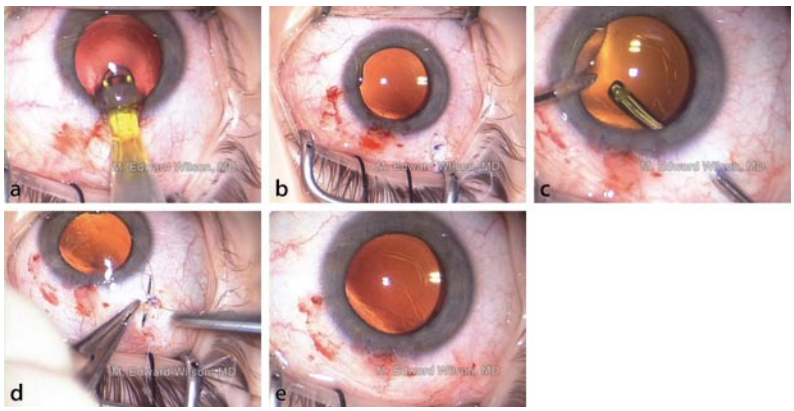

Fig. 23.3a–e **a** In-the-bag implantation of IOL. **b** In-the-bag fixation of the IOL. **c** Pars plana/plicata posterior capsulectomy and vitrectomy. **d** Suturing of pars plana/plicata incision. **e** Well-centered IOL

1% tropicamide in every 3 mL of drops. In essence, each drop delivered to the patient contains 1.3% cyclopentolate, 1.67% phenylephrine, and 0.17% tropicamide. To aid in maintaining dilation of the pupil throughout surgery, 0.5 mL epinephrine 1:1,000 solution (Hopsira, Lake Forest, IL) is added to each 500 mL bottle of irrigating solution prior to its intraoperative use during surgery. The intraoperative floppy iris syndrome (IFIS) has been reported in adults who take systemic alpha-1 antagonist medications such as tamsulosin (Flomax). IFIS is characterized by progressive pupillary miosis, and a billowing, floppy iris that prolapses easily into even the smallest of surgical entry wounds. It is caused when the pharmacological blockage from Flomax causes the normal dilator smooth muscle tone in the iris to be lost. In children, the dilator smooth muscle tone is reduced naturally, especially in infants with immature microphthalmic eyes. To combat IFIS, pediatric surgeons have used epinephrine in the intraocular irrigating fluid for more than 20 years. We recently published a pediatric case of IFIS in one eye and no IFIS in the other eye as a result of the inadvertent absence of epinephrine in the irrigating fluid of the eye demonstrating signs of IFIS [42]. We strongly recommend epinephrine in the irrigation fluid for all pediatric cataract surgeries.

Povidone iodine, diluted to a 5% solution, is applied to the eye at the end of the surgical skin and lash preparation. An additional drop is placed at the conclusion of surgery. These drops are not irrigated out after application.

23.3 Surgical Steps

23.3.1 Incision

Children have thin sclera and, as mentioned above, markedly decreased scleral rigidity when compared with adults. Scleral collapse results in increased positive vitreous pressure (also known as "vitreous upthrust"). Collapse of the anterior chamber is much more common when operating on pediatric eyes. Pediatric cataracts can be removed through a relatively small wound, as the lens has no hard nucleus. Therefore, wounds should be constructed to provide a snug fit for the instruments that pass into the anterior chamber. When an intraocular lens (IOL) is not being implanted, two stab incisions are usually made at or near the limbus (Fig. 23.1b). These incisions should not be larger than necessary for the instruments being used. For instance, a micro vitreoretinal (MVR) blade can be used that creates a 20-gauge opening for a 20-gauge vitrector/aspirator to enter the anterior chamber. A 20-gauge blunt-tipped irrigating cannula can also be used through a separate MVR blade stab incision. If the instrument positions need to be reversed, the snug fit is maintained. If 23-gauge or 25-gauge instruments are used, an MVR for that gauge opening can be utilized. While some surgeons prefer phacoaspiration (aspiration utilizing a standard phacoemulsification handpiece), a bimanual technique using an irrigating handpiece and a separate aspiration handpiece is preferred by the authors (Fig. 23.1c). Anterior chamber stability is maintained

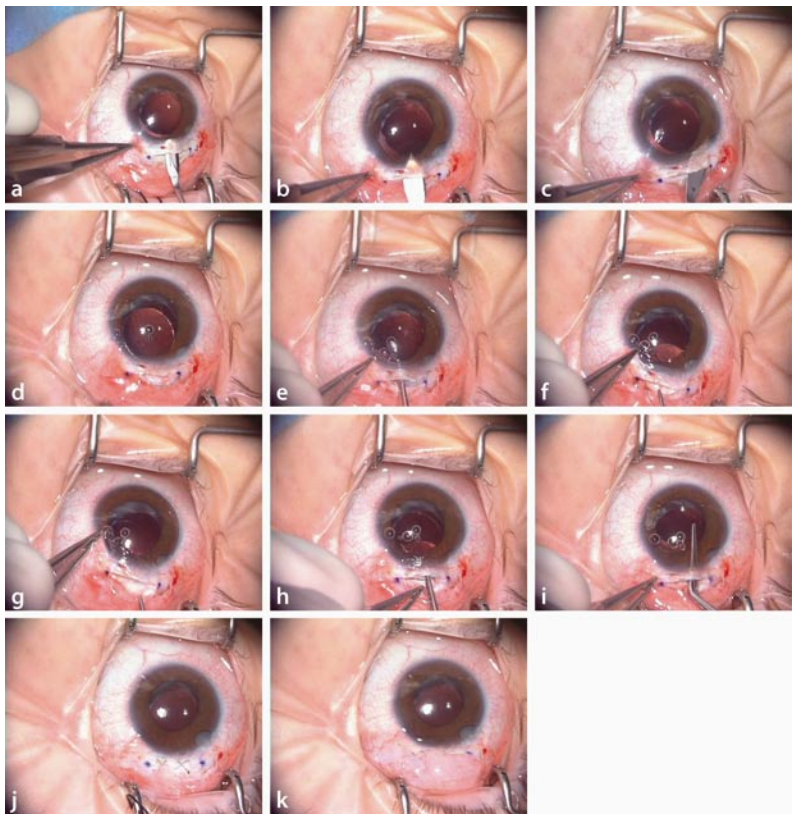

Fig. 23.4a–k Sequence of surgery of eye requiring IOL exchange. Notice use of scleral tunnel

by limiting wound leak and using a high irrigation setting.

When a foldable IOL is being implanted, a corneal tunnel is preferred since it leaves the conjunctiva undisturbed (Fig. 23.2a–c). The corneal tunnel should begin near the limbus for maximum healing and should be sutured with a synthetic absorbable suture. We prefer to use a marked caliper to outline the dimensions of the tunnel and utilize an angled crescent blade to make a groove and then a tunnel (Fig. 23.2a–c). The blade is turned up on its end to make the groove and then turned over to continue the tunnel (Fig. 23.2c).

Unlike adults, corneal incisions do not usually self-seal in children. Our 2001 survey indicated that only 20% and 3% of the American Society of Cataract and Refractive Surgeons (ASCRS) and American Association for Pediatric Ophthalmology and Strabismus (AAPOS) responders, respectively, left both tunnel and paracentesis incisions unsutured [51]. According to one study [3], self-sealing wounds failed to remain watertight in children below 11 years of age, especially when an anterior vitrectomy was combined with cataract extraction. In older (>11 years) children the wounds remained self-sealing. Even in these older children, suturing is recommended since postoperative eye rubbing is common. The authors attribute the poor self-sealing to low scleral rigidity resulting in fish mouthing of the wound leading to poor approximation of the internal corneal valve to the overlying stroma. The recommended closure material is a 10-0 synthetic absorbable suture.

In infants, a scleral tunnel is sometimes used because it heals more transparently than a corneal tunnel. In addition, a rigid IOL is implanted occasionally when sulcus placement over a large preexisting posterior capsulotomy is desired. In these instances, a scleral tunnel is utilized. An IOL exchange may require a scleral tunnel if the IOL to be removed is made of poly(methylmethacrylate) (PMMA) (Fig. 23.4). A half-thickness scleral incision is made initially approximately 2 or 2.5 mm from the limbus and dis-

sected into clear cornea. It is enlarged to the size necessary for IOL insertion. Closure is recommended using a 10-0 synthetic absorbable suture. We prefer to suture the wounds and use 10-0 polyglactic acid (Vicryl) absorbable sutures. It takes 60–90 days to completely absorb. Corneal vascularization requiring suture removal is less frequent using Vicryl suture, as opposed to non-absorbable suture (e.g., nylon). The use of non-absorbable sutures occasionally calls for an examination under anesthesia (EUA) for suture removal. Even when economic issues are a deciding factor in choice of suture material, it is better to use absorbable sutures rather than subject the child to additional anesthesia.

While the temporal wound presents the same advantages in children as it does in adults, the location is more easily traumatized by children. The superior approach allows the wound to be protected by the brow and the Bell's phenomenon in the trauma-prone childhood years. Both scleral tunnels and corneal tunnels can be easily made from a superior approach since children rarely have deep set orbits or overhanging brows. Positioning the patients on the operating table with a slight chin-up posture also helps made the superior approach easier. Locating the site of the tunnel according to the preexisting astigmatism (e.g., temporally in against-the-rule astigmatism) has not been done as often in younger children since most of these patients will wear glasses after surgery anyway. Whether the preoperative astigmatism can be altered by the site of the tunnel incision has not been studied well in children. While wound-related astigmatism is common immediately after surgery in children, due to low scleral rigidity, these eyes tend to return to their preoperative state by 1 month after surgery.

23.3.2 Anterior Capsulotomy

The anterior capsule in children is highly elastic and poses challenges in the creation of the capsulotomy [45, 48, 52]. While a manual continuous curvilinear capsulorhexis (CCC) is ideal for adults, it is more difficult to perform in young eyes. Overall, the vitrectorhexis is most commonly used in the first few years of life (Fig. 23.1b, d). Manual CCC is used most often in older children. The vitrectorhexis is very stable in the very young but can tear out to the equator more easily when used in older children (Fig. 23.5).

When performing a manual CCC in a child, the following technical recommendations are offered. Use of a highly viscous ophthalmic viscosurgical device (OVD) is recommended to fill the anterior chamber and flatten the anterior capsule (Fig. 23.2f). A slack anterior capsule will be easier to tear in a controlled fashion. Re-grasp the capsulorhexis edge frequently and begin with a smaller capsulotomy than desired. Because of the elasticity, the opening will be larger than it appears once the capsular flap is released. In order to control the turning of the CCC edge along a circular path, the tear must often be directed more toward the center of the pupil than would be necessary in an adult eye. If the capsule begins to extend peripherally, stop before the edge is out of sight under the iris. Re-grasp the capsule edge and pull directly toward the center of the pupil to recover the tear. Converting to a vitrectorhexis or a radio frequency diathermy capsulotomy may also be warranted. Using small incision capsulorhexis forceps (Fig. 23.2g) that fits easily through a paracentesis will allow conversion to vitrector instruments when needed without leakage around the vitrector handpiece during use. Recently, modifications of the manual anterior CCC technique have been published and popularized. The most common is called the two-incision push-pull (TIPP) technique. An MVR blade or a cystotome is used to puncture the anterior capsule at the superior and inferior ends of the planned CCC. The superior flap is pushed down and the inferior flap is pulled up until they meet each other. This technique keeps the tearing force directed more toward the center of the pupillary space and less toward the lens equator. The four-incision technique is similar except that four punctures are made initially and all of the ends are connected. These modifications are designed to allow more control of the CCC when the capsule is very elastic [22, 25].

While a CCC using the techniques described above is a reasonable option beyond age 4 years, it will be more difficult when attempted on children aged 4 years and younger. The vitrectorhexis is an alternative anterior capsulotomy method that will be more consistently successful than manual CCC in the youngest patients. The vitrectorhexis has been tested in both laboratory and clinical settings by the authors. This technique has proved to be very effective for young children where the CCC may be difficult to control [41, 43, 44, 48,

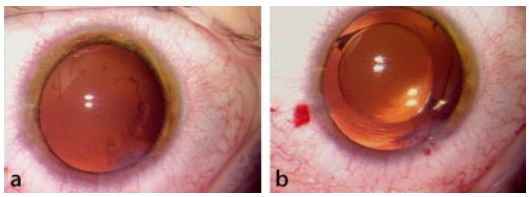

Fig. 23.5 **a** Peripheral extension of anterior capsule edge. **b** In-the-bag fixation of IOL in eye shown in **a**

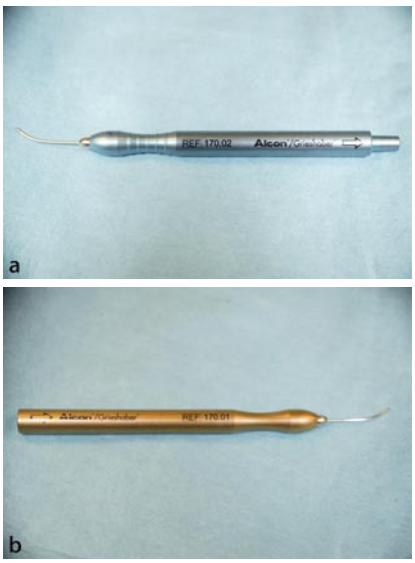

Fig. 23.6a, b Bimanual irrigation/aspiration handpiece

52]. When creating a vitrectorhexis (Fig. 23.1b), the following surgical caveats are offered. Use a vitrector supported by a Venturi pump, if possible. Peristaltic pump systems will not cut anterior capsule as easily. A bimanual technique with a separate infusion port is recommended (Fig. 23.1b). Maintain a snug fit of the instruments in the incisions through which they are placed. The anterior chamber of these soft eyes will collapse readily if leakage occurs around the instruments, making the vitrectorhexis more difficult to complete. An MVR blade can be used to enter the eye. The vitrector and a blunt-tipped irrigating cannula fit snugly into the MVR openings. We recommend either a 20-gauge Grieshaber irrigation handpiece (Alcon) (Fig. 23.6) or a Nichamin cannula (Storz). Disposable irrigation handpieces from Alcon-Grieshaber are now available as well. These work well and are beginning to replace the reusable type of cannula. An anterior chamber maintainer can also be used if the surgeon prefers. We have found that it is not necessary to begin the capsulotomy with a bent-needle cystotome. Merely place the vitrector, with its cutting port positioned posteriorly, in contact with the center of the intact anterior capsule. Turn the cutter on and increase the suction using the foot pedal until the capsule is engaged and opened. A cutting rate of 150–300 cuts per minute and an aspiration maximum of 150–250 are recommended. These settings are for currently utilized Venturi pump machines. Adjustments may be needed for other machines, especially those utilizing a peristaltic pump.

With the cutting port facing down against the capsule, engage the capsule and enlarge the round capsular opening in a spiral fashion to the desired shape and size. Any lens cortex that escapes into the anterior chamber during the vitrectorhexis is aspirated easily without interrupting the capsulotomy technique. Care should be taken to avoid leaving any right-angle edges, which could predispose to radial tear formation. The completed vitrectorhexis should be slightly smaller than the size of the IOL optic being implanted. The vitrector edge in very young children is very smooth as a result of the elasticity of the capsule. In slightly older children, the vitrector creates a slightly scalloped edge but inspection by both the dissecting microscope and the scanning electron microscope has revealed that the scallops roll outward to leave a smooth edge. Any capsular tags or points created at the apex of a scalloped cut from the vitrector are located in an area of low biomechanical stress much like an irregular outside-in completion of a CCC. These tags do not predispose to radial tear formation as demonstrated by finite element method computer modeling [16].

A third option for creating an anterior capsulotomy in a child is available with the use of high-frequency endodiathermy (Kloti radio frequency endodiathermy). This instrument cuts the capsule efficiently but results in an edge that tears easily if stretched. The Fugo plasma blade has also been used to make an anterior capsulotomy. Our experience with the Fugo blade in children is only a few cases, but the capsulotomy edge created in those cases was not very different clinically from that produced by the Kloti instrument mentioned above [48].

The use of capsular dyes has also started attracting the attention of pediatric cataract surgeons (Fig. 23.7). Visualization of the capsular flap is important to maintain control of any tears and to ensure that the edge is continuous. A report from the American Academy of Ophthalmology has concluded that "it is reasonable to consider the use of dye in cataract surgery in cases in which inadequate capsule visualization or inexperience with capsule visualization may compromise the outcome. The use of dye in routine cases cannot be recommended until a lack of toxicity is more clearly demonstrated in the event of longer duration exposure or posterior segment exposure" [14]. Both trypan blue and indocyanine green dyes provide excellent visualization of the anterior capsule flap during CCC. The United States Food and Drug Administration (FDA) approved use of trypan blue dye in December 2004 specifically as an aid in ophthalmic surgery to stain the anterior capsule of the lens. When injecting under air, the dye should be injected after the paracentesis, but prior to creating the main incision, to help with anterior chamber stability. It has been reported that staining under air versus under OVD has similar efficacy and safety [53]. In addition to better visualization, trypan blue has been reported to minimize epithelial cell proliferation in pediatric cataract surgery [15]. Staining the anterior capsule with trypan blue affected the density and viability of lens epithelial cells (LECs) [24]. The use of dyes is not advised when using hydrophilic IOLs, to avoid permanent discoloration of the IOL [40].

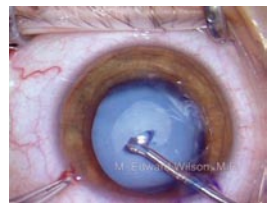

Fig. 23.7 Trypan blue for better visualization while performing manual CCC in a child with white cataract

23.3.3 Lens Substance Aspiration (Phacoaspiration)

Thorough removal of lens substance is especially crucial for pediatric eyes. When any cortical matter, which clinically may resemble a harmless strand or fiber, is left behind, it actually leaves behind a large number of mitotically active cells. These cells have the potential to grow and cause a proliferative form of visual axis opacification (VAO). The best means of reducing the incidence of this is to remove as many of these cells as possible at the time of surgery. Since VAO is one of the most frequent postoperative complications in pediatric cataract surgery, meticulous removal of the lens substance is a crucial step in the management of pediatric cataracts.

Pediatric cataracts are soft but they may be "gummy." Phacoemulsification is not needed and may be harmful in the setting of chamber instability. Lens cortex and nucleus can be aspirated in every case with an irrigation/aspiration or vitrectomy handpiece. We prefer the bimanual approach using separate irrigation and aspiration. Separate irrigation and aspiration help maintain the anterior chamber stability, decrease fluctuations of the anterior chamber, and help thorough removal of lens substance. When using the vitrector, bursts of cutting can be used intermittently to facilitate the aspiration of the more "gummy" cortex of young children. The advantage of using the vitrector is that it is possible to perform vitrectorhexis, irrigation/aspiration, posterior capsulectomy, and vitrectomy all with one instrument (the setting needs to be changed appropriately) (Fig. 23.1). This avoids extra manipulation and repeated entry into and exit from the eye. In older children, after a manual CCC we prefer 20-gauge bimanual irrigation/aspiration handpieces (Fig. 23.6) that are tapered and curved (Alcon/Grieshaber 170-01 for irrigation and Alcon/Grieshaber 170-02 for aspiration). Nearly identical disposable irrigation/aspiration handpieces are now replacing the reusable instruments mentioned here. We have not noted any technical difference when we use the disposable Alcon/Grieshaber handpieces.

Maintenance of the anterior chamber is critical when removing lens substance. Aspiration of fluid from the anterior chamber must be balanced by adequate infusion. Some surgeons also use Aqualase (Alcon) for phacoaspiration in children. It may have the advantage of better cortical clean-up with fewer mitotically active cells left behind. Further study is needed.

The addition of 0.5 mL adrenaline to the infusion bottle (1:1,000 for cardiac use) helps to maintain mydriasis and perhaps improves iris tissue tone and decreases iris floppiness [42]. Although we do not have personal experience of using heparin sodium in the

irrigating fluid, reports showing a beneficial role in preventing postoperative inflammation have appeared in the literature [4, 49]. The use of heparin should be avoided in eyes with a compromised blood-aqueous barrier (e.g., previous ocular surgery) as they are at high risk of developing postoperative hyphema.

Hydrodissection has been thought to be less useful in children than in adults. However, one study [39] has shown the intraoperative benefits of performing multiquadrant hydrodissection. The potential benefits are an overall reduction in the operative time and a reduction in the amount of irrigating solution used to facilitate lens substance removal. A fluid wave can sometimes be generated in older children but not reliably in infants and toddlers. Cortical material strips easily from the pediatric capsule even in the absence of hydrodissection if the proper technique is used (Fig. 23.2h). Attempts at hydrodelineation should be discouraged in children since it does not aid in lens removal and may lead to capsular rupture. Hydrodissection should not be done in children with posterior polar cataracts because of the fragility of the posterior capsule in these cases.

23.3.4 Posterior Capsulectomy and Vitrectomy

In young children who undergo pediatric cataract surgery, posterior capsule opacification (PCO) is rapid and virtually inevitable if the posterior capsule is left intact (Figs. 23.8, 23.9) [6, 36, 37]. PCO occurs much faster and is much more amblyogenic in younger children as compared with older children. The advent of vitreous suction cutting devices for removing the center of the posterior capsule and a portion of the anterior vitreous during the initial surgery in young children undergoing cataract surgery dramatically decreased the need for secondary surgery. A primary posterior capsulectomy and anterior vitrectomy during IOL implantation in the pediatric cataract gives the best chance for maintaining a long-term clear visual axis. Neodymium-yttrium-aluminum-garnet (Nd:YAG) laser posterior capsulotomies are usually necessary in children when the posterior capsule is left intact. Larger amounts of laser energy are often needed as compared to adults, and the posterior capsule opening may close, requiring repeated laser treatments or a secondary pars plana membranectomy.

As of 2008, primary posterior capsulectomy and anterior vitrectomy is common practice while managing younger children with cataract. An important question that remains is, when should the posterior capsule be left intact? We answer this question looking at several factors (age, association of posterior capsule plaque or defect, availability of YAG laser, expected cooperation of child approximately 12–24 months after cataract surgery for YAG). As a rough guideline, in children below 5 years of age, we prefer to do primary posterior capsulectomy and vitrectomy (Figs. 23.1, 23.3). In children, 5–8 years of age, we will do a posterior capsulectomy with or with-

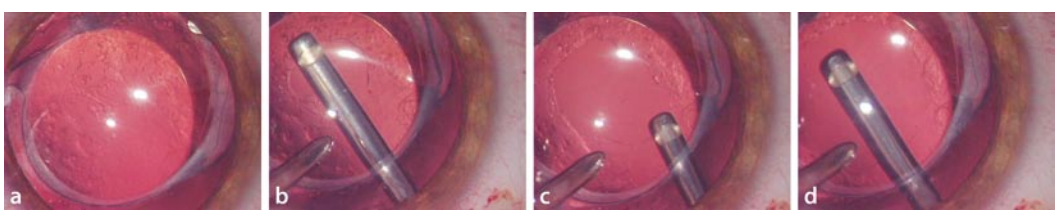

Fig. 23.8a–d Visual axis opacification requiring surgical removal to clear the visual axis

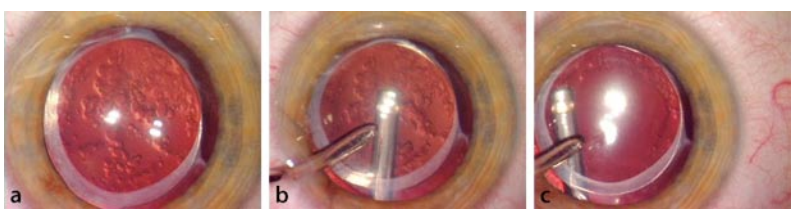

Fig. 23.9a–c Visual axis opacification requiring surgical removal to clear the visual axis

out vitrectomy, as needed. In children above 8 years of age, we keep an intact posterior capsule more often (Fig. 23.2). Anterior segment surgeons are often more accustomed to, and more comfortable with, a limbal (or anterior) approach. Our current strategy is to perform these procedures via the pars plana/plicata preferentially, whenever we intend to use a primary vitrectomy in pediatric eyes receiving IOL implantation (Fig. 23.3). The size of the posterior capsule opening should be large enough to help avoid VAO, but small enough that sufficient peripheral capsular support remains for capsular fixation of an IOL. Even if the surgeon is not planning to implant an IOL in a specific eye, it is important to leave behind sufficient anterior and posterior capsular support at the time of cataract surgery to facilitate subsequent in-the-bag or sulcus-fixated IOL implantation (if needed) (Fig. 23.1d) [33, 50]. Ideally, the surgeon should aim for a central, circular opening in the posterior capsule about 1–1.5 mm smaller than the IOL optic. We use a Venturi vacuum pump system, as in our hands it cuts the capsule more easily than a peristaltic pump. Readers should follow the manufacturer's instruction manual for using a specific machine and setting. On the Accurus machine (Alcon Laboratories, Fort Worth, Texas), an irrigation rate of 30+ cc/min and a cutting rate of 600 cuts/min have proven effective at our setting. When the pars plana/plicata approach is chosen, the IOL should be inserted into the capsular bag using OVD, while the posterior capsule is still intact (Fig. 23.3a, b). The OVD can be removed without fear of engaging vitreous, because removal precedes the posterior capsulectomy. While the irrigation cannula remains in the anterior chamber, an MVR blade is used to enter the pars plana/plicata 2–3 mm (2 mm in patients less than 1 year old, 2.5 mm in patients 1–4 years old, and 3 mm in patients over 4 years old) posterior to the limbus. The vitrector is then inserted through this incision and used to open the center of the posterior capsule. The endpoint for the vitrectomy is difficult to define. Sufficient vitreous should be removed centrally so that the LEC cannot use the vitreous face as a scaffold for VAO. Any vitreous that tracks forward past the plane of the posterior capsulectomy needs to be removed. VAO after primary posterior capsulectomy and vitrectomy is often blamed on an inadequate posterior capsule opening or an inadequate vitrectomy. These assertions have not been verified scientifically. In cataract with associated blood vessel anomalies, such as persistent fetal vasculature, vitrectomy instrumentation is used to remove the posterior lens capsule, abnormal membrane, and anterior vitreous. Intraocular scissors and intraocular cautery are also used as needed.

Intracameral triamcinolone (Kenalog) may have a potential benefit in the management of pediatric cataract. Kenalog injection into the anterior chamber provides the anterior segment surgeon with a means to localize and identify any vitreous strands remaining in the anterior chamber which otherwise might have gone unnoticed [7]. Sutureless, pars plana vitrectomy through self-sealing sclerotomies has been reported in the literature [5, 8]. No difference in the amount of visible vitreous incarceration between sutured and sutureless sclerotomies was reported, using ultrabiomicroscopy [19]. However, wound leakage, extension, dehiscence, hemorrhage, vitreous and/or retinal incarceration, retinal tear, and dialysis have been reported with this technique. Difficulty with the passage of instruments has also been observed when tunnel incisions are used. A case of successful removal of PCO in a child using a 25-gauge transconjunctival sutureless vitrectomy has been reported [21]. Although scleral rigidity in children is lower, self-sealing was seen, with the integrity of the eyes well maintained.

23.3.5 Intraocular Lens Implantation

Intraocular lens implantation in children has the benefit of providing, intraocularly, at least a partial optical correction to replace the refracting power of the crystalline lens, which is an important advantage to the visual development in amblyopia-prone eyes. While there is certainly a benefit to IOL implantation by reducing the dependency on compliance with other external optical treatments (aphakic glasses and contact lenses), implantation in pediatric eyes has remained somewhat controversial. A general consensus exists that IOL implantation is appropriate for most older children undergoing cataract surgery. In contrast, the advisability of IOL implantation during the first year of life is still being questioned. We showed a nearly 5-fold increase in the number of the ASCRS respondents and more than a 13-fold increase in the number of the AAPOS respondents implanting IOLs

in children 2 years old and younger from 1993 to 2001 [51].

It is well known that the majority of the eye's axial growth occurs during the first 2 years of life. This rapid eye growth makes selection of an IOL power for an infant difficult. Selecting the best IOL power to implant in a growing child presents unique challenges. While Gordon and Donzis [11] have documented the axial growth pattern of normal eyes in children, the axial growth of cataractous eyes is different. In the normal phakic child, there is little change in refraction (0.9 diopters from birth through adulthood on average) because the power of the natural lens decreases dramatically as the eye grows axially. However, an IOL placed in a child's eye cannot change in power to match the growth of the eye. An IOL chosen for emmetropia in early childhood is likely to leave the patient highly myopic in adulthood. For children beyond the age of 2 years, studies are available to help the surgeon predict average growth of the eye. When operating on children, many surgeons have advised selecting an IOL power that will leave mild to moderate hyperopia, leaving less hyperopia with increasing age (see Chap. 22). Other authors have advocated aiming for emmetropia regardless of age when operating beyond 2 years of age. This approach avoids potentially amblyogenic residual hyperopia but is likely to lead to the development of significant myopia later.

When placing an IOL in a child's eye, in-the-bag implantation is strongly recommended. Care should be taken to avoid asymmetrical fixation with one haptic in the capsular bag and the other in the ciliary sulcus. This can lead to decentration of the IOL. In contrast to adults, dialing of an IOL into the capsular bag can be difficult in children. Often the IOL will dial out of the capsular bag rather than into it. This tendency can be blunted somewhat by the use of highly viscous OVDs. Foldable hydrophobic acrylic IOLs are used increasingly in children. The AcrySof hydrophobic acrylic IOL (Alcon Laboratories, Fort Worth, Texas) has been shown to be very biocompatible for pediatric eyes [13, 46, 47]. The one-piece AcrySof is especially suited for small soft eyes and can be inserted into the capsular bag with ease. We use the AcrySof SN-60-IQ which has a blue-blocker chromophore and is designed using Wavefront technology. It is important to customize the "A"-constant after analysis of your own results. The "A"-constant on the IOL package is calculated using contact "A"-scan ultrasound globe axial length measurements. We recommend using immersion "A"-scan in children because of higher accuracy. The "A"-constant will usually be higher (by 0.2–0.3) when immersion measurements are used. We utilize a 118.7 "A"-constant for the SN-60-IQ IOL.

While silicone IOLs are infrequently utilized in children, the second-generation silicone material appears to be an acceptable alternative for older children. When capsular fixation is not possible, sulcus placement of an IOL in a child is acceptable. To avoid decentration, a rigid PMMA IOL should be considered or when a foldable lens (such as the three-piece AcrySof IOL) is used, optic capture through the anterior or combined anterior/posterior capsulorhexis should be attempted. Optic capture of an IOL maintained better IOL centration but was reported to predispose to an increased inflammatory response in one study [36]. Some other authors report that although technically challenging, it ensured clear visual axis and centration [9, 10, 12]. The PMMA IOL we prefer is the MC-60-BM (Alcon Laboratories, Fort Worth, Texas).

Tassignon and colleagues reported the outcome of a surgical procedure they called "bag-in-the-lens" in eyes with pediatric cataract [32]. In this technique, the anterior and posterior capsules are placed in the groove of a specially designed IOL after a capsulorhexis of the same size is created in both capsules [31, 32]. The authors reported a clear visual axis in all pediatric patients with an average follow-up of 17 months.

The ongoing development in adjustable IOL technology may prove very useful in the future of the surgical management of pediatric cataracts. The possibility of a lens that could be adjusted to counter the myopia induced by ocular growth is potentially exciting. An ideal pediatric adjustable IOL implant should be biocompatible, allow for safe repeatable adjustment procedures performed at any time after cataract surgery, and have an adequate refractive error adjustment range. As of today, this ideal adjustable IOL does not exist. However, the concept of such an IOL is being developed and, after certain modifications, such an IOL may become available [26].

The FDA recently approved the Crystalens (Eyeonics), AcrySof ReSTOR (Alcon), and ReZoom (Advanced Medical Optics) IOLs. The Crystalens accommodating IOL is engineered with a hinge designed to allow the optic to move back and forth in

response to change of focus. It is unknown whether the fibrosis that often occurs throughout the pediatric lens capsule after surgery would influence the IOL movement. This IOL is not recommended when a primary posterior capsulectomy and anterior vitrectomy has been performed. The AcrySof ReSTOR IOL is based on the AcrySof design and material platform. The ReSTOR is a pseudo-accommodative, apodized diffractive IOL with a near add of +4.00 diopters built-in. The add results in +3.20 diopters in the spectacle plane. The ReZoom multifocal IOL is a second-generation refractive redesign (using acrylic) of the original silicone Array multifocal IOL. The newest multifocal is the Tecnis aspheric optic design multifocal IOL which is engineered to reduce the spherical aberration of the average corneas.

Each of the multifocal IOLs represents a compromise based on the simultaneous vision principle. Two or more images are formed on the retina at the same time, one image at near and the other at distance focus. The brain selects the image it wants to see. Some loss of contrast is inherent to simultaneous vision since the available light is split between the near focus and the distance focus. Uncorrected refractive error (cylinder of more than 1 diopter or the changes in sphere that occur with eye growth) may result in more significant blur because of the simultaneous vision concept. Alternating vision, which is provided by a monofocal IOL and bifocal glasses, results in only one object being in focus at a time and all incoming light is directed to this focus. While the increased use of multifocal and accommodative IOLs for implantation during the teenage years is predictable, we would caution surgeons that these lenses may not be advantageous in growing or amblyopic eyes. With residual refractive error, especially the myopia that develops after eye growth, multifocality may (ironically) result in more spectacle dependence compared to a monofocal IOL with residual myopia. This deserves further study.

23.4 Postoperative Medications and Follow-up

Immediately at the end of surgery, a drop of dilute (5%) povidone iodine is placed on the operative eye. An antibiotic steroid ointment and atropine ointment are placed on the eye. A patch and Fox shield are placed over the eye. We prefer to secure the shield with two Tegaderm sheets instead of standard tape (Fig. 23.10). The patch and shield should remain on the eye until the morning after surgery. We remove it in the office, examine the eye, and show the parents how to apply the postoperative drops. There are some variances from the protocol in certain situations. With older children, the atropine may be deleted. Babies who are left aphakic do not receive the ointment. We use topical drops for these eyes, and rather than patching the eye, we apply a Silsoft contact lens (usually a 7.5 base-curve and +32 D or +29 D power) at the end of surgery. The parents can then begin the drops right away. For older children (above age 6–7 years) the parents are allowed to remove the patch and shield 4–5 h after the surgery and begin the postoperative drops. The eye is still examined on the first postoperative day. Topical atropine (0.5% in children less than 1 year of age, and 1% thereafter) is utilized once per day for 2–4 weeks in children up to age 6 years. Prednisolone acetate (1%) is used topically 6 times per day for 2 weeks and then 3–4 times per day for an additional 2 weeks. An antibiotic drop (the same fluoroquinolone used preoperatively) is used for 1 week after surgery. Any residual refractive error is corrected after the wound stabilizes and the synthetic absorbable sutures dissolve. We rarely use oral steroids except in some uveitis patients or some trauma cases. We schedule postoperative examinations at 1 week, 4 weeks, 3 months, and 6 months postoperatively. We also consider a yearly EUA in order to measure intraocular pressure, examine the peripheral retina, monitor eye growth using A-scan ul-

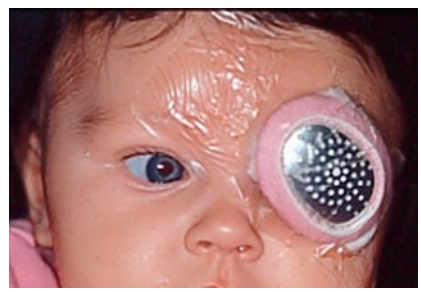

Fig. 23.10 A patch and Fox shield are placed over the eye. Note that we prefer to secure the shield with two Tegaderm sheets instead of standard tape

trasound, examine the position of the IOL, and detect any secondary membrane or after-cataract formation. Once children become old enough and cooperative enough to undergo these examinations awake, the yearly EUA becomes unnecessary.

23.5 Special Considerations

23.5.1 Traumatic Cataract

Trauma is a common cause of unilateral cataract in children. At the time of presentation after the trauma to the eye, primary repair of a corneal or scleral wound may be needed along with a complete evaluation of damage to the intraocular structures (e.g., posterior capsule rupture, vitreous hemorrhage, and retinal detachment). The authors prefer to defer cataract surgery and IOL implantation in traumatic cataract patients, even when anterior lens capsule has been ruptured. A delay of 1–4 weeks may be helpful to allow corneal healing and to reduce the inflammatory response. Longer delays are avoided in children within the amblyopic ages. Implantation of an IOL is preferred in the cases of traumatic cataracts with corneal injuries, because contact lenses may be difficult to fit. On the other hand, a rigid gas-permeable contact lens may be needed to help with control of astigmatism and, if worn, can also provide aphakic correction. For this reason, some surgeons are less likely to place an IOL primarily in these cases.

Placement of the IOL in the capsular bag is preferred when capsular support is available. When stability of the capsular bag is compromised, a capsular tension ring (CTR) can be used (Fig. 23.11). Ciliary sulcus fixation of the IOL can also be done in the absence of adequate capsular support for in-the-bag placement, but with a greater incidence of uveitis and pupillary capture [27].

23.5.2 Ectopia Lentis

Ectopia lentis is defined as displacement or malposition of the crystalline lens of the eye. The lens can be dislocated (luxated) or subluxated. Subluxation of the crystalline lens may occur as an ocular manifestation of systemic diseases including Marfan syndrome, homocystinuria, and Weil-Marchesani syndrome. It can also occur as an idiopathic isolated defect. Progressive subluxation of the lens induces large refractive errors and loss of accommodation. In addition, movement of the dislocated lens can cause the visual axis to be partly phakic and partly aphakic leading to marked visual disturbances. Surgical removal of the congenitally subluxated lens needs to be undertaken with caution. Although CTRs are useful with a moderate loss of zonular support (Figs. 23.12, 22.13), eyes with profound zonular compromise or marked lens subluxation are best treated with complete removal of the lens and capsular bag using vitrectomy instrumentation.

23.5.3 Secondary Intraocular Lens Implantation

The vast majority of children undergoing secondary IOL implantation have had a primary posterior capsulotomy and anterior vitrectomy. If adequate peripheral capsular support is present, the IOL is placed into the ciliary sulcus or in the reopened capsular bag

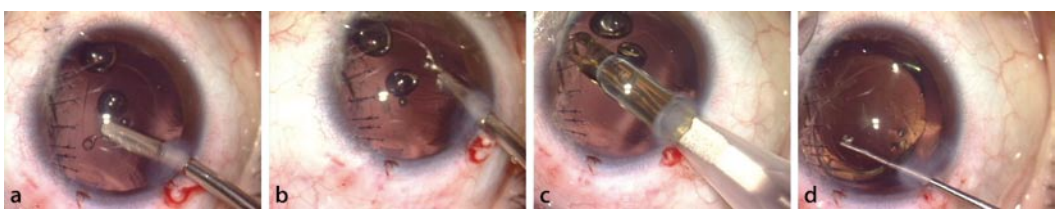

Fig. 23.11a–d Use of capsular tension ring in a child with traumatic cataract

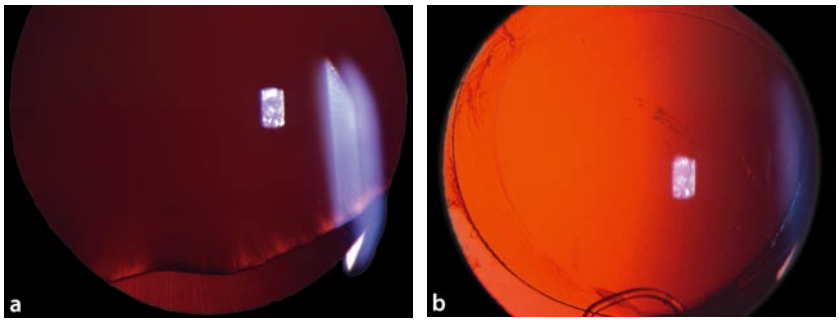

Fig. 23.12 **a** Subluxation of lens. **b** Use of Cionni ring in eye shown in **a**

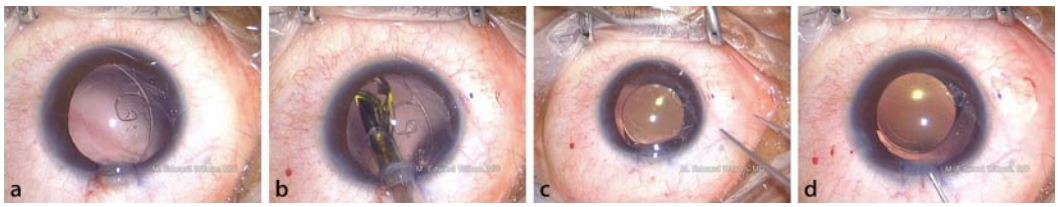

Fig. 23.13a–d Ectopia lentis and use of Cionni ring

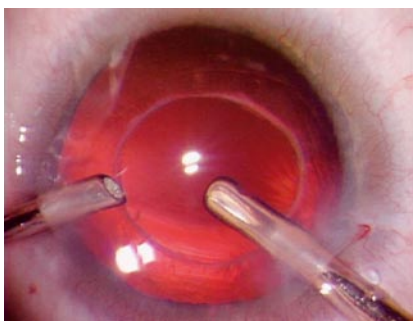

Fig. 23.14 Secondary in-the-bag: opening of capsular bag just completed with Sommerring ring removed

(Fig. 23.14) [33, 50]. Viscodissection and meticulous clearing of all posterior synechiae between the iris and the residual capsule is mandatory. An all-PMMA IOL is ideal for sulcus placement and should be considered, especially when the amount of capsule remnant is less than ideal. However, these IOLs require a larger incision for implantation. The most common IOL used in secondary implantation is the three-piece AcrySof IOL. It has a posterior angulation that helps make it suitable for the sulcus. However, the haptics are soft and decentrations can occur, especially in eyes with large anterior segments and axial length measurements greater than 23 mm. Prolapsing the IOL optic through the fused anterior and posterior capsule remnants is very useful in preventing decentration and also eliminating the possibility of inadvertent pupillary capture. When inadequate capsular support is present for sulcus fixation in a child, implantation of an IOL is not recommended unless every contact lens and spectacle option has been explored fully. Anterior chamber IOLs and scleral or iris-fixated posterior chamber IOLs are used in children when other viable options are absent, but the long-term consequences of these placements are unknown. Anterior chamber IOLs should be of an open-loop flexible design and sized appropriately for the anterior chamber. Scleral-sutured IOLs are usually fixated with 10-0 Prolene suture but concerns of biodegradation have surfaced as more late (5–15 years after surgery) IOL decentrations have been documented. A new 10-0 polyester suture has now been tried. Some surgeons are also using 9-0 Prolene. Other suture materials are in design. Iris fixation is also an alternative in children when inadequate capsule is present for sulcus or bag fixation. A three-piece acrylic lens can be placed through a pharmacologically constricted pupil so as to purposefully pupil-capture the optic. The haptics are secured to the undersurface of the iris with one full-thickness iris suture each. The sutures are placed in the immobile peripheral iris. This technique has the advantage of a small incision since a foldable IOL is utilized. Iris fixation as in the “lobster-claw” style

lenses (Verisyse) are utilized in some children as a phakic IOL for high myopia. The aphakic version of this IOL is available for compassionate use but must be requested through the FDA on a case-by-case basis. An abbreviated FDA approval process is being planned so that the aphakic IOL is easier to obtain.

23.6 Postoperative Complications and Visual Outcome

23.6.1 Visual Axis Opacification

Secondary VAO is one of the most common complications of pediatric cataract surgery, especially when the posterior capsule is left intact. PCO is generally delayed in eyes with a hydrophobic acrylic IOL as compared with a PMMA IOL. VAO after acrylic implantation with an intact posterior capsule is more "proliferative" compared to the "fibrous" reaction commonly seen in conjunction with the PMMA IOLs. After a primary posterior capsulotomy and an anterior vitrectomy, VAO is rare in older children when an acrylic IOL has been used. When VAO does occur, it is usually in a baby operated on in the first year of life. When infantile eyes are implanted with an IOL, VAO is common despite performing posterior capsulectomy and vitrectomy. Using hydrophobic acrylic IOLs, various articles have reported VAO averaging 44.0%, while ranging from 8.1% when all children under 2 years of age were reviewed to 80% when all children operated on below 6 months of age were included [18, 28, 35, 38]. Secondary VAO in eyes implanted in infancy tends to occur within the first 6 months after cataract surgery [35]. Thus, patients with longer follow-up will not likely change the incidence of VAO in infantile eyes. Eyes with associated ocular anomalies (e.g., anterior segment dysgenesis, iris hypoplasia, or persistent fetal vasculature) are at 9 times higher risk for developing VAO as compared to eyes without associated ocular anomalies [35]. In children older than 2 years of age at the time of cataract surgery, the secondary VAO rate after primary posterior capsulectomy and vitrectomy varies from 0% to 20.6% with an average of 5.1%. In older children, some authors prefer to do only posterior capsulorhexis (without vitrectomy). The average rate of secondary intervention in these eyes is 13.8% (range 0–68%). With an intact posterior capsule, various articles have reported PCO ranging from 14.7% to 100% (average 25.1%, excluding eyes with 100% PCO in children younger than 4 years of age). With longer follow-up, even for older children, the average Nd:YAG laser capsulotomy rate may be higher than the 25.1% noted here. Stager and colleagues reported that 70% maintained a clear visual axis after a single Nd:YAG procedure, 84% after two Nd:YAG procedures, and 88% after three Nd:YAG procedures [30]. Surgical intervention to clear the visual axis was needed in 8%. The probability of maintaining a clear central visual axis after 24 months with a single Nd:YAG laser procedure was 35% in children less than 24 months of age and 74% in older children.

23.6.2 Deposits and Synechiae

Increased inflammation is reported in eyes with a PMMA IOL as compared with hydrophobic acrylic IOLs [1, 17]. The incidence of deposits was reported as 6.4% [46], 25% [23], 35.9% [38], and 24.1% [35]. The incidence of deposits was significantly higher in younger age groups (age at surgery less than 2 years of age) than in the older groups ($P<0.04$) [38]. Younger age at the time of cataract surgery also increases the risk for synechiae formation. Vasavada and colleagues noted posterior synechiae in 14 eyes (13.6%). All except one were operated on during the first 2 years of life [38]. The incidence of synechiae formation was significantly higher when children were operated on before 2 years of age compared to the older age groups ($P<0.001$).

23.6.3 Glaucoma

In a multicenter retrospective review, Asrani and coworkers reported a lower incidence (0.3%, or 1 in 377 cases) of open-angle glaucoma in eyes receiving a primary IOL implant compared with those that remained aphakic (11.3%, or 14 in 124 cases) after cataract surgery [2]. We reported postoperative glaucoma in 3.8% (10 of 266) of eyes with an IOL implant and 17% (8 of 47) of aphakic eyes [34]. However, for patients who underwent surgery during the first 4.5 months of

their life, the glaucoma incidence was 24.4% (10/41) in eyes with an IOL implant and 19% (8/42) in aphakic eyes ($P=0.55$). The result of our study suggests that an IOL is not protective against the development of glaucoma [34]. Congenital cataracts that need to be operated on early in life are at higher risk for the development of glaucoma with or without an IOL. Childhood cataracts that develop after infancy are usually not associated with microphthalmia, are almost always implanted with an IOL, and are at very low risk for the development of glaucoma. Since the eyes at highest risk for glaucoma are also the eyes most likely to be left aphakic, IOL implantation may falsely appear to be protective against glaucoma.

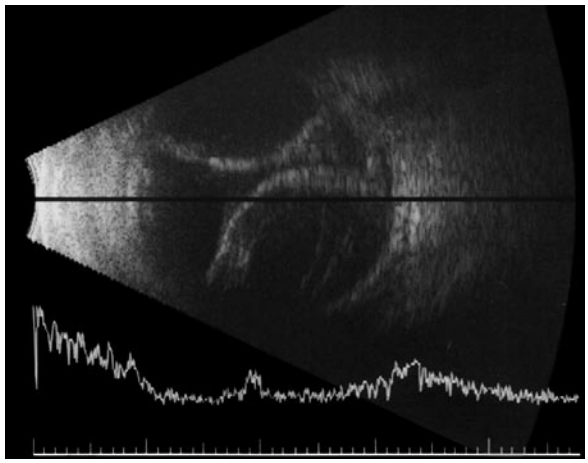

Fig. 23.15 Choroidal effusion in an eye with Sturge-Weber syndrome operated on for cataract

23.6.4 Retinal Detachment

Rabiah and colleagues noted that aphakic retinal detachment (RD) is infrequent after pediatric cataract surgery [29]. Although we have not analyzed our data for pseudophakic RD systematically, we do not recall seeing it in eyes with pediatric cataract in the absence of a predisposing etiology such as a history of RD, trauma, or retinopathy of prematurity.

23.6.5 Visual Acuity Outcome

We reported a median visual acuity of 20/30, with median visual acuity of unilateral and bilateral cases being 20/40 and 20/25, respectively [20]. Better visual acuity was associated with bilateral cataract, older age at surgery, and normal interocular axial length difference. Amblyopia was the major cause of residual visual deficit.

23.6.6 Choroidal Effusion

In eyes with Sturge-Weber syndrome, choroidal effusion can occur postoperatively (Fig. 23.15). The visual outcome of these eyes is generally good.

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References

1. Aasuri MK, Fernandes M, Pathan PP (2006) Comparison of acrylic and polymethylmethacrylate lenses in a pediatric population. Indian J Ophthalmol 54:105–109
2. Asrani S, Freedman S, Hasselblad V, Buckley EG, Egbert J, Dahan E, Gimbel H, Johnson D, McClatchey S, Parks M, Plager D, Maselli E (2000) Does primary intraocular lens implantation prevent "aphakic" glaucoma in children? J AAPOS 4:33–39
3. Basti S, Krishnamachary M, Gupta S (1996) Results of sutureless wound construction in children undergoing cataract extraction. J Pediatr Ophthalmol Strabismus 33:52–54
4. Bayramlar H, Totan Y, Borazan M (2004) Heparin in the intraocular irrigating solution in pediatric cataract surgery. J Cataract Refract Surg 30:2163–2169
5. Biglan AW, Cheng KP, Davis JS, Gerontis CC (1996) Results following secondary intraocular lens implantation in children. Trans Am Ophthalmol Soc 94:353–373
6. Buckley EG, Klombers LA, Seaber JH, Scalise-Gordy A, Minzter R (1993) Management of the posterior capsule during pediatric intraocular lens implantation. Am J Ophthalmol 115:722–728
7. Burk SE, Da Mata AP, Synder ME, Schneider S, Osher RH, Cionni RJ (2003) Visualizing vitreous using Kenalog suspension. J Cataract Refract Surg 29:645–651
8. Fujii GY, De Juan E Jr, Humayun MS, Chang TS, Pieramici DJ, Barnes A, Kent D (2002) Initial experience using the transconjunctival sutureless vitrectomy system for vitreoretinal surgery. Ophthalmology 109:1814–1820
9. Gimbel HV (1997) Posterior continuous curvilinear capsulorhexis and optic capture of the intraocular lens to prevent secondary opacification in pediatric cataract surgery. J Cataract Refract Surg 1:652–656
10. Gimbel HV, DeBroff BM (2004) Intraocular lens optic capture. J Cataract Refract Surg 30:200–206

Take Home Pearls

- Modifications of the manual CCC in children over the age of 4 years and use of the vitrectorhexis in children under the age of 4 years can lead to successful anterior management in nearly every surgery.
- The surgeon should strictly adhere to the principles of a closed-chamber technique. Proper wound construction and a tight fit around the instruments helps assure chamber stability throughout irrigation and aspiration of cortex and nucleus. No phacoemulsification is needed and suturing the wounds in children is the norm.
- Currently available single-piece acrylic IOLs have improved the intraoperative performance of pediatric cataract surgery and helped to assure the proper capsular placement of the implant.
- In children beyond the infantile age group, combined posterior capsulectomy, vitrectomy, and hydrophobic acrylic IOL implantation avoids the need for a secondary intervention in most eyes.
- In infant eyes, VAO is much more common when an IOL of any type is implanted compared with primary aphakia, even when a posterior capsulotomy and an anterior vitrectomy is performed.
- In pediatric eyes with an intact posterior capsule, PCO is almost inevitable. Nd:YAG capsulotomy can treat this complication but requires more energy and may need to be repeated.
- Patients undergoing cataract surgery during early infancy are at higher risk for the development of glaucoma with or without an IOL implant.
- Amblyopia is major cause for poor visual outcome.

11. Gordon RA, Donzis PB (1985) Refractive development of the human eye. Arch Ophthalmol 103:785–789
12. Grieshaber MC, Pienaar A, Stegmann R (2005) Posterior vertical capsulotomy with optic entrapment of the intraocular lens in congenital cataracts: prevention of capsule opacification. J Cataract Refract Surg 31:886–894
13. Hollick EJ, Spalton DJ, Ursell PG, Pande MV, Barman SA, Boyce JF, Tilling K (1999) The effect of polymethylmethacrylate, silicone, and polyacrylic intraocular lenses on posterior capsular opacification 3 years after cataract surgery. Ophthalmology 106:49–54
14. Jacobs DS, Cox TA, Wagoner MD, Ariyasu RG, Karp CL, American Academy of Ophthalmic Technology Assessment Committee Anterior Segment P (2006) Capsule staining as an adjunct to cataract surgery: a report from the American Academy of Ophthalmology. Ophthalmology 113:707–713
15. Kiel AW, Butler T, Gregson R (2003) A novel use for trypan blue to minimize epithelial cell proliferation in pediatric cataract surgery. J Pediatr Ophthalmol Strabismus 40:96–97
16. Krag S, Thim K, Corydon L, Kyster B (1994) Biomechanical aspects of the anterior capsulotomy. J Cataract Refract Surg 20:410–416
17. Kuchle M, Lausen B, Gusek-Schneider GC (2003) Results and complications of hydrophobic acrylic vs PMMA posterior chamber lenses in children under 17 years of age. Graefes Arch Clin Exp Ophthalmol 241:637–641
18. Kugelberg M, Kugelberg U, Bobrova N, Tronina S, Zetterstrom C (2006) Implantation of single-piece foldable acrylic IOLs in small children in the Ukraine. Acta Ophthalmol Scand 84:380–383
19. Kwok AK, Tham CC, Loo AV, Fan DS, Lam DS (2001) Ultrasound biomicroscopy of conventional and sutureless pars plana sclerotomies: a comparative and longitudinal study. Am J Ophthalmol 132:172–177
20. Ledoux DM, Trivedi RH, Wilson Jr ME, Payne JF (2007) Pediatric cataract extraction with intraocular lens implan-

tation: visual acuity outcome when measured at age four years and older. J AAPOS 11:218–224
21. Lee HK, Kim CY, Kwon OW, Kim EK, Lee SC, Seong GJ, Kim SS (2004) Removal of dense posterior capsule opacification after congenital cataract extraction using the transconjunctival sutureless vitrectomy system. J Cataract Refract Surg 30:1626–1628
22. Mohammadpour M (2007) Four-incision capsulorhexis in pediatric cataract surgery. J Cataract Refract Surg 33:1155–1157
23. Mullner-Eidenbock A, Amon M, Moser E, Kruger A, Abela C, Schlemmer Y, Zidek T (2003) Morphological and functional results of AcrySof intraocular lens implantation in children: prospective randomized study of age-related surgical management. J Cataract Refract Surg 29:285–293
24. Nanavaty MA, Johar K, Sivasankaran MA, Vasavada AR, Praveen MR, Zetterstrom C (2006) Effect of trypan blue staining on the density and viability of lens epithelial cells in white cataract. J Cataract Refract Surg 32:1483–1488
25. Nischal KK (2002) Two-incision push-pull capsulorhexis for pediatric cataract surgery. J Cataract Refract Surg 28:593–595
26. Nischal KK (2007) Who needs a reversibly adjustable intraocular lens? Arch Ophthalmol 125:961–962
27. Pandey SK, Ram J, Werner L, Brar GS, Jain AK, Gupta A, Apple DJ (1999) Visual results and postoperative complications of capsular bag and ciliary sulcus fixation of posterior chamber intraocular lenses in children with traumatic cataracts. J Cataract & Refract Surg 25:1576–1584
28. Plager DA, Yang S, Neely D, Sprunger D, Sondhi N (2002) Complications in the first year following cataract surgery with and without IOL in infants and older children. J AAPOS 6:9–14
29. Rabiah PK, Du H, Hahn EA (2005) Frequency and predictors of retinal detachment after pediatric cataract surgery without primary intraocular lens implantation. J AAPOS 9:152–159
30. Stager DR Jr, Wang X, Weakley DR Jr, Felius J (2006) The effectiveness of Nd:YAG laser capsulotomy for the treatment of posterior capsule opacification in children with acrylic intraocular lenses. J AAPOS 10:159–163
31. Tassignon MJ, De Groot V, Vrensen GF (2002) Bag-in-the-lens implantation of intraocular lenses. J Cataract Refract Surg 28:1182–1188
32. Tassignon MJ, De Veuster I, Godts D, Kosec D, Van den Dooren K, Gobin L (2007) Bag-in-the-lens intraocular lens implantation in the pediatric eye. J Cataract Refract Surg 33:611–617
33. Trivedi RH, Wilson ME Jr, Facciani J (2005) Secondary intraocular lens implantation for pediatric aphakia. J AAPOS 9:346–352
34. Trivedi RH, Wilson ME Jr, Golub RL (2006) Incidence and risk factors for glaucoma after pediatric cataract surgery with and without intraocular lens implantation. J AAPOS 10:117–123
35. Trivedi RH, Wilson ME Jr, Bartholomew LR, Lal G, Peterseim MM (2004) Opacification of the visual axis after cataract surgery and single acrylic intraocular lens implantation in the first year-of-life. J AAPOS 8:156–164
36. Vasavada AR, Trivedi RH (2000) Role of optic capture in congenital cataract and intraocular lens surgery in children. J Cataract Refract Surg 26:824–831
37. Vasavada AR, Trivedi RH, Singh R (2001) Necessity of vitrectomy when optic capture is performed in children older than 5 years. J Cataract Refract Surg 27:1185–1193
38. Vasavada AR, Trivedi RH, Nath V (2004) Visual axis opacification after AcrySof intraocular lens implantation in children. J Cataract Refract Surg 30:1073–1081
39. Vasavada AR, Trivedi RH, Apple DJ, Ram J, Werner L (2003) Randomized, clinical trial of multiquadrant hydrodissection in pediatric cataract surgery. Am J Ophthalmol 135:84–88
40. Werner L, Apple DJ, Crema AS, Izak AM, Pandey SK, Trivedi RH, Ma L (2002) Permanent blue discoloration of a hydrogel intraocular lens by intraoperative trypan blue. J Cataract Refract Surg 28:1279–1286
41. Wilson ME (1999) Anterior capsule management for pediatric intraocular lens implantation. J Pediatr Ophthalmol Strabismus 36:314–319
42. Wilson ME, Trivedi RH, Mistr S (2007) Pediatric intraoperative floppy-iris syndrome. J Cataract Refract Surg 33:1325–1327
43. Wilson ME, Bluestein EC, Wang XH, Apple DJ (1994) Comparison of mechanized anterior capsulectomy and manual continuous capsulorhexis in pediatric eyes. J Cataract Refract Surg 20:602–606
44. Wilson ME, Saunders RA, Roberts EL, Apple DJ (1996) Mechanized anterior capsulectomy as an alternative to manual capsulorhexis in children undergoing intraocular lens implantation. J Pediatr Ophthalmol Strabismus 33:237–240
45. Wilson ME, Trivedi RH, Bartholomew LR, Pershing S (2007) Comparison of anterior vitrectorhexis and continuous curvilinear capsulorhexis in pediatric cataract and intraocular lens implantation surgery: a 10-year analysis. J AAPOS: May 25 [Epub ahead of print]
46. Wilson ME, Elliott L, Johnson B, Peterseim MM, Rah S, Werner L, Pandey SK (2001) AcrySof acrylic intraocular lens implantation in children: clinical indications of biocompatibility. J AAPOS 5:377–380
47. Wilson ME, Trivedi RH, Buckley EG, Granet DB, Lambert SR, Plager DA, Sinskey RM, Vasavada AR (2007) ASCRS white paper: hydrophobic acrylic intraocular lenses for children. J Cataract Refract Surg 33:1966–1973
48. Wilson ME Jr (2004) Anterior lens capsule management in pediatric cataract surgery. Trans Am Ophthalmol Soc 102:391–422
49. Wilson ME Jr, Trivedi RH (2006) Low molecular-weight heparin in the intraocular irrigating solution in pediatric cataract and intraocular lens surgery. Am J Ophthalmol 141:537–538
50. Wilson ME Jr, Englert JA, Greenwald MJ (1999) In-the-bag secondary intraocular lens implantation in children. J AAPOS 3:350–355
51. Wilson ME Jr, Bartholomew LR, Trivedi RH (2003) Pediatric cataract surgery and intraocular lens implantation: practice styles and preferences of the 2001 ASCRS and AAPOS memberships. J Cataract Refract Surg 29:1811–1820

52. Wilson ME Jr, Trivedi RH, Bartholomew LR, Pershing S (2007) Comparison of anterior vitrectorhexis and continuous curvilinear capsulorhexis in pediatric cataract and intraocular lens implantation surgery: a 10-year analysis. J AAPOS 11:443–446

53. Wong VW, Lai TY, Lee GK, Lam PT, Lam DS (2006) A prospective study on trypan blue capsule staining under air vs under viscoelastic. Eye 20:820–825

Glaucoma in Infancy and Early Childhood

24

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Contents

Core Messages

- Early identification of glaucoma in infants and children by physicians and care providers maximizes the likelihood of preserving useful vision.
- Glaucomas presenting in infancy share unique features related to the corneal and overall stretching of the eye under high intraocular pressure.
- Glaucomas presenting in older children sometimes take the form of refractive error, and their timely diagnosis may rely on careful scrutiny of the optic nerve head configuration and tonometry.

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- All children with conditions predisposing to glaucoma should be regularly examined for glaucoma.
- Medical therapy is appropriate first-line therapy for many secondary glaucomas and to help clear the cornea for angle surgery in primary congenital glaucoma.
- Surgical intervention is essential for primary congenital glaucoma, and is often needed for other primary and secondary glaucomas inadequately controlled on medications.
- Successful care of childhood glaucoma requires ophthalmologists experienced in treating these rare conditions, but ultimately also requires a team approach including the family and child among other critical members.

24.1 Introduction

Childhood glaucomas are a rare, heterogeneous group of disorders which, like adult glaucoma, can have vision-threatening consequences. Diagnosis and management of the pediatric glaucomas present several unique challenges. It is often the parent, primary care or eye care provider who will first recognize glaucoma in this population and it is crucial that they are familiar with its clinical features and maintain a high index of suspicion when considering this diagnosis. In adults, glaucoma is often occult; however, in children, strong suggestive signs of glaucoma are often present. The presentation of infant and childhood glaucoma varies with the degree of pressure elevation as well as the age of onset. In addition, examination of young children can be challenging and treatment strategies less familiar than those in adult patients. Genetic, pharmacologic, and technologic advances in the diagnosis and treatment of glaucoma raise the hope that this disease will, in the near future, cease to rob children and adults of vision.

24.2 Classification

There have been several classification schemes proposed for the group of childhood glaucomas, each with its own merits and advantages [123]. One such system divides childhood glaucomas into those of primary and secondary origin, where a primary glaucoma results from an intrinsic disease of the aqueous outflow mechanism, often of genetic origin, while a secondary glaucoma results from another ocular disease, injury, drug, or systemic disease (Table 24.1). There is considerable overlap between these groups and their classification. In addition, there are some pediatric glaucomas which may have both primary and secondary etiologies (e.g., infantile-onset glaucoma in Sturge-Weber syndrome, neurofibromatosis, and even aniridia). As the genetics of conditions associated with childhood glaucoma becomes further clarified, one may expect that many of the current phenotypically driven diagnostic labels will be replaced or reorganized based upon their underlying genetic abnormalities.

Both primary and secondary pediatric glaucoma may be associated with significant systemic conditions. It is therefore important for the ophthalmologist to accurately interpret eye signs as clues for the diagnosis and classification of both the glaucoma and the associated systemic disease. It is also helpful to classify childhood glaucoma in terms of age of onset dividing glaucoma into infantile and juvenile glaucoma. Three years of age is often taken as the division between infantile and juvenile glaucoma, because it is at approximately this age that the eye no longer expands in response to elevated intraocular pressure (IOP) [29].

24.3 Signs and Symptoms of Glaucoma in Children

The signs and symptoms of glaucoma vary greatly among children, according to the age of the child and the degree of IOP elevation (see also Sect. 24.4).

Table 24.1 Classification of childhood glaucomas

Primary glaucomas	Secondary glaucomas
A. Congenital open-angle glaucoma	A. Traumatic glaucoma
1. Newborn glaucoma (iridotrabeculodysgenesis)	1. Acute glaucoma
2. Infantile glaucoma (trabeculodysgenesis)	a. Angle concussion
3. Late recognized	b. Hyphema
B. Autosomal dominant juvenile (open-angle) glaucoma	c. Ghost cell glaucoma
C. Associated with ocular abnormalities (anterior segment dysgenesis)	2. Late-onset glaucoma with angle recession
1. Iridodysgenesis	3. Arteriovenous fistula
a. Aniridia[a]	B. Secondary to intraocular neoplasm
b. Congenital iris ectropion syndrome	1. Retinoblastoma
c. Iridotrabecular dysgenesis (iris hypoplasia)	2. Juvenile xanthogranuloma
2. Corneodysgenesis (or iridocorneodysgenesis)	3. Leukemia
a. Axenfeld-Rieger anomaly	4. Melanoma
b. Peters anomaly	5. Melanocytoma
c. Congenital microcornea with myopia	6. Iris rhabdomyosarcoma
d. Sclerocornea	7. Aggressive nevi of the iris
e. Congenital hereditary endothelial dystrophy	C. Secondary to uveitis
f. Posterior polymorphous dystrophy	1. Open-angle glaucoma
g. Megalocornea	2. Angle-blockage glaucoma
D. Associated with systemic abnormalities	a. Synechial angle closure
1. Chromosomal disorders	b. Iris bombe with pupillary block
a. Trisomy 13–15 (trisomy D syndrome)	c. Trabecular endothelialization
b. Trisomy 18 (Edwards syndrome)	D. Lens-induced glaucoma
c. Trisomy 21 (Down syndrome)	1. Subluxation-dislocation and pupillary block
d. Turner syndrome (XO)	a. Marfan syndrome
2. Connective tissue abnormalities	b. Homocystinuria
a. Marfan syndrome	c. Weill-Marchesani syndrome
b. Sticklers syndrome	2. Spherophakia and pupillary block
c. Others (see under secondary glaucomas)	3. Phacolytic glaucoma
3. Metabolic disease	E. Following surgery for congenital cataract
a. Oculocerebrorenal syndrome (Lowe syndrome)	1. Lens tissue trabecular obstruction
b. Mucopolysaccharidosis (e.g., Hurlers syndrome)	2. Pupillary block
c. Others (see under secondary glaucoma)[a]	3. Chronic open-angle glaucoma associated with angle abnormalities
4. Phacomatoses	F. Steroid-induced glaucoma
a. Sturge-Weber syndrome (isolated vs with CNS involvement)	G. Secondary to rubeosis
b. Neurofibromatosis type 1	1. Retinoblastoma
c. Nevus of Ota (ocular melanosis)	2. Coats disease
d. von-Hippel-Lindau syndrome	3. Medulloepithelioma

[a] Glaucoma associated with these conditions may also be considered secondary in some cases

Table 24.1 *(continued)* Classification of childhood glaucomas

Primary glaucomas	Secondary glaucomas
5. Other	4. Familial exudative vitreoretinopathy
a. Rieger syndrome (Axenfeld-Rieger syndrome)	5. Chronic retinal detachment
b. Hepatocerebrorenal syndrome (Zellweger syndrome)	H. Secondary angle-closure glaucoma
c. Kniest dysplasia	1. Retinopathy of prematurity
d. Hallermann-Streiff syndrome	2. Microphthalmos
e. Michel syndrome	3. Nanophthalmos
f. Nail-patella syndrome	4. Retinoblastoma
g. Oculodentodigital dysplasia	5. Persistent fetal vasculature
h. Prader-Willi syndrome	6. Congenital pupillary iris-lens membrane
i. Rubinstein-Taybi syndrome	7. Topiramate
j. Waardenburg syndrome	8. Central retinal vein occlusion
k. Walker-Warburg syndrome	9. Iris stromal cysts
l. Cutis marmorata telangiectasia congenita	10.Ciliary body cysts
	11. Cystinosis
	I. Malignant glaucoma
	J. Glaucoma associated with increased episcleral venous pressure
	1. Sturge-Weber syndrome (isolated vs CNS involvement)
	2. Cavernous or dural-venous fistula
	3. Orbital disease
	K. Secondary to maternal rubella
	L. Secondary to intraocular infection
	1. Acute recurrent toxoplasmosis
	2. Acute herpetic iritis
	3. Endogenous endophthalmitis

[a] Glaucoma associated with these conditions may also be considered secondary in some cases

24.3.1 Signs and Symptoms of Glaucoma in Infancy and Early Childhood

Infants and young children with glaucoma (from any cause) usually present for ophthalmologic evaluation because the pediatrician or parents have noted something unusual about the appearance of the child's eyes or behavior. Corneal opacification and/or enlargement are the most common initial signs of glaucoma and both may progress over the first 2 years of life if IOP remains elevated (Figs. 24.1–24.3). "Buphthalmos" is a term applied to describe the abnormal enlargement of an infant's eye secondary to elevated IOP; in extreme cases these eyes are vulnerable to lens subluxation and even rupture with minor trauma (Fig. 24.4). The "classic triad" of findings: epiphora, photophobia, and blepharospasm [29] result from corneal edema often with associated breaks in Descemet's membrane called Haab's striae. The occurrence of Descemet's membrane breaks appears to be confined to the first 2 years of life; they leave permanent evidence of early-onset glaucoma, and vary with respect to the associated corneal distortion and scarring (Fig. 24.5). Breaks with more vertical orientation may be seen associated with forceps delivery [22].

Additional non-specific signs of glaucoma in early life include the presence of a deep anterior chamber and optic nerve cupping. In the absence of optic atrophy, the optic cup may decrease greatly in size

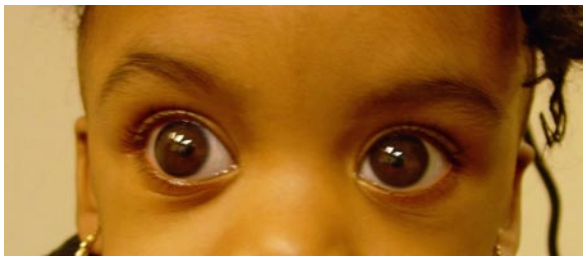

Fig. 24.1 Corneal enlargement bilaterally, with clear corneas. This infant was 2 months old at diagnosis, and responded initially to angle surgery, but subsequently required aqueous drainage device implantation in both eyes

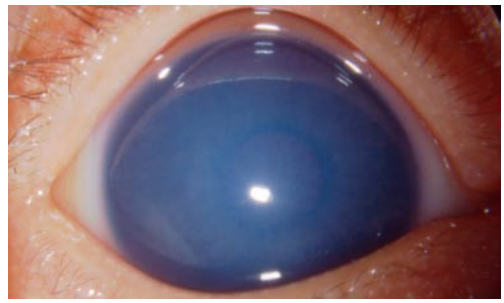

Fig. 24.2 Corneal opacification of the right eye in a 1-month-old infant with primary congenital glaucoma

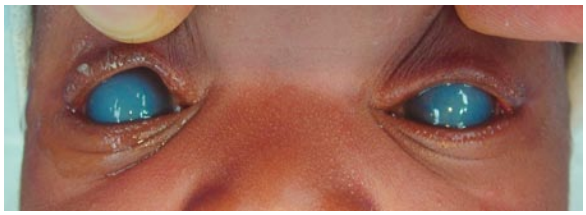

Fig. 24.3 Newborn-onset congenital glaucoma with severe bilateral corneal edema and opacification. Despite reduction of IOP after surgery, central corneal opacification did not completely clear

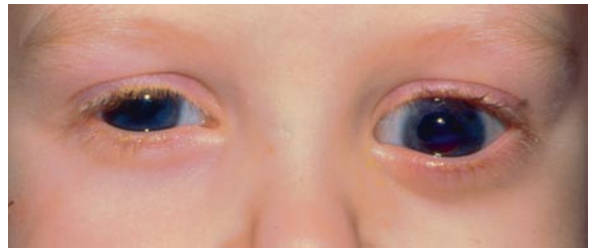

Fig. 24.4 Six-year-old boy with bilateral primary congenital glaucoma. The right eye responded well to angle surgery, while the left eye was more severely affected, became buphthalmic, and required multiple surgeries. Vision is poor in the left eye due to residual corneal scarring, and dense amblyopia

with IOP reduction, and will enlarge again if control of IOP is lost. Optic atrophy which may result from chronic or severe IOP elevation is irreversible.

24.3.2 Signs and Symptoms of Glaucoma in Older Children

Older children are typically evaluated because of decreased vision (usually from induced myopia, but sometimes from severe optic nerve damage) or circumstances in which secondary glaucoma might be suspected. While optic nerve cupping does not itself represent a reliable indicator of glaucoma, its presence should prompt thorough evaluation of that possibility in a child of any age (Fig. 24.6). Older children infrequently present with acute glaucoma inducing nauseating eye pain, headaches, and even colored haloes around lights (e.g., secondary to trauma

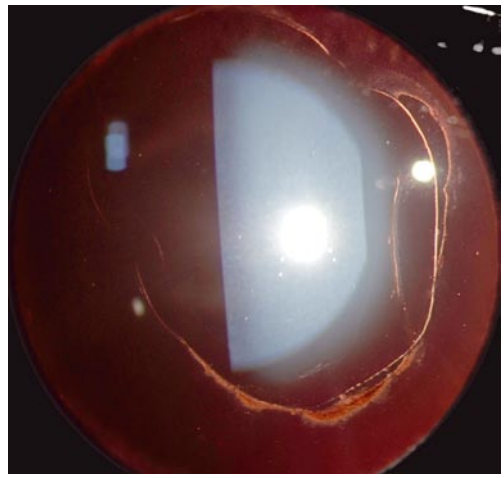

Fig. 24.5 Haab's striae seen in retroillumination in an 8-year-old boy with unilateral congenital glaucoma diagnosed at the age of 9 months, and treated with goniotomy surgery. Note the curvilinear pattern of the Descemet's membrane break, which fortunately spared the visual axis, and caused very little astigmatism in this eye. The vision in this eye is 20/25, and the IOP is normal without medications

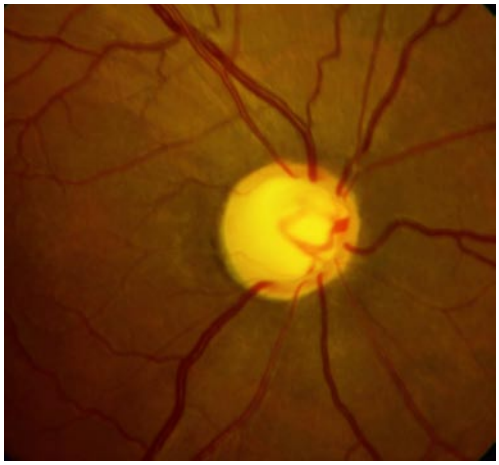

Fig. 24.6 Severe optic nerve cupping in a 13-year-old girl whose juvenile open-angle glaucoma was diagnosed 3 years after she began wearing glasses for myopia. Intraocular pressures were 40 mmHg in both eyes, and responded to medications and trabeculectomy

or angle closure as with cicatricial retinopathy of prematurity).

Loss of vision from infant and childhood glaucoma occurs secondary to pathologic changes in the eye such as corneal opacification and optic nerve damage. Poor vision may also occur secondary to the development of unilateral or bilateral refractive errors, which in turn produce amblyopia, often with associated strabismus.

24.4 Ocular Examination

While the complete pediatric eye examination best evaluates a child with suspected glaucoma, there are specific goals of the glaucoma-related examination: (a) confirming or excluding the diagnosis of glaucoma, (b) determining the etiology of the glaucoma (if present), and (c) gathering information (including any prior glaucoma interventions) vital to planning the optimal treatment. Examination under anesthesia may be avoided if the diagnosis of glaucoma can be confidently excluded (in an infant or young child) or if an older child would benefit from a medication trial. When indicated, the examination under anesthesia provides a one-stop opportunity for more detailed gonioscopy and optic nerve head evaluation, as well as measurements such as corneal diameter and pachymetry, axial length measurement, and then any needed surgical intervention.

24.4.1 Vision Testing (Acuity and Visual Fields)

Optimal vision testing methods will vary with the patient's age and cognitive function; fixation behavior and absent nystagmus are encouraging in infants, while older children should perform optotype testing. Automated visual field testing, applicable primarily to help assure the stability of older children with known glaucoma and glaucomatous field loss, often proves challenging for younger children, and children with nystagmus or poor vision. Even confrontation visual fields can often verify suspected severe nasal field loss in children with severe glaucoma and poor vision. Newer, faster testing algorithms may allow younger children to perform automated (Humphrey) visual field testing more reliably [31].

24.4.2 External Examination

External examination helps identify evidence of associated abnormalities (e.g., neurofibromatosis), buphthalmos (especially asymmetry between the eyes), photophobia, or nasolacrimal obstruction.

24.4.3 Tonometry

Measurement of the IOP (tonometry), critical to the diagnosis and treatment of children with glaucoma, belongs as part of the both the office and operating room routine. Portable applanation tonometers, such as the Perkins applanation tonometry and the Tono-Pen (a Mackay-Marg-type tonometer), prove very useful for IOP measurement in infants and young children [68, 115] whose size and attention precludes the gold-standard slit-lamp-mounted Goldmann applanation technique.

Intraocular pressure measurements are variably lowered by sedatives, narcotics, and inhalation anesthetic agents [30, 78, 125], and elevated by endotracheal intubation [29]. Ketamine anesthesia, previously reported to elevate IOP [8], has recently compared favorably with sevoflurane anesthesia in terms of minimally altering measured IOP over several minutes after induction [14]. Chloral hydrate conscious sedation, effective only in small children and with careful monitoring, reportedly minimally affects awake IOP readings [53]. Although IOP measurements taken in a sedated or anesthetic state are often less reliable than those in a calm, awake child, high preoperative IOP measurements generally remain in an abnormal range, and asymmetric IOPs between the two eyes usually remain so and often signal abnormality. Special care must be taken to avoid spuriously high IOP measured in the anesthetized child who is in laryngospasm, or "light" with eyes rolled either upward or downward compared with the midline. The normal IOP in childhood, ranging from about 10 to 22 mmHg [29], rises from infancy to reach normal adult levels by middle childhood [90].

24.4.4 Anterior Segment Examination

Anterior segment findings provide key information in the evaluation of the pediatric glaucoma patient. The cornea should be inspected and measured (holding a ruler in the frontal plane in the office, and using a caliper and ruler during anesthetized examination). Corneal changes resulting from elevated IOP often assist in diagnosing glaucoma with infant-onset, while other abnormalities may provide clues to the type of glaucoma (e.g., Peters syndrome, Axenfeld-Rieger syndrome, etc.).

Acute severe IOP elevation produces corneal enlargement, frequently accompanied by tears in Descemet's membrane (Haab's striae) than initially manifest as corneal edema/opacification, later producing variable permanent scarring and refractive errors. Moderate IOP elevation insufficient to produce noticeable corneal opacity, gradually enlarges the infant's corneas, sometimes proceeding unnoticed if symmetric, while concurrent optic nerve damage progresses to severe degrees. While the normal newborn corneal diameter ranges from 9.5 to 10.5 mm (mean 10 mm), reaching about 11.5 mm by the child's second birthday, corneal diameters of 12–12.5 mm are suggestive of glaucoma in an infant less than 12 months of age, and a measurement of 13 mm or more in childhood strongly suggests abnormality, as does asymmetry in corneal diameter between eyes [13, 29, 56, 98].

The limbus may be dramatically stretched and thinned by ocular stretching in an infant eye with glaucoma, and the anterior chamber often deepens. Abnormalities of the iris and lens may signal primary anomalies or those secondary to other eye diseases (e.g., aniridia, Axenfeld-Rieger syndrome, ectropion uvea).

24.4.5 Gonioscopy

Gonioscopy, providing vital anatomic information about the mechanism of glaucoma in a given eye, can be performed both in the office and under anesthesia. Indirect gonioscopy with a Zeiss or Sussman gonioprism proves simple to perform at the slit lamp in the older child, while Koeppe (direct) gonioscopy is useful for infants and in the operating room, facilitating detailed inspection of the iris, angle structures (and optic nerve head using a direct ophthalmoscope). In contrast to the normal adult angle, the normal infant's angle demonstrates a trabecular meshwork which appears almost as a smooth, homogeneous membrane extending from peripheral iris to Schwalbe's line. This trabecular meshwork becomes coarser and often increasingly pigmented over time [120].

In the eye with infantile glaucoma, the iris often demonstrates an insertion more anterior than normal, with altered translucency of the angle face producing an indistinct ciliary body band, trabecular mesh, and scleral spur. This translucent angle tissue has historically been dubbed "Barkan's membrane" [10]. The angle structures may reveal other features suggestive of the glaucoma etiology. For example, in glaucoma after cataract surgery, an open-angle configuration suggests trabecular meshwork dysfunction which might be amenable to initial medical therapy, while a closed angle and pupillary block may require urgent surgical intervention. An abnormally prominent Schwalbe's line, and iris adhesions to the angle structures may alternatively confirm Axenfeld-Rieger syndrome or

other anterior segment dysgenesis, while peripheral anterior synechiae may reveal the cause for IOP elevation in chronic uveitis. The eye with juvenile open-angle glaucoma often has a normal-appearing open angle, with a prominent, lacy uveal meshwork.

Taken together with other findings of anterior examination (above), the adequacy of the angle view and its findings are important guides to the appropriate surgical intervention that may be needed.

24.4.6 Optic Nerve and Fundus Examination

The optic nerve head appearance is usually the focus of the fundus examination in an eye with glaucoma, although abnormalities may help confirm the glaucoma type (e.g., a stalk in persistent fetal vasculature, foveal hypoplasia in aniridia, choroidal hemangioma in Sturge-Weber syndrome, etc.), or provide useful information for surgical planning (e.g., peripheral retinal pathology or vitreous stranding may suggest vitrectomy/peripheral laser along with aqueous drainage device placement in aphakia). Large optic nerve cups and/or asymmetry between the cupping of the two eyes suggests but does not confirm glaucoma in an infant or child. Shaffer and Heatherington reported that most eyes with primary infantile glaucoma had a cup/disc ratio larger than 0.3 (68% of 126 eyes) [102], while Richardson noted this degree of cupping in only 3% of 936 eyes of normal newborn infants [96]. Marked optic cup asymmetry was noted in only 0.6% of normal eyes in the latter series, contrasted with 89% noted for infants with monocular glaucoma.

Indirect ophthalmoscopy with a 28- or 30-diopter lens may minimize apparent optic nerve head cupping, better appreciated in the older child using binocular viewing at the slit lamp, or with a 14-diopter indirect lens or direct ophthalmoscope through a Koeppe gonioscopy lens under anesthesia. In infants and young children optic nerve cupping can occur rapidly with elevated IOP, while reversal of cupping can help confirm adequate IOP reduction, provided permanent optic nerve atrophy has not yet occurred. The older child's optic nerve cupping may also decrease with long-standing IOP reduction, but improved visual function unfortunately does not occur.

24.4.7 Other Useful Diagnostic Tests

24.4.7.1 Refraction

Refractive error determination can not only suggest possible glaucoma (as when a myopic shift occurs rapidly after cataract removal, or asymmetric relative myopia occurs in the eye with higher IOP), but also serves a critical function in maximizing the visual function of the child with glaucoma, in whom high myopia, astigmatism, or anisometropia often result from IOP-induced corneal scarring and/or ocular enlargement.

24.4.7.2 Axial Length (Ultrasound)

Measurement of the axial length (measured with ultrasound during examination under anesthesia) serves as an adjunct to serial corneal diameter determination for infants and young children being treated for glaucoma, since stabilization and even reduction in axial length can occur in the enlarged eye with stable IOP reduction [56]. This measurement also helps determine adequate size when aqueous drainage device surgery is contemplated (see Sect. 24.8). B-scan ultrasound helps confirm retinal status in eyes with opaque media, and can help confirm the patency of an aqueous drainage device (see Sect. 24.8).

24.4.7.3 Central Corneal Thickness

Ultrasound pachymetry (to measure the central corneal thickness) has become standard in the evaluation of adults with open-angle glaucoma, since this variable seems to affect not only the accuracy of the measured IOP by applanation tonometry (elevated by an unusually thick central cornea, and vice versa) [6, 48], but also the potential susceptibility of an eye to glaucomatous vision loss at elevated IOP [16, 59]. In children, the reported central corneal thickness ranges from ~540 μm (6–23 months) to ~550–560 μm for older children, with thinner central corneal thickness reported in white compared with black children [26, 27, 34, 47, 49, 52, 74], and stable measurements over at least 1 year in normal eyes and those on stable glaucoma treatment [75]. Central corneal thickness has been shown to be thinner in children with congenital glaucoma, and is probably

a function of the larger, stretched corneas of many of these children [47]. By contrast, eyes with aniridia have thicker than average central corneas [17], while those with aphakia, and particularly aphakic glaucoma, have thicker reported central corneas [76, 105, 106, 113], perhaps an acquired rather than a congenital feature [76].

The importance of central corneal thickness in the evaluation and management of children with glaucoma remains to be determined at the present time, and while this feature is worthwhile to measure and to consider when setting the target IOP, the clinician should avoid "adjusting" the measured IOP based on the pachymetry.

24.4.8 Imaging Techniques: Fundus Photography, Optical Coherence Tomography

Fundus photography of the optic nerve head has long been a mainstay in the evaluation of adults with glaucoma over time, and is useful in cooperative children with clear visual axes and without substantial nystagmus. Other imaging techniques which non-invasively image the optic nerve head (optical coherence tomography, for example, see below) may be useful in older children with glaucoma, primarily to document changes over time, rather than to diagnose glaucoma.

Optical coherence tomography, a non-invasive imaging technique able to measure the thickness of the peripapillary nerve fiber layer, as well as the macular area and volume, in adults and in children [2, 50, 97], may prove valuable to evaluate the thinning of these parameters in children with glaucoma [50, 72]. At the present time, however, their utility is limited by the need for a clear visual axis and steady fixation, as well as a wide range of normal values, and lack of longitudinal data in children with glaucoma.

24.5 Differential Diagnosis

Many conditions may produce ocular changes that could initially suggest glaucoma (Table 24.2). When faced with ocular signs or symptoms suggestive of glaucoma, the clinician must consider and rigorously rule out this diagnosis, cognizant that identification of a coexisting disorder does not by itself eliminate the possibility of glaucoma.

Table 24.2 Differential diagnosis: infant and childhood glaucoma

1. Conditions sharing cornea enlargement (without other corneal pathology)
   a. Megalocornea
   b. Megalophthalmos
   c. Axial myopia
2. Conditions sharing corneal edema or opacification
   a. Birth trauma (with Descemet's membrane ruptures)
   b. Congenital corneal malformation (e.g., Peters syndrome, sclerocornea)
   c. Corneal dystrophy (e.g., congenital hereditary endothelial dystrophy, posterior polymorphous dystrophy)
   d. Metabolic disease (e.g., mucopolysaccharidoses, cystinosis, oculocerebrorenal/Lowe syndrome)
   e. Infection (e.g., herpetic keratitis, phlyctenular)
3. Conditions sharing epiphora, and "red eye"
   a. Congenital nasolacrimal duct obstruction
   b. Conjunctivitis
   c. Corneal epithelial defect
   d. Inflammation (e.g., uveitis)
4. Conditions sharing optic nerve cupping (or abnormality)
   a. Optic nerve pit
   b. Optic disc coloboma
   c. Optic nerve atrophy
   d. Optic nerve hypoplasia
   e. Physiologic cupping (diagnosis of exclusion)

24.6 Primary Childhood Glaucoma

24.6.1 Primary Congenital/Infantile Open-angle Glaucoma

The most common of the primary pediatric glaucomas, primary congenital glaucoma (PCG) has an estimated incidence of only 1 in 10,000–20,000 live births in Western countries, as opposed to a much higher incidence in the Middle East and Slovak Romany populations, where parental consanguinity may

play a role in the increased incidence of PCG [86]. Most cases (65–80%) are bilateral, without clear gender or racial/ethnic predilection, and >75% present in the first year of life. About 25% of PCG presents in the newborn, and more than 60% are diagnosed by age 6 months [21, 29]. Although PCG always occurs early in life, with typical corneal features of enlargement, Descemet's membrane breaks, and resultant edema usually occurring during the first year of life, its phenotypic features vary greatly in severity (e.g., photophobia, corneal clouding and enlargement), so that its recognition may be delayed in milder cases, allowing time for often permanent visual loss to occur. Prompt diagnosis of glaucoma often relies on the sensitivity of parents and primary care providers to the significance of these signs and symptoms [121].

While the majority of primary infantile glaucoma cases are sporadic (no known family history), those which are familial usually show an autosomal recessive inheritance, with variable penetrance from 40% to 100% [93, 118]. Several genetic loci have been identified associated with PCG. Hence two loci, GLC3A, linked to the 2p21 region, and GLC3B, linked to the 1p36 region, have been identified, and the presence of at least a third locus in the human genome responsible for congenital glaucoma is suspected. Mutations in the CYP1B1 (cytochrome P4501B1) gene have been identified in those cases of congenital glaucoma linked to GLC3A [99, 100], with a variety of CYP1B1 mutations found in families with congenital glaucoma worldwide [3, 54, 64, 65, 77, 80, 85, 95, 107, 109, 110, 117]. The CYP1B1 gene is hypothesized to play an important role in the developing eye [101]. The routine genetic testing of children with PCG, a laudable goal for the near future, must await better funding of the laboratories currently equipped to do such testing, which is consuming of time and resources.

Although the pathogenesis of PCG is not fully understood, the increased resistance to outflow through the trabecular meshwork in PCG may well result from a developmental arrest of neural crest cell-derived anterior chamber angle tissue, with subsequent aqueous outflow obstruction by one or more mechanisms. These may include compression of the trabecular meshwork beams by a high iris and ciliary body insertion as well as abnormal development of the trabecular meshwork itself [29, 58, 66]. The inherited defect of PCG is largely limited to the filtration tissues, with typical gonioscopic abnormalities in this disease which include diminished transparency of the tissues overlying scleral spur and ciliary body band, producing the appearance of a membrane (Barkan's membrane, see Sect. 24.4.5), now thought to represent the thick, compacted trabecular meshwork itself [10].

Surgery constitutes the definitive treatment for PCG, with medical therapy reserved as brief, initial therapy to help lower the IOP and clear the cornea to facilitate surgery, and as an adjunct in those patients where IOP reduction is incomplete after surgery. Angle surgery (usually goniotomy or trabeculotomy), usually the favored initial surgery, is successful in the majority of cases, especially those with presentation between 3 and 12 months of age; surgical success drops for those with presentation at birth or after age 1–2 years (see Sect. 24.8.2.1). In certain ethnic populations, simple angle surgery has lower reported success, and experienced surgeons therefore favor combined trabeculotomy–trabeculectomy [85, 93]. Surgical options for cases of PCG refractory to angle surgery include antimetabolite-augmented filtration surgery [12, 40, 61, 104], aqueous drainage device implantation [25, 35, 39, 69, 71, 104], and cycloablation [79], with variable reported success, depending upon the reported series (see Sects. 24.8.4, 24.8.5, 24.8.6). Visual prognosis in PCG depends not only on the timely glaucoma diagnosis and IOP reduction, but also on the secondary corneal, refractive, and optic nerve changes produced by the initially elevated IOP [29].

24.6.2 Juvenile Open-angle Glaucoma

By contrast to PCG, this rare disease is an autosomal-dominant early-onset form of primary open-angle glaucoma, which has been linked in several families to mutations of the myocilin/trabecular meshwork-inducible glucocorticoid response gene at the GLC1A locus on chromosome 1q21-q31 [111]. Characterized by onset of marked bilateral IOP elevation between ages 4 and 35 years, the optic nerve cupping and visual field loss caused by IOP elevation in juvenile open-angle glaucoma (JOAG) often remain asymptomatic unless family history prompts surveillance, or the child presents with myopia and decreased dis-

tance vision. Gonioscopy reveals normal-appearing angle structures. Treatment is difficult, often beginning with medication, and proceeding to filtration or aqueous drainage device surgery, although angle surgery may be helpful in some early-onset cases (see Sect. 24.8.1.5).

24.6.3 Primary Pediatric Glaucoma Associated With Ocular Anomalies (Anterior Segment Dysgenesis)

There are a number of primary pediatric glaucomas that have associated ocular anomalies of the anterior segment (Table 24.1), involving neural crest mesenchymal tissue. Infantile-onset glaucoma may occur in many of these conditions (hence the designation primary glaucomas); later-onset glaucoma due to secondary angle outflow obstruction may also occur in some (e.g., aniridia). In some of these well-recognized disorders, systemic abnormalities may also occur (Table 24.1). Phenotypic classification schemes necessarily have significant overlap between the diagnostic categories, some of which probably share genetic abnormalities; a brief description of the features of more commonly noted diagnoses follows.

24.6.3.1 Aniridia

Children with this bilateral developmental disorder, which is characterized by congenital absence of a normal iris, develop glaucoma in at least 50% of cases, often with onset delayed until middle or late childhood (Fig. 24.7). Aniridia is associated with multiple ocular defects (and sometimes also systemic abnormalities), variably manifesting from birth to later childhood or even adulthood. Aniridia is inherited in an autosomal dominant fashion with almost complete penetrance in about two thirds of cases, with the remaining cases sporadic. This disorder results from abnormal neuroectodermal development secondary to PAX6 gene mutations at chromosome 11p13 (locus symbol AN2) [84a]. Sporadic aniridia may be associated with Wilms' tumor, genitourinary abnormalities, and mental retardation (WAGR) resulting from large deletions of 11p13, which include both the PAX6 and the adjacent Wilms tumor locus [114].

Ocular anomalies congenitally associated with aniridia include a small cornea with limbal abnormalities, hypoplastic iris leaflet, cataracts, macular hypoplasia, and angle abnormalities. Eyes with aniridia experience progressive ocular abnormalities resulting in corneal opacification, lens opacification, and glaucoma secondary to increased filtration angle dysfunction. Most aniridic eyes with acquired glaucoma demonstrate progressive trabecular blockage by movement of the residual iris tissue in front of the trabeculum [44]. Careful gonioscopic monitoring of the angle by serial anesthetic examination is recommended in aniridic infants with a strong family history of aniridic glaucoma; progressive angle narrowing and closure in these young children has been treated with prophylactic goniosurgery by some surgeons [24].

Aniridic glaucoma is difficult to treat, once it develops. Medical therapy may delay the need for surgical intervention. While no specific surgical treatment has proven best for aniridic glaucoma, angle surgery may be appropriate for early-onset cases (trabeculotomy favored by many surgeons due to the shallow anterior chamber and unprotected crystalline lens in these eyes). Trabeculectomy may be successful in older children, but is particularly challenging due to the propensity of these eyes to develop postoperative flat anterior chambers. Aqueous drainage device implantation [7] and very careful cycloablation may be needed for particularly refractory cases [1, 119, 127].

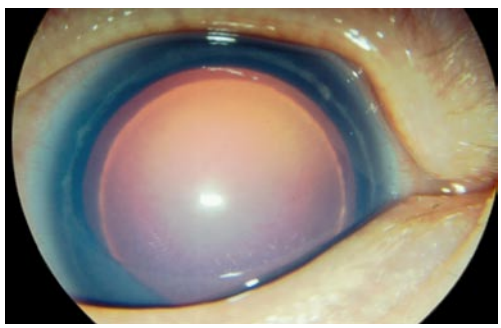

Fig. 24.7 Aniridia in an infant undergoing examination under anesthesia to allow gonioscopic examination of the angle structures. Note the limited rim of iris, and the clear outer border of the crystalline lens, in this eye with normal IOP

Extreme caution is recommended when performing filtration surgery or aqueous drainage device surgery in cases of congenital-onset aniridic glaucoma, since hypotony can result in flat chambers with subsequent corneal and lenticular opacification. Surgical interventions should maximally protect the cornea, considering the vulnerability of the cornea to later decompensation, and the poor response to penetrating keratoplasty.

24.6.3.2 Axenfeld-Rieger Syndrome

This condition represents a type of the so-called anterior chamber cleavage syndromes, in which there are variable abnormalities in the anterior segment often involving the cornea, angle, iris, and lens, and usually showing evidence of incomplete formation of the anterior chamber cavity. The collective term Axenfeld-Rieger (A-R) syndrome includes all clinical variations within this spectrum of developmental anomalies [103]. Regardless of ocular manifestations, all patients with A-R syndrome share the same general features: (a) a bilateral, developmental disorder of the eyes; (b) a frequent family history of the disorder, with an autosomal dominant mode of inheritance; (c) no sex predilection; (d) frequent systemic developmental defects; and (e) a high incidence of associated glaucoma. The iris may show hypoplasia of the anterior stromal leaf, iridotrabecular and iridocorneal processes, and posterior embryotoxon (previously termed Axenfeld anomaly). Other deformities may occur in the iris, such as corectopia (Fig. 24.8).

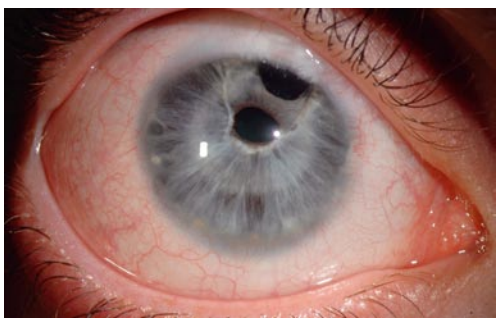

Fig. 24.8 Right eye of a 22-year-old man with Axenfeld-Rieger syndrome in both eyes. Glaucoma became uncontrolled in high school, and was managed with 5-fluorouracil-augmented trabeculectomy

Glaucoma is a common complication, occurring in more than 50% of cases, often in middle or late childhood. Dental anomalies in the form of oligodontia and anodontia, dysplasias of the skull and skeleton, and umbilical abnormalities are common.

Regarding genetics, A-R syndrome and related phenotypes have been associated with three loci, on chromosomes 4q25, 6p25, and 13q14. The genes at chromosomes 4q25 and 6p25 have been identified as PITX2 and FKHL7, respectively [5]. Axenfeld anomaly, Rieger anomaly, Rieger syndrome, iridogoniodysgenesis anomaly, iridogoniodysgenesis syndrome, iris hypoplasia, and familial glaucoma iridogoniodysplasia all have sufficient genotypic and phenotypic overlap that they should, some authors feel, be considered one condition [5].

24.6.3.3 Familial Hypoplasia of the Iris

There are some individuals demonstrating congenital hypoplasia of the iris without some of the other anterior segment abnormalities of the A-R syndrome. This autosomal dominant disorder (also termed iridogoniodysgenesis anomaly type I) demonstrates iris hypoplasia, goniodysgenesis, and early-onset glaucoma, and has been mapped to gene locus 6p26, and appears due to mutations in the gene FKHL7. A similar condition which includes non-ocular features (iridogoniodysgenesis type 2) may be allelic to A-R syndrome, mapping to 4q25, and resulting from mutations in the gene PITX2 [84b].

The risk of glaucoma in A-R and related disorders is estimated at 50–75%, with most cases presenting in childhood and early adulthood, rather than in infancy. Outflow obstruction probably results from arrested maturation of angle structures. While medical therapy may initially provide IOP control, surgical intervention is often needed. Angle surgery, while reasonable in infant-onset disease, enjoys lower success than in PCG, and other modalities may be needed for refractory cases (see Sect. 24.8).

24.6.3.4 Peters Anomaly

This congenital anomaly, usually bilateral and sporadic, a variation of the so-called anterior chamber

cleavage syndrome, consists of a posterior defect in Descemet's membrane associated with an opacity in that area with variable attachment of the iris to the periphery of the corneal leukoma (Fig. 24.9). Lens involvement is common in this condition, with cataract and/or lens adherence to the posterior corneal defect. Angle abnormalities often accompany Peters anomaly, with glaucoma incidence at least 50%. Although often occurring as an isolated ocular disorder, a wide range of associated systemic and other ocular anomalies have been reported with Peters anomaly, leading some to consider this a morphologic finding rather than a distinct entity [57]. Nonetheless, Peters anomaly can be caused by mutation in the PAX6 gene, the PITX2 gene, the CYP1B1 gene, or the FOXC1 gene [84c].

Glaucoma management in Peters anomaly, rendered difficult by the presence of corneal opacity, cataract, and shallow or absent anterior chamber, should begin with medication when angle surgery is not feasible. Surgical intervention usually includes aqueous drainage device implantation or judicious cycloablation; repeat glaucoma interventions are the rule. Corneal transplant should be avoided in favor of optical iridectomy in cases where a visual axis can be secured around a partial corneal opacity [42, 129, 130]. Phthisis and retinal detachment may result from a variety of mechanisms in these small, complex eyes.

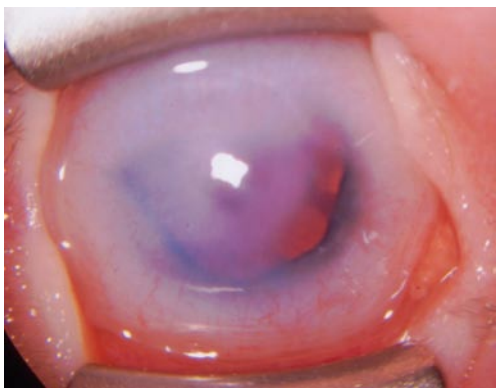

Fig. 24.9 Peters anomaly in the right eye of an infant during examination under anesthesia. Glaucoma was managed with medications in this eye (the fellow eye was more severely affected and required surgery), and the vision corrects to 20/400

24.6.3.5 Posterior Polymorphous Dystrophy

This autosomal dominant condition includes bilateral defects of the cornea at the level of Descemet's membrane with corneal opacification and variable iridocorneal adhesions, and may be mild or severe in visual consequence. Glaucoma occurs in about 15% of individuals with posterior polymorphous dystrophy; the disorder has been mapped to locus 20p11.2-q11.2 [84d].

24.6.4 Primary Pediatric Glaucoma Associated with Systemic Diseases

Primary glaucoma in children may be seen in association with certain systemic diseases in which ocular abnormalities are included in the syndrome complex (Table 24.1). A few of the clinical entities are briefly presented. See also those conditions (e.g., A-R and aniridia) listed above in Sect. 24.6.3.

24.6.4.1 Phacomatoses

Sturge-Weber Syndrome

The most common of the phacomatoses, Sturge-Weber syndrome (encephalotrigeminal angiomatosis), is a sporadic condition characterized by a congenital facial cutaneous angioma (port wine stain, nevus flammeus) affecting the facial areas innervated by the 1st and 2nd divisions of the trigeminal nerve (Fig. 24.10). Intracranial involvement may be complicated by epilepsy, paralysis, and visual field defects. Choroidal hemangiomas are present in 40% of cases, and 90% of these develop glaucoma, on the same side as the facial lesion (Figs. 24.11, 24.12a, b). Glaucoma may present at birth (goniodysgenesis suspected), but more often is acquired in childhood (the result of elevated episcleral venous pressure) [92]. Affected eyes usually demonstrate marked conjunctival and episcleral vascular prominence; gonioscopy usually reveals minor angle anatomic changes, often

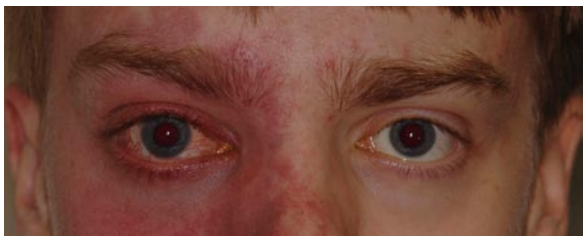

Fig. 24.10 This 18-year-old man has a port wine stain involving the right upper lid and periorbital area, associated with glaucoma in the right eye (so-called Sturge-Weber glaucoma). See also Figs. 24.11 and 24.12

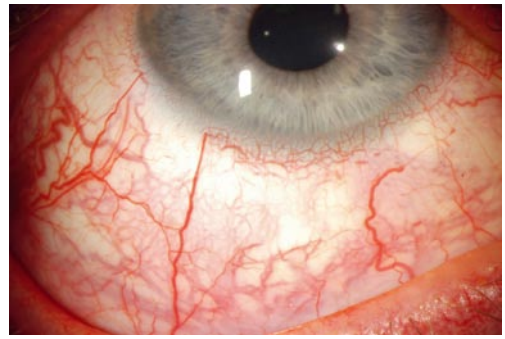

Fig. 24.11 Closer view of right eye in Sturge-Weber glaucoma (same patient as in Fig. 24.10), showing the prominent vascular pattern on the conjunctiva and episclera

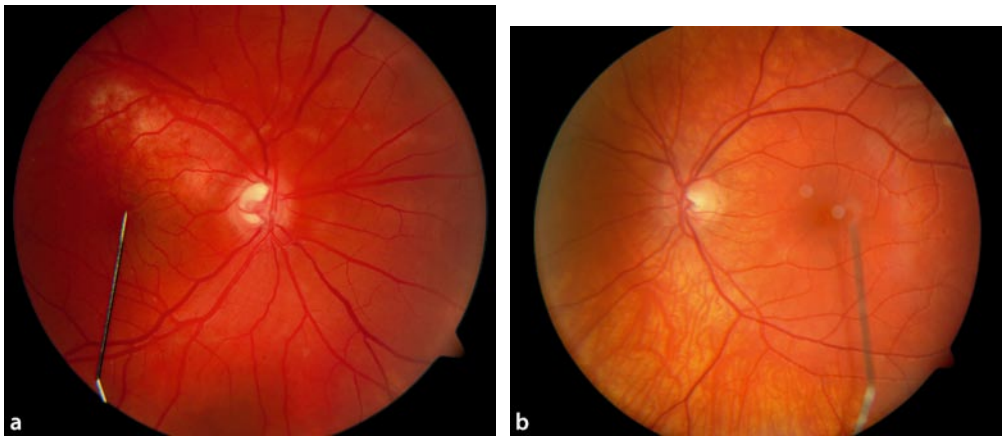

Fig. 24.12a,b Fundus view of patient with Sturge-Weber glaucoma in the right eye. **a** Right fundus, showing optic nerve cupping and choroidal hemangioma (contrast with color of fundus of normal fellow left eye (**b**). Note the pigmentary changes in the superior macular region, where leaking and macular edema from the hemangioma were successfully treated with photodynamic therapy. Vision in this eye is 20/25, and glaucoma is controlled medically. **b** Left fundus, showing normal nerve and pigmentation

with blood visible in Schlemm's canal; the iris may show increased pigmentation.

Congenital or infancy-onset glaucoma in Sturge-Weber syndrome usually requires surgical intervention. Angle surgery, although typically less effective than in cases of PCG, may prove useful; IOP reduction has been reported with both trabeculotomy and with combined trabeculotomy–trabeculectomy for these cases [60, 81]. Medication is the first-line treatment for glaucoma presenting after infancy, with aqueous suppressants the mainstay of therapy. While guarded trabeculectomy has been performed in these cases, success has also been reported with glaucoma implant surgery [19, 45], as well as with careful cycloablation [116]. Due to the presence of choroidal hemangioma in Sturge-Weber glaucoma cases, choroidal expansion and hemorrhage may complicate any intraocular surgery which rapidly decompresses the eye, either during or after the procedure.

Neurofibromatosis

This autosomal dominant systemic disease may rarely first present with congenital or infant-onset glaucoma and ectropion uvea, usually with ipsilateral plexiform neuroma of the upper eyelid, and often striking ocular enlargement of the glaucomatous eye [89]. Neurofibromatosis (NF-1) has been linked to the neurofibromin gene, located on 17q11.2 [84e]. Café au lait spots of the skin commonly appear by the end of the first year of life, with Lisch nodules on the iris usually occurring around puberty. Several possible mechanisms may explain the glaucoma in NF-1: direct effects on the normal angle development, secondary changes to the angle tissue, as well as angle closure by thickened ciliary body and choroid or directly by fibrovascular tissue [43]. Treating the glaucoma associated with NF-1 can be challenging, and should begin with medications, since angle surgery is unlikely to control IOP. Reasonable surgical options in the older child include filtration surgery, aqueous drainage device implantation, or cycloablation.

24.6.4.2 Metabolic Disease

Lowe (Oculocerebrorenal) Syndrome

Children afflicted with this rare X-linked recessive disease (linked to locus Xq26.1) [73, 84f] usually have bilateral glaucoma and cataracts, as well as associated mental retardation, renal rickets, aminoaciduria, hypotonia, acidemia, and irritability. Additional ocular abnormalities of Lowe syndrome often include microphthalmia, strabismus, nystagmus, and iris atrophy with poorly dilating pupils (which complicate cataract removal). The angle resembles that of PCG, and rarely responds to goniosurgery. Medical control rarely proves adequate, requiring additional surgery in the form of aqueous drainage device implantation and cyclodestructive surgery in refractory cases [32, 122].

24.7 Secondary Childhood Glaucoma

Pediatric glaucoma may occur secondary to a wide variety of ophthalmic conditions (see Table 24.1). While secondary glaucoma is a consequence of another eye disease rather than a primary disorder of the aqueous humor filtration mechanism, the true mechanism of glaucoma in some conditions may be both primary and secondary (see Sect. 24.6.3).

24.7.1 Trauma

Glaucoma associated with ocular trauma most often relates to an acute or secondary anterior chamber hemorrhage (hyphema). IOP elevation more commonly occurs several days following acute blunt trauma, and tends to accompany either rebleeding, or a very large initial hyphema; treatment with moderately frequent topical steroid, cycloplegics, and bedrest may decrease risk of rebleeding. Various regimens have been employed to diminish rebleeding, including antifibrinolytic agents (e.g., aminocaproic acid) and oral steroids, with variable success [38]. Children with sickle cell hemoglobinopathies are especially susceptible to optic nerve damage with moderate IOP elevation, and should be followed, as should all hyphema victims, with serial examination and IOP measurement. Initial treatment of elevated IOP with medications and gentle anterior chamber irrigation usually suffice, since IOP often normalizes after hyphema resolution. Eyes with angle recession deserve long-term follow-up, since the onset of chronic glaucoma may be delayed by years to decades.

24.7.2 Neoplasm

Neoplasms rarely produce childhood glaucoma. Advanced retinoblastoma is the most common etiology of such glaucoma, usually due to neovascular glaucoma and angle dysfunction or closure, rather than to tumor cells in the anterior chamber. Medulloepithelioma, a neoplasm of the ciliary epithelium, can also induce secondary neovascular glaucoma.

Juvenile xanthogranuloma, a rare systemic disorder sometimes associated with histiocytic infiltration of the iris, can present with glaucoma from spontaneous hyphema or due to the accumulation of histiocytes blocking the trabecular meshwork. Although glaucoma medications, along with topical and sys-

temic steroids usually suffice, difficult cases may require surgical intervention, made challenging by the tendency for continued iris bleeding whenever the IOP is lowered.

24.7.3 Inflammation and Steroid-related Glaucoma

Glaucoma secondary to chronic inflammation often presents in association with chronic anterior uveitis (e.g., ANA-associated idiopathic uveitis or arthritis), and less often with other inflammatory conditions. Glaucoma in these cases may occur by a variety of mechanisms, either acutely (e.g., trabeculitis, trabecular obstruction, iris bombe and pupillary block) or chronically (e.g., peripheral anterior synechiae, trabecular scarring/dysfunction, steroid-induced trabecular obstruction). Sometimes the diagnosis of uveitis-related glaucoma is delayed because steroid use is blamed for the IOP rise, but inflammation-related aqueous outflow reduction masks the true glaucoma when the steroid use is reduced and the inflammation not well-controlled; judicious use of systemic steroid-sparing therapy is often critical to management of difficult cases, in conjunction with pediatric rheumatologists.

Managing glaucoma secondary to uveitis requires control of the underlying inflammation, followed initially by medical management, provided the anterior chamber angle remains open. Angle surgery often controls the IOP when medication is insufficient, but success is reduced in those eyes with extensive peripheral anterior synechiae, and after cataract removal [41, 51]; tube implant surgery has also been reported quite successful in refractory cases [28, 128]. Cycloablation should be used with extreme caution in uveitic glaucoma, due to the risk of phthisis.

24.7.4 Lens-induced Glaucoma

Acute glaucoma with pupillary block and angle closure may develop in any child with ectopia lentis (from a variety of causes, e.g., homocystinuria, Weill-Marchesani syndrome, Marfan syndrome), due to forward shifting of the lens into the pupillary aperture. Non-surgical treatment can sometimes break the angle closure attack, and involves some or all of the following: supine patient positioning, manual displacement of the lens posteriorly in the eye, medication with aqueous suppressants, mydriatics, and analgesics, and subsequent miotic use. Iridectomy helps prevent repeat elevated IOP but not anterior lens displacement, and lensectomy may ultimately be needed (but is more safely performed with normalized IOP) [46].

24.7.5 Aphakic (Pseudophakic) Glaucoma

Glaucoma occurs commonly after removal of congenital or developmental cataracts (reported incidence from 3% to 41%), and represents a serious cause of late visual loss in these eyes. The glaucoma, usually of the open-angle type and often asymptomatic, is often delayed in onset for many years following cataract removal (median onset 5 years) [33, 87]. Eyes having cataract removal earlier than 1 year of age, those with associated microphthalmia, and those with persistent fetal vasculature may be at higher risk for glaucoma development. Theories of pathogenesis in open-angle glaucoma after cataract removal include both mechanical (trabecular collapse due to loss of zonular tension on the scleral spur) and chemical (postoperative inflammatory trabecular damage and/or vitreous-derived toxic factors), with no proof of either.

While peripheral iridectomy is mandatory and often curative in rare cases of angle-closure glaucoma after cataract removal, medical therapy is the first-line treatment in eyes with open angles (albeit with typical acquired angle abnormalities) [124]. Angle surgery is often disappointing in these cases, although 360-degree trabeculotomy sometimes temporizes in cases of early-onset glaucoma (personal experience). Trabeculectomy with antiproliferative agents should be used with extreme caution in aphakic or pseudophakic eyes, due to likelihood of bleb scarring and the high risk of endophthalmitis should postoperative bleb infection occur. Moderate success has been reported with aqueous drainage device sur-

gery, and cycloablation in selected refractory cases [94]. Intraocular lens implantation, either primary or secondary, does not protect against glaucoma after cataract removal.

24.7.6 Miscellaneous Causes

Secondary glaucoma in children may occur after use of steroid eye drops (see Sect. 24.7.3), and as a complication of retinopathy of prematurity. Secondary glaucoma results rarely from prenatal rubella virus infection, and a variety of other reported causes (see Table 24.1). Although there is no consensus on the ideal treatment of rare causes of secondary glaucoma, determining the etiology in each case assists the clinician in planning reasonable treatment options.

24.8 Treatment

The treatment of pediatric glaucoma varies with the type of glaucoma present, although both medical therapy and surgery often are needed (Table 24.3). Early diagnosis and adequate IOP control, the goals of treatment, maximize visual function in children with glaucoma.

24.8.1 Medical Management

While surgical intervention is the definitive treatment for children with PCG and angle-closure glaucoma cases, medical therapy should be initiated for juvenile and aphakic open-angle glaucoma, as well as for most cases of secondary open-angle glaucoma. Long-term medical therapy, which frequently plays an important role in treating children with glaucoma, proves challenging. Among the difficulties encountered when using medications in children are ensuring adequate compliance, assessing drug-induced side effects, and the possible serious adverse systemic side effects of protracted therapy. Medications are best used judiciously, with care taken to discard those drugs not providing benefit, and periodic reassessment of the adequacy of IOP control (i.e., target pressure). Let us briefly consider the five main glaucoma drug classes, and their particular application to treating pediatric glaucoma.

24.8.1.1 Beta-adrenergic Antagonists (Beta Blockers)

As effective aqueous suppressants, topical beta blockers play an important role in the treatment of children with glaucoma. Well tolerated from an ocular point of view, these drugs can produce dangerous systemic side effects in infants (especially prematurely born) and in those children prone to bronchospasm (asthma) or cardiac problems [88]. When needed in small children, beta blockers should be used at low doses (e.g., timolol, or the relatively beta-1-selective betaxolol, both at 0.25%), with punctal occlusion when possible. Topical beta blockers play an important role in treating children with glaucoma, and are appropriate first-line drugs for many.

24.8.1.2 Carbonic Anhydrase Inhibitors

Carbonic anhydrase inhibitors (CAIs) lower IOP (~20–35%) by reducing aqueous production, and are available in both oral (primary acetazolamide/Diamox) and topical (dorzolamide/Trusopt and brinzolamide/Azopt) forms. Acetazolamide lowers IOP more than its topical counterparts, is dosed at 10–20 mg/kg/day, and often produces metabolic acidosis and notable side effects that may include diarrhea, diminished energy levels, perioral and finger tingling, and loss of appetite and weight; it is therefore reserved for especially refractory cases, or those at high risk for surgical intervention. Topical dorzolamide or brinzolamide, each used b.i.d. or t.i.d., have minimal risk of systemic side effects, and serve as excellent second-line drugs in many children with glaucoma (and first-line in those unable to tolerate beta blockers).

24.8.1.3 Miotics

Miotic drugs (cholinergic stimulators) have largely been supplanted by newer medications, in the treatment of both adults and children with glaucoma. Pilocarpine retains its usefulness to induce and maintain

Table 24.3 Treatment strategy in pediatric glaucomas

I. Make the diagnosis
- A. If glaucoma suspected but not confirmed, follow carefully as indicated by findings
- B. If glaucoma confirmed, begin appropriate treatment
  1. Use medications to temporize/clear cornea in selected cases, and for most secondary glaucomas
  2. Proceed to surgery for many primary glaucomas and when secondary glaucomas uncontrolled on medications

II. Medical therapy
- A. Preoperatively, to help clear the cornea for angle surgery
- B. To temporize when infant or child is unstable for general anesthesia/surgery
- C. To assist in glaucoma control when surgery has inadequately reduced pressure
- D. To prolong visual function in cases when surgical options have been exhausted

III. Angle surgery
- A. Goniotomy (requires cornea clear enough for gonioscopic view, may repeat one or more times)
  1. Primary congenital/infantile open-angle glaucoma
  2. Other primary glaucomas (generally poorer success)
  3. Selected secondary glaucomas (especially with chronic anterior uveitis, possibly infant-onset aphakic glaucoma)
  4. Possible role vs acquired glaucoma in aniridia[a]
- B. Trabeculotomy (may repeat one time)
  1. Same as for goniotomy, but preferred in the presence of corneal opacification and by surgeons more familiar with this approach
  2. Standard with trabeculotome vs suture technique (360 degree)
  3. Perform from the side rather than superiorly unless combined with trabeculectomy
  4. May be combined with trabeculectomy (see below)

IV. Iridectomy
- A. Peripheral iridectomy for secondary pupillary block glaucoma
- B. Often combined with synechialysis
- C. Sector (optical) iridectomy when localized corneal opacity to avoid corneal transplant

V. Filtration surgery
- A. Combined trabeculotomy–trabeculectomy
  1. When trabeculotomy cannot be completed (failure to cannulate Schlemm's canal)
  2. Failed previous angle surgery (≤ 2 goniotomies and/or trabeculotomies)
- B. Trabeculectomy (usually with intraoperative mitomycin C)
  1. Any glaucoma in an eye with reasonable visual potential and unscarred conjunctiva uncontrolled on medications after angle surgery failure (or unlikely success)
  2. Must have likely faithful follow-up
  3. Not recommended in most infants or for aphakic/pseudophakic eyes

VI. Aqueous drainage device (tube shunt) surgery
- A. Infants and aphakic eyes that failed angle surgery (or low success rate with angle surgery)
- B. Failed trabeculectomy with intraoperative mitomycin C and reasonable visual potential
- C. High risk for complications with trabeculectomy (e.g., Sturge-Weber syndrome)
- D. High risk for failure with trabeculectomy from scarring (e.g., after multiple conjunctival surgeries)

[a] Should be performed only by surgeons very comfortable with goniotomy, given unprotected lens

Table 24.3 *(continued)* Treatment strategy in pediatric glaucomas

VII.	Cyclodestructive procedures (contraindicated in uveitis)
	A. Transscleral cyclophotocoagulation (diode)
	1. Failed angle surgery (or angle surgery not possible) and minimal visual potential
	2. Failed trabeculectomy and/or aqueous drainage device with poor central vision
	3. Inadequate pressure control after aqueous drainage device (encapsulated bleb)
	4. Anatomy precluding trabeculectomy or seton (e.g., disorganized anterior segment, very thin limbal tissue)
	5. Gravely ill children, poor follow-up, extremely limited remaining vision, blind in fellow eye from complication of intraocular surgery
	B. Endocyclophotocoagulation (diode)
	1. May substitute for transscleral cyclophotocoagulation (see above) in any eye with anatomy allowing limbal or pars plana approach to ciliary processes (beware cataract in phakic eyes, best in aphakic or pseudophakic eyes)
	2. Consider after transscleral cyclophotocoagulation has failed to reduce pressure
	3. May produce less inflammation than transscleral approach
	C. Cyclocryotherapy
	1. All other treatment modalities exhausted
	2. Selected cases where anatomic considerations make transscleral or endoscopic laser cyclophotocoagulation difficult or unlikely to succeed
	3. Repeat therapy in selected quadrants after previous cyclocryotherapy
VIII.	Long-term follow-up
	A. Lifetime, even when glaucoma controlled
	B. Treatment of other problems that might cause vision reduction (cataracts, refractive error, corneal opacity, potential for retinal detachment)
	C. Aggressive treatment of amblyopia
	D. Eye protection to avoid blunt trauma, especially for monocular children
	E. Appropriate visual and other support services when low vision

[a] Should be performed only by surgeons very comfortable with goniotomy, given unprotected lens

miosis before and after goniotomy or trabeculotomy for congenital glaucoma. Stronger miotics such as echothiophate iodide (Phospholine Iodide) have also been useful in selected cases of aphakic glaucoma.

24.8.1.4 Adrenergic Agonists

The topical alpha-2 agonist, brimonidine, while useful in older children with elevated IOP refractory to other medications, has produced life-threatening systemic side effects in infants (bradycardia, hypotension, hypothermia, hypotonia, and apnea), and severe somnolence in toddlers [36]. All children on brimonidine should be monitored for somnolence, and treated with the lowest effective dose (e.g., Alphagan P 0.1%). Apraclonidine (Iopidine 0.5%) helps minimize bleeding with angle surgery, and may be better tolerated than brimonidine for selected younger children requiring lower IOP (personal unpublished data), especially those intolerant to beta blockers, or after corneal transplant to avoid topical carbonic anhydrase inhibitors.

24.8.1.5 Prostaglandins

The prostaglandin analogues lower IOP mainly by enhancing uveoscleral aqueous outflow. Latanoprost has been shown to reduce IOP in some children with glaucoma, and may be especially useful in those with juvenile open-angle glaucoma [37]. Travoprost also reduces IOP in selected cases of pediatric glaucoma. While these drugs have an excellent systemic

safety profile, they do result in thick, dark, long eyelashes when used in children; iris color change has been reported in one child [18]. Excepting selected cases of juvenile open-angle glaucoma with beta blocker contraindications, prostaglandin-like agents are probably not yet appropriate first-line treatment for children.

24.8.2 Surgical Management

Surgical intervention is the indicated treatment for PCG, angle-closure glaucoma, and other cases of childhood glaucoma where medical therapy has failed to adequately control IOP. Although most experts recommend angle surgery initially to treat PCG, they often disagree regarding the optimal surgical algorithm for approaching refractory PCG and other pediatric glaucomas. Glaucoma surgery in children presents additional challenges to those encountered in adult surgery, often relating to the buphthalmic eye with stretched or distorted anatomy, and to the difficulties of postoperative evaluation and care in a young child; it is best undertaken by those with significant experience (Table 24.4). Since repeat surgery is not infrequently needed if outcomes are suboptimal, a long-term surgical strategy should preserve subsequent options and maximally prolong visual and ocular survival.

Pediatric glaucoma surgery can be divided into several broad categories: angle surgery (goniotomy or trabeculotomy), filtering surgery (trabeculectomy ± antifibrotic agents), aqueous drainage device (seton) surgery, cycloablation (cryotherapy or using laser), and others (such as peripheral iridectomy, combined trabeculotomy–trabeculectomy). Enucleation with prosthesis fitting may be the appropriate treatment for blind, disfigured, and painful eyes.

24.8.2.1 Goniotomy

Goniotomy, the surgical procedure of choice in many cases of PCG, involves incising the uveal trabecular meshwork under direct visualization. Trabeculotomy ab externo (see Sect. 24.8.2.2), an alternative and equally effective procedure, can be performed even when corneal opacity prevents adequate gonioscopic viewing of the angle structures (a prerequisite for goniotomy). The finding that approximately 70% of children with PCG can be cured by goniotomy (made by Barkan in 1942) dramatically improved the prognosis for this disease [9]. Goniotomy has also been reported as a prophylactic procedure in selected cases of congenital aniridia with progressive angle closure [23].

Goniotomy – an elegant, brief procedure which nonetheless requires great surgical precision – requires a gonioscopic view of the angle, but spares conjunctiva for later surgery, and does not alter the globe's resistance to infection or blunt trauma. Basic steps to goniotomy include: fixation of the globe, magnification and light source (loupes or microscope), operating goniotomy lens, and a sharp instrument for incision (goniotomy knife or disposable needle). Clearing of the mildly edematous cornea can be promoted by administering aqueous suppressant treatment (topical or oral carbonic anhydrase inhibitors, and timolol 0.25% in healthy infants/children) for a few days, and by application of Iopidine 0.5% as well as 5% sodium chloride drops on entering the operating room. Scraping the edematous corneal epithelium has not proved useful to the authors, who prefer trabeculotomy if the gonioscopic angle view is poor just prior to surgery. Iopidine 0.5% drops also minimize intra- and immediate postgoniotomy bleeding, and pilocarpine 2% drops induce miosis to protect the crystalline lens during the procedure, and to place the iris on stretch during and for several weeks postgoniotomy.

The authors' preferred technique utilizes a modified Barkan goniotomy lens (with a handle), placed onto the cornea on a cushion of Healon. While the surgeon sits opposite the angle to be operated on (e.g., on the temporal side for nasal goniotomy), with the microscope tilted about 45 degrees, the assistant stabilizes the eye with locking forceps placed on the Tenon's insertion near the limbus at 6 and 12 o'clock for a nasal or temporal goniotomy. Instead of a tapered knife, a disposable, 25-gauge needle on a syringe filled with Miochol or viscoelastic is used to enter the peripheral cornea on the side opposite to the intended angle incision. After the needle has been guided over the iris to engage the anterior portion of the trabecular meshwork, rotation first in one direction, and then in

Table 24.4 Tips for commonly performed surgical procedures in pediatric glaucoma

Goniotomy	
1.	Ensure adequate angle view: use aqueous suppressants before surgery, apraclonidine 0.5% drops and 5% sodium chloride just before surgery, place goniotomy lens on mound of viscoelastic, tip microscope ~45 degrees from the vertical, tip child's head toward surgical side
2.	Stabilize globe and practice rotation: use locking forceps on Tenon's insertion (usually 6 and 12 o'clock, place speculum with low profile, try globe rotation before entering eye
3.	Optimize wound entry: enter eye only one time using 25-gauge, 1.5-inch needle, make entry into peripheral cornea and parallel to iris, pass needle carefully over iris to engage anterior trabecular meshwork
4.	Perform effective trabecular meshwork incision: make incision superficial and into anterior trabecular meshwork, pass first one direction, then the other, and allow assistant to rotate globe while needle is NOT engaged in the meshwork
5.	Avoid injury to lens: constrict pupil with pilocarpine 2% before surgery, visualize tip of needle at all times and maintain plane parallel to iris for all movements
6.	Minimize bleeding: use apraclonidine drops before incision, incise the trabecular meshwork only, remove the needle carefully over the iris and have assistant "relax" any pull on locking forceps at this time, prepare to push on entry site with forceps to minimize chamber collapse, refill with balanced salt and filtered air bubble, dissolvable suture to close entry site securely
Trabeculotomy	
1.	Optimize location: unless combined with trabeculectomy, place incision temporal or nasal and just above or below the horizontal, to facilitate scleral flap and spare superior conjunctiva for possible later surgery
2.	Optimize incision and scleral flap: fornix-based conjunctival flap, triangular limbus-based scleral flap (thick enough to facilitate water-tight closure), radial scratch incision to one side of base of flap (to allow a second cut-down if needed)
3.	Maximize chances of finding Schlemm's canal: make radial incision gradually, watching for transverse fibers of canal, at sclerolimbal junction, watch for blood-aqueous reflux
4.	Minimize chance of false passage: confirm Schlemm's canal location by passing a blunted 6-0 Prolene suture into the canal, either for 360-degree suture technique, or to verify that suture remains parallel to limbus (not in anterior chamber or suprachoroidal space), 4-mirror gonioprism can sometimes visualize suture in the canal, place and rotate metal trabeculotome gently and under direct view to avoid tearing iris or stripping Descemet's membrane
5.	Secure wound and minimize bleeding: apraclonidine 0.5% and pilocarpine 2% before surgery, fill chamber with viscoelastic before pulling suture for 360-degree technique, and often after first trabeculotome pass before second pass in opposite direction, close scleral flap tightly with Vicryl suture, close conjunctiva tightly with Vicryl suture
Trabeculectomy (usually with mitomycin C)	
1.	Optimize exposure and stabilization: place 7-0 Vicryl suture into peripheral cornea in two places opposite intended surgery (e.g., at about 10:30 and 2:30 o'clock for superior site), to avoid corneal suture into thin cornea superiorly where view may be obstructed
2.	Optimize incision and future bleb morphology: fornix-based conjunctival flap for most cases, except where corneal compromised or high risk with flat chamber (e.g., aniridia)
3.	Use of antimetabolite: mitomycin C usually indicated (except in older children where 5-fluorouracil may be used intraoperatively and postoperatively), apply to broad area of uncut sclera and Tenon's capsule, but keep away from conjunctival edges and cornea, concentration usually 0.2–0.4 mg/ml for 2–5 min
4.	Scleral flap preparation, sclerostomy, and iridectomy: cut fairly thick flap with hinge at limbus, rectangular (~4×4 mm), enter under flap into cornea with supersharp (after paracentesis elsewhere), punch large (1×2 mm) opening anteriorly placed, not to edges of scleral flap hinge, make iridectomy, avoid ciliary processes if visualized
5.	Scleral flap closure: sutures at back corners of scleral flap, and two anterior releasable sutures buried into clear cornea, titrated to adequate flow, buried knots
6.	Conjunctival closure and hypotony prevention: 8-0 Vicryl on vascular needle to close "wings" of fornix-based incision, with two horizontal 10-0 Vicryl mattress sutures between, avoid covering releasable corneal portion of scleral flap sutures, fill chamber and bleb first with balanced salt then with Healon if left "leaky," leave paracentesis for office refilling in older children

Table 24.4 *(continued)*

Aqueous drainage device surgery (steps specific to children)	
1.	Choice of incision: limbus-based incision easiest to perform, consider fornix-based incision for special cases with deep chamber and corneal compromise
2.	Choice of implant and location: size the device to the eye (e.g., S-2 or FP-7 Ahmed requires axial length at least 21 mm or place very close to limbus), valved implant if immediate pressure reduction needed, otherwise Baerveldt 250 mm2 in most cases, superotemporal quadrant usual best location, suture plate 6–8 mm from limbus with 8-0 nylon suture
3.	Consider lateral rectus recession for exotropia at time of device placement: avoids need for later dissection near bleb
4.	Optimize tube position and placement: tube into anterior chamber in most cases, parallel to iris and as far back as practical to prevent exposure and corneal-tube touch, almost parallel to superior limbus rather than toward central pupil, use 30-gauge "finder" needle on viscoelastic before 23-gauge entry for tube, consider posterior chamber (over intraocular lens implant) or pars plana tube location in selected cases (need full vitrectomy if pars plana entry)
5.	Wound closure and hypotony prevention: tube completely ligated (6-0 Vicryl) if non-valved device, watertight closure of conjunctiva with 8-0 Vicryl (running closure of each wing, with "hood" onto cornea) and 10-0 Vicryl (central), chamber filled with viscoelastic unless tube ligated closed (± venting slits with 9-0 nylon needle in tube)
6.	Prophylaxis against the encapsulated bleb/high pressure phase: maintain anti-inflammatory treatment for several months (topical steroid then non-steroidals) and use aqueous suppressants liberally to keep pressure low
Cycloablation	
1.	Optimal type of ablation: transscleral vs endoscopic laser initially, cryotherapy rarely
2.	Limited treatment with transscleral and endoscopic laser to three quadrants to help avoid hypotony, vs two quadrants with cyclocryotherapy
3.	Use adequate anti-inflammatory treatment to avoid complications of inflammation
4.	Minimize risk of phthisis: keep careful records of prior treatment, rarely allow 360 degrees cumulative treatment
5.	Discuss limitations of treatment fully with parents to achieve mutual understanding of risks and alternatives

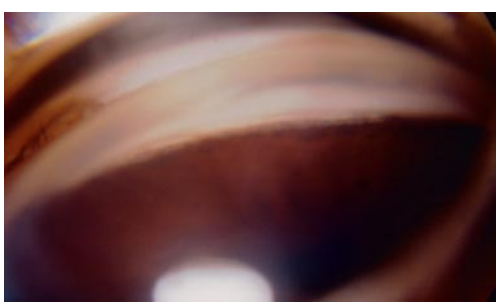

Fig. 24.13 Gonioscopic view of an eye with congenital glaucoma after successful goniotomy surgery, demonstrating a goniotomy cleft. The whitish cleft appears in the central portion of the view, where the angle is notably widened, revealing the ciliary body band

the opposite direction, produces the desired incision, which can be maximally extended to 4- to 5-clock hours, via slight globe rotation by the assistant. The resultant cleft appears in the wake of the incision, and often the peripheral iris moves posteriorly as the angle widens; blood may appear in the angle, especially if the chamber shallows after the needle is carefully withdrawn from the eye (Fig. 24.13). If used at all, a small amount of viscoelastic may be injected just as the needle is withdrawn from the eye, the chamber is refilled with balanced salt, and the entry site closed with a single 10-0 Vicryl suture. A bubble of filtered air may be placed, and helps confirm a formed chamber easily in an infant on the first postoperative day. Subconjunctival antibiotic and short-acting steroid may be injected, and the eye shielded. Postoperatively, antibiotic, steroid, and miotics (except in uveitic glaucoma) are used for various time periods by different surgeons.

Goniotomy surgery has the highest reported success rate, from 70% to more than 90%, in infants with PCG diagnosed between 3 and 12 months of age. When PCG is of birth-onset, angle surgery often fails, probably due to a more severe angle defect; PCG recognized later in childhood responds less well

to goniotomy, perhaps because of preexisting damage to the outflow system from chronically high IOP.

24.8.2.2 Trabeculotomy ab Externo

This procedure does not rely on a gonioscopic view, but instead involves the identification of Schlemm's canal in the bed of a partial-thickness scleral flap (usually via careful radial incision); the canal is then cannulated and opened from the outside inward, tearing through the poorly functioning trabecular meshwork in that area [20, 108]. While standard trabeculotomy uses a stiff curved metal trabeculotome to tear through the inner wall of Schlemm's canal, so-called suture trabeculotomy utilizes a 6-0 Prolene suture that is pulled taut after being threaded into Schlemm's canal for 180- or 360-degrees, opening the respective angle. Both goniotomy and trabeculotomy produce excellent results in selected cases of infant-onset PCG, with neither proven superior in a randomized, controlled trial. Advantages to trabeculotomy include its similarity to trabeculectomy for surgeons comfortable with the prior procedure, and ability to perform the surgery in the absence of an angle view. Disadvantages include the need to incise conjunctiva and sclera, and the possibility of being unable to locate or cannulate Schlemm's canal.

24.8.2.3 Combined Trabeculotomy–Trabeculectomy

Combined trabeculotomy and trabeculectomy has been advocated in cases resistant to goniotomy, or in selected populations where birth presentation, severely opaque corneas, and poor prior success with primary trabeculotomy have been reported. Excellent success has been reported with this technique in selected cases [62, 63].

24.8.2.4 Trabeculectomy (Filtering Surgery)

Trabeculectomy promotes filtration of aqueous humor by removing a segment of the angle tissue under a partial thickness scleral flap, creating a filtering "bleb." Usually reserved for cases where angle surgery has already failed or seems unlikely to succeed (e.g., many secondary glaucomas), simple trabeculectomy has a low success rate in children due to their healing response. Most pediatric glaucoma surgeons use antifibrotic therapy (usually intraoperative mitomycin C) and recently have advocated a fornix-based conjunctival flap superiorly, citing better bleb morphology and hopefully reduced risk of postoperative bleb infection [126]. Intraoperative 5-fluorouracil and beta irradiation have also been used with some success (Fig. 24.14) [67]. Trabeculectomy has a low success rate in infants younger than 2 years of age, and in aphakic eyes [12, 40, 112]. All children are at risk for bleb scarring and failure, and also for serious bleb-related infection, with the latter risk likely cumulative over time. Alternatives to mitomycin-enhanced trabeculectomy should be considered especially in infants, aphakic eyes, and children at high risk for inadequate infection precautions (see Sect. 24.8.2.5).

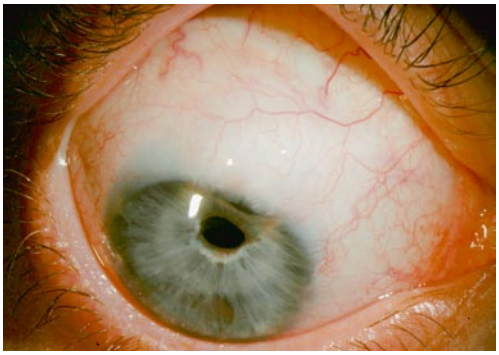

Fig. 24.14 Trabeculectomy in an eye with Axenfeld-Rieger glaucoma (same eye shown in Fig. 24.8). This partly avascular bleb was achieved in a 16-year-old boy with intra- and postoperative 5-fluorouracil injections, and has controlled glaucoma throughout 6 years of follow-up

24.8.2.5 Aqueous Drainage Device (Tube Shunt) Surgery

Initially reserved for end-stage cases, aqueous drainage device surgery has gained wider acceptance for pediatric glaucoma cases resistant to angle surgery, and having failed or not appropriate for trabeculectomy surgery. This surgery involves the placement of a flexible tube into the eye, which conducts aqueous

humor posteriorly to a reservoir (plate) sewn against the sclera, the latter becoming encapsulated to form a bleb from which trapped fluid exits into surrounding tissues. Several implant types have been widely implanted into eyes of children, including the Molteno, Baerveldt, and Ahmed glaucoma devices. Reported success and complications rates vary widely [25, 35, 39, 70, 71, 82, 83]. Less severe but more common problems include tube malposition or blockage, pupil abnormalities, cataract, motility disturbance, and encapsulation with elevation of IOP, while more severe complications such as retinal detachment (usually limited to aphakic eyes), epithelial downgrowth, and infection are fortunately fairly uncommon (Figs. 24.15, 24.16). The final IOP achieved after drainage implant surgery is not as low as after successful filtering surgery, and at least 50% of cases require continued adjunctive medication. Overall success after aqueous drainage device surgery in refractory PCG and aphakic glaucoma, approximates 75% at 2 years, but falls to ~50% after more than 5 years; success may vary with patient age and glaucoma diagnosis. In one reported series, drainage implant surgery appeared more successful at IOP control than did trabeculectomy, for children below the age of 2 years [11]. The specific devices and technique used to implant aqueous drainage devices in pediatric glaucoma cases should be adapted to the size of the eye, immediacy of the need for IOP reduction, and glaucoma type. For example, pars plana tube placement and complete vitrectomy may be needed for aqueous drainage device implantation in aphakic eyes.

24.8.2.6 Cycloablation

Cyclodestructive procedures aim to reduce IOP by damaging the ciliary processes and thereby the eye's ability to produce aqueous humor; results are often unpredictable, and complications frequent. In cases refractory to medical and other surgical interventions, cycloablation constitutes a valid means of attempting control of otherwise vision-threatening glaucoma in children. This procedure may be especially helpful as an adjunct after aqueous drainage device placement with inadequate IOP reduction.

Cyclocryotherapy

Cyclocryotherapy (freezing the ciliary processes from an external approach), the oldest cycloablative procedure, should be reserved for extremely severe cases of glaucoma where altered anatomy makes laser cycloablation unlikely to succeed. This procedure has limited success, requires repeat sessions, and has a

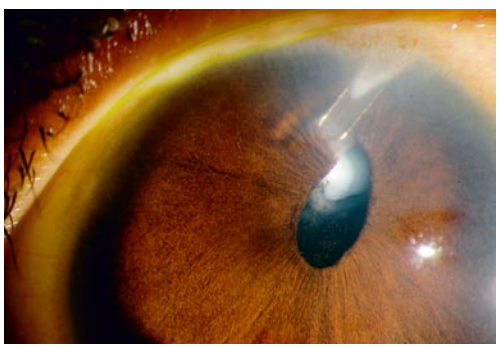

Fig. 24.15 This 8-year-old child had aqueous drainage device surgery in his eye at the age of 3 months for newborn-onset PCG. Vision is 20/60 with good IOP control off medications. Despite the fairly anterior tube position in the chamber, there is evident pupil distortion and focal cataract underlying the tube; these changes developed over several years after surgery

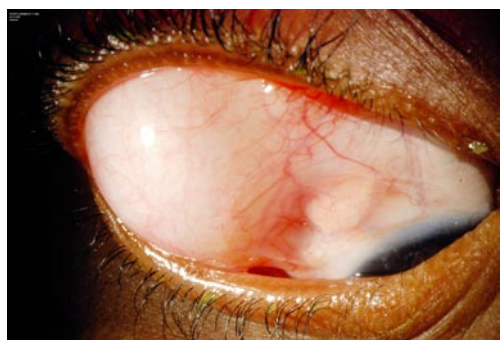

Fig. 24.16 This 11-year-old girl developed a huge, encapsulated bleb over the Ahmed aqueous drainage device which was placed in this eye with severe glaucoma after penetrating trauma and several prior related surgeries. Revision was needed due to the unacceptable resultant strabismus

significant risk of devastating complications (~15%); it should not be applied to more than 180 degrees in a single treatment (6–7 freezes of −80°C for 45–60 s) [4, 119].

Transscleral Laser Cyclophotocoagulation

Both the Nd:YAG sapphire probe and the diode laser G-probe have been used for transscleral cycloablation in children. Success has been reported at ~50% (including many retreatments), with less pain and inflammation than produced with cryotherapy, and a lower incidence of phthisis/severe complications. Problems include loss of effect over time, and inaccurate transscleral application of the laser energy to the ciliary processes [15, 55, 91].

Endoscopic Laser Cyclophotocoagulation

Endoscopic cyclophotocoagulation has the advantage of allowing direct application of laser energy to the ciliary processes with a 20-gauge probe (Microprobe; Endo Optiks, Little Silver, NJ, USA), and perhaps producing less inflammation than a transsclerally applied laser. This procedure has limited reported success, with retreatment often needed. Success of endoscopic diode cycloablation nonetheless is modest (43% in a reported series of 36 mostly aphakic eyes, after a mean cumulative arc of treatment of 260 degrees, with short mean follow-up time 19 months), and complications included retinal detachment, hypotony, and visual loss [79].

Take Home Pearls

- Infants with glaucoma often present for evaluation because the family or primary care provider has noticed signs (corneal opacity or enlargement, or tearing) or symptoms (photophobia) related to expansion of the eye under elevated pressure.
- Consider every child with myopia, optic nerve cupping, and conditions associated with glaucoma to have glaucoma until proven otherwise – check the pressure!
- Newer technologies can assist in the evaluation of the pediatric glaucoma suspect, but beware "adjusting" the measured intraocular pressure based on unusually high or low central corneal thickness. Use all available data, and if in doubt, diagnose "glaucoma suspect" and keep under surveillance.
- Most children with primary congenital glaucoma retain useful vision if diagnosed and treated early, but long-term follow-up is critical to maximizing vision and maintaining glaucoma control over time.
- All eyes are at risk for glaucoma after removal of childhood cataracts, and the risk increases over time, so life-long surveillance is needed.
- Surgery for childhood glaucoma, although sharing features with adult glaucoma surgery, is sufficiently different that it should be undertaken by a surgeon with expertise and interest in pediatric glaucoma.
- It takes a village – optimal care of the child with glaucoma requires a team effort, with members often including at least one ophthalmologist, as well as the family and child, primary care physician, school, and community members. Much improvement remains to be made in the diagnosis and care of these special children.

24.9 Long-term Follow-up of Children with Glaucoma

Every child with glaucoma must have periodic follow-up over his or her entire lifetime. Despite initial successful surgery or medical therapy, the glaucomatous eye may demonstrate asymptomatic loss of IOP control months or even decades later. Other progressive changes such as cataract or corneal decompensation may likewise occur many years after initial presentation of glaucoma, even in eyes with continued adequate IOP control. The target pressure must be continuously reevaluated, especially if progressive visual field defects or optic nerve changes occur despite previously accepted IOP levels. Eyes with functioning filtering blebs or aqueous drainage devices must be diligently followed for surgery-related complications. Young children often lose vision from glaucoma despite adequate IOP control, from corneal scarring, anisometropia, and resultant amblyopia. Children with glaucoma that is controlled without medications should be followed at least every 6 months, and young children, or those whose IOP has been controlled for less than 2 years, should probably be evaluated at least every 3 or 4 months. In spite of timely diagnosis and optimal treatment, many children with childhood glaucomas suffer visual loss from their disease; there is much room for improvement in our current understanding and treatment of these special children.

References

1. Adachi M, Dickens CJ, Hetherington J Jr, Hoskins HD, Iwach AG, Wong PC, Nguyen N, Ma AS (1997) Clinical experience of trabeculotomy for the surgical treatment of aniridic glaucoma. Ophthalmology 104:2121–2125
2. Ahn HC, Son HW, Kim JS, Lee JH (2005) Quantitative analysis of retinal nerve fiber layer thickness of normal children and adolescents. Korean J Ophthalmol 19:195–200
3. Alfadhli S, Behbehani A, Elshafey A, Abdelmoaty S, Al-Awadi S (2006) Molecular and clinical evaluation of primary congenital glaucoma in Kuwait. Am J Ophthalmol 141:512–516
4. Al Faran MF, Tomey KF, Al Mutlag FA (1990) Cyclocryotherapy in selected cases of congenital glaucoma. Ophthalmic Surg 21:794–798
5. Alward WL (2000) Axenfeld-Rieger syndrome in the age of molecular genetics. Am J Ophthalmol 130:107–115
6. Argus AA (1995) Ocular hypertension and central corneal thickness. Ophthalmology 102:1810–1812
7. Arroyave CP, Scott IU, Gedde SJ, Parrish RK II, Feuer WJ (2003) Use of glaucoma drainage devices in the management of glaucoma associated with aniridia. Am J Ophthalmol 135:155–159
8. Ausinsch B, Rayburn RL, Munson ES, Levy NS (1976) Ketamine and intraocular pressure in children. Anesth Analg 55:773–775
9. Barkan O (1942) Operation for congenital glaucoma. Am J Ophthalmol 25:552
10. Barkan O (1955) Pathogenesis of congenital glaucoma: gonioscopic and anatomic observation of the angle of the anterior chamber in the normal eye and in congenital glaucoma. Am J Ophthalmol 40:1–11
11. Beck AD, Freedman S, Kammer J, Jin J (2003) Aqueous shunt devices compared with trabeculectomy with mitomycin-C for children in the first two years of life. Am J Ophthalmol 136:994–1000
12. Beck AD, Wilson WR, Lynch MG, Lynn MJ, Noe R (1998) Trabeculectomy with adjunctive mitomycin C in pediatric glaucoma. Am J Ophthalmol 126:648–657
13. Becker B, Shaffer RN (1965) Diagnosis and therapy of the glaucomas. Mosby, St. Louis
14. Blumberg D, Congdon N, Jampel H, Gilbert D, Elliott R, Rivers R, Munoz B, Quigley H (2007) The effects of sevoflurane and ketamine on intraocular pressure in children during examination under anesthesia. Am J Ophthalmol 143:494–499
15. Bock CJ, Freedman FF, Buckley EG, Shields MB (1997) Transscleral diode laser cyclophotocoagulation for refractory pediatric glaucomas. J Pediatr Ophthalmol Strabismus 34:235–239
16. Brandt JD (2007) Central corneal thickness: tonometry artifact, or something more? Ophthalmology 114:1963–1964
17. Brandt JD, Casuso LA, Budenz DL (2004) Markedly increased central corneal thickness: an unrecognized finding in congenital aniridia. Am J Ophthalmol 137:348–350
18. Brown SM (1998) Increased iris pigment in a child due to latanoprost. Arch Ophthalmol 116:1683–1684
19. Budenz DL, Sakamoto D, Eliezer R, Varma R, Heuer DK (2000) Two-staged Baerveldt glaucoma implant for childhood glaucoma associated with Sturge-Weber syndrome. Ophthalmology 107:2105–2110
20. Burian HM (1960) A case of Marfan's syndrome with bilateral glaucoma with a description of a new type of operation for developmental glaucoma. Am J Ophthalmol 50:1187–1192
21. Chandler PA, Grant WM (1965) Lectures in glaucoma. Lea and Febiger, Philadelphia
22. Chandler PA, Grant WM (1980) Glaucoma. Lea and Febiger, Philadelphia
23. Chen TC, Walton DS (1998) Goniosurgery for prevention of aniridic glaucoma. Trans Am Ophthalmol Soc 96:155–165; discussion 165–169
24. Chen TC, Walton DS (1999) Goniosurgery for prevention of aniridic glaucoma. Arch Ophthalmol 117:1144–1148

25. Coleman AL, Smyth RJ, Wilson MR, Tam M (1997) Initial clinical experience with the Ahmed glaucoma valve implant in pediatric patients. Arch Ophthalmol 115:186–191
26. Copt RP, Thomas R, Mermoud A (1999) Corneal thickness in ocular hypertension, primary open-angle glaucoma, and normal tension glaucoma. Arch Ophthalmol 117:14–16
27. Dai E, Gunderson CA (2006) Pediatric central corneal thickness variation among major ethnic populations. J AAPOS 10:22–25
28. Da Mata A, Burk SE, Netland PA, Baltatzis S, Christen W, Foster CS (1999) Management of uveitic glaucoma with Ahmed glaucoma valve implantation. Ophthalmology 106:2168–2172
29. DeLuise VP, Anderson DR (1983) Primary infantile glaucoma (congenital glaucoma). Surv Ophthalmol 28:1–18
30. Dominiguez A, Banos MS, Alvare MG, Contra GF, Quintela FB (1974) Intraocular pressure measurement in infants under general anesthesia. Am J Ophthalmol 78:110–116
31. Donahue SP, Porter A (2001) SITA visual field testing in children. J AAPOS 5:114
32. Donahue SP, Keech RV, Munden P, Scott WE (1997) Baerveldt implant surgery in the treatment of advanced childhood glaucoma. J AAPOS 1:41–45
33. Egbert JE, Wright MM, Dahlhauser KF, Keithahn MA, Letson RD, Summers CG (1995) A prospective study of ocular hypertension and glaucoma after pediatric cataract surgery. Ophthalmology 102:1098–1101
34. Ehlers N, Sorensen T, Bramsen T, Poulsen EH (1976) Central corneal thickness in newborns and children. Acta Ophthalmol (Copenh) 54:285–290
35. Englert JA, Freedman SF, Cox TA (1999) The Ahmed valve in refractory pediatric glaucoma. Am J Ophthalmol 127:34–42
36. Enyedi LB, Freedman SF (2001) Safety and efficacy of brimonidine in children with glaucoma. J AAPOS 5:281–284
37. Enyedi LB, Freedman SF (2002) Latanoprost for the treatment of pediatric glaucoma. Surv Ophthalmol 47(suppl 1):S129–S132
38. Farber MD, Fiscella R, Goldberg MF (1991) Aminocaproic acid versus prednisone for the treatment of traumatic hyphema. A randomized clinical trial. Ophthalmology 98:279
39. Fellenbaum PS, Sidoti PA, Heuer DK, Mincker DS, Baerveldt G, Lee PP (1995) Experience with the Baerveldt implant in young patients with complicated glaucomas. J Glaucoma 4:91–97
40. Freedman SF, McCormick K, Cox TA (1999) Mitomycin C-augmented trabeculectomy with postoperative wound modulation in pediatric glaucoma. J AAPOS 3:117–124
41. Freedman SF, Rodriguez-Rosa RE, Rojas MC, Enyedi LB (2002) Goniotomy for glaucoma secondary to chronic childhood uveitis. Am J Ophthalmol 133:617–621
42. Gollamudi SR, Traboulsi EI, Chamon W, Stark WJ, Maumenee IH (1994) Visual outcome after surgery for Peters' anomaly. Ophthalmic Genet 15:31–35
43. Grant WM, Walton DS (1968) Distinctive gonioscopic findings in glaucoma due to neurofibromatosis. Arch Ophthalmol 79:127–134
44. Grant WM, Walton DS (1974) Progressive changes in the angle in congenital aniridia, with development of glaucoma. Am J Ophthalmol 78:842–847
45. Hamush NG, Coleman AL, Wilson MR (1999) Ahmed glaucoma valve implant for management of glaucoma in Sturge-Weber syndrome. Am J Ophthalmol 128:758–760
46. Harrison DA, Mullaney PB, Mesfer SA, Awad AH, Dhindsa H (1998) Management of ophthalmic complications of homocystinuria. Ophthalmology 105:1886–1890
47. Henriques MJ, Vessani RM, Reis FA, de Almeida GV, Betinjane AJ, Susanna R Jr (2004) Corneal thickness in congenital glaucoma. J Glaucoma 13:185–188
48. Herndon LW, Choudhri SA, Cox T, Damji KF, Shields MB, Allingham RR (1997) Central corneal thickness in normal, glaucomatous, and ocular hypertensive eyes. Arch Ophthalmol 115:1137–1141
49. Herse P, Weiping Y (1993) Variation in corneal thickness with age in young New Zealanders. Acta Ophthalmol 71:360–364
50. Hess DB, Asrani SG, Bhide MG, Enyedi LB, Stinnett SS, Freedman SF (2005) Macular and retinal nerve fiber layer analysis of normal and glaucomatous eyes in children using optical coherence tomography. Am J Ophthalmol 139:509–517
51. Ho CL, Walton DS (2004) Goniosurgery for glaucoma secondary to chronic anterior uveitis: prognostic factors and surgical technique. J Glaucoma 13:445–449
52. Hussein MA, Paysee EA, Bell NP, et al. (2004) Corneal thickness in children. Am J Ophthalmol 138:744–748
53. Jaafar MS, Ghulamqadir AK (1993) Effect of oral chloral hydrate sedation on the intraocular pressure measurement. J Ped Ophthalmol Strabismus 30:372–376
54. Kakiuchi-Matsumoto T, Isashiki Y, Ohba N, Kimura K, Sonoda S, Unoki K (2001) Cytochrome P450 1B1 gene mutations in Japanese patients with primary congenital glaucoma (1). Am J Ophthalmol 131:345–350
55. Kirwan JF, Shah P, Khaw PT (2002) Diode laser cyclophotocoagulation: role in the management of refractory pediatric glaucomas. Ophthalmology 109:316–323
56. Kiskis AA, Markowitz SN, Morin JD (1985) Corneal diameter and axial length in congenital glaucoma. Can J Ophthalmol 20:93
57. Kivlin JD, Fineman RM, Crandall AA, Olson RJ (1986) Peters' anomaly as a consequence of genetic and nongenetic syndromes. Arch Ophthalmol 104:61
58. Kupfer C, Kaiser-Kupfer MS (1979) Observations on the development of the anterior chamber angle with reference to the pathogenesis of congenital glaucomas. Am J Ophthalmol 88:424
59. Leske MC, Heijl A, Hyman L, Bengtsson B, Dong L, Yang Z (2007) Predictors of long-term progression in the early manifest glaucoma trial. Ophthalmology 114:1965–1972
60. Mandal AK (1999) Primary combined trabeculotomy-trabeculectomy for early-onset glaucoma in Sturge-Weber syndrome. Ophthalmology 106:1621–1627
61. Mandal AK, Prasad K, Naduvilath TJ (1999) Surgical results and complications of mitomycin C-augmented

trabeculectomy in refractory developmental glaucoma. Ophthalmic Surg Lasers 30:473–480
62. Mandal AK, Gothwal VK, Bagga H, Nutheti R, Mansoori T (2003) Outcome of surgery on infants younger than 1 month with congenital glaucoma. Ophthalmology 110:1909–1915
63. Mandal AK, Bhatia PG, Gothwal VK, Reddy VM, Sriramulu P, Prasad MS, John RK, Nutheti R, Shamanna BR (2002) Safety and efficacy of simultaneous bilateral primary combined trabeculotomy-trabeculectomy for developmental glaucoma. Indian J Ophthalmol 50:13–19
64. Martin SN, Sutherland J, Levin AV, Klose R, Priston M, Heon E (2000) Molecular characterisation of congenital glaucoma in a consanguineous Canadian community: a step towards preventing glaucoma related blindness. J Med Genet 37:422–427
65. Mashima Y, Suzuki Y, Sergeev Y, Ohtake Y, Tanino T, Kimura I, Miyata H, Aihara M, Tanihara H, Inatani M, Azuma N, Iwata T, Araie M (2001) Novel cytochrome P4501B1 (CYP1B1) gene mutations in Japanese patients with primary congenital glaucoma. Invest Ophthalmol Vis Sci 42:2211–2216
66. Maumenee AE (1963) Further observations on the pathogenesis of congenital glaucoma. Am J Ophthalmol 55:1163–1176
67. Miller MH, Rice NS (1991) Trabeculectomy combined with beta irradiation for congenital glaucoma. Br J Ophthalmol 75:584–590
68. Minckler DS, Baerveldt G, Heuer DK, Quillen-Thomas B, Walonker AF, Weiner J (1987) Clinical evaluation of the Oculab Tono-Pen. Am J Ophthalmol 104:168–173
69. Molteno AC, Ancker E, Van Biljon G (1984) Surgical technique for advanced juvenile glaucoma. Arch Ophthalmol 102:51–57
70. Molteno ACB (1973) Children with advanced glaucoma treated by draining implants. S Afr Arch Ophthalmol 1:55–61
71. Morad Y, Craig ED, Kim YM, Abdolell M, Levin AV (2003) The Ahmed drainage implant in the treatment of pediatric glaucoma. Am J Ophthalmol 135:821–829
72. Mrugacz M, Bakunowicz-Lazarczyk A (2005) Optical coherence tomography measurement of the retinal nerve fiber layer in normal and juvenile glaucomatous eyes. Ophthalmologica 219:80–85
73. Mueller OT, Hartsfield JK Jr, Gallardo LA, Essig YP, Miller KL, Papenhausen PR, Tedesco TA (1991) Lowe oculocerebrorenal syndrome in a female with a balanced X;20 translocation: mapping of the X chromosome breakpoint. Am J Hum Genet 49:804–810
74. Muir KW, Jin J, Freedman SF (2004) Central corneal thickness and its relationship to intraocular pressure in children. Ophthalmology 111:2220–2223
75. Muir KW, Duncan L, Enyedi LB, Stinnett SS, Freedman SF (2006) Central corneal thickness in children: stability over time. Am J Ophthalmol 141:955–957
76. Muir KW, Duncan L, Enyedi LB, Wallace DK, Freedman SF (2007) Central corneal thickness: congenital cataracts and aphakia. Am J Ophthalmol 144:502–506
77. Mukhopadhyay A, Acharya M, Mukherjee S, Ray J, Choudhury S, Khan M, Ray K (2002) Mutations in MYOC gene of Indian primary open angle glaucoma patients. Mol Vis 8:442–448
78. Murphy DF (1985) Anesthesia and intraocular pressure. Anesth Analg 64:520–530
79. Neely DE, Plager DA (2001) Endocyclophotocoagulation for management of difficult pediatric glaucomas. J AAPOS 5:221–229
80. Ohtake Y, Kubota R, Tanino T, Miyata H, Mashima Y (2000) Novel compound heterozygous mutations in the cytochrome P4501B1 gene (CYP1B1) in a Japanese patient with primary congenital glaucoma. Ophthalmic Genet 21:191–193
81. Olsen KE, Huang AS, Wright MM (1998) The efficacy of goniotomy/trabeculotomy in early-onset glaucoma associated with the Sturge-Weber syndrome. J AAPOS 2:365–368
82. O'Malley Schotthoefer E, Yanovitch TL, Freedman SF (2008) Aqueous drainage device surgery in refractory pediatric glaucoma. II. Ocular motility consequence. J AAPOS 12:40–45
83. O'Malley Schotthoefer E, Yanovitch TL, Freedman SF (2007) Aqueous drainage device surgery in refractory pediatric glaucomas: I. Long-term outcomes. J AAPOS 12:33–39
84a. Online Mendelian Inheritance in Man OT Johns Hopkins University, Baltimore, MD. MIM Number: {106210} {Date last edited}: 8/13/2007. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/
84b. Online Mendelian Inheritance in Man OT Johns Hopkins University, Baltimore, MD. MIM Number: {137600} {Date last edited}: 8/13/2007. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/
84c. Online Mendelian Inheritance in Man OT Johns Hopkins University, Baltimore, MD. MIM Number: {604229} World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/
84d. Online Mendelian Inheritance in Man OT Johns Hopkins University, Baltimore, MD. MIM Number: {122000}. World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/
84e. Online Mendelian Inheritance in Man OT Johns Hopkins University, Baltimore, MD. MIM Number: {162200} World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/
84f. Online Mendelian Inheritance in Man OT Johns Hopkins University, Baltimore, MD. MIM Number: {309000} World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/
85. Panicker SG, Reddy AB, Mandal AK, Ahmed N, Nagarajaram HA, Hasnain SE, Balasubramanian D (2002) Identification of novel mutations causing familial primary congenital glaucoma in Indian pedigrees. Invest Ophthalmol Vis Sci 43:1358–1366
86. Papadopoulos M, Cable N, Rahi J, Khaw PT (2007) The British Infantile and Childhood Glaucoma (BIG) Eye Study. Invest Ophthalmol Vis Sci 48:4100–4106
87. Parks MM, Johnson DA, Reed GW (1993) Long-term visual results and complications in children with aphakia. A function of cataract type. Ophthalmology 100:826–840; discussion 840–841

88. Passo MS, Palmer EA, Van Buskirk EM (1984) Plasma timolol in glaucoma patients. Ophthalmology 91:1361–1363
89. Payne MS, Nadell JM, Lacassie Y, Tilton AH (2003) Congenital glaucoma and neurofibromatosis in a monozygotic twin: case report and review of the literature. J Child Neurol 18:504–508
90. Pensiero S, DaPozza S, Perissutti P, Cavallini GM, Guerra R (1992) Normal intraocular pressure in children. J Pediatr Ophthalmol Strabismus 29:79–84
91. Phelan MJ, Higginbotham EJ (1995) Contact transscleral Nd:YAG laser cyclophotocoagulation for the treatment of refractory pediatric glaucoma. Ophthalmic Surg Lasers 26:401–403
92. Phelps CD (1978) The pathogenesis of glaucoma in Sturge-Weber syndrome. Ophthalmology 85:276–286
93. Phelps CD, Podos SM (1974) Glaucoma. Little Brown, Boston
94. Plager DA, Neely DE (1999) Intermediate-term results of endoscopic diode laser cyclophotocoagulation for pediatric glaucoma. J AAPOS 3:131–137
95. Reddy AB, Kaur K, Mandal AK, Panicker SG, Thomas R, Hasnain SE, Balasubramanian D, Chakrabarti S (2004) Mutation spectrum of the CYP1B1 gene in Indian primary congenital glaucoma patients. Mol Vis 10:696–702
96. Richardson KT (1968) Optic cup symmetry in normal newborn infants. Invest Ophthalmol 7:137–147
97. Salchow DJ, Oleynikov YS, Chiang MF, Kennedy-Salchow SE, Langton K, Tsai JC, Al-Aswad LA (2006) Retinal nerve fiber layer thickness in normal children measured with optical coherence tomography. Ophthalmology 113:786–791
98. Sampaolesi R, Caruso R (1982) Ocular echometry in the diagnosis of congenital glaucoma. Arch Ophthalmol 100:574–577
99. Sarfarazi M (1997) Recent advances in molecular genetics of glaucomas. Hum Mol Genet 6:1667–1677
100. Sarfarazi M, Akarsu AN, Hossain A, Turacli ME, Aktan SG, Barsoum-Homsy M, Chevrette L, Sayli BS (1995) Assignment of a locus (GLC3A) for primary congenital glaucoma (buphthalmos) to 2p21 and evidence for genetic heterogeneity. Genomics 30:171–177
101. Sena DF, Finzi S, Rodgers K, Del Bono E, Haines JL, Wiggs JL (2004) Founder mutations of CYP1B1 gene in patients with congenital glaucoma from the United States and Brazil. J Med Genet 41:e6
102. Shaffer RN, Heatherington J (1969) Glaucomatous disc in infants. A suggested hypothesis for disc cupping. Trans Am Acad Ophthalmol Otolaryngol 73:929–935
103. Shields MB, Buckley EG, Klintworth GK, Thresher R (1985) Axenfeld-Rieger syndrome. A spectrum of developmental disorders. Surv Ophthalmol 29:387
104. Sidoti PA, Belmonte SJ, Liebmann JM, Ritch R (2000) Trabeculectomy with mitomycin C in the treatment of pediatric glaucomas. Ophthalmology 107:422–429
105. Simon JW, O'Malley MR, Gandham SB, Ghaiy R, Zobal-Ratner J, Simmons ST (2005) Central corneal thickness and glaucoma in aphakic and pseudophakic children. J AAPOS 9:326–329
106. Simsek T, Mutluay AH, Elgin U, Gursel R, Batman A (2006) Glaucoma and increased central corneal thickness in aphakic and pseudophakic patients after congenital cataract surgery. Br J Ophthalmol 90:1103–1106
107. Sitorus R, Ardjo SM, Lorenz B, Preising M (2003) CYP1B1 gene analysis in primary congenital glaucoma in Indonesian and European patients. J Med Genet 40:e9
108. Smith R (1960) A new technique for opening the canal of Schlemm. Br J Ophthalmol 44:370–373
109. Soley GC, Bosse KA, Flikier D, Flikier P, Azofeifa J, Mardin CY, Reis A, Michels-Rautenstrauss KG, Rautenstrauss BW (2003) Primary congenital glaucoma: a novel single-nucleotide deletion and varying phenotypic expression for the 1,546-1,555dup mutation in the GLC3A (CYP1B1) gene in 2 families of different ethnic origin. J Glaucoma 12:27–30
110. Stoilov IR, Costa VP, Vasconcellos JP, Melo MB, Betinjane AJ, Carani JC, Oltrogge EV, Sarfarazi M (2002) Molecular genetics of primary congenital glaucoma in Brazil. Invest Ophthalmol Vis Sci 43:1820–1827
111. Stone DL, Fingert JH, Alward WL, et al. (1997) Identification of a gene that causes primary open angle glaucoma. Science 275:668–670
112. Susanna RJ, Oltrogge EW, Carani JCE, Nicolela MT (1995) Mitomycin as adjunct chemotherapy with trabeculectomy in congenital and developmental glaucomas. J Glaucoma 4:151–157
113. Tai TY, Mills MD, Beck AD, Joos KM, Ying GS, Liu C, Piltz-Seymour JR (2006) Central corneal thickness and corneal diameter in patients with childhood glaucoma. J Glaucoma 15:524–528
114. Turleau C, DeGrouchy J, Tournade M-F, et al. (1984) Del 11p/aniridia complex. Report of three patients and review of 37 observations from the literature. Clin Genet 26:356
115. Van Buskirk EM, Plamer EA (1979) Office assessment of young children for glaucoma. Ann Ophthalmol 11:1749
116. van Emelen C, Goethals M, Dralands L, Casteels I (2000) Treatment of glaucoma in children with Sturge-Weber syndrome. J Pediatr Ophthalmol Strabismus 37:29–34
117. Vincent AL, Billingsley G, Buys Y, Levin AV, Priston M, Trope G, Williams-Lyn D, Heon E (2002) Digenic inheritance of early-onset glaucoma: CYP1B1, a potential modifier gene. Am J Hum Genet 70:448–460
118. Waardenburg PJ, Franceschetti P, Klein D (1961) Genetics and ophthalmology. Thomas, Springfields
119. Wagle NS, Freedman SF, Buckley EG, Davis JS, Biglan AW (1998) Long-term outcome of cyclocryotherapy for refractory pediatric glaucoma. Ophthalmology 105:1921–1926; discussion 1926–1927
120. Walton DS (1979) Primary congenital open-angle glaucoma. In: Chandler PA, Grant WM (eds) Glaucoma. Lea and Febiger, Philadelphia, p 329
121. Walton DS (1979) Primary congenital open angle glaucoma: a study of the anterior segment abnormalities. Trans Am Ophthalmol Soc 77:746–768
122. Walton DS (1986) Diagnosis and treatment of glaucoma in childhood. In: Epstein DL (ed) Chandler and Grant's Glaucoma. Lea and Febinger, Philadelphia
123. Walton DS (1991) Glaucoma in infants and children. In: Nelson LB, Calhoun JH, Harley RD (eds) Pediatric ophthalmology. Saunders, Philadelphia, pp 258–270

124. Walton DS (1995) Pediatric aphakic glaucoma: a study of 65 patients. Trans Am Ophthalmol Soc 93:403–413; discussion 413–420
125. Watcha MF, Chu FC, Stevens JL, Forestner JE (1990) Effects of halothane on intraocular pressure in anesthetized children. Anesth Analg 71:181–184
126. Wells AP, Cordeiro MF, Bunce C, Khaw PT (2003) Cystic bleb formation and related complications in limbus- versus fornix-based conjunctival flaps in pediatric and young adult trabeculectomy with mitomycin C. Ophthalmology 110:2192–2197
127. Wiggins RE Jr, Tomey KF (1992) The results of glaucoma surgery in aniridia. Arch Ophthalmol 110:503–505
128. Wright MM, McGehee RF, Pederson JE (1997) Intraoperative mitomycin-C for glaucoma associated with ocular inflammation. Ophthalmic Surg Lasers 28:370–376
129. Yang LL, Lambert SR (2001) Peters' anomaly. A synopsis of surgical management and visual outcome. Ophthalmol Clin North Am 14:467–477
130. Zaidman GW, Rabinowitz Y, Forstot SL (1998) Optical iridectomy for corneal opacities in Peters' anomaly. J Cataract Refract Surg 24:719–722

Retinopathy of Prematurity

David K. Coats and Ashvini K. Reddy

25

Contents

Core Messages

- Almost seven decades after it was first described, retinopathy of prematurity (ROP) remains an important threat to pediatric vision.
- Cooperative, multicenter, prospective trials (such as CRYO-ROP and ETROP) have been useful in establishing screening and treatment guidelines for premature infants.
- An organized screening program is vital to timely detection and treatment of ROP to reduce the risk of vision loss.
- Aggressive posterior ROP is an uncommon, rapidly progressing, severe form of ROP that requires special attention.
- Documentation and communication among physicians, staff, and parents are important.
- Future advances in screening and treatment are forthcoming.

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25.1 Introduction

The search for a cure for retinopathy of prematurity (ROP) has become a priority among researchers since the disease was first described by Theodore L. Terry in 1942 [68]. ROP is a common disorder, and the risk of visual impairment can be minimized in the vast majority of affected infants with careful management. Despite this, it is estimated that ROP accounts for 19% of cases of pediatric blindness worldwide [29] and is a leading cause of blindness in children attending schools for the blind [63, 66]. Continued interest in understanding and eradicating the disorder has brought about unprecedented collaboration among scientists, ophthalmologists, and public health activists in both developed and developing nations.

25.2 A Brief History

With the introduction of and liberal use of oxygen in the neonatal population in the 1930s, rates of "retrolental fibroplasia" (as ROP was originally called) in premature infants reached epidemic proportions, resulting in blindness or severe visual impairment in thousands of children worldwide [65]. Strict oxygen curtailment subsequently resulted in extensive morbidity and mortality [12]. Oxygen was thereafter liberalized, but monitored, carefully balancing the risk of ROP against other factors. Since ROP generally afflicts only the smallest, sickest infants, it is not surprising that after decades of decline, the incidence of disease again began to rise in the 1970s [31, 44]. This was concurrent with advances in obstetrics and neonatology that permitted the survival of low birth weight premature infants.

In the 1980s the Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) study demonstrated a significant reduction in the rate of unfavorable visual, developmental, and social [49] outcomes in infants randomized to cryotherapy of the avascular retina in eyes with threshold ROP compared to untreated controls [39, 49, 53, 60, 67]. Collaborative spirit fueled further clinical trials, including the Supplemental Therapeutic Oxygen for Prethreshold ROP (STOP-ROP) study [5, 25, 32, 45], which failed to demonstrate a significant benefit to the use of supplemental oxygen therapy when administered to infants with prethreshold ROP; the Light Reduction in ROP study [4, 61], which showed no benefit to preterm infants from reduction in light exposure from birth to 32 weeks postconceptional age; and the Early Treatment for ROP (ETROP) study [36], which demonstrated that early treatment of high-risk prethreshold disease significantly reduced the risk of unfavorable outcomes and resulted in the modification of previous treatment guidelines. Currently, a cooperative study is being undertaken to evaluate the utility of biochemical cytokine modulators in ROP.

25.3 Risk Factors

Low birth weight and young gestational age are directly correlated with the most severe ROP [17, 41, 69]. Other risk factors that have inconsistently been linked to ROP severity include hypoxia [15, 75], oxygen administration [74, 75], intraventricular hemorrhage [42, 69], surfactant therapy [38], hypotension [64], fungemia [43, 47, 50], sepsis [42], and anemia [23, 28]. The overwhelming impact of both low birth weight and prematurity make establishing the full role of other risk factors difficult.

25.4 Pathogenesis

The relationship between premature birth, oxygen exposure, and ROP that eluded researchers for so long can now be explained on a molecular level, but a full appreciation of the pathogenesis of ROP still requires a basic understanding of ocular embryology and anatomy. Development of the retinal vasculature begins at the optic disc at approximately 16 weeks gestation, progresses relatively circumferentially and anteriorly, and is complete by around 40 weeks. Therefore, the proportion of mature retina at birth is determined by the degree of prematurity at birth. In full-term infants, the retina is generally fully vascularized and ROP cannot occur, but in preterm neonates, especially those born at or before 28 weeks gestation, retinal vascularization is incomplete and the normal process of development is at risk of being interrupted. Exposure to excessive concentrations of oxygen during this period can lead to vascular injury resulting in arrest of vascular development, oblitera-

tion of newly formed capillaries, and ultimately in the formation of arteriovenous shunts in the retina.

Acute ROP progresses in two main stages. Retinal vessels are capable of autoregulation and respond to increased oxygen tension after birth by constricting [14, 21]. Thus, in the first stage, postnatal hyperoxia paradoxically leads to regional ischemia of the developing retina. Hyperoxia also inhibits the release of the vasoactive cytokines, such as vascular endothelial growth factor (VEGF) [15]. In the second stage, ongoing ischemia subsequently stimulates release of excessive VEGF and other vasoactive cytokines in an attempt to reestablish retinal perfusion. Dysregulation of these vasoactive cytokines is thought to be responsible for the pathologic vascular growth, or neovascularization, seen in ROP [15]. In most cases, the fibrovascular tissue that results will involute spontaneously with little or no residual retinal damage. Vision loss and even blindness may occur in a small number of infants as a result of contraction of this neovascular tissue, leading to retinal traction and/or detachment.

Insulin-like growth factor (IGF-1) appears to be a critical oxygen-independent factor in the pathogenesis of ROP. Recent research indicates that serum levels of IGF-1 in premature babies correlate directly with the clinical severity of ROP [48, 71–73]. IGF-1 appears to act indirectly as a permissive factor by allowing maximal VEGF stimulation of vessel growth. Lack of IGF-1 in preterm infants prevents normal retinal vascular growth in phase I of ROP, despite the presence of VEGF [48]. As infants mature, rising levels of IGF-1 in phase II of ROP allow VEGF-stimulated pathologic neovascularization to occur. These findings suggest that restoration of IGF-1 to normal levels might be useful in preventing and/or reducing the severity of ROP in preterm infants.

Oxygen free radicals have also been theorized to overwhelm antioxidant enzymes and other protective mechanisms in the neonate, resulting in damage to stem cells and thus interrupting the process of normal vessel migration and vasculogenesis [37].

25.5 Classification Scheme

Clinically, ROP can be divided into two distinct phases. In the acute phase, normal vascular development is interrupted by the proliferation of abnormal vessels and fibrous tissue. In the chronic or late proliferation phase of ROP, retinal detachment, macular ectopia, and severe visual loss may occur.

Retinopathy of prematurity is generally classified according to the International Classification of ROP (ICROP) [1, 2, 7]. This classification system uses retinal landmarks to minimize interexaminer variability. ROP is classified based on the zone, stage, and extent of disease, followed by documentation of the status of the vessels in the posterior pole (plus disease).

Zone refers to the location of disease. Three zones are centered on the optic disc. (Fig. 25.1) The radius of zone I is twice the disk-to-fovea distance in all directions from the optic disk, roughly an angle of 30°. This distance is about the same as the viewing field of a 30 diopter lens. Zone II extends from the edge of zone I peripherally to the nasal ora serrata and continues temporally along the same radius of curvature. Zone III is the residual temporal crescent anterior and lateral to zone II.

Stage indicates the severity of abnormal vascular changes at the junction of the vascular and avascular retina. The vascularized retina of premature infants without ROP blends almost imperceptibly into the anterior, non-vascularized retina. The junction between the vascularized and avascularized retina becomes more pronounced with the onset of clinically apparent ROP. In stage 1 ROP, the junction is seen as a distinct white line but still lies within the plane of the retina. In stage 2 there is elevation of a white ridge that extends above the plane of the retina. Stage 3 ROP is distinguished by extraretinal neovascularization, with fibrovascular tissue extending pos-

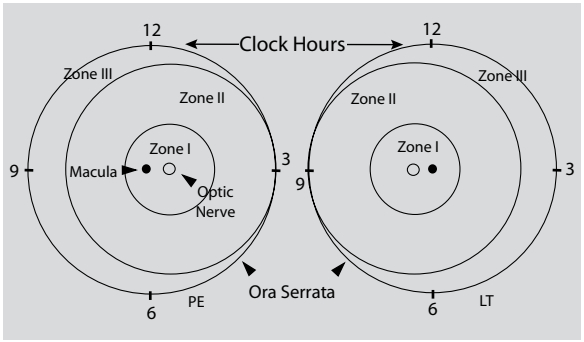

Fig. 25.1 The location of ROP is designated by zone of involvement in three zones concentric with the optic disc [7]. Source: (2005) The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol 123:991–999

teriorly from the ridge into the vitreous. Isolated tufts of "popcorn" neovascular tissue may lie posterior to the ridge, and do not constitute stage 3 ROP. Cicatricial changes in this fibrovascular tissue may result in subtotal tractional retinal detachment that spares (stage 4a ROP) or includes (stage 4b ROP) the fovea. Total retinal detachment is termed stage 5 ROP. Staging for the entire eye is determined by the most severe manifestation observed.

The extent of disease is recorded in sectors, or clock hours each subtending an angle of 30° degrees (60° arc total). Severity of the disease process is considered worse as the number of clock hours involved increases.

Plus disease refers to venous dilation and arterial tortuosity of the vasculature in the posterior pole. A standardized photograph (Fig. 25.2) is currently used to qualitatively define the minimum amount of vascular dilation and tortuosity required to make a diagnosis of plus disease. Qualifying changes must be present in at least two quadrants. Pre-plus disease refers to arterial tortuosity and venous engorgement that is outside normal limits but insufficient to qualify for plus disease. Progressive vascular disease may also manifest as iris vessel engorgement resulting in pupil rigidity.

Threshold ROP, as defined by the CRYO-ROP study [54], is defined as ROP characterized by five or more contiguous or eight cumulative clock hours of extraretinal neovascularization with plus disease involving zone I or II. Prethreshold disease was the term used by early researchers and clinicians to describe a constellation of findings associated with an increased risk of progression to threshold disease. The terms threshold and prethreshold ROP, as used in this context, are used less commonly today as newer terminology (see below) has come into favor and supplanted these older terms in many practices.

Eyes treated at threshold are more likely to have an unfavorable outcome than those with milder disease. Based on the findings of the ETROP study [36], eyes are now considered for treatment when type I (high-risk prethreshold) ROP is present. In this report, type I ROP is defined as one of the following: (1) zone I ROP, any stage with plus disease; (2) zone I ROP, stage 3, without plus disease; or (3) zone II, stage 2 or 3 with plus disease.

Eyes with type II ROP (low-risk prethreshold) are defined as one of the following: (1) zone I, stage 1 or 2 without plus disease; or (2) zone II, stage 3 without plus disease [30]. Eyes with type II ROP (low-risk prethreshold) are still at risk for further progression. Such patients therefore warrant close observation and are typically examined at least weekly until the disease is observed to be stable or regresses. However, more frequent examinations may be prudent in some cases.

Aggressive posterior ROP (AP-ROP) is an uncommon, rapidly progressing, and severe form of ROP formerly called "Rush disease." Posterior location, plus disease, and ill-defined neovascularization are the hallmarks of AP-ROP. Early in the development of AP-ROP, the posterior pole vessels usually exhibit dilation and tortuosity in all four quadrants. ROP may initially manifest as only a flat network of neovascularization at the junction of the vascularized and avascularized retina. It may extend circumferentially and is often accompanied by a circumferential vessel (Fig. 25.3). AP-ROP may rapidly progress to stage 5 disease without intervention.

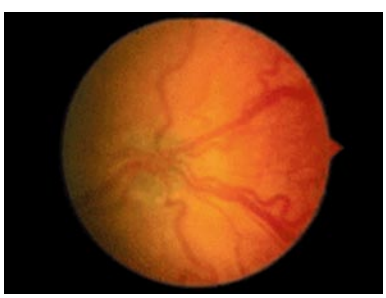

Fig. 25.2 Standard photo of minimal posterior pole vessel abnormality required for plus disease [7]. Source: (2005) The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol 123:991–999

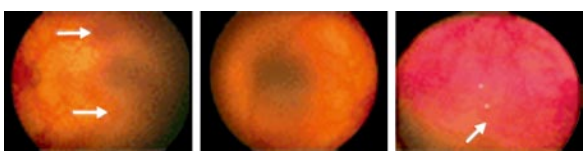

Fig. 25.3 Aggressive posterior ROP [7]. Source: (2005) The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol 123:991–999

25.6 Course of Acute Phase

In 1991, the CRYO-ROP study systematically documented ROP progression using the ICROP system [54]. The timing of retinal disease is more closely linked to postmenstrual age than postnatal age. The median postmenstrual ages of onset for stage 1, 2, and 3 disease were 34.3, 35.4, and 36.6 weeks, respectively. Plus disease manifested at a median age of 36.3 weeks. The earliest appearance of prethreshold disease was at approximately 26 weeks, of confirmed plus disease at 31 weeks, and of threshold at 31 weeks. Ninety-five percent of all infants who reached threshold did so by 42 weeks postconceptional age. The overall incidence and severity of ROP in infants was highest in the most premature infants with the lowest birth weights.

Repka and coworkers [59] noted that acute phase ROP typically began to involute at a mean age of 38.6 weeks postmenstrual age and that 90% of eyes demonstrated onset of involution prior to 44 weeks postmenstrual age. Flynn and coworkers [26] reported that ROP will last an average of 15 weeks from inception to resolution in eyes that regress.

Whereas involution generally occurs safely in most treated and untreated eyes, it can be marked by the development of detrimental vitreoretinal abnormalities that result in permanent retinal damage, including retinal detachment and blindness in some eyes. Remnant myofibroblasts in the vitreous may contract for up to 4 months following intervention [46], increasing the risk of tractional retinal detachment [40]. Extensive vitreous organization and vitreous hemorrhage were predictive for development of a retinal detachment in eyes treated at threshold in one retrospective study [18]. Full involution does not typically occur in most eyes until two or more weeks after laser intervention [18].

25.7 Setting Up an Organized Screening Program

An effective screening program identifies the small number of preterm infants who require treatment for ROP within a much larger population of at-risk infants [8, 9] while conserving resources and minimizing the number of stressful (and even potentially harmful) examinations required to diagnose ROP requiring treatment. The following screening and treatment guidelines for American hospitals were recently proposed [8]. The sensitivity of these guidelines in detecting ROP before the disease becomes severe enough to result in retinal detachment is predicted to be 99% in American institutions.

25.7.1 Infants Requiring Examination

Infants with a birth weight of less than 1,500 g or estimated gestational age (EGA) of 30 weeks or less and selected infants with a birth weight between 1,500 and 2,000 g or EGA of more than 30 weeks with an unstable clinical course who are believed to be at high risk by their neonatologist, should have dilated retinal examination performed to detect ROP. A single examination is sufficient if it unequivocally shows the retina to be fully vascularized in both eyes.

25.7.2 Timing of Examinations

Because the onset of serious ROP correlates better with postmenstrual age than with postnatal age (that is, the youngest infants at birth take the longest time to develop serious ROP), the timing of the first examination should be based on the gestational age at birth. Table 25.1 reviews the suggested timing of initial examinations. It should be noted that limited data are available to support these timing guidelines on the most premature babies, such as those born at 23–24 weeks EGA. Follow-up examinations should be conducted based on examination findings and risks as assessed by the examining ophthalmologist. Table 25.2 reviewed the proposed follow-up recommendations.

25.7.3 Retinopathy of Prematurity Requiring Treatment

Treatment should be considered for eyes with type I ROP, if the examining ophthalmologist believes

Table 25.1 Suggested timing of first eye examination based on gestational age at birth [8]

Gestational age at birth (weeks)	Age at examination (weeks)	
	Postmenstrual	Chronological
22[a]	31	9
23[a]	31	8
24	31	7
25	31	6
26	31	5
27	31	4
28	32	4
29	33	4
30	34	4

[a] This guideline should be considered tentative rather than evidence based for infants with a gestational age of 22–23 weeks because of the small number of survivors in these gestational age categories

treatment is warranted. The decision to withhold treatment despite the presence of type I ROP is based on clinical judgment after assessing a number of issues including severity of disease, postmenstrual age, progression of the disease, and other factors. Additionally, treatment may be indicated in situations not included in the standard recommendations, and such treatment must be considered on a case-by-case basis. Experience of the examiner in the management of ROP plays an important role in making these treatment decisions.

25.7.4 Cessation of Examinations

The conclusion of ROP examinations should be based on postmenstrual age and retinal ophthalmoscopic findings. Findings that suggest that examinations can be curtailed include the following: (1) retinal vascularization into zone III without previous zone I or II ROP, in infants with a postmenstrual age of less than 35 weeks, confirmatory examinations are usually warranted since vascularization into zone III is less common in infants prior to 36 weeks postmenstrual age; (2) full retinal vascularization; (3) postmenstrual age of 45 weeks and no prethreshold disease or worse ROP is present; (4) regression of ROP, and absence of abnormal vascular tissue that is capable of reactivation and progression.

25.7.5 Responsibility

Responsibility for examination and follow-up of infants at risk for ROP should be defined by the neonatal care unit. Appropriate follow-up care must be available if hospital discharge or transfer is considered while the infant is still at risk for serious ROP. A computer database, dedicated ROP coordinator, and committed staff can be invaluable aids. The transferring primary care physician, after communication with the examining ophthalmologist, generally has responsibility for communicating eye care needs to the infant's next physician. If this responsibility is

Table 25.2 Recommended follow-up schedule for infants with or at risk for ROP [8, 9]

ROP severity	Recommended follow-up
Stage 1 or 2 ROP: zone I Stage 3 ROP: zone II	1-week or less follow-up
Immature vascularization: zone I–no ROP Stage 2 ROP: zone II Regressing ROP: zone I	1- to 2-week follow-up
Stage 1 ROP: zone II Regressing ROP: zone II	2-week follow-up
Immature vascularization: zone II–no ROP Stage 1 or 2 ROP: zone III Regressing ROP: zone III	2- to 3-week follow-up
Plus disease zone I or II	The presence of plus disease in zones I or II suggests that peripheral ablation, rather than observation, is appropriate

delegated to the parents of a discharged infant, parents should be aware of the fact that there is a critical time window for evaluation and treatment should the disease progress.

25.8 Documentation and Communication

Neonatologists and pediatricians caring for a premature infant should be aware of the child's risk for ROP and should be kept informed by the examining ophthalmologist through appropriate documentation in the medical record. Optimally, parents of an affected infant should be kept informed about the status of their child's ROP and should have some understanding of the condition and how their infant may be affected. Mechanisms that may be helpful in facilitating communicating with parents include prepared written information about ROP, examination reports, formal parent lectures, bedside communication, telephone updates, etc. Documentation of such conversations and communication with parents is desirable, when possible, to minimize miscommunication and medicolegal disputes.

25.9 Treatment of Acute Phase Disease

Though most infants who develop ROP undergo spontaneous regression, intervention may be necessary to prevent progression to retinal detachment in more advanced cases. Treatment is typically considered for eyes with type I ROP (see above). The number of clock hours of stage 3 disease no longer is formally taken into consideration to identify eyes for which treatment is considered. Treatment should generally be accomplished within 72 h of determination that treatable disease is present. More urgent treatment may be warranted in selected situations, such as the presence of aggressive posterior ROP.

Transpupillary laser photocoagulation delivered through an indirect ophthalmoscope has essentially replaced cryotherapy as the preferred treatment for acute ROP, though this modality is imperfect and has known serious complications. A diode or argon laser may be used to treat the entire peripheral avascular zone, usually with the aid of scleral depression, though argon laser may be associated with an increased incidence of cataracts [51, 57]. The practitioner may choose to place laser spots approximately 1–1.5 lesion-widths apart or apply laser in a near-continuous pattern (Fig. 25.4) [56]. Photocoagulation destroys the peripheral avascular retina responsible for increased cytokine production, thereby reducing the stimulus for neovascularization and the subsequent risk of retinal damage and detachment.

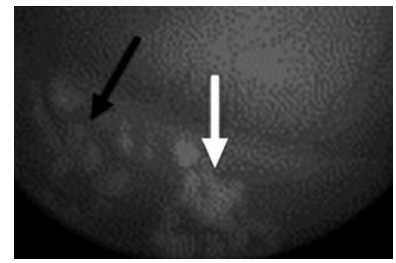

Fig. 25.4 Use of individual laser spots (*left*) versus a near-continuous laser application (*right*) [56]. Source: Paysse EA, Hussein MA, Miller AM, et al. (2007) Pulsed mode versus near-continuous mode delivery of diode laser photocoagulation for high-risk retinopathy of prematurity. J AAPOS 11:388–392

Treatment can be accomplished in the intensive care unit or operating room and under sedation, retrobulbar anesthesia, or general anesthesia [8], depending on the preferences of the neonatologist and treating ophthalmologist and the medical condition of the baby. Major potential complications of laser treatment include diminished peripheral vision, cataract formation, intraocular bleeding, myopia, and retinal detachment.

25.10 Involution and Monitoring of Infants After Treatment

There is at present no reliable means for an ophthalmologist to predict which eyes will develop a poor outcome despite timely treatment. ROP in the poste-

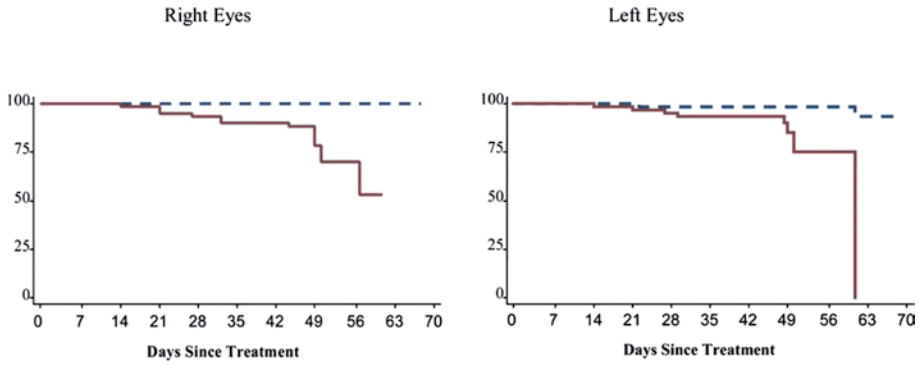

Fig. 25.5 Kaplan-Meir analysis of rate of full involution of ROP after treatment of threshold ROP in 138 patients [18]. Source: Coats D K, Miller AM, Hussein MA, et al. (2005) Involution of retinopathy of prematurity after laser treatment: factors associated with development of retinal detachment. Am J Ophthalmol 140:214–222

rior retina has the worst prognosis and such eyes often respond less favorably to laser intervention [3, 53]. "Skip lesions" (areas of the retina which have received insufficient or ineffective treatment) may be considered for supplemental laser if residual disease activity is noted in the days and weeks after treatment.

No official recommendations exist to guide the postoperative management of eyes that have been treated for ROP. Practitioners must depend almost exclusively on training and experience to guide postoperative care. In a study on ROP involution after treatment of threshold disease, complete involution occurred in the majority of eyes within 3 weeks of laser treatment and all eyes had fully involuted or developed a retinal detachment by 9±3 weeks after treatment (Fig. 25.5) [17]. Traction retinal detachments typically did not develop until several weeks after treatment, suggesting the need for close and frequent follow-up after treatment. Eyes most likely to develop a retinal detachment in this study included eyes with zone I disease, marked vitreous organization, and marked vitreous hemorrhage [17, 18].

25.11 Treatment of Chronic or Late-stage Disease

Few controlled scientific data exist to guide the management of late-stage disease, so physicians rely in large part on experience and clinical judgment to gauge the need for surgical intervention in patients who develop or who are considered at high risk for development of a traction retinal detachment. The management of stage 4a disease (extramacular, partial retinal detachment) remains controversial and there is no consensus as to the best treatment approach. Some surgeons may be reluctant to intervene when a stage 4a retinal detachment is present for several reasons, including fear of causing harm, lack of evidence-based medicine to clearly support intervention at this stage, and fear of medicolegal consequences. Recognizing the universally poor outcomes associated with more advanced detachments [27], most vitreoretinal surgeons experienced in the management of ROP-related retinal detachments do advocate treatment of stage 4a disease in selected eyes.

Anatomic and visual outcomes for treatment of stage 4a retinal detachments have generally been favorable in recent limited case series. Surgery at this stage is believed to reduce the risk of progression to more severe detachment profiles [13]. Lens-sparing vitrectomy with or without concurrent scleral buckling has been associated with non-progression of detachments beyond stage 4a in up to 90% of eyes [13]. Visual outcomes after vitreoretinal surgery for stage 4a ROP were excellent in one study which reported a mean visual acuity of 20/58 (range 20/200 to 20/20) [58]. Recently, early vitrectomy was reported as an effective means for preventing retinal detachment in aggressive posterior ROP [55].

25.12 Prognosis and Comorbidities

Treatment of type I ROP does not assure a favorable outcome. The ETROP study reported an unfavorable structural outcome in 9.0% of eyes treated at high-risk prethreshold compared with 15.6% of conventionally managed eyes [30]. The rate of unfavorable visual outcome (grating acuity <1.85 cycles per degree, low vision, or blindness) in eyes treated at prethreshold in the ETROP study was 19.8% [30]. The fact that the visual outcome is less favorable than the structural outcome underscores that factors other than traction retinal detachment can lead to poor vision in premature infants, including optic atrophy, cortical (cerebral) visual impairment, and subclinical retinal abnormalities.

While most ROP regresses spontaneously by a process of involution or evolution from a vasoproliferative phase to a fibrotic phase [7], infants with ROP are at increased risk of other vision-threatening sequelae, even if they did not require treatment for high-risk ROP. These comorbidities include, but are not limited to, high myopia, strabismus, amblyopia, and reduced contrast sensitivity [6, 70]. Potential abnormalities associated with more severe ROP include macular dragging, cataract, glaucoma, retinal detachment, and blindness.

25.13 Future Screening and Treatment Options

The advent of sophisticated imaging technology has allowed telemedicine to play an increasingly important role in the screening and management of ROP. This has been necessitated in part by a lack of willingness of ophthalmologists to remain or become involved in the care of premature infants. Semiautomated analysis of retinal vasculature using specially designed computer software to detect vessel diameter and tortuosity [16, 22, 34, 76] has performed well in pilot studies and has shown promise as a potential means of increasing precision and reducing interexaminer variability in the assessment of plus disease. Telemedicine has the potential to impact the delivery, quality, and accessibility of ophthalmic care for infants with ROP, while minimizing strain on the limited number of physicians involved in the care of ROP. Before image-based screening can be implemented on a large scale, clinical standards, diagnostic accuracy, sensitivity/specificity profiles, and reliability must be established.

Follow-up procedures must be in place to ensure that infants with ROP are seen at the indicated intervals, as failure to follow-up may result in blindness. A dedicated ROP coordinator can be very helpful in this regard.

Antioxidant therapy with vitamins E [24, 33, 35], A [52], and D-penicillamine [20] has been explored as a means of reducing oxygen free radical damage to prevent or treat ROP and remains controversial. Though each has shown some potential, concerns over side-effect profiles and efficacy have limited their use. Control of exogenous oxygen administration to maintain oxygen saturation at a level between 88% and 93%, may help avoid hypoxemia and minimize the risk of additional lung injury caused by exposure to excessive oxygen concentrations [5, 10, 11]. The finding of reduced levels of severe ROP in these studies has led many to recommend judicious oxygen use as a means to mitigate development of severe ROP [11, 32, 45].

In 2004, it was found that localized inhibition of VEGF could block pathologic retinal neovascularization without affecting preexisting retinal vessels in mouse models of ROP [62], which has fueled translational research in humans. The upcoming prospective, multicenter BLOCK-ROP trial will explore the utility of the anti-VEGF drug bevacizumab (Avastin) as local therapy for severe ROP not responsive to laser ablation.

25.14 Medicolegal Considerations

Medicolegal risk to those who examine and treat ROP is high [19]. It remains a fact that despite significant advances in both the diagnosis and management of severe ROP, infants can and still do suffer severe visual complications and even blindness as a result of the disease. This can occur despite the best of screening programs, the most experienced examiner, optimal timing of diagnosis and treatment, and the most skilled surgeon. According to the ETROP study, an unfavorable structural outcome can be ex-

Take Home Pearls

- Updated classification for acute phase disease has defined and characterized the importance of aggressive posterior and pre-plus disease.
- A dedicated coordinator can be an invaluable aid in establishing a safe and effective ROP screening and follow-up program.
- Documentation and communication with the family and within the healthcare team are important components in the process of ROP care.
- Intervention for type I ROP is associated with an incremental improvement in prognosis compared with treatment at threshold.
- Advances in the treatment of late-stage disease can be associated with good structural and functional outcome.
- Comorbidities such as visual cortical impairment and other disabilities can worsen visual prognosis.

pected to occur in approximately 10% of eyes treated at prethreshold [30].

Parents of premature infants are often unrealistic both in their understanding of their child's medical condition and their expectations regarding outcomes. Parental understanding of ROP can be similarly unrealistic. Despite frequent communication with parents about the seriousness of the disease and the risks that their infant may face, parents are sometimes surprised that their child had an unfavorable outcome. Surprise over an unfavorable outcome, other medical comorbidities, family dynamics, and the financial stress of caring for a disabled child can be overwhelming. The sympathy elicited by a blind, disabled child is often enough to interest a plaintiff attorney in the pursuit of medicolegal action, even in a properly managed case. Misguided and even frankly unethical ophthalmologists are sometimes willing to support claims of medical malpractice in these situations, an unfortunate reality that has contributed to a gradual attrition of practitioners willing to remain or become involved in the care of premature infants.

While the management of ROP cannot be distilled into a "cookbook," medicolegal risks can be mitigated through training, experience, general adherence to formal ROP screening and treatment guidelines (with documented justification for deviations), and communication with the families of at-risk infants.

References

1. (1984) An international classification of retinopathy of prematurity. II. The classification of retinal detachment. The Committee for the Classification of Retinopathy of Prematurity. Arch Ophthalmol 102:1130–1134
2. (1987) An international classification of retinopathy of prematurity. II. The classification of retinal detachment. The International Committee for the Classification of the Late Stages of Retinopathy of Prematurity. Arch Ophthalmol 105:906–912
3. (1990) Multicenter trial of cryotherapy for retinopathy of prematurity. One-year outcome: structure and function. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Arch Ophthalmol 108:1408–1416
4. (1999) The design of the multicenter study of light reduction in retinopathy of prematurity (LIGHT-ROP). J Pediatr Ophthalmol Strabismus 36:257–263
5. (2000) Supplemental Therapeutic Oxygen for Prethreshold Retinopathy Of Prematurity (STOP-ROP), a randomized, controlled trial. I. Primary outcomes. Pediatrics 105:295–310
6. Cryotherapy for Retinopathy of Prematurity Cooperative Group (2001) Contrast sensitivity at age 10 years in children who had threshold retinopathy of prematurity. Arch Ophthalmol 119:1129–1133
7. International Committee for the Classification of Retinopathy of Prematurity (2005) The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol 123:991–999
8. Section on Ophthalmology American Academy of Pediatrics; American Academy of Ophthalmology; American Association for Pediatric Ophthalmology and Strabismus (2006) Screening examination of premature infants for retinopathy of prematurity. Pediatrics 117:572–576

9. (2006) Erratum. Pediatrics. 118:1324
10. Abman S (2002) Monitoring cardiovascular function in infants with chronic lung disease of prematurity. Arch Dis Child Fetal Neonatal Ed 87:F15
11. Askie LM, Henderson-Smart DJ, Irwig L, et al. (2003) Oxygen-saturation targets and outcomes in extremely preterm infants. N Engl J Med 349:959–967
12. Avery ME (1960) Recent increase in mortality from hyaline membrane disease. J Pediatr 57:553–559
13. Capone A Jr, Trese MT (2001) Lens-sparing vitreous surgery for tractional stage 4A retinopathy of prematurity retinal detachments. Ophthalmology 108:2068–2070
14. Chan-Ling T, Tout S, Hollander H, et al. (1992) Vascular changes and their mechanisms in the feline model of retinopathy of prematurity. Invest Ophthalmol Vis Sci 33:2128–2147
15. Chen J, Smith LE (2007) Retinopathy of prematurity. Angiogenesis 10:133–140
16. Chiang MF, Jiang L, Gelman R, et al. (2007) Interexpert agreement of plus disease diagnosis in retinopathy of prematurity. Arch Ophthalmol 125:875–880
17. Coats DK (2005) Retinopathy of prematurity: involution, factors predisposing to retinal detachment, and expected utility of preemptive surgical reintervention. Trans Am Ophthalmol Soc 103:281–312
18. Coats DK, Miller AM, Hussein MA, et al. (2005) Involution of retinopathy of prematurity after laser treatment: factors associated with development of retinal detachment. Am J Ophthalmol 140:214–222
19. Demorest BH (1996) Retinopathy of prematurity requires diligent follow-up care. Surv Ophthalmol 41:175–178
20. DiBiasie A (2006) Evidence-based review of retinopathy of prematurity prevention in VLBW and ELBW infants. Neonatal Netw 25:393–403
21. Dollery CT, Bulpitt CJ, Kohner EM (1969) Oxygen supply to the retina from the retinal and choroidal circulations at normal and increased arterial oxygen tensions. Invest Ophthalmol 8:588–594
22. Ells AL, Holmes JM, Astle WF, et al. (2003) Telemedicine approach to screening for severe retinopathy of prematurity: a pilot study. Ophthalmology 110:2113–2117
23. Englert JA, Saunders RA, Purohit D, et al. (2001) The effect of anemia on retinopathy of prematurity in extremely low birth weight infants. J Perinatol 21:21–26
24. Finer NN, Schindler RF, Grant G, et al. (1982) Effect of intramuscular vitamin E on frequency and severity of retrolental fibroplasia. A controlled trial. Lancet 1:1087–1091
25. Flynn JT, Bancalari E (2000) On "supplemental therapeutic oxygen for prethreshold retinopathy of prematurity (STOP-ROP), a randomized, controlled trial. I. Primary outcomes." J AAPOS 4:65–66
26. Flynn JT, Bancalari E, Bachynski BN, et al. (1987) Retinopathy of prematurity. Diagnosis, severity, and natural history. Ophthalmology 94:620–629
27. Fuchino Y, Hayashi H, Kono T, et al. (1995) Long-term follow up of visual acuity in eyes with stage 5 retinopathy of prematurity after closed vitrectomy. Am J Ophthalmol 120:308–316
28. Gaynon MW (2006) Rethinking STOP-ROP: is it worthwhile trying to modulate excessive VEGF levels in prethreshold ROP eyes by systemic intervention? A review of the role of oxygen, light adaptation state, and anemia in prethreshold ROP. Retina 26:S18–S23
29. Gilbert C, Rahi J, Eckstein M, et al. (1997) Retinopathy of prematurity in middle-income countries. Lancet 350:12–14
30. Good WV (2004) Final results of the Early Treatment for Retinopathy of Prematurity (ETROP) randomized trial. Trans Am Ophthalmol Soc 102:233–248; discussion 248–250
31. Gunn TR, Aranda JV, Little J (1978) Incidence of retrolental fibroplasia. Lancet 1:216–217
32. Hay WW Jr, Bell EF (2000) Oxygen therapy, oxygen toxicity, and the STOP-ROP trial. Pediatrics 105:424–425
33. Hittner HM, Godio LB, Rudolph AJ, et al. (1981) Retrolental fibroplasia: efficacy of vitamin E in a double-blind clinical study of preterm infants. N Engl J Med 305:1365–1371
34. Johnson KS, Mills MD, Karp KA, et al. (2007) Semiautomated analysis of retinal vessel diameter in retinopathy of prematurity patients with and without plus disease. Am J Ophthalmol 143:723–725
35. Johnson L, Schaffer D, Boggs TR Jr (1974) The premature infant, vitamin E deficiency and retrolental fibroplasia. Am J Clin Nutr 27:1158–1173
36. Jones JG, MacKinnon B, Good WV, et al. (2005) The early treatment for ROP (ETROP) randomized trial: study results and nursing care adaptations. Insight 30:7–13
37. Katz ML, Robison WG Jr (1988) Autoxidative damage to the retina: potential role in retinopathy of prematurity. Birth Defects Orig Artic Ser 24:237–248
38. Kim TI, Sohn J, Pi SY, et al. (2004) Postnatal risk factors of retinopathy of prematurity. Paediatr Perinat Epidemiol 18:130–134
39. Kivlin JD, Biglan AW, Gordon RA, et al. (1996) Early retinal vessel development and iris vessel dilatation as factors in retinopathy of prematurity. Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) Cooperative Group. Arch Ophthalmol 114:150–154
40. Kretzer FL, Mintz-Hittner HA (1989) In: Miquel J, Quintanilha AT, Weber H (eds) Handbook of free radicals and antioxidants in biomedicine, vol 2. CRC Press, Boca Raton, pp 315–322
41. Lala-Gitteau E, Majzoub S, Saliba E, et al. (2007) [Epidemiology for retinopathy of prematurity: risk factors in the Tours hospital (France).] J Fr Ophtalmol 30:366–373
42. Liu PM, Fang PC, Huang CB, et al. (2005) Risk factors of retinopathy of prematurity in premature infants weighing less than 1600 g. Am J Perinatol 22:115–120
43. Manzoni P, Maestri A, Leonessa M, et al. (2006) Fungal and bacterial sepsis and threshold ROP in preterm very low birth weight neonates. J Perinatol 26:23–30
44. McCormick AQ (1977) Retinopathy of prematurity. Curr Probl Pediatr 7:1–28
45. Mills MD (2000) STOP-ROP results suggest selective use of supplemental oxygen for prethreshold ROP. Arch Ophthalmol 118:1121–1122
46. Mintz-Hittner HA, Kretzer FL (1990) The rationale for cryotherapy with a prophylactic scleral buckle for zone I threshold retinopathy of prematurity. Doc Ophthalmol 74:263–268

47. Mittal M, Dhanireddy R, Higgins RD (1998) Candida sepsis and association with retinopathy of prematurity. Pediatrics 101:654–657
48. Modanlou HD, Gharraee Z, Hasan J, et al. (2006) Ontogeny of VEGF, IGF-I, and GH in neonatal rat serum, vitreous fluid, and retina from birth to weaning. Invest Ophthalmol Vis Sci 47:738–744
49. Msall ME, Phelps DL, Hardy RJ, et al. (2004) Educational and social competencies at 8 years in children with threshold retinopathy of prematurity in the CRYO-ROP multicenter study. Pediatrics 113:790–799
50. Noyola DE, Bohra L, Paysse EA, et al. (2002) Association of candidemia and retinopathy of prematurity in very low birth weight infants. Ophthalmology 109:80–84
51. O'Neil JW, Hutchinson AK, Saunders RA, et al. (1998) Acquired cataracts after argon laser photocoagulation for retinopathy of prematurity. J AAPOS 2:48–51
52. Ozkan H, Duman N, Kumral A, et al. (2006) Inhibition of vascular endothelial growth factor-induced retinal neovascularization by retinoic acid in experimental retinopathy of prematurity. Physiol Res 55:267–275
53. Palmer EA (1990) Results of U.S. randomized clinical trial of cryotherapy for ROP (CRYO-ROP). Doc Ophthalmol 74:245–251
54. Palmer EA, Flynn JT, Hardy RJ, et al. (1991) Incidence and early course of retinopathy of prematurity. The Cryotherapy for Retinopathy of Prematurity Cooperative Group. Ophthalmology 98:1628–1640
55. Paysse EA, Coats DK, Hussein MA, et al. (2006) Long-term outcomes of photorefractive keratectomy for anisometropic amblyopia in children. Ophthalmology 113:169–176
56. Paysse EA, Hussein MA, Miller AM, et al. (2007) Pulsed mode versus near-continuous mode delivery of diode laser photocoagulation for high-risk retinopathy of prematurity. J AAPOS 11:388–392
57. Paysse EA, Miller A, Brady McCreery KM, et al. (2002) Acquired cataracts after diode laser photocoagulation for threshold retinopathy of prematurity. Ophthalmology 109:1662–1665
58. Prenner JL, Capone A Jr, Trese MT (2004) Visual outcomes after lens-sparing vitrectomy for stage 4A retinopathy of prematurity. Ophthalmology 111:2271–2273
59. Repka MX, Palmer EA, Tung B (2000) Involution of retinopathy of prematurity. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Arch Ophthalmol 118:645–649
60. Reynolds JD, Dobson V, Quinn GE, et al. (2002) Evidence-based screening criteria for retinopathy of prematurity: natural history data from the CRYO-ROP and LIGHT-ROP studies. Arch Ophthalmol 120:1470–1476
61. Reynolds JD, Hardy RJ, Kennedy KA, et al. (1998) Lack of efficacy of light reduction in preventing retinopathy of prematurity. Light Reduction in Retinopathy of Prematurity (LIGHT-ROP) Cooperative Group. N Engl J Med 338:1572–1576
62. Rota R, Riccioni T, Zaccarini M, et al. (2004) Marked inhibition of retinal neovascularization in rats following soluble-flt-1 gene transfer. J Gene Med 6:992–1002
63. Rudanko SL, Fellman V, Laatikainen L (2003) Visual impairment in children born prematurely from 1972 through 1989. Ophthalmology 110:1639–1645
64. Shah VA, Yeo CL, Ling YL, et al. (2005) Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. Ann Acad Med Singapore 34:169–178
65. Silverman WA (1980) In: Retrolental Fibroplasia: A Modern Parable. Grune & Stratton, New York
66. Steinkuller PG, Du L, Gilbert C, et al. (1999) Childhood blindness. J AAPOS 3:26–32
67. Tasman W (2001) Ten-year follow-up from the CRYO-ROP study. Arch Ophthalmol 119:1200–1201
68. Terry TL (1942) Fibroblastic overgrowth of persistent tunica vasculosa lentis in infants born prematurely. II. Report of cases: clinical aspects. Trans Am Ophthalmol Soc 40:262–284
69. Valcamonico A, Accorsi P, Sanzeni C, et al. (2007) Mid- and long-term outcome of extremely low birth weight (ELBW) infants: an analysis of prognostic factors. J Matern Fetal Neonatal Med 20:465–471
70. VanderVeen DK, Coats DK, Dobson V, et al. (2006) Prevalence and course of strabismus in the first year of life for infants with prethreshold retinopathy of prematurity: findings from the Early Treatment for Retinopathy of Prematurity study. Arch Ophthalmol 124:766–773
71. Villegas-Becerril E, Gonzalez-Fernandez R, Perula-Torres L, et al. (2006) [IGF-I, VEGF and bFGF as predictive factors for the onset of retinopathy of prematurity (ROP)]. Arch Soc Esp Oftalmol 81:641–646
72. Villegas Becerril E, Fernandez Molina F, Gonzalez R, et al. (2005) [Serum IGF-I levels in retinopathy of prematurity. New indications for ROP screening]. Arch Soc Esp Oftalmol 80:233–238
73. Villegas Becerril E, Gonzalez Fernandez R, Fernandez Molina F, et al. (2005) Growth factor levels and ROP. Ophthalmology 112:2238
74. Wallace DK, Veness-Meehan KA, Miller WC (2007) Incidence of severe retinopathy of prematurity before and after a modest reduction in target oxygen saturation levels. J AAPOS 11:170–174
75. Wright KW, Sami D, Thompson L, et al. (2006) A physiologic reduced oxygen protocol decreases the incidence of threshold retinopathy of prematurity. Trans Am Ophthalmol Soc 104:78–84
76. Wu C, Petersen RA, VanderVeen DK (2006) RetCam imaging for retinopathy of prematurity screening. J AAPOS 10:107–111

Pediatric Retinal Disorders

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Contents

Core Messages

Albinism

- The various subtypes of oculocutaneous albinism are typically inherited in an autosomal recessive fashion, whereas ocular albinism is inherited in an X-linked pattern.
- Decreased visual acuity occurs as a consequence of foveal hypoplasia.
- Misrouting of optic nerve fibers is common with temporal retina fibers inappropriately routed contralaterally instead of ipsilaterally, resulting in impaired stereopsis and strabismus.

Congenital X-linked Retinoschisis

- Congenital X-linked retinoschisis (CXLRS) is the most common cause of juvenile macular degeneration in males.

[1] The authors have no proprietary interests in any product mentioned herein.

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- Retinal splitting occurs in all layers of the retina.
- Foveal schisis is seen in all forms of CXLRS, while lamellar and peripheral bullous schisis are variably present.
- A selectively reduced b-wave electroretinogram (ERG) is characteristic of CXLRS, and is useful in differentiating CXLRS from other disease entities.
- Apart from foveal schisis, vision may also be compromised by amblyopia due to vitreous hemorrhage, a schisis bulla which interrupts the visual axis or extends through the macula, or a combined schisis-rhegmatogenous retinal detachment (RRD).

Heredodegenerative Retinal Degeneration

- Retinitis pigmentosa (RP) is a heterogeneous group of inherited diseases that typically results in bilateral, symmetric, progressive degeneration of photoreceptor and retinal pigment epithelial (RPE) cells.
- Pigmentary changes in the retinal mid-periphery, waxy pallor of the optic nerve, retinal arteriolar attenuation, visual field abnormalities, and a flat scotopic ERG are the characteristic features.
- Syndromic causes of RP should be excluded by careful family history, medical history, and physical examination.

Best's disease

- Best's disease is characterized by an abnormal electrooculogram.
- The clinical appearance of Best's disease is highly variable even within the same family.

Stargardt's Disease/Fundus Flavimaculatus

- Stargardt's disease/fundus flavimaculatus (STGD1/FF) is the most common recessively inherited macular degeneration.
- It is characterized histopathologically by the accumulation of lipofuscin pigment in the RPE cells.
- The phenomenon of lack of choroidal fluorescence ("dark choroid") during the fluorescein angiogram is present in at least 50% of STGD1/FF patients.

Familial Exudative Vitreoretinopathy

- Familial exudative vitreoretinopathy (FEVR) is a hereditary retinal vascular disorder characterized by an avascular peripheral retina, exudation, and traction retinal detachment.
- Eighty-five percent of eyes are bilaterally involved, and asymmetric bilaterality is common.
- Infants presenting in the first year of life usually have a worse prognosis.

Persistent Fetal Vasculature Syndrome

- The term refers to a spectrum of structural changes in which the hyaloid vessels and tunica vascular lentis persist in an eye following birth, resulting in lens and/or posterior pole abnormalities.

- Persistent fetal vasculature syndrome (PFVS) is unilateral 90% of the time, and the eye may range from small to normal in size.

Coats' Disease

- Typically a unilateral retinal vascular disorder occurring predominantly in young males in the first decade of life.
- Infants presenting in the first year of life usually have a worse prognosis.

Norrie's Disease

- Patients often present as infants with bilateral profound visual impairment, retinal dysplasia, and leukocoria.
- Sensorineural hearing loss and mental impairment occur in approximately 30% of patients.

Incontinentia Pigmenti

- Inherited as an X-linked dominant trait typically seen in only females, as it is usually lethal in males.
- Ocular findings consist of peripheral retinal non-perfusion and vitreoretinal neovascularization.
- Cutaneous involvement is characteristic with skin vesicles beginning at birth and hyper- and hypopigmented papular lesions on the trunk and extremities.
- Skin, dental, central nervous system, and skeletal involvement are associated features.

Pediatric Choroidal Neovascularization

- Typically occurs as a complication of infectious conditions, hereditary conditions, inflammatory conditions, or traumatic choroidal rupture.

Pediatric Retinal Detachment

- Though uncommon, pediatric RRD has a high rate of vision-threatening pathology in the companion eye.
- Non-traumatic retinal detachments in children are often syndromic.
- Retinal detachment is usually detected otherwise either on routine examination or routine follow-up to a prior surgical procedure.

26.1 Introduction

Pediatric retinal diseases often present with striking clinical features, and can have a profound impact on visual outcome. Alternatively, both clinical findings and visual impact can be subtle. Some of these conditions are covered elsewhere in this text: retinopathy of prematurity (ROP) (Chap. 25), retinoblastoma (Chap. 27), and pediatric uveitis (Chap. 28). The pages that follow will provide practical insight into the current thinking and practice regarding the more common heredodegenerative retinal disorders, vasoproliferative retinopathies, and retinal detachment syndromes occurring in children.

26.2 Medical Pediatric Retina

26.2.1 Albinism

Albinism is comprised of a group of clinically and genetically heterogeneous disorders characterized by

a congenital reduction in melanin pigment in the eye. Prevalence worldwide is in the order of 1/10,000 to 1/20,000. Oculocutaneous albinism (OCA) affects the eye, skin, and hair. Melanin pigment deficiency is limited to the eye in the less common ocular albinism (OA) [7].

The various subtypes of OCA are typically inherited in an autosomal recessive fashion. The most common subtypes are OCA1 and OCA2. OCA1 is associated with a varied deficiency of tyrosinase activity, an enzyme important in melanin synthesis. Patients with OCA1A have a complete absence of tyrosinase activity that does not significantly change over their lifetime. Individuals with OCA1B have varying levels of tyrosinase activity, tend to develop some pigmentation later in life, and have milder ocular findings than in OCA1A. OCA2, "tyrosinase-positive" albinism, is the most prevalent type found worldwide. OA is inherited in an X-linked pattern, thereby affecting predominantly males. Affected males and carrier females have abnormal, large melanosomes in melanocytes and keratinocytes.

Two potentially life-threatening syndromes associated with albinism are the Hermansky-Pudlak syndrome (HPS) and the Chédiak-Higashi syndrome (CHS). HPS is a genetically heterogeneous multisystem disorder with clinical findings of ocular cutaneous albinism. Affected individuals have an immune defect which predisposes them to life-threatening bacterial infections, and an increased susceptibility to lymphoproliferative disorders. Patients also have a mild bleeding dysfunction due to absent platelet dense bodies. CHS patients typically have creamy white hypopigmented skin and metallic grey hair. Defects in natural killer activity result in recurrent pyogenic bacterial infections. Bleeding and neurologic problems also tend to develop.

Clinical Findings

Diagnosis of albinism is typically based on the clinical presentation of ocular and/or systemic findings. Both types of OCA1 are born with white hair and skin, whereas OCA2 has a variable amount of visible pigmentation at birth. Clinically, the phenotype of OA is similar to that of the ocular findings observed in OCA but with normal skin and hair pigmentation. Carrier females of OA, however, may have a fundoscopic examination with a mosaic pigmentation pattern. Congenital nystagmus during the first 3 months of life may be the initial presenting ophthalmic clinical sign. Iris and fundus hypopigmentation are the hallmark diagnostic clinical findings in most OA patients. Marked iris transillumination defects and a "blonde" fundus are typical findings. Foveal hypoplasia with loss of the normal foveal depression and light reflex is characteristic of albinism, and the cause for decreased visual acuity in this disorder. Optical coherence tomography (OCT) is very useful in the diagnosis of foveal hypoplasia in otherwise normal-appearing patients with OA. Visual evoked potential studies demonstrate optic nerve fiber misrouting. HPS and CHS diagnosis is based primarily on their clinical features, although HPS has available molecular genetic testing.

Clinical Course and Management

Visual acuity will usually range from 20/40 to 20/400, with intact color vision. Misrouting of optic nerve fibers is common with temporal retina fibers inappropriately routed contralaterally instead of ipsilaterally, resulting in impaired stereopsis and strabismus. Due to potentially life threatening complications, patients suspected with HPS or CHS should be promptly referred to a hematologist for evaluation. Referral to a geneticist can facilitate DNA diagnostic evaluation, and electron microscopic testing of skin or hair bulb melanocytes can help in the diagnosis of the type of albinism and provide counseling for the family. Ongoing care with the ophthalmologist, low-vision specialist, and dermatologist is important.

26.2.2 Congenital X-linked Retinoschisis

Congenital X-linked retinoschisis (CXLRS) is predominantly inherited in an X-linked recessive distribution. It is the most common cause of juvenile macular degeneration in males affecting 5,000–25,000 live births worldwide. Affected individuals have a 96% incidence of a mutation in the *XLRS1* gene, resulting in expression of an aberrant retinoschisin protein.

Mothers are typically asymptomatic obligate carriers of the disease with normal retinal examinations and normal electroretinograms (ERG), but often have a positive family history of male members in the family with a history of vision loss [14].

Clinical Findings

Patients may present in infancy with a diagnosis of amblyopia, strabismus, or nystagmus, but most patients will present between 5 and 10 years of age with difficulties in school. The disease is characterized by structural deficits in the retinal layers resulting in foveal schisis and peripheral bullous schisis cavities most commonly affecting the inferior retinal periphery. Retinal splitting was previously thought to occur primarily in the nerve fiber layer. Analysis of the retinal layers by OCT has revealed that schisis occurs in all layers of the retina, most commonly in the outer plexiform layer. The finding on OCT of fine, coalescing extramacular intraretinal schisis cavities is referred to as lamellar schisis. Foveal schisis is seen in all forms of CXLRS, while lamellar and peripheral bullous schisis are variably present [11]. Electroretinography (ERG) typically shows an "electronegative" waveform, consisting of a normal a-wave amplitude and a selectively reduced b-wave amplitude.

Bullous peripheral schisis cavities may cause amblyopia when they extend superiorly to interrupt the visual axis. Disruption of the thin inner wall of schisis bullae may result in interruption of a retinal vessel and amblyogenic vitreous hemorrhage. Rhegmatogenous retinal detachment (RRD) is uncommon, and may be difficult to diagnose in CXLRS.

Clinical Course and Management

The clinical course is variable with severity in visual loss ranging from 20/50 to no light perception. Currently there is no treatment for foveal or lamellar schisis in CXLRS. Vitreoretinal surgery may be necessary when bullous CXLRS results in interruption of the visual axis or threatens to extend through the fovea, to address an amblyogenic vitreous hemorrhage, and to repair combined schisis-RRD. Laser retinopexy can create a mechanical barrier to prevent progression of bullous retinal schisis, but there is risk of iatrogenic full-thickness retinal break. Correction of refractive errors and early intervention with amblyopia therapy are vital during the entire visual development of the child. Low-vision aids in conjunction with a low-vision specialist can be invaluable as the child gets older. Protective eyewear is recommended.

26.2.3 Heredodegenerative Retinal Degeneration

Pigmentary retinopathy is a generalized reference to a panretinal deterioration of the retina and retinal pigment epithelium (RPE). The pigmentary retinopathies can be divided into primary retinitis pigmentosa (RP), in which the disorder is exclusively found in the eyes without any other systemic manifestations, and secondary pigmentary retinopathy, in which the retinal degeneration is associated with a multiorgan syndrome.

26.2.3.1 Primary Retinitis Pigmentosa

Retinitis pigmentosa is a heterogeneous group of inherited diseases that typically results in bilateral, symmetric, progressive degeneration of photoreceptor and RPE cells.

Inheritance Pattern

Retinitis pigmentosa is a heterogeneous assembly of gene mutations affecting various molecular pathways, and with diverse inheritance patterns [3]. Autosomal dominant (AD) RP has been estimated to comprise 10% of cases, is usually the mildest form, and is often undiagnosed until the second to fourth decade. Autosomal recessive (AR) RP comprises 84% of cases, is often more severe, usually present in the first two decades of life with significant loss of peripheral visual field and visual acuity deterioration to worse than 20/200. Forty percent of cases are associated with some form of systemic syndrome. X-linked (XL) cases constitute only 6% of all cases, yet tend to have the most severe phenotype of RP. Clinically,

affected males show early onset and present within the first decade of life with severe retinal degeneration. Carrier females can have no clinical effect to severe dysfunction depending on the lyonization of their retina and RPE cells [8].

Clinical Findings

Children with RP typically present either asymptomatic with a known family history or symptomatic with a variety of symptoms and signs: night blindness and symptoms of difficulty with dark adaptation, poor vision, nystagmus, and strabismus are common. The scotopic ERG is typically flat. Kinetic (Goldmann) visual field (VF) testing may reveal a classic "ring scotoma" caused by mid-peripheral rod degeneration early in the disease. Central vision is preserved until relatively late.

The classic triad of RP is "bone spicule" pigmentary accumulations in the mid-periphery, waxy pallor of the optic nerve, and retinal arteriolar attenuation. Older patients may develop vitreous cells, cystoid macular edema, macular pucker, and/or macular pigment migration. Optic nerve drusen and posterior subcapsular cataract may occur as well.

Clinical Course and Management

As the disease progresses, central visual acuity decreases as cone function deteriorates. A thorough history, including a detailed family history, physical examination, ERG, and kinetic visual field testing should be performed in the workup of any pigmentary retinopathy. Fluorescein angiography and OCT are useful to detect and monitor cystoid macular edema, a potentially reversible cause of vision loss in RP patients when treated with systemic or topical carbonic anhydrase inhibitors. Posterior subcapsular cataract may be disproportionately symptomatic due to the impact on central vision. Early cataract surgery is commonly necessary to maintain visual acuity. Periodic monitoring of lens and macular status, serial perimetry, genetic counseling, and working with a low-vision specialist are appropriate management considerations.

26.2.3.2 Secondary Pigmentary Retinopathies

Usher disease is a heterogeneous autosomal recessive disease, and usually manifests clinically as initial bilateral sensorineural hearing loss followed by vision loss secondary to RP in late childhood or adolescence. Total blindness can occur by the third or fourth decade. Type I Usher disease patients have severe hearing loss with vestibular dysfunction and an earlier onset of vision loss compared to type II Usher disease patients who have a milder course with normal vestibular function. Type III has a variable course with regard to onset of vision loss, vestibular dysfunction, and progressive hearing loss [6].

Leber's congenital amaurosis (LCA) presents in the first year of life with severely affected vision, poor pupillary reactions, and sensory nystagmus. Visual acuity ranges from 20/200 to no light perception when older. Clinical findings are varied as well, and patients may have a normal-appearing fundus, colobomas, bull's eye maculopathy, peripheral bone spicules, or diffuse peripheral fine white dots. Keratoconus, cataract, and hyperopia can also be associated with LCA. A markedly attenuated or non-recordable ERG in an infant is characteristic [1].

The infantile or late-infantile form of neuronal ceroid lipofuscinosis (NCL), or Batten's disease, is one of the most common neurogenic lysosomal storage diseases of childhood, and can present with visual inattention and nystagmus. Hypotonia, seizure disorder, developmental delay, vision loss, and poor motor control are trademarks of NCL.

Other syndromic causes of RP include Bardet-Biedl syndrome (polydactyly, intellectual developmental delay, hypogonadism, obesity, renal dysfunction), Kearns-Sayre syndrome (chronic progressive external ophthalmoplegia, ataxia, ptosis, sensorineural hearing loss, heart block cardiomyopathy, white matter brain disease with a mitochondrial inheritance pattern), Friedrich's ataxia (ataxia, sensory loss, cerebellar dysfunction that is associated with vitamin E deficiency), and abetalipoproteinemia, also known as Bassen-Kornzweig syndrome (characterized by ataxia, fat intolerance, sensory neuropathy, and acanthocytosis). Patients with abetalipoproteinemia should be on a fat-free diet and receive supplemental vitamin E, A, and K.

A detailed family and medical history, and physical examination should identify systemic involvement associated with a pigmentary retinopathy, and the diagnosis needs to be made such that treatable and potentially life-threatening systemic conditions can be managed.

26.2.4 Best's Disease

Best's disease is inherited in an autosomal dominant manner with variable expressivity, with phenotypes ranging from an opthalmoscopically normal-appearing fundus (seen in 5–32% of carriers) to an orange-yellow vitelliform lesion to a gliotic macular scar. The penetrance of Best's disease, however, is complete as all patients with the genetic disorder have an abnormal electrooculogram (EOG), the hallmark of this macular dystrophy. The disease locus has been mapped to 11q13, and the defective gene in Best's disease is VMD2, which encodes for the RPE transmembrane chloride channel, bestrophin [9].

Clinical Findings

The clinical appearance of Best's disease is highly variable even within the same family. The most characteristic appearance is the orange-yellow "egg-yolk" (vitelliform) lesions in the central macula. Vitelliform lesions may have a variety of appearances depending on the resorption of lipofuscin pigment. Choroidal neovascularization (CNV), a well-demarcated gliotic scar, and macular RPE atrophy may also occur. Vitelliform lesions have been reported in infants as early as 1 week old, and may persist into late adulthood. Multiple lesions have also been described in the same eye, referred to as multifocal Best's disease.

Fluorescein angiographic findings depend on the type of fundus lesion present. Lipofuscin blocks fluorescein transmission early. Resorption of lipofuscin in the vitelliform lesion and subsequent RPE atrophy results in RPE transmission defects, early hyperfluorescence that fades in the late phase of the angiogram. When present, CNV demonstrates typical early hyperfluorescence followed by late, expanding leakage. Disciform scars will stain with dye in the late phases of the angiogram.

Best's disease is characterized by an abnormal EOG (most affected patients have an Arden ratio of less than 1.5, as compared to a normal value of greater than 1.7), with a normal ERG and dark adaptation. The EOG measures the standing electric potential that exists across the RPE, which oscillates depending on illumination intensities.

Clinical Course and Management

Vision may be normal or mildly reduced even with a large subfoveal vitelliform lesion. Most (75%) patients maintain 20/40 vision or better in at least one eye through middle age. All family members of affected patients should undergo dilated funduscopic examination, and be offered genetic testing and counseling. There is no treatment for Best's disease apart from CNV, which is infrequent.

26.2.5 Stargardt's Disease/ Fundus Flavimaculatus

Stargardt's disease/fundus flavimaculatus (STGD1/FF) is the most common recessively inherited macular degeneration, affecting roughly 1 in 10,000 people. Dominant inherited pedigrees have been reported. Although controversial, Stargardt's disease (STGD) and fundus flavimaculatus (FF) are considered as part of a spectrum of the same disease entity, STGD1/FF, with different allelic expressions. Autosomal recessive STGD is caused by a mutation in the *ABCA4 (ABCR)* gene, which encodes the ATP-binding cassette transporter on chromosome 1p. FF maps to this same region. The pathologic accumulation of toxic lipofuscin pigment in the RPE cells suggests a disorder in lipopigment metabolism leading to RPE cell dysfunction, subsequent photoreceptor death, and severe vision loss in affected patients [15].

Clinical Findings

Stargardt's disease/fundus flavimaculatus is typically a bilaterally symmetric progressive retinal degeneration. The classic Stargardt phenotype is a central

beaten-bronze bull's eye maculopathy with yellow-white flecks at the level of the RPE or deep retina, usually concentrated in paracentral macula and the posterior pole. Children with STGD will usually present with visual complaints and central macular involvement in the early to mid-teens, although onset of symptoms typically starts several years prior to presentation. Patients with the FF phenotype–paracentral and more diffuse peripheral flecks as compared to STGD patients without atrophic macular involvement—will typically present in early or mid-adult life. The peripheral flecks are transitory and may appear in the second decade, and disappear and reappear over decades. The FF phenotype, however, tends to have a more severe deterioration of retinal and visual function as compared to patients with the STGD phenotype with or without typical central lesions.

Fluorescein angiography is often useful for diagnosis. The phenomenon of a "dark" or "silent" choroid describes the lack of choroidal fluorescence during the fluorescein angiogram, and this finding is present in at least 50% of STGD1/FF patients. The absence of this sign does not exclude the diagnosis of STGD1/FF. The dark choroid effect has been thought to be due to blockage of the choroidal flush by the lipofuscin-laden RPE cells. This theory has been challenged by little or lack of correlation between lipofuscin concentration and presence or absence of a dark choroid on fluorescein angiography. Flecks may be hypofluorescent, presumably because of blockage, or display adjacent hyperfluorescence secondary to RPE transmission defect.

Clinical Course and Management

Early in the disease, loss of central vision may be out of proportion to funduscopic examination. Visual dysfunction can range from mild to expanding central scotoma over time, or have peripheral degeneration with accompanying loss of peripheral visual field and ERG loss. Visual acuity typically ranges from 20/50 to 20/200. There is currently no treatment for STGD/FF.

26.3 Vasoproliferative Vitreoretinopathies

26.3.1 Familial Exudative Vitreoretinopathy

Familial exudative vitreoretinopathy (FEVR) is an inherited retinal vascular disorder characterized by an avascular peripheral retina, extraretinal fibrovascular proliferation, exudation, an abnormal vitreoretinal interface, and traction retinal detachment. Patients with the FEVR mutation may present with an avascular retinal periphery without exudation or vasoproliferative findings, or with a clinically normal retina (incomplete penetrance although mutation present). The disease may be inherited in an autosomal dominant, autosomal recessive, or X-linked manner. Family history can be instrumental in making a diagnosis. In 55% of cases there is no known family history of the disease, though on peripheral fundus examination vascular abnormalities are commonly uncovered in an asymptomatic parent. Earlier reports of retinopathy of prematurity (ROP) in full-term infants were likely, in reality, infants with FEVR and a negative family history [18].

Clinical Findings

The clinical manifestations of FEVR include an avascular peripheral retina, neovascular buds at the junction of vascular and avascular retina, fibrovascular proliferation extending into the vitreous, and often a characteristic traction detachment producing a retinal fold which extends through the macula. Subretinal exudates, dragged retinal vessels, and retinal folds that can extend to the lens may also be seen. The clinical appearance may mimic not only ROP, but also Coats' disease, Norrie's disease, incontinentia pigmenti, and retinoblastoma. The diagnosis is usually made by clinical examination, patient history, birth history, and family history. In its most severe forms, a total retinal detachment due to exudation and fibrovascular proliferation can result, and render diagnosis more challenging. FEVR is usually, but not invariably, bilateral and asymmetric. Fluorescein angiography will often unmask peripheral non-perfusion in a seemingly normal-appearing companion eye.

Clinical Course and Management

Familial exudative vitreoretinopathy is a chronic life-long disease with periods of exacerbation and remission and frequent examinations are necessary for appropriate management. Patients who present with symptomatic FEVR (strabismus, amblyopia, or leukocoria most commonly) in infancy and early childhood often have a poor prognosis. Treatment of FEVR depends on the severity of the pathology. Exudation, even if asymptomatic, is initially treated with laser ablation of the avascular retina. Fluorescein angiography can be useful to identify the extent of the avascular retina and guide peripheral ablation. Tractional retinal detachment may be managed by vitrectomy in some cases. Family members of suspected patients with FEVR should have a thorough peripheral retinal examination to aid in the diagnosis.

26.3.2 Persistent Fetal Vasculature Syndrome

Persistent fetal vasculature syndrome (PFVS), previously known as persistent hyperplastic primary vitreous (PHPV), refers to a spectrum of structural changes in which the hyaloid vessels and tunica vascular lentis (TVL) persist in an eye following birth. The hyaloid system, or primary vitreous, fills the vitreous cavity and is more than just the hyaloid vessel connecting the optic nerve to the posterior lens. The TVL extends both anterior and posterior to the lens, interweaving with the hyaloid system posteriorly and the ciliary processes as well. The hyaloid system typically regresses by 28–30 weeks of gestational age. Incomplete hyaloidal involution may result in a posterior lens opacity of variable severity, and a number of characteristic potential posterior pole abnormalities. No distinct genetic mutation has been associated for typical unilateral PFVS [19].

Clinical Findings

Ninety percent of the time PFVS is unilateral. Eyes with PFVS are typically, but not invariably, smaller compared to the normal fellow eye, with a posterior lens opacity and a stalk that connects the posterior lens to the optic disc. Anterior or posterior changes may predominate in a given eye. Visual potential is most dependent on the extent of posterior involvement (especially optic nerve and peripapillary retina) and the size of the eye. Retinal dysplasia is found in varying amounts in PFVS, and may limit visual function as well.

Clinical Course and Management

When an eye is normal in size and leukocoria is the prominent ocular finding, the most important differential diagnostic consideration is retinoblastoma. Ultrasonographic and/or radiographic imaging (CT or MRI) can be performed to detect intraocular calcifications and aid in the diagnosis.

Visual evoked potentials (VEP) are useful, comparing an affected eye to its normal companion, when trying to determine visual potential of the affected eye. If the visual evoked potential is positive, it is reasonable to consider surgical repair. With minor eccentric lens opacity, lens-sparing vitrectomy with interruption of the stalk is in order. Peripapillary retinal detachments will often resolve following vitrectomy, and the eye is allowed to grow more normally. Anatomic and visual results are variable following surgery, and depend not only on preoperative ocular anatomy but also timing of surgery, whether the lens was removed, and postoperative amblyopic therapy. Monocular precautions and the use of safety glasses lifelong are standard recommendations.

26.3.3 Coats' Disease

Coats' disease is typically a unilateral retinal vascular disorder (90%) occurring predominantly (up to 90%) in young males in the first decade of life. Inheritance is primarily sporadic. Mildly affected individuals can present late in adulthood, typically with vitreous hemorrhage in the setting of posterior vitreous detachment. Patients who are younger at presentation are affected more severely. No racial or ethnic predisposition or environmental factors have been linked to Coats' disease [12].

Clinical Findings

Children typically will present with strabismus, leukocoria, or poor vision on routine vision screening. Characteristic funduscopic findings in Coats' disease are focal vascular telangiectasias and "light bulb-shaped" aneurysmal dilatations. It is generally held that breakdown of the blood–retinal barrier of the capillary endothelium causes plasma leakage into vessel walls and ultimately form dilatations and telangiectasias. Continued leakage into nearby retinal tissue results in the characteristic intraretinal and subretinal cholesterol exudates, hemorrhage, and subretinal fluid.

More severely affected patients have an associated serous detachment of the neurosensory retina which can be localized or total. Visual compromise occurs as a consequence of accumulation of exudative material in the macular area, secondary macular changes (RPE atrophy or subfoveal fibrosis), exudative detachment involving the macula, and amblyopia.

Clinical Course and Management

If left untreated, eyes with Coats' disease deteriorate. Gomez Morales reported that 64% of untreated patients who were followed for 5 years developed total retinal detachments and 32% developed secondary glaucoma [5]. Not uncommonly, advanced unilateral Coats' disease must be differentiated from retinoblastoma. Funduscopic (microvascular dilatations), ultrasonographic, and radiographic (CT or MRI) findings (intraocular calcification) can help in the diagnosis when serous detachment or disorganization is a prominent feature.

Fluorescein angiography is helpful in juvenile Coats' disease in not only diagnosis but also identifying treatable areas. Discrete "light bulb-shaped" aneurysmal vessels hyperfluoresce early and leak late into the subretinal space. In addition, normal-appearing areas of non-perfused retina are more effectively identified for treatment.

All abnormal vasculature and areas of non-perfusion are treated with photocoagulation or cryotherapy ablation. Multiple treatment sessions are often needed to adequately treat the abnormal vasculature initially. Recurrences may occur long after successful treatment. Consequently, children with Coats' disease should be followed every 6 months to monitor for additional ablative therapy as needed. In cases of partial retinal detachment, scleral buckle may be performed with external drainage of subretinal fluid to facilitate peripheral retinal ablation and reduce exudative activity.

26.3.4 Norrie's Disease

Norrie's disease is a rare vitreoretinal dystrophy that is inherited in an X-linked recessive pattern. Patients with Norrie's disease often present with bilateral profound visual impairment, retinal dysplasia, and leukocoria. Sensorineural hearing loss and mental impairment occur in approximately 30% of patients. Ocular findings include retinal dysplasia, traction retinal detachment, vitreous hemorrhage, and persistent fetal vasculature. The retina peripheral to posterior pole detachment is often avascular. The Norrie's disease gene (*NDP*), originally known as the *EVR2* gene, encodes for the norrin protein, a member of the cysteine knot proteins, which acts as a ligand in the canonical Wnt receptor/beta-catenin signal transduction pathway. Dysregulation in *NDP* has led to a unifying classification system of congenital vitreoretinopathies as "NDP-related," and includes PFVS, Coats' disease, X-linked FEVR, and ROP [20].

Clinical Course and Management

If the patient has visual potential as demonstrated by a visual evoked potential, vitrectomy surgery can be considered to relieve the traction between the retina and the lens. Visual potential is limited to hand motions to light perception vision, even with resorption of subretinal fluid, due to the severity of retinal dysplasia. Molecular genetic analysis should be performed, and families should receive genetic counseling.

26.3.5 Incontinentia Pigmenti

Incontinentia pigmenti (IP; Bloch-Sulzberger syndrome) is inherited as an X-linked dominant trait.

Mutation of the *NEMO* gene, a defect in the NF-kB pathway, is found in 90% of patients with IP. IP is typically seen only in females, as it is usually lethal in males [4].

Skin, dental, CNS, skeletal, and ocular findings may be seen in IP. Cutaneous involvement is characteristic with skin vesicles beginning at birth and hyper- and hypopigmented papular lesions on the trunk and extremities. Delayed and disrupted dental development, delayed intellectual development, seizure disorder, strokes, microcephaly, scoliosis, and spina bifida are other features seen in IP. Ocular findings consist of peripheral retinal non-perfusion and vitreoretinal neovascularization. Cataracts, optic nerve atrophy, iris hypoplasia, nystagmus, corneal opacities, retinal folds and detachment, microphthalmia, strabismus, and macular ischemia may also be seen in IP. The differential diagnosis includes ROP, FEVR, Norrie's disease, and PFVS. Intervention treats the underlying pathology: laser or cryotherapy for active neovascularization, or vitrectomy surgery for retinal detachment.

Clinical Course and Management

Similar to ROP and FEVR, prompt prophylactic treatment of avascular peripheral retina should be performed to help prevent neovascularization and retinal detachment.

26.3.6 Pediatric Choroidal Neovascularization

Subfoveal choroidal neovascularization in children is a rare event, typically occurring as a complication of infectious conditions (e.g., toxoplasmosis, Toxocara canis, rubella retinopathy, ocular histoplasmosis syndrome), hereditary conditions (e.g., North Carolina macular dystrophy, Best's disease), inflammatory conditions (e.g., pars planitis, Vogt-Koyanagi-Harada syndrome, serpiginous choroidopathy, multifocal choroiditis, punctate inner choroidopathy), and traumatic choroidal rupture. Other etiologies include Coats' disease, pathologic myopia, angioid streaks, choroidal osteoma, chronic uveitis, fundus flavimaculatus, choroideremia, after photocoagulation, sickle cell retinopathy, optic disc drusen, congenital optic pits, or idiopathic. Visual acuity may be compromised by the subfoveal location of the choroidal neovascular complex, exudative macular detachment, subretinal or subretinal pigment epithelial hemorrhage, and cystoid degenerative changes of the neurosensory retina [13].

The prognosis of subfoveal neovascularization in children is reportedly more favorable than adult neovascularization from either exudative age-related macular degeneration (ARMD) or presumed ocular histoplasmosis. Fifty-eight percent of subretinal neovascular membranes in children and adolescents undergo spontaneous involution, with 29% achieving a final visual acuity of 20/50. Initial visual acuity is a useful predictor of final visual acuity. Nonetheless, 40% of children with subretinal neovascular membranes progress to disciform scar with loss of central vision measured at less than 20/200.

Clinical Course and Management

Photodynamic therapy (PDT) with verteporfin may be considered in the pediatric population although RPE alterations have been described in some reports. Surgical excision can be considered if the subfoveal CNV is refractory to medical therapy and tends to have a more favorable outcome than submacular surgery in adults for exudative ARMD likely due to the location of the CNV anterior to the RPE in children.

Although PDT and submacular surgery is a consideration in patients with worsening vision, their futures in the era of intravitreal anti-VEGF treatments (e.g., bevacizumab and ranibizumab) is uncertain. The safety profile of anti-VEGF treatments in children is currently not known, and they should be used with caution.

26.4 Pediatric Rhegmatogenous Retinal Detachment

Though rhegmatogenous retinal detachment (RRD) has an incidence of approximately 12.4 cases per 100,000 population, RRD occurring in the pediatric age group (birth to 18 years of age) accounts for

only 3.2–5.6% of the total (approximately 0.38–0.69 per 100,000 population). However, the rate of vision-threatening pathology in the companion eye in children may be as high as 90% [2]. Pediatric retinal detachments in children unrelated to globe-disrupting trauma or acute ROP in infancy are seen most often in association with myopia (both isolated ocular or syndrome-associated) or antecedent intraocular surgery.

Clinical Findings

Poor visual acuity is generally the presenting symptom. Retinal detachment is usually detected otherwise either on routine examination, or routine follow-up to a prior surgical procedure. The mean duration of vision loss prior to repair may be several weeks, ranging from immediate awareness to many months. The tendency to late diagnosis has predictable consequences. Pediatric RRD presents more commonly as macula-off relative to adults, with proliferative vitreoretinopathy (PVR) present at initial presentation in nearly half of all eyes. Retinal dialyses are seen most often following prior intraocular surgical procedures. Non-traumatic retinal detachments in children are often syndromic.

26.4.1 Stickler Syndromes

The Stickler syndromes (hereditary or progressive oculoarthropathy) type 1 and type 2 are the most common causes of retinal detachment in children, occurring as a consequence of mutation in a collagen gene. Myopia, an "optically empty vitreous," and retinal detachment are frequent ocular features. The most common form, type 1 Stickler's, is associated with a mutation in the type II collagen gene (collagen 2A1) located on chromosome 12q13.11-p13.2, and clinically demonstrates a "membranous" vitreous. The less commonly encountered form of Stickler's syndrome (type 2, due to a defect in the collagen 11A1 gene involved in type XI collagen production) maps to chromosomal locus 1p21. Such patients have a fibrillar or "beaded" vitreous. Mutation in the collagen 11A2 gene results in a systemic Stickler phenotype without ocular findings (type III), mapping to chromosomal locus 6p21. Direct DNA testing is available for all three loci to confirm diagnosis or for prenatal testing.

Deafness, orofacial features, and arthritis are associated components of type 1 Stickler's syndrome [17]. More than 17 mutations have been described for the highly penetrant type 1 gene, with considerable phenotypic variability. Some patients present without associated systemic features, and a fundus appearance characterized by a radial perivascular retinal degeneration. The vitreoretinal degeneration of type 1 Stickler's syndrome may be visible in the first decade, with retinal holes and tears occurring within the lesion and at its margins.

Individuals with type 1 Stickler's syndrome (col2A1 mutation) have a high risk of RRD during childhood, in the order of 50%. The RRDs seen in Stickler's syndrome are unusual as multiple retinal breaks and giant retinal tears are common.

26.4.2 Marfan Syndrome

Marfan syndrome is due to a mutation in the fibrillin 1 gene (*FBN1*, locus 15q21.1). Skeletal, cardiovascular, and ocular findings are characteristic of the autosomal dominant syndrome. Ectopia lentis with superotemporal displacement, lens coloboma, and axial high myopia with scleral thinning are common ocular findings.

Retinal detachment occurs in 5–11% of patients, increasing to 8–38% in association with ectopia lentis or following lens surgery. Retinal detachment typically occurs in the third decade, but can be see in childhood. There is high relative prevalence of giant retinal tear, bilateral retinal detachment, total retinal detachment, macula-off retinal detachment, and PVR on initial presentation [16].

Circumferential laser and silicone tamponade are commonly employed during RRD repair. Autologous plasmin enzyme can be useful as a surgical adjuvant to eliminate the need for a scleral buckle by removing the pre-retinal scaffold for posterior PVR.

26.4.3 Colobomatous Rhegmatogenous Retinal Detachment

Colobomata may occur in the iris, lens, ciliary body, retina, choroid, and optic nerve and are described

as "typical" when present inferonasally. Additional ocular findings may include microphthalmia, microcornea, cataract, and retinal detachment. The high incidence of associated systemic defects (~40%) underscores the importance of pediatric referral [10].

Optic nerve coloboma occurs as a consequence of incomplete closure of the optic stalk in weeks 5–7 of embryogenesis. Optic nerve coloboma may occur sporadically, or in association with multisystem abnormalities. In general, visual potential in an eye with an optic nerve coloboma correlates with foveal anatomy. Discerning fovea anatomy may pose a challenge due to alteration of foveal detail. Chorioretinal colobomas are known to predispose to retinal detachment (in the order of 8%). The retina overlying the choroidal defect is thin and prone to breaks within or along the margin of the coloboma.

Retinal detachments associated with coloboma may occur in infancy, but are most typically seen in childhood. Rarely, they may resolve spontaneously. Visual acuity is typically poor, even with successful repair.

Retinal detachments associated with coloboma are uniquely challenging. The retinal break occurs within the coloboma. The posterior hyaloid is typically attached firmly at the edge of the coloboma. Repair of the retinal detachment is usually by vitrectomy with silicone oil tamponade. Laser retinopexy is performed around the circumference of the coloboma to achieve chorioretinal adhesion. Without retinopexy around the coloboma there is significant probability that silicone oil will track into the subretinal space via the open break within the coloboma, the same path that accounts for the RRD.

Clinical Course and Management

Detachment of the fovea, especially repeated detachment, has a particularly devastating effect on visual acuity in children. Primary retinal detachment due to a single retinal break or idiopathic retinal dialysis with no/low-grade PVR is typically managed with a scleral buckling procedure. Predictably, such eyes have the best prognosis, with repair rates reported at 80% or more.

Rhegmatogenous retinal detachment with PVR is usually managed by combined scleral buckle and vitrectomy. Giant retinal tears are repaired with vitrectomy, endolaser, and silicone oil in most instances, and the lens is often sacrificed to facilitate meticulous vitreous removal. Autologous plasmin enzyme may be used to assist vitrectomy in colobomatous detachments and schisis-rhegmatogenous detachment.

The high rate of bilaterality of retinal detachment due to giant retinal tear in Stickler's and Marfan syndromes justifies consideration of prophylactic retinopexy of the fellow eye in these patients. Laser treatment should be circumferential, not focal, as ostensibly normal-appearing retina is vulnerable to detachment.

Though the incidence of RRD in childhood is quite low, the high incidence of bilateral ocular abnormalities is noteworthy. This tendency to bilateral ocular disease, and the finding that nearly 40% of the repaired eyes have better or equal visual acuity as compared to the companion eye at final follow-up, make a compelling case for proceeding with surgical repair. Often, it will not be "just a spare eye."

26.5 Conclusion

Pediatric retinal pathology is often challenging with respect to both diagnosis and management. Many pathologies are relatively uncommon, with diverse clinical presentations, frequent bilateral ocular involvement, and concomitant ocular and systemic abnormalities. Several pediatric retinal pathologies are potentially life-threatening themselves (such as retinoblastoma) or by virtue of their associated systemic features (Hermansky-Pudlak, Chédiak-Higashi, Kearns-Sayre, and Marfan syndromes, to name a few). Effective management of pediatric retinal pathologies often requires a multidisciplinary team to address the systemic, ocular, and visual rehabilitative needs of the affected child.

Take Home Pearls

Albinism

- Optical coherence tomography is very useful in the diagnosis of foveal hypoplasia in otherwise normal-appearing patients with ocular albinism.
- Due to potentially life-threatening complications, patients suspected with Hermansky-Pudlak syndrome and Chédiak-Higashi syndrome should be promptly referred to a hematologist for evaluation.

Congenital X-linked Retinoschisis

- Optical coherence tomography is used to determine the presence and severity of both macular schisis and lamellar extramacular schisis.
- Surgical indications include bullous schisis interrupting the visual axis or if it threatens to extend through the fovea, amblyogenic vitreous hemorrhage, and combined schisis-rhegmatogenous retinal detachment.

Heredodegenerative Retinal Degeneration

- Retinitis pigmentosa (RP) does not present in the first year of life. Consider Leber's congenital amaurosis in the differential diagnosis of infants with severe vision loss.
- X-linked cases tend to have the most severe phenotype of RP, followed by those with autosomal recessive and autosomal dominant inheritance.
- Periodic monitoring allows prompt diagnosis and management of treatable causes of visual compromise (posterior subcapsular cataract, cystoid macular edema, and macular pucker).

Best's disease

- Vitelliform lesions may be single or multiple.
- While the phenotype is variable, all patients with the genetic disorder have an abnormal electrooculogram.

Stargardt's Disease/Fundus Flavimaculatus (STGD1/FF)

- The peripheral flecks are transitory and may appear in the second decade, and disappear and reappear over decades.
- Absence of a dark choroid on fluorescein angiography does not exclude the diagnosis of STGD1/FF.

Familial Exudative Vitreoretinopathy (FEVR)

- Fluorescein angiography will often unmask peripheral non-perfusion in a seemingly normal-appearing companion eye, and is useful in guiding treatment.
- Fundus examination of the parents often uncovers a clinically asymptomatic carrier.
- Familial exudative vitreoretinopathy is a chronic vascularly active process with sometimes long quiescent periods and merits lifelong monitoring.

Persistent Fetal Vasculature Syndrome (PFVS)

- Anisometropia is a common hurdle to good visual outcome.
- Retinal dysplasia is found in varying amounts in PFVS, and may limit visual function and rehabilitation.

Coats' Disease

- One of the most common diseases requiring differentiation from retinoblastoma.
- Fluorescein angiography is helpful not only in diagnosis but also in identifying the full extent of the disease for treatment.
- Recurrences may occur long after successful treatment and merits lifelong monitoring.

Norrie's Disease

- Visual potential is limited to hand motions to light perception vision, even with resorption of subretinal fluid, due to the severity of retinal dysplasia.

Incontinentia Pigmenti

- Interventions to address the underlying pathology consist of laser or cryotherapy for active neovascularization, and vitrectomy surgery for retinal detachment.

Pediatric Choroidal Neovascularization (CNV)

- Fifty-eight percent of CNV in children and adolescents undergo spontaneous involution, with 29% achieving a final visual acuity of 20/50.
- There is no standardized therapy, although submacular surgery, photodynamic therapy, and intravitreal anti-vascular endothelial growth factor (VEGF) agents are available options.

Pediatric Rhegmatogenous Retinal Detachment

- The high rate of bilateral giant retinal tear in Stickler's and Marfan syndromes justifies prophylactic retinopexy of the fellow eye.
- In retinal detachments associated with coloboma, the retinal break occurs within the coloboma.
- Visual potential in an eye with an optic nerve coloboma generally correlates with foveal anatomy.

References

1. Ahmed E, Loewenstein J (2008) Leber congenital amaurosis: disease, genetics and therapy. Semin Ophthalmol 23:39–43
2. Capone A Jr, Trese MT (2005) Pediatric rhegmatogenous retinal detachment. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
3. Daiger SP, Bowne SJ, Sullivan LS (2007) Perspective on genes and mutations causing retinitis pigmentosa. Arch Ophthalmol 125:151–158
4. Goldberg MF, Custis PH (1993) Retinal and other manifestations of incontinentia pigmenti (Bloch-Sulzberger syndrome). Ophthalmology 100:1645–1654
5. Gomez Morales A (1965) Coats' disease. Natural history and results of treatment. Am J Ophthalmol 60:855–864
6. Keats BJB (2005) Usher disease. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
7. Marble M (2005) Albinism, lysosomal storage diseases, and other metabolic conditions. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
8. Murphy RC, Stout JT (2005) Hereditary retinitis pigmentosa. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
9. Oh KT, Parikh A (2005) Generalized retinal and choroidal dystrophies. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
10. Postel EA, Pulido JS, McNamara JA, et al. (1998) The etiology and treatment of macular detachment associated with optic nerve pits and related anomalies. Trans Am Ophthalmol Soc 96:73–88; discussion 88–93
11. Prenner JL, Capone A Jr, Ciaccia S, et al. (2006) Congenital X-linked retinoschisis classification system. Retina 26(suppl):61–64

12. Recchia FM, Capone A Jr, Trese MT (2005) Coats' disease. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
13. Sears J, Capone A Jr, Aaberg T Sr, Lewis H, Grossniklaus H, Sternberg P Jr, DeJuan E (1999) Surgical management of subfoveal neovascularization in children. Ophthalmology 106:920–924
14. Sieving PA, MacDonald IM, Trese MT (2005) Congenital X-linked retinoschisis. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
15. Sippy BD, Aaberg TA Sr (2005) Stargardt disease/fundus flavimaculatus. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
16. Sharma T, Gopal L, Shanmugam MP, et al. (2002) Retinal detachment in Marfan syndrome: clinical characteristics and surgical outcome. Retina 22:423–428
17. Snead MP, Yates JR (1999) Clinical and molecular genetics of Stickler syndrome. J Med Genet 36:353–359
18. Trese MT, Capone A Jr (2005) Familial exudative vitreoretinopathy. In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
19. Trese MT, Capone A Jr (2005) Persistent fetal vasculature syndrome (persistent hyperplastic primary vitreous). In: Hartnett ME, Trese MT, Capone A Jr, et al. (eds) Pediatric retina. Lippincott, Williams and Wilkins, Philadelphia
20. Wu WC, Drenser K, Trese M, et al. (2007) Retinal phenotype-genotype correlation of pediatric patients expressing mutations in the Norrie disease gene. Arch Ophthalmol 125:225–230

Pediatric Ocular Tumors and Simulating Lesions

27

Matthew W. Wilson

Contents

Core Messages

- The management of retinoblastoma has become more complex in the era of primary systemic chemotherapy.
- The management of retinoblastoma requires a multidisciplinary team composed of an ophthalmologist, pediatric oncologist, and radiation oncologist.
- Enucleation remains the standard of care for patients with massive unilateral disease in which the affected eye has limited visual potential and the other eye is normal.
- Any eye with limited visual potential in which retinoblastoma cannot be excluded should be enucleated.
- Retinoblastoma is a systemic disease; germ-line mutations of the *RB1* gene lead to 30% mortality from second cancers.

27.1 Retinoblastoma

Retinoblastoma is the most common primary intraocular malignancy of childhood, affecting 1/15,000 to 1/20,000 children [22, 48]. There are approximately 300 new cases per year in the USA. Over 90% of the cases are diagnosed by 3 years of age. Retinoblastoma is caused by a mutation of the *RB1* gene, a tumor sup-

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pressor gene, located at the 14 loci on the long arm of chromosome 13 (13q14). Retinoblastoma can occur in one of two forms, the most common being the unilateral sporadic form that accounts for approximately two thirds of the cases. Patients with the unilateral sporadic form of the disease are diagnosed on average between 18 and 24 months of age. They develop one tumor in one eye as a result of two independent mutations in a single retinal progenitor cell. Each mutation affects one copy of the *RB1* gene deleting the growth-regulating RB1 protein. As a result the cell enters an unregulated pattern of cell growth giving rise to the cancer. The second form of retinoblastoma is the hereditary or germ-line form of the disease. In contrast to the unilateral sporadic form of the disease, patients with germ-line mutations are diagnosed much earlier, usually by their first birthday. This, in essence, represents a systemic disease that commits the patient lifelong medical observation. The patient either inherits or develops early in utero an *RB1* mutation. The *RB1* mutation in turn is propagated through out the body as the fetus develops. As retinal progenitor cells divide, mutations in the second copy of the *RB1* gene lead to multiple tumors in one or both eyes. More importantly, the germ-line disease renders the patient susceptible to second cancers elsewhere in the body as they mature.

27.1.1 Presentation

The most common clinical manifestation of retinoblastoma is leukocoria, the white pupil (Fig. 27.1). Although screened for by pediatricians as part of the well-baby check up, leukocoria is most often first detected by the parents as either a cat's eye reflex or film over the eye. Alternatively, the white pupil may be seen on photographs and brought to the pediatrician's attention. Leukocoria is caused by light being reflected off the white surface of the tumor rather than the healthy retina, which casts a characteristic red reflex.

Leukocoria may be seen in varying brightness of light and positions of gaze. Leukocoria is best appreciated in dim light with the pupil fully dilated looking through a direct ophthalmoscope. If the tumor is located in the macula, leukocoria is seen with the child looking straight ahead. However, if the tumor

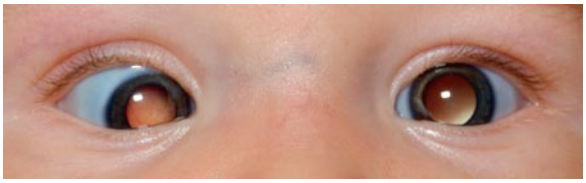

Fig. 27.1 Advanced intraocular retinoblastoma present as bilateral leukocoria and esotropia

is located in the nasal retina the leukocoria may only be with the affected eye in adduction. Similarly if the tumor is located in the temporal retina the leukocoria may only be seen with the eye in abduction. Listening to the parents as to when the abnormal reflex is seen and examining the eye in those same conditions will insure the best possible office examination for leukocoria. A chief complaint that includes some description of leukocoria necessitates a dilated ophthalmic examination with binocular indirect ophthalmoscopy. Although retinoblastoma is the most feared entity that causes leukocoria, it is the not the only one. A differential diagnosis for leukocoria and lesions simulating retinoblastoma is provided in Table 27.1 [34, 68].

Retinoblastoma may also present as a strabismus, most commonly an esotropia. The children typically affected by retinoblastoma are preverbal and cannot communicate a loss of vision. As the tumor grows, vision deteriorates and the eye most commonly deviates inward. Children with strabismus should have a dilated eye examination to exclude an intraocular tumor. It is also important to keep in mind that older children who fail visual screening examinations should also be dilated to exclude retinoblastoma.

Advanced cases of retinoblastoma have a more varied presentation. Prolonged retinal detachments from underlying tumors plus abundant vascular growth factors from the tumor itself can stimulate blood vessel growth on the iris surface, leading to ectropion uvea, heterochromia, neovascular glaucoma, and spontaneous hyphemas. Tumor cells can also enter the aqueous circulation, layering between the cornea and iris to form a pseudohypopyon (Fig. 27.2). In very advanced cases of retinoblastoma, the tumor may undergo spontaneous necrosis inside the eye, triggering a marked ocular and orbital inflammatory response. Retinoblastoma must be considered in the differential diagnosis of a child who presents with coexisting orbital cellulitis and panophthalmitis.

Table 27.1 Differential diagnosis of leukocoria and retinoblastoma

Vitreoretinopathy	Tumors	Infections	Congenital
Coats' disease	Medulloepithelioma	Toxocariasis	Cataract
Persistent fetal vasculature (persistent hyperplastic primary vitreous)	Astrocytic hamartoma	Toxoplasmosis	Coloboma
Retinopathy of prematurity	Diffuse choroidal hemangioma	Endogenous endophthalmitis	Morning glory disc
Familial exudative vitreoretinopathy	Juvenile xanthogranuloma		
X-linked retinoschisis			
Norrie's disease			
Incontinentia pigmenti			

In developed countries, the extraocular presentation of retinoblastoma is rare. However, left untreated, retinoblastoma can directly invade the orbit through emissary canals or by eroding through the overlying ocular coats. Massive proptosis will result as the tumor fills the orbit, pushing the globe forward. Retinoblastoma can also erode through the cornea, producing a friable exophytic mass that protrudes through the palpebral fissure.

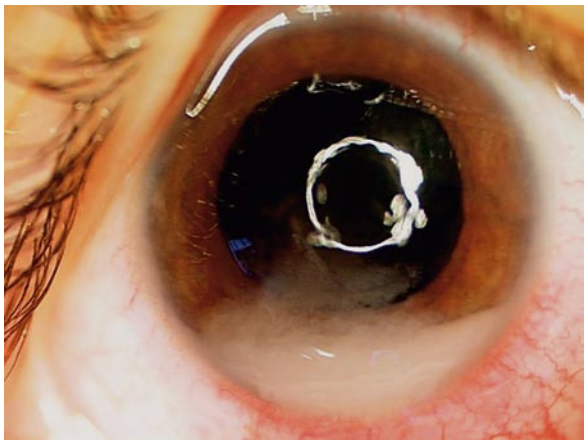

Fig. 27.2 Pseudohypopyon secondary to retinoblastoma. The tumor cells are suspended in the aqueous of the anterior chamber. In contrast to a true hypopyon the tumor cells will shift with gravity

27.1.2 Examination

Cursory ophthalmic examinations may be performed in the office with the child awake at the time of diagnosis. The history of present illness, the family's history of eye disease, and the family's history of cancer are all essential parts of the medical record. Birth history, an exposure to dogs, and systemic infections should be documented. A brief dilated examination coupled with an ultrasound documenting intraocular calcifications is sufficient to allow the ophthalmologist to make a presumptive diagnosis of retinoblastoma. During this visit, both these findings and the need for a more detailed examination under anesthesia can be discussed with the parents. The office visit also provides the opportunity to perform a dilated examination of the parents and patient's siblings, looking for evidence of spontaneously regressed retinoblastoma that might indicate a hereditary form of the disease.

Examinations under anesthesia are imperative in the diagnosis and treatment of retinoblastoma. The ora serrata must be visualized for 360° to assess the extent of intraocular disease. The eyelids, adnexa, and orbit should first be examined for anomalies. Attention is then directed to the conjunctiva, looking for circumlimbal inflammation. The diameters and clarity of the corneas should be documented. The irides should be inspected for ectropion uvea and neovascularization. The presence or absence of cataracts should be recorded, and the intraocular pressures should be measured.

Using indirect ophthalmoscopy, the vitreous should be studied first, looking for evidence of seeding from the tumor. Attention is then directed to the optic nerve and posterior pole of the eye. Examination of the retina continues until the mid-periphery and periphery have been viewed in their entirety. Each tumor with its associated clinical features such as size, growth pattern, serous retinal detachment,

subretinal retinal seeds, and vitreous seeds should be documented in a detailed fundus drawing.

Retinoblastomas appear as amelanotic masses with intrinsic calcifications. Retinoblastomas assume one or a combination of three growth patterns. Exophytic tumors grow beneath the retina. As the tumor grows, subretinal fluid accumulates around the mass leading to an exudative detachment (Fig. 27.3). In some cases the exudative detachment can be complete obscuring visualization of the tumor itself. Exophytic tumors may seed the subretinal space, as cells break free of the tumor and suspend themselves in the subretinal fluid. Exophytic tumors may also erode the overlying retina and grow into the vitreous cavity. Endophytic tumors grow on top of the retina into the vitreous cavity. It is the endophytic tumor that, in turn, seeds the vitreous cavity, as cells break free and suspend themselves in the vitreous (Fig. 27.4). Diffuse infiltrating retinoblastoma is an extremely rare growth pattern found more commonly in older children. The tumor grows within the retina and mimics a retinitis. Accompanying cells in the vitreous mimic an associated vitritis. Patients may be misdiagnosed as a unilateral recalcitrant uveitis when they fail to respond to immunosuppressive therapy. Diagnostic vitrectomies in such cases should be avoided until retinoblastoma has been excluded as a possible diagnosis. Failure to do so may lead to inadvertent extraocular spread of retinoblastoma.

Findings should also be documented with fundus photography. Older methods used handheld fundus cameras with a limited field of view. Images were stored on film, and comparisons between examinations were difficult. Newer imaging modalities, such as the RetCam (Clarity Medical Systems, Pleasanton, CA, USA), allow for wide-angle contact fundus photography. Images are digitally stored and are used to provide immediate comparisons between visits. The technology allows for the detection of the smallest change in tumors.

27.1.3 Diagnostic Testing

27.1.3.1 Ultrasound

Ultrasound typically shows an irregular heterogeneous tumor with focal areas of high internal reflectively corresponding to the intrinsic calcification within the lesion. If the calcification of the tumor is extensive, shadowing of the orbit posterior to the mass may be seen. Ultrasound can be used to provide approximate tumor measurements. Calcification within the lesion may interfere with the examiner's ability to clearly delineate the borders of the tumor. Similarly, a heavily calcified tumor can make assessments of the optic nerve difficult. Ultrasonography is

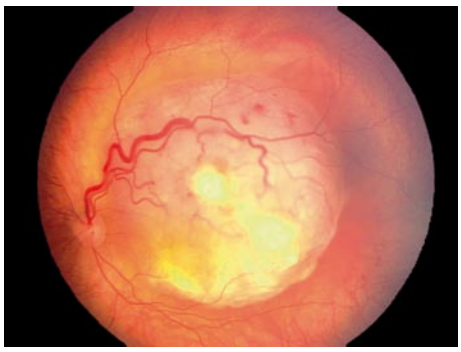

Fig. 27.3 Exophytic retinoblastoma with foci of calcification, afferent and efferent vessels, displaced luteal pigment, and a cuff of subretinal fluid

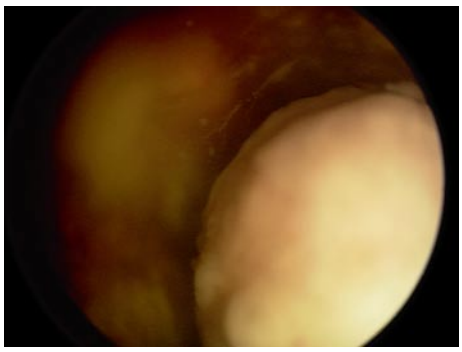

Fig. 27.4 Endophytic retinoblastoma with a paucity of overlying vessels. Parts of the tumor have broken off and seeded the vitreous cavity

most useful when the retinoblastoma is obscured by an overlying exudative retinal detachment.

27.1.3.2 Computed Tomography

Similarly computed tomography can be used to demonstrate the intraocular calcifications and to examine for extraocular extension. At the same time the brain can be examined to exclude both brain tumors and brain metastases. The fear of radiation exposure to patients with germ-line mutations has led some to advocate for magnetic resonance imaging (MRI) instead in all retinoblastoma patients.

27.1.3.3 Magnetic Resonance Imaging

Magnetic resonance imaging can be used to demonstrate intraocular retinoblastoma [19, 20]. Tumors will enhance on T1-weighted images with gadolinium. Although MRI does not show the intraocular calcifications, it provides the most reliable method for determining tumor size and assessing optic nerve involvement. MRI with gadolinium also provides a more detailed study of the pineal gland than computed tomography.

27.1.4 Grouping

Once the examination is complete, the eyes should be classified by a grouping system. Traditionally, the Reese-Ellsworth Classification has been used (Table 27.2). Algernon Reese and Robert Ellsworth based their classification on their collective experience with external beam radiation [22, 48]. Eyes were classified based on tumor size, number, and location. In summary, eyes with smaller and fewer tumors in the posterior pole were viewed more favorably than eyes with larger tumors anterior to the equator. Vitreous seeding was deemed the worst prognostic feature. In recent years, systemic chemotherapy has replaced external beam radiotherapy as the primary conservative treatment for intraocular retinoblastoma. The International Classification has, thus, been developed to better predict a response to chemotherapy (Table 27.3) [62]. The International Classification groups eyes based on tumor size, subretinal fluid, subretinal and vitreous seeding, and neovascular glaucoma. These grouping systems should not be confused with a cancer staging systems. Grouping systems relate strictly to the eye, whereas staging predicts overall extent of disease and patient survival. Retinoblastoma staging systems have been put forth both by the American Joint Commission on Cancer and St Jude Children's Research Hospital [4, 47].

27.1.5 Treatment

The goals in the treatment of intraocular retinoblastoma are to: (1) preserve life, (2) preserve the eye, and (3) preserve vision. Survival rates for retinoblastoma exceed 90% in the developed countries. Treatment decisions are based on the extent of intraocular disease, the potential for useful vision, and the status of the contralateral eye [52, 53]. An algorithm for the treatment of retinoblastoma does not exist. In the decision-making process, it must be kept in mind that patients with advanced intraocular retinoblastoma, massive tumor, and vitreous seeding require

Table 27.2 Reese-Ellsworth Classification of retinoblastoma. *DD* disc diameter

	A	B
I	Solitary tumor <4 DD	Multiple tumors, none >4 DD
II	Solitary tumor, 4–10 DD	Multiple tumors, 4–10 DD
III	Any lesion anterior to equator	Solitary tumor >10 DD
IV	Multiple tumors, some >10 DD	Any lesion anterior to ora serrata
V	Tumor involving 50% of retina	Vitreous seeding

Table 27.3 International classification

Group	Characteristics
A	Small tumors away from foveola and disc
	Tumors < 3 mm
	Located at least 3 mm from foveola and 1.5 mm from the optic disc
B	All remaining tumors confined to the retina
	All other tumors confined to retina not in group A
	Subretinal fluid < 3 mm from the base of tumor
C	Local subretinal fluid or seeding
	Local subretinal fluid alone > 3 to < 6 mm from tumor
	Vitreous seeding or subretinal seeding < 3 mm from the tumor
D	Diffuse subretinal fluid or seeding
	Subretinal fluid alone > 6 mm from tumor
	Vitreous seeding or subretinal seeding > 3 mm from tumor
E	Presence of poor prognosis features
	More than two thirds of globe filled with tumor
	Tumor in anterior segment or ciliary body
	Iris neovascularization, neovascular glaucoma
	Tumor necrosis, phthisis bulbi

prolonged multiagent chemotherapy, focal consolidation, and, most often, external beam radiotherapy. This treatment regimen necessitates not only frequent examination under anesthesia but also multiple doctor appointments to monitor the side effects of chemotherapy. In the end, even with such extensive treatments, eyes with advanced disease are frequently enucleated [79]. Moreover, the extensive treatments can increase the difficulty of the enucleation and impair the cosmetic rehabilitation of the patient [44]. Once a treatment decision is made it may be subsequently modified based on each successive examination under anesthesia. Table 27.4 provides guidelines for scheduling examinations under anesthesia.

27.1.5.1 Enucleation

Enucleation remains the treatment for massive unilateral retinoblastoma (eyes in Reese- Ellsworth group V or in International Classification groups D and E). In patients with unilateral disease, the pros and cons of conservative therapy must be weighed against the pros and cons of enucleation. In developed countries, enucleation in most cases provides definitive treatment. With proper surgical technique, the diseased eye can be removed and a deep orbital implant placed. Later, a prosthetic eye can be fitted to provide an acceptable cosmetic appearance.

Enucleation is best performed by an ophthalmologist skilled in the management of retinoblastoma. Care should be taken to minimize inadvertent perforation of the globe. No traction sutures should be placed on the eye. Rather, the insertion of the medial rectus muscle should be left long (2–3 mm). A hemostat can then be used to grasp the insertion and rotate the eye laterally. Long Metzenbaum scissors can be passed between the eye and the detached medial rectus muscle. Once the optic nerve is identified, it can be cut and the eye removed with gentle traction on the medial rectus insertion. This approach allows the surgeon to obtain a maximum length of optic nerve, usually in excess of 10 mm. As the cut end of the optic nerve represents the margin of tumor resection, it is extremely important to obtain as much nerve as possible.

Table 27.4 Recommended follow up schedule for examinations under anesthesia

Nature of examination	Follow up
Unilateral follow up after enucleation	< 1 year of age every 6 weeks 1–2 years of age every 8 weeks 3–4 years of age every 12 weeks 4–5 years of age every 16 weeks 5 years of age+, awake in clinic yearly
During chemotherapy	Every 3–6 weeks
After focal treatment	3 weeks
Stable examination	6 weeks, progressively lengthening based on disease and age
After external beam radiation	At the completion of treatment 4 weeks thereafter

The need for adjuvant chemotherapy and external beam radiotherapy are considered in those cases with high-risk pathologic features [13, 15, 64, 65]. These include massive deep choroidal invasion, ciliary body and iris involvement, and anterior chamber disease. Extension past the lamina cribrosa alone does not dictate the need for adjuvant chemotherapy provided the subarachnoid space has not been breached. Extraocular extension through the sclera or extension to the cut margin of the optic nerve requires external radiotherapy to the orbit.

27.1.5.2 Focal Treatments

Unilateral retinoblastoma with small discrete tumors may be treated with a combination of lasers, cryotherapy, and plaque brachytherapy, with or without the additive effect of systemic chemotherapy [22, 48]. Tumors posterior to the equator are more easily treated with laser, either argon or diode. The argon laser is used to encircle the tumor with a discrete double row of burns shutting down the tumor's blood supply. Alternatively, the diode laser can be applied directly to the tumor surface. Slow sustained treatment using a continuous delivery system provides hyperthermic therapy to the tumor and is directly cytotoxic. Cryotherapy is typically used to treat tumors anterior to the equator. A trans-scleral triple freeze-thaw is applied. Using direct visualization, the freeze can be seen to engulf the tumor and surrounding vitreous.

For discrete tumors too large to treat with laser or cryotherapy, episcleral plaque brachytherapy can be used [43]. An applicator loaded with one of several radioactive sources (I-125, Ru-106, Pd-103, Co-86) is sutured to the sclera underlying the tumor. Target doses of 40–45 Gy to the tumor apex are prescribed by the radiation oncologists. The plaque is left in place until the target dose is reached. Patients are reexamined 3–4 weeks after focal treatment to ensure the tumor has responded. Further treatment may be needed until the tumor regresses to a flat chorioretinal scar.

27.1.5.3 Chemotherapy

Today, bilateral retinoblastoma, and some cases of early unilateral retinoblastoma, are treated by primary systemic chemotherapy. Chemotherapy reduces the tumor's size (so-called chemoreduction), allowing for later treatment with focal therapies. Single and multiagent systemic chemotherapy using a combination of carboplatin, vincristine, etoposide, teniposide, and cyclosporine have replaced external beam radiotherapy as the primary treatment in these patients [8, 10, 21, 23, 24, 27, 28, 37, 41, 45, 53, 57, 58, 63, 80]. This is due to the increased risk of second tumors and orbital hypoplasia associated with radiation [1]. The goal of treatment in these patients is to retain some vision in one or both eyes while minimizing any risk of metastatic disease.

Chemotherapy typically is administered every 3–4 weeks for a total of 6–8 cycles. During this time, examinations under anesthesia continue to be performed every 3–6 weeks. The ophthalmologists should judge the response of the tumors to the chemotherapy and document the findings. Maximum tumor regression is normally seen after the first 2 cycles of chemotherapy. As the tumors shrink, the ophthalmologists can then apply focal therapies. Lasers, argon and diode, are typically used to treat tumors posterior to the equator. Treatment can be applied to the lesion as a whole or to selective portions of the tumor with suspected residual activity [32]. The diode laser is applied to the tumor surface, providing hyperthermia and a direct cytotoxic effect [56]. Newer models of the argon green laser can also be applied in a continuous mode to the tumor surface. Power settings should be kept low to avoid the liberation of tumor cells into the vitreous cavity. Tumors anterior to the equator are best treated with cryotherapy. As cryotherapy disrupts the blood–retina barrier, it may provide some synergy with chemotherapy in the treatment of vitreous disease by allowing greater diffusion of drugs into the vitreous cavity. For tumors too large to treat with laser or cryotherapy or for localized tumors that progress despite other focal therapies, plaque brachytherapy, as described above, can be used [43, 61].

Eyes with vitreous and subretinal seeds remain the most challenging in treatment of bilateral retinoblastoma [59, 60]. Initially, systemic chemotherapy gains access to the vitreous cavity through the incompetent tumor blood vessels. As the tumor shrinks with each progressive cycle, these vessels diminish and, in turn, so do the concentrations of chemotherapy in the vitreous. Subconjunctival chemotherapy allows a pulsed concentration of chemotherapy to be delivered to the vitreous cavity via scleral diffusion [2, 3]. Carboplatin, 20 mg in 2 ml, is the most commonly used agent to date and will be studied further in upcoming

Children's Oncology Group trials. Meanwhile, newer chemotherapeutic agents such as topotecan are being investigated for periocular delivery [11].

27.1.5.4 Radiation Therapy

External beam radiotherapy remains the gold standard for the treatment of vitreous seeds. For patients with bilateral retinoblastoma who have advanced or recalcitrant vitreous disease, external beam radiotherapy is as essential part of their treatment. External beam radiotherapy is also an important tool in the management of juxtapapillary and juxtafoveal tumors. Laser to tumors adjoining these visually sensitive areas can result in damage to adjacent healthy retina and cause visual loss. External beam radiotherapy is more likely to spare the optic nerve and retina, and preserve maximal vision. A consultation with the radiation oncologists should be made early in treatment if radiotherapy is deemed likely. Discussions should pertain to timing, the dose needed to control the intraocular disease, and potential side effects. Decisions to proceed with external beam radiotherapy should be based on the potential vision of the affected eye as well the vision of the other eye.

Newer methods of radiation such as conformal radiotherapy and intensity-modulated radiotherapy have tightened the field of radiation thereby diminishing exposure to surrounding orbital structures. More encouraging is the potential use of proton beam radiotherapy. The tightly collimated proton beam reduces spread to adjacent tissue and its depth of penetration is more strictly controlled. The long-term results and complications of these newer radiation methods have yet to be fully studied in retinoblastoma patients.

27.1.6 Genetic Testing and Counseling

Genetic counseling and testing are integral parts in the management of retinoblastoma patients and their families. Table 27.5 lists important percentages to remember in counseling a retinoblastoma family. Multiplying these independent variables can approximate an overall risk. For example, the child of a retinoblastoma survivor has a 50% chance of inheriting the *RB1* mutation from his or her parents. In such cases the gene is 90% penetrant, so there is 45% chance that the child will have retinoblastoma. Unilateral retinoblastoma survivors have a 7% risk of having an affected child. Unaffected parents of a child with retinoblastoma have less than a 5% chance of having another child with retinoblastoma. If two children of unaffected parents have retinoblastoma, the next child has a 45% chance of having retinoblastoma, as one parent is an unaffected carrier of the *RB1* mutation.

Genetic testing can better define the likelihood of having affected siblings and offspring. Identifying novel mutations in patients with bilateral retinoblastoma allows the parents to be subsequently screened. If they do not possess the detected mutation the likelihood of having future affected children decreases to less than 1%. Also testing patients with unilateral disease allows those with a germ-line mutation to be detected. This is important not only in counseling the parents regarding future children but in assessing the patient's risk for second cancers. Knowing a patient's exact mutation allows future offspring to be screened in utero or at birth. This in turn can better define the need and timing for screening examinations. As research continues in retinoblastoma and the array of detected mutations increases, it may be become possible to better correlate genotype with phenotype.

27.1.7 Long-term Follow Up

Long-term follow up of retinoblastoma patients is need. Only 5% of retinoblastoma patients will die from retinoblastoma; however, it is approximated that 30% of patients will die from second, third, and

Table 27.5 Important percentages in retinoblastoma genetic counseling

15% chance of an unilateral retinoblastoma patient having an *RB1* mutation
50% chance of inheriting an *RB1* mutation
90% penetrance
10% chance of having the retinoblastoma gene, but being an unaffected carrier
95% accuracy of genetic screening
5% chance of an *RB1* mutation being missed

fourth malignancies [29, 39]. Of these the most feared is the primitive neuroectodermal tumor that arises in the pineal gland, the pinealoblastoma. The association of bilateral retinoblastoma with an asynchronous intracranial tumor is referred to as trilateral retinoblastoma. The median age at diagnosis of trilateral retinoblastoma is 23–48 months, and the interval between the diagnosis of retinoblastoma and the brain tumor is usually more than 20 months. The prognosis for trilateral retinoblastoma is poor with patients dying from disseminated neuroaxis disease within 9 months. Other malignancies vary from osteosarcoma and rhabdomyosarcoma in childhood to lung cancer, bladder cancer, breast cancer, and melanoma in adulthood (Fig. 27.5). Long-term follow up with a pediatrician and/or oncologists is needed. Yearly screening examinations for second cancers should be performed. Diagnostic testing should be symptom directed, and geared toward minimizing cumulative radiation exposure.

For retinoblastoma patients with unilateral disease who undergo primary enucleation, continued surveillance of the remaining eye is needed to assure that no tumors develop. This remains true even in the presence of negative genetic testing as the possibility of a false-negative test exists. Intervals between examinations under anesthesia can be progressively lengthened as the child grows older and eventually transition into yearly office appointments. As for patients with germ-line mutations, close surveillance is needed to monitor the development of new intraocular tumors as well as to assure that the existing intraocular disease is stable or inactive. Intervals between examination under anesthesia can then be progressively lengthened until a thorough examination can be performed in the office. Most experts deem this to occur somewhere between 5 and 7 years of age.

When appropriate, visual rehabilitation may also begin. This can be as simple as prescribing glasses or may require more complex approaches such as patching, cataract surgery, low vision consultations, and dry eye management. The individual needs of each child must be assessed.

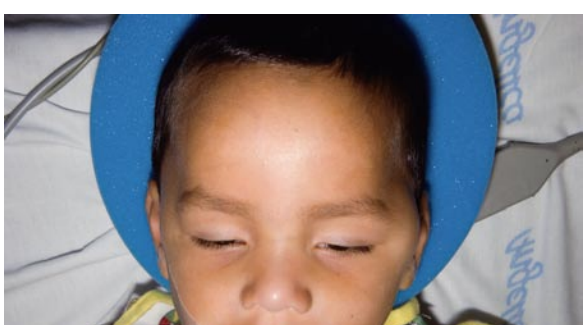

Fig. 27.5 Rhabdomyosarcoma presenting as a left temporal fossa in child with bilateral advanced intraocular retinoblastoma treated with external beam radiotherapy

27.2 Coats' Disease

Coats' disease is a retinal vascular disease of uncertain origin that is most commonly diagnosed in the first decade of life [16, 50]. Boys are eight times more likely than girls to be affected. There is no observed racial predilection. Over 90% of cases are unilateral. In its most advanced form, Coats' disease manifests itself as a complete exudative retinal detachment with prominent telangiectatic vessels. The exudative detachment with underlying cholesterol deposits casts a "white" reflection through the pupil, often leading to an initial diagnosis of retinoblastoma until a more thorough examination and complimentary diagnostic studies can be performed.

Patients with Coats' disease most often present with leukocoria or strabismus. As with retinoblastoma patients, a detailed family and medical history should be taken. Premature birth, systemic infections, and exposure to dogs or sand boxes are essential aspects of the history. A cursory office examination may be performed but a more detail examination under anesthesia is needed to determine an appropriate treatment.

The clinical examination is variable and dependent on the extent of the disease [69]. In early stages of Coats' disease, examination may show only focal areas of retinal telangiectasia anterior to the equator. These so-called telangiectasias have a dilated saccular or bulbar appearance that may be best appreciated on fluorescein angiography. Fluorescein angiography may also show large areas of capillary non-perfusion and arterial-venous shunts (Fig. 27.6a, b). Subretinal exudates with a characteristic mustard appearance may be present. These are cholesterol deposits that have accumulated as a result of the incompetent vasculature. As the disease progresses, the areas of

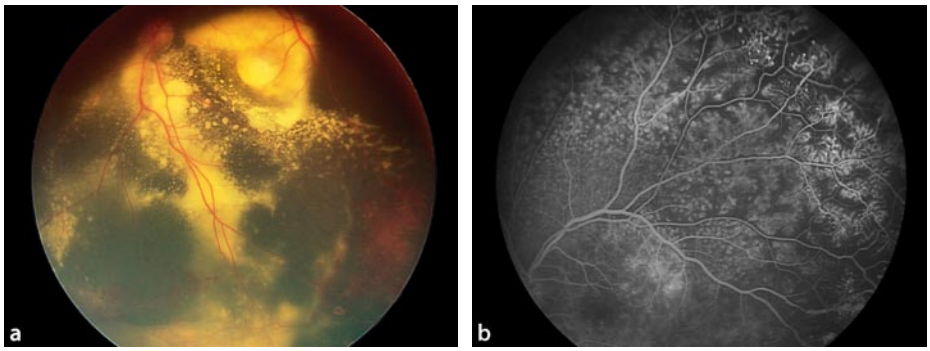

Fig. 27.6 **a** Moderately advanced Coats' disease with yellow subretinal exudates. Abnormal telangiectatic vessels can be seen in the inferior nasal quadrant. **b** Fluorescein angiography better demonstrates the abnormal retinal vessels and profound retinal capillary drop out

abnormal vessels will enlarge and coalesce. Further exudates will leach into the subretinal space causing a progressive retinal detachment as well as an overlying cystic retinal degeneration. Patches of retinal pigment epithelium may be seen on the posterior surface of the detached retina. In advanced cases iris neovascularization may develop with associated ectropion uvea and glaucoma.

Pathology shows irregular dilated retinal blood vessels [12]. There is thickening and hyalinization of the vessel walls with focal areas of necrosis. The vessel endothelium is attenuated. Cholesterol crystals appear as negative images in the subretinal exudate [31]. Both intraretinal hemorrhage and cystic degeneration may be seen. Studies have linked Coats' disease to somatic mutation in the NDP gene, postulating a role for norrin in retinal angiogenesis [9].

Ultrasound of an eye with Coats' disease mirrors the clinical findings. In early cases, low-lying shallow retinal detachments may be detected. More severe cases show a total exudative detachment with marked retinal thickening. Convection of the cholesterol in the subretinal space can also be appreciated. In contrast to an eye with advanced exophytic retinoblastoma no subretinal mass will be seen. Only in very advanced cases of Coats' disease with osseous metaplasia of the retinal pigment epithelium will intraocular calcifications be seen. This will appear as a thin linear mass that conforms to the globe. In differentiating Coats' disease from retinoblastoma, computed tomography is helpful in excluding the presence of intraocular calcification. T1-weighted images on magnetic resonance imaging show hyperintense subretinal fluid [19, 20]. Gadolinium delineates the thickened detached retina but does not reveal a tumor mass. Rarely, there are eyes in which retinoblastoma cannot be excluded. Given the severe consequences of spreading extraocular disease with attempted surgery, these eyes are best enucleated.

Treatment for Coats' disease is based on the severity of disease [70, 82]. In early cases, laser photocoagulation or cryotherapy to the focal areas of abnormal vessels may suffice. More advanced cases require drainage of the subretinal fluid in addition to laser photocoagulation and cryotherapy. Multiple treatment sessions may be needed. Eyes with advanced disease such as neovascular glaucoma may be best enucleated.

27.3 Persistent Fetal Vasculature (Primary Hyperplastic Primary Vitreous)

Persistent fetal vasculature (PFV), formerly known as persistent hyperplastic primary vitreous (PHPV) is the entity most commonly mistaken for retinoblastoma [34, 68]. PFV is a congenital anomaly, most often affecting only one eye [26, 49]. The exact etiology of PFV is not known. Clinical studies have linked some cases of PFV to mutations in the Norrie disease gene, located on the short arm of chromo-

some X at position p11.4 [81]. Such mutations have also been linked to an array of other pediatric vitreoretinopathies including retinopathy of prematurity, Coats' disease, and familial exudative vitreoretinopathy. Newer research has linked PFV to somatic mutations in the *arf* tumor suppressor gene in a murine model [73].

Persistent fetal vasculature can easily be differentiated from retinoblastoma based on history and clinical examination. PFV typically presents shortly after birth when the parents or pediatrician notice a small eye with a white pupil. The smaller eye of PFV stands in contrast to normal-sized eyes with retinoblastoma and Coats' disease. If not clearly evident, the suspicion of a smaller eye can be confirmed by measuring both the horizontal corneal diameters and the axial length of the eye on ultrasound. Anterior chamber depth is variable and dependent on the severity of the disease. More advanced cases have shallow anterior chambers with hypoplastic irides and prominent radial stromal vessels. In such cases there maybe a marked increase in the intraocular pressure. The hallmark of PFV is a prominent fibrovascular plaque that invades the posterior lens capsule accounting for the noted leukocoria. This fibrovascular plaque represents the anterior extent of the persistent hyaloid artery. The posterior fibrovascular proliferation may detach both the ciliary body and the retina (Fig. 27.7). The ciliary body detachment is appreciated clinically as anteriorly rotated ciliary processes present in the visual axis [30]. The tractional retinal detachment may not be noted clinically due to the cataract. Ultrasound is best for confirming the suspected retinal detachment.

On ultrasound, the eye with PFV will appear smaller. The lens is thin with an irregular posterior surface. The retrolental membrane connects to a prominent vitreous strand that connects posteriorly to the optic nerve head. The vitreous strand represents the persistent hyaloid artery and is of variable width. Thickened strands are those that incorporate varying degrees of retinal detachment. In contrast to retinoblastoma, intraocular calcifications are rarely present and there are no subretinal masses. Both computed tomography and magnetic resonance imaging can be used to compliment the ultrasound findings [19, 20].

Management of PFV is dependent on the extent of the disease [35]. The goal of surgery is to create a clear visual axis and release vitreoretinal traction. Eyes with marked fibrovascular proliferation and a complete tractional retinal detachment have a poor visual potential. Surgical success is limited by the difficulty in freeing the retina from the fibrovascular adhesions [17]. The pros and cons of surgical intervention should be discussed with the family.

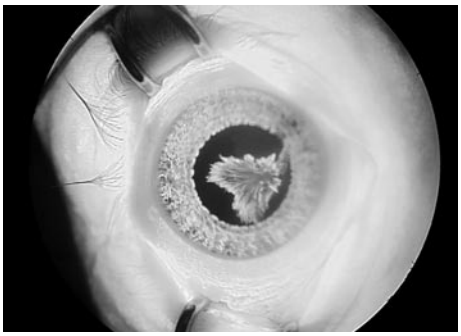

Fig. 27.7 Fluorescein angiogram of an eye with persistent fetal vasculature. Note the prominent retrolental fibrovascular membrane

27.4 Medulloepithelioma

Medulloepithelioma, or diktyoma, is a tumor that arises from primitive medullary epithelium. Most commonly they arise from the non-pigmented epithelium of the ciliary body. Medulloepitheliomas appear as variably pigmented masses that may compress or displace the lens (Fig. 27.8). The lesion may erode through the iris root to extend into the anterior chamber. Cystic spaces may be seen on the tumor's surface. Medulloepitheliomas may also arise from the retina or optic nerve [14]. The diagnosis is usually made in the first decade of life between the ages of 4 and 12 years. Presenting signs and symptoms include leukocoria, strabismus, decreased vision, and neovascular glaucoma.

Ultrasound and magnetic resonance imaging are complimentary diagnostic modalities [6, 74]. Both studies may show intralesional cystic structures. Discernable areas of calcification within the tumor should not be present.

Medulloepitheliomas are classified as non-teratoid and teratoid, and may be benign or malignant. Non-teratoid variants are composed of multilayered sheets of poorly differentiated medullary epithelial cells

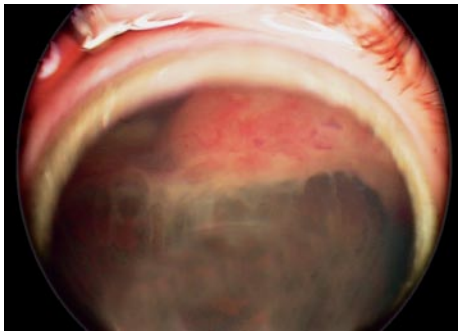

Fig. 27.8 Medulloepithelioma of the ciliary body. The tumor is variably pigmented and displaces the lens. Portions of the tumor extend into the overlying vitreous cavity

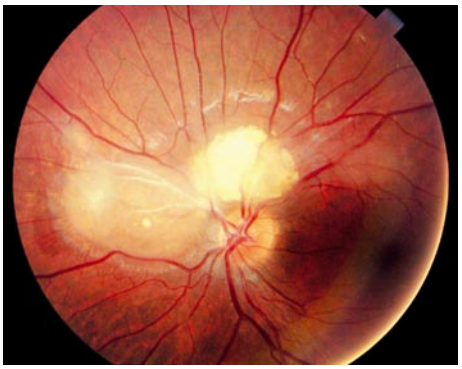

Fig. 27.9 Juxtapapillary astrocytic hamartomas in a patient with tuberous sclerosis. Note the variable appearance of the lesion, the nasalmost lesion being translucent and the superior lesion being calcified with a "mulberry" appearance

arranged in tubular or papillary structures. Homer-Wright rosettes may be present. Teratoid medulloepitheliomas contain heteroplastic tissue elements such as cartilage, muscle, and nerve. Differentiating benign from malignant tumors can be challenging. Increased mitotic rate, increased nuclear pleomorphism, poorly differentiated heteroplastic cells, and invasion of the ocular coats suggest malignancy.

Management of medulloepitheliomas includes observation, enucleation, radiation, and resection. As these are exceedingly rare tumors and most lesions are detected late, enucleation is the mainstay of treatment. Isolated cases reporting the use of episcleral brachytherapy have been published, as have cases of tumor resection [18]. Treatments strategies should be formulated based on tumor size, visual potential, and status of the contralateral eye.

27.5 Astrocytic Hamartoma

Astrocytic hamartomas are benign tumors of the retina and optic nerve typically associated with tuberosis sclerosis. Astrocytic hamartomas may also be associated with neurofibromatosis or acquired independent of a systemic disease. Astrocytic hamartomas arise from undifferentiated glioneurocytes within the developing retina. Mutations in the *TSC1* and *TSC2* genes, which express hamartin and tuberin, respectively, are thought to interrupt cell growth regulation leading to tumor formation [36, 75].

Tumors are normally detected in childhood as part of a screening process for tuberosis sclerosis or neurofibromatosis [46]. However, some patients may present as adults with metamorphosis from acquired astrocytic hamartomas that encroach on the fovea or leak subretinal fluid into the macula. On clinical examination, astrocytic hamartomas have a variable appearance, ranging from minimally elevated translucent lesions to large, elevated, multinodular calcified masses with a so-called mulberry appearance (Fig. 27.9). Multiple tumors may be present and can be observed to grow and calcify over time. Ultrasound confirms the presence of intraocular calcifications while fluorescein angiograms will show leakage into the subretinal space in the later phases.

Lesions detected in the absence of tuberosis sclerosis or neurofibromatosis may be difficult to differentiate from retinoblastoma [51]. A careful systemic examination may reveal previously undetected stigmata of tuberosis sclerosis: ash leaf spots, periungual fibromas, or adenoma sebaceum of the face [76, 78]. Internal examination including an echocardiogram and neuroimage may show tubers affecting the heart or periventricular gray matter. The patient should also be examined for the presence of café-au-lait spots, typical of neurofibromatosis.

In rare cases biopsy may be needed to confirm the diagnosis. Management most often consists of close

observation. In cases where the tumor growth threatens vision, episcleral brachytherapy may be used [66, 67]. Reports of giant astrocytomas within the eye are rare [42]. Such tumors frequently result in enucleation of the eye as the diagnosis of retinoblastoma cannot be excluded.

27.6 Toxocariasis

Toxocara canis is the dog parasite that is acquired via fecal–oral transmission [71, 72]. *Toxocara* is more common in puppies. A history of dogs or sandbox exposures should be specifically asked for when considering the diagnosis. Inside the eye, *Toxocara* causes choroidal granulomas with associated vitritis [55]. Granulomas are more often found in the peripheral choroid, but may be found in the posterior pole and peripapillary choroid. The inflammation may cause vitreous membranes and tractional retinal detachments. The diagnosis can be confirmed by testing the patient's blood or aqueous for anti-*Toxocara* IgG antibodies.

Patients typically present with leukocoria, strabismus, or decreased vision. Rarely, they may present with an incidental peripheral choroidal mass on routine eye examination. Acute *Toxocara* may be treated with albendazole and systemic corticosteroids [7]. Quiescent lesions with associated vitreous membranes may require vitrectomy to repair associated tractional retinal detachments.

27.7 Juvenile Xanthogranuloma

Juvenile xanthogranuloma (JXG) is a self-limiting, systemic disease of childhood that manifests as multiple cutaneous reddish papules of the head, neck, trunk, and upper extremities [5, 33]. Lesions are composed of non-caseating granulomas with prominent Touton giant cells. Ocular tumors most commonly present as unilateral infiltrative lesions of the iris. A yellowish cast may be imparted to the mass. The cornea, ciliary body, retina, and optic nerve may rarely be affected [14, 74, 77, 83]. The iris lesions are exceedingly well vascularized, and may bleed spontaneously causing a hyphema and secondary glaucoma.

The diagnosis of JXG is most commonly confirmed by biopsy of a skin lesion. JXG responds exceedingly well to systemic, topical, and periocular corticosteroids. If no skin lesions are present, fine-needle aspiration biopsy of the iris tumor may prove diagnostic. Hemorrhaging, hyphema, and glaucoma are expected complications in such cases. Alternatively, a trial of systemic or oral corticosteroids can be tried under close observation. If there is no response, a biopsy should be undertaken before continuing a protracted course of corticosteroids. In the presence of a hyphema with an impaired view of the retina, it is important to exclude the diagnosis of retinoblastoma using appropriate diagnostic testing before attempting an iris biopsy [25].

27.8 Leukemia

Leukemia is the most common type of pediatric cancer. The two primary pediatric leukemias are acute lymphocytic leukemia (ALL) and acute myelogenous leukemia (AML). ALL is the most commonly diagnosed malignancy in patients under 15 years of age. The peak incidence of ALL occurs before 6 years of age. ALL is derived from a B- or T-lymphocyte progenitor cell. AML accounts for 15–20% of the pediatric leukemias, and is the most common neonatal and congenital leukemia. AML arises from a pluripotent progenitor cell capable of undergoing erythroid, megakaryocytic, or granulocytic differentiation. The eye is a sanctuary site where leukemic cells can be sequestered from the effects of systemic chemotherapy. As a result, ocular involvement may be the first signs of an extramedullary relapse.

Estimates are that anywhere from 30–90% of patients with leukemia will have ocular manifestations [38, 40]. Patients may be asymptomatic or have complaints of blurred or decreased vision. Clinically, the retina is the most commonly affected intraocular structure. Leukemic retinopathy is characterized by intraretinal and subhyaloidal hemorrhages, cotton wool spots and "pseudo-Roth" spots, and white-centered intraretinal hemorrhages caused by leukemic cells or platelet-fibrin aggregates [54]. A combination of underlying anemia, hyperviscosity, and thrombocytopenia contribute to the findings. Subhyaloidal hemorrhages may break through into the vitreous

Take Home Pearls

- Leukocoria has a vast differential diagnosis of which retinoblastoma is the most feared.
- Intraocular calcifications are the hallmark of retinoblastoma.
- Coats' disease, persistent fetal vasculature, and toxocariasis are the most common pseudoretinoblastomas.
- Astrocytic hamartomas, medulloepitheliomas, and juvenile xanthogranuloma are other intraocular tumors that may mimic retinoblastoma.
- The eye acts as a sanctuary for acute lymphocytic leukemia (ALL); ocular involvement may be the first sign of an extramedullary relapse.

cavity mimicking vitreous involvement. Vitreous infiltration is exceedingly rare. Any leukemic cells found in the vitreous cavity are more likely due to hemorrhage than direct invasion.

Involvement of the iris and anterior chamber is rare, and more commonly seen in patients with ALL. Examination may show diffuse thickening of the iris with loss of normal iris crypts. Comparison with the other iris may be needed to appreciate subtle differences in architecture. Alternatively, there may be a focal area of nodular thickening in the iris. Tumor cells can also directly invade the anterior chamber producing a pseudohypopyon. Involvement of the trabecular meshwork can cause a secondary glaucoma. Infiltration of the choroid is rarely detected clinically, but is the most common histologic finding. Perivascular infiltrates can cause diffuse or patchy choroidal thickening.

Leukemic involvement of the optic nerve is a hallmark of central nervous system disease. The leukemic cells may invade both the prelaminar and retrobulbar portions of the optic nerve. The former appears as an edematous, hemorrhagic nerve. Visual acuity may be preserved. Retrobulbar infiltrates are more apt to compress the nerve resulting in visual loss. Optic nerve edema may also arise from raised intracranial pressure related to the central nervous system disease. When ophthalmic disease is detected, central nervous disease must be excluded. The eyes are treated either alone with radiation or in conjunction with intrathecal chemotherapy and craniospinal radiation for central nervous system disease elsewhere.

References

1. Abramson DH, Frank CM (1998) Second monocular tumors in survivors of bilateral retinoblastoma: a possible age effect on radiation-related risk. Ophthalmology 105:573–579
2 Abramson DH, Frank CM, Chantada GL, et al. (1999) Intraocular carboplatin concentrations following intravenous administration for human intraocular retinoblastoma. Ophthalmic Genet 20:31–36
3. Abramson DH, Frank CM, Dunkle IJ (1999) A phase I/II study of subconjunctival carboplatin for intraocular retinoblastoma. Ophthalmology 106:1947–1950
4. American Joint Commission on Cancer Definitions and Staging of Ocular Tumors, 2002
5. Ashmore ED, Wilson MW, Morris WR et al. (2003) Corneal juvenile xanthogranuloma in a 4-month-old child. Arch Ophthalmol 2003;121:117–118
6. Ayers B, Brasil OM, Klejnberg C, et al. (2006) Ciliary body medulloepithelioma: clinical, ultrasound biomicroscopic and histopathologic correlation. Clin Exp Ophthalmol 34:695–698
7. Barisani-Asenbauer T, Maca SM, Hauff W, et al. (2001) Treatment of ocular toxocariasis with albendazole. J Ocul Pharmacol Ther 17:287–294
8. Beck MN, Balmer A, Dessing C, et al. (2000) First-line chemotherapy with local treatment can prevent external-beam irradiation and enucleation in low-stage intraocular retinoblastoma. J Clin Oncol 18:2881–2887
9. Black GC, Perveen R, Bonshek R, et al. (1999) Coats' disease of the retina (unilateral retinal telangiectasis) caused by a somatic mutation in the NDP gene: a role for norrin in the retinal angiogenesis. Hum Mol Genet 8:2031–2035
10. Brichard B, Brucycker JJ, DePotter P, et al. (2002) Combined chemotherapy and local treatment in the management of intraocular retinoblastoma. Med Pediatr Oncol 38:411–415
11. Carcaboso AM, Bramuglia GF, Chantada GL, et al. (2007) Topotecan vitreous levels after periocular or intravenous

delivery in rabbits: an alternative for retinoblastoma chemotherapy. Invest Ophthalmol Vis Sci 48:3761–3767
12. Chang MM, McLean IW, Merritt JC (1984) Coats' disease: a study of 62 histologically confirmed cases. J Pediatr Ophthalmol Strabismus21:163–168
13. Chantada GL, Dunkel IJ, Antoneli CB, et al. (2007) Risk factors for extraocular relapse following enucleation after failure of chemoreduction in retinoblastoma. Pediatr Blood Cancer 49:256–260
14. Chavez M, Mafee MF, Castillo B, et al. (2004) Medulloepithelioma of the optic nerve. J Pediatr Ophthalmol Strabismus 41:48–52
15. Chong EM, Coffee RE, Chintagumpala M, et al. (2006) Extensively necrotic retinoblastoma is associated with high-risk prognostic factors. Arch Pathol Lab Med 130:1669–1672
16. Coats G (1908) Forms of retinal disease with massive exudation. R Lond Ophthalm Hosp Rep 17:440–525
17. Dass AB, Trese MT (1999) Surgical results of persistent hyperplastic primary vitreous. Ophthalmology 106:280–284
18. Davidorf FH, Craig E, Birnbaum L, Wakely P Jr (2002) Management of medulloepithelioma of the ciliary body with brachytherapy. Am J Ophthalmol 13:841–843
19. De Potter P, Flanders AE, Shields JA et al. (1994) The role of fat-suppression technique and gadopentetate dimeglumine in magnetic resonance imaging evaluation of intraocular tumors and simulation lesions. Arch Ophthalmol 112:340–348
20. De Potter P, Shields CL, Shields JA, Flanders AE (1996) The role of magnetic resonance imaging in children with intraocular tumors and simulating lesions. Ophthalmology 103:1774–1783
21. Dunkel IJ, Lee TC, Shi W, et al. (2007) A phase II clinical trial of carboplatin for intraocular retinoblastoma. Pediatri Blood Cancer 49:643–648
22. Ellsworth RM (1969) Practical management of retinoblastoma. Trans Am Ophthalmol Soc 67:464–534
23. Friedman DL, Himelstein B, Shields CL, et al. (2000) Chemoreduction and local ophthalmic therapy for intraocular retinoblastoma. J Clin Oncol 18:12–17
24. Gallie BL, Budning A, DeBoer G, et al. (1996) Chemotherapy with focal therapy can cure intraocular retinoblastoma without radiotherapy. Arch Ophthalmol 114:1321–1328
25. Gass JD (1964) Management of juvenile xanthogranuloma of the iris. Arch Ophthalmol 71:344–347
26. Goldberg MF (1997) Persistent fetal vasculature (PFV): an integrated interpretation of signs and symptoms associated with persistent hyperplastic primary vitreous (PHPV). Am J Ophthalmol 124:587–626
27. Gombos DS, Kelly A, Coen PG, et al. (2002) Retinoblastoma treated with primary chemotherapy alone: the significance of tumor size, location and age. Br J Ophthalmol 86:80–83
28. Greenwald MJ, Strauss LC (1996) Treatment of intraocular retinoblastoma with carboplatin and etoposide with retinoblastoma. Ophthalmology 103:1989–1997
29. Guerin S, Hawkins M, Shamsaldin A et al. (2007) Treatment-adjusted predisposition to second malignant neoplasms after a solid cancer in childhood: a case-control study. J Clin Oncol 25:2833–2839
30. Haddad R, Font RL, Reeser F (1978) Persistent hyperplastic primary vitreous. A clinicopathologic study of 62 cases and review of the literature. Surv Ophthalmol 23:123–134
31. Haik BG, Koizumi J, Smith ME, Ellsworth RM (1985) Fresh preparation of subretinal fluid aspirations in Coats' disease. Am J Ophthalmol 100:327–328
32. Hamel P, Heon E, Gallie BL, Budning AS (2000) Focal therapy in the management of retinoblastoma: when to start and when to stop. J AAPOS 4:334–337
33. Harley RD, Romayananda N, Chan GH (1982) Juvenile xanthogranuloma. J Pediatr Ophthalmol Strabismus 19:33–39
34. Howard GM, Ellsworth RM (1965) Differential diagnosis of retinoblastoma. A statistical survey of 500 children. I: Relative frequency of lesions that simulate retinoblastoma. Am J Ophthalmol 60:610–618
35. Hunt A, Rowe N, Lam A, Martin F (2005) Outcomes in persistent hyperplastic primary vitreous. Br J Ophhtalmol 89:859–863
36. Johnson MW, Kerfoot C, Bushnell T, et al. (2001) Hamartin and tuberin expression in human tissues. Mod Pathol 14:202–210
37. Kingston JE, Hungerford JL, Madreperla SA, Plowman PN (1996) Results of combined chemotherapy and radiotherapy for advanced intraocular retinoblastoma. Arch Ophthalmol 114:1339–1343
38. Kinkaid MC, Green WR (1983) Ocular and orbital involvement in leukemia. A review. Surv Ophthalmol 27:211–232
39. Kleinerman RA, Tucker MA, Abramson DH, et al. (2007) Risk of soft tissue sarcomas by individual subtype in survivors of hereditary retinoblastoma. J Natl Caner Inst 99:24–31
40. Leonardy NJ, Rupani M, Dent G, Klintworth GK (1990) Analysis of 135 autopsy eyes for ocular involvement of leukemia. Am J Ophthalmol 109:436–444
41. Lumbroso L, Doz F, Levy C, et al. (2003) [Diode laser thermotherapy and chemothermotherapy in the treatment of retinoblastoma.] J Fr Ophthalmol 26:154–159
42. Margo CE, Barletta JP, Staman JA (1993) Giant cell astrocytoma of the retina in tuberous sclerosis. Retina 13:155–159
43. Merchant TE, Gould CJ, Wilson MW, et al. (2004) Episcleral plaque brachytherapy for retinoblastoma. Pediatr Blood Cancer 43:134–139
44. Mulvihill A, Budning A, Jay V, et al. (2003) Ocular motility changes after subtenon carboplatin chemotherapy for retinoblastoma. Arch Ophthalmol 121:1120–1124
45. Murphree AL, Villablanca JG, Deegan WF, et al. (1996) Chemotherapy plus local treatment in the management of intraocular retinoblastoma. Arch Ophthalmol 114:1348–1356
46. Nyboer JH, Robertson DM, Gomez MR (1976) Retinal lesions in tuberosis sclerosis. Arch Ophthalmol 94:1277–1280

47. Pratt CB, Fontanesi J, Lu X et al. (1997) Proposal for a new staging scheme for intraocular and extraocular retinoblastoma based on an analysis of 103 globes. Oncologist 2:1–5
48. Reese A (1963) Retinoblastoma. In: Reese A Tumors of the eye. Harper and Row, New York
49. Reese AB (1995) Persistence and hyperplasia of the primary vitreous: The Jackson Memorial Lecture. Am J Ophthalmol 40:317–331
50. Reese AB (1956) Telangiectasis of the retina and Coats' disease. Am J Ophthalmol 42:1–8
51. Reeser FH, Aaberg TM, Van Horn DL (1978) Astrocytic hamartoma of the retina not associated with tuberous sclerosis. Am J Ophthalmol 86:699–698
52. Rodriguez-Galindo C, Chantada GL, Haik BG, Wilson MW (2007) Treatment of retinoblastoma: current status and future directions. Curr Treat Options Neurol 9:294–307
53. Rodriguez-Galindo C, Wilson MW, Haik BG, et al. (2003) Treatment of intraocular retinoblastoma with vincristine and carboplatin. J Clin Oncol 21:2019–2025
54. Rosenthal AR (1983) Ocular manifestations of leukemia. A review. Ophthalmology 90:899–905
55. Sabrosa NA, de Souza EC (2001) Nematode infections of the eye: toxocariasis and diffuse unilateral subacute neuroretinitis. Curr Opin Ophthalmol 12:450–454
56. Schueler AO, Jurklies C, Heimann H, et al. (2003) Thermochemotherapy in retinoblastoma. Br J Ophthalmol 87:90–95
57. Shields CL, De Potter P, Himelstein B, et al. (1996) Chemoreduction in the initial management of intraocular retinoblastoma. Arch Ophthalmol 114:1330–1338
58. Shields CL, Honavar SG, Meadows AT, et al. (2002) Chemoreduction for unilateral retinoblastoma. Arch Ophthalmol 120:1653–1658
59. Shields CL, Honavar SG, Meadows AT, et al. (2002) Chemoreduction plus focal therapy for retinoblastoma: factors predictive of need for treatment with external beam radiotherapy and enucleation. Am J Ophthalmol 133:657–664
60. Shields CL, Honavar SG, Shields JA, et al. (2002) Factors predictive of recurrence of retinal tumors, vitreous seeds, and subretinal seeds following chemoreduction for retinoblastoma. Arch Ophthalmol 120:460–464
61. Shields CL, Mashayekhi A, Sun H, et al. (2006) Iodine-125 plaque radiotherapy as salvage treatment for retinoblastoma recurrence after chemoreduction in 84 patients. Ophthalmology 113:2087–2092
62. Shields CL, Mashayekhi A, Au Ak, et al. (2006) The international classification of retinoblastoma predicts chemoreduction success. Ophthalmology 113:2276–2280
63. Shields CL, Shields JL, Needle M, et al. (1997) Combined chemoreduction and adjuvant treatment for intraocular retinoblastoma. Ophthalmology 104:2101–2111
64. Shields CL, Shields JA, Baez KA, et al. (1993) Choroidal invasion of retinoblastoma: metastatic potential and clinical risk factors. Br J Ophthalmol 77:544–548
65. Shields CL, Shields JA, Baez KA, et al. (1994) Optic nerve invasion of retinoblastoma: metastatic potential and clinical risk factors. Cancer 73:692–698
66. Shields CL, Shields JA, Eagle RC Jr, et al. (2004) Progressive enlargement of acquired astrocytoma in 2 cases. Ophthalmology 111:363–368
67. Shields JA, Eagle RC, Shields CL, et al. (2005) Aggressive retinal astrocytoma in 4 patients with tuberous sclerosis complex. Arch Ophthalmol 123:856–863
68. Shields JA, Parsons HM, Shields CL (1991) Lesions simulating retinoblastoma. J Pediatr Ophthalmol Strabismus 28:338–340
69. Shields JA, Shields CL (2001) Differentiation of Coats' disease and retinoblastoma. J Pediatr Ophthalmol Strabismus 38:262–266
70. Shields JA, Shields CL, Honavar SG, et al. (2001) Classification and management of Coats' disease: the 2000 Proctor Lecture. Am J Ophthalmol 131:572–583
71. Stewart JM, Cubillan LD, Cunningham ET Jr (2005) Prevalence, clinical features, and causes of vision loss among patients with ocular toxocariasis. Retina 25:1005–1013
72. Taylor MR (2001) The epidemiology of ocular toxocariasis. J Helminthol 75:119–124
73. Thorton JD, Swanson DJ, Mary MN, et al. (2007) Persistent hyperplastic primary vitreous due to somatic mosaic deletion of the arf tumor suppressor. Invest Ophthalmol Vis Sci 48:491–499
74. Vajaranant TS, Mafee MF, Kapur R, et al. (2005) Medulloepithelioma of the ciliary body and optic nerve: clinicopathologic, CT, and MR imaging features. Neuroimaging Clin N Am 15:69–83
75. Van Siegtenhorst M, Nellist M, Nagelkerken B, et al. (1998) Interaction between hamartin and tuberin, the TSC1 ad TSC2 gene products. Hum Mol Genet 7:1053–1057
76. Walsh MN, Koch FLP, Brunsting HA (1938) Syndrome of tuberous sclerosis, retinal tumors, and adenoma sebaceum: a report of a case. Mayo Clin Proc 13:155–160
77. Wertz FD, Zimmerman LE, Mc Keown CA, et al. (1982) Juvenile xanthogranuloma of the optic nerve, disc, retina, and choroid. Ophthalmology 89:1331–1335
78. Williams R, Taylor D (1985) Tuberous sclerosis. Surv Ophthalmol 30:143–154
79. Wilson MW, Haik BG, Rodriguez-Galindo C (2006) Socioeconomic impact of modern multidisciplinary management of retinoblastoma. Pediatrics 118;e331–e336
80. Wilson MW, Rodriguez-Galindo C, Haik BG, et al. (2001) Multiagent chemotherapy as neoadjuvant treatment for multifocal intraocular retinoblastoma. Ophthalmology 108:2106–2115
81. Wu WC, Drenser K, Trese M, et al. (2007) Retinal phenotype-genotype correlation of pediatric patients expressing mutations in the Norrie disease gene. Arch Ophthlmol 125:225–230
82. Yoshizumi MO, Kreiger AR, Lewis H, et al. (1995) Vitrectomy techniques in late Coats'-like exudative detachment. Doc Ophthalmol 90:387–394
83. Zimmerman LE (1965) Ocular juvenile xanthogranuloma. Nevoxanthoendothelioma. Am J Ophthalmol 60:1011–1035

The Challenges of Pediatric Uveitis

John D. Sheppard, Jeffrey Davis and Avi Meier

28

Contents

Core Messages

- A causative diagnosis is essential to proper treatment.
- There may be more than one etiology.
- There is often corollary pathology: glaucoma, synechiae, cataract, and macular edema.
- Elimination of all inflammation is the cornerstone of therapy.
- Infection should be treated prior to or simultaneous to anti-inflammatory treatment.
- Maintenance therapy, when indicated, should be minimally sufficient.
- Eyes must be completely quiet for 6 months prior to elective surgery.

28.1 Pediatric Inflammatory Disease Presents Unique Diagnostic and Therapeutic Challenges

Chronic and acute ocular inflammation can take a particularly severe toll on young patients, due both to their highly efficient immune response as well as the many potential years of inflammatory damage

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ahead. These patients require aggressive treatment and examination schedules as well as the undivided loyalty of their parents and guardians. Enlisting the assistance of pediatricians and pediatric rheumatologists is logical from a risk management as well as a patient care perspective.

Children with ocular inflammatory disease present the clinician with both diagnostic dilemmas and a requirement for treatments specifically tailored to pediatric metabolism. The patients are often poor historians. Parents are generally extremely anxious about a condition they poorly understand. Examinations are difficult, consume inordinate amounts of clinic time, and often necessitate a trip to the operating room for an examination under anesthesia. The differential diagnosis for children is significantly divergent from the adult population. Medication responses are different and require far more careful attention to dosage than an adult: young patients are truly not just smaller adults. Nevertheless, the general principles of diagnosis and care are consistent across all age ranges:

1. A causative diagnosis is essential to proper treatment.
2. There may be more than one etiology.
3. There is often corollary pathology: glaucoma, synechiae, cataract and macular edema.
4. Elimination of all inflammation is the cornerstone of therapy.
5. Infection should be treated prior to or simultaneous to anti-inflammatory treatment.
6. Maintenance therapy, when indicated, should be minimally sufficient.
7. Eyes must be completely quiet for 6 months prior to elective surgery.

There are exceptions to every rule. Fuchs' uveitis syndrome may never become completely quiet, yet patients fare well in the long term with minimized but not eliminated anterior chamber cell. Similarly Fuchs' patients usually do well with cataract surgery in their desired state of minimized rather than eliminated inflammation. Toxocara uveitis is another exception in that treatment of the infectious agent with antimicrobials can result in massive organism death and an overwhelming inflammatory response to the sudden hurricane of dead foreign antigen.

Uveitis in the pediatric population has a prevalence much lower than the adult population. Uveitis in this age group (less than 16 years of age) is relatively uncommon with a yearly incidence of 4.3–6 in 100,000 population [13, 22, 28, 45]. The prevalence has been shown to be 30 cases per 100,000 [13, 28, 45]. Children account for 5–10% of all uveitis cases seen in the tertiary care setting [46]. Historically posterior uveitis accounts for 40–50% of pediatric uveitis cases, anterior uveitis 30–40%, intermediate uveitis 20%, and panuveitis 10%. However, these numbers arise from studies conducted at tertiary care hospitals. Other population-based studies [22, 45] have suggested that anterior segment uveitis is more common in ages 0–7 years and posterior uveitis is more prevalent in ages 8–15 years. Nonetheless, pediatric uveitis as a whole has a disproportionate prevalence of posterior uveitis when compared to adult uveitis (Table 28.1). This portends a less favorable prognosis in general. The etiology depends on a wide variety of factors, including the age at presentation and previous risk factors for exposure to infectious agents (Table 28.2).

Table 28.1 Most common causes of pediatric uveitis

Adolescents	Toddlers and school children	Infants
Juvenile rheumatoid arthritis (JRA) or juvenile idiopathic arthritis (JIA)	Toxocariasis	Herpes simplex virus (HSV)
Pars planitis	Toxoplasmosis	Toxocara
Vogt-Koyanagi-Harada (VKH) syndrome	Leukemia	Congenital lues (syphilis)
Toxoplasmosis	Vogt-Koyanagi Harada (VKH) syndrome	Retinoblastoma
HLA-B27-associated disease and reactive arthritis	Diffuse unilateral sclerosing neuroretinitis (DUSN)	
Sarcoidosis	Juvenile rheumatoid arthritis (JRA)	
Behçet's disease		
Intraocular foreign body		

The incidence is about 2,250 new cases per year in the USA with a prevalence of as many as 115,000 cases [24]. Thus, with over 18,000 ophthalmologists in the USA, it is exceedingly unlikely that any one practitioner will see a significant number of cases, nor develop appreciable expertise without a concentrated effort to create a dedicated pediatric uveitis service. We find in our clinic that the greatest oversight in pediatric uveitis is undertreatment of the inflammation, both locally and systemically, for fear of creating medication-induced complications. Just the opposite is true, in that adequate treatment allows a lifetime of vision, and systemic therapy often mitigates the ravages of accompanying systemic disease.

Diagnostic challenges continuously haunt the clinician tasked with pediatric uveitis cases. Assessing visual acuity and obtaining a proper history of present illness is hindered by non-verbal patients. Examination of children in the office creates commotion, the often obligatory elimination of stereotyped white laboratory garb for the primary examiner, dancing mechanical teddy bears, bribery scenarios, foolish facial gestures with infantile mouth noises, and the recruitment of friends, siblings, staff, and parents for cooperation. The office examination is often reduced to gross analysis by external examination, digital palpation, and a handheld magnifier, retinoscope, or indirect ophthalmoscope. Slit-lamp observation often

Table 28.2 Etiology of pediatric uveitis. There are a few categories with extremely rare forms of uveitis. After the diagnostic evaluation and naming step, the most common etiologic groups in children can be conveniently meshed into a differential diagnosis from five key categories as shown

Category 1 (anterior non-granulomatous)
Idiopathic
HLA-B27-associated disease:
1. Ankylosing spondylitis
2. Reiter's disease
3. Psoriasis
4. Inflammatory bowel disease: reactive arthritis
Juvenile rheumatoid arthritis (JRA) or juvenile idiopathic arthritis (JIA)
Nephritis
Systemic lupus erythematosus
Herpes simplex virus
Lyme disease
Leukemia
Drug and medication induced

Category 2 (anterior granulomatous uveitis)
Sarcoidosis
Inflammatory bowel disease: Crohn's disease and ulcerative colitis
Lues (syphilis)
Herpes simplex virus (HSV)
Herpes zoster virus (HZV) or varicella-zoster virus (VZV)
Tuberculosis
Behçet's disease
Multiple sclerosis
Fungal disease
Whipple's disease
Leprosy

Category 3 (intermediate uveitis)
JRA or JIA
Pars planitis syndrome (a diagnosis of exclusion)
Multiple sclerosis
Lyme disease
Sarcoidosis

Category 4 (posterior uveitis, without vasculitis)
Toxocariasis
Toxoplasmosis
Leukemia
Tuberculosis
Intraocular foreign body
Vogt-Koyanagi-Harada syndrome

Category 5 (posterior uveitis, with vasculitis)
Cytomegalovirus (CMV)
Acute retinal necrosis (ARN) syndrome and bilateral disease (BARN) due to HSV and VZV
Inflammatory bowel disease
Lues (syphilis)
Behçet's disease
Systemic lupus erythematosus
Kowasaki's disease
Sarcoidosis
Polyarteritis nodosa
Wegener's granulomatosis

becomes the last frontier. Younger patients may not be able to articulate their symptoms until advanced disease is present. All of these factors can contribute to a delay in diagnosis. Early diagnosis and the initiation of treatment from an experienced uveitis specialist have been shown to directly improve outcome. Kump [34] found the length of the delay in referral to a uveitis expert at a tertiary care center strongly correlated with both complication rate and degree of vision loss. The delay in diagnosis of uveitis in non-verbal children accounts for a much higher prevalence of vision loss in pediatric uveitis when compared to adult forms [66]. Tugal-Tutkun [66] found that 26% of patients with juvenile rheumatoid arthritis, 14% with idiopathic uveitis, and 10.5% with pars planitis had final visual acuities of 20/200 or worse. Prompt treatment helps to decrease structural changes that may occur as the result of chronic inflammation, including maculopathy, cataract, synechia, and permanent disruption of the blood–brain barrier. Younger children also pose the unique challenge of dealing with amblyopia causing irreversible visual impairment long after the inflammatory disease is controlled.

Therapeutic challenges also exist when treating a pediatric disease. Compliance with oral and drop medications can be much lower in this population. Periocular injection may often require general anesthesia or sedation that can not be performed in the office. Long-term steroid and immunomodulatory medication use in young children creates the same array of potentially life-threatening side effects seen in adults, but with the additional risks of growth delay, developmental impairment, and fertility loss. These unique pediatric issues can serve to further delay or hinder treatment.

28.2 Diagnostic Approach and the Seven-Step Method

Pediatric uveitis may be classified according to numerous parameters, including patient demographics, location and character of the inflammatory process, duration, onset, clinical course, and the etiology of the inflammation (Table 28.3). The intellectual exercise of consciously identifying each parameter allows the clinician to focus on those diagnoses most likely attributable to each patient's disease. Thus, a specifically tailored, cost-effective uveitis evaluation may be obtained to further process the differential for a given constellation of parameters.

Below is a method to help the clinician with a direct and logical approach for the evaluation of pediatric uveitis referred to as the "Seven-Step Method." This method [44, 60] provides a useful road map to cost-effective and efficient clinical uveitis practice:

1. Clinical evaluation: Data collection
2. Naming: Precise methodical description of your findings
3. Meshing: Differential diagnosis ranked by probability
4. Office testing: Hone your diagnosis at the first visit
5. Specific and non-specific laboratory testing
6. Specialty consultations: Recruit help from expert colleagues
7. Clinical therapeutic trial: Test your diagnosis with the appropriate treatment

Table 28.3 Diagnostic descriptors of pediatric uveitis

1. Patient demographics: age, sex, race, domicile, travel, body habitus, immune status
2. Location of the inflammatory process:
   a. Anterior
   b. Intermediate
   c. Posterior
   d. Panuveitis
   e. Unilateral, bilateral, or alternating
3. Duration, onset, course, and therapeutic responsiveness of the inflammation:
   a. Acute, chronic, recurrent
   b. Sudden vs insidious onset
   c. Progressive vs self-limiting
   d. Responsive vs recalcitrant or non-responsive
4. Character of the inflammation:
   a. Nature of the inflammatory cells
   b. Inflammatory deposit (KP) nature: granulomatous vs non-granulomatous
   c. Keratitic precipitate (KP) distribution: classic, Arlt's triangle, diffuse stellate
   d. Presence of nodules: Busacca or Koeppe
   e. Presence of fibrin
   f. Presence of synechiae
5. Etiology of the inflammation:
   a. Infectious
   b. Autoimmune
   c. Idiopathic

28.2.1 Clinical Evaluation

A thorough clinical evaluation is the first step in evaluating any uveitis patient. Obtaining patient trust in a friendly office environment may allow for more patient cooperation. Under ideal circumstances, the clinical evaluation for the pediatric patient is similar to that of the cooperative adult patient.

A complete history of the patient's disease is important. Age, sex, race, geographic history, family history, social habits, contagious disease exposure, travel history, and duration of illness are all necessary elements in evaluation. Each one of these categories can help the clinician narrow the differential diagnosis.

During the physical examination it is important to determine the anatomic location of the patient's uveitis (anterior, intermediate, posterior, or panuveitis). The cornea should be examined for keratitic precipitates (KP) (stellate vs mutton fat), endothelial pigmentation patterns, and endothelial or stromal changes. Anterior chamber cell or fibrinoid reaction can be observed and graded. The iris should be checked for the existence of synechiae, iris nodules (Busacca/Koeppe), and areas of atrophy or discoloration. Iris atrophy may be sectorial, diffuse, superficial, or very subtle with minimal shallowing of the crypts. If possible, the iris should also be examined by gonioscopy along with the angle structures. The vitreous can also be examined for the presence of cell and overall haze and graded accordingly. The existence of snow banks, large white opacities (snowballs), or pars planitis should also be noted. Finally, the retina should be examined for findings such as the presence of masses, serous retinal detachments, areas of acute inflammation, necrosis, vessel sheathing or macular cysts, macular pigment, or macular edema. The optic disc may also show diffuse atrophy or pallor, sectorial atrophy, thinning, neovascularization, hyperemia, or edema.

Finally the clinician should look for systemic correlates such as respiratory symptoms, lymphadenopathy, joint pain, gastrointestinal problems, or cutaneous manifestations including rash, vesicles, erythema, ecchymosis, open ulcers, or signs of trauma.

28.2.2 Naming

The history and the physical evaluation must be properly organized to judiciously proceed to a differential diagnosis. Additionally, the history and the physical evaluation should be well organized using medical terminology for potential further discussion with other caregivers, including optometrists, non-ophthalmologist physicians, therapists, and primary care providers as well as other ophthalmologists.

The naming process creates a profile or template of the clinical case. All of the terms describing the salient historical and clinical facts referable to the case under study should be combined in a detailed clinical description of the patient.

Naming example: John is a 9-year-old white male from Virginia with a history of chronic, intermittent photophobia and unilateral eye pain. The boy also complains of sporadic joint pain and occasional rashes, but no known history of ocular trauma. Examination reveals normal lids, ipsilateral injection with diffuse fine KP, a clear cornea, no synechiae, mild iris atrophy, mild cell, no cataract, and no posterior segment findings.

Naming breakdown: Patient identifier, age, race, occupation, duration, character of the inflammation, location of the inflammation, and symptoms.

28.2.3 Meshing

Meshing is the process of matching up the findings in the case in question with the findings that characterize a particular entity. Generally speaking, uveitis syndromes are distinct entities. The list of likely uveitic entities in the pediatric population is surprisingly small, so the differential also covers the vast majority of uveitis cases seen in the general practice of adult ophthalmology.

By comparing patient parameters to established uveitic entities, similar profiles should be included in the preliminary differential diagnosis and then should be ranked in order of likelihood. Based on the pre-

vious clinical example, meshing would provide the following differential diagnoses: (1) herpetic uveitis without corneal involvement, (2) Fuchs' uveitis syndrome, (3) juvenile rheumatoid or idiopathic arthritis, and (4) pars planitis. Additional naming and meshing examples are noted below:

Example 1: A 10-year-old white female student and musician with bilateral chronic non-granulomatous iridocyclitis observed for the past 2 years, manifested by minimal eye symptoms and occasional knee pain. This initial mesh or differential diagnosis includes juvenile rheumatoid arthritis and sarcoidosis.

Example 2: An 18-year-old black male student and artist with bilateral acute episodic granulomatous iridocyclitis and vitritis and symptoms of blurred vision and pain over the past 3 months without systemic complaints. This initial mesh would include sarcoidosis or ankylosing spondylitis.

Example 3: A 7-year-old oriental otherwise healthy female student and gymnast with acute unilateral iridocyclitis and glaucoma complains of photophobia and blurring for the past 2 weeks. Initial mesh includes toxoplasmosis, Fuchs' uveitis syndrome, or herpetic uveitis.

28.2.4 Office Testing

Many diagnostic tests and procedures can be performed while the patient is in the clinician's office, often during the initial consultation visit. An efficient system to utilize para-professional personnel to obtain these tests greatly facilitates the workup while freeing valuable physician time:

- Delayed hypersensitivity skin testing for: (1) tuberculosis (purified protein derivative [PPD]), and rarely (2) anergy for sarcoidosis (*Candida* or mumps), or (3) histoplasmosis or coccidioidomycosis.
- Behçet's skin testing (archaic but classic practice).
- Photostress and Amsler grid (macular edema, macular retinitis).
- Fluorescein angiography (macular edema, vasculitis, papillitis, choroiditis, retinitis, posterior scleritis).
- Tear function testing: Schirmer's test and breakup time (Sjögren's syndrome, sarcoidosis, connective tissue diseases).
- Tear lysozyme or lactoferrin (Sjögren's syndrome, sarcoidosis).
- Conjunctival biopsy (sarcoidosis).
- Aqueous paracentesis (infection, antibody titer, tumor, lens-induced uveitis, eosinophilia).
- Visual fields (glaucoma, optic atrophy, papillitis).
- Contrast sensitivity, color vision (optic neuritis, papillitis).
- Glare testing (cataract, synechiae, capsular opacification).
- Ultrasonography (posterior scleritis, retinal detachment, vitreous debris).
- Electroretinogram (chloroquine toxicity, opaque media, birdshot choroidoretinopathy, retinitis pigmentosa, non-specific).
- Electrooculogram (diabetic retinopathy, siderosis retinae, vitiliginous maculopathy, and shallow retinal pigment epithelial detachments).
- Corneal topography (corneal disease seen in herpetic keratouveitis).
- Optical coherence tomography (OCT) provides quantitative data on macular edema or glaucomatous nerve fiber layer changes (optic nerve atrophy in papillitis or glaucoma, as well as macular changes seen with edema, epiretinal membrane, or atrophic maculopathy). This includes other digital imaging modalities and devices such as HRT (Heidelberg) and RTA (Marco).
- Conjunctival biopsy (sarcoidosis).
- Aqueous paracentesis (infection, antibody titer, tumor, lens-induced uveitis, eosinophilia).

28.2.5 Specific and Non-specific Laboratory Tests

Working with the small list of diagnostic possibilities generated by the naming–meshing process, laboratory tests can be ordered to systematically evaluate each possible diagnosis. Some tests arrive in the physician's office the next day, while other tests may require up to

a week. Serologic testing for unusual infections may be sent to state health departments, centrally located high-efficiency commercial laboratories such as LabCorps, or specialty university laboratories for analysis. Histocompatibility antigens often may be drawn only early in the week because lymphocytes must be processed in culture over several days to identify surface antigens. Below is a list of commonly used tests:

- Bacterial antibody testing: toxocariasis, toxoplasmosis, *Bartonella henselae*, brucellosis
- Viral antibody testing: herpes simplex virus (HSV), cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus (EBV), hepatitis, human immunodeficiency virus (HIV), human T-lymphotropic virus (HTLV)
- Luetic serology: treponemal tests (fluorescent treponemal antibody absorption [FTA-ABS] test, microhemagglutination-Treponema pallidum [MHA-TP]) and non-treponemal tests (rapid plasma reagin [RPR], Venereal Disease Research Laboratory [VDRL] test)
- Lyme disease testing: serology, western blot confirmation, and polymerase chain reaction (PCR)
- Leptospirosis serology
- Fungal serology: blastomycosis, coccidioidomycosis, histoplasmosis serum antibodies
- Connective tissue disease: rheumatoid factor (RF), antinuclear antibody (ANA), lupus anticoagulant, complement, protein electrophoresis, antineutrophil cytoplasmic antibody (ANCA), Sjögren's syndrome antibodies (SS-A, SS-B), and specific antinuclear antibodies (single-stranded, double-stranded DNA, Smith, ribonucleoprotein)
- Non-specific inflammation: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), high sensitivity, low specificity testing, useful for following systemic therapy and vasculitis or arteritis, generally lower in children than adults
- Feces for parasites: *Ascaris*, *Entamoeba histolytica, Escherichia coli, Endolimax nana, Giardia lamblia*
- Angiotensin-converting enzyme (ACE) for sarcoidosis
- Lysozyme: sarcoidosis, tuberculosis
- Major histocompatibility antigens: HLA-B27 syndromes and HLA-A29 in birdshot chorioretinopathy are by far the most useful clinically
- Standard tests: complete blood count (CBC), differential, clotting factors, chemistry, urinalysis
- Cryoglobulins: myeloma and other myeloproliferative neoplasms, rheumatoid arthritis, Sjögren's syndrome, lupus erythematosus, Waldenström's macroglobulinemia, hepatitis, CMV infections, infective endocarditis, mononucleosis, leprosy
- Complement levels, interleukin levels, circulating immune complexes
- Chlamydial complement-fixation test
- AIDS tests: enzyme-linked immunosorbent assay (ELISA), viral load, and western blot
- Diagnostic imaging:
  - Chest x-ray: tuberculosis, sarcoidosis, histoplasmosis, tumor
  - Sacroiliac films: HLA-B27, Reiter's syndrome, ankylosing spondylitis
  - Orbital films, CT scan, or MRI: tumor, foreign body, thyroid, scleritis
  - Skull films: congenital toxoplasmosis
  - Joint films: rheumatoid arthritis, HLA-B27, JIA, lupus, gonorrhea
  - Gallium scan: sarcoidosis
- Invasive diagnostic testing:
  - Diagnostic vitrectomy: acute or chronic endophthalmitis for *Propionibacterium acnes*, or viral antibodies
  - Aqueous paracentesis: tumor cells, or adjunctive to vitreous tap
  - Vitreous tap: in office abbreviated form of diagnostic vitrectomy
  - Corneal biopsy: important for *Acanthamoeba* and fungal lesions
  - Conjunctival biopsy: sarcoidosis for focal nodules
  - Retinal biopsy: viral disease
  - Choroidal biopsy: idiopathic focal lesions
  - Conjunctival impression cytology: neoplasia, severe dry eye

28.2.6 Specialty Consultations

The assistance of colleagues in other specialties is essential for excellence and standardization of medical care. Particularly useful collaborations include those with specialists in internal medicine, pediatrics, infectious diseases, oncology, rheumatology, radiology, nuclear medicine, dentistry, neurology, and dermatology.

28.2.7 Therapeutic Diagnostic Trials

Many times, a diagnosis can be firmly established only if the patient actually responds to specific medical therapy, usually an antibiotic. The most significant uveitic diseases responding to antimicrobial therapy include toxoplasmosis, Lyme disease, leptospirosis, tuberculosis, coccidioidomycosis, cryptococcosis, and, of course, infectious postoperative endophthalmitis. Many patients with toxocariasis, on the other hand, will worsen when given antihelmintic drugs and instead will fare better with only anti-inflammatory treatment.

Modern HIV treatment with highly aggressive antiretroviral therapy (HAART) has markedly altered the prognosis for HIV infection and the attendant opportunistic infections such as ocular toxoplasmosis or CMV retinitis. Viral disease leading to uveitis often responds remarkably well to concomitant systemic antiviral therapy and local ocular anti-inflammatory medications.

An entirely new entity of immune recovery uveitis can occur with the rejuvenation of immune competency following successful specific antiretroviral therapy. Patients experience an unwelcomed renaissance of their intraocular inflammation with reinvigoration of autoimmunity while remaining on previously adequate doses of anti-inflammatory medication. Treatment logically consists of sufficiently increased potency, dosage, and frequency of anti-inflammatory medications to control intraocular inflammation.

28.3 Important Uveitis Entities in the Pediatric Population

28.3.1 Toxocariasis

Toxocariasis is an uncommon disease in the general population, but represents a sizably concerning cause of posterior uveitis in the pediatric clinic. Toxocariasis is the result of parasitic nematode larvae that have been found to live in up to 80% of young dog (*Toxocara canis*) and cat (*Toxocara cati*) intestines. One study showed that 81.8% of patients diagnosed with toxocariasis had significant household exposure to either puppies or kittens [63]. The disease is usually contracted by the ingestion of dirt or food that has been contaminated by dog or cat feces containing the ova. The ova reach the intestine producing larvae that enter both the blood and lymphatic circulation. From there they reach sites including the liver, lungs, and eye. Although largely considered a pediatric disease, a large study by Stewart found ocular toxocariasis in patients aged 1–37 years with an average age of 16.5 years and a median of 14 years [63].

Toxocariasis is usually a unilateral disease with one study showing 9.1% of cases being bilateral [63]. Common presenting complaints include blurred vision, photophobia, floaters, eye redness, or strabismus secondary to poor vision. Visual acuity can widely vary from normal to very poor depending on macular involvement and vitreous clarity. Systemic infection with toxocariasis is referred to as visceral larval migrans (VLM) and can be associated with malaise, fever, poor appetite, or may be asymptomatic. Eye manifestations can occur outside of any other systemic symptoms, which is the norm. In fact most patients with VLM do not have ocular nematode disease.

Ocular toxocariasis can present as an intermediate, posterior, or panuveitis and is not usually seen as an isolated anterior uveitis. Toxocariasis can typically present with a granuloma located peripherally or localized to the posterior pole and macula. Leukocoria from chronic endophthalmitis is also a common but unfortunate presentation. Less commonly a granuloma on the optic nerve can be seen. The location of the granuloma is dependent on the entrance arterial vascular access route of the nematode. Entrance via the central retinal artery usually results in peripheral granulomas while entrance through the short posterior ciliary artery can result in posterior pole, macula, or optic disc granulomas. This phenomenon is due to lumen diameter restriction of distal arterial flow within the posterior polar circulation. Cystoid macular edema and vitreoretinal traction creating tension on the macula can occur as well and commonly cause reduced vision in these patients. Ocular toxocariasis is a common cause of pseudoretinoblastoma in the published literature and should be considered in the differential diagnosis of leukocoria to avoid misdiagnosing pediatric patients with retinoblastoma [8].

Diagnosis of toxocariasis is largely dependent on fundus examination and a proper patient history that includes exposure to pets. Serum ELISA for antibod-

ies to *Toxocara* is instrumental in the diagnosis. However, ocular toxocariasis patients may routinely have low to absent serum titers. Therefore, positive serum results may help support the diagnosis, yet a negative serum antibody does not rule out the diagnosis. For VLM, the ELISA cutoff dilution of 1:32 is used to indicate a positive result. Since serum antibody levels may be much lower or even absent in ocular toxocariasis, any antibody titer, including undiluted, should be considered significant when there is also a suspicious clinical examination. Aqueous or vitreous fluid has been found to yield much higher sensitivity making diagnostic vitrectomy or anterior chamber tap an option in difficult cases.

Loss of vision is often due to chronic inflammation as the body reacts to the larvae. Therefore the mainstay of treatment in these patients focuses on steroid therapy during the acute inflammatory phases. Topical, periocular, or systemic steroids are commonly used. Other studies have found mixed success with the use of cyclosporine A in conjunction with systemic steroids [42]. In cases where there is retinal traction or severe vitreous opacity, vitrectomy may become necessary. In most cases, laser photocoagulation or cryoretinopexy of the larvae is not suggested since destruction of the nematode may cause a severe inflammatory process. The use of antihelmintic medications such as albendazole or thiabendazole are common in treating systemic disease, but remain controversial with ocular disease [3]. As with laser photocoagulation, it is believed that the destroyed larvae are responsible for a severe inflammatory reaction. In the case of peripheral lesions that are asymptomatic, simple observation may be recommended while host immunity controls and eliminates the infection over time.

28.3.2 Traumatic Iritis, Blunt Injury, and Hyphema

Blunt trauma is a common emergent presentation in pediatrics. Traumatic iritis is generally self-limited, but far less symptomatic and persistent when effectively and proactively treated with topical steroids and dilation. A wide variety of findings and sequelae result from blunt trauma, as indicated in Table 28.4. Acute iritis following blunt trauma should be aggressively treated with topical steroids and cycloplegics until all cellular response in the anterior chamber has disappeared, then topical steroids weaning judiciously in order to prevent rebound inflammation. Patients and their family should be informed that the injured eye is forever thereafter subject to a litany of potential complications, most important of which are cataract, glaucoma, and retinal detachment. These patients should have regular eye examinations for the remainder of their lives to ensure early detection of these sequelae. In cases of anisocoria, proper wristband, medical record, and driver's license documentation of pupillary asymmetry should be ascertained.

Hyphema is also a common result of blunt ocular trauma in the pediatric population. As many as 90% of hyphemas occur in boys, in concordance with other data regarding blunt and penetrating injury. The mechanism of injury can vary widely and should be ascertained. Non-accidental trauma in these patients should also be ruled out. A hyphema is usually caused

Table 28.4 Sequelae of blunt ocular trauma

Traumatic iritis
Traumatic iridocyclitis
Traumatic hyphema
Secondary glaucoma due to meshwork inflammation
Secondary glaucoma due to crenated red blood cell obstruction of the meshwork
Hypotony due to ciliary body inflammation or dislocation
Angle recession and angle-recession glaucoma
Iris sphincter rupture
Temporary and permanent ipsilateral pupillary dilation and anisocoria
Traumatic cataract
Traumatic zonular dehiscence, and subsequent lenticular dislocation or phacodinesis
Refractive or deprivation amblyopia
Posterior vitreous detachment
Symptomatic syneresis
Retinal detachment
Commotio retinae and optic nerve head hemorrhage
Vitreous hemorrhage
Rhegmatogenous retinal detachment
Orbital blow-out fracture, and subsequent diplopia, fatty atrophy, and enophthalmos
Ruptured globe, usually at the muscle insertions or optic nerve insertion

by blunt force that when applied to the eye displaces the aqueous fluid out peripherally. This results in increased hydraulic pressure to the iris root and angle structures. If this pressure is great enough, bleeding will occur from broken vessels usually located within the peripheral iris and ciliary body. Such injury may also be great enough to cause scleral rupture; therefore ruptured globe should always be excluded in these patients. Spontaneous hyphema is less common, but should raise the concern for juvenile xanthogranuloma, retinoblastoma, and leukemia. Iris rubeosis, clotting disorders, Fuchs' uveitis syndrome, and herpes are also possible causes of spontaneous hyphema.

The degree of bleeding can vary from microscopic red blood cells visible under the slit lamp to complete filling of the anterior chamber, the proverbial "eight-ball." Less than 50% of hyphemas will fill greater than one third of the anterior chamber and less than 10% will fill the entire chamber [17]. The prognosis of these patients usually is rather good, but largely depends on whether the patient develops complications from the hyphema. The common complications are glaucoma, optic atrophy secondary to glaucoma, corneal blood staining, uveitis, and rebleeding. Evidence of rebleeding should be of high concern to the physician and is a poor prognostic factor of future visually acuity. Rebleeding occurs most frequently between days 2 and 5.

The first step in treating a hyphema begins with a thorough history. The mechanism of injury is important and the clinician should rule out penetrating injury when applicable. The date of injury is helpful in assessing the likelihood of rebleeding and to aid in determining a proper follow-up schedule. The child should be screened for any preexisting eye diseases such as glaucoma, corneal diseases, or amblyopia. It should also be known whether the child has any clotting disorder, or is on systemic anticoagulation.

All African American patients should be tested for sickle cell disease. Sickle cell patients are at risk for sickling of red blood cells in the anterior chamber. The abnormal red blood cells can inhibit outflow through the trabecular meshwork and lead to increased intraocular pressure (IOP). Sickle cell patients are also at a greater risk for optic neuropathy which has been theorized to be due to decreased blood flow to the optic nerve head making it more susceptible to IOP increases.

During serial examinations, the size of the hyphema should be documented and followed for improvement. The cornea should be evaluated for evidence of blood staining. The cornea should also be assessed for evidence of any preexisting conditions that may increase the patient's risk for blood staining. The iris and lens should also be examined for evidence of cyclodialysis or subluxation. If possible, the fundus should also be assessed for vitreous hemorrhage or retinal detachment. Often, the fundus view is obscured necessitating B-scan ultrasound to rule out retinal detachment or a mass in the fundus. Gonioscopy should be delayed for up to 6 weeks to avoid the chance of causing a rebleed. Gonioscopy is eventually necessary to examine for angle recession, a condition that necessitates closer follow-up for the increased risk of open-angle glaucoma. IOP measurement is very important as glaucoma is a common and serious complication with hyphema patients and may dictate the course of treatment.

Treatment of hyphema begins with having the child refrain from physical activity and sleeping with the head elevated 35 degrees to avoid obscuration of the entire trabecular meshwork circumference. The use of a hard eye shield is also helpful to prevent further trauma, but employed only for appropriate cases. Hospitalization was often used with pediatric cases in the past, but has largely fallen out of favor. However, hospitalization is still considered reasonable during the first 5 days of treatment to closely monitor for development of a rebleed [23]. Patients who are at a high risk for developing complications such as children with glaucoma, sickle cell, or who have already developed a rebleed during follow-up are also good candidates for hospitalization. Bilateral pressure patching to immobilize the eyes during the first five critical days post-injury has also largely fallen out of favor.

Medical therapy includes long-term dilation with either homatropine, Cyclogyl, or atropine which helps with patient pain and may reduce the risk of rebleed and the formation of synechiae. Prednisolone acetate is also used four times per day (q.i.d.) or more depending on the degree of inflammation. Oral prednisone has also been used at 0.75–1.00 mg/kg in a divided dose and has been shown in some studies to prevent rebleed. Antifibrinolytics such as oral aminocaproic acid (Amicar) are well studied and shown to prevent rebleed in high-risk patients. While systemic

Amicar has well-known systemic side effects including vomiting, topical aminocaproic acid gel (Caprogel; Ista Pharmaceuticals, Irvine) has been shown to significantly reduce the risk of rebleed while avoiding systemic side effects [10–12, 35].

Because elevated IOP can lead to corneal blood staining and optic atrophy, patients with increasing IOP should be placed on a topical beta-blocker or other appropriate topical agent. Carbonic anhydrase inhibitors and adrenergics need to be avoided in sickle cell patients as these medications can induce sickling in the anterior chamber.

Generally, corneal blood staining can occur with IOPs that are greater than 25 for a period greater than 6 days. Blood staining can be seen histologically as blood products in the corneal stroma which may take from months to years to fully resolve. The clinician should always be mindful of earlier development of staining, as this would be an indication of surgical evacuation of the hyphema. Blood staining may also occur earlier or under a lower IOP in patients with complete hyphemas or who have preexisting corneal pathology. Blood staining in younger children presents the challenge of dealing with amblyopia. Severe staining may necessitate corneal transplantation.

While a hyphema is generally managed medically, surgical intervention is necessary at times. IOPs greater than 35 for more than 2–3 days despite medical therapy may lead to corneal blood staining and therefore indicate an anterior chamber washout. Sickle cell patients who have pressures greater than 25 for more than 24 h also require a washout. Surgical washout is usually performed using a simple irrigation/aspiration technique. Vitreous cutting instrumentation with aspiration may also be used if a large clot does not aspirate well.

28.3.3 Fuchs' Uveitis Syndrome

Fuchs' uveitis syndrome (FUS), previously known as Fuchs' heterochromic iridocyclitis, is a condition that was first described by the legendary Austrian ophthalmologist Ernst Fuchs in 1906. For many years, standard terminology termed this condition Fuchs' heterochromic uveitis due to the characteristic heterochromia seen in most cases by simple external examination. FUS is largely (over 90%) a unilateral, chronic iridocyclitis that is usually seen with heterochromia, which may be subtle in early cases. Likely because of the paucity of symptoms, FUS is an uncommon presentation in the pediatric ophthalmologist's practice. However, in some studies 2–11% of childhood uveitis patients had FUS [56]. FUS has no racial or sex predilection and can present anywhere from late adolescence to adulthood. While some studies show the average age of presentation at 40 years old, pediatric FUS is well reported and should be included in any uveitis differential diagnosis. FUS diagnosis in the pediatric population is important because proper diagnosis may allow the clinician to avoid the use of chronic immunosuppressive medication and the resultant side effects.

Fuchs' uveitis syndrome is a low-grade inflammatory process that leads to iris atrophy and potential secondary glaucoma and cataract. Vitreous opacification can rarely occur, but posterior synechiae formation is unusual. While the cause of FUS is not known, several theories exist including infectious and autoimmune. Multiple autoimmune mechanisms have been implicated. Of those theories the most studied is with retinitis pigmentosa. In 2000, Chowers et al. studied 338 patients with retinitis pigmentosa finding a statistically significant connection between FUS and retinitis pigmentosa. However, no significant positive human leukocyte antigen (HLA) associations have been found.

The infectious mechanisms that have been theorized to cause FUS include rubella, toxoplasmosis, toxocariasis, and herpes simplex. Some studies have shown toxoplasmosis to have a significant link to FUS [4, 48, 56]. In a 25-patient study by Schwab, 16 FUS patients had fundus lesions that were suspicious for ocular toxoplasmosis while 13 of these had positive serology for toxoplasmosis [56]. Recently, rubella has been heavily studied and then implicated in its association with FUS. A study by de Groot-Mijnes confirmed earlier work by Quentin which showed intraocular antibodies against rubella virus in FUS patients [15, 48]. In 2007, Birnbaum showed a statistically significant decrease in the number of American-born FUS patients, when compared to other forms of uveitis, after the advent of rubella vaccination in the USA [4].

Fuchs' uveitis syndrome is often an asymptomatic disease, particularly in younger patients. A paper by La Hey found that none of the studied FUS

patients presented with photophobia or eye redness [36]. When symptomatic, patients may complain of decreased vision secondary to cataracts or vitreous haze. The diagnosis is one of exclusion and based principally on physical examination. The diagnostic triad consists of stellate KP, cataract, and iris atrophy leading to heterochromia. The conjunctiva and sclera are usually white and quiet; however, vessels may be prominent on the sclera or conjunctiva.

The La Hey study showed stellate KP in 86% of patients [36]. Although stellate KP is highly suggestive of FUS, these KP are also evident in toxoplasmosis, herpes simplex, herpes zoster, and CMV infectious uveitis cases. The anterior chamber may or may not show a low-grade cell and flare even in the presence of stellate KP. Stellate KP are characterized by a diffuse distribution throughout the endothelium, without an obvious predilection for Arlt's triangle inferiorly. Furthermore, stellate KP show definitive dendritic or stellate projections from a central core when viewed at high magnification, unlike the characteristically discoid morphology of the more common non-granulomatous KP or the globular appearance of granulomatous KP.

Heterochromia can be seen in 82% of patients, but in the same Le Hey study, iris stromal atrophy was seen in 100% of patients [36]. Normally a lighter colored iris becomes darker when stromal loss causes the underlying densely pigmented posterior iris pigmented epithelium to show through. Conversely, a darker colored iris becomes lighter as the deep brown iris stroma slowly melts away leaving more muscle fibers and less melanin visible. Koeppe and Busacca nodules may also be seen. Posterior synechiae are uncommon in FUS patients. The presence of posterior synechiae should in fact lead the clinician away from a diagnosis of FUS. Neovascularization of the iris and chamber angle can lead to bleeding and hyphema during procedures such as paracentesis or cataract surgery. A wispy filiform angle hemorrhage after diagnostic aqueous paracentesis forms the basis of Arlt's sign, thought in the early twentieth century to be diagnostic for FUS. The vitreous may have opacities that at times can lead to decreased vision and necessitate surgical intervention. Cystoid macular edema is usually not present differentiating it from other uveitis syndromes.

The low-grade inflammation seen in FUS usually does not require aggressive treatment. However, periodic flare-ups may require corticosteroids, but chronic therapy is not indicated. Many patients fare well on a single dose of topical steroid such as Pred Forte (prednisolone acetate; Allergan, Irvine) or Lotemax (loteprednol etabonate; Bausch & Lomb, Rochester). The elimination of all aqueous cell and flare should not necessarily be the goal of therapy in these patients and may only predispose the patient to the complications of chronic steroid use.

The two main complications of FUS stem from cataract and glaucoma. A rapidly progressing posterior subcapsular cataract has been found in 80–90% of patients. Secondary glaucoma is also another serious complication seen in 22–59% of patients studied. Posterior subcapsular cataract, a common complication of FUS, will eventually require surgical intervention in every patient, especially in pediatric patients in the amblyogenic age group. Studies have found these patients do well with small incision, clear cornea phacoemulsification with an intraocular lens placed in the capsular bag. Pretreatment with prednisolone q.i.d. 4 days prior to surgery and continued postoperatively aid in reducing postoperative inflammation. The surgeon should also be mindful that FUS patients often have abnormal iris and anterior angle vessels which may cause excessive bleeding during procedures leading to an iatrogenic hyphema.

Glaucoma in an FUS patient is initially treated with topical medications. When medication fails the surgical options include trabeculectomy and glaucoma drainage implant. Laser procedures such as argon laser trabeculoplasty (ALT) and selective laser trabeculoplasty (SLT) are often not effective in these patients, but should be attempted prior to surgery. The customarily dense meshwork pigmentation seen in FUS may be more amenable to SLT therapy. The tendency of pediatric uveitis patients to form fibrous tissue quickly can lead to the failure of the surgical bleb. However, the success of trabeculectomy in the pediatric uveitis patient has been increased since the advent of antimetabolites. Glaucoma drainage implants are also a common choice for these patients where scar formation and bleb failure is a concern.

A small group of patients may experience vision loss secondary to vitreous floaters or debris. In these patients, pars plana vitrectomy has been shown in some studies to be an effective treatment and may in theory also protect against inflammatory damage to the posterior pole [57]. Planned elective pars plana

vitrectomy can be performed at the time of cataract extraction and intraocular lens implantation in selected patients.

28.3.4 Toxoplasmosis

Toxoplasma gondii is an obligate intracellular protozoan parasite that can infect any organ system in the human body. It is highly neurotrophic with a predilection for ocular and brain tissues. An estimated 13–50% of the world's population is infected, with higher prevalence in areas of South America, Europe, and Africa, particularly where raw meat such as steak tartare is commonly ingested [18, 33]. However, most exposed individuals demonstrate no symptoms of disease. More virulent strains have been identified in South America and Africa with ocular involvement in up to 20% of infected persons [29]. The third National Health and Nutrition Examination Survey found a seroprevalence of *Toxoplasma gondii* in the USA of 23% in 17,658 persons and ocular toxoplasmosis is estimated to occur in 2% of seropositive patients. In 2001 the CDC/American Academy of Ophthalmology survey estimated 30,000 visits to ophthalmologists for ocular toxoplasmosis. These data presume as many as 1.26 million Americans could have ocular toxoplasmosis, active or inactive [33].

Infection occurs either by ingestion of fruits, vegetables, or undercooked meat containing the cystic bradyzoite form or through contamination by cat feces that may contain oocysts. Infected water sources have been recently proven a source of infection and cause for several epidemics in South America and Canada. In the USA most toxoplasmosis is thought to be acquired congenitally.

The life cycle of *Toxoplasma gondii* is complex starting with feline hosts where sexual reproduction of the protozoa produces oocysts in the intestinal tract of the host. These oocysts are quite resistant to environmental damage and can remain viable for long periods of time. Ingestion of oocysts causes activation and transformation into the active tachyzoite which replicates quickly, destroying host cells, and releasing more tachyzoites into the bloodstream. Immune regulation in immunocompetent hosts controls disease in a host–parasite stalemate in which the tachyzoite form transforms to the morphologically identical bradyzoite form with much slower replication rates. Bradyzoites can persist in a host for a lifetime and evade immune detection in cystic form which can also be shed in feces and remain infective. Bradyzoites can be released from cysts and transform into actively replicating tachyzoites at any time within a host. Reactivation of latent toxoplasmosis can occur at any time of decreased host immune control, such as immune-suppression for transplant patients, AIDS, severe illness, major trauma, childbirth, or general surgery [18, 29, 33].

Congenital toxoplasmosis occurs with primary maternal infection and dissemination to the placenta with protozoa crossing into the fetal circulation. The classic triad of congenital toxoplasmosis is chorioretinitis, intracranial calcifications, and hydrocephalus. Other signs include anemia, jaundice, rash, hepatosplenomegaly, and low birth weight. Infection during the first or second trimester can severely affect the fetus causing significant morbidity and mortality. Infection during the third trimester can have little effect with normal-appearing newborns. However, if treatment is not given, children can develop chorioretinitis and growth delay. Treatment is recommended for all pregnant women who develop toxoplasmosis during their pregnancy and to all newborns for a duration of 1 year [2, 51].

In the USA an estimated 3,000 newborns are infected with *Toxoplasma gondii* per year. Approximately 10% of infected infants have noted chorioretinal lesions soon after birth although new lesions can appear at any time. Recent studies of 281 infected newborns in Europe showed 17% had developed retinal lesions at the 5-year follow-up mark with nearly two thirds having posterior pole lesions and almost 15% having bilateral posterior pole lesions. Eyes with posterior pole lesions had normal vision in that eye 52% of the time measured at 3 years of age, and 84% had normal vision in eyes with only peripheral lesions. Patients with ocular involvement had normal vision greater than 90% of the time in at least one eye and only 9% of patients had vision worse than 20/40 in both eyes [2, 51].

Ocular toxoplasmosis is thought to occur by parasite infection breaking down the blood–eye barrier with direct infection into the eye. This disrupts innate immune privilege within the eye and induces a hyperimmune response, involving CD4, CD8, along with interleukins and cytokines, against the protozoans

[29]. This immune response, however, also causes collateral damage to uninfected cells within the eye. Systemic corticosteroids are therefore necessarily used concurrently with antiprotozoan treatment by many clinicians to reduce the detrimental effects of the host immune response within the eye. Periocular injections of steroids, however, are contraindicated due to an overwhelming inhibition of host immunity and subsequent rampant replication of toxoplasmal organisms. Periocular steroid injections have led to the loss of infected eyes that may otherwise have been saved with systemic steroid and antiprotozoan agents [59].

The "classic" appearance of ocular toxoplasmosis is a focal necrotizing chorioretinitis accompanied by a vitreous inflammatory reaction. Commonly, this focal area arises from the border of an old chorioretinal scar. Immunocompetent patients almost always have only one area of active toxoplasmosis on examination whereas patients with decreased immunity can have several active lesions. The congenital form tends to be a bilateral disease with multiple satellite lesions located seemingly preferentially within the macula. Ocular toxoplasmosis typically involves 8–16 weeks of active inflammation then periods of inactivity for several years. Recurrence rates vary and in a study of 154 patients with ocular toxoplasmosis 79% of patients had a recurrence within a 5-year follow-up period despite antiparasitic treatment [64].

Optic nerve involvement can have many different presentations typified by four presentations: (1) disc edema with distant retinal lesions, (2) juxtapapillary lesions (Jensen's disease), (3) serous macular detachment, and (4) rarely with no other active lesions. Prognosis is still good with optic nerve involvement in 71% of patients showing improvement of vision with treatment [21]. IOP can be elevated in many cases of ocular toxoplasmosis due to trabeculitis, a phenomenon also observed in the other uveitic entities manifesting stellate KP. Westfall's retrospective review of 61 patients showed IOP >21 in nearly 40% of patients and >30 in almost 30% [59]. Ocular toxoplasmosis can lead to severe vision loss with about one fourth of patients legally blind in at least one eye from the disease [64].

Diagnosis of ocular toxoplasmosis can usually be made on clinical grounds alone through documentation of the characteristic funduscopic lesions. If the diagnosis is questionable, laboratory tests can be used to confirm the initial impression. Typically, serum antibody testing is obtained, but aqueous paracentesis specimens are also very useful. Recent comparative testing of PCR versus WDC (Goldmann-Witmer coefficient) was performed on 189 patients in India, 25 of these with clinical ocular toxoplasmosis and 164 controls. Toxoplasma PCR was determined a fast and effective test requiring only 50 μL of intraocular fluid, with a specificity of 100% and sensitivity of 59.1%. PCR testing takes 5–12 h and is cheaper than other tests. WDC requires 100 μL of intraocular fluid, takes 12–48 h for results, and is 2–3 times more expensive than PCR. Specificity of WDC was also 100% with a sensitivity of 72.7%, slightly higher than PCR. *Toxoplasma gondii* immunoglobulin titers from peripheral blood may also be used when intraocular fluid testing is impractical [18].

Many treatment regimens for toxoplasmosis exist and usually multiple drugs are used to treat this fastidious protozoa. More studies are needed to compare efficacy, ocular disease response, and maintenance suppression therapy. Standard or classic treatment consists of systemic pyrimethamine and sulfadiazine with folinic acid supplementation. However, these drugs can have significant side effects including bone marrow suppression and Stevens-Johnson syndrome. Weekly initial blood counts followed by less frequent testing is needed when patients take pyrimethamine. Clindamycin can be added to pyrimethamine, sulfadiazine, and oral steroids as "quadruple therapy" [33]. A recent prospective randomized trial by Soheilian compared trimethoprim/sulfamethoxazole 960 mg (generic Bactrim or Septra) alone for 6 weeks versus combination therapy with pyrimethamine and sulfadiazine, and found both treatments to be equally effective. Trimethoprim/sulfamethoxazole has improved the side effect profile of quadruple or classic treatment and provides the busy clinician with an effective alternative first-line therapy, obviating supplemental folinic acid [18].

Atovaquone is an antiprotozoa medication that affects mitochondrial electron transport and has been shown to be effective against central nervous system *Toxoplasma gondii*. Atovaquone is generally much better tolerated than classic therapy but it is much more expensive. Tetracycline antibiotics are also effective for treating toxoplasmosis with minimal and familiar side effects. Young children with immature dentition cannot use tetracyclines due to discolor-

ation of teeth and bone deposition. The macrolide antibiotics azithromycin and spiramycin have demonstrated effectiveness, and spiramycin is commonly used for pregnant women due to its low fetal toxicity [18, 33].

Small case series of patients non-responsive to oral medications and with vision-threatening disease have shown success with off-label usage of intravitreal clindamycin 1 mg with and without systemic steroid use. Systemic corticosteroids are usually added either concurrently or within the first few days after antimicrobial treatment is initiated to help control inflammation that can be detrimental within the eye. The use of steroids in immunosuppressed patients is controversial especially since inflammatory responses are usually mild [33]. Animal studies have shown that supplementation with zinc and melatonin could improve chorioretinitis seen in toxoplasmosis, although no corresponding human studies have been reported [2].

Prophylaxis is usually reserved for significantly immunocompromised patients and has been shown to reduce recurrences. Specific prophylactic regimens for these patients vary by clinician. With so many different accepted treatment options available and a lack of controlled trials, recommendations vary widely and no consensus has been determined regarding optimal treatment for ocular toxoplasmosis [33]. Hopefully future research can determine safe and effective treatment guidelines for toxoplasmosis, particularly in children.

28.3.5 Seronegative Spondyloarthropathies

Seronegative spondyloarthropathies (SS) are a heterogeneous group of disorders characterized by inflammatory joint disease predominantly affecting the lower limbs. They are all rheumatoid factor (RF) negative, and thus seronegative. The main disorders include ankylosing spondylitis (AS), Reiter's syndrome (reactive arthritis), psoriatic arthritis, arthritis associated with inflammatory bowel disease (Crohn's disease, Whipple's disease, idiopathic), and juvenile-onset spondyloarthropathies. These patients also show a common link with a large percentage HLA-B27 positive. This major histocompatibility allele was the first ever reported in the literature as a risk factor or in association with human disease. The relative risk of a person with the HLA-B27 allele for developing AS is approximately 85:1, which means this person is about 85 times more likely to develop AS then a B27-negative individual. This relative risk remains among the highest in all of human genetics [58].

The high association with HLA-B27 and enteric infections has lead to the hypothesis that these disorders are related to a genetic predisposition for immune system dysfunction to form autoantibodies after exposure to certain bacteria (*Shigella, Campylobacter, Yersinia, Salmonella*). Small retrospective studies on spondyloarthropathies and HLA-B27-positive patients showed that the HLA-B*2705 allele, a subtype of HLA-B27, was found in 100% of patients with uveitis. The actual gene involved may be in close linkage equilibrium with the B27 locus, or it may act through molecular mimicry with certain foreign genes to initiate an autoimmune response [1]. The gram-negative lipopolysaccharide (surface LPS) may have highly similar surface antigenicity when compares to the B27 gene, thus creating a hit-and-run scenario wherein the instigating infectious agent induces autoimmunity, is eliminated by routine host defenses, but initiates a perpetual cascade of inflammatory events even in the absence of the initial offending organism [1, 58].

Ocular involvement is common in these disorders and uveitis is one of the most common ocular manifestations associated with SS. Other important ocular manifestations include band keratopathy, scleritis and episcleritis, blepharitis, secondary glaucoma, cataract formation, conjunctivitis, posterior synechiae formation, macular edema, and amblyopia in the pediatric population. Uveitis, seen in 15–25% of B27-positive AS patients, presents classically as acute or hyperacute recurrent alternating or bilateral anterior uveitis with rare posterior involvement. SS, along with Behçet's syndrome, are in the short differential diagnosis of non-infectious causes of non-infectious, atraumatic hypopyon [1, 40]. With such a high association with ocular disease, all patients with SS should be screened and followed by an eye-care professional conversant with the widespread ramifications of uveitic disease, as complications can be avoided with proper early treatment.

Uveitis associated with SS typically shows excellent response with topical steroids. Severe cases require additional steroids through adjunctive ocular injections or systemic therapy. In approximately 10% of patients chronic uveitis persists or the side effects of steroids are sufficiently prohibitive to their continued use. Chronic uveitis is frequently due to delayed diagnosis, insufficient medication recommendations, poor compliance, and resultant permanent damage to the blood–aqueous and blood–retina barriers. In other successfully treated cases, steroid side effects including intractable glaucoma may be sufficiently prohibitive to chronic steroid use. In all of these cases, a now vast array of adjunctive non-steroidal immunosuppressants and disease-modifying antirheumatologic drugs (DMARDs) such as methotrexate, cyclosporine, mycophenolate and the TNF-α inhibitors have shown good success in adult populations [49, 50]. Caution should be taken in the pediatric population where newer medications have not been as well studied, and these medications should be started only by physicians experienced in their use and side effects. This juncture in the therapeutic decision tree clearly involves close collaboration with a pediatric rheumatologist or hematologist.

An important point regarding TNF-α inhibitors is that they increase the risk of tuberculosis reactivation and other infections. One case report of tuberculosis uveitis in a patient on etanercept has been reported, further emphasizing the need for continued vigilance and perpetual suspicion of an infectious etiology in patients with atypical presentations. There are several case reports of patients with SS on etanercept treatment with either the new development of uveitis or exacerbations of preexisting uveitis following etanercept injections. Some have hypothesized that perhaps etanercept therapy could induce an autoimmune uveitis in rare instances, although no animal model or human studies have corroborated this theory [49].

Intraocular surgery in patients with SS and a history of uveitis can be challenging. As with any patient with recurrent uveitis, surgery should be delayed, if possible, until inflammation is completely resolved for a period of at least 3 months in adults and 6 months in children. Even with adequate control, these patients are at higher risk of complications and recurrence of inflammation. The most common uveitis-related postoperative complications of cataract surgery include cystoid macular edema, hypotony, and synechia formation. Patients with immobile pupils and synechiae are more likely to have postoperative pupillary complications, including anisocoria, irregular iris sphincter margins, iris atrophy, transillumination defects, and synechiae formation between the sphincter and the anterior capsule [1].

28.3.5.1 Ankylosing Spondylitis

Ankylosing spondylitis is an idiopathic rheumatologic disorder of chronic inflammation primarily affecting the sacroiliac joints, spine, and entheses (muscle insertions to bone). The male:female ratio is at least 5:1 and as high as 9:1 in some epidemiologic studies. The peak incidence is in ages 15–35 years with a prevalence of 0.1–2% in different populations, and 90–95% of patients will be HLA-B27 positive, compared to 8% in the general population. The relative risk that a patient with the B27 allele will develop AS is approximately 88 times higher than a B27-negative patient. This important relative risk for the HLA-B27 allele was the first ever reported for any genetic marker for any disease in the literature. Most patients will also have elevated CRP and ESR although these do not correlate well with disease activity as in other inflammatory conditions [39].

The hallmark of AS is sacroiliitis, with involvement of the lower third of the sacroiliac joints. Radiographic evidence in early disease is best seen with MRI of the sacroiliac joints showing early sacroiliitis. Early or moderate sacroiliitis can be missed in routine hip or pelvis x-rays because the pathology is best seen with an angled tunnel view parallel to each sacroiliac joint. Disease progression can lead to joint erosion, bony formation bridging vertebrae, and ultimately complete spinal fusion (bamboo spine) [39, 49, 50].

Because of a characteristically insidious onset, diagnosis may be delayed. Primary complaints are back pain with rest, especially on awakening, that improves with exercise. On examination, tenderness of joints and entheses is readily demonstrable, and decreased forward lumbar flexion and decreased lung expansion may be noted [39].

Rates of uveitis associated with AS range from 14% to 40%. Uveitis in AS has been associated with juvenile disease onset and the involvement of the lower limbs, especially the Achilles and plantar entheses. Conjunctivitis is the second most common oc-

ular manifestation in AS, which is typically bilateral, non-purulent, and self limited [1, 40, 49, 50, 54].

Besides ocular and joint involvement, patients with AS can develop aortic incompetence, cardiac conduction disturbances, and pulmonary fibrosis. Rarely, aortitis occurs with a significant mortality rate when undetected or undertreated [39].

Treatment of AS joint disease has historically employed physical therapy and non-steroidal anti-inflammatory drugs (NSAIDs). Local steroid injections to affected joints are frequently recommended as well, despite the fact that newer analyses have shown good responses to the TNF inhibitors so commonly utilized against rheumatoid arthritis [1, 39].

28.3.5.2 Reiter's Syndrome

Reiter's syndrome (RS) is a clinically diagnosed disorder historically defined by the presence of arthritis, non-gonococcal urethritis, and conjunctivitis. A relatively rare disorder, diagnosed RS is seen in ~1–3% of men following non-specific urethritis, and 4% or more of persons, male and female, after enteric infections with gram-negative bacteria. RS typically develops within 1 month of preceding infection. A high association with HLA-B27 antigen (75–90%) is seen with RS, however, the presence of this allele is not a part of the diagnostic criteria, so absence of HLA-B27 does not exclude RS. RS is a spectrum of disease with pathology that can be categorized by four subgroups of related signs and symptoms: (1) arthritis, either acute or chronic, with migratory and asymmetric joint pain, usually involving the lower extremities; (2) enthesopathy presenting with localized pain at muscle tendon insertion to bone most frequently seen as heel pain; (3) sacroiliitis and spondylitis causing lower back pain most highly associated with HLA-B27 antigen; and (4) extra-articular with systemic symptoms including ocular symptoms, mucocutaneous lesions, and idiopathic inflammation of virtually any organ. Highly characteristic but non-diagnostic lesions include circinate balanitis of the penis, and keratoderma blennorrhagicum, seen primarily on the feet [32, 50].

Conjunctivitis is the most common ocular manifestation of RS occurring in up to 60% of patients in some publications. Conjunctivitis typically presents within a month of urethritis and arthritis with bilateral asymmetric mucopurulent discharge, negative conjunctival cultures, and non-specific inflammation of the eyelids. Conjunctivitis is usually self-limited and resolves within 10 days. The second most common ocular pathology is uveitis, seen in ~12% of RS patients. Uveitis most commonly presents as non-granulomatous anterior disease. Uveitis is more common in patients positive for HLA-B27 [1, 32, 49, 50, 54]. Treatment of uveitis in RS includes topical and systemic steroids along with other steroid-sparing immunosuppressants when necessary. Oral NSAIDs have also been used for maintenance regimens. Additional reported ocular pathology includes scleritis, disc swelling, macular and retinal edema, vasculitis, and keratitis, although none of these are typical of the disease [32, 50].

28.3.5.3 Psoriatic Arthritis

Psoriatic arthritis (PsA) is a chronic systemic inflammatory disorder associated with cutaneous psoriasis, which in turn afflicts up to 1% of the population. The clinical presentations can resemble oligoarticular juvenile rheumatoid arthritis. Distinct features of this disease are the association with cutaneous psoriasis, bony formation seen on radiographs of the distal interphalangeal joints, and dactylitis and psoriatic nail changes. Diagnosis can be difficult especially in the ~13% of patients with PsA who are rheumatoid factor positive. Spondylitis is seen in ~40% of patients, however PsA typically has a more widespread arthritis than the other spondyloarthropathies [37]. The presence of skin psoriasis, typically described as salmon pink patches with a silver scale on extensor surfaces and scalp, is the most distinguishing feature although it is not required for the diagnosis. These often disfiguring cutaneous lesions are especially tragic in a young child. HLA-B27 is positive in 20–60% of patients with PsA and spondylitis [39, 50].

Uveitis is seen in 10–20% of patients with PsA. A feature that distinguishes uveitis in PsA is more common posterior involvement than other SS [37]. Two distinct subgroups of PsA exist: early childhood presentation and late childhood presentation. In patients presenting in early childhood, uveitis is typically chronic with insidious onset, bilateral involvement, and asymptomatic in a white eye. Because uveitis is typically asymptomatic in this group, patients can

present later in the disease and have more complications than symptomatic patients. Uveitis in patients with arthritis developing in later childhood is most commonly symptomatic with recurrent acute anterior uveitis associated with significant fibrin reaction in the anterior chamber. Treatment of uveitis is essential and visual prognosis is relatively good in these patients. Severity of spine involvement is associated with a higher likelihood of uveitis. HLA subtyping has shown a strong association with uveitis and HLA-DR13, however no association was noted for HLA-B27.

The German Uveitis in Childhood Study Group recommends ophthalmologic screening every 6 weeks in early childhood PsA and every 6 months for late childhood presentation where uveitis is usually symptomatic [69].

28.3.5.4 Inflammatory Bowel Disease (Crohn's Disease, Ulcerative Colitis, Whipple's Disease)

Crohn's disease and ulcerative colitis are autoimmune inflammatory bowel diseases (IBD) with primarily gastrointestinal morbidity including abdominal pain, malabsorption, and weight loss. HLA-B27 correlation is not as strongly associated as other disease processes, however increased incidence is found in the IBD. P-ANCA is positive in nearly 70% of ulcerative colitis patients and almost 20% of Crohn's disease patients. There is increasing evidence of a role for *Mycobacterium paratuberculosis* in Crohn's disease and rifabutin and clarithromycin are being increasingly used in treatment [65]. Similar microscopic inflammatory lesions to those seen in Crohn's disease have been noted in ~50% of AS on ileoscopy giving evidence to speculation that many of these disorders involve genetic predisposition and perhaps an inciting enteric infection [49].

Ten to twenty percent of IBD may initially present with extraintestinal manifestations prior to the onset of intestinal disease. Ocular manifestations are reported in 2–12% of patients with IBD and usually coexisting with arthritis and erythema nodosum. A small cohort study in Turkey found higher rates with ocular involvement seen in 60% of Crohn's disease and 23% of ulcerative colitis [49, 65]. Ocular complications in IBD can result in significant morbidity as they are underdiagnosed and may present late to ophthalmologists.

Episcleritis was the most common symptom seen in up to 29% of patients, however, it is often underdiagnosed due to a mild and self-limited disease course. Uveitis is the most commonly diagnosed ocular manifestation occurring in as many as 17% of patients with IBD. Uveitis is more commonly seen in women with IBD and strongly correlates to disease activity, improving with treatment for IBD. IBD-associated uveitis most commonly is a non-granulomatous, low-grade, recurrent, acute anterior uveitis which accounts for 60% of cases. Ten percent of patients have an isolated episode of non-recurrent acute anterior uveitis and the remaining 30% have panuveitis with associated vasculitis in a majority of these patients. Posterior involvement is seen in less than 1% of patients with IBD, however they can have significant visual morbidity from vasculitis and vitritis. Inflammation typically responds better to topical, periocular, and systemic steroids in IBD than other HLA-B27 disorders [1, 49, 65].

Whipple's disease is a rare bacterial infection caused by *Tropheryma whippelii*, affecting mostly the gastrointestinal tract although any organ can be involved. Ocular symptoms of Whipple's disease are rare (about 5%) and include uveitis, vitritis, retinitis, optic neuritis, papilledema, and direct involvement of the lens epithelium. Ocular involvement in usually never seen without concurrent intestinal disease [20].

Helicobacter pylori, a gram-negative rod associated with gastroesophageal reflux disease, gastritis, gastrointestinal ulcers, and gastric carcinoma has been implicated in the development of uveitis and spondyloarthropathies. Significantly higher levels of *H. pylori* antibodies have been documented in affected patients compared with controls. Treatment of *H. pylori* with multidrug regimens may be a therapeutic consideration although more research is needed to demonstrate improvement of ocular disease with standard gastric treatment protocols. Other gram-negative rods associated with gastrointestinal infections and diarrhea include *Salmonella, Shigella, Klebsiella*, and *Yersinia*. These organisms have a strong association with reactive arthritis and uveitis. A recent survey of patients with confirmed *Salmonella* infection showed 34% of children with ocular complaints [1].

28.3.6 Sarcoid Uveitis

Sarcoidosis is an inflammatory disease of unknown etiology that can affect virtually every organ in the body. Lung involvement is seen in 90% of patients' disease course and can range from asymptomatic to severe lung disease. Uveitis is the most common extrapulmonary symptom seen in sarcoid patients with incidence ranging from 22% to 47% in various studies [5, 39, 53]. Spagnolo et al. studied single nucleotide polymorphisms (SNPs) in patients with sarcoidosis, and found a 2.5-fold increase in sarcoid patients with uveitis with HSP-70 haplotype 2 compared to patients with sarcoid and no uveitis and non-sarcoid patients [62].

Additional ocular manifestations include conjunctival granulomas, episcleritis, scleritis, and interstitial keratitis. Inflammatory optic neuritis either anterior with disc edema or posterior without acute disc changes can also be seen in sarcoidosis. Extraocular muscle involvement can lead to painful ophthalmoplegia and diplopia. Lacrimal involvement in the form of adenitis or asymptomatic enlargement can occur. Chronic inflammation of the lacrimal gland can lead to fibrosis and decreased tear production causing severe keratoconjunctivitis sicca. Periocular cutaneous involvement creating a wide variety of nodules may be painful and disfiguring, as well as associated with ptosis and other lid deformities [5, 39, 53].

Sarcoidosis is characterized by non-caseating granulomatous inflammation seen on biopsy, and currently biopsy is required for definitive diagnosis. Histologically non-caseating granulomatous inflammation is manifest by epithelioid cells and multinucleated giant cells, Langhans type, with peripheral pallisading nuclei. The most common source of a diagnostic biopsy is the mediastinal lymph node plexus retrieved by mediastinoscopy. Other reliable sources include cutaneous nodules, swollen cervical and axillary lymph nodes, brain tissue, kidney and liver specimens, and conjunctiva.

With lung involvement being so frequent, chest radiograph is part of the standard workup. Diagnosis by transbronchial mediastinoscopic biopsy, a fairly invasive procedure, is required when more accessible lesions are not present. For this reason, a search for extrapulmonary involvement is performed looking for nodules, lymphadenopathy, or other lesions throughout the body. Gallium 67 scanning may help identify other areas of sarcoid involvement where biopsy could prove easier and safer [5]. A small study in China evaluated the utility of blind conjunctival biopsy in sarcoidosis patients. Of the 26 patients enrolled 19 had "eye-related problems," however no conjunctival nodules or follicles were noted. Blind biopsies, 1×3 cm, were obtained from bilateral lower fornices. Biopsy results were positive for sarcoidosis in ~37% of patients with sarcoidosis [9]. These results could prove very useful in diagnosing suspected sarcoidosis as conjunctival biopsy is much less invasive with relatively few complications, especially when compared to lung and mediastinal biopsy. More research needs to be performed, however blind bilateral conjunctival biopsy may be an excellent initial test for sarcoidosis diagnosis.

Serum angiotensin-converting enzyme (ACE) level is elevated in 56–86% of patients and is a useful test in suspected sarcoidosis. Elevated ACE levels and a positive gallium scan are quite sensitive (83–99%) for diagnosis of sarcoidosis, however biopsy is still currently required for diagnosis [5]. Disease course can range from asymptomatic lymphadenopathy to life threatening with CNS involvement.

Sarcoidosis can affect people of any age, gender, race, and ethnicity. More common presentations include women, people of African descent, and patients in their third and fourth decades. In the USA African-Americans are at a 10-fold increased risk for developing sarcoidosis. Population studies have shown sarcoidosis incidence ranging from 1 to 150 per 100,000 in various groups [39]. Some regions of the country have disproportionately high prevalence levels of sarcoidosis, including North Carolina and Virginia, leading to the suspicions of an environmental factor such as atypical *Mycobacteria* or pine pollen.

Uveitis in sarcoidosis is classically chronic bilateral granulomatous iridocyclitis with mutton fat KP and iris nodules (Koeppe and Busacca), however acute anterior uveitis with fine KP can also be seen. Intermediate and posterior uveitis can also occur. Retinal granulomas can be seen on dilated examination ranging from small one quarter disc diameter lesions to large granulomata up to four disc diameters. In adults and older adolescent children, severe retinal periphlebitis with exudate, resembling "candle-wax drippings" can be seen, the classic "taches de bou-

gie." Interestingly, retinal periphlebitis has not been described in pediatric sarcoidosis uveitis [5]. Treatment of uveitis involves topical steroids and cycloplegia, however systemic steroids and non-steroidal immunosuppressants are usually required in advanced cases, as inflammation can be difficult to control. This is particularly common in advanced cases and those presenting late in their course with significant permanent damage to the blood–aqueous barrier.

Sarcoidosis in the pediatric population is less common than adult-diagnosed sarcoidosis, representing at most 15% of all sarcoidosis with about a 60% female preponderance. Pediatric sarcoidosis exists in two distinct forms with differing characteristic features. Infantile sarcoidosis, approximately 70% of pediatric sarcoidosis, typically is seen in ages 0–5 years and is characterized by uveitis, arthritis, and skin rash. Anterior uveitis is seen in ~77% of patients with infantile sarcoidosis. Blau syndrome is an autosomal dominant autoimmune disorder mapped to the CARD15 gene on chromosome 16 in most cases. It presents with signs associated with infantile sarcoidosis, noncaseating granulomatous arthritis, uveitis, and dermatitis, along with camptodactyly, which describes hand deformities similar to those seen in advanced rheumatoid arthritis. The rash is typically described as a tan-colored, scaly, ichthyosiform rash. Recent studies have shown that infantile sarcoidosis and Blau syndrome are a spectrum of the same disease associated with mutations in the CARD15 gene in 50–100% of patients studied. More research is being performed attempting to establish genetic testing for CARD15 gene mutations as a less invasive and more accurate method for diagnosis of Blau syndrome and infantile uveitis compared to biopsy [53].

Sarcoidosis diagnosed in school-aged and an adolescent patients, ~30% of pediatric sarcoidosis cases, more closely resembles adult sarcoidosis with primarily lung involvement and absence of rash and arthritis. Anterior uveitis in these patients is seen in ~30% of patients, about the same prevalence as in adult sarcoidosis [53].

In studies of patients with sarcoid uveitis at the onset, the most commonly involved extraocular organ was the lung in ~35%. Spread to other organ systems occurred in ~17% of patients, with a majority of these suffering neurosarcoidosis. Treatment of uveitis reported by uveitis referral centers in cohort studies showed that ~50% of patients required systemic steroids with ~10% requiring additional immunosuppressants [5, 39, 47]. These statistics demonstrate the challenges in treating uveitis related to sarcoidosis.

28.3.7 Pars Planitis Syndrome

Pars planitis syndrome is an idiopathic inflammatory condition with uveitis characterized by inflammatory cellular infiltration over the pars plana and adjacent vitreous body. Associated with only mild anterior segment inflammation, pars planitis is considered an intermediate uveitis. The Standardization of Uveitis Nomenclature working group has recommended that the term "pars planitis" or "pars planitis syndrome" be reserved for "that subset of intermediate uveitis associated with snowbank or snowball formation in the absence of an associated infection or systemic disease" [19]. Therefore, before a diagnosis of pars planitis is made, infectious causes must be ruled out, including Lyme disease, Epstein-Barr virus (EBV) infection, West Nile virus, tuberculosis, cat-scratch disease, toxocariasis, sarcoidosis, and Behçet's disease. Pars planitis is a diagnosis of exclusion.

Pars planitis is a rare disorder with an incidence of approximately 1.5–2 per 100,000. It is mostly a disease of childhood and young adulthood with presentations above 40 years of age exceedingly rare. Pars planitis and intermediate uveitis represent 8–22% of all uveitis cases and 18–33% of uveitis in patients less than 16 years of age. The most frequent symptoms include decreased vision and floater, which are typically bilateral and asymmetric ~80% of the time. Rarely patients may report pain, photophobia, and redness. Patients may also be asymptomatic with snowballs and vitreous cells noted on routine examination [14, 19, 27, 52]. Visual acuity is typically well preserved with average best corrected visual acuity at presentation 20/25 [19]. Anterior uveitis can be seen in roughly 30% of cases, however vitreous cell is seen in ~90%. Snowbanks describe the typical inflammatory pars plana exudates seen in all but very mild cases. Snowballs are large aggregates of vitreous cells seen in approximately 75% of cases of pars planitis. Peripheral vascular sheathing may also be present leading up to snowbanks along with neovascularization in the periphery. These localized lesions may require focal laser or cryotherapy.

Complications of pars planitis are related to the chronic inflammation in these patients. Epiretinal membranes (ERMs) are seen in almost 50% of patients, although rarely severe enough to require surgery. Cataract formation, typically posterior subcapsular, occurs in a third of patients on average 10 years after their diagnosis of pars planitis. Cataract development results from the disease itself as well as steroid treatment. Cystoid macular edema (CME) is seen in roughly 40% of cases in various studies. Control and prevention of CME is essential in preserving good visual acuity in these patients. Many patients may be asymptomatic with 20/20 vision, yet demonstrate significant macular involvement by OCT or fluorescein angiography. These patients should be treated to prevent subsequent macular damage and visual loss [14]. A relatively large retrospective review of pediatric pars planitis and intermediate uveitis in the Netherlands noted optic disc edema in 71% of patients, although other studies have shown much lower rates of 2–20%. Increased IOP occurs rarely and topical agents can be used to treat high pressures. Chronic inflammation and periphlebitis can lead to neovascularization in as many as 5–10% of patients. Vitreous hemorrhage, and even retinal detachment are seen in less than 5% of pars planitis cases. Chronic inflammation can also lead to posterior synechiae and band keratopathy [14].

Treatment of intermediate uveitis depends on the underlying etiology which should be treated according to the specific organism or disease process. If all testing is negative, then the diagnosis of pars planitis can be made. Treatment of pars planitis depends on clinical severity. Asymptomatic patients with normal vision may be observed and no treatment may be necessary. These patients still require close follow-up as the disease course can be quite variable. Topical, periocular, and systemic steroids can then be used as needed, titrated to disease severity [14]. Even young patients 5 years of age and over can be taught to cooperate for periocular steroid injections, avoiding systemic agents or trips to the operating room for sedation.

Oral steroids are usually started at 1.0–1.5 mg/kg dose with gradual taper to the lowest effective dose and a short-term goal of less than 15 mg per day. Cryotherapy or laser therapy to snowbanks can also be performed if not improving with steroid therapy or when peripheral neovascularization develops. Cryotherapy should be avoided in areas of retinal traction as this could worsen the traction in treated areas. Laser photocoagulation should be employed in these instances. Rarely, vitrectomy may be performed for inflammation not responding well to steroids. The pars plana vitrectomy approach allows separation of the posterior hyaloid membrane and endolaser treatment to snowbanks. Vitrectomy can also be used to treat non-clearing vitreous cell or debris obscuring vision, and repair of tractional retinal detachment and non-clearing vitreous hemorrhage [14, 19]. Steroid-sparing immunosuppressants may rarely be required, including methotrexate and TNF inhibitors.

Visual outcome is relatively good in pars planitis with three fourths of patients retaining 20/40 vision or better in long-term follow-up. Most patients have vision in the 20/25–20/30 range, with acuity loss usually attributed to ERM, cataract, and CME [19]. Worse visual loss is seen in patients with optic nerve involvement. The clinical course tends to be less favorable with younger age of onset in some studies. Within the pediatric population, age was not noted to be a risk factor for disease severity. This same study showed an almost 50% "remission" rate in treated patients at the 5-year follow-up [14].

Correlation between cigarette smoking and pars planitis was noted recently in population studies of Olmstead County, MN. Although not noted in previous studies, recommending smoking cessation to patients is worthwhile. Multiple sclerosis (MS) and pars planitis correlation has been firmly established in many studies with prevalence of 12–16% of patients with pars planitis diagnosed with MS when compared to 0.1% of US population with MS [19]. A significant association between HLA-DR2 subtype and pars planitis has been determined, which is also seen in MS.

28.3.8 Juvenile Idiopathic Arthritis and Juvenile Rheumatoid Arthritis

Juvenile rheumatoid arthritis (JRA) is now grouped into a broader category of juvenile idiopathic arthritis (JIA), an autoimmune disease that affects 1–2 per 1,000 children, with incidence ranging from 11 to 14

new cases per 100,000 children per year [55]. Early diagnosis is important to reduce morbidity from joint involvement and to prevent serious complications of uveitis commonly seen in the disease. Referral to an ophthalmologist is indicated in all patients suspected of JRA to rule out uveitis, especially as ocular inflammation is usually asymptomatic in JRA. Meticulously frequent follow-up care is mandatory to ensure uveitis does not develop. Arthritis-related uveitis in children can devastate an eye in short order despite the lack of symptoms other than the often-ignored unilateral blurring or floaters.

Classifications of childhood arthritis conditions are changing as we learn more about these related disease processes, while multiple classifications exist in different countries and among different specialties. In many European countries the term juvenile idiopathic arthritis (JIA) is used which encompasses JRA along with other autoimmune arthropathies, including psoriatic arthritis and ankylosing spondylitis. The American College of Rheumatology diagnostic criteria, first established in 1977, defines JRA as a chronic arthritis lasting longer than 6 weeks, with onset before the age of 16 years, excluding other forms of pediatric arthritis. JRA is the most common systemic disease associated with pediatric uveitis [7, 67].

Three main types of JRA are defined by the systemic symptoms seen within the first 6 months of onset. These types are:

1. Oligoarticular (pauciarticular) with <5 joints involved
2. Polyarticular with 5 or more joints involved
3. Systemic onset with arthritis associated with fevers

Pauciarticular JRA (<5 joints) accounts for ~60% of JRA cases. There is a strong female sex predilection with female:male ratio of 5:1. The age of onset is usually in early childhood with peak incidence in ages 1 through 3 years. Pauciarticular-type JRA is the type most frequently associated with uveitis, seen in 15–20% of cases. Serologic studies show rheumatoid factor (RF) to be rarely positive in these patients while a positive antinuclear antibody (ANA), on the other hand, is found in a vast majority of cases, reportedly ~75–85% of patients. Many times a negative or low titer ANA will rise sharply with subsequent testing or a proximal flare in systemic disease. The course of therapy as well as the natural history of the disease process itself can often be followed with ANA serology, the ESR, or the CRP. Pauciarticular arthritis can persist into adulthood in 40–50% of cases. Many children experience a welcome diminution in the severity of their ocular and joint disease as they complete puberty [67, 69].

Polyarticular type (≥5 joints) represents ~30% of JRA cases. Polyarticular type can present throughout childhood up to the age of 16 years with a peak at 1–3 years. Once again there is a significantly higher incidence in girls with a female:male ratio of 3:1. Uveitis is seen in approximately 5% of polyarticular JRA cases. Serologic tests show a positive RF in ~10% and a positive ANA in 40–50% of cases [7, 69].

Systemic JRA, characterized by multijoint arthritis and fever, is the diagnosis in ~10% of JRA cases. Systemic JRA, in contradistinction to the oligoarticular and the polyarticular forms of arthritis in children, is rarely associated with uveitis. Serologic studies show RF is rarely positive and a positive ANA is found in only 10% of these patients. Sex predilection is equal. This is the most severe type of JRA; it can cause profound joint destruction and has a mortality rate of 0.5–2.0% [7].

Ophthalmologists are rarely the first physician seeing JRA patients, particularly in light of the frighteningly negative symptoms produced by even advanced ocular disease. Most patients already carry the diagnosis since their joint involvement usually precedes uveitis, and is more readily apparent and symptomatic. Referrals most frequently arise from pediatric rheumatologists and primary care pediatricians. However, ophthalmology may occasionally be the first to see a patient in rare cases of uveitis presenting before arthritis or poor school vision screening. Any child with idiopathic uveitis warrants referral to rheumatology not only for appropriate rheumatologic workup of possible systemic disease, but also for assistance in guiding therapy in these notoriously difficult uveitis patients.

Early detection and treatment of uveitis is essential for preservation of normal vision and ocular anatomy. Studies have shown later presentation, and, specifically, formation of posterior synechia, is associated with worse visual outcomes and earlier cataract formation requiring surgery. Intense screening should be performed for JRA and other rheumatologic conditions (e.g., ankylosing spondylitis, psoriatic arthritis) to detect uveitis earlier and prevent the manifold complications associated with late presentation [61].

Table 28.5 Frequency of ophthalmologic examination for patients with JRA; American Academy of Pediatrics Recommendations

Type	ANA	Age at onset (years)	Duration of disease (years)	Risk category	Eye examination frequency (months)
Oligoarthritis or polyarthritis	+	≤6	≤4	High	3
	+	≤6	>4	Moderate	6
	+	≤6	>7	Low	12
	+	>6	≤4	Moderate	6
	+	>6	>4	Low	12
	–	≤6	≤4	Moderate	6
	–	≤6	>4	Low	12
	–	>6	NA	Low	12
Systemic disease (fever, rash)	NA	NA	NA	Low	12

The American Academy of Pediatrics have devised ophthalmologic screening guidelines for patients with JRA based on several key factors shown to have increased risk and complications due to uveitis. Female sex, age <4 years, and a positive ANA titer are considered high-risk factors for developing uveitis (Table 28.5). Recent population studies from Canada show a small predisposition for JRA and uveitis associated with JRA among patients of European ancestry and a lower relative risk for children of African, Asian, and Indian ancestry. These population studies also concluded that female gender showed increased risk of asymptomatic uveitis compared to males with JRA [6].

Aggressive treatment of uveitis is required in these patients and usually only mild cases can be treated successfully with topical steroids. Monotherapy with topical NSAIDs alone has not been effective in controlling uveitis in these patients, although a concurrent topical NSAID can provide sufficient anti-inflammatory benefits to reduce the overall necessary dosage of topical steroids. A combination of topical and systemic steroids is usually instituted in JRA patients with moderate to severe uveitis. High-frequency topical prednisolone drops along with high induction dosages of oral prednisone (up to 2 mg/kg p.o. daily) or IV methylprednisone have been suggested. Tapering of steroids to avoid long-term complications of topical and systemic steroid use has been successful with adjunctive disease-modifying agents, or DMARDs. Methotrexate is the most commonly used of these medications as its safety profile in the pediatric population and success is well documented. Oral naproxen is also useful in this age group, although less potent than the DMARDs. Cyclosporine, azathioprine, and newer TNF-inhibiting drugs like infliximab and etanercept have been used in small studies with moderate improvement. Long-term success and safety data are not as extensive as methotrexate in treating these patients, but results are extremely encouraging [67, 69].

Long-term studies on JRA patients have shown that a majority of the patients had a favorable outcome. Approximately 50% of patients have persistent disease activity and continued joint pain and edema with only 14% of patients with continued uveitis [67]. On the other hand, JRA-associated uveitis when undertreated or untreated due to delayed diagnosis can devastate an eye with permanent cicatricial or inflammatory damage.

28.3.9 Herpetic Uveitis

Human herpes virus (HHV) family is a group of eight viruses ubiquitous in human hosts due to their characteristic ability to establish a persistent latent ganglionic infection. After initial exposure these viruses lie dormant in a latency stage within various neural cells and are capable of reactivation at any time, usually during periods of host immune susceptibility. The most prevalent pathologic viruses being herpes simplex-1 (HSV-1, commonly called oral herpes),

herpes simplex-2 (HSV-2, commonly called genital herpes), varicella-zoster virus (VZV, virus implicated in chickenpox and shingles), cytomegalovirus (CMV), and Epstein-Barr virus (EBV). Human herpes virus type 8 has been strongly associated with Kaposi sarcoma [30].

The herpes viruses are the causative agent in many ocular diseases, including blepharitis/dermatitis, conjunctivitis, dendritic epithelial keratitis, corneal ulceration, stromal keratitis, endotheliitis, trabeculitis, episcleritis, scleritis, iridocyclitis, and acute retinal necrosis (ARN) syndrome. HSV ocular involvement is almost always unilateral with less than 3% of patients in the HEDS trial having bilateral disease [26]. The location of herpetic reactivation can be virtually anywhere in the eye, including multiple anatomic locations, none of which are either mutually exclusive or mandatory in combination (Table 28.6). Thus, a wide variety of presentations can occur, most commonly epithelial keratitis, stromal keratitis, herpetic uveitis, and cutaneous vesicular eruptions. Trabeculitis is common with keratitis or uveitis, creating an elevated IOP in contradistinction to most uveitis entities that lead to depressed IOP. Other uveitic conditions creating high IOPs include toxoplasmosis, Fuchs' uveitis syndrome, and Posner-Schlossman syndrome [26, 30].

Herpetic corneal disease is an important cause of blindness, accounting for up to an estimated 500,000 cases annually in the USA. After active infection, herpes viruses lie dormant within the trigeminal ganglion or in corneal nerves and may reactivate to produce any of the many varieties of ocular herpetic disease [26]. The average age of onset for HSV uveitis is 46 years, accounting for approximately 9% of non-traumatic iritis cases in a referral clinic setting. The onset of HSV uveitis generally decreases with age, whereas VZV reactivation increases with age. About one in four individuals over the age of 80 years will suffer a bout of shingles, and one fourth of them will have trigeminal zoster. VZV is also triggered by periods of stress or impaired immunity [41].

Table 28.6 Ocular localization of human herpes simplex virus may occur in any combination

Eyelids
Periocular skin
Corneal epithelium
Corneal stroma
Corneal endothelium
Trabecular meshwork
Iris stroma
Iris sphincter
Vitritis
Retinitis
Papillitis

Corneal epithelial involvement can be seen as a dendrite or pseudodentrite thought to contain active virus. Many patients with VZV or HSV uveitis do not have any evidence of active or inactive corneal disease, however, careful examination may often reveal a previously undetected subtle postinflammatory corneal scar or ectasia characteristic of herpetic disease. Therefore steroids should be avoided in patients with active or potentially active severe axial epithelial disease.

Herpes viruses can damage nerves during active inflammation, and decreased corneal sensation can be noted acutely or after resolution of corneal disease. Since the HEDS trial much more information regarding the treatment of HSV ocular disease is available. Treatment of HSV epithelial keratitis with topical trifluridine drops with or without debridement can shorten the duration of disease. Herpetic uveitis develops in ~10% of patients with epithelial keratitis. The HEDS trial noted no benefit of adding oral acyclovir for epithelial disease in preventing development of iritis. Corneal stromal involvement can be seen with or without epithelial defect and up to 20% of patients with epithelial HSV keratitis will develop stromal keratitis within 2 years. Stromal keratitis is thought to be a non-infectious immune reaction and should be treated with topical corticosteroids and either topical or systemic antiviral medications. The HEDS trial showed a 68% decrease in stromal keratitis progressing to keratouveitis with steroid use, and a significant decrease in recurrence of stromal keratitis with long-term acyclovir prophylaxis. Topical steroids and oral acyclovir is also the recommended treatment for herpetic endotheliitis [26].

Herpetic uveitis is most often an acute, anterior, non-granulomatous uveitis. A more severe granulomatous reaction, however can cause inflammation anywhere in the eye with herpetic reactivation. Herpes uveitis needs to be kept in the differential for any unilateral uveitis of unknown etiology. Prompt aggressive treatment of stromal herpetic keratitis often

avoids progression to anterior uveitis. Recurrence of HSV uveitis is common, occurring in around 70% of patients and is more frequent in non-whites. Anterior chamber cell can vary depending on severity, and hypopyon and hyphema have both been described in HSV uveitis.

Patients with anterior uveitis from any of the human herpes viruses characteristically develop stellate KP. These unique lesions are defined by a diffuse homogeneous distribution differing extensively from KP from other etiologies. Stellate KP also appear as wispy dendritic or starfish-shaped deposits throughout the endothelium. They are much smaller than either granulomatous or non-granulomatous KP which themselves are usually far more prominent in the inferior one third of the cornea known as Arlt's triangle. Either coincidentally or by a pathophysiologic mechanism, the uveitic entities that create an elevated IOP are also those entities that produce stellate KP. Thus, stellate KP may result from a fluidic pathologic state that simultaneously creates trabecular meshwork congestion and subsequent aqueous humor outflow obstruction [26, 30].

Primary infection with VZV, better known as chickenpox, can occasionally cause a bilateral, self-limited, mild anterior uveitis. Reactivation VZV, or shingles, causes ipsilateral uveitis, usually concurrent with periocular skin involvement. Ocular involvement is said to occur in up to 70% of patients with involvement of the V1 or ophthalmic branch of the trigeminal nerve. Eye involvement is more likely with involvement on the tip of the nose (Hutchinson's sign) indicating reactivation through the nasociliary nerve, an inferior branch of V1 traveling through the orbit [68].

Herpetic uveitis is associated with iris stromal necrosis leading to atrophy, best seen by slit-lamp retroillumination, and pupillary irregularity as a result. Typically VZV iris atrophy is described as sectorial while HSV-1 and HSV-2 causes more diffuse iris atrophy. Recent reports of aqueous humor samples in a small number of patients with VZV uveitis demonstrated that higher VZV DNA levels detected in aqueous samples correlated with more severe iris atrophy and pupil irregularity [41, 68].

Glaucoma is an important diagnostic sign in herpetic uveitis. Unlike most uveitis where IOP is decreased due to decreased aqueous production by the inflamed ciliary body, herpetic uveitis can result in increased IOP resulting from trabeculitis. Chronic inflammation can cause scarring of the trabecular meshwork and chronic glaucoma. This elevation in IOP responds well to corticosteroid therapy. Posterior synechiae are another common outcome of HSV iridocyclitis, occurring in 58% of patients. Secondary glaucoma association with HSV was seen in up to 54% of patients and 38% of patients with VZV. This increase in pressure can be quite pronounced with IOP as high as 50–60 [30].

Intermediate, posterior, and panuveitis uveitis are also seen in herpetic ocular disease. Somewhat unique to the herpes family of viruses is the development of retinitis, particularly in immunocompromised patients. Posterior involvement is more common with VZV than HSV. Herpes infection (HSV-1, HSV-2, CMV, VZV) can cause ARN or bilateral acute retinal necrosis (BARN), although VZV and HSV-1 are most commonly implicated. ARN is a syndrome characterized by peripheral necrotizing retinitis and vasculitis, accompanied by variable degrees of vitritis, papillitis, and anterior granulomatous uveitis. Predominately a disease of healthy people, ARN can be visually devastating [25, 26, 41, 68]. Causative organisms have been identified from vitreous sampling in several clinical reports. These studies have shown that ARN is most likely caused by VZV or HSV-1 in patients over 25 years of age. In patients less than 25 years old, HSV-1 and HSV-2 were the most likely organisms identified [41].

Severely immunocompromised patients can develop peripheral outer retinal necrosis (PORN). This rare syndrome reveals significant peripheral retinal necrosis, vasculitis, retinal artery occlusions, anterior segment ischemia, cranial nerve palsies, orbital involvement, and positive VZV titers in the majority of cases [25, 38, 68].

Herpetic retinal necrosis is rapidly progressive and visually devastating thus requiring aggressive systemic antivirals specifically directed against the presumed causative organism. These medications include acyclovir, foscarnet, and ganciclovir. Valacyclovir and valganciclovir are newer prodrugs that facilitate superior gastrointestinal absorption profiles and often allow early outpatient management of highly responsive cases. Augmentation with intravitreal injections of ganciclovir or foscarnet or intraocular implants of ganciclovir (Vitrasert; Bausch & Lomb, Rochester, NY) are also used to halt dis-

ease and preserve vision. Retinal detachment is frequently caused by the severe retinal necrosis seen in herpetic disease. Thus, prophylactic laser photocoagulation is sometimes used around areas of necrosis to prevent detachment, with variable degrees of success [25, 26, 68].

A Goldmann-Witmer coefficient antibody analysis (GWC) value >2 has proved to be a useful tool in determining the etiology of infectious uveitis. The sensitivity of these tests has an excellent correlation to vitreous PCR, with 91% true positives and 9% false-negative GWC tests. The accuracy of GWC may suffer in comparison to PCR in immune-compromised patients due to impaired antibody production in AIDS and other immune deficiencies [16].

Animal and human studies have demonstrated a failure to develop delayed-type hypersensitivity skin reactions to herpes viruses in patients who have significant uveitis or acute retinal necrosis associated with either VZV or HSV [31]. This lack of delayed hypersensitivity may prove to be a helpful diagnostic tool. Also, this lack of responsiveness may reveal more insight regarding the pathophysiologic mechanism and immune dysfunction leading to ocular involvement from these ubiquitous viruses.

Comparison studies between VZV- and HSV-associated uveitis demonstrated that HSV presents with a more recurrent and remitting course whereas VZV was more typically a chronic uveitis. Secondary glaucoma association with HSV was seen in up to 54% of patients and 38% with VZV. Periocular and systemic steroids were required in 60% of patients with HSV uveitis and only 25% of patients with VZV. The same study showed approximately 20% of eyes were ultimately legally blind as a result of uveitis in both VZV and HSV [30].

Treatment of acute herpes zoster (shingles) with oral antivirals (acyclovir, valacyclovir, famciclovir) for 7–10 days has been proven to decrease episode time, severity, and complications if instituted within the first 72 h after vesicles first appear. There have been some reports of improvement after 72 h as well. The development of new skin lesions may also be an indication to start antiviral therapy even after 72 h. The use of concurrent systemic steroids in VZV has shown decreased pain and increased healing rates of cutaneous lesions, and may be considered particularly for severely afflicted patients. Live attenuated vaccine to VZV was approved by the FDA in 1995 and significantly decreased the incidence of VZV and subsequent complications. This vaccine, similar to the virus itself, can lie dormant in the trigeminal ganglion and reactivation can cause zoster in immune-compromised patients [43]. Rarely VZV can develop resistance to acyclovir usually from long-term low-dose therapy, especially in immune-compromised patients. Foscarnet is recommended for this scenario [38].

Treatment of herpetic anterior uveitis consists of cycloplegics and topical steroid drops with slow taper over weeks to months. Some patients may need chronic low-dose topical steroid therapy to remain quiescent, especially with VZV. Severe uveitis may benefit from systemic antivirals, as demonstrated in a small controlled trial. In this trial, patients with herpetic iridocyclitis using oral acyclovir 400 mg 5 times per day showed a trend toward improvement. IOP increase can be treated with glaucoma medications, although pressure usually returns to normal quickly with decreasing inflammation. Many patients who present with elevated IOP will return with normal pressures simply as a result of improved trabeculitis treated with topical steroids alone [30].

Oral acyclovir 400 mg twice daily for 1 year is recommended in patients who have two or more scarring epithelial infections per year or any stromal disease. Valacyclovir has recently been proven as effective as acyclovir and requires less frequent dosing. Unfortunately, there is no generic equivalent to valacyclovir in the USA, markedly increasing the cost [26]. A 7- to 10-day course of oral acyclovir, valacyclovir, or famciclovir is recommended within the first 72 h of a herpes zoster outbreak to reduce uveitis duration and severity [38]. Longer therapy may be beneficial as studies have shown active virus from cutaneous cultures up to 32 days after starting antiviral therapy. Adding oral steroids may help with resolution, and low-dose tricyclic antidepressants have been used to prevent post-herpetic neuralgia. Post-herpetic neuralgia can be extremely difficult to treat, testing the acumen of the managing physician and the psychologic fortitude of the patient [38]. A wide variety of treatments are available, including sophisticated pain management techniques, stellate ganglion and peripheral trigeminal nerve blocks, and multiple pharmaceutical agents. Post-herpetic neuralgia is less common and less severe in younger adults and children when compared to older adults and senior citizens.

Take Home Pearls

- A methodical and reproducible approach to each uveitis patient will improve clinic flow as well as cost effectiveness of treatment.
- In ocular toxocariasis laser photocoagulation or cryoretinopexy of the larvae is not suggested because destruction of the nematode may cause a severe inflammatory reaction.
- Topical aminocaproic acid gel (Caprogel; Ista Pharmaceuticals, Irvine) has been shown to significantly reduce the risk of rebleeding during the critical first 5 days following blunt trauma causing a hyphema, while also avoiding systemic side effects.
- In FUS, heterochromia can be seen in 82% of patients. Normally a lighter colored iris becomes darker when stromal loss causes the underlying densely pigmented posterior iris pigmented epithelium to show through. Conversely, a darker colored iris becomes lighter as the deep brown iris stroma slowly melts away leaving more muscle fibers and less melanin visible.
- Ocular toxoplasmosis responds to a wide variety of therapies including systemic steroids and antibiotics. However, periocular and intravitreal steroids are absolutely contraindicated due to predictably poor outcomes resulting from a loss of immune control of the intraretinal protozoan parasites.
- Seronegative spondyloarthropathies constitute a spectrum of diseases frequently associated with the HLA B27 locus. This allele, along with HLA B29 associated birdshot chorioretinopathy, are the two truly useful genetic determinants employed in the judicious laboratory evaluation of uveitis patients.
- Sarcoid uveitis can occur with or without signs of systemic sarcoidosis. High-frequency topical, injection, or systemic steroid administration is often necessary in these patients to achieve the universal goal of a completely quiet eye. Failure to do so leads to permanent breakdown of the blood–aqueous barrier and thereby chronic flare, cystoid macular edema, and expectedly poor surgical outcomes.
- Pars planitis syndrome, an idiopathic intermediate uveitis, is a diagnosis of exclusion that is often associated with multiple sclerosis. However, a wide variety of uveitic syndromes may present with intermediate uveitis and must be ruled out first. These diseases include: Lyme disease, Epstein-Barr virus (EBV) infection, West Nile virus, tuberculosis, cat-scratch disease, toxocariasis, sarcoidosis, and Behçet's disease.
- Juvenile idiopathic arthritis associated uveitis is most commonly seen in pauciarticular-type females who are ANA positive. This ocular disease is known also as "white iritis" due to the absence of classic symptoms including redness. It is frequently asymptomatic, necessitating regular screening examinations by an ophthalmologist familiar with pediatric uveitis.
- Herpetic uveitis is not necessarily associated with corneal disease as the herpes virus may present in virtually any ocular tissue. Trabeculitis frequently accompanies herpes uveitis making this one of the few uveitic conditions associated with IOP elevation.

References

1. Ali A, Samson CM (2007) Seronegative spondyloarthropathies and the eye. Curr Opin Ophthalmol 18:476–480
2. Avunduk AM, Avunduk MC, Baltaci AK, et al. (2007) Effect of melatonin and zinc on the immune response in experimental Toxoplasma retinochoroiditis. Ophthalmologica 221:421–425
3. Barisani-Asenbauer T, et al. (2001) Treatment of ocular toxocariasis with albendazole. J Ocular Pharmacol Ther 3:287–294
4. Birnbaum AD, Tessler HH, Schultz KA, et al. (2007) Epidemiologic relationship between Fuchs heterochromic iridocyclitis and the United States Rubella Vaccination Program. Am J Ophthalmol 144:447–448
5. Braswell RA, Kline LB (2007) Neuro-ophthalmologic manifestations of sarcoidosis. Int Ophthalmol Clin 47:67–77
6. Cassidy J, Kivlin J, Lindsley C, Nocton J; Section on Rheumatology; Section on Ophthalmology (2006) Ophthalmologic examinations in children with juvenile rheumatoid arthritis. Pediatrics 117:1843–1845
7. Cassidy J, Levinson JE, Bass JC, Baum J, et al. (1986) A study of classification criteria for a diagnosis of juvenile rheumatoid arthritis. Arthritis Rheum 29:274–281
8. Chuah CT, Lim MC, Seah LL, et al. (2006) Pseudoretinoblastoma in enucleated eyes of Asian patients. Singapore Med J 47:617–620
9. Chung YM, Lin YC, Huang DF, et al. (2006) Conjunctival biopsy in sarcoidosis. J Chin Med Assoc 69:472–477
10. Crouch ER Jr, Crouch ER (1999) Management of traumatic hyphema: therapeutic options. J Pediatr Ophthalmol Strabismus 36:238–250
11. Crouch ER Jr, Williams PB (1997) Topical aminocaproic acid in the treatment of traumatic hyphema. Arch Ophthalmol 115:1106–1112
12. Crouch ER Jr, Williams PB (1992) Secondary hemorrhage in traumatic hyphema. Am J Ophthalmol 113:344–346
13. Darrell RW, Wagener HP, Kurland LT (1962) Epidemiology of uveitis. Arch Ophthalmol 68:100–112
14. de Boer J, Berendschot TT, van der Does P, Rothova A (2006) Long-term follow-up of intermediate uveitis in children. Am J Ophthalmol 141:616–621
15. de Groot-Mijnes JD, de Visser L, Rothova A (2006) Rubella virus is associated with Fuchs heterochromic iridocyclitis. Am J Ophthalmol 141:212–214
16. De Groot-Mijnes JD, Rothova A, Van Loon AM, Schuller M, et al. (2006) Polymerase chain reaction and Goldmann-Witmer coefficient analysis are complimentary for the diagnosis of infectious uveitis. Am J Ophthalmol 141:313–318
17. Deutsch TA, Goldbery MF (1984) Traumatic hyphema: medical and surgical management. Focal points: clinical modules for ophthalmologists, module 5. American Academy of Ophthalmology, San Francisco
18. Dodds E (2006) Toxoplasmosis. Curr Opin Ophthalmol 17:557–561
19. Donaldson MJ, Pulido JS, Herman DC, et al. (2007) Pars planitis: a 20-year study of incidence, clinical features, and outcomes. Am J Ophthalmol 144:812–817
20. Dutly F, Altwegg M (2001) Whipple's disease and "Tropheryma whippelii." Clin Microbiol Rev 14:561–583
21. Eckert GU, Melamed J, Menegaz B (2007) Optic nerve changes in ocular toxoplasmosis. Eye 21:746–751
22. Edelsten C, Reddy MA, Stanford M, Graham EM (2003) Visual loss associated with pediatric uveitis in English primary and referral centers. Am J Ophthalmol 135:676–680
23. Fong LP (1994) Secondary hemorrhage in traumatic hyphema. Predictive factors for selective prophylaxis. Ophthalmology 101:1583–1588
24. Foster CS (2008) Pediatric uveitis. http://www.uveitis.org/medical/articles/clinical/ pediatricuv.html
25. Ganatra JB, Chandler D, Santos C, Kuppermann B, et al. (2000) Viral causes of the acute retinal necrosis syndrome. Am J Ophthalmol 129:166–172
26. Green LK, Pavan-Langston D (2006) Herpes simplex ocular inflammatory disease. Int Ophthalmol Clin 46:27–37
27. Holland GN (2006) The enigma of pars planitis, revisited. Am J Ophthalmol 141:729–730
28. Holland GN, Stiehm ER (2003) Special considerations in the evaluation and management of uveitis in children. Am J Ophthalmol 135:676–680
29. Jones LA, Alexander J, Roberts CW (2006) Ocular toxoplasmosis: in the storm of the eye. Parasite Immunol 28:635–642
30. Jones R 3rd, Pasquale LR, Pavan-Langston D (2007) Herpes simplex virus: an important etiology for secondary glaucoma. Int Ophthalmol Clin 47:99–107
31. Kezuka T, Sakai J, Minoda H, et al. (2002) A relationship between varicella-zoster virus-specific delayed hypersensitivity and varicella-zoster virus-induced anterior uveitis. Arch Ophthalmol 120:1183–1188
32. Kiss S, Letko E, Qamruddin S, et al. (2003) Long-term progression, prognosis, and treatment of patients with recurrent ocular manifestations of Reiter's syndrome. Ophthalmology 110:1764–1769
33. Koo L, Young LH (2006) Management of ocular toxoplasmosis. Int Ophthalmol Clin 46:183–193
34. Kump L (2005) Analysis of pediatric uveitis cases at a tertiary referral center. Ophthalmology 112:1287–1292
35. Kutner BN, Fourman SB, Sheppard JD, et al. (1987) Aminocaproic acid reduces the risk of secondary hemorrhage in patients with traumatic hyphema. Arch Ophthalmol 105:206–208
36. La Hey E, Baarsma GS, De Vries J, Kijlstra A (1991) Clinical analysis of Fuchs' heterochromic cyclitis. Doc Ophthalmol 78:225–235
37. Leung YY, Tam LS, Kun EW, et al. (2007) Psoriatic arthritis as a distinct disease entity. J Postgrad Med 53:63–71
38. Liesegang TJ (2004) Herpes zoster virus infection. Curr Opin Ophthalmol 15:531–536
39. Mavrikakis I, Rootman J (2007) Diverse clinical presentations of orbital sarcoid. Am J Ophthalmol 144:769–775
40. McVeigh CM, Cairns AP (2006) Diagnosis and management of ankylosing spondylitis. BMJ 333:581–585
41. Miserocchi E, Waheed NK, Dios E, et al. (2002) Visual outcome in herpes simplex virus and varicella zoster virus uveitis: a clinical evaluation and comparison. Ophthalmology 109:1532–1537

42. Mora P (2006) Use of systemic cyclosporin A in a case of severe Toxocara uveitis. J Infect 52:159–161
43. Naseri A, Good WV, Cunningham ET Jr (2003) Herpes zoster virus sclerokeratitis and anterior uveitis in a child following varicella vaccination. Am J Ophthalmol 135:415–417
44. Nozik RA, Smith RE (1989) Uveitis: a clinical approach to diagnosis and management, 2nd edn. Williams and Wilkins, Baltimore, pp 85
45. Paivonsalo-Hietanen T, Tuominen J, Saari KM (2000) Uveitis in children: population-based study in Finland. Acta Ophthalmol Scand 78:84–88
46. Perkins ES (1966) Pattern of uveitis in children. Br J Ophthalmol 50:169–185
47. Prabhakaran VC, Saeed P, Esmaeli B, et al. (2007) Orbital and adnexal sarcoidosis. Arch Ophthalmol 125:1657–1662
48. Quentin CD, Reiber H (2004) Fuchs heterochromic cyclitis: rubella virus antibodies and genome in aqueous humor. Am J Ophthalmol 138:46–54
49. Reveille JD, Arnett FC (2005) Spondyloarthritis: update on pathogenesis and management. Am J Med 118:592–603
50. Ritchlin (2006) Newer therapeutic approaches: spondyloarthritis and uveitis. Rheum Dis Clin North Am 32:75–90, viii
51. Roizen N, Kasza K, et al. (2006) Impact of visual impairment on measures of cognitive function for children with congenital toxoplasmosis: implications for compensatory intervention strategies. Pediatrics 118:e379–e390
52. Romero R, Peralta J, Sendagorta E, et al. (2007) Pars planitis in children: epidemiologic, clinical, and therapeutic characteristics. J Pediatr Ophthalmol Strabismus 44:288–293
53. Rose CD, Wouters CH, Meiorin S (2006) Pediatric granulomatous arthritis: an international registry. Arthritis Rheum 54:3337–3344
54. Sampaio-Barros PD (2006) Characterization and outcome of uveitis in 350 patients with spondyloarthropathies. Rheumatol Int 26:1143–1146
55. Saurenmann RK, Rose JB, Tyrrell P (2007) Epidemiology of juvenile idiopathic arthritis in a multiethnic cohort: ethnicity as a risk factor. Arthritis Rheum 56:1974–1984
56. Schwab IR (1991) The epidemiologic association of Fuchs' heterochromic iridocyclitis and ocular toxoplasmosis. Am J Ophthalmol 111:356–362
57. Scott RA (2001) The effect of pars plana vitrectomy in the management of Fuchs heterochromic cyclitis. Retina 21:312–316
58. Sheppard JD, Garovoy MR (1999) The major histocompatibility complex. In: Friedlander MH (ed) Basic ophthalmologic science, vol 1, chap 38. Lippincott, Philadelphia
59. Sheppard JD (1993) Posterior uveitis. In: Nozik RA, Michaelson JB (eds) Ophthalmology clinics of North America, vol 6, no 1. Saunders, Philadelphia
60. Sheppard JD, Nozik RA (1989) Practical diagnostic approach to uveitis. In: Duane TA, Jaeger WE (eds) Clinical ophthalmology, vol 4, chap 33. Lippincott, Philadelphia
61. Sijssens KM, Rothova A, Van De Vijver DA (2007) Risk factors for the development of cataract requiring surgery in uveitis associated with juvenile idiopathic arthritis. Am J Ophthalmol 144:574–579
62. Spagnolo P, Sato H, Marshall SE, et al. (2007)Association between heat shock protein 70/Hom genetic polymorphisms and uveitis in patients with sarcoidosis. Invest Ophthalmol Visual Sci 48:3019–3025
63. Stewart JM, Cubillan LD, Cunningham ET (2005) Prevalence, clinical features, and causes of vision loss among patients with ocular toxocariasis. Retina 25:1005–1013
64. Tan HK, Schmidt D, Stanford M, et al. (2007) European Multicentre Study on Congenital Toxoplasmosis (EMSCOT). Risk of visual impairment in children with congenital toxoplasmic retinochoroiditis. Am J Ophthalmol 144:648–653
65. Taylor SR, McCluskey P, Lightman S (2006) The ocular manifestations of inflammatory bowel disease. Curr Opin Ophthalmol 17:538–544
66. Tugal-Tutkun I, Havrlikova K, Power WJ, et al. (1966) Changing patterns in uveitis of childhood. Ophthalmology 103:375–383
67. Wright T, Cron RQ (2007) Pediatric rheumatology for the adult rheumatologist II: uveitis in juvenile idiopathic arthritis. J Clin Rheumatol 13:205–210
68. Zamir E (2005) Herpetic posterior uveitis. Int Ophthalmol Clin 45:89–97
69. Zierhut M, Michels H, Stubiger N, et al. (2005) Uveitis in children. Int Ophthalmol Clin 45:135–156

Common Conditions Affecting the External Eye

29

Cintia F. Gomi and David B. Granet

Contents

Core Messages

- Hordeolum and chalazion are the most common eyelid lesions in childhood.
- Nevi are the most common conjunctival pigmented lesion with less than 1% of risk of malignant transformation.
- The nevus of Ota predisposes to development of uveal malignant melanoma, but not conjunctival melanoma.
- Besides cosmetic issues, dermoids may cause visual impairment, requiring surgery.
- Molluscum contagiosum is a common viral disease that occurs in clusters in the skin and may resolve spontaneously over the course of several months.
- Prophylaxis for neonatal conjunctivitis is mandatory due to well-known complications and sequelae.
- Acute conjunctivitis is a common cause of pediatric primary care visits. Although it is a self-limited condition, the majority of cases are infectious and contagious, urging for treatment.
- Allergy is the most common cause of chronic conjunctivitis, affecting more than 15% of the world population. Topical combinations of mast cell stabilizers and antihistamine drops are currently the best choice of treatment.

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29.1 Introduction

The "external eye" comprises the eyelids, eyelashes, conjunctiva, sclera, and cornea. Several diseases can affect and compromise these structures. This chapter will update the most common pathologies and their treatment.

29.2 Hordeolum/Chalazion

Hordeolum and chalazion are the most common eyelid lesions in childhood [1]. They are usually diagnosed and treated on the basis of clinical examination alone. Hordeolum is an obstruction of the sebaceous gland with subsequent infection of the gland and abscess formation. It is usually self-limited and subsides with conservative treatment. Chalazion may evolve from internal hordeolum, but usually arises secondarily to non-infectious obstruction of sebaceous gland duct. Although these lesions are generally not visually threatening, there have been reports of large chalazia causing amblyopia due to mechanical ptosis, hypermetropia, and astigmatism [2–4].

A study published in 2004 by Dhaliwal et al. [5] showed cytopathologic responses of fine-needle aspiration smears from chalazia. They found two broad patterns of granulomatous reaction with some overlapping features. They termed the first group "mixed-cell granuloma" and the second "suppurative granuloma." In the first type, the smear showed few neutrophils with a predominant population of plasma cells, lymphocytes, and macrophages. Fibroblasts and capillary fragments (granulation tissue) were also present and probably represent the concomitant repair process in the evolution of the lesion. In the suppurative type, the granuloma contained numerous neutrophils in a proteinaceous background. Relative paucity of lymphocytes, plasma cells, isolated macrophages, giant cells, and granulation tissue distinguished this pattern from the previous one. The authors believe that they represent different stages of the inflammatory process of chalazia, thus explaining the overlap of features between them. Since the evolution of the lesion represents a continuous process, this classification is somewhat arbitrary and depends on the relative proportions of the various cell types seen in the aspirates.

Classic conservative management of hordeolum and chalazion (i.e., warm compresses, hygiene measures) typically present a high success rate. When this approach fails, other interventions include incision and curettage of contents, and/or intralesional steroid injections. Other techniques have been described such as chalazion removal with CO_2 laser and perilesional steroid injection [6, 7].

In their follow-up work from 2005, Dhaliwal and Bhatia [8] compared incision and curettage with intralesional steroid injections and, based on the results of the chalazion aspiration smears, the suppurative granuloma type responded significantly better to incision and curettage while the mixed-cell type responded equally to both treatments.

29.3 Pinguecula/Pterygium

Pterygium (Fig. 29.1) and pinguecula are uncommon entities in childhood, although they have been described in children as young as 4 years of age.

New research has shown evidence that questions if a pterygium really represents a chronic degenerative condition. This research suggests that the pathologic mechanism could be an ultraviolet-related tumor rather than degenerative disease [9–13]. Other studies report that pterygium could also be associated with oncogenic viruses such as human papillomavirus virus and herpes simplex virus [14]. Because these lesions are relatively uncommon in children, masquerade conditions should be suspected and pathologic analysis of the tissue should be requested on removal.

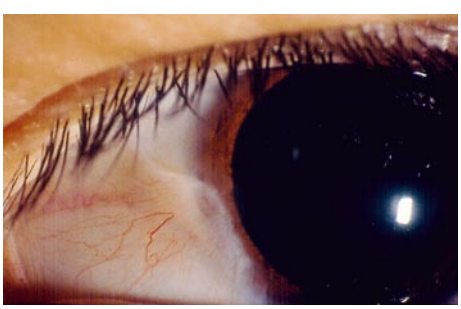

Fig. 29.1 Fourteen-year-old boy with large nasal pterygium invading the limbus

29.4 Pigmented Lesions of the Conjunctiva

Nevi are the most common conjunctival pigmented lesion. They are usually congenital and present as a variably pigmented, flat or slightly elevated mass. They usually remain stationary throughout life with less than 1% of risk of malignant transformation. With age, these lesions may vary in pigmentation in about 5% of the cases and in size in about 7% [15]. Periodic observation with photographic documentation for comparison is ideal. If suspicious changes occur or if growth is observed, local excision of the lesion should be considered. When performing the surgery, the mass should be removed entirely as one single piece using a "no-touch" technique. Cryotherapy should be applied at the margins of excision to help prevent recurrence of the nevus and also to prevent recurrence if the lesion should prove to be malignant [15]. The other indication for excision is cosmetic. For this purpose, the use of laser treatment has been used to treat many pigmented cutaneous lesions by dermatologists [16]. Overall it has been found to be a safe and effective procedure. Kwon et al. [17] reported the results of laser photoablation for conjunctival nevus in carefully selected patients. They performed this technique in 30 eyes of 28 patients with good results and no scar formation or recurrence during the follow-up period. However, long-term outcomes are not yet available. The main disadvantage of the laser treatment is that it does not allow for histopathology and carries the risk of destroying a malignant primary lesion without a diagnosis. The authors recommend that laser photoablation should be performed only on patients with no evidence or suspicion of malignancy and for those who refuse surgical alternatives.

Melanosis is a term used to describe excessive melanotic pigmentation in tissues, but in the absence of a mass. In ocular melanocytosis, the congenital increase in pigmentation of the melanocytes can be found in the uvea, sclera, episcleral, and orbit; typically, there is no pigment in the conjunctiva. Some cases are also accompanied by hyperpigmentation of the dermis of the eyelids and periocular skin, characterizing the nevus of Ota. The nevus of Ota is more frequently seen in Asian and African descendents than in Caucasians. Both pathologies predispose to development of uveal malignant melanoma, but not conjunctival melanoma [18]. Cosmetically, the hyperpigmentation can be bothersome but the treatment for the melanosis has been limited to the skin. Several types of laser have been used and reports show good results. For the ocular hyperpigmentation, Kim et al. [19] reported in 2005 a series of six cases in which a flipped scleral flap surgery was performed. In this technique, a partial-thickness scleral flap is dissected from just posterior to the limbus to the muscle insertion site. The free flap is then flipped and reattached to the scleral bed with sutures, hiding the pigmented face internally. This results in a less pigmented surface being visible. They performed the surgery on the nasal and temporal sclera with a satisfactory outcome in all patients during the follow-up period (average of 37 months).

29.5 Choristomas

Choristomas are lesions composed of tissue not normally found in the affected area, whereas hamartomas are anomalous development of tissue natural to the affected area [20]. Dermoids are the most common type of choristomas (Fig. 29.2). Besides cosmetic issues, they may also cause visual impairment due to astigmatism, blocking of the visual axis by the lesion, or other corneal lesions resulting from the elevated mass such as dellen formation, drying, and superficial keratitis. When indicated, surgical treatment is still the only way to deal with limbal dermoids. Surgical techniques include simple excision, excision with lamellar keratoplasty, and excision with penetrating keratoplasty. Although a less complex surgery,

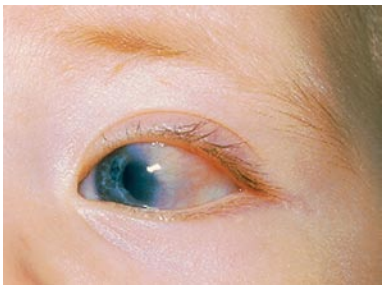

Fig. 29.2 Two-year-old boy with large corneal dermoid affecting the visual axis

simple excision may cause complications such as residual opacity, neovascularization, pseudopterygium formation, and globe perforation during surgery. Excision of the lesion with lamellar keratoscleroplasty offers good outcome without the problem of vascularization and pseudopterygium seen after simple excision or shaving of the dermoid [21]. This technique is complex and time consuming, as the donor tissue has to be dissected to match the host corneal bed thickness. In 2005, Shen et al. [22] published a series of 10 patients in which a full-thickness corneal graft was used in lamellar keratoplasty instead of a partial-thickness one. To reduce complications, the corneal endothelium from the donor was removed. The authors reported that this technique is simpler than the customized thickness grafts and suggested that, because Descemet's membrane is not violated, it results in a smoother posterior surface providing an optically better graft–host interface; also it can provide additional support for dangerously thin corneas. They concluded that this technique provides satisfactory visual and cosmetic outcomes. This technique, however, is not exempt from complications such as graft rejection.

29.6 Molluscum Contagiosum

Molluscum contagiosum is a common viral disease that affects mainly children and immunocompromised patients. It is caused by a large DNA poxvirus that produces benign, small umbilicated papules on the skin and mucous membranes. Molluscum usually occurs in clusters and most lesions resolve spontaneously but may take several months to years. In the meantime, it can lead to widespread cutaneous dissemination, dermatitis, pruritus, discomfort, bacterial superinfection, acute inflammatory and chronic granulomatous reactions, and scar formation, and most important it is contagious to other children [23]. Therefore, treatment is recommended. Medical and surgical options exist, with the treatment of choice depending on the physician's and parents' preferences. Treatment can be divided into three categories: destructive (chemical and physical), immunomodulatory, and antiviral [23]. Destructive therapies are the most commonly used and include cryotherapy, curettage, topical application of keratolytics or vesicants, pulsed dye laser, and photodynamic therapy. Immunomodulatory treatments include imiquimod and cimetidine. Studies with cimetidine showed inconclusive results, but it appears that this drug is more effective in atopic children [23–25]. Treatment with antiviral medications is available, but rarely used for treatment of poxvirus infections in immunocompetent patients; however studies suggest that it may play an important role in the treatment of immunocompromised patients [23, 26].

29.7 Neonatal Conjunctivitis

Neonatal conjunctivitis is usually a hyperacute papillary conjunctivitis that affects infants during the first month after birth. The time of the first manifestations of conjunctivitis is helpful in suggesting the etiologic cause. Conjunctivitis caused by *Neisseria gonorrhoeae* was the single greatest cause of blindness in European infants in the nineteenth century [27]. After the introduction of prophylaxis, the most common etiologic agent in the USA and Europe during the 1990s was *Chlamydia trachomatis* [28]. Since this is an entity with well-known complications and sequelae, prophylaxis is mandatory and widely accepted. Several chemical agents have been used, including erythromycin, tetracycline, and silver nitrate. Reports of outbreaks of antibiotic-resistant bacterial conjunctivitis in neonates pushed for a new prophylactic agent that would be effective against the most common etiologic pathogens without increasing resistance. After a pilot study performed in the USA [29], a larger clinical trial conducted by Isenberg et al. was performed in Kenya, comparing erythromycin, silver nitrate, and povidone-iodine (PVP-I) [30]. The authors concluded that povidone-iodine 2.5% was more effective preventing conjunctivitis than the other two drugs. Later, they performed another trial to evaluate if a second dose of PVP-I applied 24 h after the first instillation would achieve better prophylaxis than a single drop and concluded that the second drop provided no further benefit [31]. There are several advantages of using PVP-I for prophylaxis, including the low risk of inducing drug resistance, low cost, and broad antimicrobial spectrum for bacteria, fungi, viruses, and protozoa. In 2006, Richter et al., in a prospective controlled randomized study, evaluated the

effects of the iodine drops on thyroid hormone levels and renal excretion. They observed that after instillation of PVP-I eye drops, both urinary iodine excretion and thyroid-stimulating hormone levels ranged within physiological levels. Therefore the authors concluded that administration of 1.25% PVP-I eye drops in healthy term newborns may be regarded as safe. However, they did not evaluate the safety of this drug in preterm newborns [32].

29.8 Conjunctivitis

Acute conjunctivitis is a common cause of pediatric primary care visits. Most cases of acute conjunctivitis are infectious and therefore contagious. The etiology has been documented as bacterial in 50–75% of pediatric cases [33–37]. The fear of spreading the disease in day-care centers and schools leading to missed classes and absence of parents from work has culminated in a pressure for early treatment. This behavior raised concern regarding drug-resistant pathogens, overprescription, increased cost of health care, and increased adverse events related to those drugs. Although most cases of infective conjunctivitis are self-limited, it can take weeks for the infection to clear. Various reports have demonstrated that treatment does help shorten the clinical course, reduces contagious spreading, and allows the patient to return to daily routine earlier [38–40]. Physicians, especially general practitioners and pediatricians, face this dilemma of overprescribing or dealing with the pressure of the social impact and morbidity of this disease. A recent study conducted by Patel et al. [39] in a pediatric emergency department showed that antibiotics were prescribed 83% of the time and were correctly prescribed 86% of the time. This high statistic has been shown before. A survey performed in England with 234 general practitioners [41] showed that 95% of the physicians prescribed topical antibiotics for acute infective conjunctivitis, with 20% of those prescribing for every case. In spite of that, in the 67% of the practitioners that reported ever collecting a swab sample of the conjunctiva, the majority (84%) did so only in selected cases (less than 10% of cases seen).

Streptococcus pneumoniae and *Haemophilus influenzae* are the most common etiologic agents isolated in bacterial conjunctivitis in children. Several studies have shown that both bacteria have developed resistance to some drugs. In a study published in 2000, Block et al. [36] performed cultures of conjunctival swabs in 250 children with acute conjunctivitis. They found that one-fourth of the cases of pneumococcal conjunctivitis were resistant to high levels of penicillin and over two-thirds of isolated *H. influenza* produce beta-lactamase. It is likely that the resistance seen is from the systemic use of antibiotics or the chronic use of topicals rather than short courses of topical therapy.

The diagnosis of conjunctivitis is straightforward, but the differentiation between viral and bacterial is clinically difficult, as the signs and symptoms overlap. Being a self-limited condition with high spontaneous resolution rate without treatment that may also be viral, one could argue against the real necessity of antibiotic treatment for every case of conjunctivitis. However, it is known that the treatment is more effective if applied in the first few days of infection [40]. Bacteriologic examination and cultures are not commonly requested for every case due to the costs of the examinations and the time delay to get the results back. They are especially requested in severe cases, outbreaks, neonates, and recurrences. If prescribing antibiotics for every case of conjunctivitis becomes the exception, not the rule, it is possible that the incidence of bacterial conjunctivitis as a contagion will increase, but it should not affect the incidence of viral conjunctivitis.

As most practitioners treat those cases empirically with topical antibiotics, first-line treatment should provide coverage for the most common infective agents. The ideal antibiotic would offer broad antimicrobial spectrum with low dosing frequency, fast bactericidal effect, and low rate of adverse effects (including risk of resistance). Several drugs are effective against bacterial conjunctivitis, but fluoroquinolones are the most used ocular drops. It should be noted this class of medication is not approved "on label" in infants and children less than 1 year of age [42, 43]. The American Academy of Pediatrics recommends that the use of systemic fourth-generation fluoroquinolones should be restricted to situations in which there is no safe and effective alternative [42]. Fortunately this admonition dramatically decreases the chance of resistance formation to their topical cousins. New drugs and formulations are constantly

being developed due to the necessity to overcome the resistance to older drugs. For example in 2007, some studies have been published regarding new ocular formulations for azithromycin [44, 45]. This older drug had a wide in vitro antimicrobial spectrum against gram-positive and gram-negative bacteria. The AzaSite Clinical Study Group conducted a phase 3 clinical trial to assess the safety and tolerability of a 5-day regimen of AzaSite, a formulation of 1% azithromycin in DuraSite, a polymeric mucoadhesive delivery system (InSite Vision, Alameda, CA), and compared it with tobramycin 0.3% ophthalmic solution [44]. This technology (DuraSite) allows the active component of this medication to stay on the ocular surface longer than the conventional aqueous eye drops; a potential concern for resistance that led to an FDA warning on their package insert regarding the missing of doses. This study showed that 1% azithromycin in DuraSite used twice a day for the first 2 days, and then daily for 3 days could achieve a success profile similar to tobramycin at four doses a day for 5 days only if combined with extra drops of vehicle in preservative to total four applications per day. No significant differences in the overall incidence of adverse events were detected between the treatment groups.

The American Academy of Pediatrics Red Book and the National Health and Safety Performance Standards guidelines suggest that children with bacterial conjunctivitis without systemic illness should be allowed to return to school once therapy is implemented [46]. The problem with the implementation of this guideline is the difficulty to clinically differentiate bacterial from viral conjunctivitis [43].

Thus bacterial conjunctivitis should be treated to decrease patient morbidity, allow an earlier return to work and school, as well as to prevent contagion. Given that conjunctivitis is generally treated by non-ophthalmic specialists, failure to improve on topical antibiotics after a few days of therapy may well indicate a "masquerade disease" such as herpes, iritis, corneal abrasion, etc. Thus in the pediatric age group, topical therapy should consist of fast-acting, effective bactericidal treatment with broad-spectrum coverage unlikely to cause resistance, dosed in a manner geared to enhance compliance.

Adenovirus is the most common etiologic agent for red or pink eye worldwide. It is known to spread easily and cause outbreaks. Laboratory tests to diagnosis adenoviral infections currently include viral cell culture with confirmatory immunofluorescence staining (CC-IFA), polymerase chain reaction (PCR), serologic methods, and antigen detection. Cell culture with immunofluorescence staining is the gold standard but PCR has shown better sensitivity compared to cell culture [47–53]. Despite the availability of these tests, few physicians order them before starting treatment. Several attempts to create a reliable and easy method to identify adenovirus have been done with no success. They proved to be either too sensitive, not specific enough, or technically challenging to be performed in office. In 2006, Sambursky et al. evaluated a new method to screen suspected cases of adenovirus [54]. The Rapid Pathogen Screening (RPS) Adeno Detector (Rapid Pathogen Screening, South Williamsport, PA) is based on the principle of lateral flow immunochromatography. It detects common epitopes on the hexon protein of the adenovirus within a conserved region among the serotypes, allowing it to detect all known serotypes. The authors reported that it is a rapid test requiring 10 min for a result and uses a sample of tear fluid. They compared the results obtained with the RPS Adeno Detector with CC-IFA and PCR. Using the CC-IFA as reference, the RPS Adeno Detector demonstrated a sensitivity of 88% and a specificity of 91% with overall agreement of 90%. When PCR was used as the reference method, the RPS Adeno Detector showed a sensitivity of 89%, specificity of 94%, and overall agreement of 92%. The comparison of the two reference methods showed a sensitivity of 91% and specificity of 100%. The authors believe that this test's ability to provide an immediate result will help the practitioner decide the best treatment for the patient, thus decreasing the current practice of empirically treating every case of conjunctivitis with antibiotics. Adenovirus, although self-limited, may cause significant morbidity such as persistent subepithelial infiltrates, chronic epiphora, dry eyes, conjunctival foreshortening, and symblepharon formation. In severe cases, additional treatment is required. Traditional diagnostic tests require time and the delay in treatment could increase the risk of complications. Therefore, if a fast and reliable test is available, it could help guide the physician on treatment and follow-up schedule.

29.9 Allergies

Allergy is the most common cause of chronic conjunctivitis, affecting more than 15% of the world population with higher incidence in industrialized countries [55, 56]. Over the past 30–40 years, an increase in the incidence of atopic diseases was observed [57, 58]. In 1989, Strachan published a possible explanation for this rise, which became known as the "hygiene hypothesis" [59]. This hypothesis was later expanded and it is believed that the declining microbial exposure is a major cause in the increasing incidence of atopy. However, the mechanism by which this reduced exposure to pathogenic or nonpathogenic microbes results in a higher prevalence of allergic disease is of debate [60, 61].

Allergic conjunctivitis presents a peak during late childhood and young adulthood. The ocular allergic response results from exposure of the conjunctiva to allergens. In children, the most common types are seasonal/perennial conjunctivitis and less frequently vernal keratoconjunctivitis.

Seasonal and perennial conjunctivitis are IgE-mediated (humoral response) and are induced typically by airborne allergens. Perennial allergy presents with symptoms throughout the year with seasonal exacerbations and it is often less severe than the seasonal type. This type of atopy carries a strong family history. The treatment for this condition starts with avoidance or elimination of the causative agents. Studies have shown that the bedroom is the part of the house that often contains more house dust mites. Thus, preventive measures should be applied, such as removing stuffed toys, duvets, and carpeting from the bedroom and washing bedding material more frequently and properly [57].

For symptomatic relief, cold compresses and over-the-counter lubricant drops can be of mild help. Of all the mediators involved in the allergic response, the clinical signs and symptoms are predominantly caused by histamine. Topical combination of mast cell stabilizers and antihistamine drops are currently the best choice of treatment. Several drugs are currently available, affecting different steps of the humoral allergic reaction when tested in vitro [62]. Azelastine is an H1 antagonist, and a study with human cord blood stem cell-derived mast cell showed that it inhibits the release of tryptase, IL-6, IL-8, and TNF-α. Epinastine is an H1 and H2 antagonist that showed no effect on membrane fluidity, and yet inhibits calcium uptake and release from intracellular stores and dose dependently suppresses calmodulin in guinea-pig mast cells. Ketotifen is an H1 and H2 antagonist, and studies showed that it inhibits eosinophil oxidative metabolism and eosinophil chemotaxis. Olopatadine is an H1 antagonist and studies with human conjunctival mast cells showed that it inhibits the release of TNF-α and has inhibitory effects on eosinophils and neutrophils in tears. A study in vivo comparing nedocromil, a drug considered the gold standard mast cell stabilizer, epinastine, and olopatadine showed that the effect on reducing redness was comparable between the three drops. Epinastine and olopatadine are also antihistamines, therefore it is expected that they would inhibit histamine-mediated vasodilation via H1 (and H2) receptor antagonism. All three drugs significantly decreased eosinophil infiltration [62].

A post hoc study published in 2006 compared the clinical effects of olopatadine with epinastine [56]. The results from this analysis suggested that olopatadine is more efficacious in treating ocular itching and conjunctival redness compared with epinastine even as the severity of the reaction increases.

Another study published in 2005 compared olopatadine, ketotifen, and preservative-free artificial tear substitutes [63]. They asked physicians to rate the effect of the active drugs on redness, eyelid swelling, and chemosis. While some signs of allergic conjunctivitis were unchanged, both ketotifen and olopatadine were more effective in relieving itching and tearing than preservative-free artificial tears.

In conjunctival allergen challenge studies, the allergic gold standard test, olopatadine was reported to be more comfortable or better tolerated than ketotifen [64], ketorolac [65], loteprednol [66], and nedocromil [67].

These recent studies suggest that due to the fact that these drug combinations affect different paths in the allergic reaction cascade, the treatment for this condition might be improved by combining or alternating the different anti-allergic drops. For now the initial treatment should be with the drop most likely to improve as many of the signs and symptoms of allergic conjunctivitis as possible. These would include: (1) itching, (2) redness, (3) tearing, (4) chemosis, and (5) lid swelling. Further, since these are

chronically used, ease of administration and dosing profile should be considered. Currently, only olopatadine 0.1% is FDA-approved for the signs and symptoms of allergic conjunctivitis. The other drugs have only received itchy as their indication [68].

In severe cases, steroid drops can be used, but have several limitations due to their potential adverse effects. Steroids are potent anti-inflammatory drugs but carry risks of complications with prolonged use. This class of drug does not block histamine receptors like antihistamines, but they inhibit the synthesis of histamine in the mast cells and also deplete the free histamine by increasing the stores of histaminase, the enzyme that catalyzes the histamine into an inactive metabolite, thus having an anti-allergic role [69]. This mechanism plus their anti-inflammatory action would make this drug ideal to treat all signs and symptoms of allergic conjunctivitis. However, the potential side effects of prolonged use make them the last choice as first-line agents to treat this condition. New steroid-based ocular medications have been developed with formulations geared to have the same clinical potency and yet decreased adverse effects. Long-term studies are necessary to evaluate the safety of these drugs as first-line choice of treatment.

Another important aspect of seasonal and perennial allergic conjunctivitis is the change in microbiota of the conjunctiva. In 2005 a Brazilian group analyzed the conjunctival microbiota in patients with any type of allergic conjunctivitis with non-atopic patients [70]. They found more positive cultures of the conjunctival sac of allergic patients than normal. The authors hypothesized that rubbing the eyes could transfer bacteria from the hands and eyelids/lashes to the conjunctiva. However, the increased discharge seen in allergic patients could provide a better sample for analysis, perhaps creating a bias of the study.

Vernal keratoconjunctivitis (VKC) is a chronic recurrent allergic disease, potentially severe with periods of exacerbation and difficult control. Visual complications can be due as a result of the condition itself or complications associated with treatment. Studies have shown that in long-standing cases, topographic changes may occur, leading to disturbances in visual performance, such as below normal best-corrected visual acuity, low contrast sensibility, and subjective visual symptoms. Lapid-Gortzak et al. [71] found an abnormal pattern of corneal topography in nearly 71% of VKC patients. They found that those patients had more significantly abnormal corneal videokeratographic patterns, higher maximal corneal dioptric power, and increased superior-to-inferior asymmetry, with a tendency to more superior corneal steepening. Dantas et al. [72] studied the videokeratography of 142 eyes from 71 patients with VKC and compared with 200 eyes of 100 control patients and found that the mean anterior corneal curvature was more accentuated in VKC patients, associated with low corneal uniformity index and consequently poor visual performance. They also found that 22% of the VKC patients had keratoconus diagnosed by corneal topography. In these particular patients, the authors found that the initial allergic symptoms presented later and remained for a longer time when compared to VKC patients with no signs of keratoconus, suggesting that the chronicity of the condition could be related to the severity of the corneal changes. In 2007 Dada et al. [73] showed that patients with VKC associated with steroid-induced glaucoma presented an increase in the corneal curvature, a significant increase in posterior corneal elevation, and a reduction in the central corneal pachymetry. They also reported that these changes may be reversed by a reduction in the intraocular pressure with medical therapy.

Another rare but severe visual-threatening complication is shield ulcer and plaque affecting from 3% to 20% of VKC patients [74, 75]. The pathophysiology of these lesions is not yet well established but it is believed to involve a combination of mechanical damage from the giant papillae to the corneal epithelium as well as toxic epitheliopathy caused by inflammatory mediators. Inflammatory debris that deposits in the base of the ulcer forms a plaque. Shield ulcers are difficult to treat and some cases may be unresponsive to medical therapy, requiring surgical intervention. They also carry a risk of secondary infection and corneal perforation in severe cases.

The standard protocol for treating VKC includes antihistamines, mast cell stabilizers, and steroids. However, the first two classes of drugs do not perform well in severe cases and steroids carry potential adverse effects, especially when used for extensive periods of time. Several studies have shown that cyclosporine A may be of great advantage in the treatment of these patients [75, 76]. Cyclosporine A is an immunomodulator that inhibits CD4 T-lymphocyte proliferation by blocking the interleukin-2 receptor expression. It also presents direct inhibitory effects

Take Home Pearls

- Cytopathology of chalazion may influence type of treatment.
- Studies regarding cosmetic laser treatment for pigmented conjunctival lesions have shown good short-term results.
- A new technique for treatment of dermoid involving the cornea was published using full-thickness corneal graft instead of partial-thickness.
- Destructive therapies are still the most common treatment for molluscum contagiosum.
- Povidone-iodine has been used for prophylaxis of neonatal conjunctivitis with good results.
- Fourth-generation fluoroquinolones are recommended for treatment of acute bacterial conjunctivitis.
- A new in-office test for quick diagnosis of adenovirus has been developed.
- Combination of antihistamine and mast cell stabilizer still is the best choice for allergic conjunctivitis treatment.
- Vernal keratoconjunctivitis can affect corneal contour and topography, causing decrease in visual acuity.

on eosinophils and mast cell activation and release of mediators. An advantage of this drug is that it inhibits the phagocytic system to a lesser extent than steroids do, thus having less impact on wound healing. Further, serious ocular side effects, such as cataract formation and glaucoma, and systemic adverse reactions have not been reported with prolonged use of topical cyclosporine A for treatment of VKC.

References

1. Lederman C, Miller M (1999) Hordeola and chalazia. Pediatr Rev 20:283–284
2. Donaldson MJ, Gole GA (2005) Amblyopia due to inflamed chalazion in a 13-month-old infant. Clin Exp Ophthalmol 33:332–333
3. Ormond AW (1921) Notes on three cases of acquired astigmatism associated with meibomian cysts. Br J Ophthalmol 5:117–118
4. Santa Cruz C, Culotta T, Cohen EJ, Rapuano CJ (1997) Chalazion-induced hyperopia as a cause of decreased vision. Ophthalmic Surg Lasers 28:683–684
5. Dhaliwal U, Arora VK, Singh N, Bhatia A (2004) Cytopathology of chalazia. Diagn Cytopathol 31:118–122
6. Korn EL (1988) Laser chalazion removal. Ophthalmic Surg 19:428–431
7. Chung CF, Lai JS, Li PS (2006) Subcutaneous extralesional triamcinolone acetonide injection versus conservative management in the treatment of chalazion. Hong Kong Med J 12:278–281
8. Dhaliwal U, Bhatia A (2005) A rationale for therapeutic decision-making in chalazia. Orbit 24:227–230
9. Chiang CC, Cheng YW, Lin CL, Lee H, Tsai FJ, Tseng SH, Tsai YY (2007) Cyclooxygenase 2 expression in pterygium. Mol Vis 13:635–638
10. Tan DT, Lim AS, Goh HS, Smith DR (1997) Abnormal expression of the p53 tumor suppressor gene in the conjunctiva of patients with pterygium. Am J Ophthalmol 123:404–405
11. Dushku N, Reid TW (1997) P53 expression in altered limbal basal cells of pingueculae, pterygia, and limbal tumors. Curr Eye Res 16:1179–1192
12. Tan DT, Tang WY, Liu YP, Goh HS, Smith DR (2000) Apoptosis and apoptosis related gene expression in normal conjunctiva and pterygium. Br J Ophthalmol 84:212–216
13. Weinstein O, Rosenthal G, Zirkin H, Monos T, Lifshitz T, Argov S (2002) Overexpression of p53 tumor suppressor gene in pterygia. Eye 16:619–621
14. Dushku N, Hatcher SL, Albert DM, Reid TW (1999) p53 expression and relation to human papillomavirus infection in pingueculae, pterygia, and limbal tumors. Arch Ophthalmol 117:1593–1599
15. Shields CL, Shields JA (2007) Conjunctival tumors in children. Curr Opin Ophthalmol 18:351–360

16. Ferguson RE Jr, Vasconez HC (2005) Laser treatment of congenital nevi. J Craniofac Surg 16:908–914
17. Kwon JW, Jeoung JW, Kim TI, Lee JH, Wee WR (2006) Argon laser photoablation of conjunctival pigmented nevus. Am J Ophthalmol 141:383–386
18. Shields CL, Shields JA (2004) Tumors of the conjunctiva and cornea. Surv Ophthalmol 49:3–24
19. Kim TI, Yoon J, Choi J, Tchah H (2005) Flipped scleral flap surgery for reduction of ocular pigmentation in oculodermal melanosis. Cornea 24:482–485
20. Gomi CF, Robbins SL, Heichel CW, Gross RD, Granet DB (2005) Conjunctival diseases. In: Harley RD (ed) Pediatric ophthalmology, 5th edn. Lippincott Williams and Wilkins, Baltimore, pp 201–216
21. Watts P, Michaeli-Cohen A, Abdolell M, Rootman D (2002) Outcome of lamellar keratoplasty for limbal dermoids in children. J AAPOS 6:209–215
22. Shen YD, Chen WL, Wang IJ, Hou YC, Hu FR (2005) Full-thickness central corneal grafts in lamellar keratoscleroplasty to treat limbal dermoids. Ophthalmology 112:1955
23. Hanna D, Hatami A, Powell J, Marcoux D, Maari C, Savard P, Thibeault H, McCuaig C (2006) A prospective randomized trial comparing the efficacy and adverse effects of four recognized treatments of molluscum contagiosum in children. Pediatr Dermatol 23:574–579
24. Cunningham BB, Paller AS, Garzon M (1998) Inefficacy of oral cimetidine for nonatopic children with molluscum contagiosum. Pediatr Dermatol 15:71–72
25. Brown J, Janniger CK, Schwartz RA, Silverberg NB (2006) Childhood molluscum contagiosum. Int J Dermatol 45:93–99
26. Toutous-Trellu L (2004) Treatment of cutaneous human papilloma virus, poxvirus and herpes simplex virus infections with topical cidofovir 1% in HIV positive patients. Ann Dermatol Venereol 131:445–449
27. Fransen L, Klauss V (1988) Neonatal ophthalmia in the developing world. Epidemiology, etiology, management and control. Int Ophthalmol 11:189–196
28. Yip TP, Chan WH, Yip KT, Que TL, Lee MM, Kwong NS, Ho CK (2007) Incidence of neonatal chlamydial conjunctivitis and its association with nasopharyngeal colonisation in a Hong Kong hospital, assessed by polymerase chain reaction. Hong Kong Med J 13:22–26
29. Isenberg SJ, Apt L, Yoshimori R, Leake RD, Rich R (1994) Povidone-iodine for ophthalmia neonatorum prophylaxis. Am J Ophthalmol 118:701–706
30. Isenberg SJ, Apt L, Wood M (1995) A controlled trial of povidone-iodine as prophylaxis against ophthalmia neonatorum. N Engl J Med 332:562–566
31. Isenberg SJ, Apt L, Del Signore M, Gichuhi S, Berman NG (2003) A double application approach to ophthalmia neonatorum prophylaxis. Br J Ophthalmol 87:1449–1452
32. Richter R, Below H, Kadow I, Kramer A, Muller C, Fusch C (2006) Effect of topical 1.25% povidone-iodine eyedrops used for prophylaxis of ophthalmia neonatorum on renal iodine excretion and thyroid-stimulating hormone level. J Pediatr 148:401–403
33. Buznach N, Dagan R, Greenberg D (2005) Clinical and bacterial characteristics of acute bacterial conjunctivitis in children in the antibiotic resistance era. Pediatr Infect Dis J 24:823–828
34. Høvding G (2007) Acute bacterial conjunctivitis. Acta Ophthalmol Scand 29: [Epub ahead of print]
35. Gigliotti F (1995) Acute conjunctivitis. Pediatr Rev 16:203–207
36. Block SL, Hedrick J, Tyler R, Smith A, Findlay R, Keegan E, Stroman DW (2000) Increasing bacterial resistance in pediatric acute conjunctivitis (1997–1998). Antimicrob Agents Chemother 44:1650–1654
37. Weiss A (1994) Acute conjunctivitis in childhood. Curr Probl Pediatr 24:4–11
38. Mah F (2006) Bacterial conjunctivitis in pediatrics and primary care. Pediatr Clin North Am 53(suppl 1):7–10
39. Patel PB, Diaz MC, Bennett JE, Attia MW (2007) Clinical features of bacterial conjunctivitis in children. Acad Emerg Med 14:1–5
40. Rose P (2007) Management strategies for acute infective conjunctivitis in primary care: a systematic review. Expert Opin Pharmacother 8:1903–1921
41. Everitt H, Little P (2002) How do GPs diagnose and manage acute infective conjunctivitis? A GP survey. Fam Pract 19:658–660
42. Committee on Infectious Diseases (2006) The use of systemic fluoroquinolones. Pediatrics 118:1287–1292
43. Chalumeau M, Tonnelier S, D'Athis P, Tréluyer JM, Gendrel D, Bréart G, Pons G; Pediatric Fluoroquinolone Safety Study Investigators (2003) Fluoroquinolone safety in pediatric patients: a prospective, multicenter, comparative cohort study in France. Pediatrics 111:e714–e719
44. Protzko E, Bowman L, Abelson M, Shapiro A; AzaSite Clinical Study Group (2007) Phase 3 safety comparisons for 1.0% azithromycin in polymeric mucoadhesive eye drops versus 0.3% tobramycin eye drops for bacterial conjunctivitis. Invest Ophthalmol Vis Sci 48:3425–3429
45. Cochereau I, Meddeb-Ouertani A, Khairallah M, Amraoui A, Zaghloul K, Pop M, Delval L, Pouliquen P, Tandon R, Garg P, Goldschmidt P, Bourcier T (2007) 3-day treatment with azithromycin 1.5% eye drops versus 7-day treatment with tobramycin 0.3% for purulent bacterial conjunctivitis: multicentre, randomised and controlled trial in adults and children. Br J Ophthalmol 91:465–469
46. American Academy of Pediatrics (2003) Red Book: 2003 Report of the Committee on Infectious Diseases, 26th edn. American Academy of Pediatrics, Grove Village, IL, pp 141–142
47. Pring-Akerblom P, Adrian T (1994) Type- and group-specific polymerase chain reaction for adenovirus detection. Res Virol 145:25–35
48. Saitoh-Inagawa W, Oshima A, Aoki K, et al. (1996) Rapid diagnosis of adenoviral conjunctivitis by PCR and restriction fragment length polymorphism analysis. J Clin Microbiol 34:2113–2116
49. Morris DJ, Bailey AS, Cooper RJ, et al. (1995) Polymerase chain reaction for rapid detection of ocular adenovirus infection. J Med Virol 46:126–132
50. Elnifro EM, Cooper RJ, Klapper PE, et al. (2000) Multiplex polymerase chain reaction for diagnosis of viral and chlamydial keratoconjunctivitis. Invest Ophthalmol Vis Sci 41:1818–1822

51. Cooper RJ, Yeo AC, Bailey AS, Tullo AB (1999) Adenovirus polymerase chain reaction assay for rapid diagnosis of conjunctivitis. Invest Ophthalmol Vis Sci 40:90–95
52. Madhavan HN (1999) Laboratory investigations on viral and Chlamydia trachomatis infections of the eye: Sankara Nethralaya experiences. Indian J Ophthalmol 47:241–246
53. Koidl C, Bozic M, Mossböck G, et al. (2005) Rapid diagnosis of adenoviral keratoconjunctivitis by a fully automated molecular assay. Ophthalmology 112:1521–1528
54. Sambursky R, Tauber S, Schirra F, Kozich K, Davidson R, Cohen EJ (2006) The RPS adeno detector for diagnosing adenoviral conjunctivitis. Ophthalmology 113:1758–1764
55. Phipatanakul W (2005) Allergic rhinoconjunctivitis: epidemiology. Immunol Allergy Clin North Am 25:263–281, vi
56. Finegold I, Granet DB, D'Arienzo PA, Epstein AB (2007) Efficacy and response with olopatadine versus epinastine in ocular allergic symptoms: a post hoc analysis of data from a conjunctival allergen challenge study. Clin Ther 28:1630–1638
57. Van Gysel D, Govaere E, Verhamme K, Doli E, De Baets F (2007) The influence of bedroom environment on sensitization and allergic symptoms in schoolchildren. J Investig Allergol Clin Immunol 17:227–235
58. Isolauri E, Huurre A, Salminen S, Impivaara O (2004) The allergy epidemic extends beyond the past few decades. Clin Exp Allergy 34:1007–1010
59. Strachan DP (1989) Hay fever, hygiene, and household size. BMJ 299:1259–1260
60. Kemp A, Bjorksten B (2003) Immune deviation and the hygiene hypothesis: a review of the epidemiological evidence. Pediatr Allergy Immunol 14:74–80
61. Romagnani S (2004) The increased prevalence of allergy and the hygiene hypothesis: missing immune deviation, reduced immune suppression, or both? Immunology 112:352–363
62. Galatowicz G, Ajayi Y, Stern ME, Calder VL Ocular anti-allergic compounds selectively inhibit human mast cell cytokines in vitro and conjunctival cell infiltration in vivo. Clin Exp Allergy 37:1648–1656
63. Avunduk AM, Tekelioglu Y, Turk A, Akyol N (2005) Comparison of the effects of ketotifen fumarate 0.025% and olopatadine HCl 0.1% ophthalmic solutions in seasonal allergic conjunctivities: a 30-day, randomized, double-masked, artificial tear substitute-controlled trial. Clin Ther 27:1392–1402
64. Berdy GJ, Spangler DL, Bensch G, Berdy SS, Brusatti RC (2000) A comparison of the relative efficacy and clinical performance of olopatadine hydrochloride 0.1% ophthalmic solution and ketotifen fumarate 0.025% ophthalmic solution in the conjunctival antigen challenge model. Clin Ther 22:826–833
65. Yaylali V, Demirlenk I, Tatlipinar S, Ozbay D, Esme A, Yildirim C, Ozden S (2003) Comparative study of 0.1% olopatadine hydrochloride and 0.5% ketorolac tromethamine in the treatment of seasonal allergic conjunctivitis. Acta Ophthalmol Scand 81:378–382
66. Berdy GJ, Stoppel JO, Epstein AB (2002) Comparison of the clinical efficacy and tolerability of olopatadine hydrochloride 0.1% ophthalmic solution and loteprednol etabonate 0.2% ophthalmic suspension in the conjunctival allergen challenge model. Clin Ther 24:918–929
67. Butrus S, Greiner JV, Discepola M, Finegold I (2000) Comparison of the clinical efficacy and comfort of olopatadine hydrochloride 0.1% ophthalmic solution and nedocromil sodium 2% ophthalmic solution in the human conjunctival allergen challenge model. Clin Ther 22:1462–1472
68. U.S. Food and Drug Administration (2007) New drug application (NDA) approved labels. Available at: http://www.fda.gov/cder/foi/label/1999/21066lbl.pdf, http://www.fda.gov/cder/foi/label/2004/021545lbl.pdf, http://www.fda.gov/cder/foi/label/2000/21127lbl.pdf. Accessed December 21, 2007
69. Ilyas H, Slonim CB, Braswell GR, Favetta JR, Schulman M (2004) Long-term safety of loteprednol etabonate 0.2% in the treatment of seasonal and perennial allergic conjunctivitis. Eye Contact Lens 30:10–13
70. Libório AM, Nishiwaki-Dantas MC, Mimica LM, Dantas PE, Lima AL (2005) [Conjunctival microbiota in patients with ocular allergy.] Arq Bras Oftalmol 68:824–827
71. Lapid-Gortzak R, Rosen S, Weitzman S, Lifshitz T (2002) Videokeratography findings in children with vernal keratoconjunctivitis versus those of healthy children. Ophthalmology 109:2018–2023
72. Dantas PE, Alves MR, Nishiwaki-Dantas MC (2005) Topographic corneal changes in patients with vernal keratoconjunctivitis. Arq Bras Oftalmol 68:593–598
73. Dada T, Konkal V, Tandon R, Singh R, Sihota R (2007) Corneal topographic response to intraocular pressure reduction in patients with vernal keratoconjunctivitis and steroid-induced glaucoma. Eye 21:158–163
74. Solomon A, Zamir E, Levartovsky S, Frucht-Pery J (2004) Surgical management of corneal plaques in vernal keratoconjunctivitis: a clinicopathologic study. Cornea 23:608–612
75. Cetinkaya A, Akova YA, Dursun D, Pelit A (2004) Topical cyclosporine in the management of shield ulcers. Cornea 23:194–200
76. Spadavecchia L, Fanelli P, Tesse R, Brunetti L, Cardinale F, Bellizzi M, Rizzo G, Procoli U, Bellizzi G, Armenio L (2006) Efficacy of 1.25% and 1% topical cyclosporine in the treatment of severe vernal keratoconjunctivitis in childhood. Pediatr Allergy Immunol 17:527–532

Pediatric Low Vision

Linda Lawrence and M. Edward Wilson

30

Contents

Core Messages

- The goal of pediatric low vision services is to help each child achieve maximum potential, regardless of diagnosis or disability.
- Visual impairment in the first years of life requires immediate attention, just as any other developmental delay.
- Children with visual impairment or who are blind have a right to education.
- Visual acuity does not equal visual functioning. Each aspect of the evaluation of a visually impaired child must take this into consideration.

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30.1 Introduction

A child with a visual impairment is one who has impaired visual functioning even after treatment and/or standard refractive correction, but who uses, or is potentially able to use, vision for the planning or execution of a task [7]. Training as ophthalmologists in the clinical, acute care setting may not provide adequate preparation for the evaluations and recommendations that are needed in the educational/rehabilitation setting. Every child is a unique individual, with the adaptation for low vision or blindness unique for each. In order for the child to receive the maximum benefit from educational and rehabilitation services, the ophthalmologist must learn how to partner effectively with the other members of the educational/rehabilitation team. Without the support, advocacy, and medical advice from the ophthalmologist, the team will not be able to properly individualize the services, interventions, and training to the unique needs of each visually impaired child.

30.2 Services Provided by a Transdisciplinary Team

30.2.1 The Ophthalmologist's Role

The ophthalmologist is responsible for the initial ophthalmic diagnoses and for the prescribing of medical and surgical interventions for the infant/child with low vision or blindness. The ophthalmologist is also responsible for referring the child/family to appropriate intervention/educational services. Eye examination information needs to be communicated to the parents and the rehabilitation team by the ophthalmologist in a comprehensive and family-centered manner. The ophthalmic information combined with other pertinent medical information will enable the rehabilitation team plan and implement services that are specifically designed to meet the child's individualized needs. The ophthalmologist should provide ocular and visual system related medical information for the team, but delegate the interventions to those who are professionals in the field of education and rehabilitation. This should be applied for each child, regardless of abilities. The child needs to have access to the entire (core) school curriculum, not only for literacy (reading, writing, and communication), but also to include physical education, arts and music education, etc. The final aim is to increase independence and improve quality of life.

Expected information from the ophthalmologist in regards to the pediatric low vision evaluation is covered later in the chapter. However, in general terms, the following advice is offered so that the ophthalmologist can help set the stage for the rehabilitation program that will follow.

Be positive in your approach with the child and family, they will remember what you say to them for the rest of their lives. Allow the family and child time to ask and have questions answered.

The ophthalmologist is the expert of, and the best teacher of how the ocular pathology and visual system and neurological development affect the child's use of vision. Encourage, as appropriate, the attendance of a teacher of students who are blind or visually impaired (TVI; previously TVI was defined as teacher for visually impaired), classroom and special education teachers, paraprofessionals, or a therapist at examinations with parent and child. This facilitates communication among the team, and allows for quicker institution of recommendations. Write down the diagnoses and the recommended interventions, and anything else you feel important for the parents and the team, in clear and concise language. A form is helpful.

The more the ophthalmologist knows about the educational and rehabilitation services process, the better able he/she will be to provide useful medical information and help guide the parents and the team.

30.2.2 Educational Services/Intervention

Educational services and interventions for the visually impaired child vary from state to state, and even from community to community. In some states a Functional Vision Assessment must be completed to determine eligibility. Although states are allowed to set some parameters about who is eligible, all states participating in part C of the Individuals with Disabilities Education Act (IDEA) must provide services to children who have an established disability [5]. The visually disabled child may have additional mul-

tiple disabilities which must be planned for when the individualized education and rehabilitation program is designed.

Family, educators, and therapists are all part of the educational team. This may also include community health nurses, social workers and case managers, occupational therapists to assist with feeding issues and fine motor development, physical therapists for mobility, TVIs, early childhood special education teachers, and orientation and mobility instructors.

Children who are visually impaired are often classified into four groups for educational purposes. They are: (1) the very young, (2) Braille readers, (3) children with low vision, and (4) children with additional disabilities [3].

30.2.3 Early Intervention Services (Newborn to Age 3)

The group of children with additional disabilities is the fastest growing group of infants/toddlers with visual impairment. This is influenced by the high survival rate of very low birth weight and premature infants, as well as increased survival rates of infants and children with other types of brain injury. The latest statistics from Babies Count [1], the national registry for children with visual impairment, birth to 3 years, shows out of 2,155 children in the registry, 26% had cortical visual impairment (CVI) as the main reason for visual disability, and 18% had retinopathy of immaturity (ROP). In infants and toddlers with CVI, 35% had developmental delay, 61% cerebral palsy, and 67% brain injury. In children with ROP as the primary cause of visual delays, 48% also were diagnosed with developmental delays, and 13% with cerebral palsy. The leading diagnosed conditions associated with visual loss require a transdisciplinary team.

The Individual Family Service Plan (IFSP) is the intervention plan for infants and toddlers (birth to 3 years) with disabilities who are served under part C of IDEA (1997) [6]. Part C Infant-Toddler Services may provide funding that can be used for vision services. In some states, the Infant-Toddler Services may be coordinated by the Department of Health and Environmental Services, or by the Department of Social and Rehabilitative Services. Each state is different. IFSPs were first mandated by Public Law 99-457 in 1986 to assure that families would be included in the development and implementation of early intervention services. A multidisciplinary team that includes the family should develop the IFSP. Early intervention services are to be provided within the child's natural environment. This is generally a home-based service for the infant and his/her family. The pediatrician, family doctor, community health nurses, and the ophthalmologists may make referrals to the child/family's early intervention program. Early referral will help direct the team's interventions based on priorities set in partnership with the family. These interventions aim to support and promote the child's growth and development. The local team may consult a TVI. A TVI is a special educator, with either a certification in visual impairment, or with Masters or PhD level training, who specializes in consulting/coaching the early interventionist and the educational team. These teachers are typically part of the local school system's regional services centers, cooperatives, or are part of the state school for the blind.

The ophthalmologist, at the initial assessment can suggest or endorse interventions for the child with vision loss, especially those with CVI. Some of the adaptations that can be made are reducing visual clutter, increasing or decreasing lighting depending on the pathology, and allowing the child plenty of time to respond to the stimulation offered. Toys may need to be placed in closer proximity, at the level the child can see them, and in consistent order. The child needs to be encouraged to reach beyond himself/herself and to explore and control the environment.

30.2.4 Preschool (3–5 Years)

The federal definition in IDEA states that visual impairment including blindness means impairment in vision that, even with optical correction, adversely affects a child's educational performance. This term applies to both partial sight and blindness. All children with low vision or blindness deserve an Individualized Educational Plan (IEP) developed by the educational team. The ophthalmologist should ask the parent specifically if there has been an IEP, and what the team discussed. Be sure the team has the

proper information from the medical evaluation, so that appropriate interventions can be discussed. The child/student's primary learning modality (visual or tactile) needs to be determined.

A 504 plan is another type of plan under IDEA. However, it only requires schools to provide assistance to children with disabilities to ensure a safe environment. It does not mandate educational interventions. Vision issues may not be addressed if there are other issues such as cognitive or motor delays, which are more obvious to the educational team. The ophthalmologist should recommend that the parents ask for a TVI to be present for the child's IEP planning. Ophthalmologists can and should be strong advocates for their young patients and their families.

Many of our communities have "Head Start" preschools where children with delays or disabilities including visual can receive more concentrated educational interventions. This is a good time for the child to be evaluated for low vision devices. The follow-up of the effectiveness of these devices can be assessed by the TVI in the classroom.

30.2.5 School Age (Kindergarten to 12th Grade)

The older child can vocalize what they are able to see in the classroom and what services they are receiving. The IEP is individualized, specialized, and has curriculum modifications. There may be experimental learning, and teaching of compensatory skills. Parents and professionals can enhance the learning opportunities and advocate for the best learning environments.

30.2.6 Role of Schools for the Blind

The trend in education is from institutionalization to integration in the child's hometown local school. However, state schools for the blind, special schools for students with visual impairments, continue to have a valuable role. Enrollment, at no charge to the parents, is recommended by the IEP team with involvement from the child's local school district, the family, and the school for the blind's evaluation team. Placement is time-limited, and designed to return the student to their own hometown school district as soon as the IEP team determines the student will be academically and socially successful at the local level. The school for the blind provides a highly individualized curriculum and may include: (1) enrollment in the range of 2–3 years to build blindness skills (Braille, orientation and mobility, access technology), (2) short-term programs where children come from integrated classroom settings into the school for the blind for a week or so to focus on a particular skill area such as assistive technology, or (3) outreach service to parents and school districts, generally in a technical assistance model [4].

30.3 Evaluation by the Ophthalmologist as a Member of the Educational/ Rehabilitation Team

30.3.1 Introduction and Overview

As stated earlier, the ophthalmologist is an integral part of the transdisciplinary team that will determine the best rehabilitation plan for each visually impaired child. It is crucial that the ophthalmologist provide the best possible explanation of the child's visual condition and prognosis. In addition, the evaluation and examination may need to be structured differently than it is for children without permanent visual disability. In addition to the information available from the standard pediatric ophthalmology examination note, several special requests will be made of the ophthalmologist. The educational/rehabilitation team will specifically want to know how secondary visual conditions will affect the primary visual condition. An example would be a child with visual loss from ROP who also has strabismus or aphakia. The ophthalmologist will need to make a statement about whether there are any activity restrictions resulting from the visual condition. Any advice with regard to lighting, positioning, and magnification will be very helpful. The ophthalmologist may refer the child to a low vision center for further assessment or may feel

comfortable providing the initial low vision services himself/herself. Medical information from the ophthalmologist should be in a form that is legible, and in lay terms that parents, educational, and rehabilitation teams can understand and utilize.

Another concept to remember is the "four-leaf clover" of vision. Vision is used for:

1. Communication and interaction
2. Activities of daily life
3. Orientation and moving in space
4. Sustained near vision tasks [7]

This may sound obvious, but in the ophthalmic evaluation, the emphasis may be on treating the disease rather than how the disease affects the overall functioning, not only of the eye itself and visual system, but also of the entire child.

30.3.2 Pediatric Functional Vision Assessment

Visual function does not necessarily correlate with visual acuity. Visual acuity measures the function of the eye; functional assessment measures the use of vision. The clinical eye examination in a child with low vision is different than simply assessing pathology. Diagnosis, prognosis, and visual acuity may not reflect how the child uses his/her vision in the environment within activities of daily life. The visual system is immature at birth, and children's neurological systems, including vision, may develop at different rates. Visual acuity, refraction, motility, binocular visual acuity, contrast, color vision, visual fields, and examination of ocular structures are all important to evaluate and record as part of the pediatric functional low vision assessment.

Pediatric low vision assessment starts at the time of diagnosis or suspicion of delays in visual development and continues at regular intervals, independent of ocular pathology. At a minimum, low vision evaluations should be at the child's transition times in the educational system. This would start with the early intervention services at newborn to age 3, next at admission to preschool (3–5 years), then at the beginning of elementary school (age 6). In the 3rd and 4th grades, print in textbooks gets smaller, and the child moves from learning to read, to reading to learn. Middle school, high school, and entry into university or vocational training are additional transition times. The child's environment is continually changing, so the evaluations and modifications to maximize vision and learning also need continuous reevaluation.

The pediatric low vision assessment should be performed in a consistent manner. The low vision assessment is in addition to the comprehensive ophthalmologic examination that prescribes medical and surgical interventions, and not meant to replace it.

30.3.3 History Taking for the Visually Impaired Child

The initial step in any assessment is history. For the infant or child with low vision, this should include pertinent medical and ocular history as well as social and educational histories.

Ocular history should include the age at onset of symptoms, as well as results from prior eye examinations. An example would be eye poking, which indicates retinal etiology rather than neurological or optic nerve. What are the responses to light? Night blindness may indicate retinal dystrophy. Photophobia and light gazing may indicate CVI. What is the response to parent's face, to toys, or other objects? Is the child aware of or will they track a favorite color?

Medical history affects the overall development of the infant and the visual functioning. Perinatal history of the mother and baby are both important. For the maternal history, what was the estimated date of confinement? How was mother's general health? What drugs were taken either prescribed or illegal? Alcohol intake, trauma, multiple births, infections, steroids, hypertension, preeclampsia, and nutritional status during pregnancy are all important questions. History of the baby includes gestational age at birth and birth weight. Did the baby move in utero? Was the prenatal growth normal or was there intrauterine growth retardation (IUGR)? How was the birthing process, and was resuscitation required?

The postnatal history adds additional information. How was the nursery stay? Risk factors for ROP in-

clude sepsis, transfusions, unstable nursery course, and mechanical ventilation. Risk factors for CVI include the same, as well as history of intraventricular hemorrhage. What were the findings on head ultrasounds, or other forms of neuroimaging (such as CT, MRI)?

Current medical conditions should be identified such as seizure disorders, traumatic injuries, congenital anomalies, "birth marks," attention-deficit hyperactivity disorder (ADHD), hearing deficiency, or speech delay. Hospitalization, frequent visits to the doctor, surgeries, and other diagnoses should be noted. What other medications including steroids, seizure medications, chronic antibiotics, and other chronic medications is the child taking?

Family history may provide more clues to etiologies of low vision. Specific questions about familial or inherited eye diseases should be elicited. This should include strabismus, amblyopia, and refractive errors, eye patching, or thick glasses as a child. Knowing about familial medical problems or disabilities and the results of examination of family members may help in identifying underlying pathology. An example is a history of deafness in relatives. This may help identify those with Usher's syndrome or Waardenburg's syndrome. Children with these diagnoses may have combined hearing and vision losses which would require modified interventions.

Taking the developmental history is a skill the ophthalmologist and his/her office team may have to improve on. It is important to identify visual, motor, cognitive, and hearing delays. For example, an infant may initially raise its head, but this developmental milestone may regress in a baby with severe visual impairments. Developmental assessments completed by professionals on the infant-child teams specifically trained in developmental assessments are important to gather. The pediatrician may also provide some of this information.

Educational history and terminology is an area that the ophthalmologist who takes care of children, especially with vision loss should become familiar with. How is the child performing in school? What type of school is the child attending and what is the classroom setting? Does the child have an IFSP, and IEP, or a 504 plan? Other related or educational services the ophthalmologist needs to ask about are: is the child receiving occupational therapy, physical therapy, and/or speech therapy, vision services by a TVI, orientation and mobility instruction? Does the child use low vision aid devices, or an augmentative communication device? If the child is not getting timely low vision evaluations, the optical and non-optical devices may be outdated for the education level and tasks of the child.

30.3.4 General Assessment of the Child

Assess the child's overall physical appearance. The examiner can assess overall muscle tone, head control, and fixation by holding the infant. Assessment of the infant's vision can be performed by using the examiner's face as a target. Watching the child move from lap or chair, or walk in the room is helpful. How does the child interact with the environment, with the parent, with the examiner? The examination should be performed quickly, keeping the child engaged, and in a compassionate manner.

30.3.5 Visual Acuity Testing

Visual acuity should not be the only measure to determine eligibility for service. If the child's functional vision, even with correction, adversely affects his/her educational performance, this information should be used to determine eligibility and entitlement to educational services. There is a difference between tests of visual acuity and visual function. Testing should be age and ability dependent.

There are different types of acuity measurements. Always measure the child's distance and near acuity. Try binocular vision first, then separate eyes for acuity measurement. Remember the four-leaf clover of vision; near acuity is used for sustained near tasks, distance acuity for functioning in the larger environment and for orientation and mobility.

Recognition acuity consists of Snellen charts (which are age, visual acuity, and culture dependent), as well as LEA and Lighthouse symbols (Pediatric Low Vision Care (LV11), Lighthouse International, 111 E. 59th Street, New York, USA), the logMar (early treatment of diabetic retinopathy study; ETDRS) chart, and matching charts using the letters H, O, T, and V. These can be used in prereaders or non-verbal children if they can perform matching.

Fig. 30.1 Grating paddles can be used to resolution acuity in infants

Resolution acuity is often tested using a forced choice preferential looking method. These include Teller cards, or the less expensive, grating paddles (Fig. 30.1).

In general, there is central, steady, and maintained fixation by 3 months, binocular vision by 3–7 months, and by 3–5 years the visual acuity should reach 20/20 on a Snellen chart. For infants at birth to 18 months, object awareness develops beginning with lighted objects and human faces. Preferential looking with the Teller cards and grating paddles gives a baseline to communicate with the intervention team. For toddlers, 18 months to 3 years, matching or naming objects such as LEA or Lighthouse symbols, matching tests such as HOTV, or Teller acuity cards can be used. Grating paddles can be used in young children who may not have the communication or developmental skills to match or name letters. In preschool, ages 3–5 years, LEA and Lighthouse symbols, matching tests with the HOTV, or naming objects may be used. Near acuity can be measured using the same. For children with disabilities, including visual disabilities, school age is considered age 5–21. For distance visual acuity testing, ETDRS/Lighthouse charts are used, and Snellen acuity may be able to be measured. For near acuity, Lighthouse cards, HOTV, and numbers may be used.

Visual evoked potential (VEP), electroretinography (ERG), and electro-oculography (EOG) have some usefulness in the assessment of low vision or blindness. However, these tests are often inaccessible in the average community and may be expensive and time consuming.

30.3.6 Refraction

All visually impaired children should have a cycloplegic refraction. Dry retinoscopy or dynamic retinoscopy gives a rough estimate only. When using dilating and cycloplegic drop combinations, phenylephrine may need to be left off in a medically fragile child. Current nursing manuals for babies in the intensive care unit recommend holding feedings for 4 hours before dilation because of the anticholinergic effects of the drops. Phenylephrine may cause tachycardia and a rise in blood pressure when used in the very young. Atropine and cyclopentolate may have side effects in children with neurological disease. Flushing is very common with the use of cyclopentolate, and occasionally children have hallucinations when these drops are administered.

30.3.7 Assessment of Ocular Pathology

For the ophthalmologist, it is imperative to know the extent of the pathology of the ocular and visual systems, to properly evaluate and recommend low vision interventions.

For the anterior segment, the direct ophthalmoscope is an underutilized tool for rapid assessment. The red reflex, clarity of media, pupillary reactions, and fixation can be quickly evaluated. The baby can be held up to the slit lamp or a handheld slit lamp can be used. The indirect ophthalmoscope, with a 20D lens used as a simple magnifier, can provide a view of the anterior segment. Surgical loupes can also be used for this purpose. Intraocular pressure can often be measured using a Tono-Pen or a handheld applanation tonometer in the infant while he/she is sucking on a pacifier or while being bottle-fed in its mother's arms.

Examination of the posterior segment after pupil dilation should always be performed. Indirect examination of the fundus is performed using a 28D and/or 20D aspheric lenses. Subtle optic nerve atrophy and

macular dragging from regressed ROP are two common findings that may affect visual functioning.

30.3.8 Eye Movements

It is important to evaluate for nystagmus. A face turn or head tilt may help the child compensate. The educational team is often very concerned about these mannerisms, and may try to discourage them. They need to understand that this is part of the child's compensatory mechanism. Children with torticollis should be evaluated for congenital fourth cranial nerve palsy and for nystagmus. Infants may have already been referred to early intervention programs for therapy for the torticollis, when the real problem is ocular dysmotility. Shift of gaze, localization of objects, fixation on the caregiver's face, versions and ductions, smooth pursuits, and convergence all have a bearing on the child's overall development.

30.3.9 Motility/Binocular Vision

Stereopsis testing, using the Titmus fly, may be performed even at age 1 with coaxing and patience. A child with a significant chin up position from congenital ptosis may actually have difficulty with tripping over objects, and present as a child with visual impairment. A head turn may be a compensatory movement for Duane's syndrome, or other duction defects.

30.3.10 Visual Fields

Full visual fields are not present at birth. Test by confrontation for a younger child with a face, toy, or lighted object. Babies will often follow the light spot from a direct ophthalmoscope around the room if the examiner makes a game of it. If the child can sit, rolling color balls to the child from his/her peripheral field can be used. Older children can do automated perimetry. Try automated perimetry early, even by age 5. Let the technician introduce the child to the perimetry machine. Have a practice session when there is no rush for time. Inferior visual field defects are often found in children with brain injury, and this can affect the approach of all other midline functions, such as eating, playing with toys, reading, use of communication devices, and mobility. A child with an inferior visual field defect may have good visual acuity, but require a cane for safe and independent travel, or need reading material on a slant board to bring into the useful field of vision. Scanning techniques can be taught.

30.3.11 Color Vision

Accurate color vision testing can be usually be achieved by age 3. Eight percent of males have difficulty with red/green color vision. This has no bearing on visual acuity. Identification is important so the educational team can be notified. Color may also impact how a child uses vision. Red and yellow may be preferred colors for children with CVI. The mechanism for this is not well defined. Color preference can help promote the use of vision in the intervention setting.

30.3.12 Contrast Sensitivity

There are symbol tests for young children to measure contrast sensitivity. For infants, an object such as a piece of tan-colored cereal on the examiner's hand can be used to measure contrast. This is important in the early intervention and classroom setting, as far as suggestions for lighting and contrast for reading material. The examiner may be able to predict contrast difficulties based on the underlying pathology.

30.4 Pediatric Low Vision Interventions

Following the assessment, the visually impaired child should have appropriate interventions and referrals. The ophthalmologist should obtain or design a form

for the parent/teacher that has the diagnosis, pertinent findings, and recommendations. It is assumed for this discussion that the appropriate medical or surgical treatment for the underlying ocular or visual system pathology is already being addressed. IDEA allows states to determine the criteria for what constitutes a developmental delay. The areas considered are typically cognitive, motor, social-emotional, communication, and adaptive skills [2]. Children with associated multiple disabilities should be entitled to the same ophthalmic interventions as the typically developing child. This includes correction of refractive errors and amblyopia therapy. The child with other associated disabilities may need strabismus surgery or unilateral patching to bring one or both eyes to midline for better use of communication devices, and other educational materials.

30.4.1 Correction of Refractive Errors: A Key Part of Intervention

In pediatric low vision interventions, correction of refractive error is a key part of the intervention. For children with low vision and especially those with additional disabilities, an individualized approach is needed. These children do not follow typical guidelines for when lenses should be prescribed.

Glasses may benefit children with other developmental delays at lower hyperopic powers than the typically developing child. Medications may influence accommodation. Children with CVI may have poor accommodative effort and benefit from bifocals or low hyperopic prescriptions. Bifocals may cause difficulty in ambulation in some children.

Children with low vision and significant myopia may achieve better function by removing their glasses and bringing objects closer. Let the educators know this is okay since it increases magnification and thus serves as a compensatory mechanism for the low vision.

Be creative in your fitting of contact lenses. The family/parents must be comfortable with the insertion, and the child willing to accept. A child in a wheelchair may have great difficulty in keeping glasses on. The glasses may be uncomfortable, and if head activated devices are used, the glasses with always be out of alignment. In a child needing bifocals, contact lenses can be fit for near, and glasses used over them for distance viewing. Children who swim or participate in other sports, and even in recess, have to remove glasses, which can cause difficulty in functioning visually and may interfere with the treatment of refractive amblyopia and accommodative esotropia. Be open to using contact lenses and glasses for visually impaired children in a slightly different manner than would be routine in typically developing children.

30.4.2 Low Vision Optical and Non-optical Aids

Low vision optical aids may include telescopes for distance viewing, stand and handheld magnifiers, and prism glasses with magnifications for near viewing. Adequate spectacle correction needs to be employed if indicated. Increased magnification may help if there is decreased contrast.

Children should be encouraged to use residual vision with the use of optical and non-optical aids. The use of vision can help the child function in the world, even if he/she is a Braille reader. Children with visual impairment should be evaluated with a Learning Media Assessment (LMA) by a TVI. Reading speed is important to assess. A child with low vision may be able to read Braille at a faster rate than standard or enlarged print with a magnifier. Building the skill of the student in both Braille and print reading will enable the student to choose one method or the other depending on the specific reading task.

A low vision specialist (ophthalmologist or optometrist) trained in the proper selection and fitting of optical devices should evaluate the child and prescribe the devices. Around age 3–5 is the best time to introduce low vision devices. This again varies with each child. Abilities (motor and cognitive), maturity, and responsibility determine which low vision devices are prescribed and used. Personnel with appropriate training then instruct the child and parent in the proper use and care of the optical devices. This is typically the TVI or an orientation and mobility specialist.

Low-cost, high-quality low vision devices are available. The next question is who will pay for the devices? This varies in each school system. The cost of the devices may be a barrier. Often older children will not use devices because it draws attention to them. There may be hesitation to use devices because of inadequate initial and on-going training or support in the classroom.

30.4.3 Low and High Assistive Technology

The learning environment should be adapted to the specific diagnosis and to the functional abilities of the child. Functional toys can help the child develop concepts and skills needed for later learning devices. Toys with switches that do something help the child with control of the environment.

There is adaptive software available such as JAWS, a screen reader that voices printed material. Most current computer software has the ability to change font size, contrast, and other parameters to improve usage for those with low vision.

Closed circuit television (CCTV) can often be helpful for appropriate children. These can be cumbersome and expensive but the pricing is improving. The ophthalmologist and the educational/rehabilitation team need to advocate for children who would benefit from CCTV technology to have both a unit at home and a unit at school. Loaner programs or grants from service clubs may help achieve this goal.

30.4.4 Orientation and Mobility Training

Orientation and mobility (O&M) training helps develop the child's orientation in space, as well as movement and safety in traveling. This is not dependent solely on visual acuity. A child with significant visual field loss may need O&M training to help adapt to the loss of field. Concepts of space and time may need to be taught. While this training is often reserved for children with very severe visual loss, O&M instruction may also be very helpful to the mild or moderately visually impaired but multihandicapped child.

Take Home Pearls

- The ophthalmologist is a member of a transdisciplinary pediatric low vision team for children with visual impairment and blindness.
- The ophthalmologist's chief role is to supply the proper medical information in a manner that the educational team can understand and utilize to maximize outcomes for the child.
- When evaluating visually impaired children, the ophthalmologist's history, examination, and treatment decisions must be customized with the concepts of functional vision in mind.

References

1. Hatton DD, Schwietz E, Boyer B (2007) Babies Count: the national registry for children with visual impairments, birth to 3 years. J Am Pediatr Assoc Ophthalmol Strabismus 11:351–355
2. Hyvarinen L (2005) CVI lectures series. Logan, UT; Ski-Hi Institute, HOPE
3. Hyvarinen L (2003) Classification of visual impairment in children. Presentation at WHO meeting, Sept 2003, p 11
4. Texas School for the Blind and Visually Impaired (2008) http://www.tsbvi.edu/. Accessed 14 May 2008
5. Tracking services for infants, toddlers, and their families: a look at the Federal Early Childhood Services and the Roles of State and Local Governments (2007) www.zerotothree.org/policy. Accessed Nov 2007, p 5
6. Policy guidelines on Education of Blind and Visually Impaired Students, www.ed.gov/legislation/Fedregistar/other/2000-2/060800.pdf. Accessed Nov 2007
7. Management of low vision in children. Report of a WHO consultation, Bangkok, 23–24 July, 1992. WHO/PBL/93.37, p 7

Pediatric Ocular Trauma

Scott R. Lambert and Amy K. Hutchinson

31

Contents

Core Messages

- Most traumatic corneal abrasions should not be patched. Topical non-steroidal anti-inflammatory drugs are helpful in reducing the associated pain.
- Children with sickle cell hemoglobinopathy are at greater risk of developing optic nerve ischemia and secondary hemorrhages with traumatic hyphemas.
- Vitreous hemorrhages in children can cause amblyopia and axial elongation and should be treated with a vitrectomy if the hemorrhages persist for 1 month or more.
- Open globes secondary to lacerations of the cornea generally have a favorable visual prognosis whereas open globes rupturing after blunt injuries generally have an unfavorable visual prognosis.

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- Post-traumatic macular holes in children can resolve spontaneously.
- Children with muscle entrapment secondary to "trapdoor" injuries of the orbital floor should undergo early surgical repair.

31.1 Traumatic Corneal Abrasion

Corneal abrasions are one of the most common ocular injuries occurring in children. The size of the abrasion usually dictates the rate of healing, but most traumatic corneal abrasions heal within 12–72 h. The pain associated with traumatic corneal abrasions can be severe and often prevents children from engaging in their normal activities. In the past, cornea abrasions were often treated with topical antibiotic ointment, cycloplegia, and patching. Many studies have shown that patching neither reduces the pain associated with corneal abrasions nor the healing time [31]. Moreover, patching may increase the risk of keratitis by decreasing the oxygen supply to the cornea, increasing the surface temperature of the cornea, and reducing tear turnover. On the other hand, the topical application of non-steroidal anti-inflammatory drugs has been shown in many high-quality randomized clinical trials to reduce the associated pain [27, 38, 54]. However, transient stinging may accompany their instillation. Low power "bandage" contact lenses have also been used in an attempt to reduce the pain associated with traumatic corneal abrasions, but their efficacy has not been established in a randomized clinical trial. Because of the increased risk of developing bacterial keratitis, the use of antibiotic ointment is recommended until the corneal epithelium has fully healed.

31.2 Traumatic Hyphema

Traumatic hyphema can occur following blunt or penetrating trauma. Although traumatic hyphema often resolves without sequelae, the potential for severe and permanent visual loss should not be underestimated. The diagnosis of hyphema is usually straightforward and in most cases can be diagnosed with a penlight examination. Hyphemas may be associated with increased intraocular pressure, the formation of peripheral anterior synechiae, optic atrophy, corneal blood staining, and secondary hemorrhage ("rebleeding"). It is important to identify patients with sickle cell hemoglobinopathy because these children are at greater risk of optic nerve atrophy when the intraocular pressure is moderately elevated and secondary hemorrhage compared to children with normal hemoglobin [60]. In addition, children with clotting disorders should be identified as they are more likely to experience secondary hemorrhage.

31.2.1 Outpatient Versus Inpatient Management

The appropriate management of traumatic hyphema in children is controversial. It is generally recognized that activity should be limited in children with traumatic hyphema in order to prevent secondary hemorrhage. Strict bedrest with hospital admission has often been recommended in the past, but a benefit remains unproven. Several studies have shown that outpatient management of children with hyphema can be safe. In some children, however, bedrest and hospital admission may be preferable, especially when adequate supervision is in question, the hyphema is large (more than one third of the anterior chamber volume), or the child has sickle cell disease or trait. The involved eye should be shielded and the head of the bed elevated. Aspirin or aspirin-containing products should be avoided [12]. Physical activity should be limited for at least 5 days after the occurrence of a hyphema.

31.2.2 Medical Therapy

Medical therapy is initiated to reduce the risk of secondary hemorrhage and intraocular inflammation. Although many studies have shown that the oral administration of ε-aminocaproic acid (50 mg/kg

every 4 h for 5 days) can decrease the incidence of rebleeding, its use in children remains controversial. Several studies have concluded that ε-aminocaproic acid is not beneficial in children. Furthermore, it has been associated with a high rate of nausea in children [28, 58]. ε-Aminocaproic acid prolongs blood clot resorption, so its use is not indicated in total hyphemas. Oral prednisone, which has been shown to have equal efficacy to ε-aminocaproic acid in preventing rebleeding, may be preferable in children [16]. An additional advantage to oral prednisone is that it may allow for a "no-touch" treatment paradigm, consisting of oral prednisone 0.6 mg/kg/day for 5–7 days instead of topical medications. Topically administered steroids are commonly used in children and adults to reduce inflammation and to stabilize the blood–aqueous barrier. Cycloplegia also reduces iris and ciliary body movement thereby facilitating clot stability. Several studies have shown that topically administered ε-aminocaproic acid is associated with a lower rebleeding rate and a trend toward a better visual outcome. However, it is not currently available in the USA [40]. Topical and systemic glaucoma medications should be administered as needed to control intraocular pressure.

31.2.3 Surgical Management

Surgical intervention may be required in children with a hyphema if the intraocular pressure cannot be lowered with medical therapy or if the hyphema persists long enough to put the eye at risk of developing corneal blood staining or amblyopia. Empirical criteria for surgical intervention have been determined and are listed in Table 31.1. In some cases a washout of the anterior chamber is sufficient. If a clot is present, it may need to be surgically excised using a vitreous cutting instrument. Great care must be taken to avoid damaging the iris or lens while removing the clot. Rebleeding may occur both intraoperatively or postoperatively.

31.2.4 Sickle Cell Hemoglobinopathy

Management of hyphema in children with sickle cell hemoglobinopathy differs somewhat because of the greater likelihood of optic nerve atrophy and secondary hemorrhage. Patients with sickle cell hemoglobinopathy are more susceptible to vascular occlusion when the intraocular pressure is elevated. In addition, systemic carbonic anhydrase agents (particularly acetazolamide) and repeated doses of hyperosmotic or diuretic agents should be avoided since either treatment can induce erythrocyte sickling by promoting metabolic acidosis.

31.2.5 Angle-recession Glaucoma

After a hyphema, children are at increased risk for developing angle-recession glaucoma. Intraocular pressure should be monitored on a regular basis since the onset of glaucoma can occur even months to years after the original injury.

31.3 Open Globes

Open globes (full-thickness wounds of the eyewall) arise most commonly in children when sharp objects penetrate the eye. When the open globe arises from a corneal laceration, a hyphema and corectopia are

Table 31.1 Criteria for surgical intervention of hyphema [14]

1.	Intractably elevated intraocular pressure despite medical treatment (greater than 60 mm Hg for 2 days in sickle-negative patient, or mean intraocular pressure greater than 24 mm Hg over the first 24 h or repeated spikes over 30 mm Hg in the setting of sickle cell disease)
2.	Intraocular pressure greater than 25 mm Hg for 5 days in the presence of a total hyphema
3.	Microscopic corneal blood staining present
4.	Persistence of hyphema occupying more than 50% of the anterior chamber volume for more than 1 week

usually present and uveal tissue may adhere to or prolapse through the wound. Most of these injuries occur at home during unsupervised play and are more common in boys than girls [59]. Open globes caused by sharp objects penetrating the eye are associated with the best visual prognoses, particularly if the injury is confined to the cornea (Fig. 31.1) [3, 34, 57]. Open globes can occur as a consequence of objects thrown or shot at the eye. Air gun injuries are a serious problem in young males and are frequently associated with poor visual outcomes [35]. One study reported that only 14% of eyes with BB gun-related injuries achieved a visual acuity better than or equal to 5/200 and 64% required enucleation [39]. Open globes may also arise when the sclera ruptures after blunt trauma. The site of rupture usually occurs posterior to the insertions of the extraocular muscles where the sclera is thinnest. Signs suggestive of scleral rupture include: (1) intraocular or subconjunctival hemorrhage; (2) an intraocular pressure <5 mm Hg; (3) light perception or worse vision; (4) an abnormally deep or shallow anterior chamber; and (5) flattening of the sclera with computed tomography (CT) [29]. Open globes secondary to blunt trauma are associated with particularly poor visual outcomes.

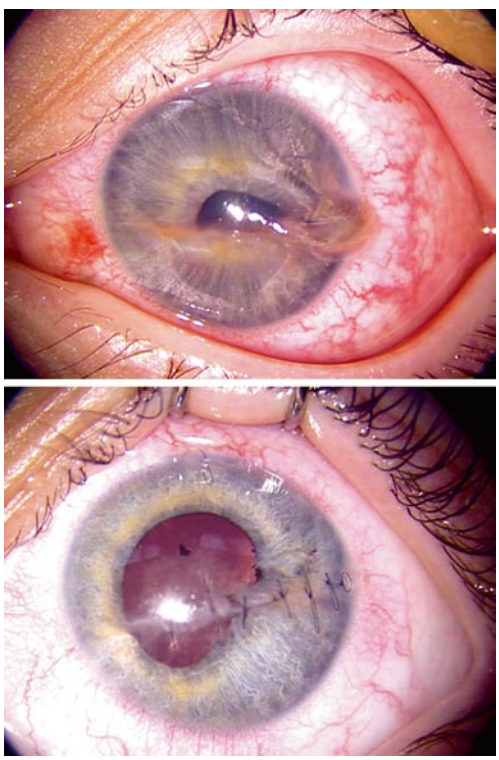

Fig. 31.1 Open globe in a 5-year-old boy following an unwitnessed accident (*top*). The corneal laceration was sutured closed 4 days later (*bottom*). He subsequently developed a posterior subcapsular cataract and underwent cataract extraction and intraocular lens implantation. Two years later, his visual acuity was correctable to 20/20 in the injured eye with spectacles

31.3.1 Surgical Management

The defect in the eyewall should be closed surgically as soon as possible to restore the structural integrity of the globe. A delay in closing the wound may increase the risk of endophthalmitis or result in prolapsed uveal tissue becoming epithelialized. It may not be possible to primarily close some catastrophic wounds such as those arising from firearms or high-speed motor vehicle accidents. For this reason, it should be explained to parents at the time of the initial repair that primary enucleation may be necessary. Linear wounds are usually easier to close than stellate wounds or wounds where tissue is missing. Great care should be taken to free all uveal tissue from the corneal wound to normalize pupillary function. Uveal tissue may generally be repositioned in the eye if it has been externalized for less than 24 h. This can be facilitated by creating a paracentesis site and filling the anterior chamber with a viscoelastic agent prior to closing the corneal laceration. For simple lacerations, the viscoelastic agent should be removed after water-tight closure of the wound. However, for complex lacerations it is sometimes better to leave the viscoelastic agent in the anterior chamber to prevent the anterior chamber from collapsing during the immediate postoperative period as a result of a slow leak from the wound. An added benefit of leaving the viscoelastic agent in the anterior chamber is that usually fewer sutures are needed to close the wound thereby minimizing the size of the resultant corneal leukoma (Fig. 31.2).

31.3.2 Secondary Enucleation

If the eye is found to have no light perception postoperatively, secondary enucleation may be indicated to prevent the occurrence of sympathetic ophthalmia

[13]. Secondary enucleations are performed in about 10% of children after primary repair of an open globe injury. Preoperative risk factors for secondary enucleation include: (1) the presence of a relative afferent pupillary defect; (2) the absence of a red reflex; (3) an associated lid laceration; (4) a blunt mechanism of injury; and (5) a preoperative visual acuity <20/200 [43].

31.3.3 Intraocular Foreign Body

If a foreign body is present in the eye, the eye is usually closed primarily, but a reoperation is scheduled soon afterward to remove the intraocular foreign body. CT is an excellent means of localizing and identifying intraocular foreign bodies, but each scan exposes a child to 15–30 millisieverts (mSv) of radiation with all of its attendant risks [8]. Ultrasonography can also be helpful in identifying intraocular foreign bodies and in evaluating the status of the retina [22]. If performed by an experienced ultrasonographer through the eyelid, it is safe even in open globes at high risk of extruding intraocular contents. Magnetic resonance imaging should only be performed if an intraocular metallic foreign body has been previously ruled out either by CT or ultrasonography.

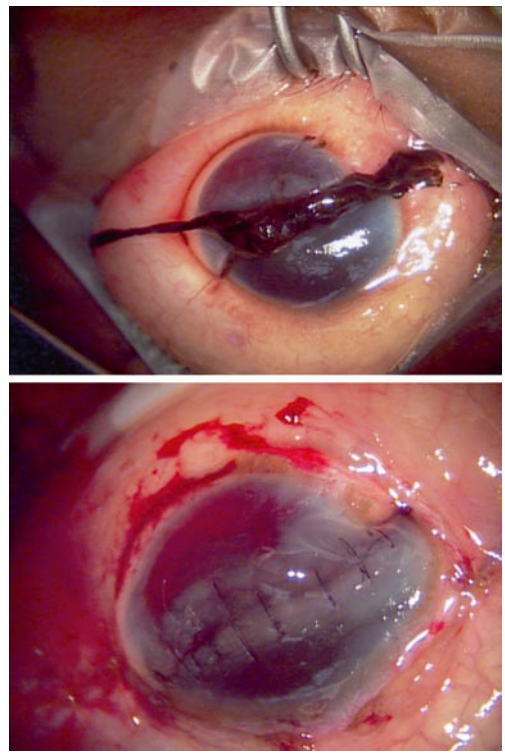

Fig. 31.2 Corneoscleral laceration in a 9-year-old boy who had a rock intentionally thrown at him by an older child (*top*). The wound was sutured closed the following day (*bottom*). The child developed an inoperable retinal detachment in the injured eye and had no light perception vision. Four weeks later the eye was enucleated

31.3.4 Endophthalmitis

Traumatic endophthalmitis occurs in about 5% of open globes. The presence of an intraocular foreign body, a delay in wound closure, an injury to the crystalline lens, and the occurrence of the injury in a rural setting have been shown to increase the risk of endophthalmitis. The administration of intravitreous or oral antibiotics may decrease this risk [17, 53].

31.4 Traumatic Cataracts

Trauma is one of the leading causes of cataracts in children. Traumatic cataracts may occur in association with an open globe due to a penetrating injury of the lens capsule or secondary to a contusion injury of the eye (Fig. 31.3). Usually the lens opacifies rapidly once a rent develops in the lens capsule although a small rent on occasion will be self-sealing (Fig. 31.4). Contusion injuries to the eye often produce capsular or subcapsular opacities. In some cases traumatic cataracts may not develop for days or longer after an ocular injury. Zonular dehiscence and lens subluxation is less common in children than adults.

31.4.1 Cataract Surgery

It is important to have a formed anterior chamber when performing cataract surgery. Good visualization of the lens capsule is required for placement of the intraocular lens in the capsular bag. For this reason, cataract surgery is usually not performed con-

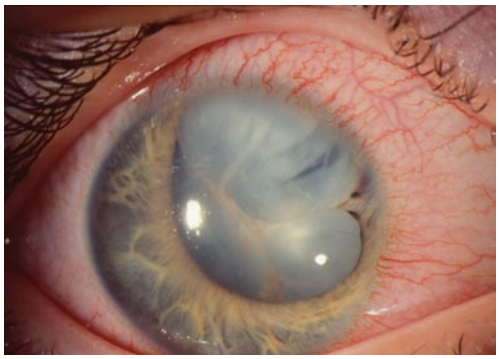

Fig. 31.3 Traumatic cataract and iridodialysis in a boy following a BB injury

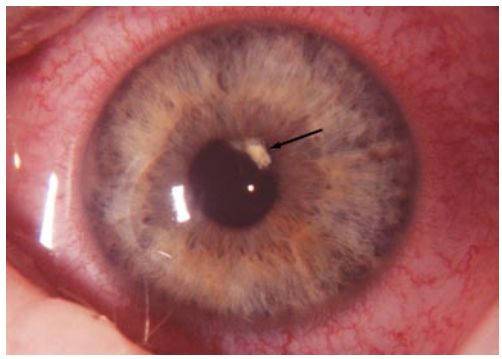

Fig. 31.4 Focal cataract *(arrow)* in a 6-year-old boy who had a sliver of metal that penetrated through his cornea and become lodged in the anterior lens cortex. After surgical removal, the child developed a focal cataract which has not progressed after 6 years. His visual acuity has remained 20/25 in this eye

currently with the primary repair of an open globe. The exception to this rule would be a small eyewall laceration that can be closed securely prior to cataract surgery and that does not interfere with visualization of the cataract. If cataract surgery is delayed for several weeks, the procedure can be combined with the removal of the sutures used to close the corneal laceration thereby minimizing the number of times the child has to be anesthetized. If it is uncertain as to the visual significance of the cataract, surgery should be delayed until the cornea is fully healed and the child's vision can be tested with an optical correction. If the cataract is visually significant, cataract extraction should not be delayed because of the potential for the development of amblyopia and loss of binocularity.

31.4.2 Intraocular Lens Implantation

An intraocular lens (IOL) should be implanted whenever possible in children with traumatic cataracts even if a rigid gas permeable contact lens will be needed postoperatively to neutralize irregular astigmatism. The IOL will ensure that at least a partial optical correction is present at all times. It may not be possible to obtain accurate keratometry measurements in an eye with a corneal leukoma following the repair of a corneal laceration. In these cases, the keratometry readings from the fellow eye are usually sufficient. In young children, it is generally best to optically undercorrect an eye in anticipation of a myopic shift as the child becomes older. IOLs can safely be implanted in most eyes with traumatic cataracts even if the posterior capsule is damaged at the time of the injury [6]. Care should be taken to position the haptics of the IOL over the most stable remnants of the lens capsule. Suture fixation of IOLs into the sulcus should generally be avoided because of the risk of these IOLs dislocating into the vitreous chamber [37, 41].

31.5 Airbag Injuries

While airbags have been shown to reduce the fatality rate and the rate of head injuries arising from motor vehicle accidents, they may severely injure the eye [56]. Corneal abrasion is the most common ocular injury caused by airbag deployment. In some cases there may also be generalized corneal stromal edema and the permanent loss of corneal endothelial cells. Chemical keratitis caused by the combustible powder, sodium azide, in airbags may result in severe alkali injuries to the cornea. Deformation of the globe by the airbag may also cause hyphema, vitreous hemorrhages, angle recession, irido- and cyclodialysis, and anterior capsular cataracts (Fig. 31.5). Anterior capsular cataracts are believed to be caused by direct

contact between the corneal endothelium and anterior lens surface. The most common retinal injuries are retinal breaks at the vitreous base. Children with ocular injuries following airbag deployment should undergo a careful examination of the retinal periphery using indirect ophthalmoscopy.

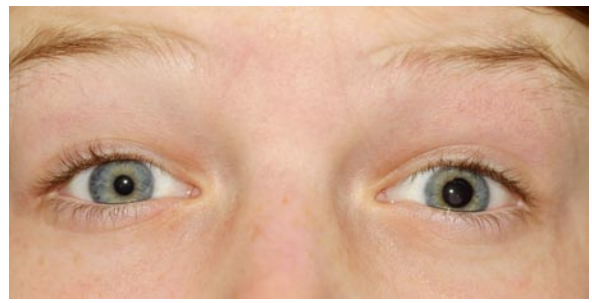

Fig. 31.5 Traumatic mydriasis and a subcapsular cataract in a 12-year-old following an airbag injury

31.6 Traumatic Vitreous Hemorrhage

Vitreous hemorrhage can occur in the setting of open or closed globe injuries and can preclude good visualization of the fundus as well as reduce the patient's visual acuity and lead to amblyopia. Trauma, both manifest and occult, is the most common cause of vitreous hemorrhage in children [55, 62]. Ultrasonography is invaluable in evaluating children with dense vitreous hemorrhage and can be used to identify retinal detachments and other associated retinal pathology [42]. Mild vitreous hemorrhages can often be treated with topical corticosteroids and safely observed. However, dense vitreous hemorrhages associated with ocular trauma involving the posterior segment often lead to poor visual outcomes. Early vitrectomy is used to clear the visual axis in infants and young children who are at risk for form deprivation amblyopia and myopia. Vitrectomy is also useful in identifying and treating underlying pathology such as retinal tears, choroidal rupture, and macular holes [50].

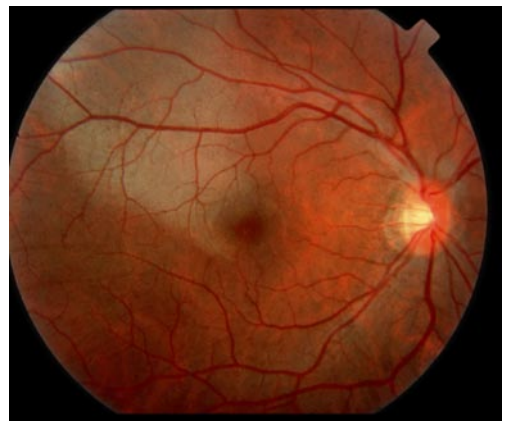

Fig. 31.6 Mild commotio retinae following blunt trauma to the eye. Note opacification of the outer retina and absence of retinal hemorrhage. This patient's vision returned to 20/20 without intervention

31.7 Commotio Retinae

Commotio retinae (Berlin's edema) was first described by a German oculist, Rudolf Berlin, in 1873 as a transient grey-white opacification of the macular or peripheral retina that occurs following blunt trauma to the eye. There are two variations of commotio retinae. The first, retinal concussion, is a milder injury with less dramatic grey-white change and is less frequently associated with hemorrhage (Fig. 31.6). The retina usually recovers spontaneously without permanent loss of vision. In contrast, retinal contusion is a more severe injury accompanied by dramatic retinal whitening and hemorrhage, and is more commonly associated with permanent visual loss, especially with macular involvement. Histologic studies of commotio retinae in animals and humans reveal disruption of the outer segments of photoreceptors. No acute treatment has proven to be beneficial.

31.8 Traumatic Retinal Tears and Detachment

Traumatic retinal tears and detachment can occur in the setting of both open and closed globe injuries [47]. Even though trauma is a leading cause of retinal detachment in children [46], it is relatively uncommon for a child to develop an acute rhegmatogenous

retinal detachment after blunt trauma because the solid vitreous provides internal tamponade to the retina despite tears or dialyses [45]. Nevertheless, it is important to identify tears since vitreous liquefaction occurs with age, and traumatic retinal detachments have been reported to present as late as 40 years after the initial injury [11]. In the population at large, retinal dialysis has been reported to be the most common type of break observed after blunt trauma. It tends to occur in the inferotemporal and supranasal quadrants [15, 21]. However, a recent series pertaining to traumatic retinal detachment in children found rhegmatogenous retinal detachments to be more common than retinal dialyses [47]. When a tear or dialysis is identified, prophylactic photocoagulation or cryopexy is recommended [38]. Traumatic retinal detachments are treated with conventional scleral buckling surgery or with vitrectomy. Treatment can be difficult in children and poor outcomes are frequently associated with postoperative proliferative vitreoretinopathy [9, 49].

31.9 Traumatic Macular Hole

Macular holes can occur in children following blunt trauma to the eye (Fig. 31.7). The pathophysiology of traumatic macular hole formation includes some combination of contusion necrosis with cystoid degeneration, subfoveal hemorrhage, choroidal rupture, and anteroposterior vitreous traction [18]. Recent studies using high-resolution cross-sectional retinal images obtained with optical coherence tomography (OCT) suggest that there might be two distinct types of traumatic macular hole resulting in either immediate visual loss (caused by primary dehiscence of the fovea) or delayed visual loss (caused by persistent vitreofoveal adhesion leading to secondary foveal dehiscence) [65]. Spontaneous closure of traumatic macular holes is not uncommon, especially in children, and therefore the timing of treatment is somewhat controversial [67]. If the hole is small, observation for several months is sometimes recommended. Vitrectomy and fluid–gas exchange is the current surgical approach. It has good success both anatomically and functionally with many patients achieving vision of 20/40 or better [10, 25].

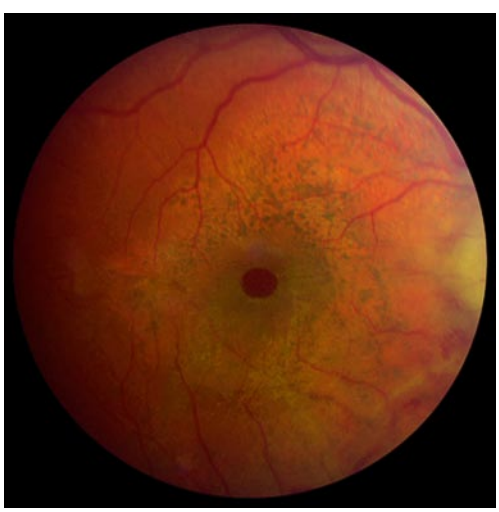

Fig. 31.7 Post-traumatic macular hole following severe blunt trauma to the eye

31.10 Choroidal Rupture

Traumatic choroidal rupture in children can occur at all ages following blunt injury and has even been reported in a newborn infant after forceps delivery [18]. Choroidal rupture occurs when the eye is compressed along its anterior-posterior plane, resulting in stretching of the horizontal plane with tearing of the relatively inelastic Bruch's membrane. Damage to the overlying retinal pigment epithelium (RPE) and choriocapillaris can also occur. Traumatic choroidal ruptures tend to be concentric with the optic nerve and vertically oriented [64]. The most common location is temporal to the optic nerve and through the macula. Single or multiple ruptures can occur (Fig. 31.8). Although no immediate treatment is indicated, visual prognosis depends on the severity of associated eye injuries, the location of the rupture, and the presence or absence of subsequent choroidal neovascular membrane formation. Up to 20% of adults with choroidal rupture will develop choroidal neovascular membranes, usually occurring in the first year after the injury, but often following weeks to months of relative visual stability [48]. Risk factors for choroidal neovascular membrane formation

include increased age, proximity of rupture to the fovea, and length of rupture. Peripherally located choroidal ruptures are less likely to be associated with neovascular membrane formation, but are more likely to be associated with retinal detachments [4]. Treatment options for choroidal neovascular membranes associated with traumatic choroidal rupture include: observation, submacular surgery, photocoagulation, and photodynamic therapy. Visual outcomes vary, but most patients with choroidal rupture do not obtain visual acuity of 20/40 or better. On the whole, visual outcomes tend to be better in children, who are also less likely than adults to develop choroidal neovascular membranes [1, 44].

31.11 Traumatic Chorioretinal Rupture (Sclopetaria)

Traumatic chorioretinal rupture (sclopetaria) is a full-thickness rupture of the retina and choroid that occurs when the shock wave from a high-velocity missile, such as a BB pellet traveling in close proximity to the globe, causes rapid deformation of the globe rupturing the choroid and retina but sparing the sclera [33]. Treatment is unnecessary because the intact posterior hyaloid over the chorioretinal rupture prevents acute retinal detachment, and subsequently the choroid and retina become firmly adherent to the sclera by the proliferation of fibrous tissue. Associated retinal detachment is usually due to simultaneously occurring peripheral retinal tears.

31.12 Canalicular Laceration

Canalicular lacerations are usually the result of indirect trauma to the eyelids. In children, they frequently arise from the lower eyelid being stretched and then avulsing in the region of the canaliculus which is generally the weakest point of the lower eyelid [63]. Dog bites are a common cause of canalicular lacerations in children (Fig. 31.9) [52]. The canaliculus should be repaired soon after the injury. A stent (we prefer the Mini Monika; Fayette & Bernard, Issy-Les-Moulineaux, France) is first threaded into the puncta and then through the distal end of the torn canaliculus. The proximal end of the torn canaliculus is then located by direct visualization in the medial canthal area. The procedure can often be facilitated by using an operating microscope. After placing the stent into the proximal end of the canaliculus, the distal and proximal ends of the canaliculus are sutured together. Last, the lid laceration is sutured closed. The stent should be left in place for several months to ensure patency of the lacrimal system.

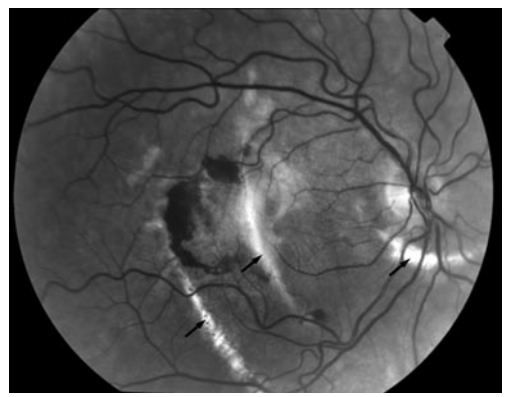

Fig. 31.8 Red-free photograph taken several weeks after blunt trauma reveals resolving retinal hemorrhage and multiple choroidal ruptures (*arrows*). The ruptures are concentric with the optic nerve and located temporal to the optic nerve and through the macula

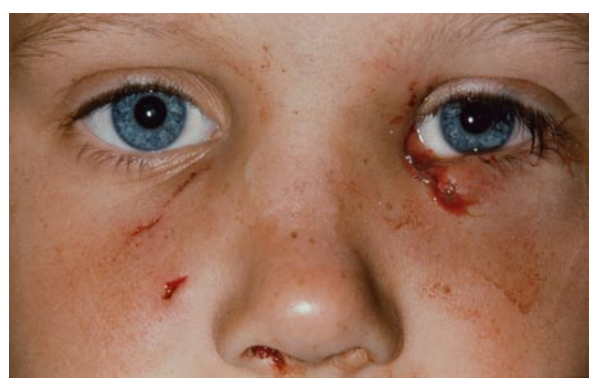

Fig. 31.9 Avulsion of the lower eyelid resulting in a tear of the inferior canaliculus in a 9-year-old girl following a dog bite

31.13 Orbital Fracture

Orbital fractures in children frequently result from sports injuries, physical assault, or motor vehicle accidents and are more common in boys [23]. They most frequently involve the orbital floor (67%) followed by combined orbital floor and medial wall fractures (14%), isolated medial wall fractures (8%), and orbital roof fractures (6%). Orbital roof fractures are more common in younger children because they have a higher cranium-to-face ratio rendering the skull more vulnerable to injury and because incomplete pneumatization of the frontal sinuses results in less even distribution of force. Signs and symptoms of orbital fractures vary. Some patients can be asymptomatic, but most patients will have some degree of bruising and swelling. Other signs and symptoms include diplopia, enophthalmos, hypoglobus, and hypoesthesia in the distribution of the infraorbital nerve. Children, because they have flexible and more elastic facial bones are particularly susceptible to "trapdoor" fractures which occur when an elliptical segment of the bony orbit is displaced, while still remaining attached on one side. Muscle entrapment can occur (Fig. 31.10) and is frequently associated with nausea and vomiting as well as a marked motility restriction despite a relatively quiet looking eye ("white-eyed blowout fracture") [5]. Expeditious repair is often recommended to prevent tissue ischemia and necrosis and bradycardia [51].

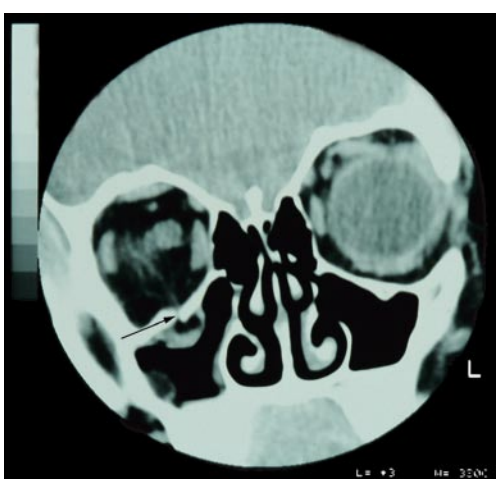

Fig. 31.10 This "trapdoor" type fracture of the orbital floor occurred in a child following blunt injury. Note inferior rectus muscle entrapment (*arrow*), which is likely to result in ischemia and permanent muscle damage if not repaired expeditiously

31.13.1 Surgical Management

Management of orbital fractures in children includes CT to identify fractures and a complete ophthalmic examination to rule out associated ocular injuries. Patients with orbital roof fractures should also be evaluated for possible intracranial injury. Indication for surgical intervention is controversial. A conservative approach is to perform surgery within 2 weeks in patients with symptomatic diplopia and positive forced ductions, CT evidence of muscle entrapment, enophthalmos of 3 mm or more, or large defects (>50%) of the orbital floor [26]. More urgent repair may be indicated in cases of "trapdoor" fractures or globe herniation into the maxillary sinus.

31.14 Traumatic Retrobulbar Hemorrhage

Orbital or facial trauma can result in retrobulbar hemorrhage which, if left untreated, can cause permanent visual impairment and even blindness. Patients generally present with decreased visual acuity, pain, proptosis, increased intraocular pressure, and limited ocular motility. Other signs include a hard, tense eye, optic disc pallor, afferent pupillary defect, pulsating central retinal artery and, less commonly, a cherry red spot from central retinal artery occlusion. Visual loss is thought to result from an orbital compartment syndrome leading to ischemic or direct injury to the optic nerve [61]. Associated displaced orbital fractures can be protective since blood can drain into the paranasal sinuses, thereby avoiding an orbital compartment syndrome. Permanent visual loss can occur 90–120 minutes after hemorrhage, so treatment includes both medical and surgical intervention. CT or ultrasound can be useful to confirm the diagnosis, but should not delay treatment if unavailable. Lateral canthotomy and cantholysis can be effective in producing urgent decompression, but surgical

evacuation of the hematoma is sometimes necessary. Medical treatment includes topical intraocular pressure lowering drops, and intravenous corticosteroids to reduce inflammation and stabilize cell membranes. Diuretics may also shrink the vitreous and reduce intraocular pressure.

31.15 Traumatic Optic Neuropathy

Traumatic optic neuropathy results from either direct or indirect trauma to the optic nerve. The most common site of injury is in the optic canal where the nerve is tethered and confined to a narrow boney space. Injury can also occur in the orbit or intracranial space. The optic nerve may be compressed by boney fragments or a hematoma or have its vascular supply disrupted. In most cases, it results in a retrobulbar optic neuropathy with a normal-appearing optic nerve initially. It is not until weeks later that pallor of the optic nerve may become visible. The swinging flashlight test to check for a relative afferent papillary defect is the most helpful clinical sign for detecting a traumatic optic neuropathy in a child. The condition is usually unilateral and a child may not notice the unilateral loss of vision immediately. Traumatic optic neuropathy is most commonly caused by motor vehicle accidents, falls, and sports-related injuries [19]. High-resolution CT of the orbit is helpful in evaluating fractures in the optic canal, although CT underestimates the true incidence of these fractures.

31.15.1 Treatment

The treatment of traumatic optic neuropathy is largely based on retrospective series. An attempt was made to perform a randomized clinical trial of traumatic optic neuropathy (International Optic Nerve Trauma Study), but it was changed to an observational study due to low recruitment [32]. High doses of intravenous corticosteroids have been shown to be effective in the treatment of acute spinal cord injuries [7], but their efficacy in patients with traumatic optic neuropathy has not been established. It remains unclear whether intravenous steroids in fact improve visual outcome. Nor is it clear how soon after optic nerve injury steroids need to be administered. Others have recommended decompression of the optic canal, particularly when a boney fragment is compressing the optic nerve. Decompression can be performed through an anterior approach along the medial orbital wall, a transnasal endoscopic approach, or intracranially [20, 66]. In a large series from Taiwan, Yang et al. [66] reported that the initial visual acuity was the most important factor in predicting the visual outcome. Nonetheless, many children with traumatic optic neuropathy who initially had no light perception vision have recovered vision.

31.16 In Utero Trauma

Mid-trimester amniocentesis rarely results in traumatic injury to the eye. Injuries are usually due to the amniocentesis needle penetrating the cornea or the sclera. In one report, a scleral opening plugged by uveal tissue was noted in the eye of a newborn with a retinal detachment who had undergone amniocentesis during the 17th week of pregnancy [2]. Corneal scars with peaked pupils have also been reported following amniocentesis [36]. The use of high-resolution real-time ultrasonography and smaller bore needles have reduced the incidence of ocular injuries following amniocentesis.

31.17 Birth Injuries

Ocular injuries may occur at the time of delivery particularly when forceps are used. The injuries may include eyelid lacerations, hyphemas, tears in Descemet's membrane, retinal hemorrhages, and choroidal ruptures (Fig. 31.11) [24]. Tears in Descemet's membranes after forceps deliveries are generally oriented vertically and may be single or multiple. These eyes frequently present with marked corneal edema, hyphema, and ecchymoses of the eyelids. While the corneal edema usually resolves in a few days, high astigmatic refractive errors often develop. If left untreated, these eyes often develop dense anisometropic amblyopia. Favorable visual results have been reported when the refractive errors have been treated from infancy with gas-permeable contact lenses [30].

Take Home Pearls

- The greater magnification that can be achieved with an operating microscope can be helpful in visualizing the proximal end of a torn canaliculus.
- Leaving a viscoelastic agent in the anterior chamber may temporarily seal a complex corneoscleral laceration that might otherwise continue to leak regardless of the number of sutures used to close the wound.
- Intraocular lenses can safely be implanted in the capsular bag or sulcus of most eyes with traumatic cataracts even if the posterior capsule is damaged at the time of the injury.
- Ultrasonography may be used to evaluate the status of the retina and to identify intraocular foreign bodies in open globes with a low risk of extruding intraocular contents.

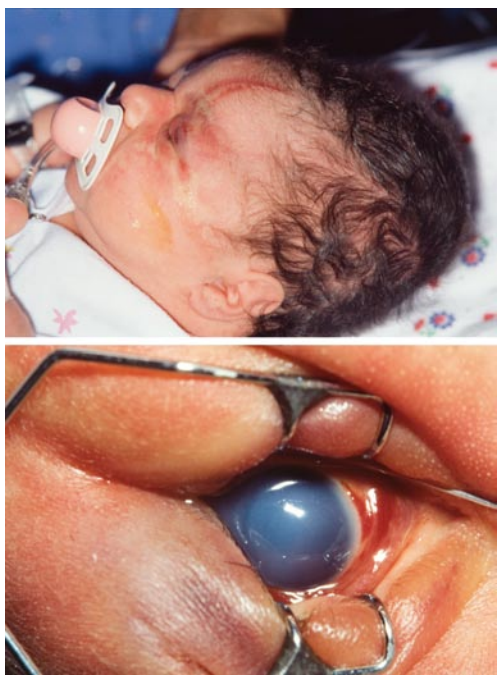

Fig. 31.11 Ocular forceps injury in a newborn (*top*) associated with corneal edema (*bottom*), a hyphema, and a high astigmatic refractive error

References

1. Abri A, Binder S, Pavelka M, et al. (2006) Choroidal neovascularization in a child with traumatic choroidal rupture: clinical and ultrastructural findings. Clin Exp Ophthalmol 34:460–463
2. Admoni MM, BenEzra D (1988) Ocular trauma following amniocentesis as the cause of leukocoria. J Pediatr Ophthalmol Strabismus 25:196–197
3. Alfaro DV, Chaudhry NA, Walonker AF, et al. (1994) Penetrating eye injuries in young children. Retina 14:201–205
4. Ament CS, Zacks DN, Lane AM, et al. (2006) Predictors of visual outcome and choroidal neovascular membrane formation after traumatic choroidal rupture. Arch Ophthalmol 124:957–966
5. Bansagi ZC, Meyer DR (2000) Internal orbital fractures in the pediatric age group: characterization and management. Ophthalmology 107:829–836
6. Bowman RJC, Yorston D, Wood M, et al. (1998) Primary intraocular lens implantation for penetrating lens trauma in Africa. Ophthalmology 105:1770–1774
7. Bracken MB, Shepard MJ, Holford TR, et al. (1997) Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. JAMA 277:1597–1604
8. Brenner DJ, Hall EJ (2007) Computed tomography: an increasing source of radiation exposure. N Engl J Med 357:2277–2284
9. Cekic O, Batman C, Totan Y, et al. (1999) Management of traumatic retinal detachment with vitreon in children. Int Ophthalmol 23:145–148
10. Chow DR, Willams GA, Trese MT, et al. (1999) Successful closure of traumatic retinal holes. Retina 19:405–409

11. Cox MS, Schepens CL, Freeman HM (1966) Retinal detachment due to ocular contusion. Arch Ophthalmol 76:678–685
12. Crawford JS, Lewandowski JS, Chan W (1975) The effect of aspirin on rebleeding in traumatic hyphema. Am J Ophthalmol 80:543–575
13. Damico FM, Kiss S, Young LH (2005) Sympathetic ophthalmia. Semin Ophthalmol 20:191–197
14. Deutsch TA, Weinreb RN, Goldberg MF (1984) Indications for surgical management of hyphema in patients with sickle cell trait. Arch Ophthalmol 102:566–569
15. Dumas JJ (1967) Retinal detachment following contusion of the eye. Int Ophthalmol Clin 7:19–38
16. Edwards WC, Layden WE (1973) Traumatic hyphema. A report of 184 consecutive cases. Am J Ophthalmol 75:110–116
17. Essex RW, Yi Q, Charles PG, et al. (2004) Post-traumatic endophthalmitis. Ophthalmology 111:2015–2022
18. Estafanous MF, Seeley M, Traboulsi EI (2000) Choroidal rupture associated with forceps delivery. Am J Ophthalmol 129:819–820

18a. Gass DM (1997) Stereoscopic atlas of macular diseases: diagnosis and treatment, 4th edn. Mosby, St Louis

19. Goldenberg-Cohen N, Miller NR, Repka MX (2004) Traumatic optic neuropathy in children and adolescents. J AAPOS 8:20–27
20. Gupta AK, Gupta AK, Gupta A, et al. (2007) Traumatic optic neuropathy in pediatric population: early intervention or delayed intervention? Int J Pediatr Otorhinolaryngol 71:559–562
21. Hagler WS (1980) Retinal dialysis: a statistical and genetic study to determine pathogenetic factors. Trans Am Ophthalmol Soc 78:686–733
22. Harlan JB Jr, Pieramici DJ (2002) Evaluation of patients with ocular trauma. Ophthalmol Clin North Am 15:153–161
23. Hatton MP, Watkins LM, Rubin PA (2001) Orbital fractures in children. Ophthal Plast Reconstr Surg 17:174–179
24. Honig MA, Barraquer J, Perry HD, et al. (1996) Forceps and vacuum injuries to the cornea: histopathologic features of twelve cases and review of the literature. Cornea 15:463–472
25. Johnson RN, McDonald HR, Lewis H, et al. (2001) Traumatic macular hole: observations, pathogenesis, and results of vitrectomy surgery. Ophthalmology 108:853–857
26. Jordan DR, Allen LH, White J, et al. (1998) Intervention within days for some orbital floor fractures: the white-eyed blowout [see comment]. Ophthal Plast Reconstr Surg 14:379–390
27. Kaiser PK, Pineda R (1997) The corneal abrasion patching study group. A study of topical nonsteroidal anti-inflammatory drops and no pressure patching in the treatment of corneal abrasions. Ophthalmology 104:1353–1359
28. Kraft SP, Christianson MD, Crawford JS, et al. (1987) Traumatic hyphema in children. Treatment with epsilon-aminocaproic acid. Ophthalmology 94:1232–1237
29. Kylstra JA, Lamkin JC, Runyan DK (1993) Clinical predictors of scleral rupture after blunt ocular trauma. Am J Ophthalmol 115:530–535
30. Lambert SR, Drack AV, Hutchinson AK (2004) Longitudinal changes in the refractive errors of children with tears in Descemet's membrane following forceps injuries. J AAPOS 8:368–370
31. LeSage N, Verreault R, Rochette L (2001) Efficacy of eye patching for traumatic corneal abrasions: a controlled clinical trial. Ann Emerg Med 38:129–134
32. Levin LA, Beck RW, Joseph MP, et al. (1999) The treatment of traumatic optic neuropathy: the International Optic Nerve Trauma Study. Ophthalmology 106:1268–1277
33. Martin DF, Awh CC, McCuen BW 2nd (1994) Treatment and pathogenesis of traumatic chorioretinal rupture (sclopetaria). Am J Ophthalmol 117:190–200
34. Maw R, Pineda R, Pasquale LR, et al. (2002) Traumatic ruptured globe injuries in children. Int Ophthalmol Clin 42:157–165
35. McGwin G Jr, Hall TA, Xie A, et al. (2006) Gun-related eye injury in the United States, 1993–2002. Ophthalmic Epidemiol 13:15–21
36. Naylor G, Roper JP, Willshaw HE (1990) Ophthalmic complications of amniocentesis. Eye 4:845–849
37. Parekh P, Green WR, Stark WJ, et al. (2007) Subluxation of suture-fixated posterior chamber intraocular lenses a clinicopathologic study. Ophthalmology 114:232–237
38. Patrone G, Sacca SC, Macri A, et al. (1999) Evaluation of the analgesic effect of 0.1% indomethacin solution on corneal abrasions. Ophthalmologica 213:350–354
39. Pieramici DJ, MacCumber MW, Humayun MU, et al. (1996) Open-globe injury. Update on types of injuries and visual results. Ophthalmology 103:1798–1803
40. Pieramici DJ, Goldberg MF, Melia M, et al. (2003) A phase III, multicenter, randomized, placebo-controlled clinical trial of topical aminocaproic acid (Caprogel) in the management of traumatic hyphema. Ophthalmology 110:2106–2112
41. Price MO, Price FW Jr, Werner L, et al. (2005) Late dislocation of scleral-sutured posterior chamber intraocular lenses. J Cataract Refract Surg 31:1320–1326
42. Rabinowitz R, Yagev R, Shoham A, et al. (2004) Comparison between clinical and ultrasound findings in patients with vitreous hemorrhage. Eye 18:253–256
43. Rahman I, Maino A, Devadason D, et al. (2006) Open globe injuries: factors predictive of poor outcome. Eye 20:1336–1341
44. Raman SV, Desai UR, Anderson S, et al. (2004) Visual prognosis in patients with traumatic choroidal rupture. Can J Ophthalmol 39:260–266
45. Recchia FM, Aaberg TA, Sternberg PS (2006) Trauma: principles and techniques of treatment, 4th edn. Retina. Elsevier Mosby, Philadelphia, pp 2379–2401
46. Rosner M, Treister G, Belkin M (1987) Epidemiology of retinal detachment in childhood and adolescence. J Pediatric Ophthalmol Strabismus 24:42–44
47. Sarrazin L, Averbukh E, Halpert M, et al. (2004) Traumatic pediatric retinal detachment: a comparison between open and closed globe injuries. Am J Ophthalmol 137:1042–1049

48. Secretan M, Sickenberg M, Zografos L, et al. (1998) Morphometric characteristics of traumatic choroidal ruptures associated with neovascularization. Retina 18:62–66
49. Sheard RM, Mireskandari K, Ezra E, et al. (2007) Vitreoretinal surgery after childhood ocular trauma. Eye 21:793–798
50. Simon J, Sood S, Yoon MK, et al. (2005) Vitrectomy for dense vitreous hemorrhage in infancy. J Pediatr Ophthalmol Strabismus 42:18–22
51. Sires BS, Stanley RB, Levine LM (1998) Oculocardiac reflex caused by orbital floor trapdoor fracture: an indication for urgent repair. Arch Ophthalmol 116:955–956
52. Slonim CB (1996) Dog bite-induced canalicular lacerations: a review of 17 cases. Ophthal Plast Reconstr Surg 12:218–222
53. Soheilian M, Rafati N, Mohebbi MR, et al. (2007) Prophylaxis of acute posttraumatic bacterial endophthalmitis: a multicenter, randomized clinical trial of intraocular antibiotic injection, report 2. Arch Ophthalmol 125:460–465
54. Solomon A, Halpert M, Frucht-Pery J (2000) Comparison of topical indomethacin and eye patching for minor corneal trauma. Ann Ophthalmol 32:316–319
55. Spirn MJ, Lynn MJ, Hubbard GB 3rd (2006) Vitreous hemorrhage in children Ophthalmology 113:848–852
56. Stein JD, Jaeger EA, Jeffers JB (1999) Air bags and ocular injuries. Trans Am Ophthalmol Soc 97:59–82; discussion 82–86
57. Sternberg P Jr, de Juan E Jr, Michels RG (1984) Penetrating ocular injuries in young patients. Initial injuries and visual results. Retina 4:5–8
58. Teboul BK, Jacob JL, Barsoum-Homsy M, et al. (1995) Clinical evaluation of aminocaproic acid for managing traumatic hyphema in children. Ophthalmology 102:1646–1653
59. Thompson CG, Kumar N, Billson FA, et al. (2002) The aetiology of perforating ocular injuries in children. Br J Ophthalmol 86:920–922
60. Walton W, Von Hagen S, Grigorian R, et al. (2002) Management of traumatic hyphema. Surv Ophthalmol 47:297–334
61. Winterton JV, Patel K, Mizen KD (2007) Review of management options for a retrobulbar hemorrhage. J Oral Maxillofac Surg 65:296–299
62. Wirth MG, Helbig H (2006) Vitreous haemorrhage in children. Klin Monatsbl Augenheilkd 223:440–442
63. Wulc AE, Arterberry JF (1991) The pathogenesis of canalicular laceration. Ophthalmology 98:1243–1249
64. Wyszynski RE, Grossniklaus HE, Frank KE (1988) Indirect choroidal rupture secondary to blunt ocular trauma. A review of eight eyes. Retina 8:237–243
65. Yamashita T, Uemara A, Uchino E, et al. (2002) Spontaneous closure of traumatic macular hole. Am J Ophthalmol 133:230–235
66. Yang WG, Chen CT, Tsay PK, et al. (2004) Outcome for traumatic optic neuropathy: surgical versus nonsurgical treatment. Ann Plast Surg 52:36–42
67. Yeshurun I, Guerrero-Naranjo JL, Quiroz-Mercado H (2002) Spontaneous closure of a large traumatic macular hole in a young patient. Am J Ophthalmol 134:602–603

Subject Index

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