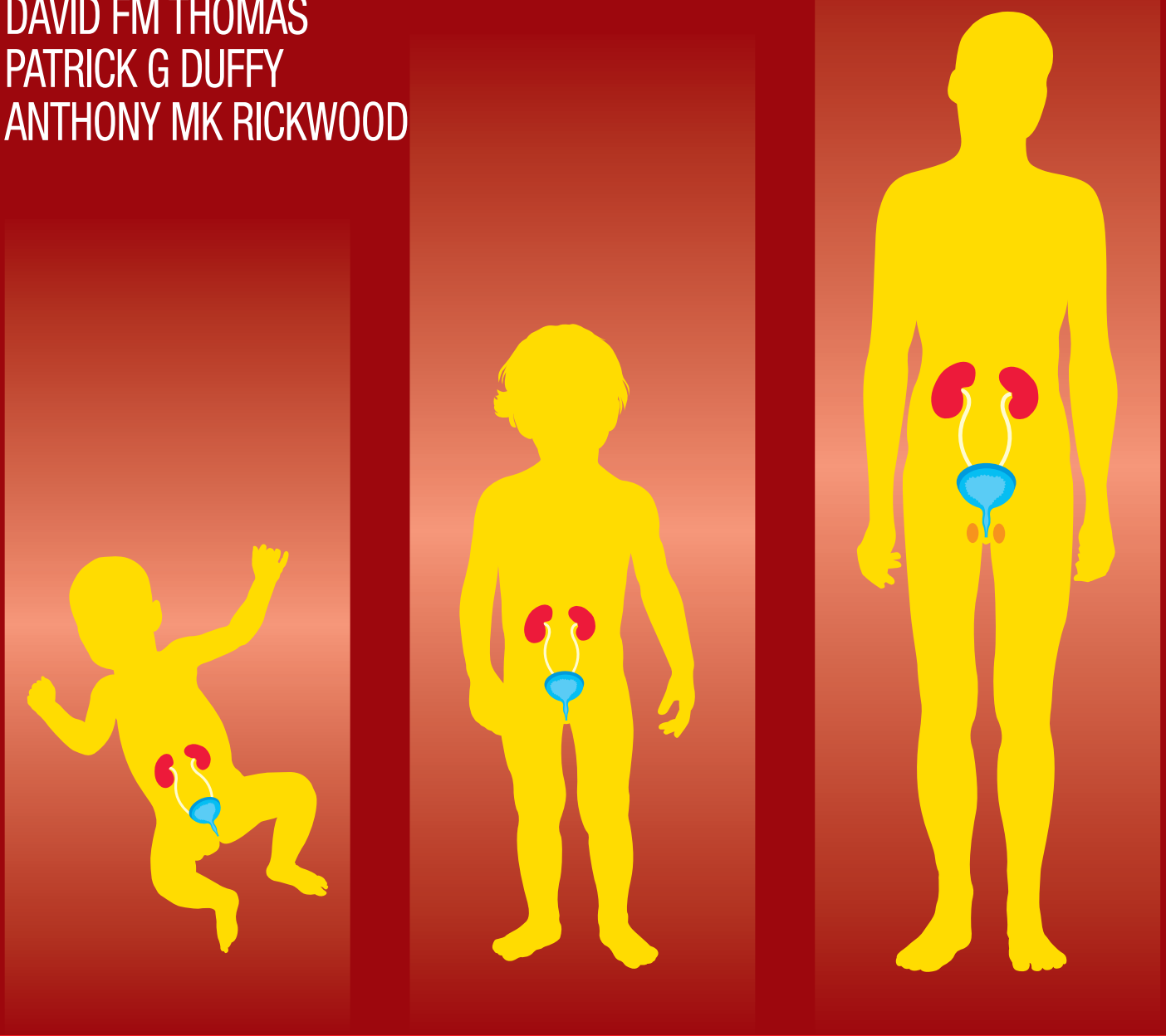
ESSENTIALS OF PAEDIATRIC UROLOGY

SECOND EDITION

EDITED BY
DAVID FM THOMAS
PATRICK G DUFFY
ANTHONY MK RICKWOOD



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Edited by

David FM Thomas FRCP FRCPCH FRCS
St James's University Hospital
Leeds, UK

Patrick G Duffy MB BCH BAO FRCS(I) FEBU
Great Ormond Street
Hospital for Sick Children
London, UK

Anthony MK Rickwood MA FRCS
Formerly of Royal Liverpool
Hospital for Sick Children
Liverpool, UK

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To our wives: Marilyn, Zara and Valerie.

Contents

Contributors

Su-Anna M Boddy MS FRCS
Department of Paediatric Urology
St George's Hospital
London
UK

Peter Cuckow MB BS FRCS (Paed)
Department of Paediatric Urology
Great Ormond Street Hospital for Sick Children
London
UK

Divyesh Y Desai MBBS MS MCHIR (UROL) FEAPU
Department of Paediatric Urology
Great Ormond Street Hospital for Sick Children
London
UK

HK Dhillon FRCS (ED)
Department of Paediatric Urology
Great Ormond Street Hospital for Sick Children
London
UK

Patrick G Duffy MB BCH BAO FRCS (I) FEBU
Department of Paediatric Urology
Great Ormond Street Hospital for Sick Children
London
UK

Martyn E Flett MB MCH BSC FRCS (PAED)
Department of Paediatric Urology
Great Ormond Street Hospital for Sick Children
London
UK

Melanie P Hiorns MRCP FRCR
Department of Radiology
Great Ormond Street Hospital for Sick Children
London
UK

Kim AR Hutton MBCHB CHM FRCS (PAED)
Department of Paediatric Surgery
University Hospital of Wales
Cardiff
Wales
UK

Henri Lottman MD FEBU
Hôspital Necker-Enfants Malades
Service de Chirurgie Viscérale Pédiatrique
Paris
France

Nicholas P Madden MA FRCS
Department of Paediatric Surgery and Urology
Chelsea and Westminster Hospital
London
UK

Padraig S Malone MB MCH FRCSI FRCS
Department of Paediatric Urology
Southampton General Hospital
Southampton
UK

Pierre DE Mouriquand MD FRCS (ENG) EFAPU
Department of Paediatric Urology
Claude-Bernard University
Debrousse Hospital
Lyon
France

Imran Mushtaq MD FRCS (PAEDS)
Department of Paediatric Urology
Great Ormond Street Hospital for Sick Children
London
UK

Stuart J O'Toole MD FRCS (PAEDS)
Department of Surgical Paediatrics
Royal Hospital for Sick Children
Glasgow
Scotland
UK

Anthony MK Rickwood MA FRCS
(Formerly)
Department of Paediatric Urology
Royal Liverpool Hospital for Sick Children
Liverpool
UK

Neil J Sebire MB BS BCLINSCI DRCOG MD MRCPATH
Institute of Child Health and
Department of Paediatric Urology
Great Ormond Street Hospital for Sick Children
London
UK

Henrik A Steinbrecher BSC MS FRCS (PAEDS)
Department of Paediatric Urology
Southampton University Hospital
Southampton
UK

Ram Subramaniam MD
Department of Paediatric Surgery
St James's University Hospital
Leeds
UK

David FM Thomas FRCP FRCPCH FRCS
Department of Paediatric Surgery
St James's University Hospital
Leeds
UK

Richard Trompetor MB FRCP FRCPCH
Department of Nephrology
Great Ormond Street Hospital for Sick Children
London
UK

Duncan T Wilcox MD FRCS
Department of Paediatric Urology
University of Texas
Southwestern Medical Center
Dallas, TX
USA

Christopher RJ Woodhouse MB BS FRCS FEBU
Department of Paediatric Urology
The Institute of Urology
London
UK

Preface

The specialty of paediatric urology has seen many advances and innovations since the publication of the first edition of *Essentials of Paediatric Urology*. This new edition has been extensively updated, revised and rewritten to reflect exciting developments in areas such as laparoscopic paediatric urology, endoscopic correction of reflux, the increasing use of MRI and the introduction of new surgical procedures for hypospadias and bladder exstrophy. The scope of this new edition ranges from complex anomalies managed by specialist paediatric urologists to common conditions such as testicular maldescent, urinary infection and incontinence, which constitute a substantial part of everyday practice for urologists, general paediatric surgeons and paediatricians.

We have sought to retain the accessible, didactic format that proved a popular feature of the first edition and wherever possible have also endeavoured to include suggestions and helpful feedback from trainees and other readers of the first edition. Throughout the book our over-riding aim has been to provide a concise and up-to-date account of the diagnosis and management of the urological conditions of childhood which is factual and evidence-based.

The contributors include internationally recognised authorities in their field – many of whom are regular contributors to the British Association of Paediatric Urologists postgraduate training course held annually in Cambridge.

The content of the new edition has been designed to encompass the syllabus tested by the intercollegiate examinations in Urology and Paediatric Surgery, the Fellowship of the European Board of Urology and the in-service examination of the European Society of Paediatric Urology. A new feature of the second edition is a self-assessment section of multiple choice questions which is intended to provide a valuable learning and revision aid for surgeons preparing for British, European and North American Board Examinations.

It has also been our intention that the second edition of *Essentials of Paediatric Urology* should retain the book's role as a source of easy reference for paediatricians, paediatric nephrologists, radiologists and nurse specialists.

David FM Thomas
Patrick G Duffy
Anthony MK Rickwood

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Finally, we owe a debt of gratitude to our publishing team at Informa Healthcare, especially Alan Burgess and his colleagues, Jonathan Mazliah and Oliver Walter; they ensured that the second edition of 'Essentials' made crucial deadlines.

Embryology

1

David FM Thomas

Topics covered
Genetic basis of genitourinary malformations
Embryogenesis
Upper urinary tract
Lower urinary tract
Genital tracts

Introduction

A working knowledge of the embryology of the genitourinary tract provides the basis for understanding the structural anomalies encountered in paediatric urological practice. Although this chapter will concentrate predominantly on the clinical aspects of embryology of the genitourinary tract it will also touch on some of the relevant basic science and summarise developments in the rapidly advancing field of developmental biology.

Genetic basis of genitourinary tract malformations

Chromosomal abnormalities

The nuclear DNA present in the normal human somatic cell is represented by 23 pairs of chromosomes: 22 pairs of autosomes and one pair of sex chromosomes, a karyotype expressed as 46XY (male) or 46XX (female).

Following the sequence of two meiotic divisions during **gametogenesis** each spermatazoon or oocyte carries only one unpaired copy of each autosome and one sex chromosome – either X or Y. Fusion of the nuclear DNA of the gametes at the time of fertilisation imparts the normal diploid status to the fertilised zygote.

Structural chromosomal abnormalities occur either during the formation of the gametes (gametogenesis) or during the first few cell divisions of the fertilised zygote. Examination of spontaneously aborted embryos reveals a high percentage of profound chromosomal abnormalities inconsistent with survival of the embryo. The most serious chromosomal abnormalities compatible with survival to term are **trisomy** 21 – Down's syndrome (47XX or 47XY) – and trisomies 13 and 18.

Trisomies result from the failure of a pair of chromosomes to separate fully during gametogenesis, with the result that an additional copy of a chromosome or fragment of chromosome becomes incorporated into the nucleus of a gamete (usually by a process termed **translocation** or **non-disjunction)**. The converse of the process, which gives rise to trisomic states, also results in the formation of a gamete that is lacking a copy of a particular chromosome. The zygote formed by fertilisation will therefore have only one copy of this chromosome – termed **monosomy**. Complete autosomal monosomic states are uniformly lethal but some partial monosomies created by deletion of part of a chromosome are compatible with survival and are associated with specific syndromes. Deletion of a particular portion of chromosome 11 has been implicated in the aetiology of some Wilms' tumours.

A similar process of faulty separation affecting the sex chromosomes is encountered in, for example, Klinefelter's syndrome (47XXY) or Turner syndrome (45X). Monosomic forms (45X) account for approximately 50% of cases of Turner

syndrome, mosaicism (45X/46XX) is present in approximately 30% of cases while a structural deletion on one of the X chromosomes accounts for approximately 20%. Abnormalities of the sex chromosomes often occur in mosaic form, **mosaicism** being defined as the presence of two chromosomally distinct cell lines derived from the same zygote. In addition to translocation and non-disjunction, structural defects involving identifiable segments of chromosomes include deletion, inversion, duplication and substitution.

The genetic imbalance arising from structural chromosomal abnormalities is expressed as profound disturbances of embryological development across a number of systems, including the genitourinary tract (Table 1.1).

Gene mutations occur in structurally intact chromosomes at the level of the nucleotides comprising the individual genes. Such mutations are not visible on microscopy but are amenable to study by techniques such as **PCR (polymerase chain reaction)** and **FISH (fluorescent in situ hybridisation)**. The role of individual genes can be elucidated by studying the effects of so-called 'knock out' deletion in transgenic mice.

Specific gene mutations have been identified in a number of inherited conditions affecting the genitourinary tract, e.g. autosomal dominant polycystic kidney disease, X-linked Kallmann's syndrome and renal coloboma syndrome (mutation of the *PAX2* gene encoding for a transcription factor expressed during development of the eye and urinary tract).

However, the majority of the congenital anomalies encountered in paediatric urology do not have such a clearly defined genetic basis. They either arise sporadically or are inherited as autosomal dominant traits with variable expression and penetrance. Conditions such as vesicoureteric reflux, upper tract duplication, hypospadias, etc., which exhibit a familial tendency are generally believed to represent the interaction of multiple genes, rather than a single gene mutation. The extent to which external factors in the fetal or the wider environment influence the expression of genes involved in regulating the development of the genitourinary tract is poorly understood. However, it is known, for example, that gene expression and regulation within the differentiating fetal kidney is markedly affected by early urinary tract obstruction.

Table 1.1 Chromosome defects associated with urinary tract anomalies

Chromosome defect or syndrome	Frequency (%)	Genitourinary anomalies
Turner syndrome 45X0	60–80	Horseshoe kidney Duplication
Trisomy 18 (Edwards' syndrome)	70	Horseshoe kidney Renal ectopia Duplication Hydronephrosis
Trisomy 13 (Patau syndrome)	60–80	Cystic kidney Hydronephrosis Horseshoe kidney Ureteric duplication
4p (Wolf–Hirschorn syndrome)	33	Hypospadias Cystic kidney Hydronephrosis
Trisomy 21 (Down's syndrome)	3–7	Renal agenesis Horseshoe kidney

Embryogenesis

Human gestation spans a period of 38 weeks, from fertilisation to birth. Conventionally, pregnancy is divided into three trimesters, each of 3 months' duration. The formation of organs and systems (embryogenesis) takes place principally between the third and 10th weeks of gestation. Throughout the remainder, the fetal organs undergo differentiation, branching, maturation and growth. In each ovulatory cycle a small number of germ cells (primary oocytes) within the ovary are stimulated to resume the long-arrested meiotic division. Of these, usually only one progresses to be extruded from the ovary into the fallopian tube at the midpoint of the menstrual cycle. At the time of fertilisation the protective zona pellucida of the oocyte is penetrated by the fertilising spermatazoon, thereby triggering the final meiotic division to create the definitive oocyte and second polar body (consisting of non-functional DNA). Fertilisation is defined as the fusion of the nuclear DNA of the male and female gametes (spermatazoon and definitive oocyte). In the ensuing 5 days, the fertilised zygote undergoes a series of mitotic doubling cell divisions termed cleavage (Figure 1.1).

Implantation of the spherical mass of cells (blastocyst) into the primed uterine endometrium occurs approximately 6 days after fertilisation. Proliferation of the embryonic cell mass over the ensuing 10 days is accompanied by the appearance of two cavities – the amniotic cavity and the yolk sac. The embryo is destined to develop from the cells interposed between these two cavities. The ectodermal tissues of the embryo derives from the layer of cells on the amniotic surface of the embryonic disc, whereas the endodermal derivatives have their origins in the layer of cells adjacent to the yolk sac (Figure 1.2). Inpouring of cells from the amniotic surface via the primitive streak creates a third layer of embryonic tissue, the intraembryonic mesoderm, which subdivides into paraxial, intermediate and lateral plate mesoderm. It is from the intermediate block of intraembryonic mesoderm that much of the genitourinary tract is derived. Segmentation and folding of the embryo begins during the third and fourth weeks of gestation, and towards the end of this period the precursor of the embryonic kidney begins to take shape.

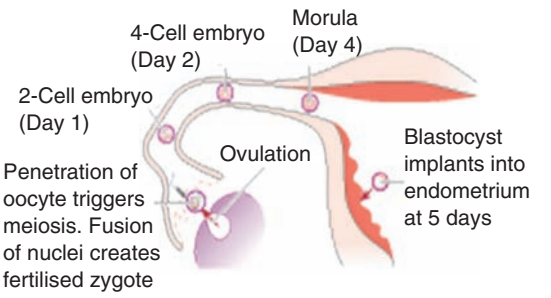

Figure 1.1 Key stages in the 5–6 days from fertilisation to implantation.

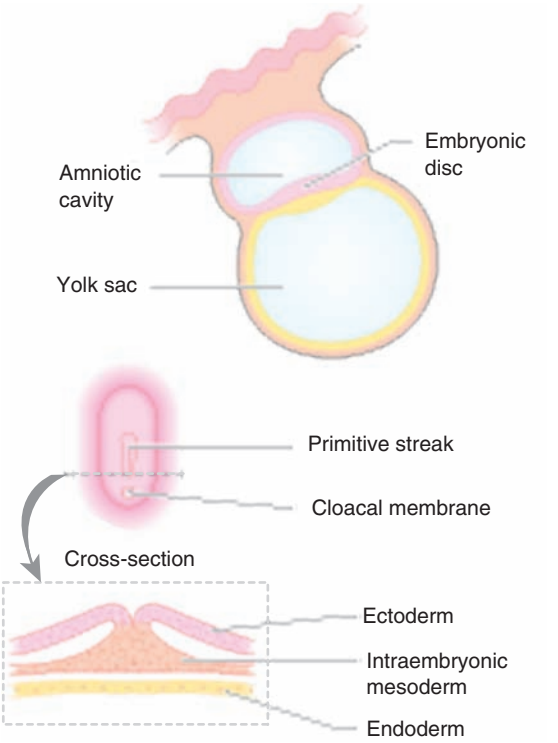

Figure 1.2 Embryonic disc at 16 days. Formation of intraembryonic mesoderm by inpouring of cells at the primitive streak.

In vitro fertilisation (IVF)

Many of the more severe congenital abnormalities of the genitourinary tract frequently carry a significant risk of infertility or subfertility. Examples in males include oligospermia or azoospermia due to cryptorchidism, impaired ejaculation in men with a history of posterior urethral valves or bladder exstrophy and erectile dysfunction in men with neurological impairment associated with spina bifida. Causes of infertility or reduced fertility in females include Turner syndrome, spina bifida and cloacal anomalies. With the development of in vitro techniques, the outlook for fertility is not always as bleak as was once the case. In the technique of intracytoplasmic sperm injection (ICSI), spermatozoa are harvested directly from the testis or epididymis and a single spermatozoon is selected and injected into an oocyte. The fertilised zygote is then inserted into the uterus. This technique is particularly applicable to men with obstructive azoospermia or oligospermia. Other techniques such as gamete intrafallopian transfer (GIFT) or zygote intrafallopian transfer (ZIFT) may also be applicable, depending upon the cause of infertility.

Upper urinary tract (Figure 1.3)

In the cervical portions of the paired blocks of intermediate mesoderm the primitive precursor of the kidney, the pronephros, first appears in the fourth week of gestation. This structure rapidly regresses in the human embryo. The midzone mesonephros, however, continues to differentiate, giving rise to tubular structures which, although ultimately destined to contribute to the definitive gonad, function briefly in an excretory role. In the mesenchyme lying lateral to the developing mesonephros, the mesonephric ducts appear, advancing caudally to fuse with the terminal portion of the hindgut (the primitive cloaca). Canalisation of the mesonephric ducts creates a patent excretory unit which is believed to function transiently.

At the beginning of the fifth week, the ureteric buds arise from the distal portion of the paired

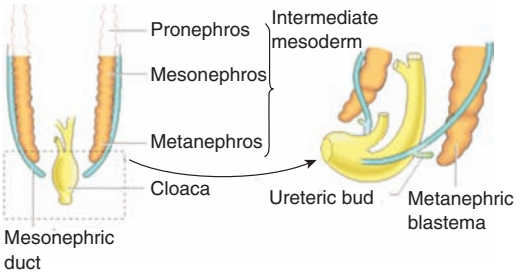

Figure 1.3 Embryonic precursors of the upper urinary tract, metanephros (kidney), ureteric bud.

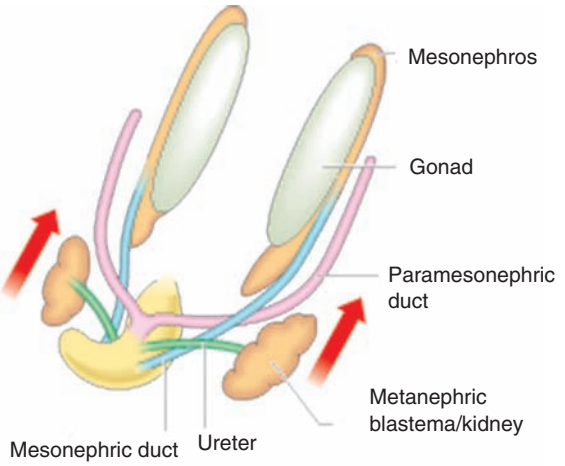

Figure 1.4 Embryonic genitourinary tract at 6–8 weeks.

mesonephric ducts and advance towards the most caudal portion of the blocks of intraembryonic mesoderm – the metanephros. Fusion of the ureteric bud and metanephric blastema at around 32 days initiates the process of nephrogenesis. Between the sixth and 10th weeks the lobulated embryonic kidneys ascend up the posterior abdominal wall, deriving their blood supply sequentially at different levels until the definitive lumbar position is achieved (Figure 1.4).

Nephrogenesis

The formation of nephrons within the developing kidney is an example of 'reciprocal induction'. The

ureteric bud derivatives give rise to the renal pelvis, major calyces, minor calyces and collecting ducts, whereas the glomeruli, convoluted tubules and loop of Henle are derived from metanephric mesenchyme. Urine production commences at around the 10th week, when continuity is established between the distal convoluted tubules and collecting ducts. Proliferation of the ureteric bud derivatives ceases at around 15 weeks, but new generations of nephrons continue to appear sequentially within the renal cortex until 36 weeks. At that time the process of nephrogenesis ceases and the number of nephrons within each kidney remains fixed for life. There is considerable variation in the number of nephrons within a normal kidney, with a median value of approximately 700 000.

Nephrogenesis is the subject of extensive research to identify the molecules responsible for cell-to-cell signalling. A large number have already been identified, including growth factors, transcription factors (DNA-binding proteins that regulate gene expression) and adhesion molecules. The rennin–angiotensin system has recently been found to play an important role in regulating early differentiation and development of the urinary tract. Two different tissue receptors are responsible for mediating the actions of angiotensin 2. Whereas stimulation of the angiotensin type 1 receptor promotes cellular proliferation and the release of growth factors, stimulation of the angiotensin type 2 receptor, which is expressed mainly in the embryo and fetus, mediates apoptosis (programmed cell death) and diminished cell growth. Differing patterns of renal malformation are observed in transgenic 'knock out' mice, depending on whether the gene encoding for the type 1 or the type 2 receptor is deleted. Targeted ablation of the uroplakin 3 gene results in a convincing experimental model of primary vesicoureteric reflux. But, whereas the wealth of information being revealed by molecular biology is advancing our understanding of inherited renal disease, experimental findings do not always translate readily into the clinical setting. For example, screening of patients with vesicoureteric reflux for mutations of the angiotensin receptor 2 gene and uroplakin 3 gene have yielded uniformly negative results.

Clinical considerations

The normal embryological development of the upper tract is heavily dependent on the role of the ureteric bud. Faulty or failed interaction between the ureteric bud and metanephric mesenchyme results in renal agenesis or differing patterns of renal dysplasia.

Renal agenesis

One or both kidneys may be congenitally absent, either as part of a syndrome or as an isolated anomaly. The origins of renal agenesis include:

- Intrinsic defect of embryonic mesenchyme. The association between unilateral renal agenesis and ipsilateral agenesis of the paramesonephric duct derivatives in girls provides evidence of a fundamental defect of mesenchymal tissue (see below).
- Failed induction of nephrogenesis.
- Involution of a multicystic dysplastic kidney. This common renal anomaly has been shown to involute both in utero and in postnatal life to mimic the findings of renal agenesis.

The empirical recurrence risk of bilateral renal agenesis is 3.5%. In contrast, unilateral renal agenesis is often a 'silent' condition and its inheritance is poorly documented.

Renal dysplasia

'Dysplasia' is a histological diagnosis in which the internal architecture is disordered and characterised by the presence of immature 'primitive' undifferentiated tubules and the inappropriate (metaplastic) presence of cartilage and fibromuscular tissue. The kidney is usually smaller than normal. Renal dysplasia results from faulty interaction between the ureteric bud and metanephric tissue, or from a major insult to the embryonic and fetal kidney, e.g. severe obstructive uropathy.

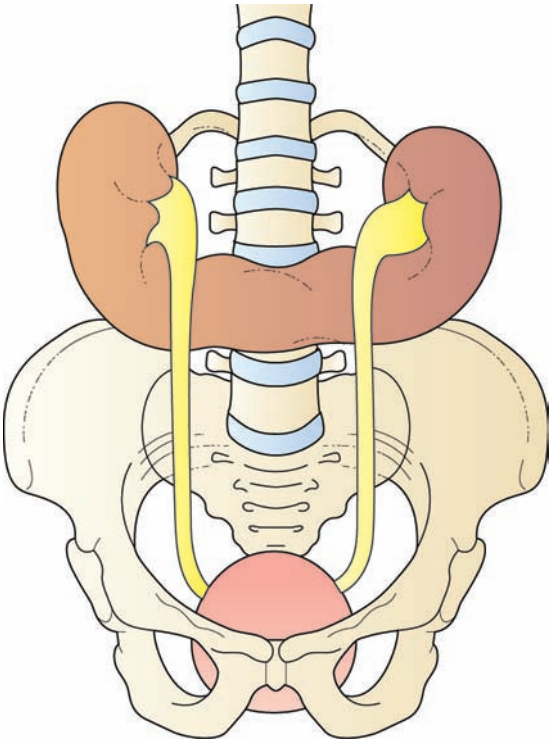

Figure 1.5 Abnormality of renal ascent and fusion – horseshoe kidney.

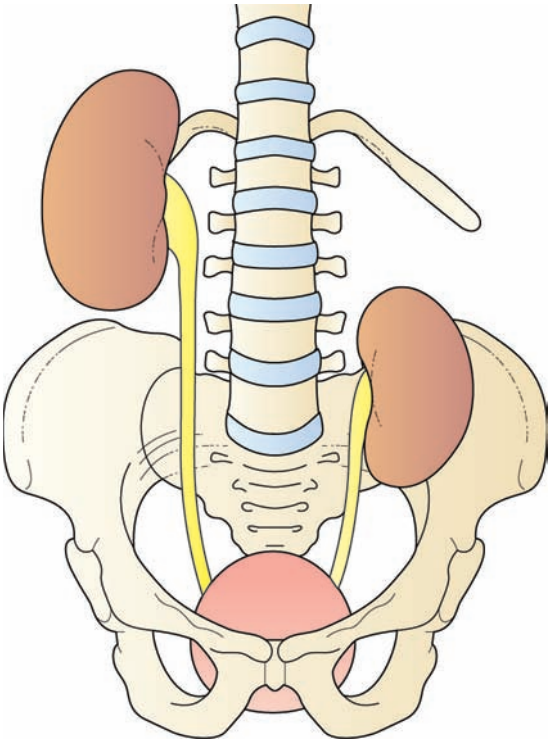

Figure 1.6 Abnormality of ascent – pelvic kidney.

Cystic anomalies

The patterns of cystic renal disease and their aetiology are considered in Chapter 9. There is some evidence to suggest that defective development of the ureteric bud is implicated in the causation of multicystic dysplastic kidney.

Abnormalities of renal ascent and fusion

This spectrum of renal anomalies including pelvic kidney, horseshoe kidney and crossed renal ectopia dates from the sixth to the ninth weeks of gestation, when the embryonic kidney is ascending to its definitive lumbar position. Horseshoe kidney has a reported autopsy incidence of 1:400 (Figure 1.5). Fusion of the lower poles of metanephric tissue interferes with the normal process of renal ascent, vascularisation and rotation. Pelvic kidney (Figure 1.6) and crossed fused renal ectopia (Figure 1.7) provide further examples of anomalies resulting from defects of ascent and fusion of the embryonic kidney.

Fetal renal function

The fetus is in effect, dialysed by the placenta, which fulfils the homeostatic excretory role of the kidney until the time of delivery. For this reason, anephric fetuses may survive until term. The fetal kidneys, however, do serve the important role of producing increasing volumes of urine, the most important constituent of amniotic fluid. By the 36th week of gestation it is estimated that fetal urine accounts for approximately 90% of the amniotic liquor. A reduction in the production of fetal urine as a result of renal damage (agenesis or dysplasia) or obstructive uropathy causes oligohydramnios and consequent moulding deformities of the fetus and pulmonary hypoplasia. Amniotic fluid in sufficient volume is an essential factor contributing to normal fetal lung development.

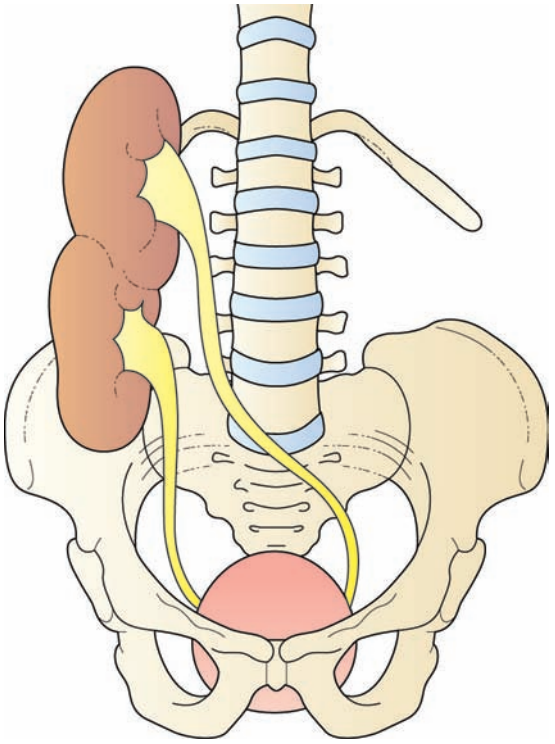

Figure 1.7 Abnormality of ascent and fusion – crossed fused renal ectopia.

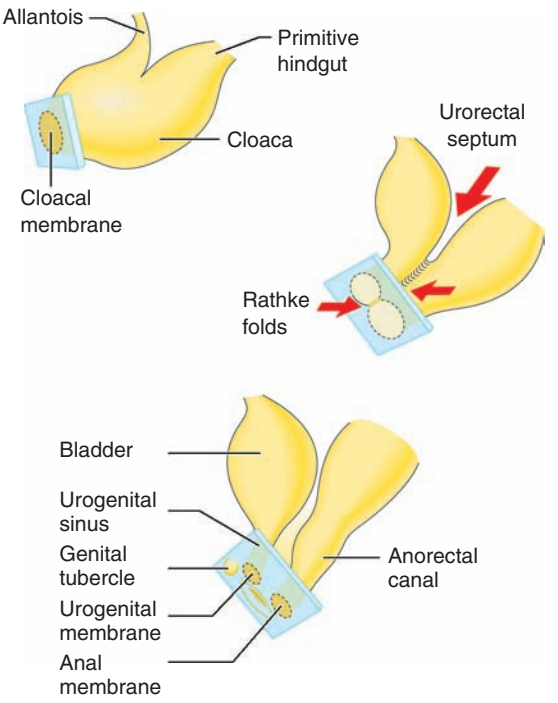

Figure 1.8 Compartmentalisation of cloaca into the urogenital compartment and anorectum by the descent of the urorectal septum – 4–6 weeks.

Lower urinary tract (Figure 1.8)

The lower urinary tract originates from the cloaca, the section of primitive hindgut into which the mesonephric ducts and embryonic ureters drain. Between the fourth and sixth weeks of gestation, the cloaca is subdivided by the descent of the urorectal septum towards the perineum and by lateral ingrowth of the folds of Rathke. The effect is to compartmentalise the cloaca into the urogenital canal anteriorly and the anorectal canal posteriorly. While the bladder is taking shape in the upper portion of the urogenital canal, the distal ureter and mesonephric duct begin to separate. The mesonephric ducts migrate caudally to join into the developing posterior urethra, whereas the ureters remain relatively fixed at their point of entry in the developing bladder (Figure 1.9). The adjacent mesenchyme of the pelvis undergoes differentiation into the detrusor, a smooth muscle component of the bladder wall, in response to induction by contact with the embryonic urothelium. In the female the urethra is derived entirely from the distal portion of the urogenital canal, whereas in the male the urogenital canal gives rise to the posterior urethra and the anterior urethra is created by the closure of the urogenital groove. The allantois protrudes from the dome of the fetal bladder like an elongated diverticulum, extending into the umbilical cord. Subsequently, the obliterated allantois persists as the median umbilical ligament. Rarely, the allantois remains patent, giving rise to a congenital umblical urinary fistula (patent urachus) or an encysted remnant.

Clinical considerations

The spectrum of cloacal anomalies encountered in clinical practice correlates closely with varying degrees of failed or incomplete descent of the urorectal septum. The embryological origins of

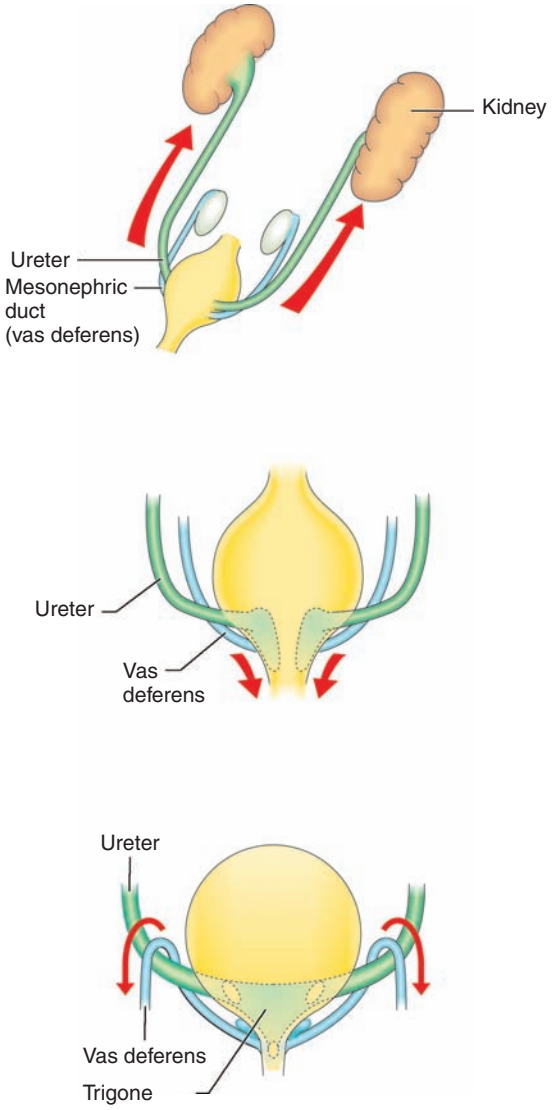

Figure 1.9 Changing anatomical relationships of ureters and mesonephric duct derivatives.

bladder exstrophy and epispadias are less readily apparent, but probably result from early defects of the cloacal membrane. Incomplete ureteric duplication results from bifurcation of the ureteric bud. Complete ureteric duplication is characterised by a pattern of ureteric anatomy in which the ureter draining the upper pole paradoxically enters the urinary tract more distally than the lower pole ureter (in some cases draining ectopically into the vagina). This anatomical configuration (described by the Meyer–Weigert law) occurs when the mesonephric duct separates from the embryonic lower pole ureter and descends towards the developing posterior urethra (with a tendency to take the upper pole ureter with it).

Genital tracts

The internal and external genitalia of both sexes are genetically 'programmed' to differentiate passively down a 'default' female pathway unless actively switched down a male pathway by the genetic information carried by the testis-determining gene (*SRY*). Until the sixth week of gestation, the genitalia of both sexes share identical embryonic precursors. Differentiation of the gonads and genital tracts is initiated by the migration of primordial germ cells from the yolk sac, across the coelomic cavity to condensations of primitive mesenchyme in the lumbar region of the embryo. By a process of reciprocal interaction, the germ cells and surrounding mesenchyme form the primitive sex cords within the embryonic gonad. At around this time (6 weeks), the paired paramesonephric ducts appear as cords of coelomic epithelium lying lateral to the mesonephric ducts. From this stage onwards, the pathways of male and female differentiation diverge.

Female

Internal genitalia (Figure 1.10)

Although the primitive sex cords degenerate, secondary sex cords derived from genital ridge mesoderm enfold the primordial germ cells to form primitive follicles. Differentiation of the genitalia down a female pathway cannot be entirely explained by the absence of the *SRY* gene. Normal development of the ovary does appear to at least be partly dependent on the presence of the two normal X chromosomes, since patients with Turner syndrome who have a single X chromosome (X karyotype) typically have poorly formed, dysgenetic ovaries.

In the female, the initial phase of gametogenesis (transition from primordial germ cell to primary

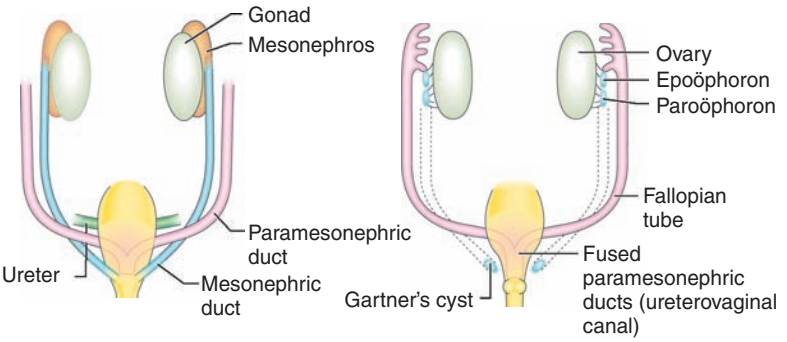

Figure 1.10 The undifferentiated genital tract is genetically programmed to proceed down the pathway of female differentiation unless switched down the male pathway by the *SRY* gene.

oocyte) occurs within the fetal ovaries. During fetal life these primary oocytes embark on the first phase of meiotic division before entering a long phase of arrested division, which resumes again only at puberty. In the absence of testosterone, the mesonephric ducts regress (leaving only vestigial remnants – the epoöphoron, paroöphoron and Gartner's cysts). The paramesonephric ducts persist in the form of the fallopian tubes. Distally, the fused portions of the paramesonephric ducts give rise to the uterus and upper two-thirds of the vagina.

At the junction of the paired paramesonephric ducts with the urogenital sinus a condensation of tissue, the sinuvaginal bulb, develops. Between the 10th and 20th weeks of gestation displacement of the sinuvaginal bulb in the direction of the fetal perineum separates the developing vagina from the urethra. During this process, canalisation of the vagina occurs. The upper two-thirds of the vagina is derived from the paramesonephric ducts, whereas the distal third has its origins in the urogenital sinus and the introitus and external genitalia are derived from ectoderm (Figure 1.11).

External genitalia

In the absence of androgenic stimulation, the external genitalia of the embryo and fetus differentiate passively down a female pathway. The genital tubercle gives rise to the clitoris, the urogenital sinus contributes the vestibule of the vagina, while the urogenital folds persist as the labia minora, and the labioscrotal folds persist as the labia majora.

Male

Internal genitalia (Figure 1.12)

Current evidence indicates that differentiation of the male genitalia is initiated by a single testis-determining gene (*SRY*) located on the Y chromosome and then mediated through other Y chromosomal and autosomal 'downstream' genes. The gene product expressed by the *SRY* gene is responsible for stimulating the medullary sex cords to differentiate into secretory pre-Sertoli cells. From the seventh week onwards these pre-Sertoli cells secrete anti-müllerian hormone (AMH) – otherwise termed müllerian inhibiting substance (MIS), a glycoprotein that plays a central role in subsequent differentiation of the male genital tract.

In the male the paramesonephric ducts disappear completely, with the exception of vestigial remnants (the appendix testis and utriculus). At least three important properties are ascribed to MIS:

1. MIS stimulates regression of the paramesonephric ducts.
2. Production of testosterone by the Leydig cells of the embryonic testis is initiated by MIS from the ninth week of gestation. During the 12th to 14th weeks of gestation the fetus is exposed to very high levels of androgenic stimulation.
3. The first stage of testicular descent is mediated by the action of MIS on the gubernaculum, which anchors the embryonic testis in the vicinity of the developing inguinal canal.

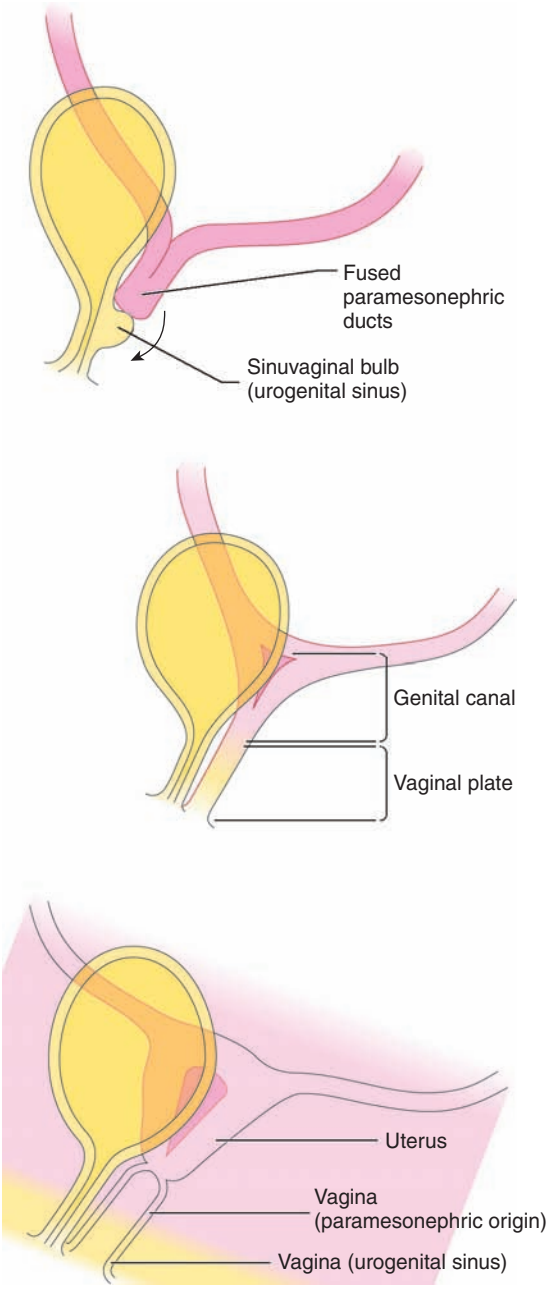

Figure 1.11 Development of the lower female genital tract between 10 and 20 weeks.

In contrast to the germ cell differentiation initiated in the female embryo, male primordial germ cells are inhibited from further division within the embryonic gonad. Although gametogenesis does not commence until after puberty the testis is not entirely quiescent in childhood since there is evidence that the fetal gonocyte germ cell pool transforms into adult type gonocytes in early childhood. The mesonephric duct derivatives differentiate between the eighth and 12th weeks of gestation to give rise to the epididymis, rete testis, vas deferens, ejaculatory ducts and seminal vesicles. This occurs in response to exposure to testosterone (probably by diffusion) from the developing testis.

The development of the prostate gland is dependent upon circulating testosterone and provides a further example of reciprocal induction. Proliferation and branching of the endodermal lining of the urethra (which gives rise to the ducts and glanular acini of the prostate gland) induces differentiation of surrounding mesenchyme to form the capsule and smooth muscle, a process that ceases after the 15th week of gestation.

External genitalia (Figure 1.13)

A number of factors are responsible for the differentiation of the male external genitalia, including the synthesis of testosterone by the fetal testis, the conversion of testosterone into dihydrotestosterone by the enzyme 5α-reductase and the presence of androgen receptors within the target cells. Androgenic stimulation of the genital tubercle results in the development of the male phallus. From the seventh week of gestation the male urogenital sinus advances on to the phallus as the urethral groove. Ingrowth of this urethral groove is associated with the appearance of urethral plate tissue destined to canalise and form the definitive male anterior urethra. Closure of the urethra is complete by around 15 weeks, with ingrowth of ectoderm from the tip of the glans forming the terminal portion of the urethra.

The testis

Tesicular descent is believed to occur in two distinct phases, the first initiated by MIS, the second being dependent upon exposure to testosterone. Experimental studies in rats have indicated that the gubernaculum plays a key role in testicular descent (although the precise mechanism may

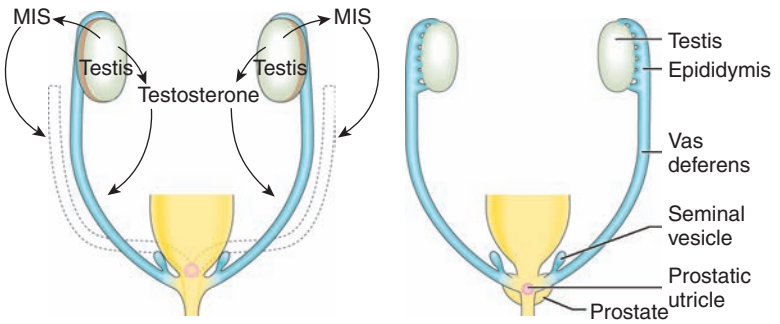

Figure 1.12 Differentiation of the male genital tract in response to müllerian inhibitory substance and testosterone.

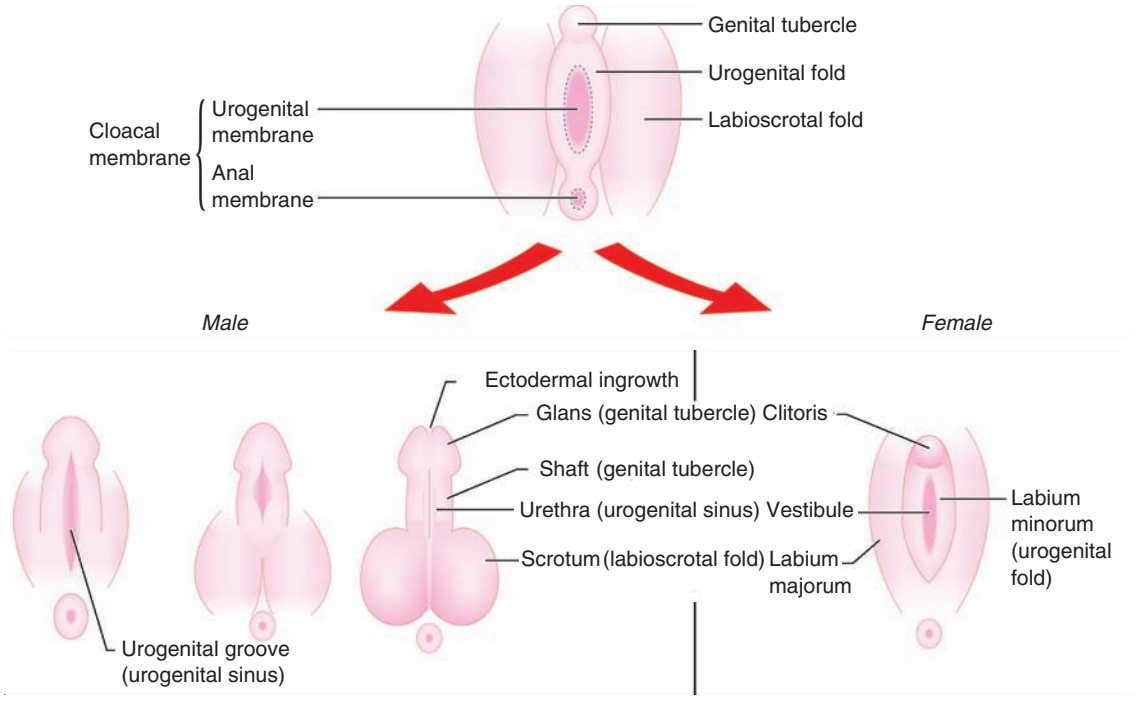

Figure 1.13 Differentiation of the external genitalia determined by androgenic stimulation.

be subject to some species variation). Extending from the testis down to the region of the labioscrotal swellings, the gubernaculum has the effect of anchoring the fetal testis in the proximity of the future inguinal canal. Under the influence of testosterone, a second more active phase of testicular descent occurs between 25 and 30 weeks, when the gubernaculum contracts in length, dragging the testis down the inguinal canal into the scrotal position it occupies at birth. During the course of its descent the testis is accompanied by a sac-like protrusion of peritoneum, the processus vaginalis.

Clinical considerations

Abnormalities of female internal genitalia

Patterns of faulty development of the paramesonephric duct derivatives include agenesis, hypoplasia, defective

canalisation and duplication. Unilateral agenesis of paramesonephric duct derivatives (absent fallopian tube, hemiuterus, etc.) may be accompanied by unilateral renal agenesis, suggesting a fundamental underlying defect of the original ipsilateral intermediate mesoderm. Agenesis of the upper two-thirds of the vagina (Rokitansky syndrome) reflects a failure of the paramesonephric ducts to fuse distally and merge with the urogenital sinus. Transverse vaginal septa and short atretic segments can be attributed to defective canalisation (Figure 1.14), whereas duplication anomalies such as bicornuate uterus represent incomplete fusion of the distal paramesonephric ducts (Figure 1.15).

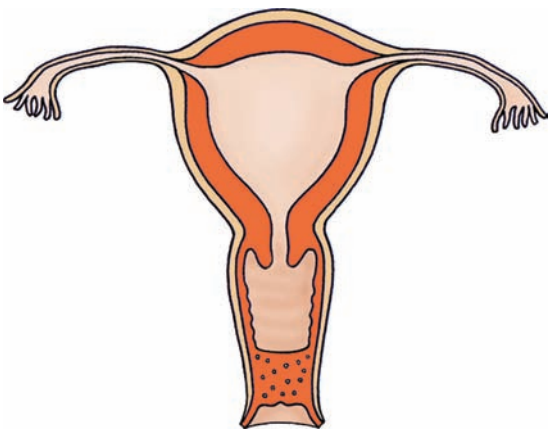

Figure 1.14 Canalisation defect – transverse vaginal septum.

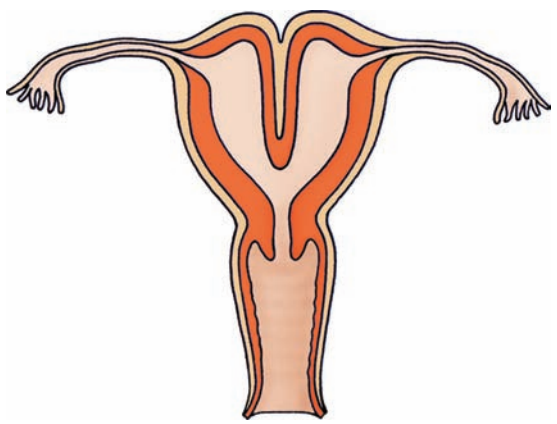

Figure 1.15 Fusion defect – bicornuate uterus.

Female external genitalia

The aetiology and classification of disorders of sexual development (DSD) are considered in more detail in Chapter 20. The most commonly encountered example in Western Europe is virilisation of the external genitalia in a female with a 46XX genotype resulting from congenital adrenal hyperplasia. In affected individuals, the internal reproductive tract differentiates normally but the external genitalia virilise in response to high levels of circulating androgens of adrenal origin.

Male internal genitalia

The rare genetically determined syndrome of MIS deficiency is characterised by bilateral undescended testes accompanied by the presence of persistent paramesonephric duct structures, including fallopian tubes and uterus. A receptor defect is responsible for approximately 50% of cases, whereas the remaining cases are genuinely attributable to a deficiency of this hormone. With the exception of the undescended testes, the external genitalia virilise normally as this is not dependent on MIS.

The persistence of a müllerian sac-like prostatic utricle is predominantly a feature of impaired virilisation and patients with proximal hypospadias or DSD account for more than 90% of cases.

In the syndrome of androgen insensitivity, the external genitalia exhibit a receptor defect to dihydrotestosterone (the derivative of testosterone active in the peripheral tissues). As a result, the external genitalia differentiate passively down the female pathway despite a male phenotype and normal male internal genitalia.

Male external genitalia

Hypospadias results from varying degrees of incomplete closure of the urethral groove (although distal glanular hypospadias may simply represent failure of ectodermal ingrowth). Severe hypospadias, particularly when accompanied by cryptorchidism and a persistent müllerian utriculus, is evidently the outcome of a generalised virilisation defect. However, although isolated endocrinopathies have

occasionally been identified in such cases, as yet no single endocrine defect has been implicated in the aetiology of hypospadias.

Similarly, there is no single unifying aetiology for cryptorchidism. Bilateral cryptorchidism is more likely to represent the influence of an endocrinopathy or imbalance of the pituitary–gonadal axis, whereas local mechanical factors (possibly related to the gubernaculum or the processus vaginalis) are likely to play a more important role in the unilateral cryptorchidism. The combination of a blind-ending vas and histological findings of calcification and haemosiderin in 'nubbins' of residual testicular tissue suggests that most cases of so-called testicular 'agenesis' result from testicular torsion in utero.

Key points

- The genitourinary tract is commonly affected in children with chromosomal abnormalities.
- The ureteric bud plays a pivotal role in nephrogenesis and the embryological development of the upper tract.
- A number of important congenital anomalies can be ascribed to defects of the ureteric bud.
- The undifferentiated genital tract of both sexes is 'programmed' to differentiate passively down a female pathway unless positively directed down a male pathway by the presence of the *SRY* gene and associated downstream genes and their products.
- Although single gene mutations have been implicated in the aetiology of some inherited genitourinary abnormalities, most of the conditions encountered in paediatric urology occur on a sporadic basis or result from the interaction of multiple genes.
- In vitro fertilisation techniques (IVF) offer the prospect of fertility to some patients whose genitourinary malformations would previously have been a bar to parenthood.

Further reading

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Renal physiology and renal failure

2

Richard Trompetor

Topics covered
Fetal and neonatal renal function
Renal impairment in infancy and childhood
Medical management
Renal replacement therapy

Renal physiology in the fetus and newborn

Introduction

Although the kidney plays a key role in enabling the newborn infant to adapt to the postnatal physiological environment, it is immature and its ability to regulate and maintain normal homeostasis is reduced, particularly in premature neonates. A variety of different pathological insults and metabolic demands can further impair the physiological function of the kidney in this age group. As a consequence, the nephrological management of neonates differs in several important respects from the management of older children.

In the later stages of pregnancy the fetus is in a state of physiological volume expansion. Amniotic fluid is swallowed, absorbed in the gastrointestinal tract and 'recycled' into the amniotic cavity via the kidneys. Fetal urine is the major constituent of amniotic fluid and production increases with gestational age from approximately 10 ml/h at 23 weeks' gestation to approximately 30 ml/h at 32 weeks' gestation and continuing at that rate until the end of pregnancy. Oligohydramnios is usually a consequence of renal dysfunction or urinary tract obstruction.

The formation of new nephrons (nephrogenesis) in humans is confined to intrauterine life and is complete by 36 weeks' gestation – although in premature infants born before 36 weeks the normal pattern of nephrogenesis continues after birth. Nephrogenesis may be affected by a number of prenatal factors, notably early urinary tract obstruction.

In the fetus, glomerular filtration rate (GFR) is proportional to body weight, but even when the fetal GFR has been corrected for body weight it remains considerably reduced, corresponding to 30–50% of the weight-corrected adult value. Creatinine is not a useful indicator of fetal renal function as it freely crosses the placental barrier – with the result that fetal plasma creatinine values mirror those in the maternal circulation. Amniotic fluid volume is a crude index of urine production and thus of fetal renal function, and measurement of electrolytes and osmolality in amniotic fluid and fetal urine can also provide a guide to fetal renal function. Normal fetal urine is characterised by a high flow rate (>5 ml/kg/h), a low osmolality and relatively low sodium concentration.

The GFR at birth correlates closely with gestational age, being approximately 5 ml/min/m^2 in premature infants born at 28 weeks' gestation and 12 ml/min/m^2 in infants born at term (40 weeks). Postnatally there is a sharp increase in GFR, which doubles by 2 weeks of age; however, it is not until 2 years of age that the corrected GFR reaches the corresponding adult-corrected value.

The low GFR in newborn infants is of considerable relevance to clinical management: e.g. in the interpretation of laboratory results and the calculation of fluid requirements and drug

dosages. This is particularly important in sick premature babies. Although the neonatal kidney can cope with most normal demands its functional reserve is limited and may be overwhelmed by some of the stresses commonly encountered in the neonatal period. Several vasoactive systems, such as the renin–angiotensin system, intrarenal adenosine, the prostaglandins and atrial natriuretic peptide, are up-regulated in the neonatal period and are important for the maintenance of GFR. Overstimulation of the renin–angiotensin system (for example by hypoxia) or inhibition of the renin–angiotensin system (by angiotensin-converting enzyme inhibitors) can both predispose to renal failure.

Water metabolism

Newborn infants are born in a state of overexpansion of extracellular water, which is inversely proportional to maturity. Following delivery, an acute isotonic volume contraction occurs with corresponding weight loss. This phenomenon, which is part of the normal physiological adaptation to extrauterine life, is most pronounced and prolonged in premature infants.

The ability of the kidney to regulate water balance is not fully developed at birth. In response to a hypotonic fluid challenge, term and preterm neonates produce urine with an osmolality of 50 and 70 mosm/kg H_2O, respectively. At this age the kidney has the capacity to increase urine flow and water clearance in response to a waterload, but this response is impaired and water excretion is prolonged. As a consequence, newborn infants are poorly equipped to cope with fluid overload and are at greater risk of dilutional hyponatraemia.

The capacity of the neonatal kidney to produce concentrated urine is also limited and, in the first week of life, the maximum urine concentrations achieved by preterm and term neonates following fluid restriction are 600 and 800 mosm/kg H_2O, respectively. This limited concentrating capacity reflects a reduced responsiveness of the immature kidney to vasopressin and an inability to maintain a corticomedullary osmotic gradient.

Sodium balance

Newborn infants have a limited capacity to conserve sodium when challenged by sodium restriction and a limited ability to excrete sodium in response to a sodium load. In the first week of life, urinary sodium excretion is high and inversely proportional to the maturity of the neonate. Premature infants have an obligatory urinary sodium loss with consequent negative sodium balance. Plasma sodium and chloride concentrations often fall to low levels and urinary sodium excretion remains high relative to plasma sodium. This imbalance is thought to be a consequence of renal immaturity rather than redistribution of sodium within body fluid compartments.

Disturbances in plasma sodium include:

1. **Early-onset hyponatraemia** (plasma sodium <130 mmol/l) occurring in the first week of life. This is due to water retention and sodium depletion.
2. **Late-onset hyponatraemia**. This is usually the result of inadequate sodium intake, renal sodium wasting and free water retention.
3. **Early-onset hypernatraemia** (plasma sodium >150 mmol/l). This is usually iatrogenic in aetiology, resulting from repeated administration of hypertonic sodium bicarbonate solution to correct acidosis in severely ill neonates.
4. **Late-onset hypernatraemia** is due to the administration of sodium supplements and inadequate free water.

The clinical consequences of excessive or inadequate sodium intake are potentially serious, and careful monitoring of sodium and water balance is essential in at-risk infants.

Potassium balance

Postnatal plasma potassium levels differ in term and preterm infants. In the term infant potassium levels fall rapidly in the first week of life (although there is considerable individual variation). In contrast, a gradual rise in the plasma level of potassium is seen

in preterm infants, reaching a maximum at about the third to fourth week of life. Elevated plasma potassium levels may be a consequence of hypoxia, metabolic acidosis, catabolic stress, oliguric renal failure and inadequate excretion by the immature distal nephron. The impaired ability of renal tubules to respond to aldosterone coupled with low ATPase activity in the potassium-secreting epithelial cells of the distal nephron contribute to impaired potassium excretion.

Acid–base balance

By comparison with adults, neonates are acidotic: this is both respiratory and metabolic in aetiology and is usually accompanied by cardiopulmonary compensation. The capacity of the newborn infant to excrete an acid load is limited but the renal threshold for bicarbonate resorption increases with advancing maturation as the renal acidification mechanisms develop. Although late-onset metabolic acidosis in premature infants is usually mild and rarely associated with clinical symptoms, more severe acidosis gives rise to poor feeding and growth impairment. Supplements may be needed to ensure that plasma bicarbonate concentration is maintained above 17 mmol/l.

Renal impairment in infancy and childhood

Introduction

A major reduction in the number of functioning nephrons as a result of congenital or acquired damage gives rise to two distinct but related pathological states: first, since damaged nephrons are incapable of repair or regeneration, renal dysfunction occurs; second, a series of secondary physiological, metabolic and hormonal changes then ensue as renal function progressively declines. Treatment is directed at decreasing the rate of progression of chronic renal failure (CRF) and addressing the sequelae of renal dysfunction. The principal consequences of untreated CRF in children are:

- growth retardation
- sexual immaturity
- psychomotor or intellectual retardation.

Treatment must be initiated early in the course of renal dysfunction and should generally increase in intensity in parallel with progression of the disease. Chronic renal failure supervenes when the GFR decreases to less than 25–30% of normal (corresponding to a plasma creatinine concentration of approximately 150–200 μmol/l) and clinical manifestations usually become apparent at this stage.

Incidence

Data from the United States and European registries indicate that the incidence of chronic renal failure is approximately 10–12 per million children in the age group 0–19 years. Since the number of children with CRF is small compared with the adult population, there are fewer centres specialising in the treatment of renal failure in this age group.

The term end-stage renal disease (ESRD) is used to describe the phase when renal dysfunction has progressed to the point where native renal function has failed and the individual becomes dependent on either dialysis or renal transplantation for survival. According to data from the North American Pediatric Renal Transplant Cooperative Study, the most common renal disease diagnoses in children aged 0–17 years undergoing transplantation were hypoplastic–dysplastic kidneys, obstructive uropathy, focal segmental glomerulosclerosis, reflux nephropathy and systemic immunological disease. Congenital renal disorders accounted for 50% of renal failure in children under the age of 5 years.

Chronic renal failure

Measurement

In adults, the progression of renal disease can be demonstrated by a significant decline from a predictable normal adult value for GFR. In children, this calculation is inherently more difficult since both absolute GFR and actual GFR

Table 2.1 Relationship between renal function at 6 months and onset of end-stage renal disease (ESRD)

Serum creatinine (μmol/l) at 6 months of age	Prognosis (predicted age of onset of end-stage renal disease)
<150	Good prognosis
150–300	ESRD 10+ years
200–350	ESRD 5–10 years
350–600	ESRD <5 years
>600	Uncertain outcome

must be adjusted for surface area during early childhood. In addition, corrected values for GFR normally increase in the first year of life. Against the background of evolving function it is more difficult to define the progression of renal impairment. Formulae based on the logarithmic value for serum creatinine concentration or reciprocal serum creatinine concentration versus time have been derived to predict the interval before dialysis or transplantation is required. However, the predictive value of these formulae is subject to the limited reliability of creatinine clearance as a measure of GFR in the later stages of deteriorating function. As a broad guide, the serum creatinine concentration at 6 months of age can be used to predict the timing of renal replacement therapy (Table 2.1).

The point at which dialysis treatment becomes necessary varies between individual children but once the serum creatinine exceeds 500 μmol/l it becomes unlikely that even the optimal medical management can avert the need for renal replacement therapy.

Growth and development

The causes of growth failure and poor intellectual development in children with CRF are multifactorial but the principal factors involved are poor nutrition, renal osteodystrophy, salt wasting, metabolic acidosis, anaemia and hormonal changes.

Malnutrition

Malnutrition in children with CRF is characterised by food refusal, anorexia, nausea and vomiting. Anorexia is common in children with CRF and may be secondary to increased levels of gastric polypeptide; in addition, an increased incidence of foregut motility disorders predispose to gastrointestinal reflux and vomiting. Growth velocity in childhood is greatest in the first year of life and thus the impact of chronic disease and malnutrition is correspondingly more severe in this age group. Early therapeutic intervention is vital in order to prevent growth failure and **indications for intervention** include:

- failure to maintain expected weight gain despite the addition of calorie supplements to the diet
- recurrent vomiting, despite the use of prokinetic medications
- parental stress.

In a significant percentage of infants, voluntary oral intake is inadequate to meet energy or volume requirements and feeding by nasogastric, nasojejunal or gastrostomy tube is necessary to ensure adequate water and dietary intake. Supplemental feeding is given either by bolus or as a continuous overnight infusion. Infants who are tube fed at night can be fed orally during the day. In those children in whom it is necessary to administer the entire diet via tube feeding it is nevertheless important to maintain oral stimulation to help them to eat normally following renal transplantation.

In infancy, the dietary protein intake can be controlled and the most appropriate food is either human milk or a humanised milk formula with a low phosphate content. At any given level of protein intake, increasing the overall energy intake will enhance the efficient utilisation of protein. Most humanised milks have a protein-to-calorie

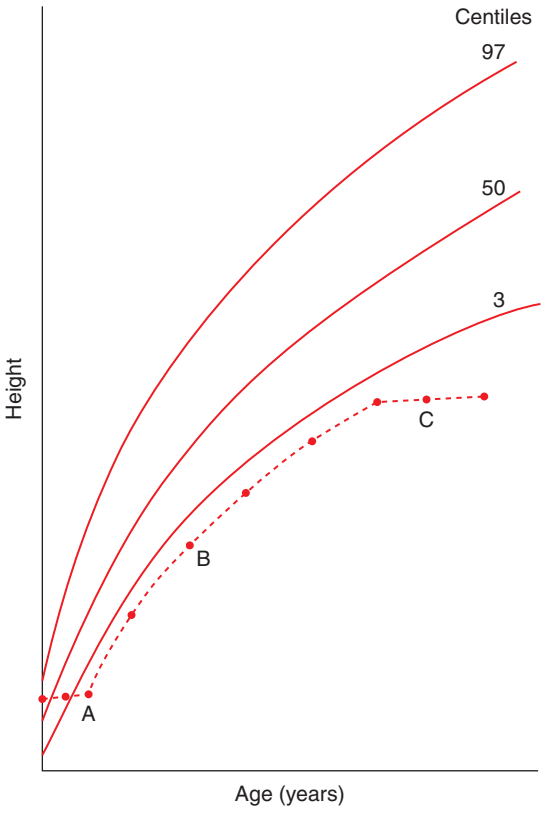


Figure 2.1 Growth pattern (height) in a child with untreated chronic renal failure. Growth maintained below the third percentile with downward deviation from the centile at puberty.

ratio of 2–3 g of protein per 100 kcal (8–12% calories as protein). Human milk has a protein-to-calorie ratio of 1.6 kcal per 100 kcal (approximately 6% calories as protein). Infant formulas containing 1.6–2 g of protein per 100 kcal are safe and meet the recommended dietary allowance (RDA) for protein intake in infancy.

Whenever possible, the serum urea level should be kept <20 mmol/l by maintaining adequate calorie intake and ensuring sufficient water is available to avoid extracellular fluid volume depletion. There is a consensus that dietary intake of carbohydrate should approximate to 100% of the RDA for the appropriate height and age. Calculated energy intake may need to be increased in children with a low weight to height ratio. Energy supplements such as polyunsaturated corn oil, complex carbohydrates or medium-chain triglycerides are widely favoured because of their high calorie density and low cost.

A typical growth pattern in infancy and childhood is illustrated in Figure 2.1. In this case growth (weight) remains below the third percentile and deviates from this percentile with the onset of puberty.

Figure 2.2 illustrates the growth pattern for both height and weight in an infant in whom nasogastric tube feeding was instituted at the age of 2 years, with resulting improvement in both weight and height. At approximately 3 years of age, overnight feeding was commenced, with further improvement in both weight and height reflected in growth lines crossing the percentiles.

Renal osteodystrophy (Figure 2.3)

Disorders of mineral metabolism in children with CRF invariably affect skeletal growth and development, with resultant bone deformities and, in most cases, deceleration of linear growth.

The crucial roles played by the kidney in bone and mineral homeostasis include:

- regulating calcium, phosphorus and magnesium metabolism
- participating in the catabolism of parathyroid hormone (PTH)
- excreting aluminium and β_2-microglobulin
- synthesizing calcitriol or 1,25-hydroxyvitamin D_3.

The primary site of vitamin D synthesis is located in the proximal nephron, where 25-hydroxyvitamin D is converted by the action of the 1α-hydroxylase enzyme to 1,25-dihydroxyvitamin D_3 (calcitriol) – its most potent and active metabolite (Figure 2.3). In renal failure, enzymatic activity decreases, leading to reduced production of calcitriol and the development of secondary hyperparathyroidism. In addition, urinary excretion of aluminium and

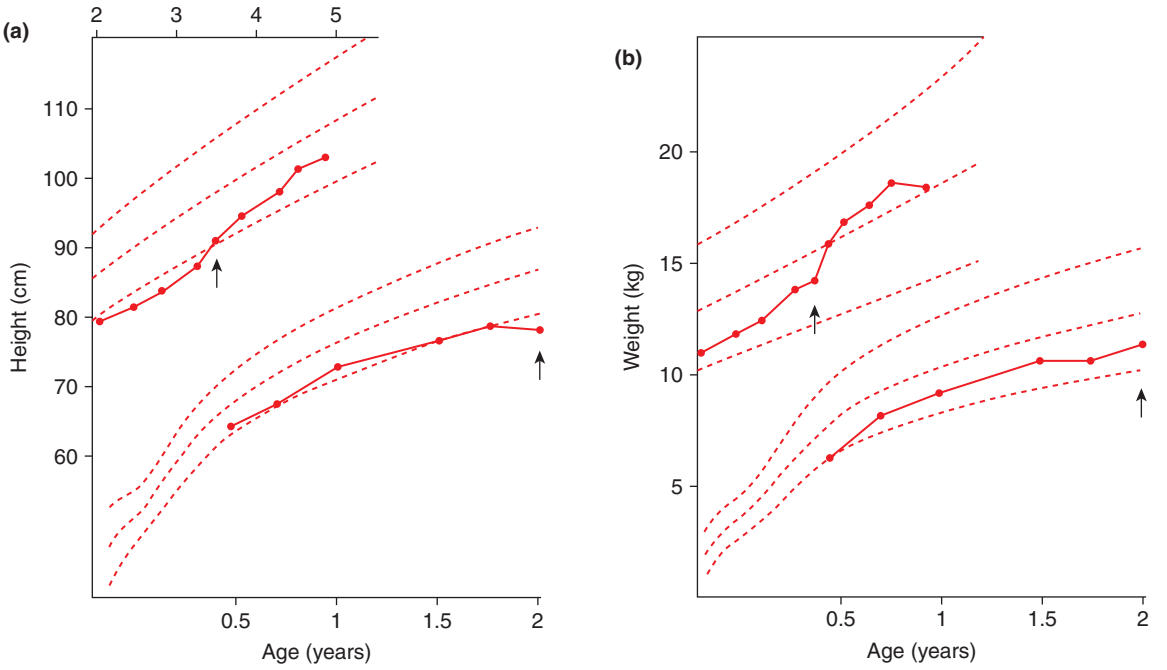


Figure 2.2 (a) Impact on growth (height) with the introduction of nasogastric enteral feeding in a 2-year-old child with CRF. (b) Improved weight gain following introduction of nasogastric feeding in the same child.

β_2-microglobulin is impaired and may contribute to certain forms of renal osteodystrophy.

Secondary hyperparathyroidism

This common feature of ESRD has a number of contributory factors:

- phosphate retention
- hypocalcaemia
- impaired calcitriol synthesis
- alterations in secretion of PTH and reduced sensitivity of the skeleton to the calcaemic actions of PTH.

Clinical manifestations

Osteodystrophy can present with non-specific signs and symptoms or may go unnoticed. A reduction in physical activity can be a subtle early symptom and it is important to be aware that radiographic changes are not always a reliable guide to the severity of the underlying bone disease.

Approximately 30–50% of children with CRF exhibit short stature and in 60% of children receiving regular dialysis treatment growth velocity is below the normal range. In early renal osteodystrophy bone pain is non-specific, but as the disease progresses pain may be localised to the lower back and weight-bearing joints in ambulatory patients. The onset of a limp should be thoroughly evaluated because of the prevalence of slipped femoral epiphysis; indeed, all epiphyses can be affected and fractures can occur.

Skeletal deformity is a significant feature of long-standing untreated CRF in children, with the patterns of deformity being age-related. In younger children skeletal abnormalities are similar to those due to vitamin D-deficient rickets, i.e. rachitic rosary, metaphyseal widening at the wrist and ankle, craniotabes and frontal bossing. In older

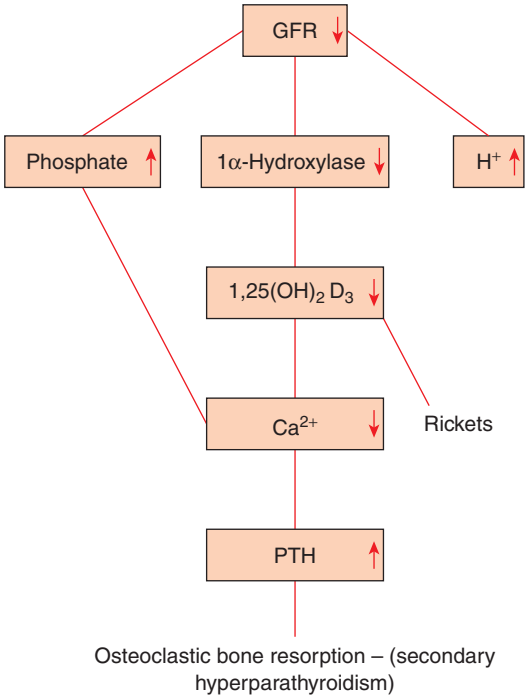


Figure 2.3 Pathogenesis of renal osteodystrophy.

children deformities of the long bones are more evident, particularly affecting the lower extremities, i.e. valgus and varus deformity of the knee.

Muscle weakness and a waddling gait are characteristic of the myopathy associated with CRF and resemble the proximal muscle weakness seen in patients with vitamin D deficiency. Although soft tissue calcification is seen more frequently in adults, it can also occur in children with ESRD: the most commonly affected sites are blood vessels, lung, kidney, myocardium, central nervous system and gastric mucosa. The aetiology of soft tissue calcification is usually a high serum calcium–phosphate product resulting from poor control of secondary hyperparathyroidism.

The principal radiographic features of renal osteodystrophy relate to increased bone resorption, typically at the subperiosteal or endosteal surfaces of cortical bones. The extent of bone resorption correlates with parathyroid hormone levels and the sites involved characteristically include the distal ends of the clavicles, ischial and pubic surfaces, sacroiliac joints, junction of the metaphysis and diaphysis of long bones, and the phalanges. The radiological appearances are characterised by a diffuse 'ground-glass' appearance, generalised mottling and focal lucent or sclerotic areas.

Treatment of osteodystrophy

Even in the earliest phase of chronic renal insufficiency, i.e. a GFR of 50–80 ml/min/1.73 m^2, some patients have a raised level of parathyroid hormone, and if untreated the severity of secondary hyperparathyroidism worsens as renal function further declines.

Dietary manipulation

When the GFR falls to less than 30 ml/min/1.73 m^2 phosphate excretion decreases and it is necessary to restrict dietary phosphate intake. Phosphorus is present in nearly all foods and its highest concentration is in meat and dairy products. The average dietary phosphate intake is between 900 and 1500 mg per 24 hours, of which approximately 50% is absorbed. Restriction to below 800 mg in 24 hours is desirable, but such a diet may become unpalatable, with implications for long-term compliance; the use of phosphate-binding agents then plays an integral role in management.

Phosphate-binding agents

Calcium-containing salts such as calcium carbonate and calcium acetate are currently the major phosphate-binding agents used for limiting intestinal phosphate absorption. Calcium carbonate is the most widely used calcium salt as it is inexpensive, well tolerated and contains 40% elemental calcium. The dosage of calcium carbonate is matched to dietary intake and should be taken with or immediately after food. Hypercalcaemia is the most important complication associated with long-term use.

Vitamin D therapy

Vitamin D replacement is indicated in patients with chronic renal failure. A number of vitamin D

sterols have been used to control secondary hyperparathyroidism, including dihydrotachysterol, 25-hydroxyvitamin D_3, 1α-hydroxyvitamin D_3 and 1,25-dihydroxyvitamin D_3. Of these, 1α-hydroxyvitamin D_3 is the most widely used vitamin D analogue and, at a daily dosage of 0.02–0.1 μg/kg/day, it is both safe and effective. Hypercalcaemia is the main side effect, but calcium levels will fall in response to a temporary reduction or cessation of therapy.

Assessment of therapy

Serial measurements of total serum calcium, ionised calcium, phosphate and intact PTH levels are important in assessing the efficacy of dietary and therapeutic intervention. Calcium and phosphate levels should be maintained within normal ranges for age (total calcium 2.41–2.77 mmol/l; ionised calcium 1.16–1.45 mmol/l; phosphate 1.2–2.1 mmol/l), whereas intact PTH levels should be below 6.0 pmol/l.

Sodium chloride and bicarbonate

Obligatory urinary salt loss is a common feature of chronic renal failure in infants with structural abnormalities of the urinary tract – notably renal dysplasia (with or without posterior urethral valves). Since the sodium concentration of most infant formula feeds is low, affected infants are frequently in negative sodium balance and salt and sodium bicarbonate supplementation is therefore required to maintain adequate extracellular fluid volume and prevent metabolic acidosis. Sodium chloride is added to the feed or diet until the serum sodium concentration rises to 135–140 mmol/l. Up to 5 mmol/kg body weight per day may be required and the level of supplementation is decreased if oedema or hypertension supervenes.

Treatment of anaemia

The availability of recombinant human erythropoietin (r-Hu EPO) has proved a major advance in the treatment of anaemia associated with CRF or ESRD in children. The benefits include:

- correction of the anaemia of renal failure, improvement in tissue oxygenation, exercise tolerance and haemostatic activity
- improved myocardial function resulting from reduction in the ventricular hypertrophy associated with anaemia
- reduced risk of developing HLA antibodies by obviating the need for blood transfusion.

Subcutaneous administration is practical for predialysis patients and for those on peritoneal dialysis, whereas the intravenous route is used to administer erythropoietin to patients on haemodialysis. Most children require between 100 and 200 international units per kg body weight per week and it is often necessary to prescribe iron in conjunction with r-Hu EPO to treat the functional iron deficiency. The target haemoglobin concentration should be 10.5–12.5 g/dl (9.5–11.5 g/dl for children <6 months).

Treatment of growth failure

Even with assiduous control of nutrition, bone disease, anaemia, salt wasting and acidosis, the majority of children probably do not achieve their genetic growth potential. Recombinant human growth hormone is effective in improving growth velocity both before and after renal transplantation.

Renal replacement therapy

A detailed review of chronic dialysis and renal transplantation in children is beyond the scope of this chapter. As a modality of long-term treatment, **peritoneal dialysis (PD)** is extremely successful in children of all ages, including very small infants. Continuous cycling peritoneal dialysis (CCPD) utilising an automated cycler overnight has become the system of choice, allowing relative freedom from therapy during the day (Figure 2.4).

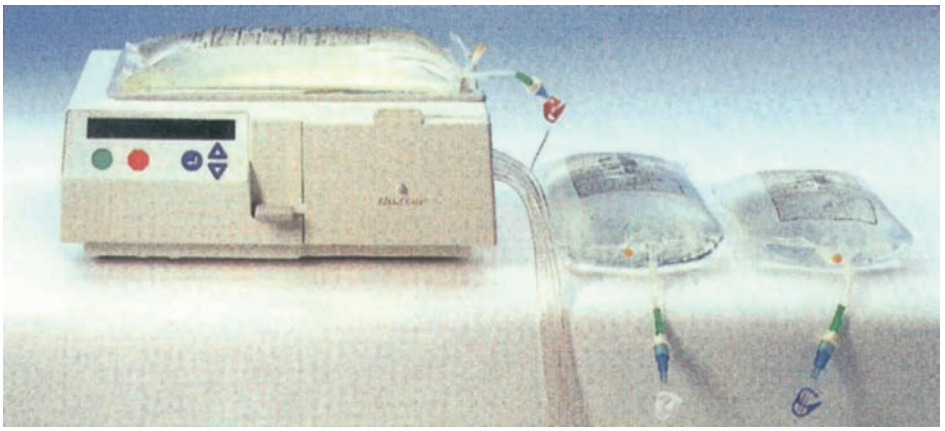


Figure 2.4 Compact peritoneal dialysis machine for automated overnight home dialysis.

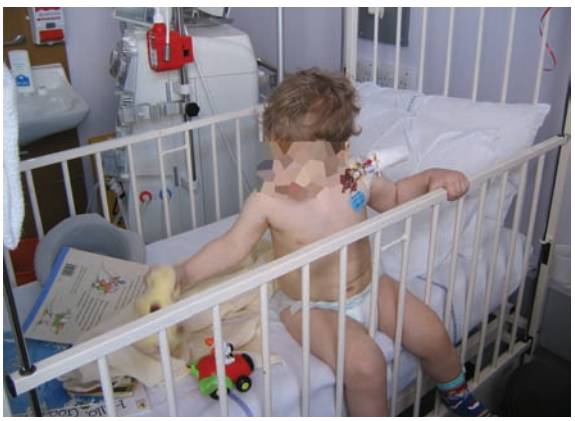


Figure 2.5 Haemodialysis via a subclavian vascular access catheter.

Continuous ambulatory peritoneal dialysis (CAPD) using a portable or wearable system is also widely used and is not dependent on access to machines.

A reliable peritoneal catheter is the cornerstone of successful PD and this should be inserted by a surgeon who has expertise in this area of work. Evidence is emerging to indicate that the complication rate is lower when a laparoscopic technique is used for dialysis catheter insertion. Exemplary PD technique and attention to detail are necessary if complications such as peritonitis are to be avoided.

Chronic haemodialysis may be required while a patient is being assessed for peritoneal dialysis, or when it has been necessary to abandon PD following repeated infections or a loss of ultrafiltration capacity. Chronic haemodialysis is not the long-term management of choice since it invariably relies on access to a dialysis centre and the services of highly skilled nursing and support staff. This form of dialysis is dependent on adequate vascular access such as internal jugular catheters or an arteriovenous fistula (Figure 2.5). Haemodialysis treatment is performed intermittently and its effectiveness is therefore transient.

Renal transplantation is the treatment of choice for any child with ESRD. Successful transplantation overcomes the problems of providing adequate nutrition, corrects renal osteodystrophy, improves growth and avoids the frequently disfiguring operations associated with dialysis access.

Outcome data from both single-centre studies and large registries demonstrate that the outlook for successful transplantation is continuing to improve and recipient age at the time of transplantation no longer has a negative effect on outcome. The overall relative risk of death, however, is approximately 13 times higher than that of the age-related population of children in the UK. Over the past three decades, there has been a steady increase in living donor recipients, which can account for up to 60% of transplants in some paediatric centres, with parents representing over

80% of living donors. In order to obviate the need for dialysis, pre-emptive renal transplantation is recommended whenever possible, thus optimising the potential for growth and neurodevelopment. Increasingly, laparoscopic living related organ donation is practised and data from single-centre studies would indicate that this method of harvesting does not have a negative effect on outcome.

Patient survival exceeds 95% at 5 years and beyond. The most common cause of graft loss is chronic rejection (40%), with other causes, including acute rejection, renal vascular thrombosis, recurrence of primary disease and poor compliance with medication, each accounting for less than 10%. Figures for graft survival indicate that graft retention has improved over the last decade. For living related recipients the current figure is 85% graft survival at 5 years, and 75% graft survival at 5 years for kidneys derived from deceased donors. Causes of death following transplantation in children are infection (25%), cardiovascular events, haemorrhage (25%) and malignancy (8%). There has been a changing trend in immunosuppressive treatment in childhood renal transplantation over the past two decades, with the use of less corticosteroid therapy, a switch from ciclosporin A to tacrolimus as the calcineurin inhibitor of choice and an increasing use of monoclonal antibodies that prevent T-cell proliferation.

The care of infants and children with CRF/ESRD and their families is complex and dependent upon a multidisciplinary approach utilising the skills of doctors, nursing staff, dieticians, teachers, psychologists and social workers. Although it is now technically possible to treat CRF/ESRD in an infant or child of virtually any age or size, the parental expectation of such treatment must be explored before embarking upon a course of lifelong therapy. After careful consideration, some parents of small infants with very severe renal pathology may opt for non-treatment in view of the profound impact of CRF/ESRD and its treatment on the quality of life of affected children.

Key points

- The immature kidney has limited capacity to respond to physiological stress. Careful management of fluid and electrolyte balance is important in sick or compromised infants.
- Chronic renal failure in children is rare. Its management is complex and demands the expertise and resources of a skilled multiprofessional team.
- Renal transplantation is the treatment of choice for end-stage renal disease in children.
- Chronic renal failure and its treatment carries major implications for quality of life and in some situations parents may take the ethically justifiable decision not to initiate treatment.

Further reading

Barratt TM, Avnel ED, Harmon WE (eds). Paediatric Nephrology, 4th edn. Baltimore: Lippincott Williams and Wilkins, 1999

Kher KK, Makker SP, Schnaper HW (eds). Clinical Pediatric Nephrology, 2nd edn. London: Martin Dunitz, 2006

Diagnostic imaging 3

Melanie P Hiorns

Topics covered

Diagnostic imaging
- Ultrasound or ultrasonography (US)
- Micturating cystourethrography (MCUG)
- Alternative methods of cystography (DIC and IRC)
- DMSA scintigraphy
- Dynamic diuresis renography (MAG3 and DTPA)
- Cross-sectional imaging: magnetic resonance imaging (MRI) and computed tomography (CT)
- Intravenous urography or urogram (IVU)
- Abdominal X-ray (AXR)

Interventional techniques

Introduction

Imaging departments make a crucial contribution both to the diagnosis of urological conditions and to their treatment – in the form of interventional radiology. The child's age and ability to cooperate are important considerations when determining the choice of investigations. These factors also dictate the possible need for sedation or general anaesthesia. Many departments now offer dedicated child-friendly facilities and play therapists whose involvement can be invaluable in alleviating the distress of children undergoing the more invasive investigations. Imaging of the urinary tract provides information on anatomy, function, or frequently, both. In most instances a combination of imaging modalities will be required to provide the information needed to plan the most appropriate form of management. The most commonly used imaging tests are ultrasound (US), dimercaptosuccinic acid (DMSA) scintigraphy, mercaptoacetyltriglycine (MAG3) dynamic diuresis renography with or without cystography and micturating cystourethrography (MCUG).

Magnetic resonance imaging (MRI) is also being used increasingly to provide both morphological and functional information. Computed tomography (CT) may occasionally be used in children, but in the majority of cases the clinical question can be answered by the modalities listed above without the need for ionising radiation. For this reason, CT should never be employed as the first-line investigation.

Although the plain abdominal X-ray (AXR) still has role to play when looking for calcification and for underlying skeletal abnormalities, it is now used on a very selective basis. Similarly, the intravenous urogram (IVU) is now performed only infrequently.

Interventional radiological techniques are being increasingly used as an alternative to open surgery for procedures such as drainage and stenting, removal of calculi and percutaneous guided tumour biopsy.

Ultrasound and Doppler

Ultrasound is almost invariably the investigation of first choice for suspected urinary tract pathology in children. The **advantages** include:

- no exposure to ionising radiation
- low cost
- non-invasive and painless
- excellent anatomical resolution, due to the lower amount of fat present in children, and their small body habitus
- high sensitivity for the detection of renal stones, cysts and for conditions causing dilatation.

The **limitations of ultrasound** include:

- observer dependence
- poor sensitivity in the detection of renal scarring
- limited anatomical delineation of complex malformations
- lack of functional information
- poor visualisation of pathology in non-dilated ureters.

Scanning technique

Scanning should be performed with a full bladder to facilitate visualisation of any dilatation of the distal ureter and to identify intravesical lesions such as ureteroceles.

Since a degree of upper tract dilatation may result solely from an overfull bladder, the kidneys should be rescanned following voiding.

Doppler ultrasound to assess perfusion is also performed if there are concerns regarding renal blood flow: for example, in renal artery stenosis, arteriovenous malformations, hypertension and transplant kidneys.

Measurements in the lower urinary tract

A bladder wall thickness of up to 3 mm is considered normal. Thickening of the bladder wall, if associated with significant residual volume, is suggestive of bladder outflow obstruction. Other causes of bladder wall thickening include inflammation and infiltration.

A significant residual volume of urine is defined as one exceeding 10% of age-adjusted expected capacity.

The bladder volume is either calculated automatically using the software provided, or as follows:

- In children under 2 years of age, bladder volume (ml) = 0.49 × depth × height × width (cm) + 3.
- In older children, bladder volume (ml) = depth × height × width (cm) × 0.9.

These formulae cannot be applied to patients with an irregular bladder or those who have undergone bladder augmentation.

Assessment of the upper urinary tract

Measurements of renal length are obtained with the child supine and values compared with published age-adjusted data. Renal echogenicity is assessed by comparison with an adjacent organ, typically the spleen or liver. The kidneys are often hyperechoic compared to the liver in the first few months of life or in premature infants, but then revert to being hypoechoic. End-stage kidneys are also echo-bright and lose their normal internal architecture.

It is very important to note that reflux cannot be reliably detected or assessed by conventional ultrasound and that additional investigations will be required if reflux is suspected.

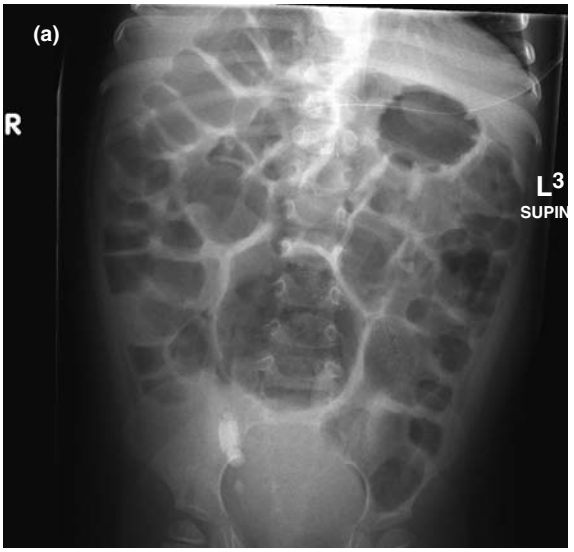
Indications

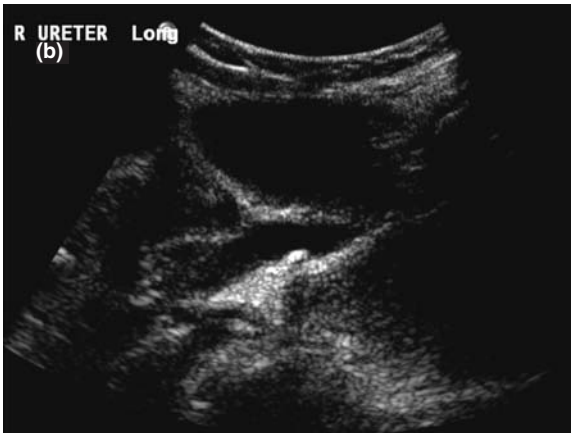
The most common indications for renal ultrasound include the investigation of **congenital abnormalities** (including antenatally diagnosed hydronephrosis), urinary tract infection, stone disease (Figure 3.1) or nephrocalcinosis (Figure 3.2).

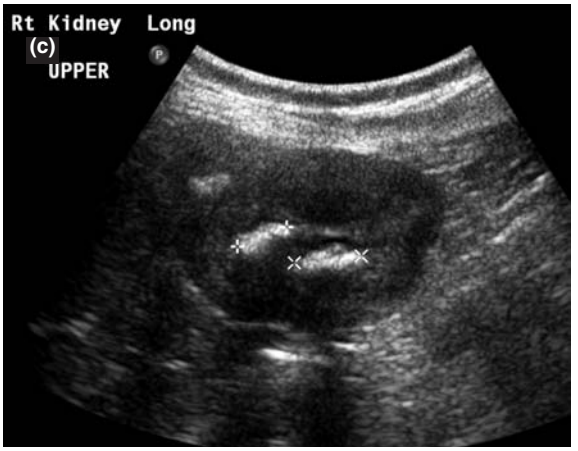
An anterior–posterior (AP) renal pelvis measurement of up to 7 mm is considered normal, whereas 7–10 mm is equivocal and over 10 mm abnormal (although not necessarily indicative of pathology).

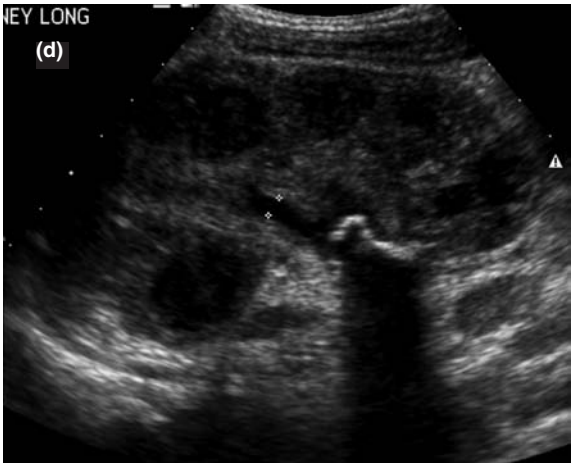
Urinary tract infection (UTI) is a common reason for referral for US and in the acute phase may confirm the presence of an obstructed or dilated system and/or the presence of calculi or debris within it. Ultrasound may also demonstrate evidence of focal pyelonephritis within the renal parenchyma. Although US is capable of detecting renal scars, it is considerably less sensitive than DMSA for this purpose.

Calculi as small as 1–2 mm can be visualised in the renal pelvis or upper ureter but the mid-ureter is difficult to examine by US due to overlying bowel gas and bowel contents. A stone at the vesicoureteric junction may also be demonstrated if the patient has a full bladder, allowing visualisation of this area. US is more sensitive than plain radiography in the assessment of calculi in the kidney. It is the first examination in the suspected diagnosis of









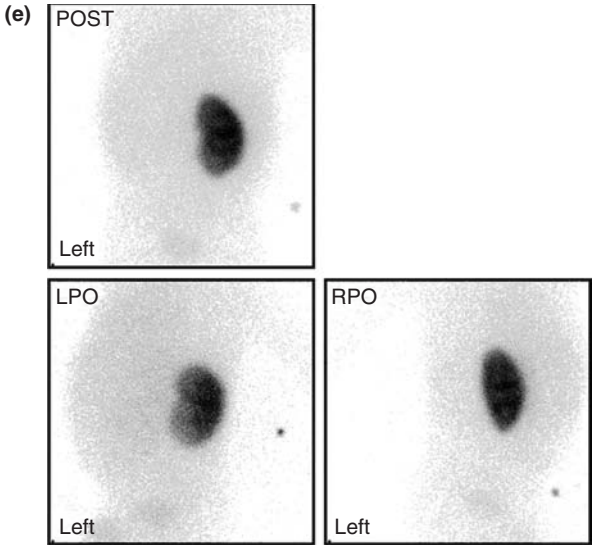
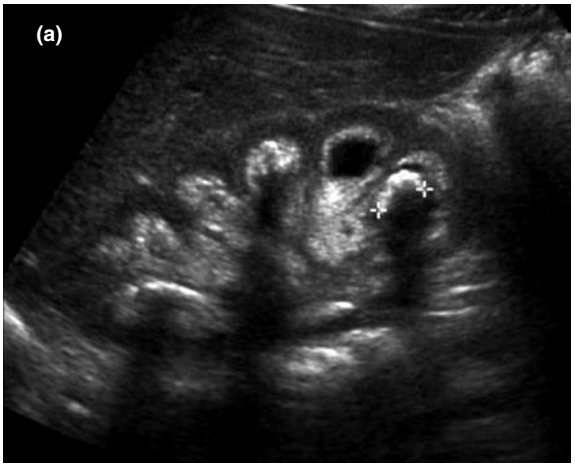
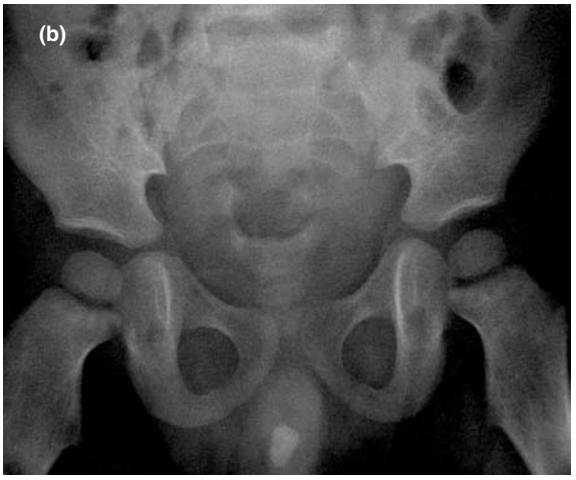
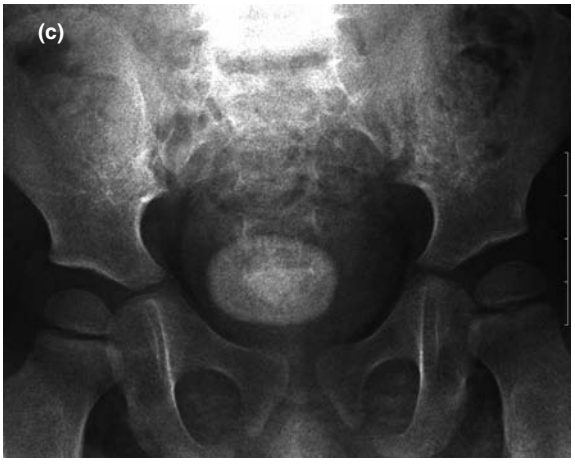
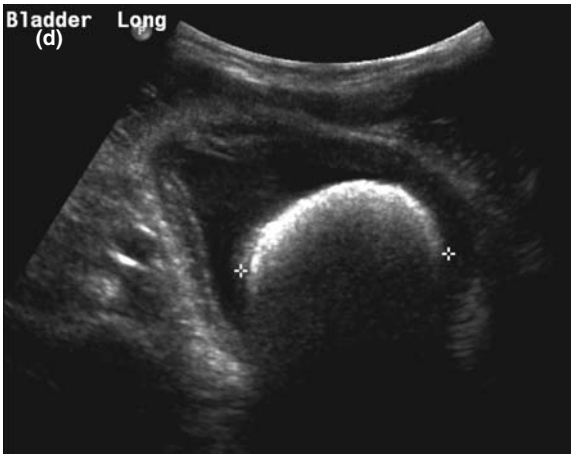


Figure 3.1 Urinary calculi. (a) Abdominal X-ray shows stones in the right ureter. (b) Ultrasound (US) demonstrating the same stones in the lower ureter by US. (c) Further calculi are shown in the kidney with characteristic acoustic shadowing. (d) US in a different patient showing a staghorn calculus and (e) DMSA demonstrating complete loss of function in the affected kidney.









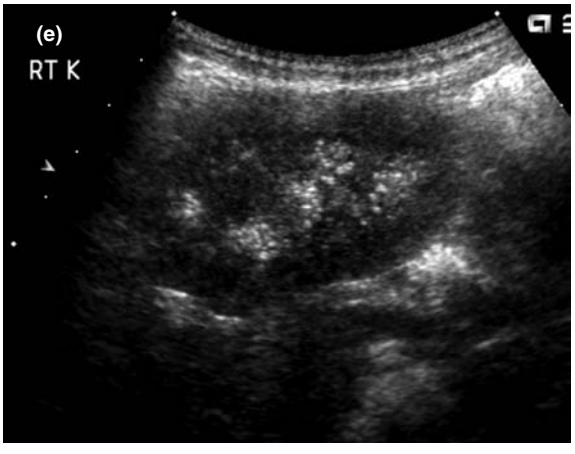


Figure 3.2 Other examples of calcification in the urinary tract. (a) Ultrasound (US) showing nephrocalcinosis and calculi occurring together in the same kidney. The nephrocalcinosis shows the typical arching calcification around the renal pyramids and the stone casts an acoustic shadow. (b) Calculus in the urethra demonstrated on plain X-ray. (c) Bladder stone on abdominal X-ray. (d) US appearances of the same stone. (e) US in a different patient showing the specks of echogenicity in medullary calcinosis.

renal calculi in children; however, if the findings are inconclusive, it may still be appropriate to progress to other forms of imaging such as CT.

US provides valuable anatomical information on a range of anatomical abnormalities such as **upper tract duplication** (Figure 3.3) but additional imaging (e.g. DMSA, MRI) is generally required if surgical intervention is envisaged.

Renal cystic disease is optimally imaged by US but it is important for the operator to accurately distinguish true cystic disease from hydronephrosis (Figures 3.4 and 3.5).

US plays a role in the investigation of some urethral abnormalities, including syringocele, posterior urethral valves or stone disease, but full assessment invariably requires a micturating cystogram.

US is generally the initial modality used to assess an **abdominal or pelvic mass**, or a mass arising within the kidney, yielding information which typically includes the organ of origin, the presence of solid or cystic components and the presence of calcification. Ultrasound may also detect **metastases** in other solid abdominal organs such as the liver. In the case of suspected renal tumours it also permits evaluation of the contralateral kidney, the integrity of the capsule of the affected kidney and the presence or absence of tumour extension within the renal vein or the inferior vena cava (IVC).

Finally, US plays an important role in the initial imaging of **renal trauma**, yielding information on the integrity of the kidney and the renal capsule and the presence of haematoma. It can also provide some information on renal blood flow and perfusion (Figure 3.6).

Doppler ultrasonography

In addition to their use in renal trauma, Doppler studies of the renal artery or vein are used for the assessment of tumour extension within the renal vein or IVC, in suspected renal vein thrombosis and in the investigation of hypertension.

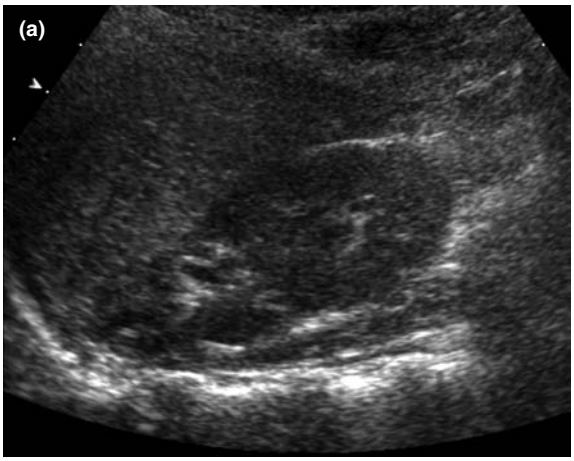
Micturating cystourethrography (voiding cystourethrography)

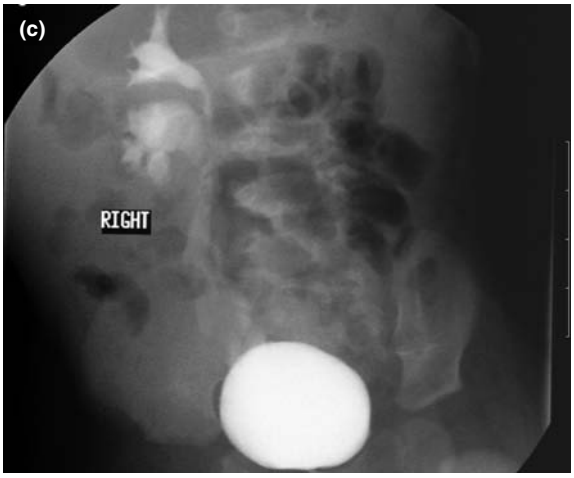
The MCUG, also known as a voiding cystourethrogram (VCUG), remains a key investigation in the examination of the bladder and the urethra for anatomical abnormalities (Figure 3.7). MCUG is indicated in male infants with bilateral hydronephrosis to look for urethral obstruction. It should also be performed in any child with a thickened bladder wall, poor stream and incomplete emptying in whom there is a need to exclude a urethral abnormality or other cause of outflow obstruction.

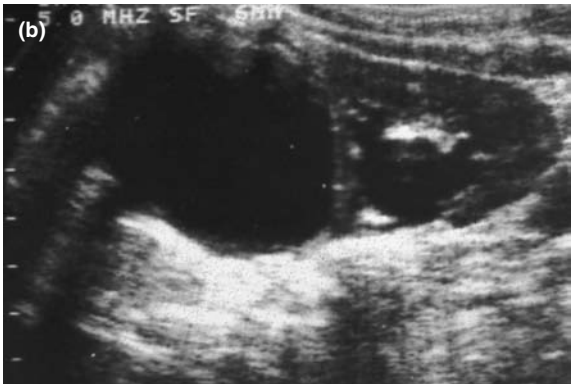
Urethral trauma is still most commonly examined by MCUG, although this may be supplemented by a retrograde urethrogram in male patients. The MCUG also retains a central role in the diagnosis and assessment of vesicoureteric reflux, albeit on a more selective basis than in the past (see Chapter 5).

Technique

The procedure should be covered by the administration of a prophylactic antibiotic and should ideally be delayed for 4–6 weeks after any acute infective episode has been treated. The child is positioned on the fluoroscopy table and, using a sterile technique, a small-calibre (6F) catheter is passed per urethra and water-soluble contrast media is introduced. Steep oblique or true lateral views are needed to demonstrate posterior urethral valves and ectopically inserted ureters while early filling views are best for visualising ureteroceles (Figure 3.8). One of the principal drawbacks of MCUG is the burden of ionising radiation, although this can be substantially reduced by using 'grabbed' digital images and by removing the grid on the imaging intensifier. Although MCUG is still considered the gold standard technique for demonstrating reflux it is important to note that reflux may occur intermittently throughout the course of an examination or may be seen on one occasion but not on another. It







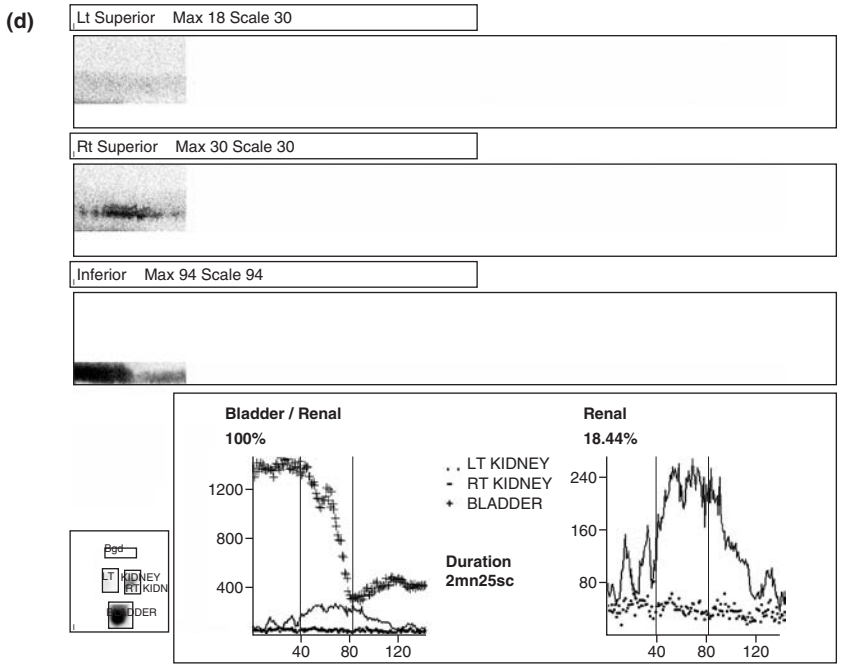
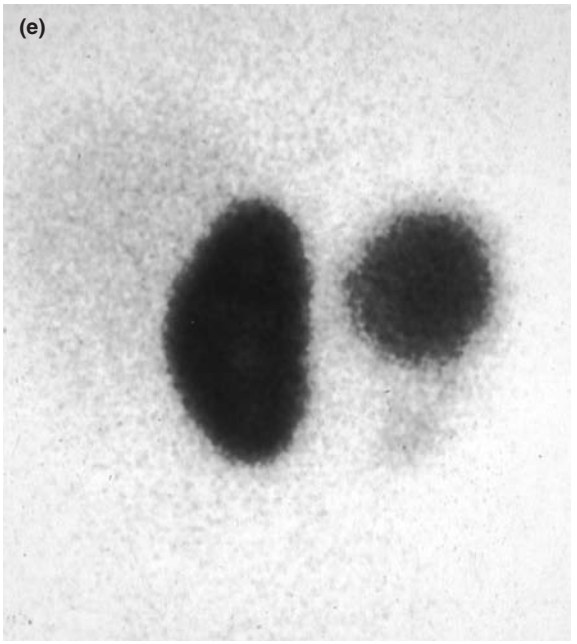


Figure 3.3 (Continued)



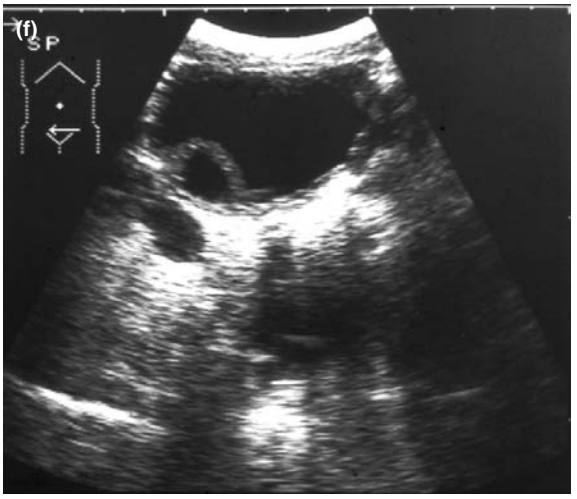


Figure 3.3 Imaging of duplex kidneys in different patients. (a) Ultrasound (US) showing a scarred upper pole in the right upper moiety. (b) US in another patient demonstrating marked dilatation of the upper pole due to distal ureteric obstruction by a ureterocele and moderate lower pole dilatation associated with lower pole reflux. (c) MCUG in a different patient showing reflux into both the upper and lower moiety on the right. (d) Reflux demonstrated in the same patient by indirect MAG3 cystogram showing an increase over the right kidney during voiding. (e) DMSA scan in another patient demonstrating near total loss of function in the lower pole of duplex kidney due to scarring/dysplasia. (f) Dilated distal ureter and associated ureterocele visualised on US.

is important to recognise that the possibility of reflux cannot be entirely discounted by a single negative MCUG.

Isotope cystography

Direct radionuclide cystography

Direct radionuclide cystography (DIC) is a sensitive test for reflux and carries a lower radiation dose than MCUG. However, it still entails a requirement for urethral catheterisation to permit instillation of the radionuclide, technetium-99m (^{99m}Tc) (20 MBq). Unlike the contrast MCUG, it provides no anatomical information and does not permit grading of severity. For these reasons its use is limited and largely confined to follow-up.

Indirect MAG3 renocystography

Indirect MAG3 renocystography (IRC) avoids the need for urethral catheterisation since the MAG3 radionuclide is injected intravenously. In essence, it follows the same pattern as a conventional dynamic renogram, with extended imaging in an area of interest over the ureter and bladder. The principal limitation is the low sensitivity for the detection of lower grades of vesicoureteric reflux. The examination is also unreliable in the presence of dilated upper urinary tracts since in this situation it becomes impossible to determine how much isotope has been retained in the collecting system as a consequence of stasis/hydronephrosis and how much has returned to the kidney because of reflux from the bladder. Adequate hydration is crucial for a good-quality examination and visualisation of reflux is generally limited to the resting and voiding phases of bladder function. Since this technique is limited to cooperative potty-trained children, its use lies mainly in excluding clinically significant reflux in older girls with UTIs, and for the follow-up of known reflux.

DMSA scintigraphy (static renography)

Technetium-99m DMSA binds to the proximal convoluted tubules, with only 10% of the injected

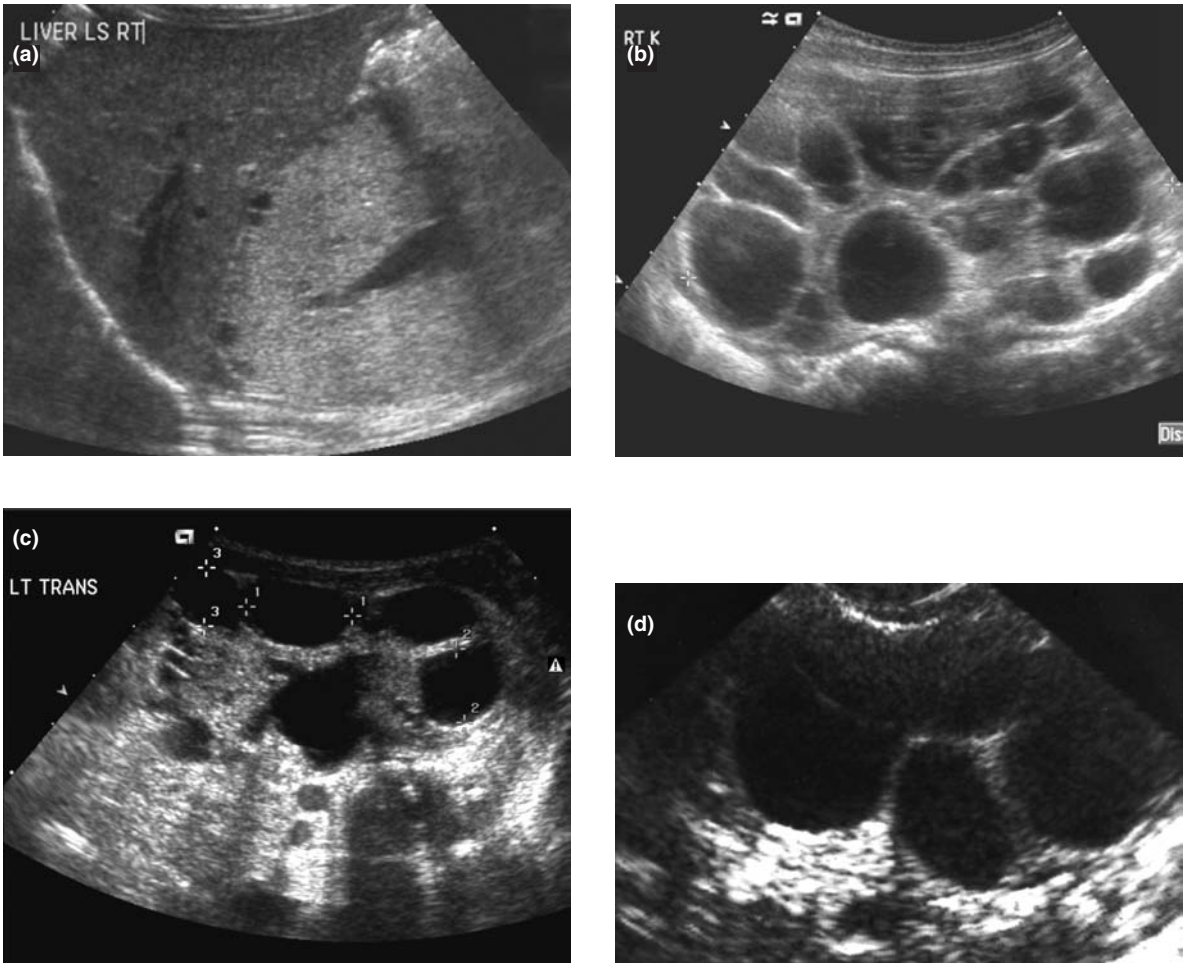


Figure 3.4 Cystic disease. Ultrasound appearances of (a) autosomal recessive polycystic kidney disease with bright parenchyma and multiple tiny cysts compared with (b) autosomal dominant polycystic kidney disease with multiple large hypoechoic cysts, (c) cystic dysplasia with scattered cysts and (d) multicystic dysplastic kidney with multiple cysts and septa containing no intervening renal parenchyma.

dose being excreted in the urine. It provides static images of functioning renal tissue and generates a measure of relative rather than absolute renal function. DMSA plays a valuable role in documenting the presence and progression of renal scarring and is also the modality of choice for identifying small, poorly functioning kidneys, ectopic renal tissue and cryptic or occult duplication anomalies (Figures 3.9 and 3.10). DMSA is also a valuable modality for demonstrating fusion anomalies such as horseshoe kidney (Figure 3.11). It may be used in the acute phase of a UTI to show areas of the renal parenchyma that may be involved in pyelonephritis and can also be used in the assessment of renal trauma to delineate which areas of renal tissue are still functioning (see Figure 3.6).

Technique

The dose of injected ^{99m}Tc DMSA is dependent on body surface area, which is calculated from the patient's age and weight. Typically, between 15 MBq and a maximum of 100 MBq are given. Images are then acquired approximately 2–3 hours after the tracer has been injected.

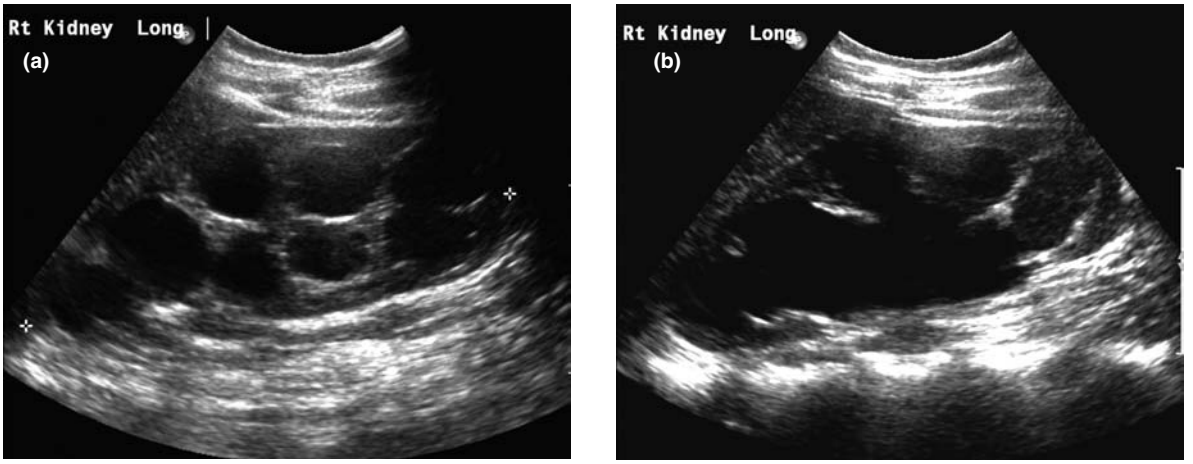


Figure 3.5 Ultrasound in a patient with (a) autosomal dominant polycystic kidney disease compared with a different patient with (b) marked hydronephrosis. Initial appearances are very similar but a skilled sonographer will be able to demonstrate that in the case of the hydronephrosis (b) the 'cysts' all interconnect since they are, in fact, calyces in a dilated collecting system.

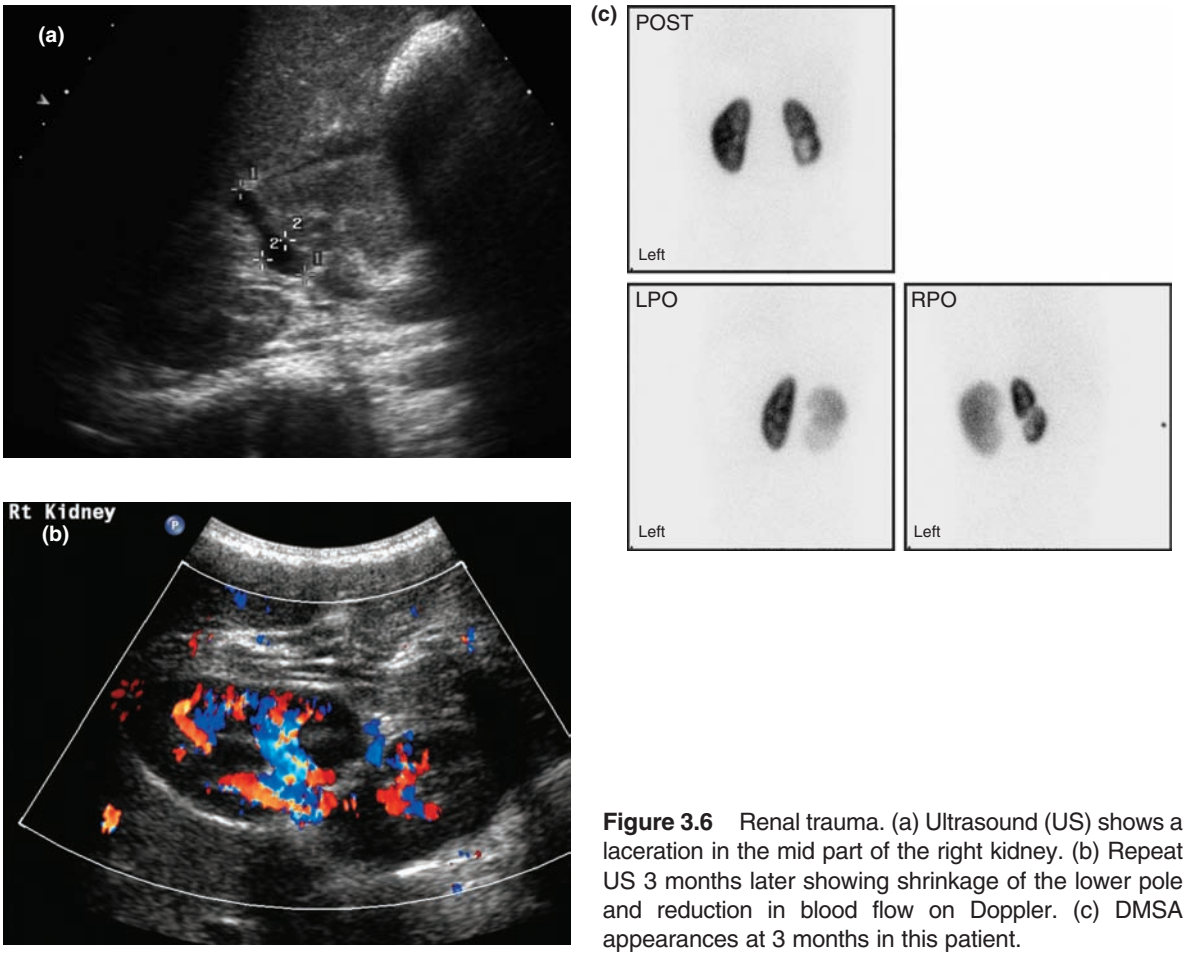


Figure 3.6 Renal trauma. (a) Ultrasound (US) shows a laceration in the mid part of the right kidney. (b) Repeat US 3 months later showing shrinkage of the lower pole and reduction in blood flow on Doppler. (c) DMSA appearances at 3 months in this patient.

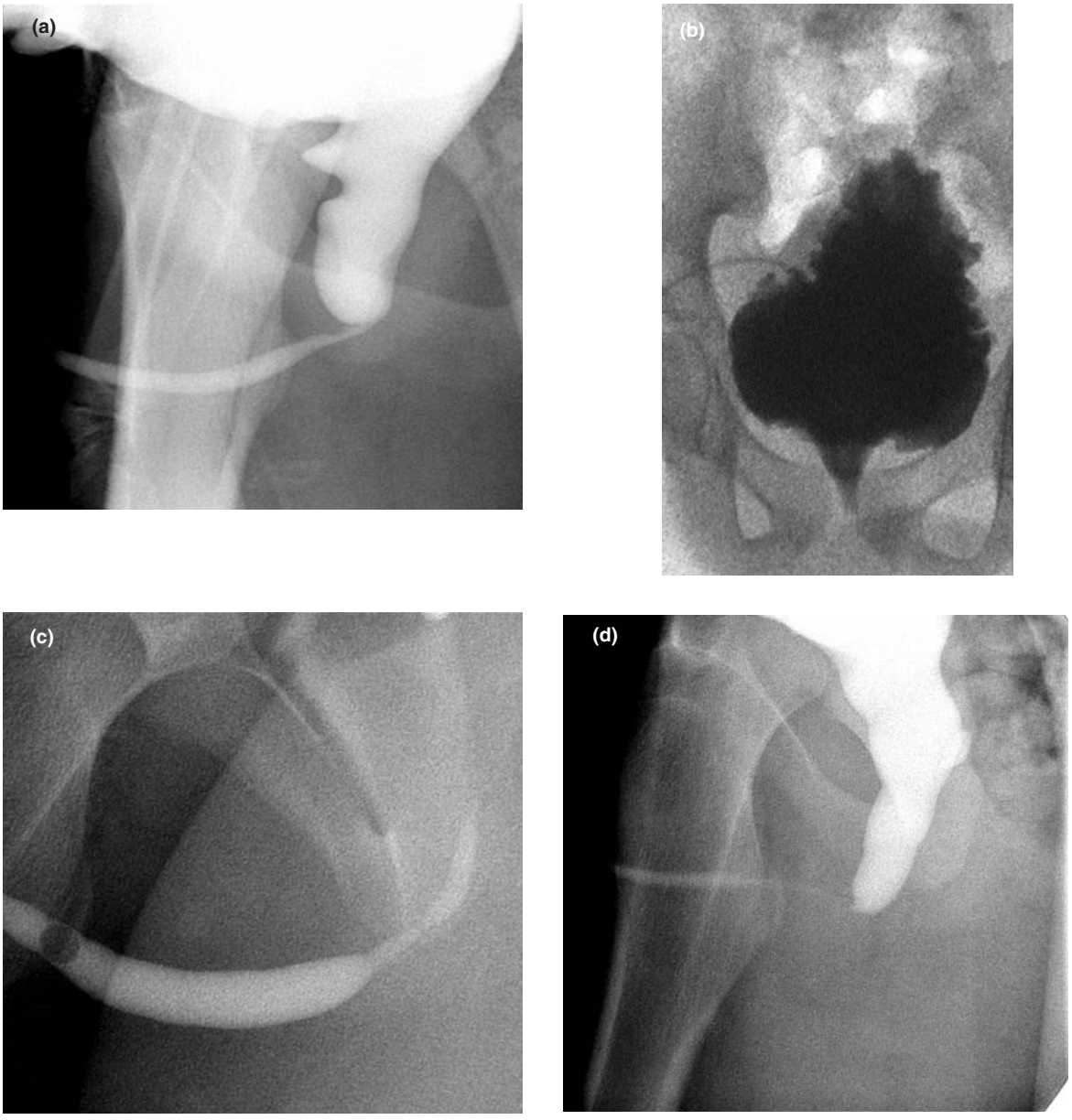


Figure 3.7 Examples of urethral abnormalities demonstrated by MCUG. (a) Typical appearance of a posterior urethral valve with an abrupt change in calibre of the urethra at the level of the valve leaflet with (b) a heavily trabeculated bladder indicating long-standing outflow obstruction. (c) Urethral stricture best demonstrated with a simultaneous retrograde urethrogram. MCUG alone (d) does not delineate the distal extent of the stricture.

The advantages of ^{99m}Tc DMSA include the high sensitivity in the detection of parenchymal pathology, measurement of differential renal function and the visualisation of ectopic kidneys. Disadvantages include the need for intravenous cannulation and the delay between injection and the acquisition of images. The radiation burden is higher than in dynamic renography (such as MAG 3), as the isotope is largely 'trapped' in the kidney until it decays.

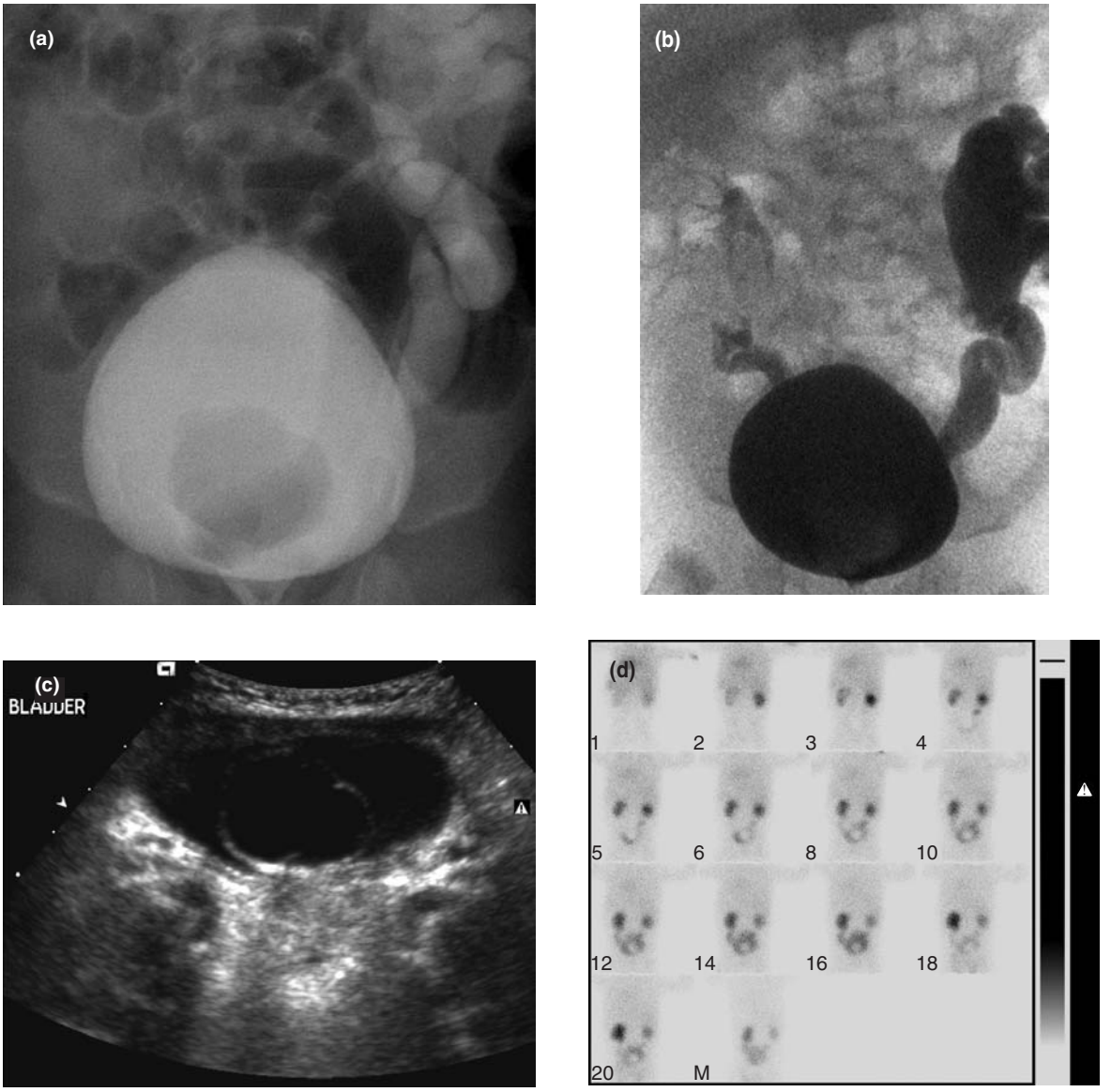


Figure 3.8 Ureterocele. (a) MCUG shows a large ureterocele as a filling defect at the bladder base with (b) associated reflux into the dilated lower moiety of a duplex kidney. (c) Ultrasound showing the ureterocele at the bladder base and (d) MAG3 renogram shows reflux on the left and the photopenic area of the ureterocele in the bladder.

Dynamic renography (MAG3 and DTPA)

It seems increasingly likely that dynamic renography will ultimately be replaced by functional MRI but, for the time being, it remains the standard diagnostic investigation for obstruction in most units. The dynamic renogram permits simultaneous assessment of renal function and drainage and is therefore used in the assessment of upper tract dilatation and for certain forms of duplex system (see Figure 3.3).

Differential renal function data are usually acquired at about 1–2 minutes after the injection of the isotope, whereas drainage is estimated by assessing the renogram curve (the normal pattern being

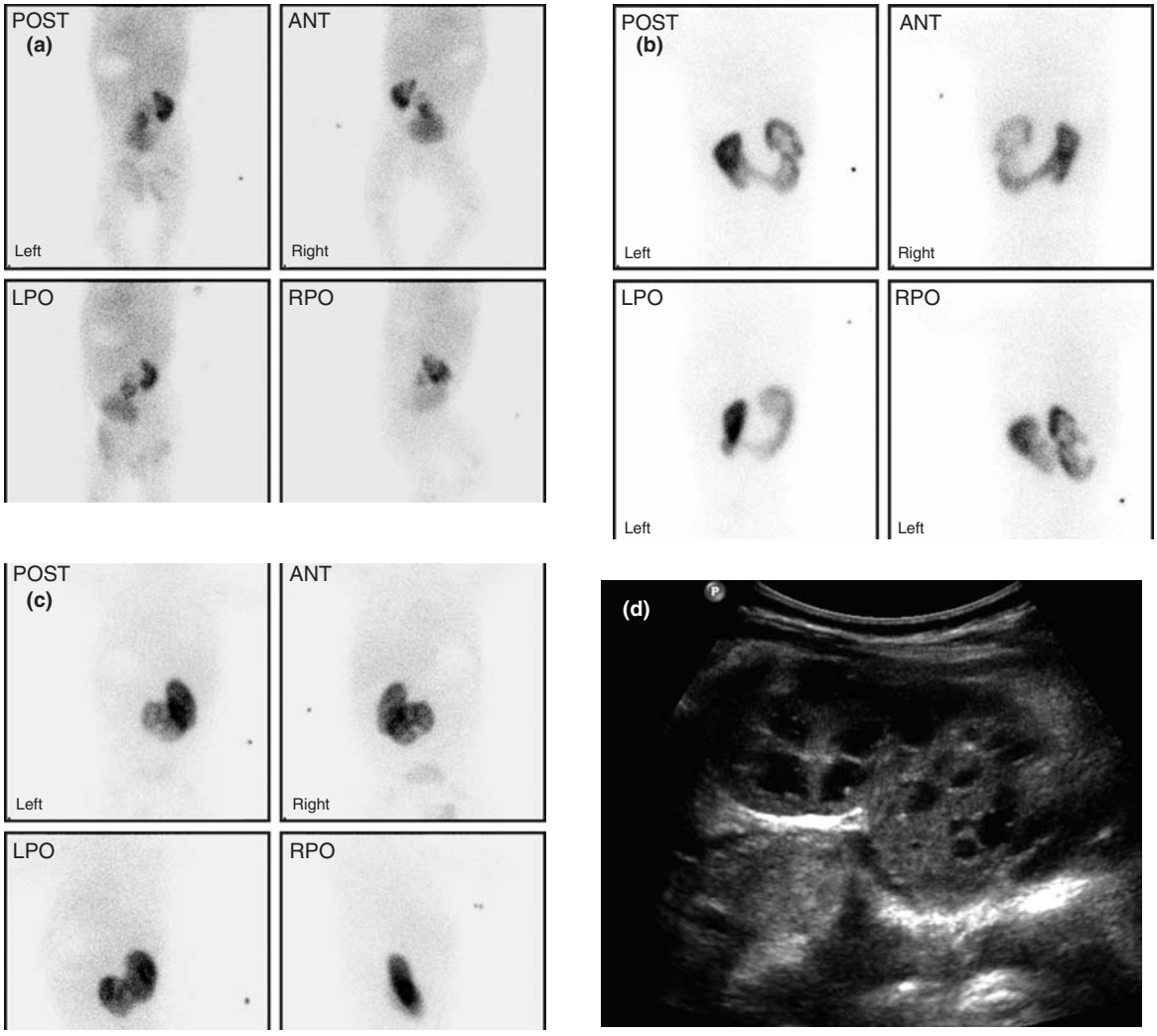


Figure 3.9 DMSA images of ectopically located renal tissue: (a) ectopic left pelvic kidney; (b) horseshoe kidney with functioning tissue crossing the midline; and (c) crossed fused ectopic kidney with (d) ultrasound demonstrating the two fused moieties in this patient.

an early peak followed by a rapidly descending phase) – see also Chapter 6.

The most commonly used isotope is now ^{99m}Tc MAG3, which relies on tubular extraction (Figure 3.12). This has the advantage of lower background activity and a higher kidney to background ratio than diethylenetriamine pentaacetic acid (DTPA), which is excreted by filtration. However, DTPA does have the advantage that it offers the possibility of simultaneous imaging and formal measurement of glomerular filtration rate (GFR), by taking timed blood samples to measure clearance of DTPA.

Cross-sectional imaging

Whereas US is a form of 'cross-sectional' technique, the term is more commonly applied to CT and MRI. The role of CT in paediatric imaging is limited by the high ionising radiation dose. MRI does not involve exposure to radiation but does require patients to remain still (or to be sedated or anaesthetised). It is contraindicated in patients with most types of metallic implants, although this is not a common consideration in children.

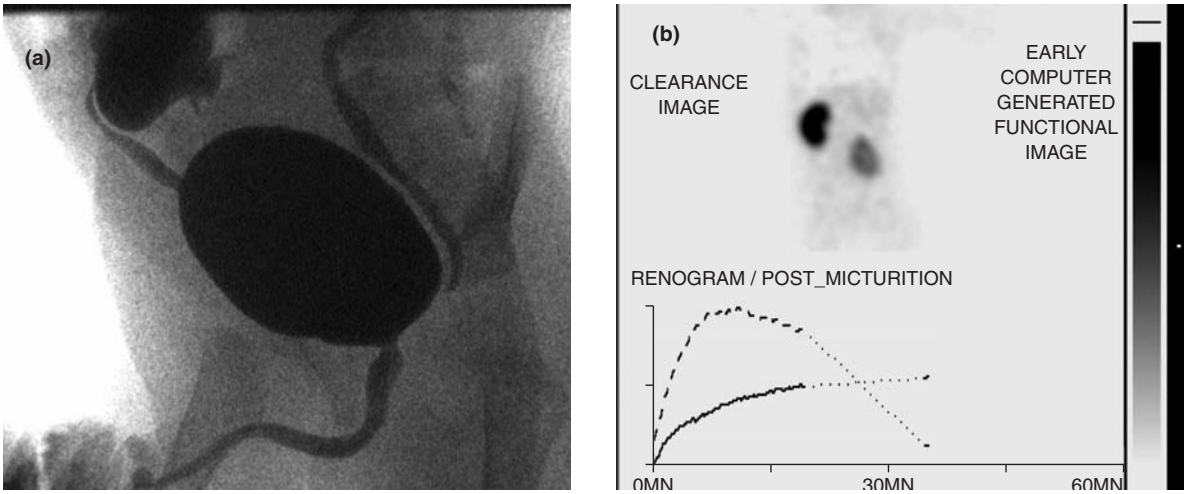


Figure 3.10 Pelvic kidney. (a) MCU shows reflux into an abnormally sited kidney. (b) MAG3 demonstrates functioning parenchyma in an abnormal pelvic position with rising renogram curve.

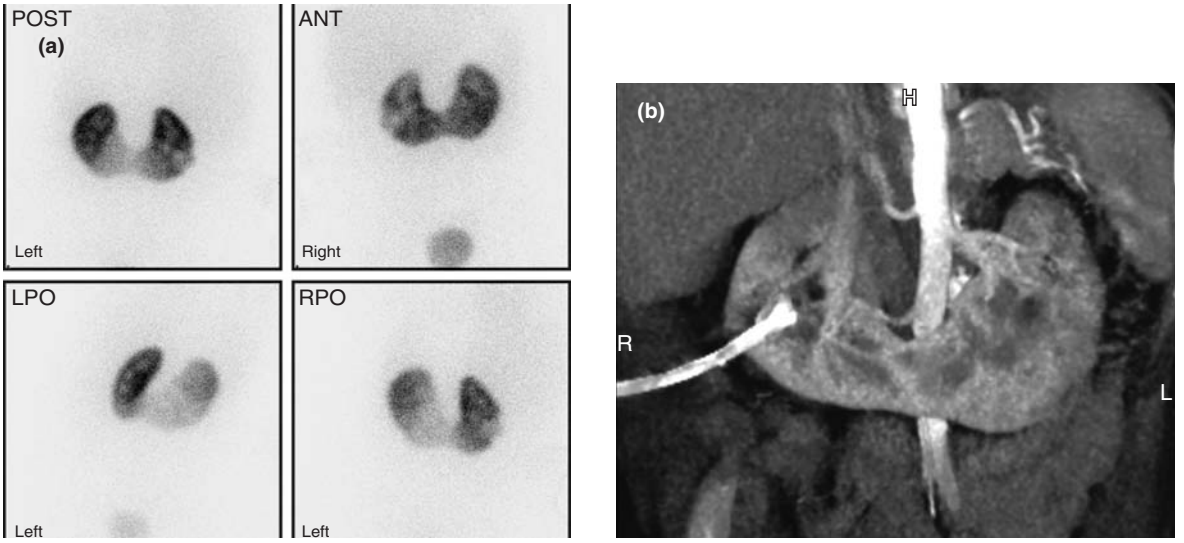


Figure 3.11 Horseshoe kidney. (a) DMSA demonstrates the presence of functioning renal tissue across the midline in this patient. (b) Coronal reconstruction from a CT angiogram for vascular anatomy presurgery also demonstrates the configuration of the kidney (a nephrostomy tube is in place in the right moiety).

MRI

Apart from the lack of ionising radiation, the advantages of MRI over CT are the multiplanar images and the superior delineation of different tissue types. In this context MRI is particularly suited to urological imaging because of its excellent delineation of water/urine-containing structures.

T_1-weighted images provide anatomical detail, whereas T_2 images are a better guide to pathology. Fat suppression techniques can also be added to enhance pathological diagnosis as they allow differentiation between fat and pathological tissue, both of which may be bright (high signal) on non-fat suppressed T_2 sequences. Gadolinium enhancement (an intravenous MRI contrast medium) is extremely

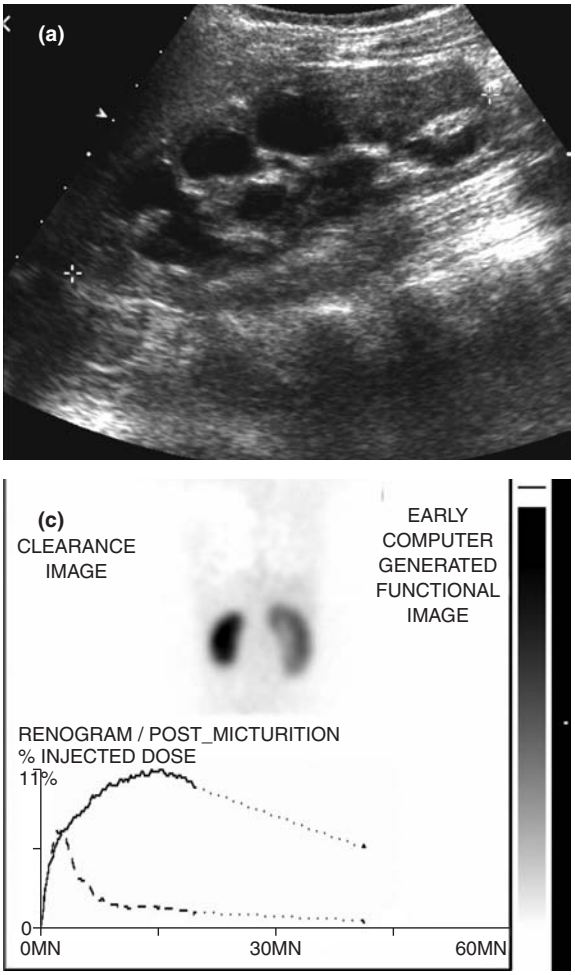


Figure 3.12 Pelviureteric junction obstruction. (a) Ultrasound shows hydronephrosis of the right kidney and the associated (b) MAG3 demonstrating delayed transit of isotope with poor drainage after micturition in the kidney and (c) rising excretion curve in the right kidney indicating accumulating isotope and poor drainage.

helpful in assessing tumour vascularity and in demonstrating kidney function and excretion.

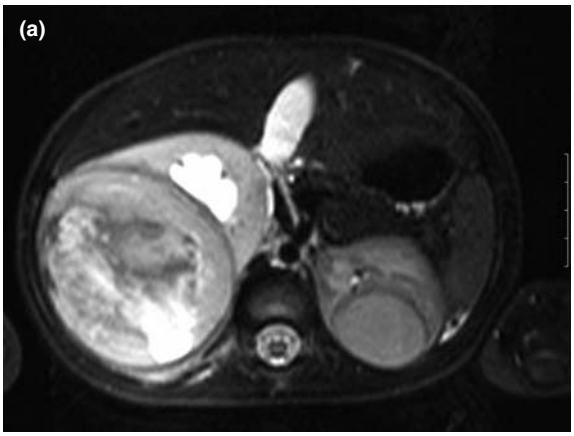
MRI in children

This technique remains challenging, as scan times can be up to 30 minutes or even longer, and the patient must remain absolutely still for the duration of the scan. Infants under 6 months can be immobilised using a 'feed and wrap' technique, in which they sleep through the study. Beyond this age, general anaesthesia is usually required to permit a satisfactory MRI scan in patients up to about the age of 7 or 8, after which they can lie still on their own.

As a result of recent technical developments, sequences are getting faster and, for the main part, images in children are now extremely good.

Techniques and indications

MRI is now the examination of choice for the assessment of renal tumours (Figures 3.13 and 3.14). MR angiography (MRA) also makes an informative contribution. For example, it is possible to confirm the presence of aberrant 'crossing vessels' giving rise to pelviureteric obstruction (Figure 3.15). MR angiography is also used in the preoperative evaluation of abdominal vasculature in children prior to renal transplantation (Figure 3.16).



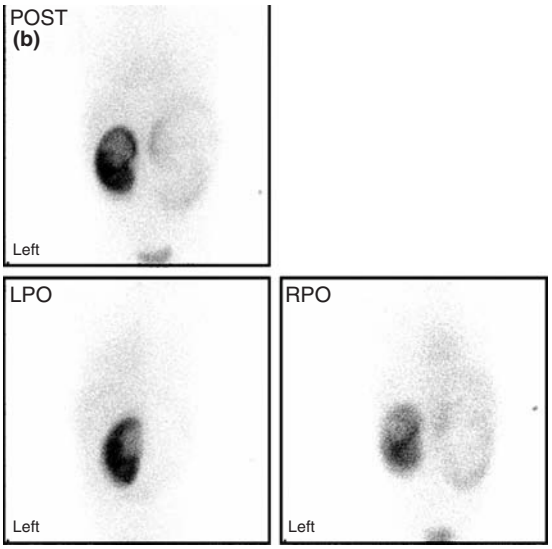
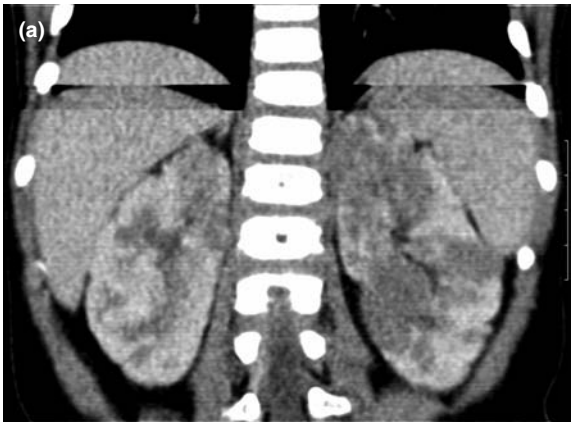


Figure 3.13 Wilms' tumour. (a) MRI with intravenous contrast in the transverse plane shows bilateral Wilms' tumour in a horseshoe kidney. (b) DMSA in the same patient showing the bilateral tumours as photopenic areas since they do not contain normally functioning renal tissue.



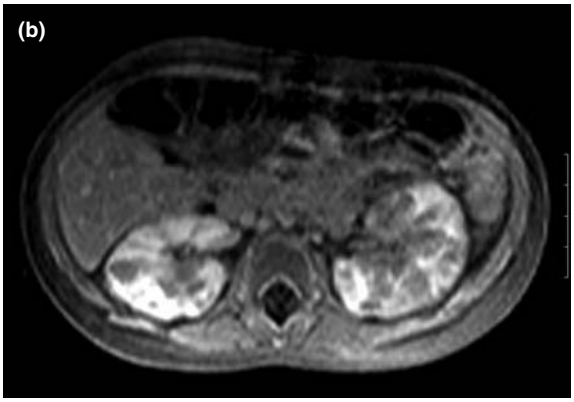


Figure 3.14 Nephroblastomatosis. (a) CT with intravenous contrast reconstructed in the coronal plane showing extensive nephroblastomatosis in both kidneys (the misregistration at the level of the diaphragm is due to the patient taking a breath during the scan). (b) MRI in the same patient demonstrates the same finding (in the transverse plane) but without the need for ionising radiation.

In specialist centres, MR urography (MRU) is now being increasingly applied to the evaluation of both upper and lower tract abnormalities. It provides high resolution images of the parenchyma and collecting system at all phases of kidney function (vascular, filtration, excretion) and also provides high-quality images of the ureters. It is likely that this technique will become increasingly widespread in children who are old enough to cooperate. Heavily T_2-weighted sequences are generally used for MRU, as these highlight water/urine-containing structures, which is an extremely useful property in the morphological assessment of the urinary tract.

MRI has the potential to combine anatomical detail with the functional information conventionally obtained from MAG3 or DMSA scans. Studies are being undertaken to validate the quality and reliability of the functional information yielded by MRI against DMSA. If it emerges that MRU is capable of yielding functional information of

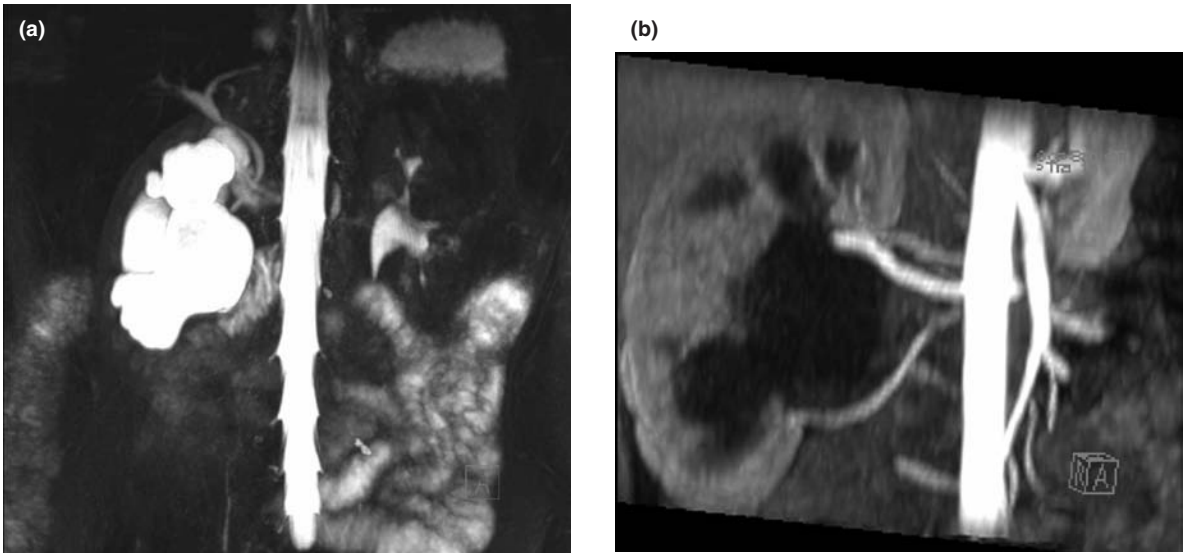


Figure 3.15 MRI in a patient with a 'crossing vessel' causing pelviureteric obstruction. (a) The heavily T_2-weighted sequence shows the marked hydronephrosis of the right kidney. (b) A T_1-weighted sequence after gadolinium shows the main right renal artery but also an accessory right renal artery 'crossing' the distended renal pelvis to cause the right pelviureteric junction obstruction. MRI has shown both the renal pelvic anatomy and the dynamic vascular anatomy in the same examination.

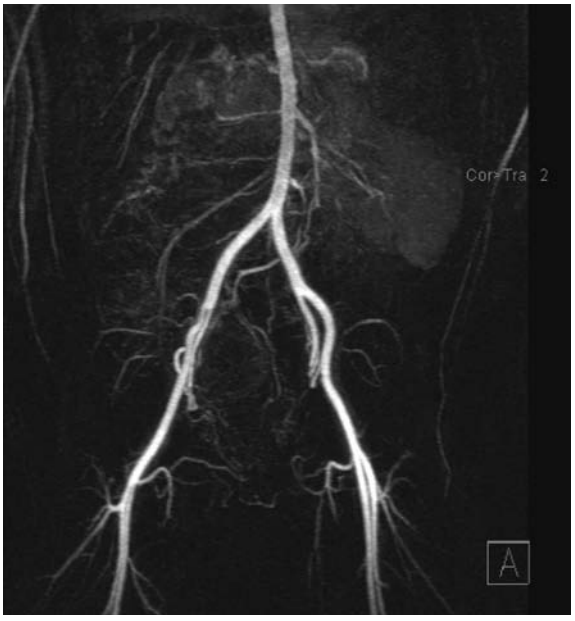


Figure 3.16 MR angiography: coronal images following intravenous gadolinium performed in the work-up for renal transplant showing a normal aorta, iliac and femoral arteries.

comparable quality, it will be increasingly adopted in the routine investigation of upper tract pathology.

Computed tomography

US can answer many of the questions in children that are more commonly addressed by CT in adults, and for this reason CT should not be considered as a first-line investigation in children. The principal exception is in children who have suffered multiple injuries and in whom additional information is simultaneously required on several organ systems. CT is highly sensitive for detecting contusions, lacerations, perinephric fluid collections and areas of avascularity. Pelvic CT should also be included in the study to look for evidence of bladder rupture and extra- or intraperitoneal leakage of urine

Although CT has previously been used as the main modality for the assessment of tumours, MRI is fast becoming the preferred technique. CT also has a role in the investigation of stone disease

in patients in whom US has been unsuccessful. This consideration may apply to patients with a very marked scoliosis or those who are obese.

Technique

Intravenous access is usually required for the administration of contrast material, although the scan can be performed without the need for contrast if it is being performed solely to look for calcification. Very young children may be able to sleep through the scan if they are fed directly prior to the study but toddlers may need sedation or a general anaesthetic. By 4 or 5 years of age, however, most children will tolerate a CT scan without the need for sedation or anaesthetic.

Modern multi-detector CT scanners acquire the images very rapidly, typically in 10–15 seconds following the start of the scan. A vascular lesion would typically be imaged at approximately 15 seconds after the start of injection and, for tumours or trauma, imaging is performed 25–30 seconds after injection (therefore in the late arterial/early venous phase). Every effort should be made to keep the radiation dose to a minimum. In this context, the clinician should be aware that even with modern CT scanners the dose from a combined abdominal and pelvic CT examination is in the region of 200–300 times greater than the dose of a chest X-ray.

Intravenous urogram

Although the IVU has largely been replaced by the combination of US, DMSA and MRI, it retains a limited role in providing information in certain specific areas such as:

- delineating the level of an acute obstruction, e.g. due to calculi
- correlating the position of calculi demonstrated on US with the exact anatomy of the collecting system to allow planning for percutaneous nephrolithotomy or for lithotripsy.

Abdominal X-ray

Historically, the plain abdominal X-ray was often a starting point in the investigation of abdominal or loin pain. However, the diagnostic yield is low and abnormal findings of urological relevance are generally restricted to the detection of urinary tract calculi, spinal anomalies (although MRI is preferable), abdominal or pelvic mass lesions and constipation. US can provide most of the information previously sought by abdominal X-ray and has rendered this investigation largely redundant.

Interventional techniques

Before any interventional technique is undertaken, it is important to ensure that all the relevant preoperative investigations (notably clotting studies) have been undertaken and full informed consent has been obtained.

Arteriography

Arteriography may be indicated when renal artery stenosis is suspected. However, this diagnosis is usually pursued firstly by US, and then by MRI. Conventional arteriography for suspected renal artery stenosis does, however, have the advantage that it can be combined with angioplasty under the same anaesthetic. Arteriography is also useful in middle aortic syndrome, and again angioplasty may be used. Some renal and bladder arteriovenous malformations are treatable by embolisation.

Venography

Selective sampling of renal veins (for renin) and the inferior vena cava may be indicated in children whose hypertension is thought to arise from excessive renin production by a scarred or dysplastic kidney. Venography and embolisation is a widely accepted technique for the treatment of varicoceles.

Antegrade pyelography

Nowadays, the principal indication lies in the investigation of distal obstruction in the upper

urinary tract. Antegrade pyelography via percutaneous renal puncture can be performed by an interventional radiologist or by a urologist.

Percutaneous nephrostomy

Percutaneous nephrostomy is often performed under US control but may be combined with fluoroscopy. The procedure is usually performed under general anaesthesia in children. Percutaneous nephrostomy is generally preferred to open surgical nephrostomy and drainage, the main indication being decompression and drainage of acutely obstructed or infected hydronephrosis usually due to pelviureteric junction (PUJ) obstruction.

Renal and tumour biopsy

Although ultrasound-guided procedures can generally be performed using sedation and local anaesthesia in compliant older children, general anaesthesia is required for the younger age group. Multiple cores should be acquired, and these should preferably undergo immediate microscopic examination to confirm that adequate tissue has been obtained. This is important to minimise the possible need for a repeat procedure and further anaesthetic.

Key points

- Many of the conditions encountered in paediatric urological practice are related to underlying congenital abnormalities of the urinary tract. A combination of imaging techniques is usually required to provide the degree of anatomical and functional information needed to plan surgical management.
- Ultrasound is invariably the initial investigation of choice in children. Intravenous urography is no longer employed routinely and its use in this age group is now limited to a few selective indications.
- Dynamic and/or static renography is routinely used to assess functional parameters across a broad range of paediatric urological conditions. With further development, however, it is possible that MR urography will take over this role for the investigation of upper tract obstruction.
- MRI is being increasingly adopted in paediatric practice because of its ability to combine excellent anatomical detail with functional information, without exposure to radiation. The principal limitation is the need for sedation or general anaesthesia in younger children.
- The role of CT in children is limited by the high radiation dosage. The only indication for CT as a first-line investigation is in the evaluation of major abdominal trauma.
- Interventional techniques such as percutaneous nephrostomy and guided tumour biopsy have largely replaced open surgery for these indications.

Further reading

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Urinary tract infection 4

Stuart J O'Toole

Topics covered

Epidemiology of childhood urinary infection
Pathogenesis
  Infecting organisms
  Host factors
Diagnosis
  Specimen collection, urine analysis
Clinical features
  Age differences
  Upper and lower tract infection
Investigation
  NICE guidelines
Management

Introduction

Urinary tract infection (UTI) is one of the commonest disorders of childhood, affecting an estimated 82 000 children a year in the UK. The investigation and management of children with UTI generates a substantial workload for paediatric urologists and paediatric nephrologists as well as for general paediatricians. The presentation of UTI in this age group is varied and the diagnosis can sometimes be problematic, particularly in young infants in whom the clinical picture is often non-specific and reliable urine samples are difficult to obtain. Despite these diagnostic difficulties, the greater awareness of the importance and prevalence of UTI in children coupled with the availability of sensitive dipstick reagent strips has resulted in the detection of UTI on a far greater scale than in the past. As a consequence of better diagnosis of UTI by general practitioners, many more children with mild or asymptomatic lower tract urinary infections are now being referred for investigation. To a large extent, however, recent protocols for the investigation and management of childhood UTI date from a time when children referred for investigation tended to be those with more severe infection. The use of outdated protocols has had the result that many children with lower tract UTIs have been subjected to unnecessary (and often needlessly invasive) investigations. Moreover, the burden of unnecessary investigations has significant financial implications for the National Health Service. To address these concerns the UK's National Institute for Health and Clinical Excellence (NICE) has recently produced new guidelines based on an extensive analysis of the published evidence. These guidelines are intended to encompass referral practice, a more selective approach to diagnostic imaging and evidence-based recommendations on management. The NICE guidelines have been criticised by some clinicians on the grounds that they might lead to under investigation of some children with clinically significant UTIs, scarring and reflux. Where appropriate, reference will be made to the 2007 NICE guidelines in this chapter.

Epidemiology

Urinary infection is one of the commonest bacterial infections occurring in children and, with improved diagnostic sensitivity, it is apparent that the true incidence is far higher than was previously thought: in the 1960s this was put at 0.02% for boys and 0.04% for girls, whereas current estimates have increased 20-fold (Table 4.1). In

Table 4.1 The age-related incidence of urinary tract infection in boys and girls

Age (years)	Boys (%)	Girls (%)
<1	1.0	0.8
<3	2.2	2.1
<7	2.8	8.2
<16	3.6	11.3
Lifetime	13.7	53.1

the first 12 months of life urinary infections are more common in boys but thereafter (and particularly above 3 years of age) UTIs occur predominantly in girls.

Pathogenesis of urinary tract infection

Although urinary tract infection can arise through haematogenous spread (or direct transmission of bacteria from other organs in the case of vesicointestinal and genitourinary fistulae), most UTIs are caused by urethral ascent of organisms which colonise the perineum or preputial sac. Once organisms have gained access to the lower urinary tract, whether they go on to produce an established infection is determined by the interplay of a number of factors set out in Figure 4.1. Recent research in experimental animals indicates that the concept of organisms multiplying within bladder urine is misconceived and that bacterial replication occurs predominantly at an intracellular level, with organisms being shed into the urine from infected urothelial cells.

Organisms

In the urinary tract, as in other systems, the occurrence of infection depends upon the balance between host resistance and the virulence of the infecting organism. *Escherichia coli* is the causative organism in some 85% of cases of UTI. The fimbriated forms of *E. coli* have the ability to adhere to receptors on the urothelial surface and

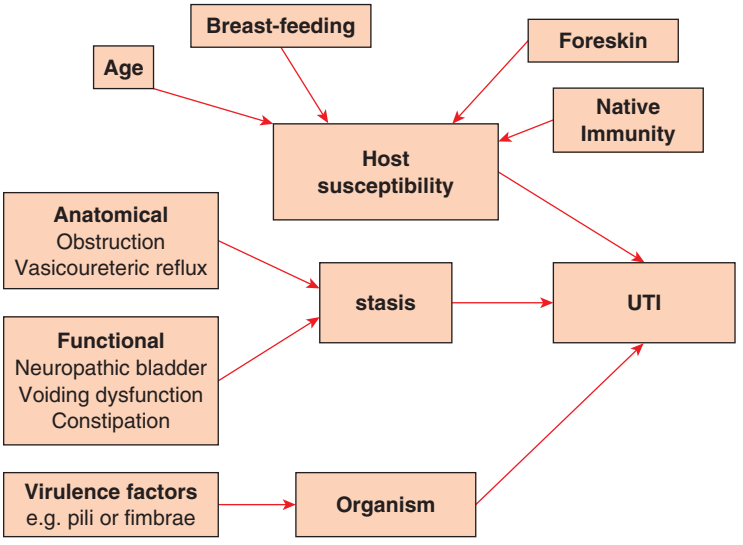

Figure 4.1 Host and pathogen factors involved in the pathogenesis of UTI in children.

are thus particularly effective at colonising the urinary tract. These are classified on the basis of haemagglutination of red blood cells and expression of the P blood group antigen. P-fimbriated *E. coli* are particularly potent pathogens by virtue of their adherence properties. Other common infecting organisms, in approximately descending order of frequency, are *Proteus vulgaris*, *Klebsiella*, *Enterobacter* and *Pseudomonas*.

Urinary stasis

Scientifically robust evidence linking urinary stasis to urinary infection is sparse, especially with regard to vesicoureteric reflux (VUR). Nonetheless, there is a large accumulated body of clinical experience to indicate that factors which impair the effectiveness with which organisms are cleared from the urinary tract do indeed predispose to urinary infection. Stasis may result from anatomical abnormalities producing obstruction or reflux, or from functional disorders interfering with bladder emptying.

Anatomical abnormalities

Increased awareness of urinary infection in children coupled with better diagnosis has had the result that many more children with mild, lower tract infections are now being referred for investigation than in the past. Consequently, the relative proportion of children with significant underlying urological abnormalities has decreased and whereas previous studies reported an incidence of underlying abnormalities of up to 30% in children with UTI more recent estimates have put the figure closer to 10%. Even when anomalies are identified on investigation many, such as minor grades of VUR, incomplete duplication anomalies, anomalies of position or fusion, etc., are of little clinical significance. In practice, dysfunctional voiding characterized by infrequent toileting and impaired bladder emptying is now a much more common predisposing cause of urinary infection, particularly in girls.

Host susceptibility

Many host factors can increase a child's susceptibility to urine infection. Premature infants are at increased risk (although breast-feeding appears to confer some protection). Other host factors including immunoglobulin A (IgA) secretion and blood group secretor status have also been linked to susceptibility to UTI. The presence of a foreskin is an undoubted risk factor, the reported incidence of urinary infection being 10–20 times higher in uncircumcised boys compared with their circumcised peers. However, this increased susceptibility occurs predominantly in the first year of life. Although the increased risk of urinary infection in uncircumcised boys has been cited as one of the justifications for routine neonatal circumcision, calculations based on a recent meta-analysis of 400 000 boys suggest that over 100 boys would have to be circumcised in order to prevent one boy with a normal urinary tract developing urinary infection.

Although routine neonatal circumcision cannot be regarded as a cost-effective public health measure for preventing UTIs, the benefit of circumcision is more apparent in boys with recurrent UTIs and those with urinary tract abnormalities. For example, there is some persuasive anecdotal evidence (backed by limited evidence from a small number of observational studies) that circumcision reduces the risk of UTI in boys with posterior urethral valves. However, this has never been subjected to a prospective controlled study.

Laboratory diagnosis of urinary tract infection

Urine collection

'Clean catch' midstream urine sample

A midstream urine (MSU) sample yields the most reliable results and children who are toilet-trained can nearly always cooperate with this method of collection.

For infants and children unable to provide a midstream specimen, there are **non-invasive** alternatives.

Non-invasive alternatives

- **Adhesive collection bags** attached around the genitalia represent the easiest and most commonly employed means of collecting urine specimens in the very young, However, the results are only reliable if the appropriate precautions have been taken and the voided specimen is sent promptly for culture. When these criteria are not met, contamination is common.
- **Absorbent urine collection pads** placed inside the nappy are being used increasingly as an alternative to collection bags. Cotton wool balls may also be used but are less reliable. Urine which has soaked into the pad is aspirated with a syringe and sent for microscopy and culture. Contamination is common.

Invasive techniques

- **Suprapubic needle aspiration** is the ideal method of collection in sick infants in whom an urgent diagnosis is required. The procedure should be performed under ultrasound guidance, with prior confirmation that there is urine in the bladder.
- **Urethral catheterisation** is invasive and unpleasant, and is rarely used for these reasons.

Although it is always preferable to obtain a urine sample before commencing treatment, there may be situations (e.g. a severely ill infant) when antibiotic treatment is justified even if a urine sample cannot be obtained.

Urine storage and transport

Once collected, the specimen should ideally be cultured within 4 hours to minimise the risk of contaminating organisms multiplying and yielding a false-positive result. Where this is not possible (for example in children presenting outside working hours), the sample can be refrigerated for up to 24 hours at +4.0ºC or transferred to a vessel containing boric acid preservative.

Urine dipsticks

The introduction of urine dipsticks with leucocyte esterase and nitrite reagents has made an important contribution to the earlier diagnosis of UTI.

NICE makes the following recommendations:

- **Leucocyte esterase and nitrite both positive** – definite evidence of UTI. Antibiotic treatment should be commenced.
- **Leucocyte esterase negative, nitrite positive** – presumptive evidence of UTI. Antibiotic treatment should be commenced and a urine sample sent for culture.
- **Leucocyte esterase positive, nitrite negative** – a urine sample should be sent for microscopy and culture but antibiotic treatment should not be commenced unless there is good clinical evidence of UTI.
- **Leucocyte esterase negative, nitrite negative** – negative result. Antibiotic treatment should not be started. Nor is it necessary to send urine for microscopy and culture.

A positive result for protein does not denote infection. A trace of proteinuria is a common finding and is not a cause for concern. Heavier proteinuria may, however, signify renal disease and referral to a paediatric nephrologist should be considered if the finding is confirmed on a further test.

Urine microscopy

When performed on a fresh uncentrifuged sample of urine, microscopy can be very useful in facilitating a prompt diagnosis. This is of particular importance in the acute situation when there is a need to commence treatment without awaiting the results of culture. Different techniques are available, but results are generally expressed as absolute values or counts per high-powered field. Significant pyuria is defined as >10 WBC/mm^3. The concentration of motile bacteria can also be quantified, with 10^7 bacteria per ml being deemed significant. This figure corresponds to 8 organisms per high-powered field. The interpretation of microscopy findings is summarised in Table 4.2.

Table 4.2 NICE guidelines on the interpretation of urine microscopy

Microscopy results	Pyuria positive	Pyuria negative
Bacteriuria positive	The infant or child should be regarded as having UTI	The infant or child should be regarded as having UTI
Bacteriuria negative	Antibiotic treatment should be started if clinically UTI	The infant or child should be regarded as not having UTI

Urine culture

Provided the urine sample has been collected without contamination, the criterion for the bacteriological diagnosis of urinary infection is a pure growth of $>10^5$ bacterial colony-forming units (CFUs) per ml. On the other hand, in specimens obtained by suprapubic aspiration, *any* growth of a Gram-negative organism is significant, as is a growth of greater than >500–1000 Gram-positive organisms. With the availability of sensitive combination dipsticks, it has been questioned whether urine culture is routinely necessary in all cases. According to NICE guidelines, it is not necessary when both leucocyte esterase and nitrite dipstick results are positive. Although urine culture may not be strictly necessary to confirm the diagnosis of UTI, there is, nevertheless, a strong argument for sending a urine specimen for culture to identify the causative organism and establish its antibiotic sensitivities. This procedure may be an important consideration at a time when multiple antibiotic resistance is becoming more prevalent.

Clinical presentation and diagnosis

History and examination

It is important, to establish whether there is any family history of urological abnormalities, particularly VUR. The antenatal history is also important, specifically whether any abnormality was detected on antenatal ultrasound. In older, toilet-trained children it should also be routine to enquire about:

- voiding history (volume, frequency, stream, urgency)
- fluid intake (volume, type)
- bowel habit.

Although **physical examination** is usually unrewarding, it should be routinely performed and include the abdomen, genitalia, spine and lower limbs, plus, in all cases, measurement of blood pressure. This can be difficult in small children but all paediatric outpatient departments should have the appropriate equipment and paediatric blood pressure cuffs.

Clinical features

Early diagnosis and prompt treatment of UTI is important, but the presentation can be non-specific and dependent on the nature of the infection and the age of the patient. Table 4.3 summarises the clinical features of UTI in children at different ages. It is important to maintain a high degree of suspicion and ensure that a urine sample is collected and tested for infection in any child with an unexplained fever exceeding 38.0°C.

In addition to age-related differences, the other principal determinant of clinical presentation is whether the child is suffering from lower or upper urinary tract infection (Table 4.4).

Lower tract infection

The symptoms are typically those of cystitis, with dysuria being almost universal. In addition, urinary frequency is common and often associated with secondary enuresis. By contrast, suprapubic pain occurs comparatively rarely. There is no fever

Table 4.3 Presenting features of UTI in children at different ages

Frequency	Infant and toddler	Older child
Common	Fever Irritability Vomiting Lethargy	Frequency Dysuria
Less common	Offensive urine Poor feeding Failure to thrive	Offensive urine Incontinence Abdominal pain
Uncommon	Jaundice Failure to thrive Haematuria	Fever Vomiting Haematuria Loin tenderness

Table 4.4 Symptoms of urinary tract infections

Lower urinary tract	Upper urinary tract
Frequency/nocturia	Fever
Dysuria	Vomiting
Secondary enuresis	General malaise
Suprapubic pain	Loin pain
Hesitancy	Upper/central abdominal pain

or any general malaise; indeed, many older children are able to continue attending school during the course of their illness.

Upper tract infection (pyelonephritis)

Fever is the most reliable clinical feature of upper urinary tract infection and, indeed, it is doubtful whether pyelonephritis ever occurs in its absence. Although the fever associated with pyelonephritis is usually high, any temperature exceeding 38°C should be regarded as suspicious. In children who have been admitted as emergencies or seen in Accident and Emergency Departments, fever, or its absence, is nearly always recorded but this is less well documented in referrals from general practice.

In this context, the 2007 NICE guidelines state:

> Infants and children who have bacteriuria and fever of 38°C or higher should be considered to have acute pyelonephritis/upper urinary tract infection. Infants and children presenting with fever lower than 38°C with loin pain/tenderness and bacteriuria should also be considered to have acute pyelonephritis/upper urinary tract infection. All other infants and children who have bacteriuria but no systemic symptoms or signs should be considered to have cystitis/lower urinary tract infection.

Other presenting features of UTI

The occurrence of haematuria is not in itself indicative of the severity of the infection or of its site. Haemorrhagic cystitis is the commonest cause, although urinary tract calculi should be suspected whenever the infecting agent *is Proteus.* Stones may be present in the upper urinary tract even in the absence of any constitutional symptoms. In some boys referred with haematuria (with or without documented infection), the history may be one of postmicturition bleeding rather than haematuria proper. This is usually due to urethritis.

Epididymo-orchitis is an occasional presentation of urinary infection in boys of all ages and

should arouse suspicion of some predisposing abnormality, such as urethral obstruction distal to the ejaculatory ducts or a duplication anomaly with the upper pole ureter draining ectopically into an ejaculatory duct (see Chapter 7).

Neonates and infants

With few exceptions, the clinical presentation is with a non-specific febrile illness, usually accompanied by vomiting and quite often by diarrhoea. Because there are many possible explanations for this clinical picture, it is advisable to perform appropriate dipstick analysis – or ideally send urine for microscopy and culture in any infant with an otherwise unexplained febrile illness. In practice, however, obtaining a reliable sample for microscopy and culture may be difficult. Other, rarer, non-specific features of urinary infection in this age group include failure to thrive (or frank weight loss) and prolonged jaundice in neonates. The occurrence of haematuria can occasionally serve as a sign of urinary tract infection, which usually manifest as a blood-stained nappy. In male infants, UTI occasionally presents with epididymo-orchitis.

Children aged 2 years and older

Even as early as 2 years of age most children can give some account of their symptoms and by 4 years, if not earlier, an accurate history can nearly always be obtained. Furthermore, except when the symptoms relate entirely to the upper renal tracts, it usually becomes apparent from the history that urinary infection is the likeliest diagnosis. Equally, in the majority of cases it is possible to determine, on clinical grounds, whether the infection involved the upper urinary or the lower urinary tract.

Upper abdominal pain is an occasional symptom of renal infection but it may be difficult to distinguish this from the non-specific pattern of central abdominal pain, which is a common symptom in children. True loin pain is rare and, if prolonged, with or without associated vomiting, is more likely to signify urinary obstruction than infection.

Potential pitfalls and sources of diagnostic confusion include:

- **Fever, loin pain and dysuria in an older child.** This triad of urinary tract symptoms associated with pyelonephritis can also be mimicked by acute inflammation of a retrocecal or pelvic appendix. In acute appendicitis, a carefully taken history should reveal that any pain on voiding is localized to the abdomen rather than the urinary tract. Moreover, the fever is usually lower in appendicitis than pyelonephritis and the pain associated with appendicitis is more likely to be provoked or exacerbated by extension of the hip.
- **Dysuria in the absence of other features of UTI**. Symptoms associated with vulvovaginitis in young girls are not uncommonly ascribed to UTI. Moreover, pyuria may be evident on urine microscopy. Whereas urine culture is generally negative, it may reveal a mixed growth of organisms. From the history it should be possible to distinguish between localized symptoms of dysuria due to vulvovaginitis and dysuria, which is included as part of a broader clinical picture of genuine lower urinary tract infection.
- Likewise, dysuria associated with **balanitis** may be confused with UTI in boys.

Investigation: diagnostic imaging

Established protocols and previous guidelines have been increasingly questioned on the grounds that they have resulted in overinvestigation of children with lower tract infections and are not cost-effective.

Whereas the rationale for new guidelines is widely accepted, it nevertheless remains likely that the majority of paediatric clinicians (including paediatric urologists) will continue to advise that all children presenting with proven urinary infection should undergo some form of investigation. However, it is important to adopt a selective

Table 4.5 Strengths and weaknesses ('pros and cons') of the different imaging modalities available for the investigation of UTI in children

Investigation	Pros	Cons
Renal ultrasound with postvoid bladder views	Detects dilatation and allows measurement of renal size Detects major scarring Provides information on bladder dysfunction Visualises calculi Cheap and well tolerated	Poor at detecting scarring or reflux Operator dependent
DMSA	Most sensitive test for renal scarring and differential function	Relatively expensive and time consuming Requires IV cannulation
Indirect cystogram (MAG3)	Detects reflux during normal voiding Provides differential renal function Avoids the need for urethral catheterisation	Child must be cooperative and potty trained Misses low-grade reflux Requires IV cannulation
Contrast micturating cystourethrogram (MCUG)	Most reliable test for detection of reflux Excludes urethral and other bladder pathology	Requires urethral catheterisation and incurs exposure to radiation

approach which avoids submitting normal children to unnecessarily invasive and costly investigations while at the same time identifying those children who have significant abnormalities such as reflux and renal scarring.

The technical aspects of the most widely used investigations – ultrasonography, dimercaptoruccinic acid (DMSA) scintigraphy, micturating cystourethrography (MCUG), indirect isotope cystography – are considered in Chapter 3.

The strengths and weaknesses of the different imaging modalities are summarised in Table 4.5.

Ultrasonography

Ultrasonography is non-invasive and entails no exposure to radiation. Consequently, it represents the ideal initial screening procedure and should be undertaken in all cases. Ultrasonography reliably detects obstructive and non-obstructive urinary tract dilatation, major degrees of renal scarring or dysplasia, most urinary calculi and almost all clinically significant duplication anomalies. Other, more subtle, indicators of pathology detected by ultrasonography include disparity in renal size (>1 cm difference in length measurement), abnormalities of renal echo-texture and distal ureteric dilatation suggestive of VUR.

Because false-positive results are rare, all children found to have any of these abnormalities should be investigated further. Ultrasonography is also of value in detecting evidence of voiding dysfunction (bladder wall thickening, significant residual urine).

When an abnormality has been revealed by ultrasonography, the choice of further imaging is guided by a combination of factors, including the nature of the abnormality detected on ultrasound, the severity of infection (upper or lower tract) and

Table 4.6 Clinical features which merit further investigation (including those identified by NICE as denoting 'atypical' infection)

- Severe infection with systemic symptoms indicating upper tract infection (pyelonephritis)
- Family history of VUR and/or renal scarring
- Poor urinary stream
- Palpable bladder or other abdominal mass (although these will generally be evident as abnormalities on ultrasound)
- Raised creatinine
- Failure to respond to treatment with suitable antibiotics within 48 hours
- Infection with organisms other than *E. coli*
- Age – although this is a weak discriminator, it is a factor when considering further investigation in view of the greater susceptibility of infants and young children to renal scarring. Most paediatric urologists would continue to advise further investigation in boys presenting with UTI in the first 6 months of life, more with a view to the detection of reflux than urethral obstruction (which usually gives rise to detectable abnormalities on ultrasound)
- Recurrent infection, defined by the NICE guidelines as:
  - two or more episodes of UTI with acute pyelonephritis/upper urinary tract infection, or
  - one episode of UTI with acute pyelonephritis/upper urinary tract infection plus one or more episodes of UTI with cystitis/lower urinary tract infection, or
  - three or more episodes of UTI with cystitis/lower urinary tract infection

the age of the child. The most widely used investigations are DMSA (and MCUG if VUR is suspected) or mercaptoacetyltriglycine (MAG3) in the case of suspected upper tract obstruction.

In the majority of cases, however, ultrasonography is normal, in part because of the high false-negative rates in the detection of renal scarring and mild to moderate reflux. For example, grade III VUR is associated with a false-negative rate of 25–50%, whereas renal scarring is missed on ultrasound in 15–45% of cases.

The most controversial aspects of diagnostic imaging therefore relate to children with urinary infection whose ultrasound findings are normal.

Indications for further imaging

The 2007 NICE guidelines advocate a far more limited use of DMSA and MCUG than was practised previously. For example, according to the NICE guidelines, DMSA and MCUG are no longer routinely indicated for infants under 6 months of age whose urinary infection 'responds well to treatment within 48 hours'.

Likewise, for children in the age range 6 months to 3 years with normal ultrasound findings the NICE guidelines recommend that DMSA should be reserved for those with recurrent or 'atypical' UTIs, as defined by the criteria listed in Table 4.6.

However, many children are treated initially with antibiotics in a community setting and it may be difficult to establish in retrospect whether their UTI was accompanied by fever or not. Similarly, when children are seen for the first time as outpatients it may not be apparent from the information accompanying the referral whether their UTI 'responded well to treatment within 48 hours'. Ultrasound is not a sensitive test for renal scarring in young children and it has been argued by the critics of the guidelines that without a DMSA scan many children with scarring and underlying VUR will be missed. However, the guidelines do envisage an MCUG for younger children in whom there is evidence of dilatation on ultrasound, a family history of VUR or a non-*E. coli* infection.

For urologists, perhaps the most contentious aspect of the NICE guidelines relates to the imaging schedule for children aged 3 years and

upwards which makes no provision for an MCUG, even for children with recurrent or 'atypical' UTIs. In view of the well-documented failings of ultrasound as a means of detecting low-to-moderate grade VUR, it is evident that many children with these grades of VUR will be missed on the imaging protocol recommended by NICE. Does this matter? Although the risk of new scarring is admittedly low in children aged 3 years, it undoubtedly occurs. Moreover, scarring is not the only factor of importance when considering possible investigation for VUR. Children whose VUR is associated with urinary infection may experience recurrent episodes of symptoms and ill health which interferes with schooling and generates considerable anxiety within the family. For these reasons, it seems likely that the majority of paediatric urologists will continue to consider an MCUG for older children experiencing recurrent symptomatic UTIs since the information on whether or not they have reflux is clinically relevant to the management options, particularly endoscopic correction.

Some suggested imaging protocols incorporating modified NICE guidelines are illustrated in Figures 4.2a, 4.2b and 4.2c.

Management

Initial management

Older children and those with mild to moderate UTI are mostly treated by their general practitioner in the first instance and then referred subsequently for investigation on an outpatient basis. However, the NICE guidelines recommend that infants under 3 months of age and older children with a clinical picture of pyelonephritis should be referred promptly to a paediatric specialist.

For infants under 3 months of age and for older children with presumed pyelonephritis (the groups at particular risk of renal scarring) treatment usually comprises an intravenously administered antibiotic such as cefotaxime or ceftriaxone. The NICE guidelines recommend intravenous (IV) antibiotics for 2–4 days followed by an oral antibiotic for a total duration of 10 days. If an aminoglycoside such as gentamicin is used, it is important to monitor blood levels.

Alternatively, oral antibiotics may be considered (e.g. a 7–10-day course of cephalosporin or co-amoxiclav) depending upon the severity of the clinical picture.

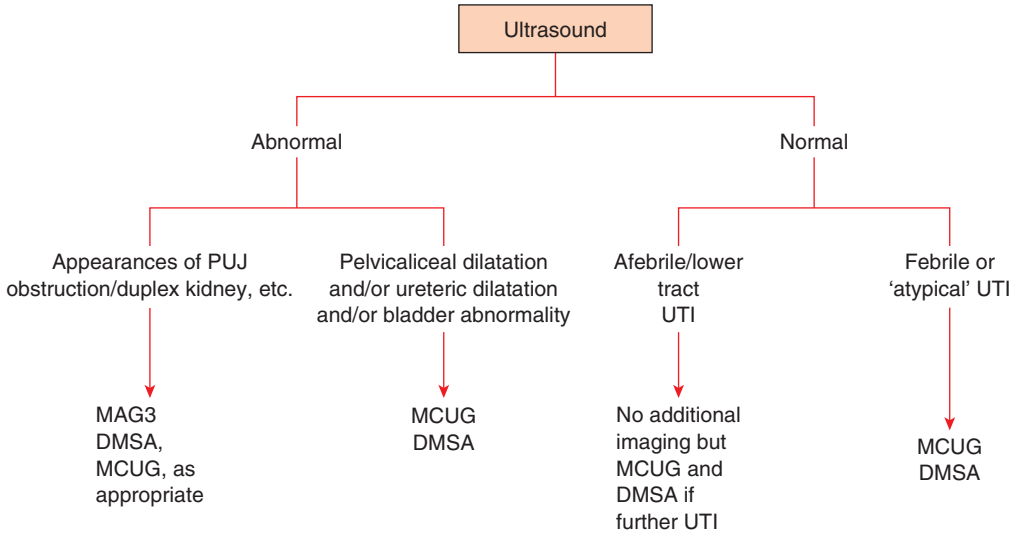

Figure 4.2a Imaging protocol incorporating modified NICE guidelines for infants aged 0–6 months.

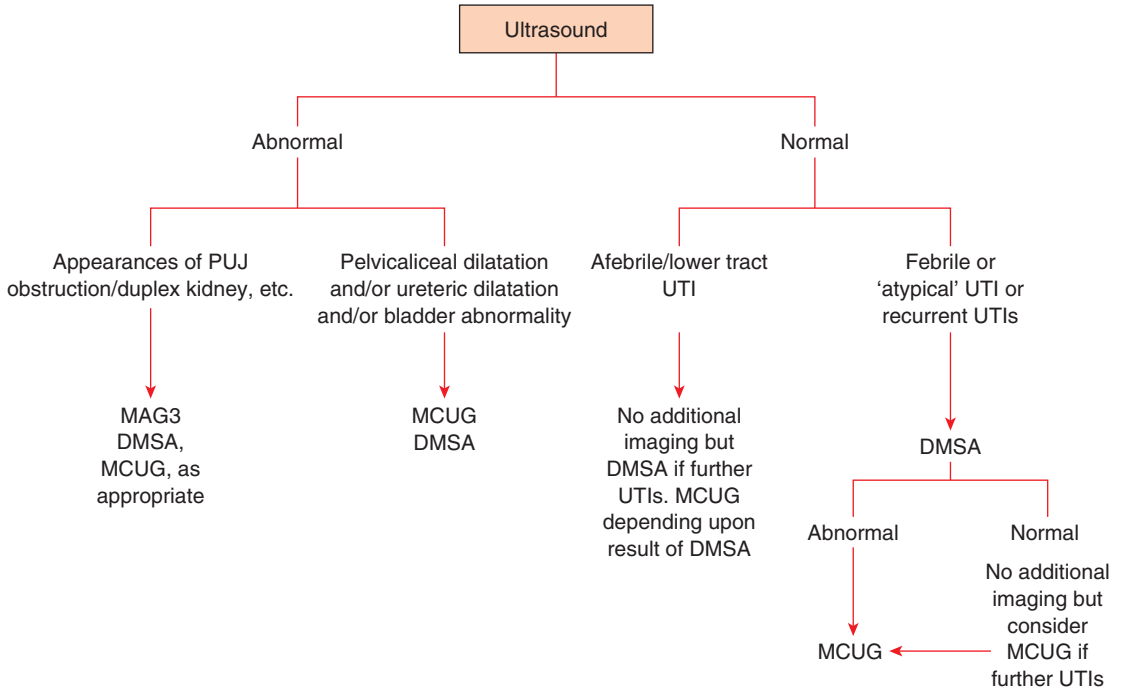

Figure 4.2b Imaging protocol incorporating modified NICE guidelines for young children aged 6 months to 3 years.

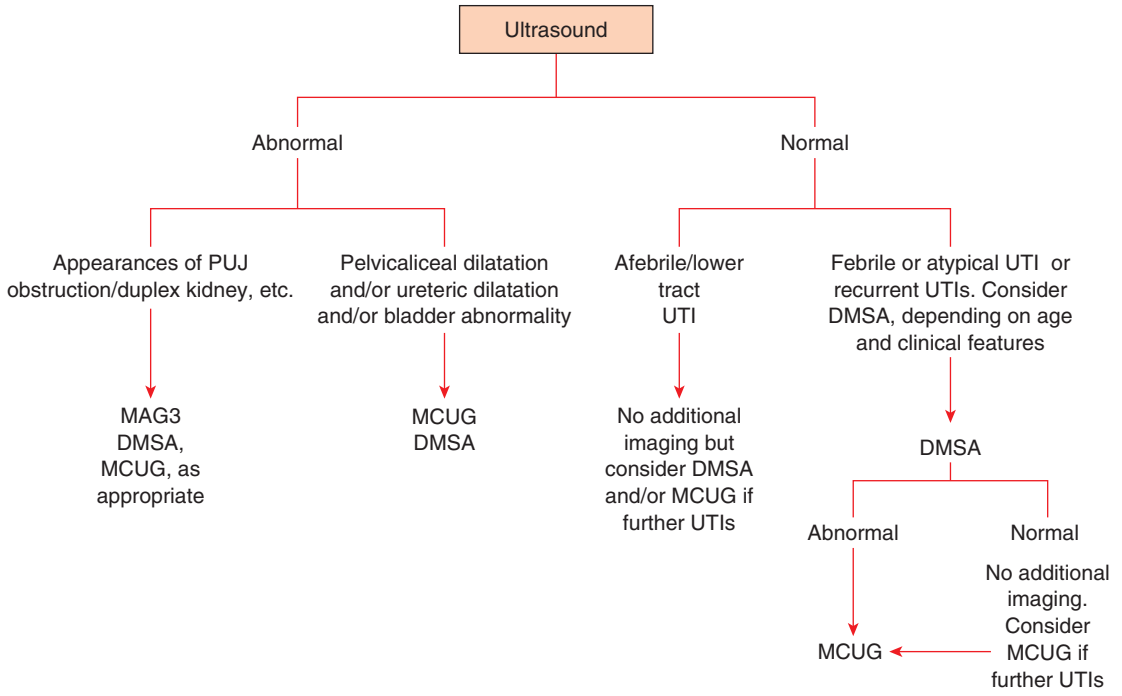

Figure 4.2c Imaging protocol incorporating modified NICE guidelines for children aged 3 years and upwards.

An early ultrasound scan is advisable in all children admitted to hospital since they may have an abnormality needing urgent drainage before the infection can be brought under control. Examples include upper tract obstruction complicated by pyonephrosis for which percutaneous nephrostomy is required or, rarely, infravesical obstruction requiring percutaneous suprapubic catheterisation.

Oral antibiotics are the first-line treatment for afebrile, lower urinary tract infection after the age of 3 months. Although the NICE guidelines advocate a course of an agent such as trimethoprim, cephalosporin, nitrofurantoin or amoxicillin limited to 3 days, many clinicians still favour a longer course. The antibiotic should be switched to a more appropriate alternative if this is indicated by the results of sensitivities obtained from the MSU.

Longer-term management

In a small number of children investigations will identify a significant urinary tract abnormality requiring surgical intervention or other ongoing management. However, the majority of children do not fall into this category and most do not require routine urological follow-up. Nevertheless, some children, predominantly girls, are troubled by recurrent UTIs despite the absence of any underlying urological abnormality. For these children it is essential to identify and treat any predisposing factors, of which dysfunctional voiding is by far the most important (see Chapter 12). The role of constipation is more difficult to define, but there is undoubtedly an association between these two 'elimination disorders'.

Treatment is aimed at establishing a routine of regular and complete voiding coupled with measures designed to break the cycle of 'holding back' in children who also have habitual constipation. Even in the absence of VUR, a period of antibiotic prophylaxis may be helpful in breaking the cycle of infection and allowing the bladder to settle down.

Other conservative measures

The parents of children with recurrent UTI are very keen to do whatever they can to prevent further infections. In recent years cranberry juice has become increasingly popular as prophylaxis against infection and although robust evidence demonstrating its effectiveness in children is lacking, some benefit has been shown in adult women. Probiotic yoghurts have also increased in popularity and, while there is little in the way of scientific evidence supporting their use, anecdotally they do seem to be effective in some children. If parents do opt for these alternative therapies, this should not be at the expense of the three most important measures – increased fluid intake, treatment of constipation and, most importantly, treatment of voiding dysfunction to improve the frequency and effectiveness of bladder emptying.

Key points

- Urinary tract infection is one of the commonest disorders of childhood and many more children with relatively asymptomatic lower tract urinary infections are now being referred for investigation than in the past.
- Care is needed to obtain an uncontaminated urine sample for reagent dipstick testing and microscopy and culture whenever possible.
- It is important to confirm the diagnosis of urinary infection before submitting a child to any investigation more invasive than ultrasonography.
- Ultrasonography is the investigation of first choice, but it is not a sensitive test for detecting vesicoureteric reflux and scarring.

- Further investigation is indicated if the initial ultrasound scan reveals an abnormality of the urinary tract. The choice of further imaging tests is guided largely by the ultrasound appearances.
- Further investigation (to look primarily for vesicoureteric reflux and/or renal scarring) may also be justified despite normal ultrasound findings. The indications for further investigation and the choice of imaging are determined by the age of the child, severity of infection and factors such as family history.
- Dysfunctional voiding is an important factor predisposing to lower tract urinary infection in girls with normal urinary tracts. Management should be directed towards improving voiding function and treating constipation when present.

Further reading

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Vesicoureteric reflux

5

David FM Thomas and Ram Subramaniam

Topics covered
Aetiology and genetic basis of reflux
Reflux nephropathy
Clinical features
Investigation; diagnostic imaging
Conservative management
Endoscopic correction and other surgical options
Current controversies

Introduction

Reflux can be defined as the retrograde flow of urine within the upper urinary tract. Whereas the term is often used synonymously with vesicoureteric reflux (VUR), it can also occur at the level of the renal papilla – intrarenal reflux (IRR).

VUR is not a single pathological entity; rather, it represents a pattern of disordered function which has different causes, exhibits varying patterns of natural history and has a broad spectrum of clinical significance.

When complicated by urinary tract infection in childhood, VUR is an important cause of symptomatic ill health, which, if undiagnosed and untreated can result in failure to thrive. In the longer term, renal scarring (reflux nephropathy) poses threats of late morbidity which include hypertension, complications of pregnancy, renal impairment and end-stage renal failure.

During the last two decades the conventional management of VUR has been based upon experimental and clinical studies undertaken in the 1970s and early 1980s. More recently, some of the accepted principles of management have been challenged by the findings of newer studies and the introduction of new treatment modalities. After a period of two or three decades which saw a broad consensus on the investigation and management of VUR, this common urological condition of childhood is once again generating controversy.

The aim of this chapter is to summarise what is known of the aetiology, pathophysiology and natural history of VUR and to provide an overview of current thinking on the clinical management. In addition, it will highlight some of the current controversies and areas of research.

Aetiology of vesicoureteric reflux

The anatomy of a normal vesicoureteric junction provides a valvular mechanism which prevents the retrograde flow of urine into the upper tract, even at increased pressure during voiding. The terminal ureter transverses the bladder wall and runs in a submucosal tunnel to open on the trigone. This anatomical arrangement imparts a flap-valve mechanism in which the intramural and submucosal portions of the distal ureter are compressed against the backing of the detrusor muscle by the pressure of urine within the bladder. The competence of this passive flap-valve mechanism may be reinforced at the time of voiding by active elongation of the intravesical ureter within a Waldeyer's sheath. In addition, there is experimental evidence to suggest that concentric contraction of smooth muscle within the distal ureteric wall may confer a further active protection against reflux.

In children with significant primary VUR, the ureteric orifice is characteristically located laterally

on the base of the bladder rather than in the normal anatomical position on the trigone. The resulting length of intramural and submucosal ureter is shorter, creating a deficiency of the flap-valve mechanism. Both the absolute and relative lengths of the submucosal tunnel tend to increase with age, thus accounting for the spontaneous resolution of VUR.

Ureteric duplication provides a clear example of the role of the ureteric bud as a crucial determinant of the position of the ureteric orifice and the potential for reflux.

Classification of vesicoureteric reflux

Reflux has been traditionally classified into primary and secondary VUR.

Primary VUR

This form of VUR is due to an anatomical abnormality of the vesicoureteric junction, which results in weakness of the normal flap-valve antireflux mechanism described above.

Secondary VUR

The term secondary VUR describes VUR associated with abnormal bladder function and elevated intravesical pressure due to conditions such as neuropathic bladder (Figure 5.1) and posterior urethral valves. Secondary VUR has a tendency to resolve when bladder pressures are restored to more physiological levels: for example, after bladder augmentation for neuropathic bladder or following resection of posterior urethral valves.

VUR and voiding dysfunction

It is now apparent that the traditional distinction between primary and secondary VUR was oversimplistic. Non-neuropathic bladder dysfunction is now thought to play a significant role in the aetiology of many instances of so-called 'primary VUR' (Figure 5.2). This is particularly true of girls

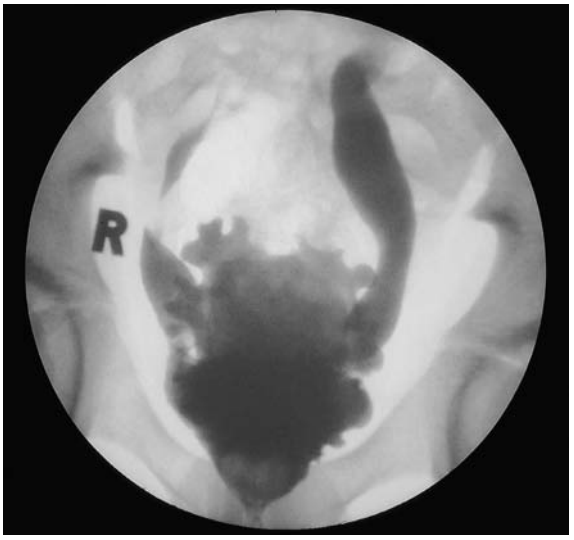

Figure 5.1 Secondary reflux. Characteristic appearances of reflux associated with trabeculated neuropathic bladder in a child with spina bifida.

with low-grade VUR in whom voiding dysfunction (characterised by detrusor instability or detrusor–sphincter dyssynergia) is coupled with 'borderline' competence of the ureterovesical junction. Typically, these girls present with daytime wetting and urinary infection (Figure 5.3).

The aetiology of high-grade primary VUR in infant boys, which had previously been regarded as a purely anatomical abnormality, has been called into question by the findings of urodynamic studies revealing markedly elevated intravesical pressures. Moreover, appearances of increased bladder wall thickness on ultrasound and subtle radiological abnormalities in the urethra have also been invoked as possible evidence of transient intravesical obstruction in utero.

There is growing evidence of a two-way interaction between VUR and bladder function in some patients with high-grade reflux. At the time of voiding, large volumes of urine reflux into the capacious dilated upper tracts, thus impairing the efficiency of bladder emptying. Urine which has refluxed into the upper tracts then returns to the bladder to refill it almost immediately after voiding. In these circumstances, it is very difficult

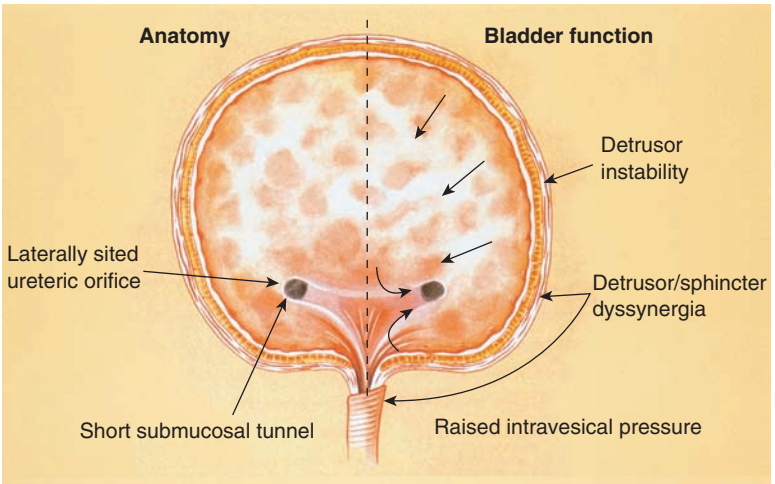

Figure 5.2 The balance between functional and anatomical factors in the aetiology of VUR.

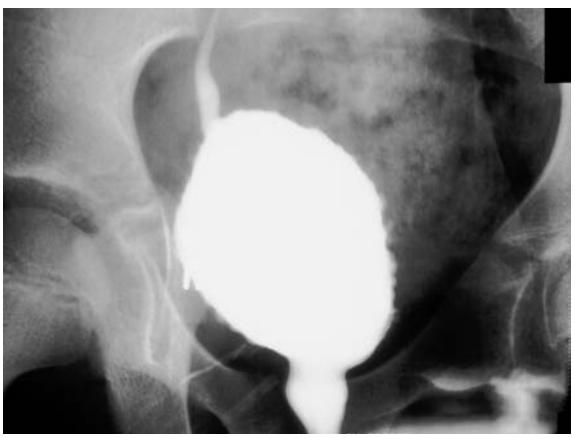

Figure 5.3 Micturating cystourethrogram illustrating the importance of bladder dysfunction in the aetiology of 'primary' VUR. Five-year-old girl presenting with wetting and recurrent UTIs. No neurological abnormality. MCU demonstrates low-grade right VUR, fine trabeculation and probable sphincter–detrusor dyssynergia. Good response to antibiotic prophylaxis, anticholinergic and voiding regimen.

for the bladder to function effectively as a storage organ. Evidence is emerging to indicate that successful correction of the reflux can result in marked improvement in voiding function in some of these patients.

Incidence and genetic factors

Our knowledge of the incidence of VUR dates largely from studies undertaken in healthy children in the 1950s and 1960s which identified an incidence of 1–2% in the general paediatric population.

The familial component of VUR is well recognised. **VUR can be demonstrated in more than 30% of the infant siblings of children with known VUR, and in up to 50% of the offspring of affected parents.**

The mode of inheritance remains unclear but the high incidence of VUR in siblings and patterns of vertical transmission have previously been interpreted as evidence of autosomal dominant inheritance with variable penetrance.

Despite the widely accepted genetic basis of VUR, disappointing progress has been made in identifying the causative gene(s). Although mutation of the *PAX2* gene has been identified in some familial cases of VUR linked to a syndrome characterised by optic nerve defects, screening studies for *PAX2* mutations in children with non-syndromic VUR have yielded uniformly negative results. Likewise, screening studies in patients with primary VUR have failed to identify any evidence of mutations of other putative genes such as *AGTR2* or *UP3*.

Nevertheless, some valuable insights are emerging from genetic research. For example, a major research programme in Dublin has identified evidence of an X-linked form of familial VUR. Moreover, familial VUR in boys appears to carry a higher risk of congenital renal damage than girls, regardless of grade of reflux.

This is a rapidly changing area of research but current knowledge suggests that most instances of familial VUR result from the interaction of multiple genes rather than an isolated single gene mutation.

Gender differences

Important differences in the aetiology, natural history and presentation of VUR between boys and girls are summarised in Table 5.1.

Reflux nephropathy

Aetiology of reflux nephropathy

Infective

The experimental work published by Hodson and by Ransley and Risden in the 1970s identified the role of IRR in the aetiology of infective scarring. Whereas the conical outline of the normal renal papilla prevents the reflux of urine into the parenchyma from the collecting system, morphologically abnormal 'compound' papillae permit IRR. In the presence of VUR and lower tract infection, organisms are transported to the renal collecting system and parenchyma, where pyelonephritis and scarring ensue if the infection remains untreated. Fimbriated strains of *Escherichia coli* are particularly virulent because of their ability to adhere to urothelial surface receptors.

It is important to recognise, however, that while most renal scarring is associated with VUR, the appearances of postinfective scarring can occasionally be seen in children with no evidence of VUR. In such cases, it is assumed that either VUR was present previously but subsequently resolved or, alternatively, that scarring resulted from the occurrence of pyelonephritis (possibly by blood-borne infection) in a non-refluxing system.

Acquired renal scarring may coexist with pre-existing congenital renal damage. But once infection has supervened, it becomes virtually impossible to determine the relative contributions of congenital and acquired renal components, except in those cases which come to nephrectomy.

Table 5.1 Summary of gender-related differences in vesicoureteric reflux between males and females

Female
Presents clinically – usually with urinary infection
Peak incidence in early to mid-childhood – age 2–7 years
VUR generally low grade, i.e. grades I–III
Functional factors important in aetiology: dysfunctional voiding, detrusor instability, constipation
Male
Presents clinically or detected prenatally
Clinical presentation usually in infancy or early childhood – 0–2 years
Often moderate to high-grade VUR, i.e. grades III–V
Anatomical factors important in aetiology (+ intrauterine bladder dysfunction???)

Congenital

The prenatal detection of VUR provides an opportunity to study patterns of renal damage in infants and children (predominantly males with high-grade VUR) whose kidneys have never been exposed to infection. Sibling screening provides a further valuable means of investigating congenital reflux nephropathy.

The findings of these studies, coupled with other recent evidence, can be summarised as follows:

- Severe renal damage (renal dysplasia) is predominantly a feature of grade V reflux and is probably a consequence of faulty interaction between the ureteric bud and the metanephric blasphema (Figure 5.4).

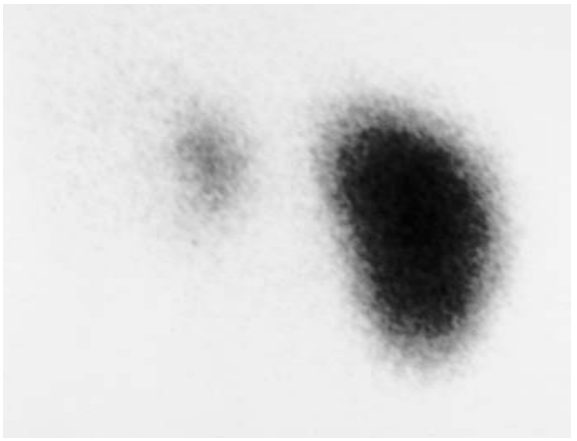

Figure 5.4 DMSA scan at around 1 month of age in an infant with unilateral grade V reflux detected prenatally; 9% differential function in the affected kidney. No urinary infection prior to DMSA imaging.

- Lesser degrees of congenital renal damage tend to take the form of global reduction in functioning renal tissue (renal hypoplasia) rather than focal scarring.
- The development of mild to moderate renal scarring appears to be mainly dependent on urinary tract infection.
- By contrast, congenital factors play a greater role in severe scarring, which is seen predominantly in conjunction with high-grade reflux, particularly in males.

Aetiology of Reflux Nephropathy: implications for management

Although a detailed review of the evidence is beyond the scope of this chapter, the key points can be summarised as follows:

- Reflux of sterile urine at physiological voiding pressures does not result in renal scarring and does not impede renal growth.
- The occurrence of pyelonephritis and development of renal scarring are not always related to VUR. In most instances, however, acquired renal scarring is the consequence of symptomatic upper tract infection associated with VUR and IRR.
- Renal scarring occurs maximally after the first episode of pyelonephritis (Ransley's 'big bang' hypothesis).
- The risk of renal scarring is greatest in infancy and early childhood.
- Conversely, the risk of infective scarring decreases significantly beyond the age of 4 years, although a small risk persists throughout childhood.
- Pyelonephritis is more likely to give rise to focal scarring of mild to moderate severity, whereas gross functional impairment is more commonly congenital in origin.
- To pose a risk of renal scarring, urinary infection must be sufficiently severe to give rise to symptomatic pyelonephritis. Asymptomatic bacteriuria, a relatively common finding in older girls, does not give rise to renal scarring.
- The bulk of infective scarring has already occurred when children are first diagnosed and are referred for investigation. Although fresh scars can develop thereafter, the risk is low providing surveillance is maintained and further infections do not go unrecognised or untreated.

Clinical significance of reflux nephropathy

Renal tissue which is congenitally dysplastic or has been scarred by pyelonephritis becomes non-functioning and, when extensive, results in significantly reduced overall renal functional reserve. Reflux nephropathy accounts for 22% of cases of end-stage renal failure in children and young people in the UK.

Even when renal damage is not sufficient to result in end-stage renal failure, long-term studies have demonstrated significant reduction in glomerular filtration rate (GFR) in individuals with bilateral scarring dating from childhood. Hyperperfusion and hyperfiltration damage in the remaining non-scarred tissue are believed to be the mechanisms largely responsible for progressive deterioration, leading to chronic renal failure.

The reported incidence of hypertension attributable to reflux nephropathy varies from less than

5% in paediatric studies to 25–40% in some late-outcome studies. However, it should be noted that the long-term studies have mostly looked at the outcome of patients who experienced severe urinary infections in childhood at a time when scarring was assessed by intravenous urography (IVU). It seems unlikely that the more subtle scars which can now be identified by the more sensitive modality of dimercaptosuccinic acid (DMSA) imaging will carry a comparable long-term risk of hypertension.

In one large UK study of children with hypertension, reflux nephropathy was the most common single cause, accounting for 14% of cases. For an individual child with evidence of renal scarring, the risk of progressing to renal failure is difficult to quantify, but is currently likely to be substantially less than the figure of 0.1% historically quoted in the literature.

Presentation of vesicoureteric reflux

Symptomatic

Symptomatic **urinary tract infection (UTI)** remains by far the commonest form of clinical presentation. The incidence of VUR in children undergoing investigation for UTIs is traditionally quoted as around 30%. However, this figure dates from a time when children being referred for investigation tended to have infections at the more severe end of the spectrum. Nowadays, the increased awareness of UTI amongst general practitioners, coupled with the availability of simple sensitive diagnostic reagent stick tests, has resulted in far larger numbers of children being diagnosed with mild, predominantly lower tract infections.

It would be difficult to document the incidence of VUR in children currently being diagnosed with UTI because the indications for micturating cystourethrography (MCU) are far more selective.

Pain is not generally regarded as a symptom of primary VUR. However, loin pain is a well-recognised feature of **pyelonephritis** and the occurrence of pain may also signal the presence of **secondary pelviureteric junction** obstruction or some other complicating factor.

VUR occasionally comes to light for the first time in individuals presenting with **renal insufficiency and/or hypertension** who have little, if any, history of urinary infection. Congenital nephropathy and renal dysplasia are the most likely explanations in this situation.

Asymptomatic

The term 'prenatally diagnosed VUR' describes a diagnostic sequence in which prenatally detected dilatation of the fetal urinary tract leads to postnatal investigations which may include MCU.

Primary VUR (usually of moderate to high grade) accounts for 15–20% of clinically significant prenatally detected uropathies. Published reports of prenatally detected VUR have consistently identified a predominance of males, with a male to female ratio of around 5 to 1.

Asymptomatic VUR also comes to light during the course of sibling screening. Data derived from 159 families with known familial reflux demonstrated that sisters of index female patients had a significantly higher incidence of reflux than brothers of female patients. The Dublin group also found that when reflux occurred in brothers, it tended to be high grade and carried a greater risk of congenital renal damage.

Investigations

The investigations of urinary tract infection are described in more detail in Chapters 3 and 4. The following diagnostic considerations apply specifically to VUR.

Ultrasound

Although non-invasive, ultrasound has a high false-negative rate when used as the first-line test for the investigation of urinary infections in children. Comparing ultrasound and MCU in 272

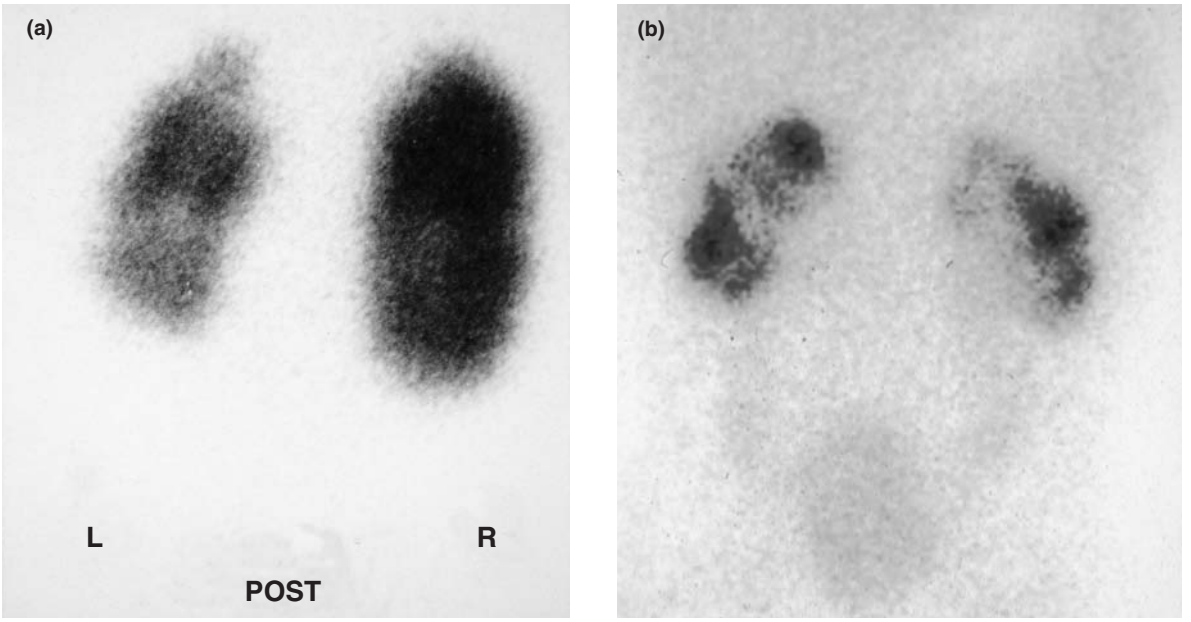

Figure 5.5 (a) DMSA scan demonstrating renal scarring with patchy cortical damage to the left kidney on initial investigation of a child presenting with urinary infection. (b) DMSA demonstrating bilateral focal scarring in a boy with bilateral VUR and a history of recurrent pyelonephritis. Differential function: 51% left; 49% right. Differential function is an unreliable guide to individual kidney function in the presence of symmetrical renal damage.

refluxing units, one large American study found normal ultrasound appearances in 201 (74%). Of the refluxing units missed on ultrasound, 28% were grade III VUR or higher.

DMSA

DMSA is the most sensitive modality for visualising scarring and quantifying differential renal function (Figure 5.5a and b). It is not, however, a test for VUR per se. Indeed, as a means of indirectly identifying children with VUR, the sensitivity of DMSA is less than 50%. In practice this high false-negative rate may not be too important since there is growing evidence that VUR associated with normal DMSA findings is generally low-grade reflux with a high spontaneous resolution rate. Moreover, there is also some evidence to suggest that kidneys exposed to VUR which nevertheless appear normal on the initial DMSA scan are less susceptible to scarring.

Micturating cystourethrography

Although invasive, the conventional radiological contrast study remains the gold standard investigation for the diagnosis and evaluation of VUR. It permits accurate grading of the severity of VUR, which is important when assessing prognosis and planning treatment. The most widely used grading system is the one devised by the International Reflux Study Committee (Figure 5.6).

Unlike indirect isotope cystography, MCU permits anatomical visualisation: for example, of the male urethra, bladder trabeculation, paraureteric diverticula, etc.

The role of the MCU in follow-up is controversial, but as a rule this invasive investigation should only be performed if the findings are likely to influence management. An MCU need not be performed routinely after ureteric reimplantation, since this is an operation with a uniformly high

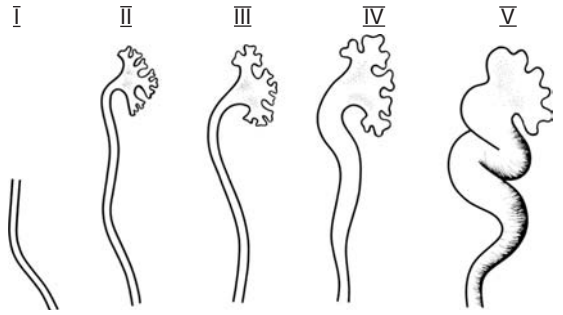

Figure 5.6 Grades of reflux (International Reflux Study Committee classification). Grade I: into ureter only; grade II: to upper tract (pelvic calyces), no dilatation; grade III: mild to moderate dilatation but minimal blunting of calyces; grade IV: moderate dilatation, loss of angles of fornices, papillary impressions in calyces still present; grade V: gross dilatation and tortuosity, and the impressions of papillae no longer visible.

success rate. Likewise, an MCU is not required before discontinuing prophylaxis in children who have been well and infection free.

Indirect micturating cystourethrography

This investigation, which utilises intravenously injected mercaptoactyletriglycine (MAG3), is less invasive than a contrast study since it does not require urethral catheterisation. However, it does entail the need for intravenous injection and exposure to radiation, albeit of a lower dosage than an MCU. The technique is best suited to children who have acquired bladder control and, conversely, is of much more limited value in infants and young children – the age group at the greatest risk of infective renal scarring. A further drawback is that indirect cystography is considerably less sensitive than a contrast MCU for the detection of low-grade VUR.

The main role of indirect cystography is therefore as a follow-up investigation, particularly in older children.

Intravenous urography

Intravenous urography (IVU) is rarely performed, having been superseded by DMSA for the visualisation of renal scarring.

Videourodynamics

Videourodynamic investigations have been used for research studies and have demonstrated urodynamic evidence of voiding dysfunction in up to 50% of girls with low to moderate grade VUR. In routine clinical practice, however, there is little place for urodynamics except, perhaps, in cases associated with neuropathic bladder dysfunction.

Sibling screening

It would clearly be desirable to look for VUR in the siblings of children with known VUR and the offspring of affected parents. In practice, however, routine screening is limited by the lack of a reliable non-invasive screening test. Ultrasound has a high false-negative rate; indirect nuclear cystography is unsuited to use in young infants; and contrast micturating cystography is an invasive investigation which carries a risk of morbidity in this age group. Ideally, the options, benefits and potential drawbacks should be discussed with parents of siblings of children with known VUR.

Despite limited sensitivity for the detection of low or moderate grades of VUR, ultrasound is a reasonable first-line screening test. If this is negative or if parents opt to forego screening, it is important that they and the general practitioner are aware of the importance of checking an MSU promptly if there is any suspicion of UTI or unexplained febrile illness. Screening is most worthwhile in the first year of life but, conversely, serves little useful purpose in siblings who are already beyond the age of 5 years.

Management of VUR

The rationale for medical or 'conservative' management is based on the evidence that sterile

Table 5.2 Distribution of grades of reflux and spontaneous resolution for each grade in 844 refluxing ureters. Data from the Children's Hospital National Medical Centre, Washington. Skoog SJ, Bellman AB, Majd M, 1987

Grade of reflux	Distribution of different grades of reflux (%)	Spontaneous resolution rate for each grade (%)
I	7	83
II	53	60
III	32	46
IV	6	9
V	2	0

VUR does not give rise to renal scarring, coupled with the well-documented tendency for mild or moderate VUR to resolve spontaneously (Table 5.2).

Conservative or 'medical' management

The conventional approach to medical management comprises:

- **Continuous antibiotic prophylaxis**: typically, trimethoprim 1–2 mg/kg/day, usually as a single night-time dose.
- **Urine surveillance**: the availability of reagent strips which test for nitrites and leucocytes make it much easier for parents or general practitioners to make a provisional diagnosis. Nevertheless, wherever possible, a freshly collected midstream urine (MSU) specimen should be examined by microscopy and culture.
- **Treatment of any underlying bladder dysfunction**: a regular voiding regimen, including double voiding where there is evidence of significant postvoid residual on bladder ultrasound. Anticholinergics, e.g. oxybutynin, should be considered if there are symptoms suggesting detrusor instability.
- **Treatment of constipation**: similar to other forms of habitual constipation; i.e. a regimen comprising a faecal softener and a laxative, with the dosage titrated against the child's response.
- **Commitment**: medical management should not be confused with benign neglect. Parental commitment is vital to ensure compliance with the medical regimen. Older children must be motivated to modify their voiding habits to correct voiding dysfunction. Effective arrangements are needed to ensure that urine samples are collected and examined promptly to facilitate diagnosis and treatment of breakthrough infections. If this commitment is lacking or the necessary level of primary healthcare support is not available, surgical intervention may be preferable.

Controversies surrounding medical management

Although the pattern of medical management described above has been the mainstay of treatment since the 1970s, it is being increasingly challenged. A number of well-designed studies are underway or are planned to address a number of important questions. For example:

- **What is the most effective regimen for administering antibiotic prophylaxis** – continuous treatment with a single agent or alternating courses of two antibiotic agents?
- **Does continuous prophylaxis have any advantage over treatment of individual infections as and when they occur?** At least one randomised prospective controlled study failed to demonstrate a difference in the number of UTIs experienced by girls on prophylaxis compared with those who were not.
- **What is the optimum duration of prophylaxis?** (There is already a trend to earlier cessation

of prophylaxis – particularly in boys once they are out of nappies and have achieved bladder control.)

- **Can endoscopic treatment now be regarded as a reasonable first-line alternative to medical management in children with low to moderate grades of VUR?** Although low to moderate grade VUR has a high tendency to resolve spontaneously, it is also the case that these grades of VUR can usually be corrected with a single endoscopic injection. Opinion remains divided.
- **Finally** comes the contentious question – **is there any benefit in treating VUR at all?** This viewpoint cites evidence that severe reflux-related renal damage is largely congenital, and thus not amenable to treatment. Moreover, the low rate of new scars in children on follow-up can be advanced as evidence that most infective scarring has already occurred and that any further intervention is a waste of time.

These arguments can be countered by the large body of clinical and experimental evidence indicating that pyelonephritis does indeed cause renal scarring. Moreover, sibling studies have found a significantly higher incidence of renal damage in index patients (those whose VUR came to light following infection) compared with their infant siblings whose VUR has been detected by screening (i.e. before the occurrence of infection).

This finding can be interpreted as evidence that acquired infective damage is not uncommon.

Finally, the theoretical arguments for ignoring VUR tend to focus on renal scarring and renal failure, while ignoring the impact of recurrent infection and ill health on schooling and well-being of affected individuals in childhood.

Indications for surgical intervention

Indications for surgery are relative rather than absolute and fall into three broad categories:

Functional

The occurrence of symptomatic breakthrough infection despite medical management represents the most common indication to proceed to surgical intervention. The options are endoscopic treatment or ureteric reimplantation.

Anatomical

VUR that occurs in conjunction with abnormalities such as paraureteric diverticulum or ureteric duplication has a lower tendency to resolve than uncomplicated primary reflux. Nevertheless, the presence of VUR into the lower pole of a duplex system is not an automatic indication for surgical intervention. High-grade reflux (grade IV or V), which is associated with significant functional impairment in the ipsilateral kidney, is very unlikely to resolve spontaneously. Surgery (usually ureteric reimplantation) is a reasonable first-line option in such cases after the age of 12 months.

Parental preference

In the internet age, parents are increasingly aware of the arguments supporting early endoscopic treatment for low to moderate grade VUR as an alternative to long-term continuous antibiotic prophylaxis.

Endoscopic correction

Since the first experimental description in 1984, endoscopic correction of VUR has become an established and widely used form of management. Several implant materials have been used for subureteric injections, including polytetrafluoroethylene (PTFE, Teflon), collagen, polydimethylsiloxane (PDMS, Macroplastique), autologous chondrocytes and Deflux (dextranomer–hyaluronic acid copolymer).

The technique of subureteric injections was first popularised by O'Donnell and Puri who published high success rates for the correction of VUR using Teflon as the injectable implant material. The

suburetic injection of Teflon acquired the acronym of the STING procedure.

Implant material

Teflon paste is a suspension of PTFE particles in glycerin. It is inert, highly crystalline and has a low coefficient of friction. After injection, the glycerin is absorbed into the tissues, the implant achieves a firm consistency and is subsequently encapsulated by thin fibrous tissue. Following the introduction of the STING procedure, concerns were expressed regarding the potential for distant migration of PTFE particles. These concerns centred on the non-biodegradable nature of PTFE and the findings of animal studies. (Although these have been challenged by other authors.)

Dextranomer–hyaluronic acid copolymer (Deflux) consists of dextranomer microspheres of an average size of 80–250 μm in sodium hyaluronate: 1 ml of the mixture consists of 0.5 ml microspheres and 0.5 ml sodium hyaluronate. Experimental work has shown that by 1 year the microspheres are surrounded by fibroblasts and collagen. This biodegradable substance has been extensively tested and, so far, there has been no evidence of immunogenic properties or potential for malignant transformation.

Macroplastique (PDMS) consists of a paste of silicone particles whose size is designed to prevent migration.

Because of its availability, ease of injection and the low theoretical risks of particle migration, Deflux is currently the most widely used injectable material.

Technique of injection

Under general anaesthesia, a cystoscope with a working channel (9–14 Fr) is introduced into the bladder. Under direct vision, a rigid or flexible needle is introduced through the working channel and advanced under the mucosa at a 6 o'clock position at the ureteric orifice (Figure 5.7a). If the refluxing ureteric orifice is wide enough to admit the tip of the scope, then an intraureteric injection is preferred. The implant is injected until a mound or 'volcanic' bulge is visualised (Figure 5.7b). The endpoint is reached when the ureteric orifice is elevated sufficiently as to create a crescent-shaped or slit-like orifice at the top of the mound, which gives the appearance of a nipple (Figure 5.7c).

Once the injection is completed satisfactorily, the needle is left in place for a further 10–15 seconds to allow the gel to set. This is particularly important if Deflux is used. Multiple punctures in the mucosa are undesirable because they permit leakage of the implant and it becomes difficult to achieve the 'mound' configuration needed to achieve satisfactory correction of VUR.

Results

Some authors have reported success rates in excess of over 93% with endoscopic correction for reflux. However, a high percentage of patients in these reported series had low-grade reflux, which has a high potential for spontaneous resolution (and for which antibiotic prophylaxis may not always be warranted).

The use of endoscopic treatment for low-grade VUR has been heavily criticised by some paediatric urologists as unnecessary intervention. These criticisms have, however, been countered by the arguments that the need for prolonged administration of prophylactic antibiotics can be averted by a single day-case procedure. Between these points of view there is general acceptance that endoscopic correction has a distinct role in the algorithm of management of VUR, along with conservative management and surgical reimplantation.

Endoscopic correction is probably most beneficial in grade III–IV VUR associated with breakthrough UTIs. The indications for treating asymptomatic low or moderate grades VUR are more controversial. Endoscopic treatment is much less successful in correcting severe VUR (grade V) and reflux may persist despite repeated injections.

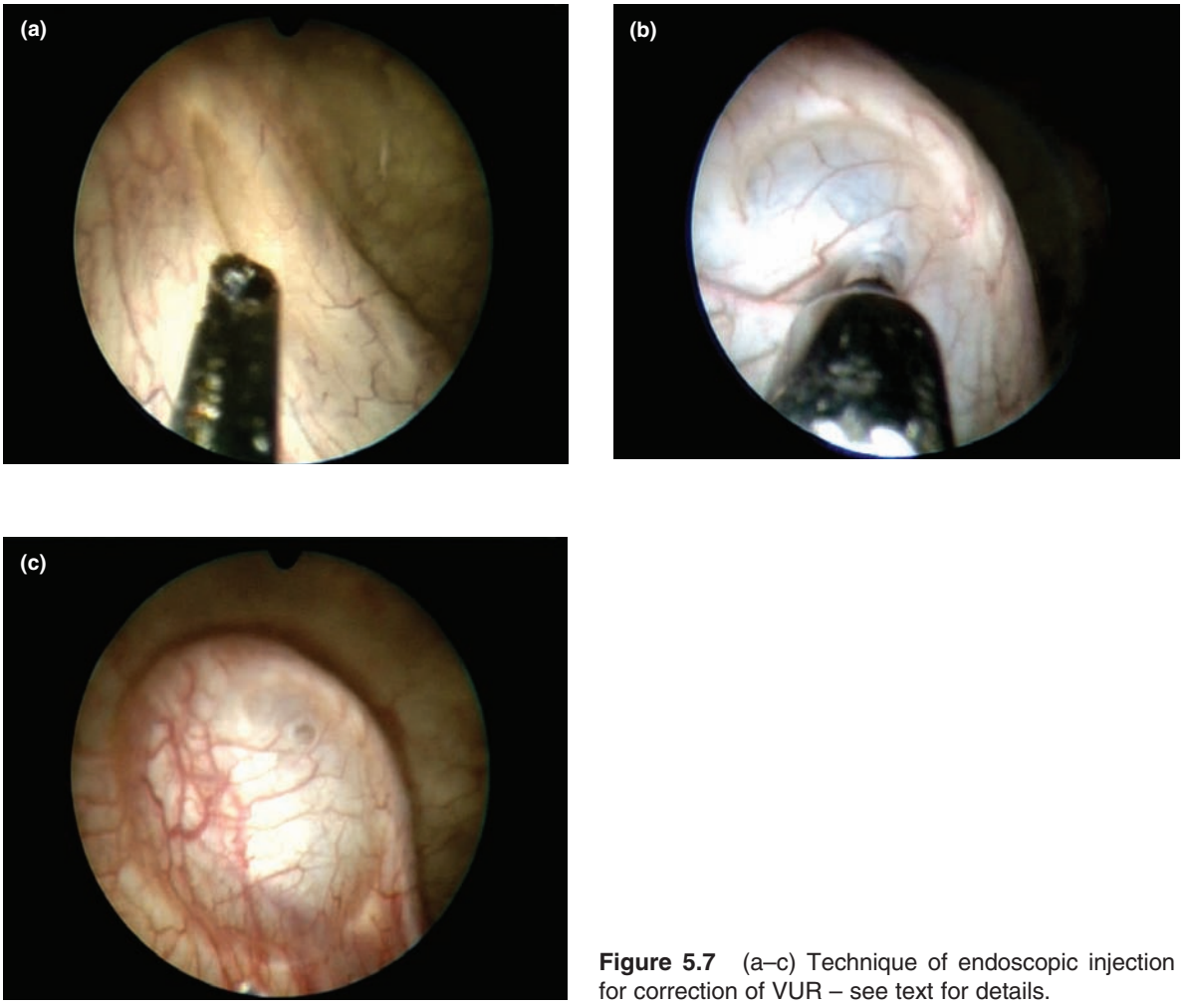

Figure 5.7 (a–c) Technique of endoscopic injection for correction of VUR – see text for details.

A study undertaken using data recorded on the Pediatric Health Information System in the United States reviewed over 4500 recorded antireflux procedures (open reimplantation and endoscopic correction) performed in children in 2002–2004. It was found that since the introduction of minimally invasive procedures the overall number of interventions for reflux had increased – although open surgery rates remained unchanged. From these findings, it is apparent that in the United States, at least, endoscopic correction is being increasingly favoured as an alternative to conservative management.

Ureteric reimplantation

The cross-trigonal advancement procedure devised by Cohen remains the open operation of choice for the majority of paediatric urologists (Figure 5.8). The appeal of this procedure lies in its relative simplicity, its high success rate in correcting VUR (97% or thereabouts) and the low incidence of postoperative obstruction.

Postoperative stenting of the reimplanted ureter is not routinely necessary, but the bladder is drained for a short period postoperatively with either a suprapubic or urethral catheter. Creating

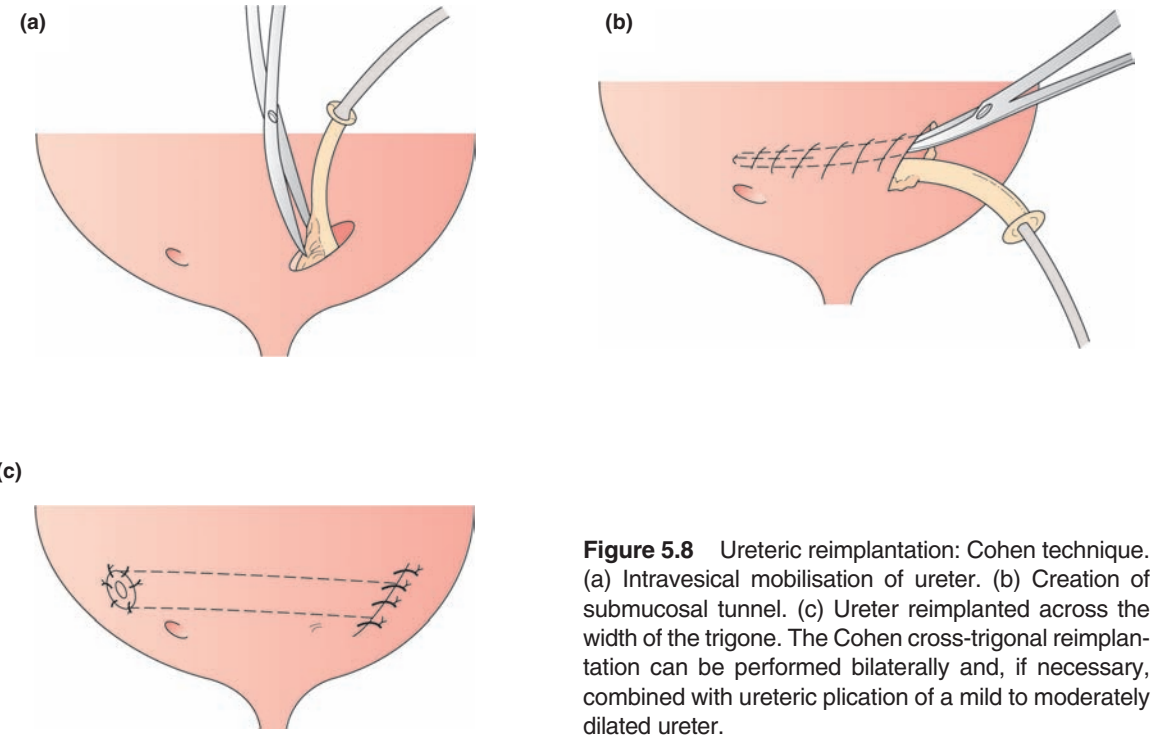

Figure 5.8 Ureteric reimplantation: Cohen technique. (a) Intravesical mobilisation of ureter. (b) Creation of submucosal tunnel. (c) Ureter reimplanted across the width of the trigone. The Cohen cross-trigonal reimplantation can be performed bilaterally and, if necessary, combined with ureteric plication of a mild to moderately dilated ureter.

an effective antireflux flap valve requires a submucosal tunnel with a length approximately three or four times greater than the diameter of the reimplanted ureter. Achieving this ratio when reimplanting a dilated ureter into a small bladder is not always technically feasible. In this situation, the diameter of the distal ureter can be reduced by plication, e.g. the Starr technique.

The Politano–Leadbetter type of reimplantation, coupled with a psoas hitch, is often preferable to the Cohen technique when reimplanting a grossly dilated megaureter.

Extravesical antireflux operations of the type originally described by Lich and Gregoir (Figure 5.9) are favoured by some paediatric urologists. The benefits centre on the reduced incidence of postoperative haematuria and discomfort. However, extravesical techniques are less suited to dilated ureters. There is also evidence of postoperative voiding dysfunction, which may amount to urinary retention in rare cases.

Endoscopic reimplantation

This technique is being developed in some specialist centres as a minimally invasive alternative to conventional open reimplantation. The bladder is filled with carbon dioxide and a Cohen reimplantation performed using endoscopes introduced percutaneously into the bladder. There is a considerable technical 'learning curve', but in skilled and experienced hands the results are comparable to those obtained by open surgery.

Alternatives to ureteric reimplantation

Circumcision

There is some anecdotal evidence that circumcision may be beneficial in reducing the incidence of urinary infection in boys with high-grade VUR. But in the absence of any formal prospective trial, there is insufficient evidence to justify routinely

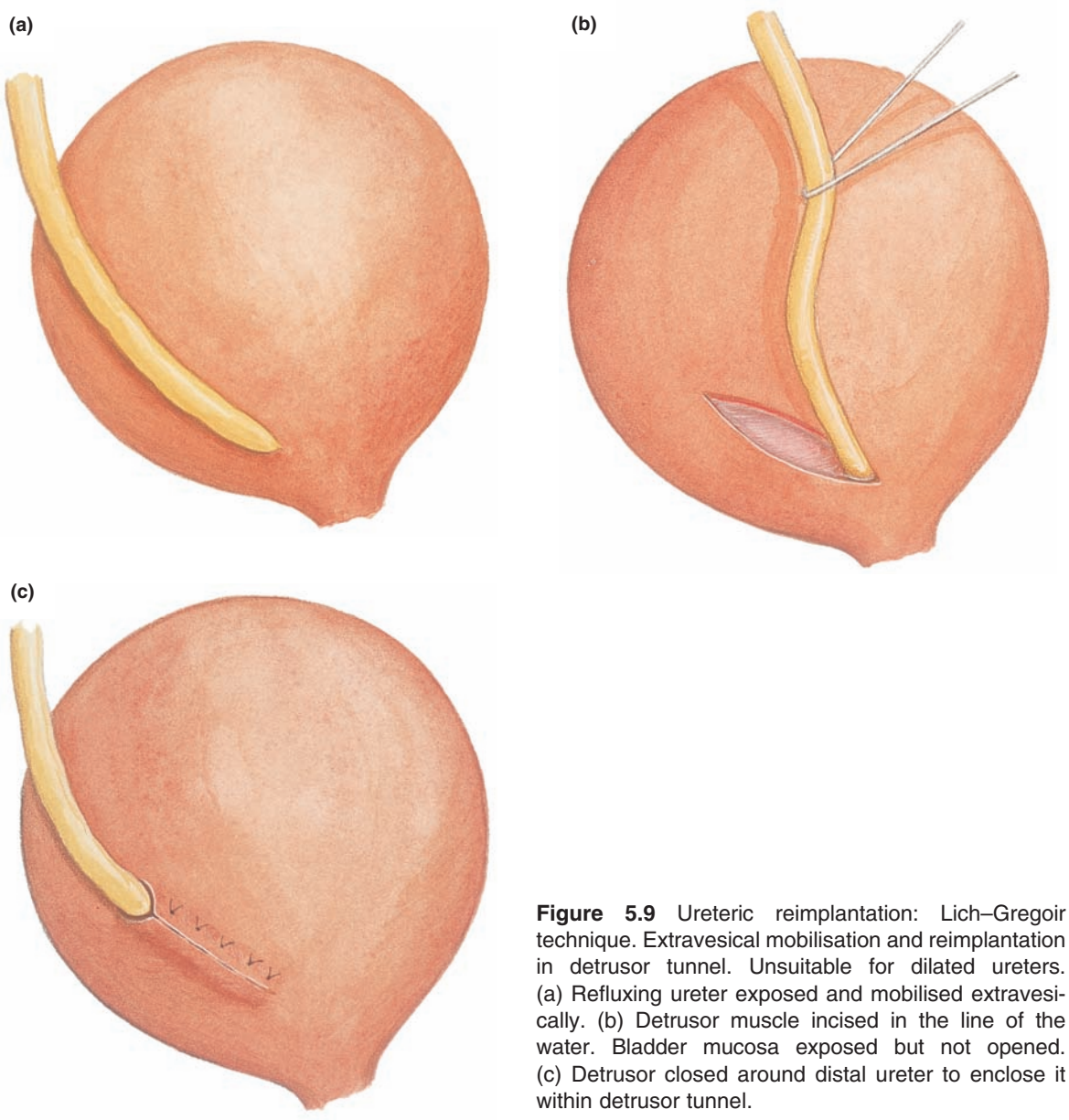

Figure 5.9 Ureteric reimplantation: Lich–Gregoir technique. Extravesical mobilisation and reimplantation in detrusor tunnel. Unsuitable for dilated ureters. (a) Refluxing ureter exposed and mobilised extravesically. (b) Detrusor muscle incised in the line of the water. Bladder mucosa exposed but not opened. (c) Detrusor closed around distal ureter to enclose it within detrusor tunnel.

performing 'prophylactic' circumcision on all boys with prenatally detected VUR or sibling VUR. Nevertheless, it is a reasonable option to consider on a selected basis.

Vesicostomy

The creation of a temporary bladder stoma is an effective way of decompressing the refluxing upper tracts and facilitating drainage. The procedure is well tolerated and the incidence of complications is low. Cutaneous vesicostomy has largely replaced ureterostomy in young infants whose VUR is complicated by sepsis or impaired renal function. Closure of the vesicostomy can be undertaken as an isolated procedure or in combination with definitive correction of VUR during the second or third year of life (Figure 5.10).

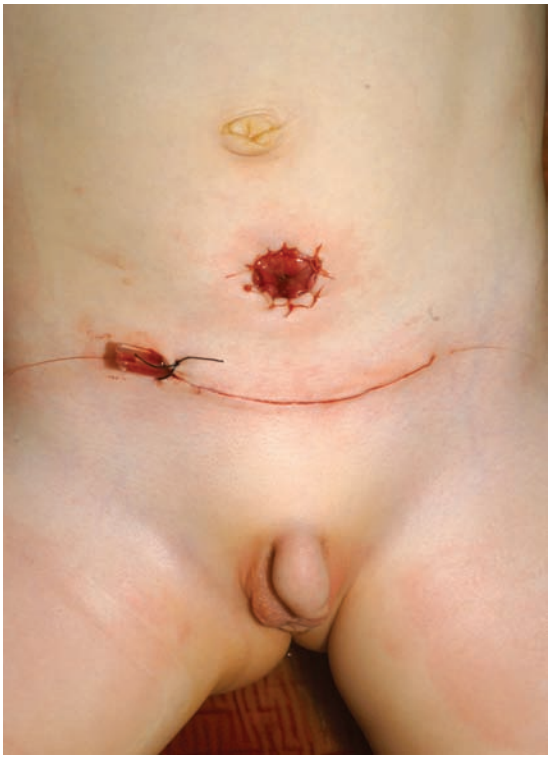

Figure 5.10 Immediate postoperative appearances of cutaneous vesicostomy performed in a male infant with high-grade primary VUR-breakthrough infections and failure of conservative management.

Nephroureterectomy

The role of nephrectomy is being reappraised in the light of concerns regarding the potential long-term risk of hyperfiltration damage to the remaining solitary kidney. However, this risk may be more than offset by the risk of hypertensive damage generated by a grossly scarred kidney which is left in situ.

The occurrence of infection strengthens the arguments for nephrectomy, particularly when differential function in the affected kidney is less than 10% and the contralateral kidney is normal.

When removing the kidney, it is also important to ensure that the ureter is also removed in its entirety to avert the risk of infection associated with a residual 'refluxing stump'. Removing the entire length of the ureter by open surgery usually requires two incisions, and for this reason laparoscopic nephroureterectomy is becoming an increasingly attractive alternative.

Transureteroureterostomy (TUU)

This is a useful procedure to manage recurrent VUR or ureteric obstruction following failed ureteric reimplantation. One ureter is reimplanted using the Politano–Leadbetter technique; the contralateral ureter is disconnected from the bladder, swung across the midline retroperitoneally and anastomosed to the reimplanted ureter.

Management of secondary VUR

Secondary VUR has a tendency to improve or resolve completely when more physiological bladder pressures have been restored by the treatment of outflow obstruction or bladder augmentation. Although it may occasionally prove necessary to resort to open antireflux surgery for secondary VUR, reimplanting dilating ureters into thick-walled neuropathic or 'valve' bladders can be technically difficult and is best avoided unless there are compelling indications. The failure rate (persisting reflux) and incidence of complications are both higher than for primary VUR.

As for primary VUR, however, the treatment algorithm has been changed by the introduction of an endoscopic treatment. Favourable results have been reported for endoscopic treatment and this approach is certainly a simpler alternative to open surgery in the thick-walled bladder.

Which is more effective: medical or surgical management?

Although a number of prospective controlled trials have been undertaken to answer this question, none have demonstrated a clear advantage of one treatment modality over the other.

An analysis of eight trials found no difference in the overall frequency of UTIs after 1–2 years and 5 years, although the incidence of febrile UTIs was lower following reimplantation. Controlled trials have not demonstrated any difference in the incidence of fresh renal scars, which in any event are relatively rare in both surgically and medically treated groups.

In everyday clinical practice, however, medical and surgical treatments do not prove equally effective. Whereas some children thrive and remain infection-free on antibiotic prophylaxis, others experience symptomatic breakthrough infections which are only controlled by endoscopic correction or ureteric reimplantation.

This paradox probably reflects the difficulty of designing trial methodologies to encompass the many different variables, which include age, gender, grade of reflux, patterns of bladder dysfunction, constipation, patient and parental compliance with voiding regimens and antibiotic prophylaxis, etc.

The principal conclusion that can be drawn from the trial data is that medical management can be safely adopted as the first-line treatment for the majority of children with VUR.

Surgical treatment is undertaken for specific indications. Nowadays, if there is an informed parental preference, endoscopic treatment may be considered as an alternative to long-term antibiotic prophylaxis.

Key points

- Voiding dysfunction plays an important role in the aetiology of 'primary' VUR, particularly in girls. Active treatment of voiding dysfunction is an important aspect of medical management.
- Reflux nephropathy may result from congenital damage (dysplasia), infective scarring or a combination of both.
- VUR is not a single entity. Management should be individualised to encompass individual contributory factors.
- Endoscopic correction is particularly indicated for moderate-grade reflux associated with breakthrough infection. The role of endoscopic correction as an alternative to long-term antibiotic prophylaxis for asymptomatic low-grade reflux is controversial.

Further reading

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Upper tract obstruction

6

David FM Thomas

Topics covered
Pathophysiology of acute and chronic upper tract obstruction
Diagnosis
Ultrasound
Isotope renography
Other modalities
Pelviureteric junction obstruction
Vesicoureteric junction obstruction

Introduction

Despite the important role of upper tract obstruction within paediatric and adult urology, there is no satisfactory scientific definition of what constitutes obstruction. One useful working definition, however, characterises obstruction as 'some impedence to the flow of urine, which causes gradual and progressive damage to the kidney'.

The terminology used by urologists and radiologists has not been helpful in advancing our understanding of obstruction, particularly when pathological and descriptive terms such as 'pelviureteric junction (PUJ) obstruction', 'idiopathic hydronephrosis' or 'vesicoureteric junction obstruction' and 'primary megaureter' have often been used interchangeably.

This confusion is exemplified by the use of the term 'hydronephrosis'. Although this is often used to denote pelviureteric junction obstruction, it is important to note that hydronephrosis is not a diagnosis in itself but a descriptive term denoting pathological dilatation of the renal pelvis and calyces. When this is accompanied by dilatation of the ureter, the corresponding term 'hydroureteronephrosis' is used. Hydronephrosis (upper tract dilatation), may be a feature of a number of acquired or developmental urological disorders, including:

- obstruction to urinary drainage
- vesicoureteric reflux
- dysplasia and developmental abnormalities of the upper urinary tract
- pathologically high urinary output (flow uropathy).

The introduction of isotope renography was a major advance in the diagnosis of obstruction, but even this can be unreliable or potentially misleading in certain clinical situations. In the absence of a precise scientific definition of obstruction or a universally reliable test, clinical decision-making will continue to depend upon information from a number of different investigations, each with its own limitations.

Pathophysiology of obstruction

Acute obstruction can be reproduced experimentally, thus allowing the sequence of physiological events within the obstructed kidney to be studied in some detail. However, acute obstruction is relatively uncommon in children and is generally the result of acute pelviureteric junction obstruction or impaction of a urinary calculus at the pelviureteric or vesicoureteric junction. Within the acutely obstructed kidney, urine is reabsorbed from the collecting system into the interstitium, intrarenal pressure rises and renal blood flow falls. Unless there is prompt relief of obstruction, progressive nephron damage supervenes, leading

to the loss of approximately 50% of functioning nephrons after 6 days and the irreversible loss of all renal function within 6 weeks. The timescale of renal damage is rapidly accelerated by the presence of urinary infection (pyonephrosis).

In clinical paediatric practice, chronic or intermittent obstruction is far more common than acute upper tract obstruction, but because of the difficulty in creating reliable experimental models we have far less understanding of the relevant pathophysiology. Investigating chronic or intermittent obstruction in a clinical setting is also more problematic and the risk of functional deterioration is more difficult to predict.

In the past, the majority of children with upper tract obstruction presented clinically with symptoms such as pain or urinary infection and the decision to advise surgical intervention was easier to justify.

However, with the advent of prenatal detection of upper tract dilatation, it has become apparent that mild to moderate upper tract dilatation is more prevalent in healthy, asymptomatic infants than was previously recognised. In many cases the presence of dilatation is not associated with active obstruction or renal impairment. In such cases, the natural history is often one of progressive improvement. Even when the presence of obstruction is established by appropriate investigation, the potential still exists for spontaneous resolution.

The natural history of asymptomatic upper tract obstruction is not always benign, and some obstructed kidneys are at undoubted risk of progressive functional deterioration which may prove irreversible. The paediatric urologist is therefore faced with the practical dilemma of distinguishing those infants whose dilatation/obstruction is destined to follow a benign course from those who are destined to suffer functional deterioration in the affected kidney unless the obstruction is relieved.

Investigation of upper tract obstruction

Although the presence of dilatation does not necessarily signify active obstruction, it is generally true that obstruction does not occur without evidence of dilatation. The early stage of acute obstruction, for example by an impacted calculus, is a rare exception to this rule.

Ultrasound

Nowadays, the diagnostic pathway almost invariably starts with the ultrasound finding of dilatation (Figure 6.1). It should be emphasised, however, that it is not possible to distinguish reliably between different causes of dilatation nor to establish the diagnosis of obstruction purely on the basis of ultrasound findings.

The measurement that has proved to be of most value is the anteroposterior (AP) diameter of the renal pelvis measured at the renal hilum. In the neonate, this figure should not normally exceed 6 mm. Significant obstruction that represents a threat to renal function is most unlikely to be present when the AP diameter is less than 15 mm. Conversely, an AP diameter exceeding 50 mm is almost invariably associated with diminished function, either at the time of initial assessment or during the course of follow-up.

The sensitivity of ultrasound in the diagnosis of obstruction can be enhanced by including an assessment of the renal cortex and the degree of calyceal dilatation.

Ureteric dilatation must always be regarded as an abnormal finding, as the normal-calibre ureter cannot be visualised on ultrasound.

Resistive index

Resistive index is measured by the use of a Doppler ultrasound probe directed at a branch of the renal artery. Studies aimed at identifying the correlation between resistive index and various parameters of obstruction have generally been unrewarding. Measurement of resistive index is not a sufficiently sensitive measure of obstruction to serve any useful role in clinical practice. In a different context, colour Doppler has also been used to visualise jets of urine emerging from the ureteric orifice. Whereas a correlation has been described between reduced frequency of ureteric jets and upper tract

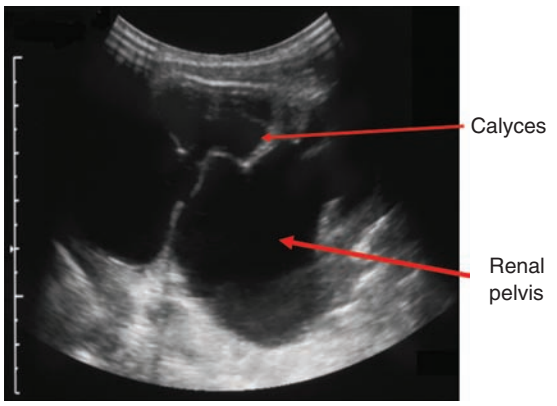


Figure 6.1 Postnatal ultrasound confirming antenatal ultrasound appearances of grossly hydronephrotic (dilated) right kidney with marked dilatation of renal pelvis and calyces with thinned cortex (renal pelvic AP diameter = 32 mm).

obstruction, it is unlikely that the technique will prove sufficiently sensitive to replace standard diagnostic modalities.

Isotope renography

Isotope renography is the principal investigation used to diagnose upper tract obstruction. Technetium-99m (^{99m}Tc) MAG3 (mercaptoacetyltriglycine) is the radiopharmaceutical agent of choice for this purpose and has largely replaced ^{99m}Tc DTPA (diethylenetriamine pentaacetic acid). ^{99m}Tc MAG3 has the advantage of superior gamma camera images to DTPA, coupled with faster clearance rate and lower background activity. Studies can be performed more rapidly and background subtraction calculations are easier. However, DTPA renography has the advantage that diagnostic imaging can be combined with a clearance study for the purpose of calculating glomerular filtration rate (GFR).

The following phases of the dynamic renogram are routinely analysed in the investigation of obstruction.

Differential renal function

Differential renal function is derived by comparing isotope uptake in the two kidneys, which in turn is a reflection of renal blood flow. Although ^{99m}Tc MAG3 is superior to DTPA for the calculation of differential function, static scintigraphy with DMSA (dimercaptosuccinic acid) remains the gold standard since it provides a more reproducible value for differential function, particularly when function is severely impaired. Regardless of whether differential function is assessed by ^{99m}Tc MAG3 or ^{99m}Tc DMSA, the values provide a comparative (i.e. differential) rather than absolute measure of renal function.

Renogram curves

Diuresis renography provides a means of distinguishing between obstructed and non-obstructed dilatation.

The characteristics of the uptake and drainage curves, as defined by O'Reilly and associates, fall into four patterns (Figure 6.2):

- Type 1. Normal uptake with prompt washout.
- Type 2. Rising uptake curve; no response to diuretic (obstruction).
- Type 3a. Initially rising curve, that falls rapidly in response to diuretic (non-obstructive dilatation).
- Type 3b. Initially rising curve which neither falls promptly nor continues to rise.

Whereas type 1 and type 3a curves are normal and non-obstructed, the clinical significance of type 2 and type 3b curves remains problematic. Drainage curves can be particularly difficult to interpret in the first few months of life (the period of so-called 'transitional nephrology') when immaturity of the renal tubules may impair the response of the kidney to diuretic stimulation. Many paediatric urologists have sought to overcome this difficulty by basing their decision on whether or not to proceed to pyeloplasty in infants with an asymptomatic, prenatally detected PUJ obstruction not on drainage curve data, but on differential function in the affected kidney.

Pressure/flow studies

Developed and popularised by Whitaker in the 1970s, this investigation was designed to quantify obstruction by measuring the hydrostatic pressure

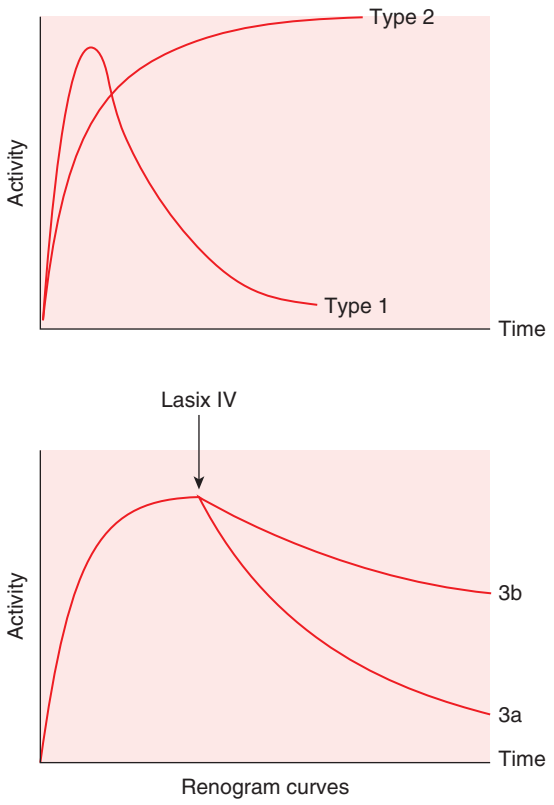


Figure 6.2 Patterns of uptake and drainage curves on isotope renography, as classified by O'Reilly and associates.

within the kidney when the collecting system is directly filled with fluid at different flow rates. It is an invasive investigation, requiring percutaneous renal puncture under general anaesthesia. Pressure/flow studies are now rarely performed, having been largely superseded by dynamic renography.

Intravenous urography

Although the intravenous urogram (IVU) has been superseded by dynamic renography, there are rare situations when it can provide valuable anatomical information which is not forthcoming from other imaging modalities. Examples include, PUJ obstruction in a duplex kidney (Figure 6.3), mid ureteric obstruction and retrocaval ureter, although this is also well demonstrated on computed tomography (CT) and magnetic resonance imaging (MRI).

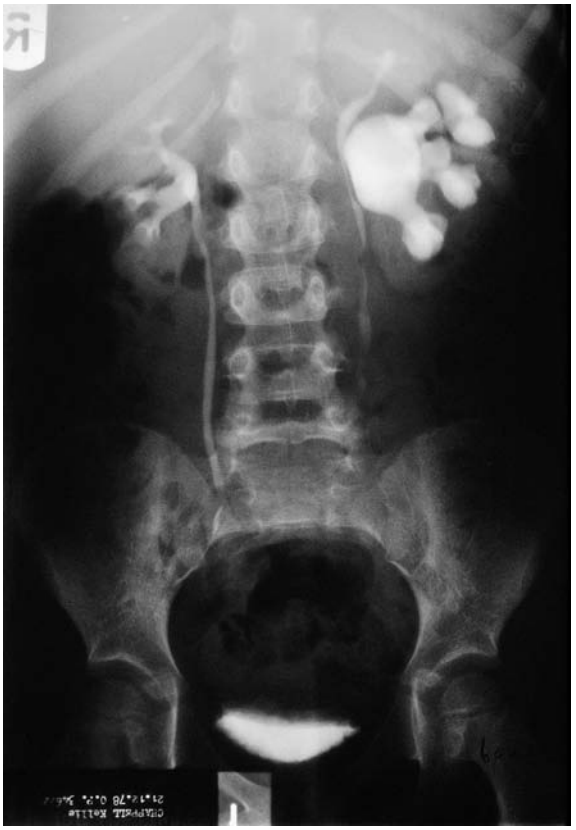


Figure 6.3 Intravenous urogram demonstrating dilatation confined to the lower pole of a duplex kidney (PUJ obstruction in an incomplete duplication – 'bifid system'). The IVU retains a useful role in delineating ureteric or caliceal anatomy in unusual variants of upper tract obstruction.

Magnetic resonance imaging (Figure 6.4)

Dynamic contrast-enhanced MR imaging has the potential to combine the anatomical information yielded by ultrasound with the functional information provided by renal scintigraphy. The information is provided by a single study that does not entail exposure of the child to ionising radiation. Practical drawbacks include the significantly higher cost and the requirement for general anaesthesia or sedation to facilitate MR imaging in infants and younger children. Furthermore, in its current stage of development, the information provided by the functional

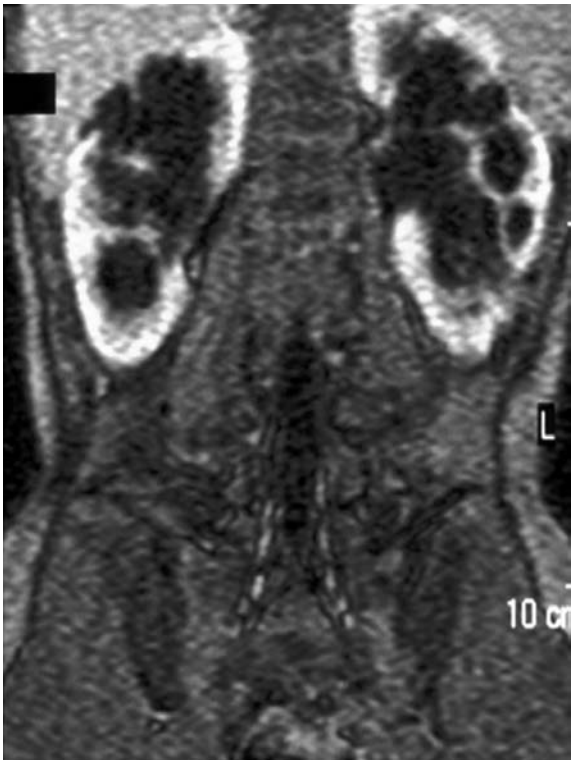


Figure 6.4 Magnetic resonance scan with contrast demonstrating bilateral PUJ obstruction.

component of dynamic contrast-enhanced MR is less reliable than the information on differential function and drainage provided by ^{99m}Tc MAG3.

Nevertheless, anyone who has seen the images produced by this new imaging modality cannot fail to be impressed by the quality of the anatomical detail. The technique is currently under evaluation in a number of specialist centres and it is too early to say whether the overall value of the additional information provided by dynamic contrast-enhanced MR will be sufficient to justify its widespread introduction as the gold standard investigation for obstruction.

It is quite possible that the information obtained at less cost from ultrasound and dynamic renography will be judged to be sufficient for the purposes of routine investigation.

Even if this proves to be the verdict on the use of MR in uncomplicated upper tract obstruction, this imaging modality will undoubtedly play a valuable role in helping to delineate the anatomy of unusual forms of obstruction such as retrocaval ureter.

Retrograde pyelography

Although this was once performed routinely to confirm the anatomical level of obstruction prior to surgery, it has been largely rendered redundant by the introduction of other imaging modalities, notably ultrasound. However, there are still occasional situations where a retrograde pyelogram may be very helpful in establishing the level of obstruction where this is in doubt.

Antegrade pyelography

Renal puncture under ultrasound guidance and the injection of contrast into the collecting system can be particularly helpful in visualising obstruction distal to the pelviureteric junction and also in the investigation of suspected recurrent PUJ obstruction following previous pyeloplasty.

Diagnostic pathway

In summary, the clinical investigation of the dilated upper tract is designed to answer the following questions:

- **Is the dilatation due to active obstruction?** Isotope renography is the first-line investigation, but other modalities may be needed to exclude reflux and non-obstructive dilatation.
- **At what anatomical level is the obstruction (and what is the most likely pathology)?** Ultrasound generally provides this information but contrast-enhanced MR urography should now be considered the next investigation of choice. Antegrade or retrograde pyelography may occasionally be required.
- **Is the function in the obstructed kidney sufficient to justify a conservative procedure**

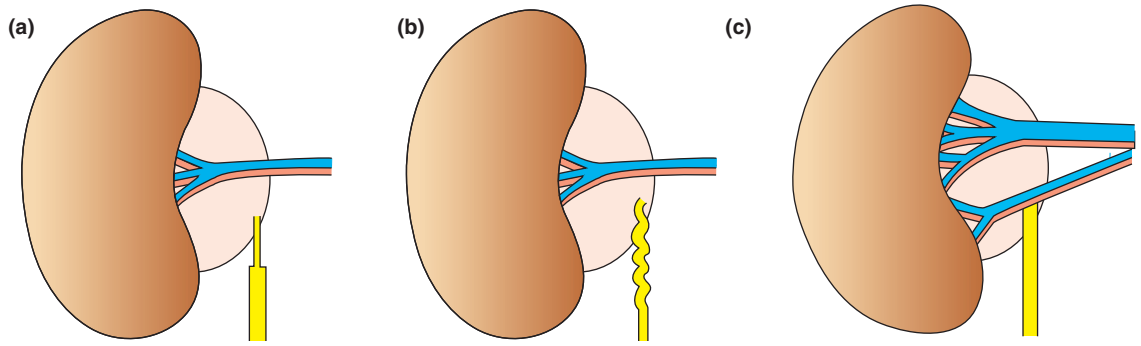


Figure 6.5 Aetiology of pelviureteric junction obstruction. (a) Intrinsic stenosis. Obstruction due to narrowing of a segment of ureter which is usually localised to the region of the pelviureteric junction but may extend over a length of several centimetres. (b) Ureteric folds. Tortuous segment of proximal ureter giving rise to varying degrees of obstruction. Straightening of this segment with growth may explain the spontaneous resolution of obstruction observed in a proportion of prenatally detected cases. (c) Extrinsic obstruction by crossing lower pole vessels.

or would nephrectomy be more appropriate? Isotope renography with ^{99m}Tc MAG3 will generally suffice but where renal function is grossly impaired ^{99m}Tc DMSA is a more accurate measure of function and a more reliable predictor of potential functional recovery.

Summary

- There is no scientifically rigorous definition of obstruction and, at present, no gold standard diagnostic test.
- Dynamic contrast-enhanced MR imaging is a promising new diagnostic modality since it provides both anatomical and functional information. But further evaluation is required before it can be considered as a viable alternative to ultrasound and dynamic renography for the routine investigation of upper tract obstruction. Cost and the need for general anaesthesia or sedation in younger children are significant drawbacks.
- Although ^{99m}Tc MAG3 is the isotope of choice for most aspects of investigation of obstruction, ^{99m}Tc DMSA provides more reliable information on differential function in poorly functioning kidneys and is a more reliable predictor of the functional outcome to be anticipated following pyeloplasty.

Pelviureteric junction obstruction

PUJ obstruction is a heterogeneous disorder with a number of different anatomical causes. Moreover, there is considerable variation both in the severity of obstruction and in the natural history of the condition. Estimates derived from antenatal screening place the incidence of PUJ obstruction in the range 1:750–1:1000. Analysis of data held on the US Pediatric Health Information System database showed that the pyeloplasty rate had doubled from 74 per 100 000 in 1992 to 140 per 100 000 in 2004.

The male to female ratio is approximately equal and the left kidney is more commonly affected than the right, by a ratio of approximately 2:1.

The condition usually occurs on a sporadic basis, but familial inheritance has been reported. PUJ obstruction is more common in children with other urinary tract anomalies such as multicystic dysplastic kidneys and the VACTERL spectrum of anorectal and vertebral anomalies.

Pathology and aetiology of PUJ obstruction

Although the findings on diagnostic imaging, notably MR urography, can be helpful in pointing to the likely anatomical cause of the obstruction, it is not usually until the time of operation that this can be established with certainty.

Intrinsic obstruction (Figure 6.5a)

Typically, the obstruction is caused by a short stenotic segment at the pelviureteric junction. However, in some cases, the stenosis may extend distally from the PUJ to involve a more extensive segment of the proximal ureter.

Ureteric folds (Figure 6.5b)

In these cases, the PUJ is of normal calibre but the proximal ureter is tortuous and kinked. This anatomical variant may be associated with self-limiting obstruction, which resolves as the proximal ureter straightens with growth.

High insertion of the pelviureteric junction

The PUJ is sited high on the dilated renal pelvis rather than at its most dependent part. Although this may be a primary abnormality, it is generally thought to be a secondary phenomenon resulting from upwards displacement of the PUJ by the dilating pelvis; i.e. an effect rather than a cause of the obstruction.

Extrinsic obstruction: lower pole or 'crossing vessels' (Figure 6.5c)

Aberrant or crossing lower pole vessels are found in more than 30% of older children and adults undergoing pyeloplasty.

In some cases, the lower pole vessels appear to be incidental to an intrinsic PUJ obstruction but in other cases, particularly older children presenting with intermittent loin pain, the operative findings strongly suggest that the crossing vessels are indeed responsible for the obstruction.

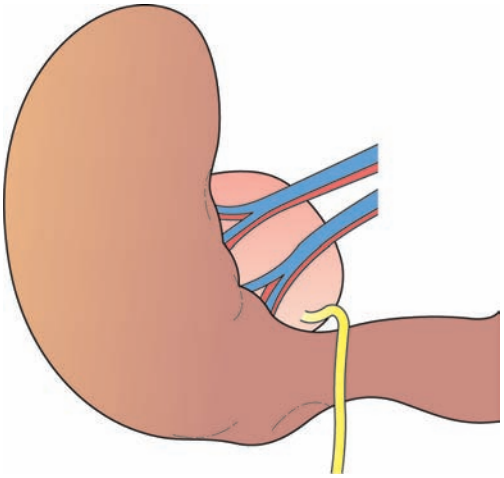


Figure 6.6 PUJ obstruction in a horseshoe kidney caused by distortion of the proximal ureter looping over the renal isthmus (or compression by aberrant vasculature).

This impression is reinforced by the observation that symptoms are invariably relieved following pyeloplasty, in which the reconstructed pelviureteric junction is relocated anterior to the vessels.

Further evidence of the causative role of lower pole vessels can be deduced from reports that symptoms can be relieved by laparoscopic mobilisation and repositioning of the PUJ in relation to the vessels, without the need for dismembered pyeloplasty (see Chapter 23).

In contrast to older children, lower pole vessels account for less than 5% of infants with prenatally detected PUJ obstruction requiring pyeloplasty.

Variants of PUJ obstruction

Horseshoe kidney

The majority of horseshoe kidneys are asymptomatic and of no urological concern. Of the complications that can occur, obstructed drainage is the most common. This may be due to distortion of the proximal ureter as it loops over the renal isthmus or compression from the aberrant vasculature found at the renal hilum of horseshoe kidneys (Figures 6.6 and 6.7).

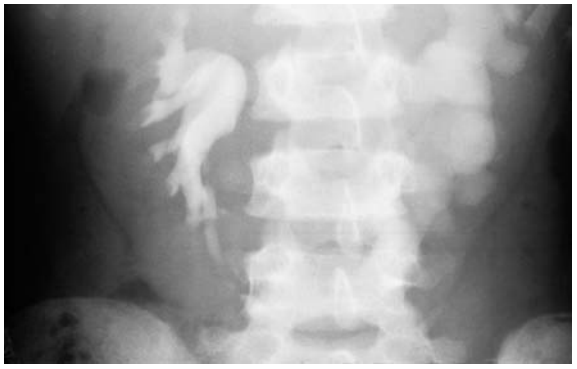


Figure 6.7 Intravenous urogram demonstrating dilatation associated with obstruction in the left limb of a horseshoe kidney.

Retrocaval ureter

This rare anomaly, which more commonly affects the right ureter, is a consequence of the abnormal development of the posterior cardinal veins, the precursors of the inferior vena cava. A number of anatomical patterns have been described. If this diagnosis is raised by the ultrasound findings, MR urography should then be performed as the investigation of choice. Laparoscopic correction is preferable to open surgery, provided this is undertaken by an experienced minimally invasive surgeon.

Intraluminal obstruction

Rare cases of ureteric obstruction caused by intraluminal fibroepithelial polyps have been described; they occur more frequently in the midureter than the pelviureteric junction.

Idiopathic 'functional' obstruction

The renal pelvis normally expels urine by peristaltic contraction initiated from pacemaker sites located in the minor calyces. Failure of peristaltic activity or discoordination of the pacemaker activity is believed to account for cases of 'obstruction' in which the pelviureteric junction is patent and no extrinsic compression can be identified. Although such cases are encountered in adult practice, they are rare in children, in whom one of the anatomical factors listed above is almost invariably present.

Secondary PUJ obstruction

Gross vesicoureteric reflux (e.g. grades IV and V) can result in tortuosity and kinking of the proximal ureter, which can occasionally cause obstructed drainage from the kidneys. This phenomenon is best seen on MCUG films taken after voiding

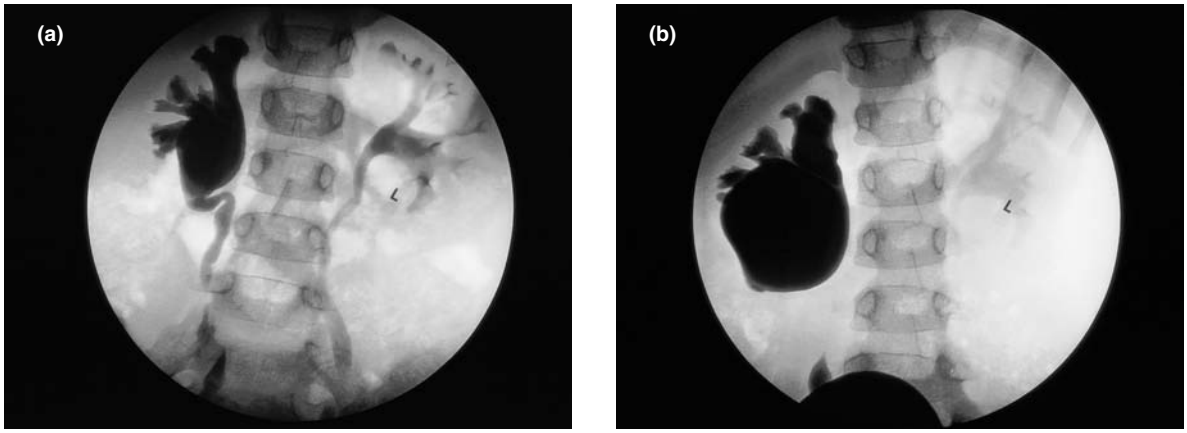


Figure 6.8 'Secondary' PUJ obstruction associated with vesicoureteric reflux. (a) Dilatation of the right renal collecting system seen on the early phase of a micturating cystogram. (b) Progressive dilatation throughout the course of the MCU study. The degree of dilatation is grossly disproportionate to the severity of the reflux. PUJ obstruction subsequently confirmed by isotope renography (performed with a bladder catheter in situ to eliminate confusion due to reflux of isotope).

(Figure 6.8). A dynamic renogram performed with a bladder catheter in situ can also be very helpful in establishing the diagnosis of secondary PUJ obstruction in the presence of reflux.

Natural history of PUJ obstruction

The natural history of PUJ obstruction is variable. Whereas the obstruction resolves spontaneously in some cases, in others it increases in severity, giving rise to progressive functional deterioration. In a substantial proportion of cases, the obstruction remains stable for many years, with little or no impact on renal function. In a study of the conservative management of prenatally detected PUJ obstruction, undertaken at Great Ormond Street Hospital, 17% of obstructed kidneys required pyeloplasty because of deteriorating function, 27% showed evidence of resolving obstruction and 56% remained stable, with persisting obstruction but no functional deterioration over the course of the study. To confuse the picture further, it is well documented that progressive obstruction and dilatation can arise de novo in a previously normal or mildly dilated kidney. Likewise, antenatally detected dilatation can resolve completely in infancy, only to recur as symptomatic, 'full blown' obstruction in later childhood (Figure 6.9).

Presentation

PUJ obstruction is the most common clinically significant uropathy detected on **prenatal ultrasound** (Figure 6.10). It should be noted, however, that mild to moderate degrees of obstruction may not be present or may not have given rise to detectable dilatation at the time when routine fetal anomaly scans are performed in the second trimester. Mild to moderate PUJ obstruction more commonly comes to light on scans performed in later pregnancy, or may remain undetected if no further scans are performed after the second trimester. The severity of the dilatation (AP diameter of the renal pelvis) is a more accurate predictor of functional impairment than the gestational age at which dilatation was first detected. Where the AP diameter exceeds 50 mm, differential function is almost invariably impaired.

Urinary tract infection used to be the commonest mode of presentation in infants and young children before the advent of prenatal ultrasound. Infection within the obstructed system may progress to pyonephrosis, characterised by high fever, systemic ill health and ultrasound findings of debris within the dilated collecting system.

It is not uncommon for PUJ obstruction to present with **pain**, typically in children aged 4 years and upwards. Unlike non-specific abdominal pain, the symptoms arising from an obstructed kidney usually last for several hours or several days. Although the pain is typically sited in the region of the loin, it may be experienced predominantly in the epigastrium and central abdomen, giving rise to possible diagnostic difficulties. In older children whose PUJ obstruction presents with intermittent pain, the underlying cause of obstruction is often related to aberrant crossing vessels.

Haematuria may occur spontaneously, but is more commonly the consequence of minor trauma – to which obstructed kidneys are more susceptible (Figure 6.11). A grossly dilated kidney can sometimes present as an **abdominal mass** mimicking a Wilms' tumour. However, the distinction can be readily made with ultrasound and CT or MRI if necessary.

Occasionally, a dilated kidney comes to light as an **incidental finding** on an ultrasound scan performed for unrelated symptoms such as abdominal pain. In these circumstances, it is important to take a careful history to establish whether the pain is genuinely related to PUJ obstruction or whether the dilatation is an incidental finding in a child with non-specific abdominal pain or abdominal pain of some unrelated aetiology.

Investigation

The diagnostic pathway has already been considered above. Typically, the sequence comprises ultrasound followed by ^{99m}Tc MAG3 dynamic renography. The use of DMSA scintigraphy or ^{99m}Tc DMSA scintigraphy is reserved for poorly

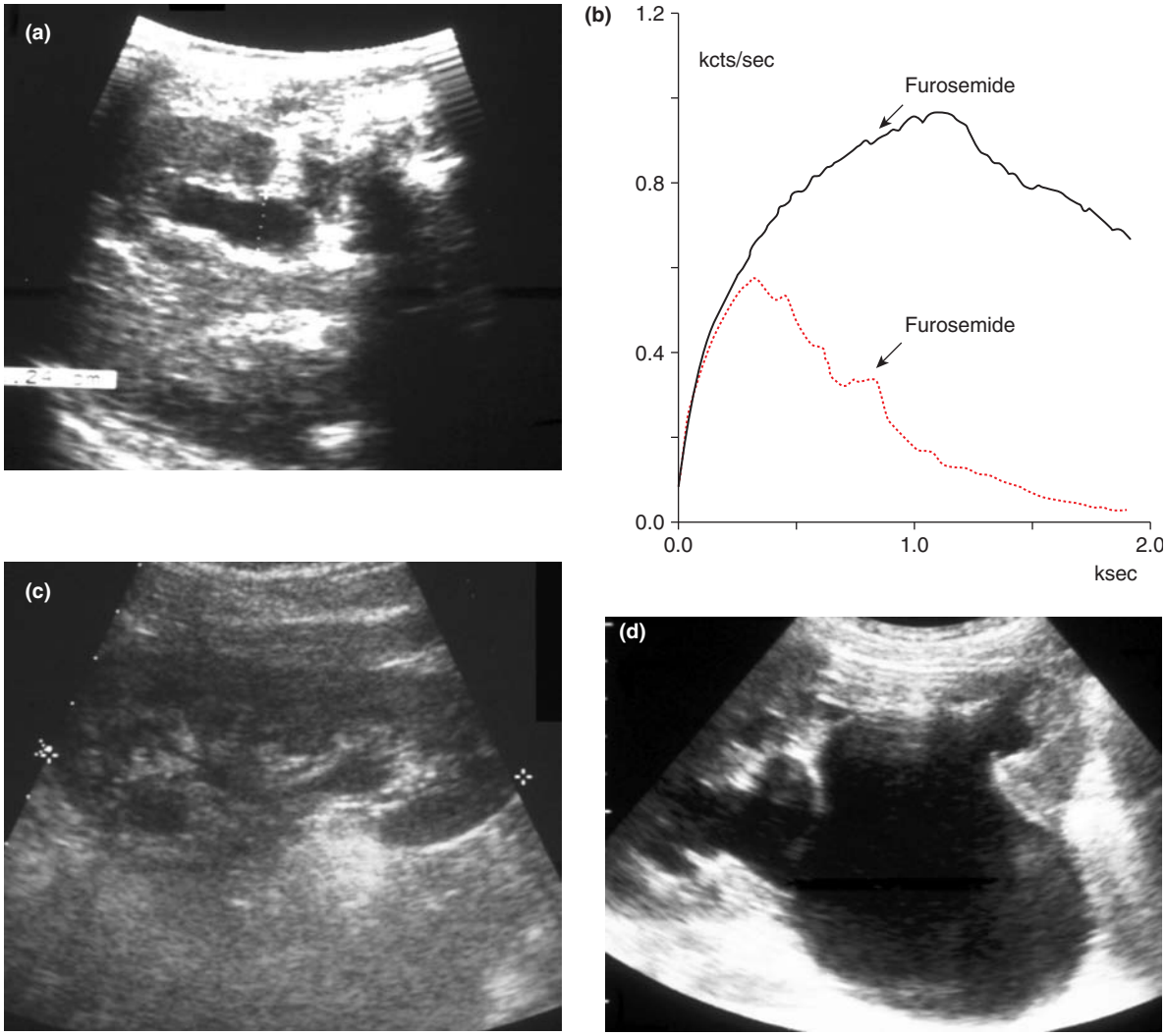


Figure 6.9 Unpredictable natural history of PUJ obstruction. (a) An ultrasound at 1 month of age. Appearances suggestive of PUJ obstruction – with good thickness renal cortex, AP diameter of renal pelvis (not shown) 18 mm. Conservative management was adopted. (b) Follow-up MAG3 study at 36 months showing type 3a O'Reilly curve (non-obstructed). Conservative management was maintained. (c) Ultrasound at 4 years of age. Complete resolution of dilatation, normal appearances of kidney. The child was discharged from further follow-up. (d) At 9 years of age he represented acutely with pain and infection. This ultrasound scan demonstrates severe dilatation due to recurrent PUJ obstruction. Pyeloplasty was curative.

functioning obstructed kidneys where the choice of procedure lies between pyeloplasty or nephrectomy. Other imaging modalities are only required in complicated cases: for example, to investigate secondary PUJ obstruction in the presence of gross vesicoureteric reflux.

Management

In the past, children with PUJ obstruction almost invariably presented with symptoms and in this situation it was not difficult to justify the decision to proceed to surgery.

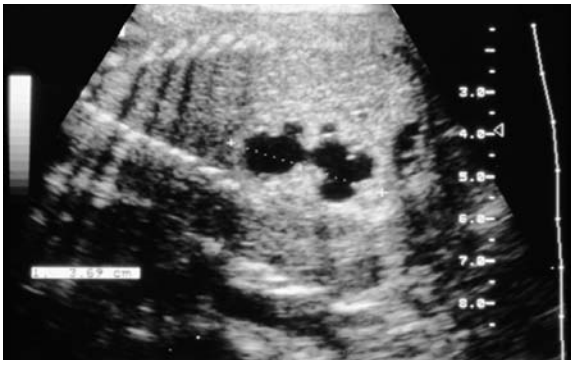


Figure 6.10 Prenatal ultrasound. Marked dilatation of a fetal kidney – PUJ obstruction confirmed by postnatal investigations.

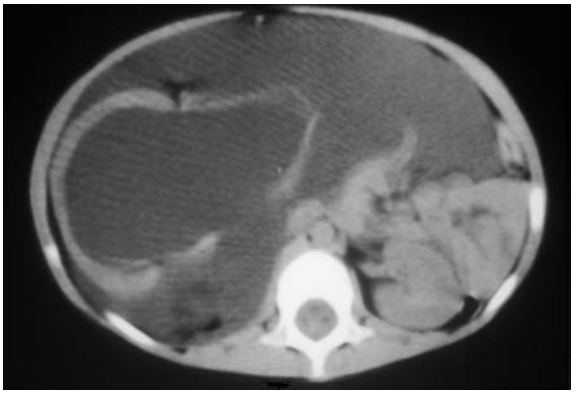


Figure 6.11 CT scan demonstrating a grossly dilated right kidney with a thin rim of renal cortex. This kidney has ruptured after trauma, leading to extensive extravasation.

By contrast, the majority of infants with prenatally detected PUJ obstruction are asymptomatic and their pathology would have remained undiagnosed (at least in infancy) if it had not been for the information yielded by the antenatal ultrasound scan.

The indications for pyeloplasty in children with prenatally detected PUJ obstruction remain controversial, although there is a broad consensus in favour of conservative management in the presence of normal differential function (defined as greater than 40% in the affected kidney).

Conservative management is therefore initiated when differential function in the obstructed kidney exceeds 40%. In practice, kidneys with well-preserved differential function usually have a renal pelvic AP diameter of less than 30 mm. In 15–20% of infants with prenatally detected PUJ obstruction, the dilatation is present bilaterally. In this situation, less reliance can be placed on the renographic assessment of differential function and greater weight must be attached to the severity of dilatation. Bilateral pyeloplasty may occasionally be indicated when the dilatation is of equal severity and both drainage curves have a symetrically obstructed pattern. In practice, however, it is rare to encounter bilateral obstruction of equal severity, and in this situation it may be appropriate to operate on a more severely dilated kidney and monitor the contralateral kidney.

The indications for pyeloplasty can be briefly summarised as:

- **Symptomatic PUJ obstruction**, e.g. pain, infection, palpable renal mass.
- **Asymptomatic obstruction with reduced function** (less than 35–40%) at the time of initial evaluation, particularly if the AP diameter of the renal pelvis exceeds 30 mm.
- **Failure of conservative management**, i.e. deteriorating function or increasing dilatation (which often precedes functional deterioration).
- **Persisting asymptomatic obstruction which shows no evidence of resolution (on ultrasound and ^{99m}Tc MAG3), despite stable differential function.**

The point at which conservative management should be abandoned in an asymptomatic child with stable obstruction is determined by clinical judgement and by the outcome of informed discussion with the parents. Rather than persist for an unspecified period with repeated ultrasound and isotope imaging, it may be thought preferable to proceed to pyeloplasty or, in some circumstances, to discharge the child from further formal follow-up.

Surgical options

Whether performed by an open approach or laparoscopically, the **Anderson–Hynes dismembered**

pyeloplasty is universally regarded as the operation of choice.

Operative technique (Figure 6.12)

Once the anatomy of the pelviureteric junction has been displayed, the ureter is divided and incised for a short length ('spatulated') just distal to the pelviureteric junction. A portion of the redundant dilated renal pelvis is then excised. For the initial stages of the anastomosis, most paediatric urologists favour interrupted sutures and, even in unstented pyeloplasty, it is advisable to minimise the risk of stenosis by performing the anastomosis over a tube, which is then withdrawn prior to closure of the renal pelvis. If a transanastomotic stent is positioned to facilitate postoperative drainage, this can be introduced before, during or after the construction of the anastomosis.

Much has been written about the different methods of postoperative drainage, but published studies have mostly failed to demonstrate any statistically significant advantage of one method over another.

Currently, the most widely used techniques include the use of an **in-dwelling JJ stent** (which is removed cystoscopically some weeks after the pyeloplasty) or a **nephro stent** – in effect a JJ stent with an extension which traverses the renal pelvis, exits through the parenchyma and emerges from the skin. This is left on free drainage for the first day or two then clamped prior to discharge from hospital.

The soft, deformable characteristics of the nephro stent are such that it can subsequently be removed without difficulty by simple traction on the length of tube emerging from the skin (usually around the 10th to 14th postoperative day). Many surgeons prefer to avoid any form of transanastomotic stent, relying instead on simple extrarenal drainage. Nephrostomy drainage alone is thought to be inadvisable since diversion of urine above an unstented anastomosis may encourage adherence of the edges of anastomosis, leading to a greater risk of recurrent obstruction.

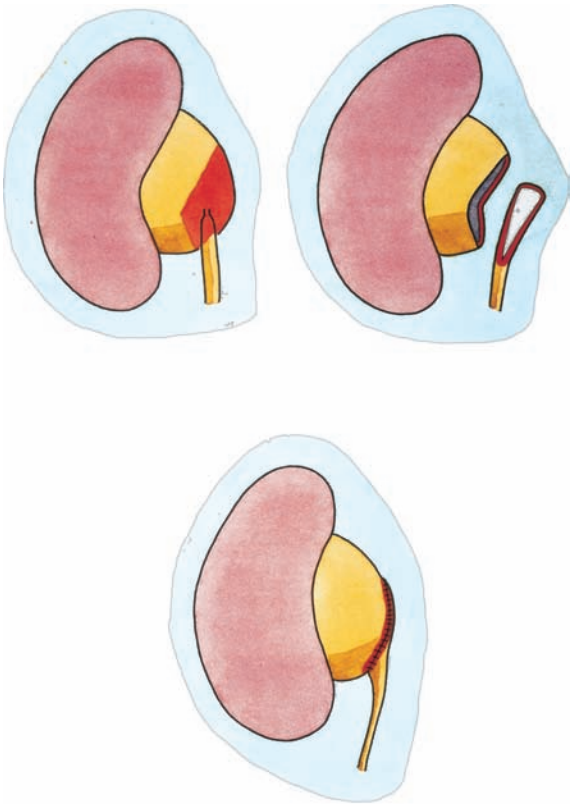


Figure 6.12 Anderson–Hynes dismembered pyeloplasty. The procedure of choice in children.

Open pyeloplasty

For open pyeloplasty the anterior extraperitoneal approach is ideally suited to infants and young children (Figure 6.13a) but access is more limited in older children with a narrower subcostal angle. The posterior lumbotomy approach (Figure 6.13b) is favoured by some surgeons but offers less flexibility to deal with unexpected operative findings. The supra-12 loin approach (Figure 6.13c), conserving the 12th rib, can be employed for all ages and can be readily extended to afford greater access if unexpected problems are encountered. However, it is associated with greater postoperative discomfort and carries a risk of subcostal nerve neuropraxia in infants.

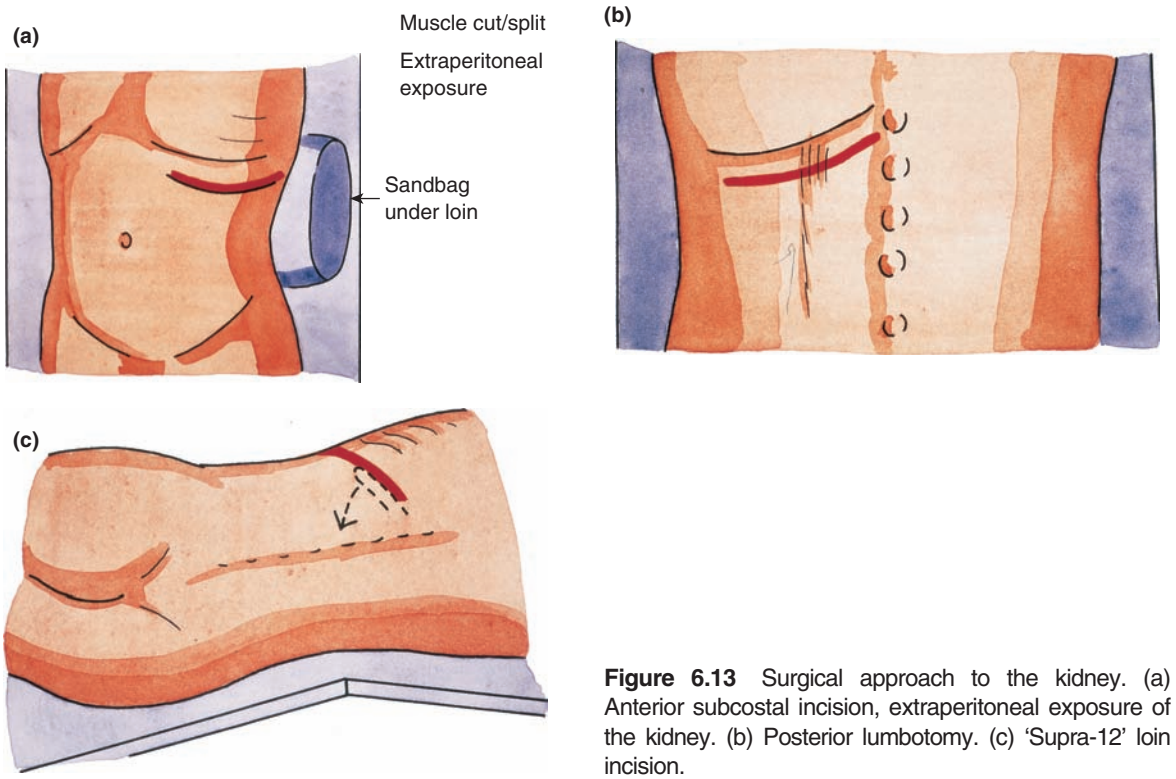


Figure 6.13 Surgical approach to the kidney. (a) Anterior subcostal incision, extraperitoneal exposure of the kidney. (b) Posterior lumbotomy. (c) 'Supra-12' loin incision.

Laparoscopic pyeloplasty

Laparoscopic pyeloplasty was introduced into adult urological practice in the mid 1990s and thereafter gained acceptance to the point that it is now increasingly regarded as the gold standard for adult pyeloplasty. The first series of laparoscopic pyeloplasties in children appeared in the literature toward the end of the 1990s and, with the introduction of better instrumentation for children, paediatric laparoscopic pyeloplasty has subsequently gained growing acceptance. The operative details are considered at greater length in Chapter 23.

Laparoscopic vs open pyeloplasty?

The experience of laparoscopic pyeloplasty to date and the relative merits and drawbacks can be briefly summarised as follows:

- The cosmetic outcome of laparoscopic pyeloplasty is superior to a conventional surgical incision. This advantage is particularly relevant to older children in whom a supra-12 loin incision can leave a relatively conspicuous scar. The cosmetic benefit is more arguable in infants, since pyeloplasty can be accomplished through a small anterolateral abdominal incision in this age group.
- Laparoscopic pyeloplasty is associated with a shorter hospital stay and reduced postoperative analgesic requirement. However, the operative time can be significantly longer than for open pyeloplasty.
- The retroperitoneal laparoscopic approach is preferable to the transperitoneal approach in view of the risk of intraperitoneal urinary leakage and the potential for adhesion formation. However, the retroperitoneal approach is

more technically challenging, particularly in infants and young children.
- Robotic pyeloplasty is limited to a small number of centres and is currently under evaluation. The operative time is longer than for conventional laparoscopic pyeloplasty and substantially longer than the operative time for open pyeloplasty.
- Laparoscopic pyeloplasty has a significant 'learning curve', during which time the early complication rate is higher than that for open pyeloplasty. In the hands of an experienced laparoscopic surgeon, however, the complication rates and overall success rates are likely to be comparable to those obtained by open pyeloplasty, i.e. overall long-term success rate of greater than 95%.
- The laparoscopic approach offers considerable ergonomic advantages over open surgery for the correction of certain variants of PUJ obstruction: for example, PUJ obstruction occurring in a horseshoe or pelvic kidney and retrocaval ureter.
- Although laparoscopic surgery is best suited to older children, its use has been safely extended to pyeloplasty in infants under 1 year of age. However, the benefits, in terms of reduced hospital stay and analgesic requirement are very marginal in view of the ease of approach offered by an anterolateral muscle-splitting subcostal incision in this age group.

Postoperative follow-up

Postoperative follow-up typically comprises ultrasound and isotope renography. Some paediatric urologists do not feel it is necessary to submit the child to a MAG3 study if ultrasonography at 6–12 months clearly demonstrates resolution of the dilatation, indicating that obstruction has been successfully relieved. Assessing the postoperative ultrasound findings in a grossly dilated system can prove problematic, as considerable dilatation often persists for a long time, despite a technically successful pyeloplasty. Similarly, it may be a matter of years rather than months before the isotope renogram drainage curve reverts to normal in these cases. In the longer term, pyeloplasty has been shown to be a highly effective operation with a very low incidence of recurrent obstruction.

Other surgical options

Percutaneous nephrostomy

The insertion of a pigtail nephrostomy catheter into the collecting system to provide temporary drainage is a particularly valuable manoeuvre in children presenting with pyonephrosis. Temporary percutaneous drainage usually permits rapid control of infection and enables potential recovery of function to be assessed with a DMSA scan prior to definitive surgery.

Ureterocalicostomy (Figure 6.14)

In this procedure, the ureter is detached from the renal pelvis and anastomosed directly to the most dependent lower pole calyx. Although it is rarely appropriate in the primary management of PUJ obstruction, ureterocalicostomy may ensure more effective drainage than pyeloplasty in, for example, recurrent PUJ obstruction or PUJ obstruction complicating a horseshoe kidney.

Endopyelotomy and balloon dilatation

Although these techniques have been described as alternatives to open pyeloplasty in children, the results are markedly inferior to those obtained by open pyeloplasty. There is little evidence to justify this form of intervention as a primary treatment. Balloon dilatation may, however, have a very limited role in the treatment of mild to moderate recurrent PUJ obstruction in older children.

Nephrectomy

When deciding whether to advise pyeloplasty or nephrectomy, most paediatric urologists supply an arbitrary 'cut off' for differential function in the range of 10–15%. Functional imaging with DMSA provides more reliable information on which to base a decision whether to proceed to

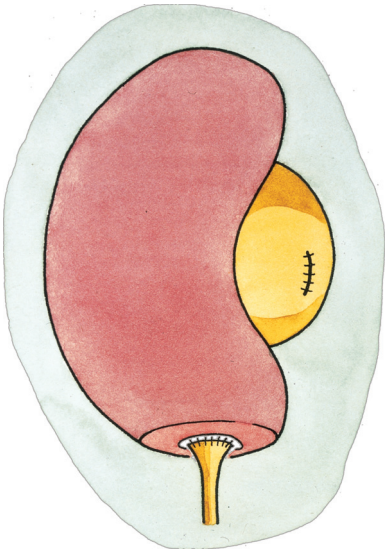


Figure 6.14 Ureterocalicostomy. The ureter is disconnected from the renal pelvis and the pelviureteric junction closed. The ureter is then anastomosed directly to the lower pole calyx. A useful procedure to facilitate dependent drainage in a grossly dilated system or horseshoe kidney and in cases of recurrent PUJ obstruction.

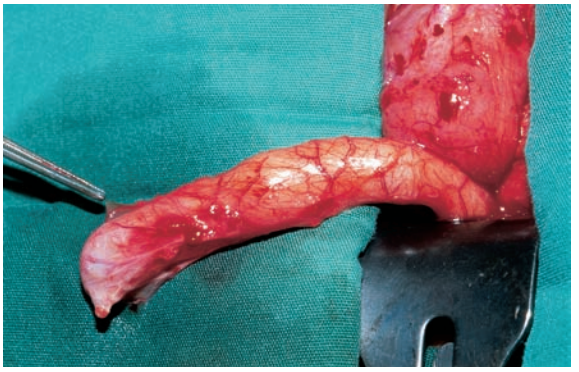


Figure 6.15 Obstructed megaureter. The ureter has been mobilised and divided at the level of the bladder. Dilatation of the ureter proximal to a short stenotic segment at the vesicoureteric junction.

nephrectomy or pyeloplasty. As already indicated, a period of temporary percutaneous nephrostomy drainage may be helpful in borderline case.

Vesicoureteric junction obstruction

The classification of ureteric dilatation (megaureter) and its causes can be simplified into three broad categories:

- **Obstructed megaureter**: the obstruction is usually intrinsic, i.e. primary stenosis of the distal ureter or vesicoureteric junction, but occasionally, the obstruction may be extrinsic and secondary to, for example, a tumour or scarring/fibrosis. Most cases are due to primary obstruction at the vesicoureteric junction, and hence the synonym **'VUJ obstruction'.**
- **Non-refluxing, non-obstructed megaureter**: the ureter is dilated but is not actively obstructed. The aetiology of such cases is often unclear but it is believed that many represent the legacy of 'burnt-out' VUJ obstruction, in which the original obstruction has resolved, leaving residual dilatation of a 'flabby' ureter.
- **Refluxing megaureter**.

Obstructed megaureter

This condition is usually characterised by a marked discrepancy between the calibre of the distal ureteric segment and the dilated, tortuous ureter proximal to it. In cases coming to surgery, the obstruction is usually found to be associated with the presence of a stenotic ureteric segment of varying length above the vesicoureteric junction (Figure 6.15). In occasional cases, however, the calibre of the distal ureter is normal and is only narrow in relation to the dilated ureter above it. In the absence of demonstrable stenosis, this form of megaureter is presumed to result from an adynamic, aperistaltic distal segment of ureter, which fails to propagate bolus transmission of urine into the bladder.

The true prevalence of megaureter is difficult to quantify since, in the days before prenatal diagnosis, many cases almost certainly did not come to light. Figures derived from routine prenatal ultrasound screening suggest an overall incidence in the range of 1:1500–1:2000. Megaureter occurs more frequently in males and the left side is more

commonly affected than the right. It generally occurs on a sporadic basis.

Presentation

Prenatal detection

Obstructed megaureter constitutes approximately 10% of prenatally detected uropathies of clinical significance. Although the dilated ureter may be visualised on prenatal ultrasonography, it is often the dilatation of the renal collecting system that is detected initially. The distinction between obstructed and refluxing megaureters can never be made by ultrasound alone and a postnatal MCUG should be undertaken routinely to exclude VUR or, in boys, outflow obstruction due to posterior urethral valves.

Symptomatic presentation

Urinary infection used to be the most common form of presentation and, despite the advent of prenatal diagnosis, unsuspected cases can still occasionally present in this fashion.

The spectrum of severity may vary from mild, predominantly lower tract symptoms to a severe systemic febrile illness caused by the presence of pus and infected debris within the obstructed collecting system (pyoureteronephrosis).

Vesicoureteric junction obstruction can also present occasionally with intermittent loin and abdominal pain, in a manner similar to intermittent PUJ obstruction (Figure 6.16). Other modes of presentation include abdominal swelling (rare) or complications secondary to the presence of calculi within the obstructed system.

Investigations

Ultrasound

Ultrasound is a valuable investigation for demonstrating ureteric dilatation, particularly when renal function is poor and the excretion of isotope tracer or radiological contrast is impaired. The ultrasound scan should visualise the dilated ureter throughout its course and should also assess the severity of pelvicalyceal dilatation. Where the ureteric diameter is less than 1 cm, significant obstruction is unlikely to be present and differential function in the affected kidney is usually well preserved. Even when the ureteric diameter exceeds 1 cm, differential renal function may still be normal and the degree of caliceal dilatation may be mild in relation to the extent of the ureteric dilatation. Such findings usually denote low-grade obstruction, with little threat to renal function.

Micturating cystourethrogram

As already stated, an MCUG should always be undertaken to distinguish between obstruction and vesicoureteric reflux as the possible cause of ureteric dilatation.

Isotope renography

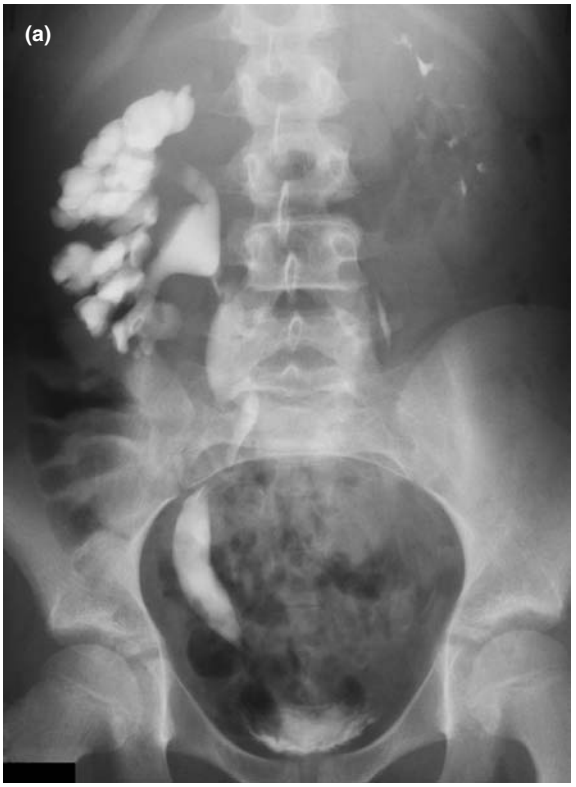
Drainage curve data can be very difficult to assess in grossly dilated ureters. In particular, clearance of isotope from the kidney may be interpreted as evidence of a non-obstructed system, whereas closer scrutiny of the 'hard copy' gamma camera images reveals that the tracer has simply emptied from the kidney into a capacious dilated ureter.

The sensitivity of isotope renography can be improved by drawing regions of interest over different portions of the ureter to estimate ureteric emptying, but, even with this modification, it may still prove very difficult to distinguish between obstructed and non-obstructed dilatation from the drainage curve. Differential function may prove to be the most helpful piece of information when planning management.

Management

Prenatally detected obstructed megaureter

The majority of infected infants are healthy and asymptomatic at birth. Conservative management is initiated where differential renal function is greater than 35–40%, with surgery being undertaken on a selective basis for the indications set out below. In



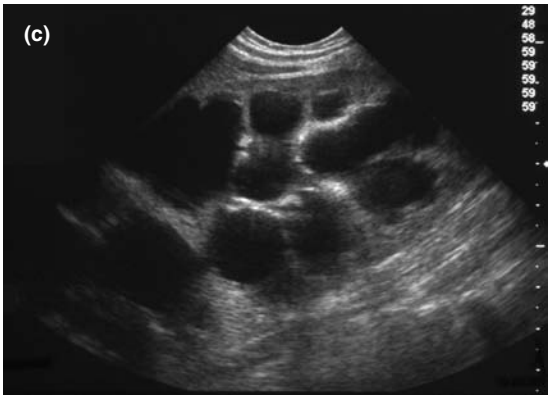


Figure 6.16 (a) Intravenous urogram in a 12-year-old girl with a long history of intermittent abdominal pain diagnosed as 'abdominal migraine'. Ultrasound (not shown) and IVU performed between episodes of pain were consistent with non-obstructive dilatation. (b) MAG3 renogram shows good preservation of function and a washout response to diuretic. The findings were interpreted as non-obstructive dilatation consistent with 'burnt out' obstructed megaureter. (c) However, an ultrasound scan performed acutely during an episode of pain demonstrated a dramatic increase in the severity of caliceal dilatation. Diagnosis: intermittent vesicoureteric junction obstruction. Her symptoms resolved completely following surgery.

one series of 40 patients with 57 megaureters, only 10% required surgery because of impaired renal function on initial assessment. Of those managed conservatively, 53% showed complete resolution on ultrasonography, while 43% remained stable or improved on follow-up. However, another group of authors who analysed the longer-term outcome in 79 children reported an operation rate of 30%, citing indications which included differential function <40%, ureteric diameter >1.3 cm and severe pelvicaliceal dilatation. The mean age at operation in this series was 14.3 months.

A high incidence of resolution or improvement in infants with prenatally detected primary

megaureter has now been reported by a number of studies. The optimum duration of follow-up is not known, but, in practice, if the dilatation resolves or shows progressive improvement on ultrasound and if differential function was normal on initial assessment, children can probably be safely discharged after 4–5 years. Where there is evidence of persisting dilatation, it is probably prudent to maintain ultrasound follow-up on an infrequent basis until the teens in view of the low risk of deterioration.

Indications for surgery

Prenatally detected obstructed megaureter

Surgical intervention should be considered if differential function is impaired on initial assessment (differential function less than 35%). Ideally, however, the study should be repeated at 3–6 months of age before proceeding to intervention.

Deteriorating renal functional follow-up is a further indication for surgery, although this is a rare occurrence.

Symptomatic complications

Mild to moderate urinary infection is not an automatic indication to proceed to surgery if the other parameters (differential function, ureteric diameter 1 cm or less) are favourable. A period of antibiotic prophylaxis and a trial of conservative management is appropriate in such cases, but when obstructed megaureter is complicated by recurrent or severe infections, it should be managed surgically. Other indications include pain or, rarely, abdominal mass.

Surgical treatment

Definitive treatment consists of excising the obstructing distal segment and reimplanting the ureter into the bladder by a technique which facilitates good upper tract drainage without permitting vesicoureteric reflux. However, these twin goals may be difficult to achieve, particularly in infants with grossly dilated ureters and relatively small bladders.

Wherever possible, reimplantation of a megaureter should be avoided in the first year of life, because of these technical difficulties and growing anecdotal evidence that dissection in the region of the distal ureter and bladder neck can result in a degree of neurological impairment, with a possible impact on continence in later childhood.

Alternatives to open surgery in the first year of life

Successful medium-term drainage with a paediatric in-dwelling ureteric JJ stent has been reported from a number of centres. If endoscopic insertion is not feasible, open cystostomy, dilatation of the ureteric orifice and insertion of a JJ stent is well tolerated. The stent can usually be safely left in situ for up to 6 months, after which time it may be feasible to proceed to definitive surgery. However, it is apparent that, in some infants, the combination of dilatation and prolonged in-dwelling stent drainage is sufficient to correct the obstruction without the need for further surgery.

Although upper tract diversion by terminal or ring ureterostomy was once widely practised in infants with obstructed megaureter, there are now very few indications for this approach. Ureteric reimplantation is best deferred until 12 months of age upwards, but, depending on the circumstances, may be considered from 6 months upwards, according to the anatomical features and the experience of the surgeon.

Surgical treatment from 1 year of age upwards

Mild ureteric dilatation (ureteric diameter approximately 1 cm or less)

In these cases the ureter can be mobilised intravesically, as for a conventional ureteric reimplantation, and the ureter reimplanted in a conventional Cohen cross-trigonal tunnel after excision of the stenotic distal segment.

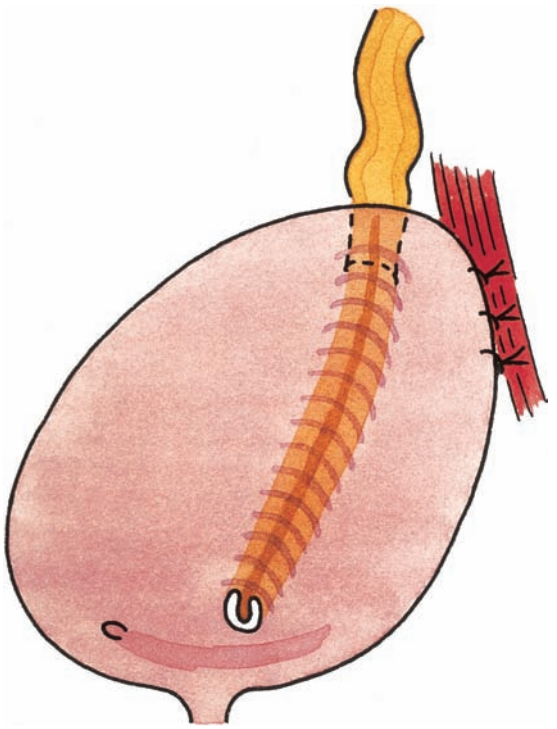


Figure 6.17 The Politano–Leadbetter reimplantation procedure combined with psoas hitch, which is often better suited to megaureters than the Cohen cross-trigonal reimplantation technique.

Moderate to severe dilatation

The dilated ureter is identified extravesically and mobilised down to the bladder, where the stenotic segment is identified and excised. In older children, it may be feasible to reimplant the ureter via the original hiatus, but because of the difficulty in creating the optimum ratio of ureteric width to length of submucosal tunnel required to prevent reflux, plication or tapering of the distal ureter is usually advisable. Where the ureter is grossly dilated, plication or tapering of the distal ureter is combined with a Politano–Leadbetter reimplantation, which creates a longer antireflux submucosal tunnel (Figure 6.17).

A psoas hitch procedure is also performed to anchor the bladder to the psoas muscle in the region of the entry point of the ureter into the bladder. This manoeuvre minimises the risk of kinking and obstruction during bladder filling. Although tapering ('remodelling') of the distal ureter has been claimed to restore ureteric peristalsis, this is very doubtful. Plication by the Starr or Kalicinski technique is more straightforward but creates a bulkier ureter and, theoretically, a greater risk of postoperative reflux (Figure 6.18).

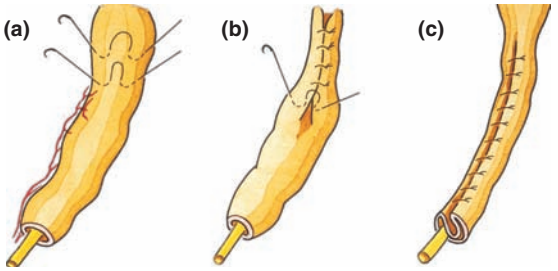


Figure 6.18 Method of ureteric plication using the Starr technique.

The presence of bilateral obstructed megaureters represents an indication for transureteroureterostomy, in which one ureter is reimplanted using the Leadbetter–Politano procedure and psoas hitch while the contralateral ureter is disconnected from the bladder, rerouted across the midline and anastomosed to the reimplanted ureter.

Follow-up

Postoperative imaging with ultrasound and isotope renography is undertaken after 6–12 months. However, a longer period of follow-up may be required before there are demonstrable improvements in the drainage curve component of an MAG3 study. Likewise, where the ureter has been grossly dilated for a prolonged period before surgery, considerable patience may be needed before significant improvement is seen on ultrasound. Any postoperative vesicoureteric reflux is usually mild and self-limiting but, when it occurs, a more prolonged period of postoperative antibiotic prophylaxis may be indicated.

Key points

- PUJ obstruction is a heterogeneous condition with a number of different causes and a variable natural history.
- Hydronephrosis due to PUJ obstruction accounts for 30–50% of clinically significant prenatally detected uropathies. A renal pelvic AP diameter exceeding 30 mm is associated with a significant likelihood of functional impairment. Conversely, an AP diameter of less than 15 mm is most unlikely to denote significant obstruction.
- Conservative management of prenatally detected PUJ obstruction is appropriate when differential function is well preserved and dilatation is mild to moderate in severity.
- Magnetic resonance imaging can combine anatomical and functional information in a single investigation. Further evaluation is required to determine whether the benefits justify the additional cost and the requirement for anaesthesia in younger children.
- The advantages of laparoscopic pyeloplasty (ideally via a retroperitoneal approach) include better cosmesis, reduced postoperative pain and shorter hospital stay. Current evidence suggests the technique is better suited to older children and has few advantages over open pyeloplasty in infants.
- Reimplantation of an obstructed megaureter should be avoided in the first year of life, when it has a higher failure rate and carries a greater risk of morbidity.

Further reading

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Duplication anomalies, ureterocoeles and ectopic ureters

7

Anthony MK Rickwood, Nicholas P Madden and Su-Anna M Boddy

Topics covered
Embryology and classification
Pathology
Clinical presentation
Investigations
Management Duplex-system ureterocoele
Suprasphincteric ectopic ureter
Infrasphincteric ectopic ureter
Duplex-system vesicoureteric reflux
Single-system ureterocoele and ectopic ureter

Introduction

Some degree of upper urinary tract duplication is found in 0.8% of postmortem examinations and in a rather higher proportion (2–3%) of patients undergoing intravenous urography (IVU) for various indications. In approximately 40% of cases the condition is bilateral. The anomaly is transmitted as an autosomal dominant trait with incomplete penetrance, so that among members of affected families the incidence is of the order of 8%.

The great majority of duplications are of the incomplete variety, with confluence of the ureters occurring at some point above the ureteric orifice. These forms of duplication rarely give rise to clinical problems. In contrast, complete duplication anomalies are often of clinical significance in terms of symptoms, renal function or both. However, complete duplication anomalies are far rarer, affecting appreciably less than 0.1% of individuals, the majority being females. Clinical presentation is nearly always during childhood, and nowadays around 50% of patients are detected by prenatal ultrasonography. Complete duplication occurs bilaterally in approximately 25% of cases but in cases of bilateral duplication the pattern of abnormal anatomy is not symmetrical. So, for example, it is possible for the child to have a ureterocoele on one side and an ectopic ureter in the contralateral upper tract.

Table 7.1 Classification of complete duplication anomalies

Lower polar
Vesicoureteric reflux

Upper polar
Duplex-system ureterocoele
Suprasphincteric ureteric ectopia
  Boys – vas, seminal vesicle, ejaculatory duct
  Girls – bladder neck, proximal urethra
Infrasphincteric ureteric ectopia
  Girls *only* – introitus, distal vagina

Duplication anomalies (Table 7.1)

Embryology

Normal ureteric and renal embryogenesis are described in Chapter 1. A single ureteric bud which arises normally from the mesonephric duct but which then undergoes bifurcation leads to a variable degree

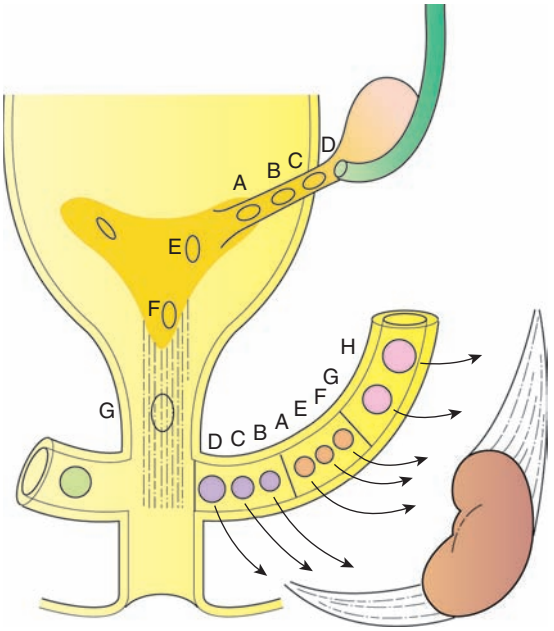

Figure 7.1 Stephen's hypothesis (see 'Further reading'). A ureteric bud arising from the normal region of origin on the mesonephric duct (AEF) makes contact with the central zone of metanephric blastema, initiating normal nephrogenesis, the formation of a healthy kidney and a ureteric orifice located on the trigone. By contrast, a ureteric bud arising from an abnormal site on the ureteric bud is more likely to make contact with a peripheral zone of metanephric blastema, with consequent renal dysplasia and an ectopic ureteric orifice.

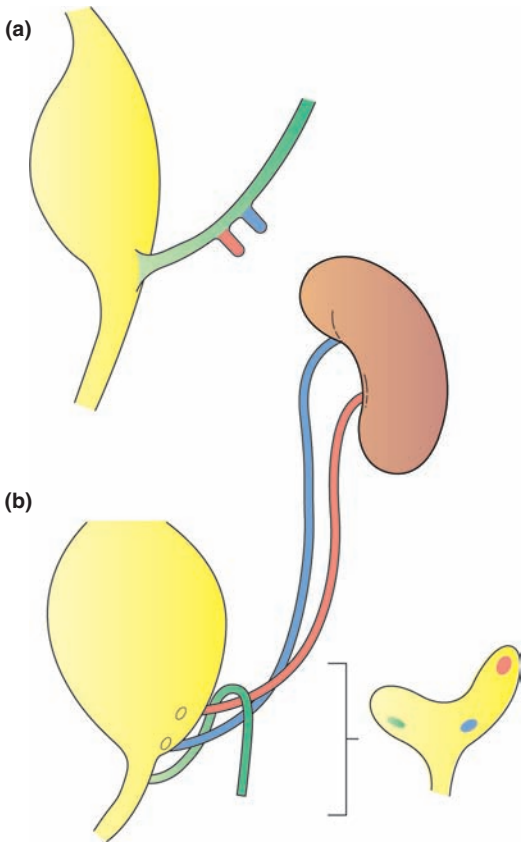

Figure 7.2 Embryological basis of complete duplication with lower pole reflux. (a) Accessory ureteric bud (red) arising caudally on the mesonephric duct (green) at around 6 weeks subsequently becomes incorporated into the superolateral portion of the trigone (b), with a short submucosal tunnel predisposing to reflux. Relative positions of ureteric orifices on trigone also illustrated.

of incomplete duplication of the upper renal tract. Complete duplication occurs when two ureteric buds arise separately from the mesonephric duct.

As a rule, the more extreme the degree of ectopia of the ureteric bud the greater the likelihood that it will come to penetrate an abnormal zone of metanephric tissue with resultant dysplasia (Figure 7.1). An accessory ureteric bud which arises in a caudal position on the mesonephric duct and connects with the lower renal pole is absorbed into the urogenital sinus, so that the ureteric orifice opens in a superior and lateral position in relation to the trigone, an anatomical configuration commonly predisposing to vesicoureteric reflux to the lower pole of the kidney (Figure 7.2).

An accessory bud that arises from the mesonephric duct in a more cephalad position than the normal site and which drains the upper renal pole will come to enter the urinary tract in a distally ectopic location (Meyer–Weigart law). It may drain into either the bladder, the urethra or the urogenital sinus (Figure 7.3). In females, such ectopic ureters may be sited above the sphincter mechanism (suprasphincteric), close to or at the level of the striated sphincter (although usually below the bladder neck), or distal to the sphincter (infrasphincteric), either at the introitus or in the distal vagina. In males, the termination is always suprasphincteric, connecting with the vas, the seminal vesicle or, most often, the ejaculatory duct.

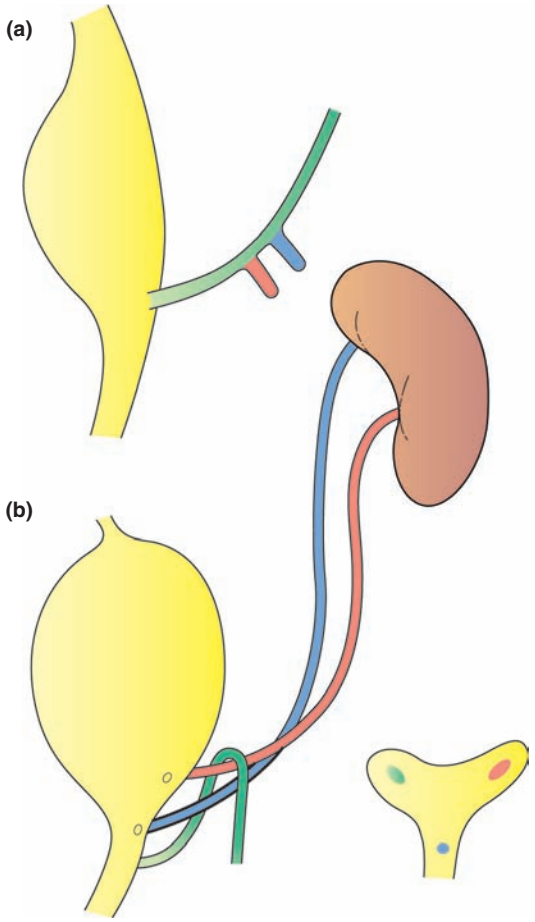

Figure 7.3 Embryological basis of complete duplication with upper pole ureteric ectopia. (a) Accessory ureteric bud (blue) with an abnormally cephalad site of origin on the mesonephric duct (green). (b) By 12 weeks the upper pole ureter has been carried with the mesonephric duct to an abnormally distal ectopic location (Meyer–Weigart law). Relative positions of ureteric orifices on trigone/bladder neck also illustrated.

Pathology

Ureteric ectopia is usually associated with a dysplastic renal pole, while the ureter itself is frequently dilated, either as a consequence of reflux, obstruction or dysmorphism. Even in the absence of dysplasia, the affected pole typically exhibits some degree of dilatation, the only common exception being in some girls with infrasphincteric ectopia.

Duplex-system ureterocoeles (defined as cystic dilatation of the terminal portion of the ureter draining the upper pole) may lie entirely within the bladder (Figure 7.4a,b) or may encroach beyond the bladder neck (ectopic ureterocoele) (Figure 7.4c,d). In the rare and most extreme form, caecoureterocoele, which is confined to girls, the ureterocoele prolapses deeply posterior to the urethra (Figure 7.4e). As would be expected, dysplasia of the upper pole parenchyma is the rule with duplex-system ureterocoeles, usually to the extent that the upper pole has little if any useful function.

In addition to the primary anomaly, duplex-system ureterocoeles may be associated with one or more of the following:

- **Coexisting vesicoureteric reflux to the ipsilateral lower pole** is present in 50% of cases and is usually of moderate severity (e.g. grade I–III reflux). More severe lower pole reflux is generally associated with significantly impaired function of that pole.
- **Obstruction of the ipsilateral lower pole ureter** is rare but when it occurs is due to extrinsic compression by a tense ureterocoele or dilated upper pole ureter. In this situation lower pole function is usually well preserved as the obstruction is a secondary phenomenon and hence is not associated with dysplasia.
- **Dilatation of the ipsilateral upper pole ureter** is usually, although not always, associated with corresponding dysplasia of the upper pole. Although conventionally ascribed to obstruction by a stenotic ureteric orifice, this dilatation (which may be massive) in reality represents primary dysmorphism of the ureteric wall.
- **Bladder outflow obstruction** is usually caused by an ectopic ureterocoele. This can compromise upper tract renal function on the contralateral side.
- **Contralateral vesicoureteric reflux** is often an incidental finding and is present in 25% of cases but seldom exceeds grade III in severity.
- **Prolapse of the ureterocoele into the urethra** is a rare complication confined to girls.

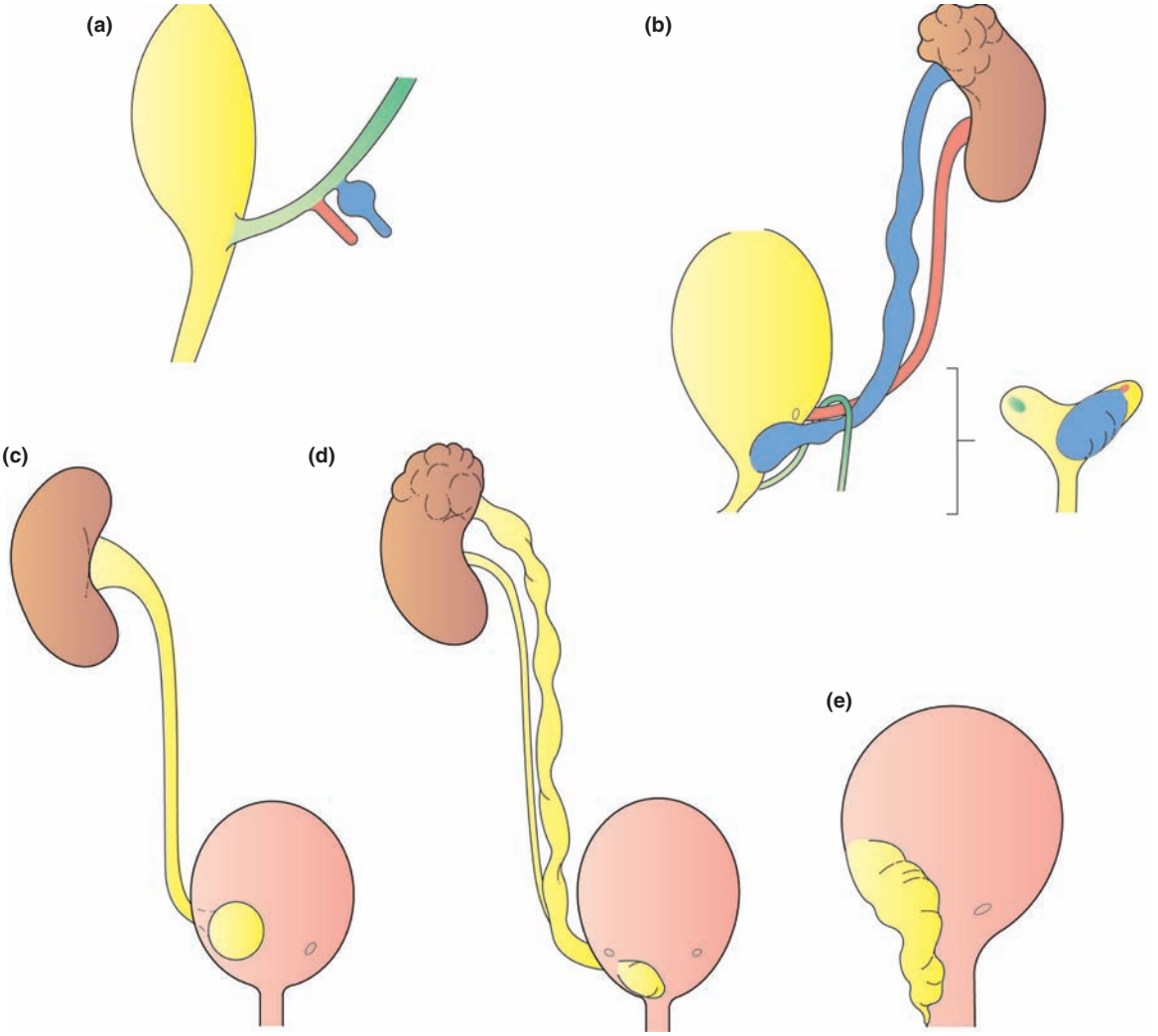

Figure 7.4 Ureterocoeles: embryology and classification. (a) Delay in canalisation of the upper ureteric bud at around the time it makes contact with the upper pole metanephric blastema results in cystic dilatation subsequently resulting (b) in the formation of a duplex ureterocoele. (c) Single-system orthotopic ureterocoele. (d) Duplex ectopic ureterocoele. (e) Caecoureterocoele. Large ureterocoele extending distally downward from the deficient trigone towards the perineum in a plane between the urethra anteriorly and the vagina posteriorly.

Incidence

Duplex-system ureterocoeles occur in approximately 0.02% of individuals, of whom 80% are female. A slight majority of ureterocoeles are left-sided and in 10% of cases the lesion is bilateral.

Ectopic ureter is still rarer, affecting some 0.01% of individuals, mostly females.

Some degree of contralateral duplication, usually incomplete, is found in 80% of cases, and in 10% of cases of infrasphincteric ectopia the anomaly exists bilaterally. The incidence of complete duplication with lower pole reflux is difficult to determine as not all cases can be detected by prenatal ultrasonography, nor do all affected individuals present clinically. At a best

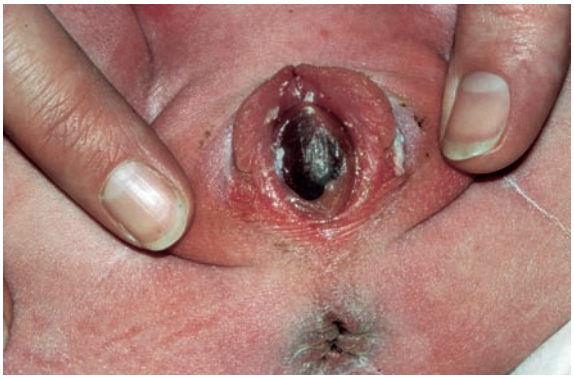

Figure 7.5 Prolapsed ureterocoele emerging at the introitus of a newborn infant.

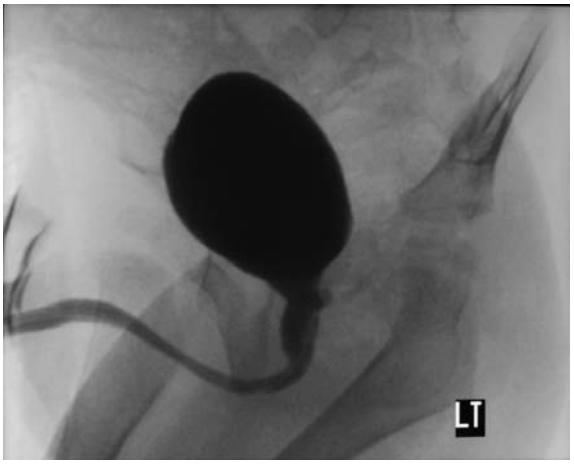

Figure 7.6 Micturating cystogram showing reflux into distal portion of an ectopic upper pole ureter in a male.

estimate, no more than 0.04% of the population are affected.

Clinical presentation

Duplex-system ureterocoele

Approximately 60% of children with these anomalies are currently identified by prenatal ultrasonography. Clinical presentation, usually during infancy, is most commonly with urinary infection, typically with marked constitutional upset and occasionally with Gram-negative septicaemia. Other, rarer, modes of presentation include acute or chronic urinary retention and, in females, urethral prolapse of the ureterocoele (Figure 7.5).

Suprasphincteric ectopic ureter

These anomalies are frequently detected prenatally by virtue of dilatation of the upper pole ureter or collecting system. Clinical presentation is almost invariably with urinary infection, which, in males, may be manifest as epididymo-orchitis (Figure 7.6).

Infrasphincteric ectopic ureter (Figure 7.7)

If not picked up prenatally, the clinical presentation is classically characterised by constant dribbling of urine superimposed upon an otherwise normal pattern of micturition, a clinical picture that distinguishes it from all other causes of incontinence.

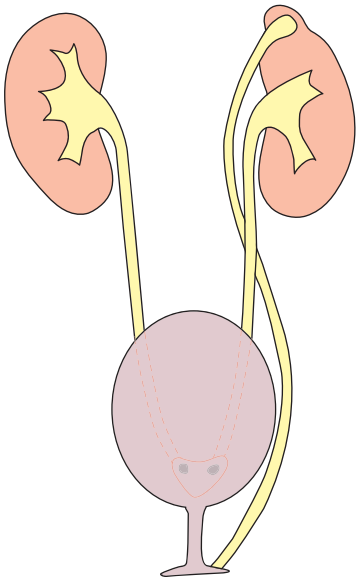

Figure 7.7 Diagrammatic representation of duplex-system infrasphincteric ureter.

However, the history is not always so straightforward. Some girls remain dry overnight, whereas others with a vaginal ectopic ureter are nevertheless able to remain dry for brief periods during the day. Occasionally the clinical picture is further confused by secondary changes in the pattern of normal

micturition: for example, marked urinary frequency prompted by the parents' increasingly desperate efforts get their daughter dry. Lastly, where the affected upper renal pole is severely dysplastic, the quantity of urine produced by it may be so reduced that it pools within the vagina, becomes infected and presents as vaginal discharge. Vaginal discharge is a relatively common complaint and this rare presentation of ureteric ectopia represents one of the few significant underlying causes.

Physical examination is usually unrewarding, although occasionally the presence of constant, slight, urinary leakage may be observed at the introitus.

Investigations

Ultrasound

Ultrasound is the investigation of first choice by virtue of its ability to pick up dilatation of the upper or lower pole of the duplex kidney. Dilatation confined to the *lower* pole may be due to:

- **Vesicoureteric reflux**. In this situation it is usually also possible to visualise a dilated ureter behind the bladder.
- **Pelviureteric junction obstruction**. When PUJ obstruction affects a duplex kidney, it almost always involves the lower pole (see Chapter 6).

Dilatation affecting only the upper renal pole may be due to:

- **Duplex-system ureterocoele**. In such cases the associated ureterocoele is always readily imaged within the bladder (Figure 7.8), provided it is full.
- **Ureteric ectopia**. As a rule, the dilated distal ureter can be visualised behind the bladder. In some girls with infrasphincteric ectopia the upper renal pole is not hydronephrotic but is small and dysplastic and consequently difficult or impossible to detect by ultrasonography ('cryptic duplication').

Dilatation affecting *both* renal poles is almost always due to **duplex-system ureterocoele**.

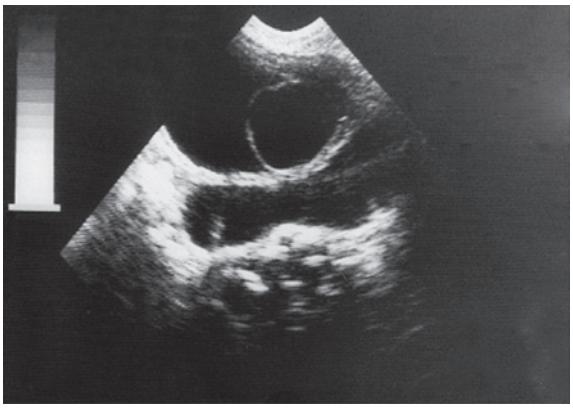

Figure 7.8 Bladder ultrasonography demonstrating a large ureterocoele within the bladder and the dilated upper pole ureter behind the bladder.

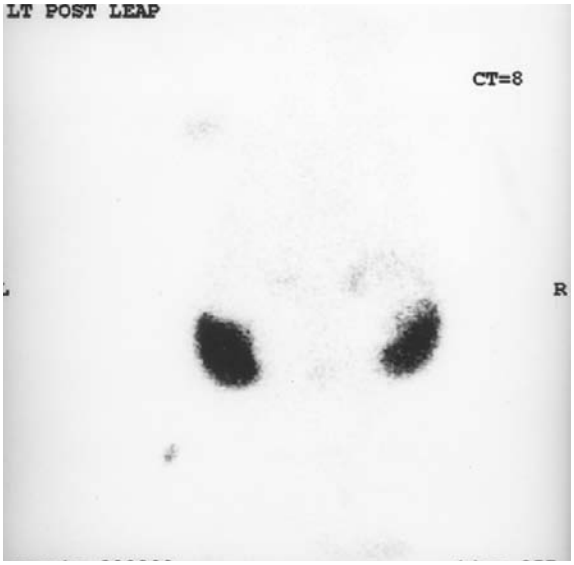

Figure 7.9 DMSA scintigrapy in a child with bilateral duplex-system ureterocoeles. Left upper renal pole is non-functioning and there is only minimal function in the thin rim of renal parenchyma overlying the grossly dilated right upper pole. Both lower poles exhibit normal function.

DMSA scintigraphy

Dimercaptosuccinic acid (DMSA) scintigraphy should be undertaken routinely to assess the distribution of function in the duplex kidney (Figure 7.9). Areas of interest drawn around the upper and lower

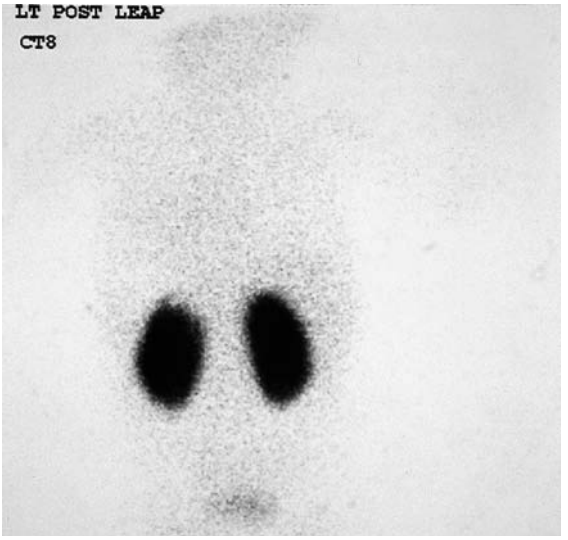

Figure 7.10 DMSA scintigraphy in a case of 'cryptic' duplication. The subtle defect at the left upper pole represents a non-functioning, non-dilated moiety.

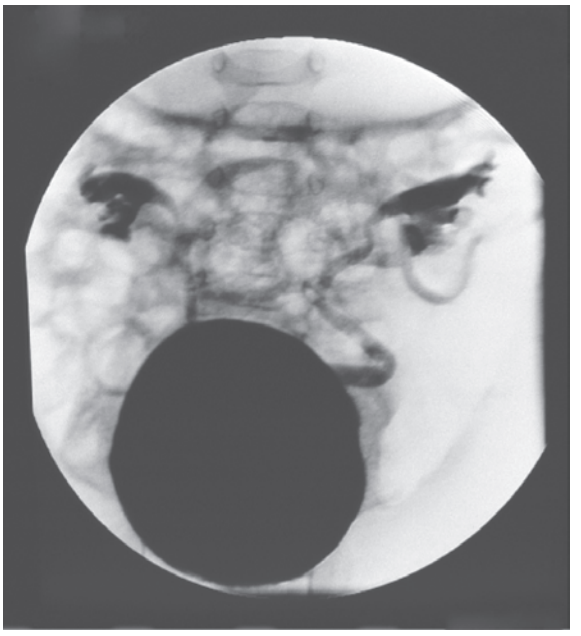

Figure 7.11 Micturating cystogram demonstrating bilateral lower pole vesicoureteric reflux. Note the absence of upper pole calyces and 'drooping flower' appearance of the lower pole pelvicaliceal systems. On the left there is lateral displacement of the kidney and 'scalloping' of the ureter, owing to the presence of a grossly dilated upper pole ureter terminating ectopically.

poles enable the differential function of each moiety to be calculated. DMSA is also of occasional use in detecting 'cryptic duplication' (Figure 7.10) (see Chapter 3).

Micturating cystourethrography (MCU)

An MCU is an essential investigation for patients suspected of having lower pole vesicoureteric reflux. In the presence of a complete duplication anomaly, reflux is almost always restricted to the lower renal pole (Figure 7.11). Reflux into both poles is usually indicative of incomplete duplication. Where the reflux differs in severity between the two moieties and is more marked in the lower pole (Figure 7.12), the ureteric confluence is likely to be very low, and immediately proximal to the ureteric orifice. Cystography is also routinely advisable in patients with duplex-system ureterocoele in view of the high incidence of reflux, both ipsilateral and contralateral. Similarly, in supra-sphincteric ectopia, the cystogram may demonstrate reflux to the upper pole during voiding.

Intravenous urography

The IVU retains an occasional role in the evaluation of duplex systems, particularly in the detection of 'cryptic duplication', the radiological signs of which may include an 'absent' upper calyx and lateral and downward displacement of the lower moiety, an appearance on IVU which has been likened to a 'drooping flower' (Figure 7.13). A further radiological sign is the 'scalloped' appearance of the lower polar ureter. With the exception of the 'absent' upper pole calyx, these radiological signs are caused by the presence of a dilated, non-visualised, drainage system arising from the upper renal pole. In addition, the discovery of an incomplete duplication anomaly on one side may raise the possibility of 'cryptic duplication' in the contralateral upper tract.

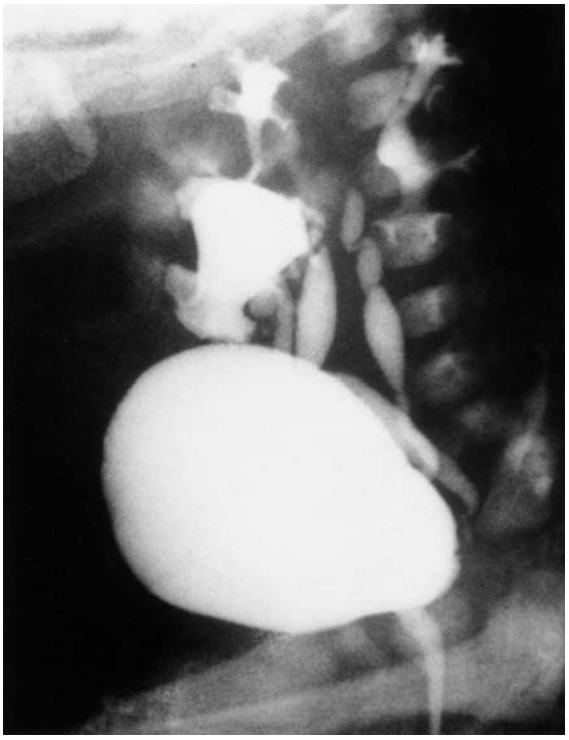

Figure 7.12 Micturating cystography demonstrating bilateral vesicoureteric reflux. Incomplete duplication on the right. (The disparity between the upper and lower pole reflux on the right is indicative of ureteric confluence just proximal to the ureteric orifice.)

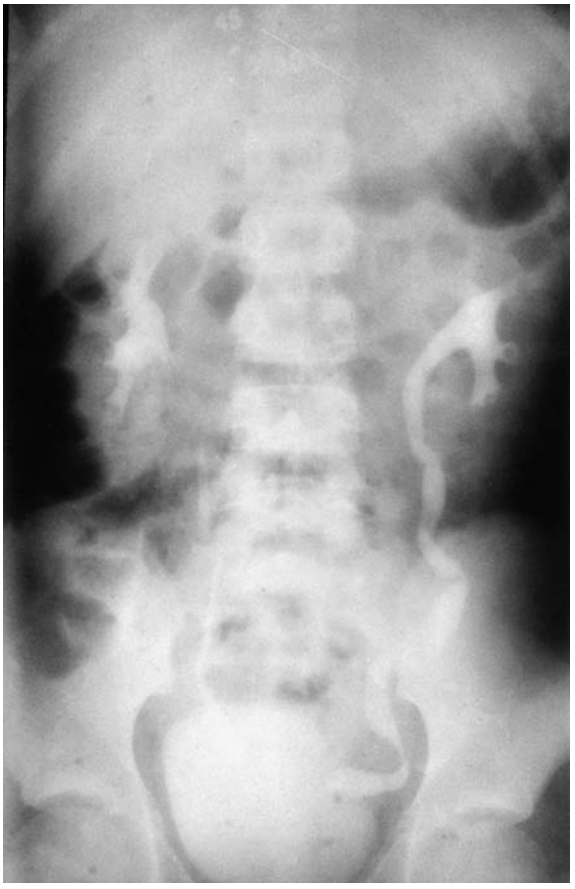

Figure 7.13 Intravenous urogram demonstrating left duplication with non-functioning upper pole. A left upper calyx is not visualised, the lower pole is displaced laterally and downwards ('drooping flower') and the lower pole ureter is deviated ('scalloped') by the presence of the grossly dilated upper pole ureter.

Cystoscopy and examination under anaesthetic

Cystoscopy is routinely advisable for the assessment of duplex-system ureterocoeles, principally in order to determine whether or not the lesion is ectopic (Figure 7.14). In girls with a suprasphincteric ectopic ureter, the ectopic ureteric orifice is visualised on cystoscopy immediately below the bladder neck. Examination under anaesthetic may also reveal an ectopic orifice in girls with infrasphincteric ectopia, although failure to identify an ectopic orifice is not unusual and by no means excludes this diagnosis.

Methylene blue test

With the introduction of magnetic resonance imaging (MRI), the methylene blue test for an ectopic ureter associated with a 'cryptic duplication' is now of largely historic interest. Methylene blue is instilled into the bladder via a catheter, which is then removed, and a pad is placed upon the vulva. If subsequent wetting of the pad is 'blue' the incontinence is due to a bladder problem, but if the fluid on the pad is 'clear' the diagnosis of infrasphincteric ectopia is confirmed.

Magnetic resonance imaging (Figure 7.15)

MRI is an attractive form of investigation, since it has the potential to clarify anatomy and provide

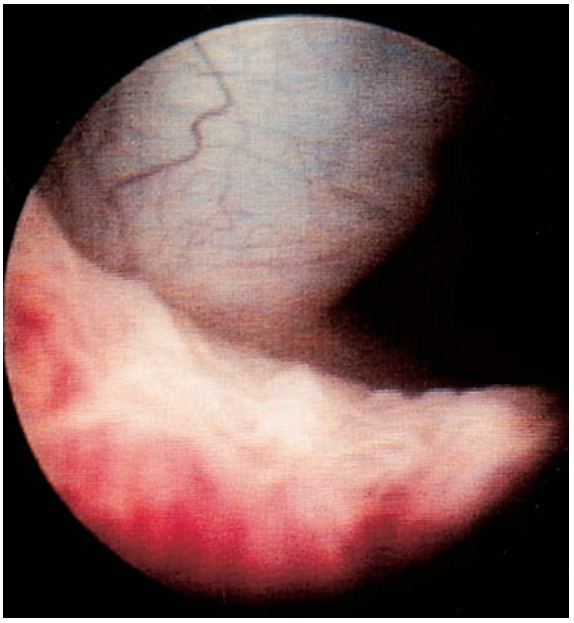

Figure 7.14 Endoscopic appearances of a duplex ureterocoele at the level of the bladder neck.

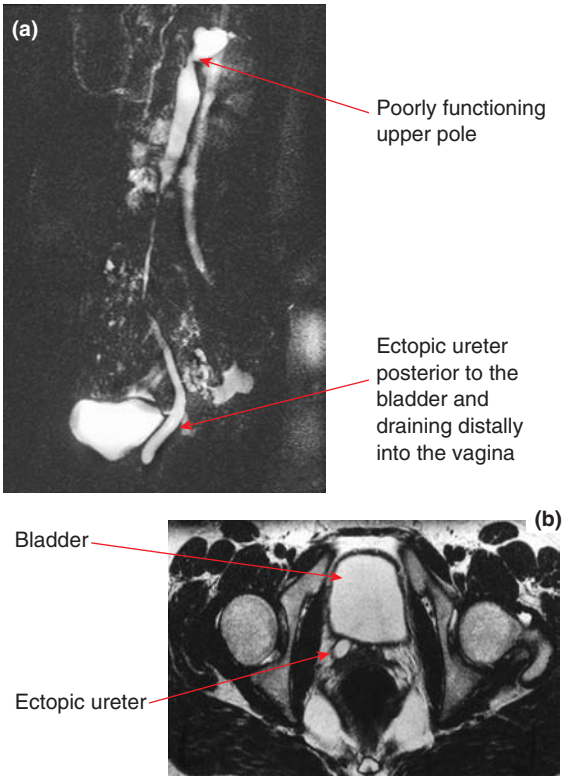

Figure 7.15 MR urogram demonstrating an 'occult' duplex ectopic ureter which had been suspected from the history but could not be confirmed by conventional imaging techniques: (a) upper pole moiety and associated ectopic ureter clearly visualised; (b) transverse image demonstrating the ectopic ureter lying posterior to the bladder base.

functional information without exposure to radiation. The major disadvantage is the requirement for general anaesthesia or sedation in children to ensure they remain still while the scan is being performed (see also Chapter 3). Nevertheless, this investigation is undoubtedly justified in children with complex or elusive forms of duplication in view of the superior quality of the images and anatomical information yielded by MRI. Indeed, the recent development of fast three-dimensional scanners, combined with MR urography, represents a major advance in the investigation of duplex systems.

Management

Duplex-system ureterocoele

Management of this anomaly is influenced by a number of factors, including the mode of presentation and the presence of any associated or secondary effects of the ureterocoele on the upper renal pole, the ipsilateral lower renal pole, the bladder and the contralateral upper renal tract.

In an appreciable proportion of cases detected by prenatal ultrasonography, none of these considerations apply as the affected infants are asymptomatic and the urinary tract is normal, apart from the ureterocoele itself and the small and severely dysplastic upper renal pole. Whether any surgical intervention is indicated in such cases, especially for those with small ureterocoeles, remains debatable.

There are several options for surgical intervention.

Endoscopic ureterocoele incision (Figure 7.16)

The indications for this technique of decompressing a ureterocoele are:

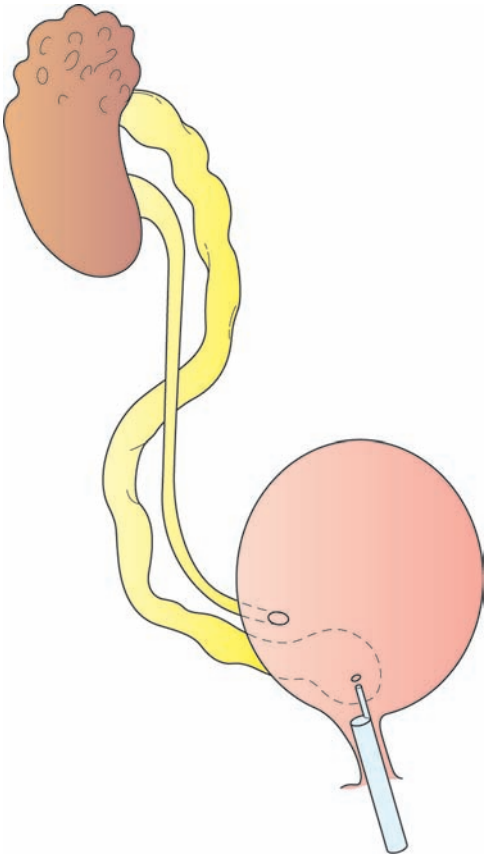

Figure 7.16 Diagrammatic illustration of the simplest form of intervention – endoscopic puncture.

- in antenatally detected cases where the ureterocoele is prolapsing, or risks obstructing the bladder outlet
- as a temporising measure in patients presenting acutely with gross upper polar sepsis.

Although endoscopic incision is the least-invasive form of intervention, it does carry the risk of inducing upper pole reflux. To minimise this risk, it is important to make the incision in the ureterocoele as close to the bladder wall as possible. Favourable medium-term results published from some centres indicate that endoscopic incision alone may represent adequate treatment in selected cases, principally those detected antenatally. However, in other cases, and probably a majority, some more definitive form of surgery is eventually required. Further long-term outcome studies are required to fully evaluate the indications and effectiveness of endoscopic incision.

Upper pole heminephrectomy

This procedure is usually the first choice in cases where upper polar function is severely compromised. When performed via an open surgical approach, the upper moiety is excised, together with as much of the ureter as can be safely mobilised and excised through the same incision. The ureterocoele is aspirated and drained via the ureteric stump, which is left in situ (Figure 7.17a). The laparoscopic approach is being used increasingly and has the advantage that the ureter can be removed almost in its entirety (see Chapter 23). Surgery confined to removal of the upper pole and a varying length of ureter (the 'simplified approach') represents definitive treatment in the majority of patients, with subsequent excision of the ureteric stump and ureterocoele and reimplantation of the lower polar ureter being required in only 10–20% of cases.

Pyelopyelostomy (Figure 7.17b)

This procedure is only appropriate for the small percentage of cases in which there is a useful degree of function in the upper pole which is accompanied by a degree of dilatation of the lower renal pole pelvis/proximal ureter. The upper pole pelvis is divided, separated from the ureter and anastomosed to the pelvis of the lower pole. The defunctioned upper pole ureter and ureterocoele are then aspirated to ensure they are emptied and fully decompressed.

Ureterocoele excision and reimplantation (Figure 7.17c)

This procedure is employed when there is useful upper pole function and no dilatation of the lower pole. In these circumstances the ureterocoele is usually intravesical and the upper pole ureter only moderately dilated, thereby enabling straightforward reimplantation of the conjoined ureters (Figure 7.18), once the ureterocoele has been

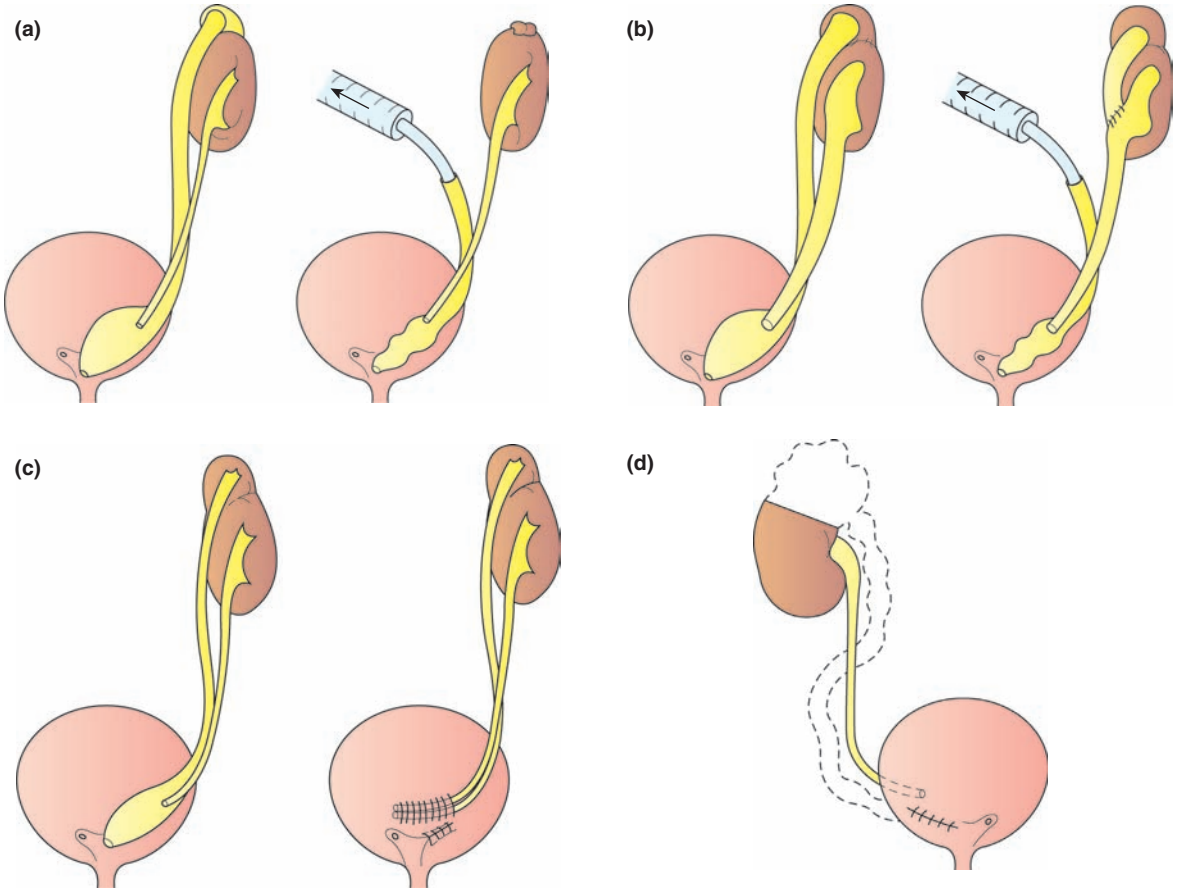

Figure 7.17 Open surgical options. (a) Normal lower pole, non-functioning upper pole – managed by upper pole heminephrectomy, excision of the proximal ureter via the same incision, and aspiration of the residual upper pole ureteric stump ('simplified approach'). (b) Functioning upper pole, dilated lower pole – management by pyelopyelostomy. Excision of proximal upper pole ureter and aspiration of ureteric stump. (c) Functioning upper pole, non-dilated lower pole – management by excision of ureterocoele and reimplantation of conjoined duplex ureters. (d) Heminephroureterectomy with excision of ureterocoele (often necessitating lower pole ureteric reimplantation). Definitive surgical treatment, but a major procedure requiring two separate incisions.

excised. As a rule it is preferable to delay this operation until after 1 year of age, because of the risk of interfering with bladder function.

Nephrectomy

Nephrectomy is appropriate when the function of both renal poles is severely compromised. Refluxing ureters should be excised, but a non-refluxing ureteric stump may be left in situ provided the ureterocoele is aspirated.

Upper pole heminephrectomy, ureterectomy and ureterocoele excision (Figure 7.17d)

This is the most extensive operation for a duplex-system ureterocoele. It requires the use of two incisions and is a potentially lengthy and technically challenging surgical undertaking (Figure 7.19). Particular care is required when excising a caecoureterocoele in view of the risk of damage to the bladder neck and striated sphincter mechanism. Other

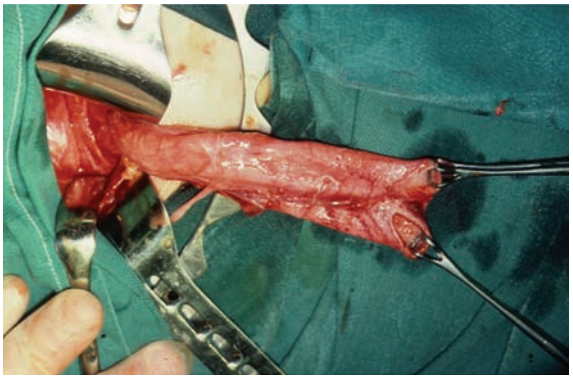

Figure 7.18 Duplex ureters in common sheath after transvesical mobilisation.

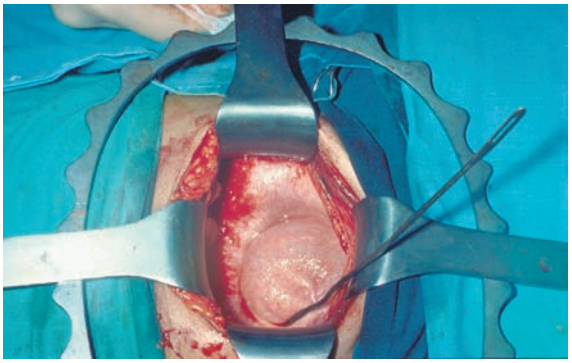

Figure 7.19 Intraoperative appearance of large ureterocoele exposed transvesically.

possible iatrogenic complications include vesicovaginal fistula. To minimise the risk of complications the bulk of the ureterocoele should be excised from above, the detrusor and mucosal defect closed, and any remaining distal lip resected endoscopically from below. Reimplantation of the ipsilateral lower pole ureter is often required, and care is needed when mobilising the dilated upper pole ureter to avoid damaging or devascularising the healthy lower pole ureter. An alternative approach consists of laparoscopic upper tract surgery (heminephroureterectomy) coupled with an open bladder procedure to accomplish excision of the ureterocoele and any associated intravesical procedures.

Suprasphincteric ectopic ureter

Indications for surgical intervention are relative, not absolute, and centre on recurrent urinary infection resulting from the presence of the ectopic ureter. In the great majority of cases, with negligible upper polar function, heminephrectomy is sufficient. However, when this form of ectopic ureter is also associated with upper pole reflux it is necessary to remove the ureter. This can be achieved by an open approach, using a separate abdominal incision to take the dissection and excision of the ureter down as close to the urethra as is practicable. Alternatively, this procedure can be performed laparoscopically. In the rare case with a useful degree of function in the upper pole, the ectopic ureter may be reimplanted into the bladder. If, as is usual, the distal ureters are conjoined, it is necessary to reimplant them both together en bloc.

Infrasphincteric ectopic ureter

As previously indicated, the main problem with this anomaly lies in its diagnosis rather than treatment. It is always worth bearing in mind that in some 10% of cases the lesion is bilateral and that the finding of a duplex system on one side should always prompt consideration of the possible presence of a cryptic contralateral upper pole associated with an ectopic ureter. Excision of the affected upper renal pole(s) invariably cures the presenting complaint. Ureteric reimplantation (or pyelopyelostomy) may be considered for the very occasional case having useful function in the upper pole.

Vesicoureteric reflux

As a rule, management of vesicoureteric reflux in the presence of a duplication anomaly runs along the same lines described for reflux generally (Chapter 5). There are, however, two particular features relating to complete duplication anomalies which may influence management.

Persistent reflux, lower pole reflux

This condition, especially if severe, is less likely to resolve spontaneously than is the case with

single-system reflux. For this reason antireflux surgery is more commonly required (although only where there are positive indications, such as breakthrough infections while on antibiotic prophylaxis, or infections following discontinuation of prophylaxis). Because endoscopic correction (STING procedure) tends to be less effective in the presence of complete duplication, open surgical reimplantation is more often required than with reflux into single ureters. The adjacent ureteric orifices are circumcised together and the underlying ureters then mobilised en bloc in their common sheath.

Lower pole dysplasia

In a proportion of cases DMSA scintigraphy demonstrates grossly impaired function in the affected lower pole that almost invariably represents congenital dysplasia rather than acquired infective scarring. When surgical intervention is indicated, this should take the form of lower pole nephrectomy, along with excision of the ureter down to the point where it enters a common sheath with the upper polar ureter.

Pelviureteric junction obstruction

This condition almost invariably affects the lower pole and is managed as other PUJ obstructions (see Chapter 6).

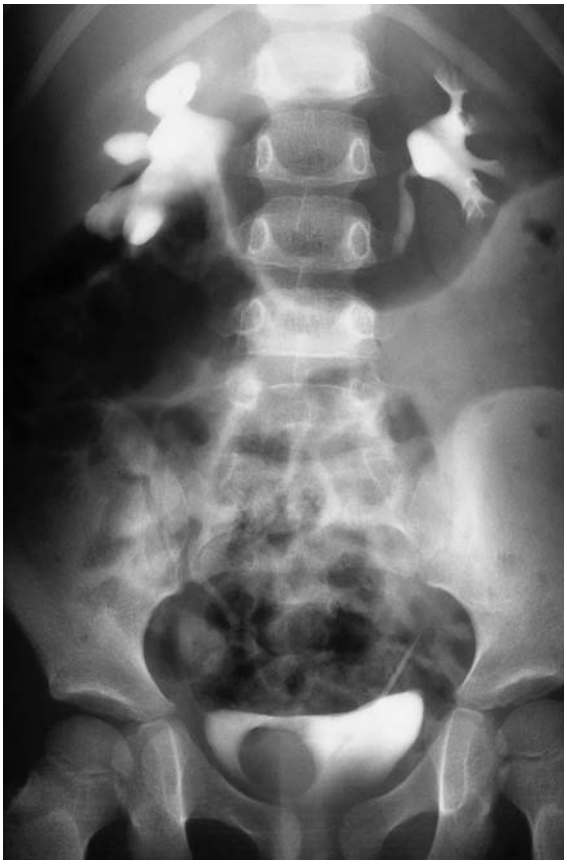

Figure 7.20 Intravenous urogram demonstrating a right-sided orthotopic (single-system) ureterocoele with brisk uptake of contrast, indicating good preservation of renal function.

Single-system ureterocoele and ectopic ureter

Single-system ureterocoeles

Clinical features

These lesions, which occur more commonly in boys than girls, almost always lie entirely within the bladder (orthotopic ureterocoeles). Whereas the anomaly can be detected prenatally, it also comes to light in later childhood as a largely incidental finding on ultrasonography or intravenous urography.

Single-system ureteroceles which present clinically usually do so with urinary infection but, very occasionally, they may also present with bladder outflow obstruction causing intermittent retention, or symptoms related to calculi. Upper tract dilatation is absent or of mild to moderate severity and, in most cases, renal function is normally preserved (Figure 7.20).

Management

Indications for surgical intervention comprise:

- symptoms
- upper renal tract obstruction.

Endoscopic incision is the simplest and least-invasive form of treatment but, because of the risk

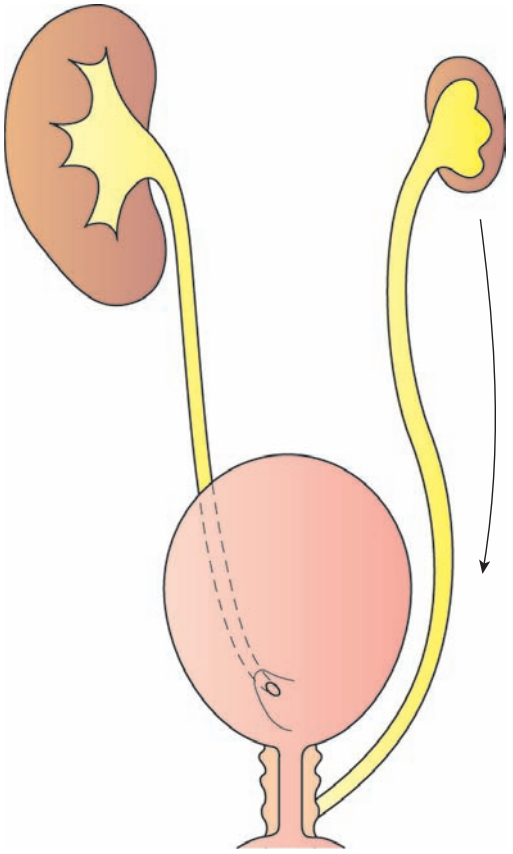

Figure 7.21 The anatomy of a single-system infrasphincteric ectopic ureter. The arrow indicates that the affected kidney may be sited ectopically.

of inducing reflux, some paediatric urologists believe it is preferable to excise the ureterocoele and to reimplant the underlying ureter.

Opinion is divided on the management of small orthotopic ureterocoeles, with some advocating 'prophylactic' endoscopic incision and others favouring simple observation.

Single-system ectopic ureter

Single vaginal ectopic ureter (Figure 7.21)

This anomaly is less common than duplex-system ectopia as a cause of urinary incontinence in girls. The ureter terminates ectopically in the vagina, usually around the junction of the middle and distal thirds, and the clinical presentation is the same as for infrasphincteric duplex-system ectopia, namely continuous dribbling of urine superimposed upon otherwise normal micturition. Similarly, this condition presents diagnostic rather than therapeutic difficulties, partly because the affected kidney, being small and dysplastic, is difficult to image, and partly because it may lie ectopically anywhere from the lumbar region to the pelvis.

An initial ultrasound examination often reports 'unilateral renal agenesis', but a more purposeful search may locate the kidney. DMSA scintigraphy and MRI may be helpful in locating a small kidney which cannot be visualised by ultrasound. The diagnosis may also be confirmed by identification of the ectopic orifice and retrograde contrast studies or, as a last resort, by laparoscopy. Nephrectomy is curative.

Unilateral urethral ectopic ureter

In this rare anomaly, virtually confined to girls, the single ureter terminates ectopically in the proximal urethra. The function of the overlying kidney is usually impaired – sometimes severely so – presumably as a result of congenital dysplasia. The ureter is usually sufficiently dilated to be detectable by ultrasonography.

When not picked up by prenatal ultrasonography, the anomaly generally presents with urinary infection. In symptomatic cases with useful renal function, the ureter can be reimplanted into the bladder, if necessary with trimming if the ureter is markedly dilated. Otherwise, nephrectomy is indicated.

Bilateral single ectopic ureters

This exceptionally rare anomaly affects girls more often than boys. Both single ureters terminate ectopically in the proximal urethra. The bladder neck and external urethral sphincter are

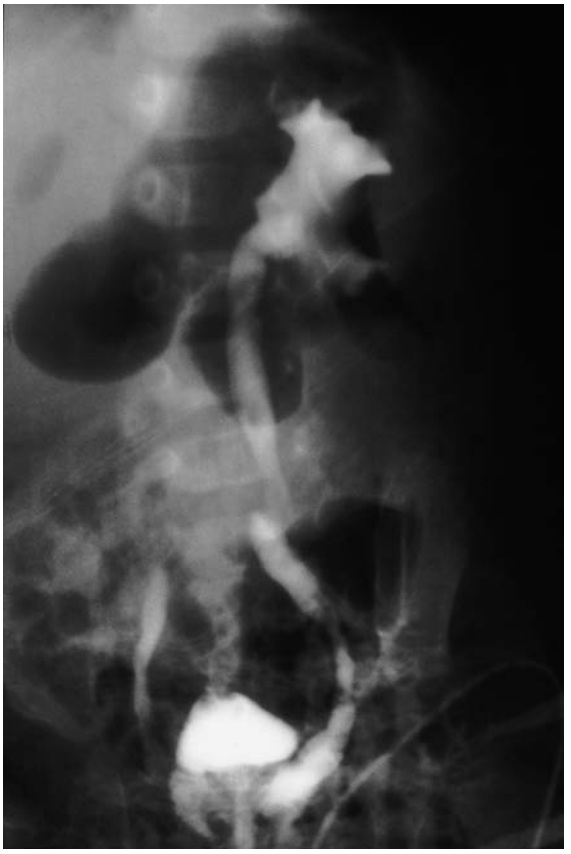

Figure 7.22 Intravenous urogram in a child with bilateral single ectopic ureters. Both ureters drain infravesically and the bladder is of small capacity.

incompetent, and the bladder itself is usually small (Figure 7.22). As a rule both kidneys are affected by a degree of dysplasia (sometimes severely so), while the ureters tend to be dilated and are thus detectable by ultrasonography. Presentation may be either with continuous dribbling incontinence in childhood or with symptoms of renal insufficiency in infancy.

Treatment requires reimplantation of the ectopic ureters into the bladder, plus augmentation cystoplasty when the bladder is small. Finally, it is necessary to deal with the sphincteric incompetence, either by bladder neck repair or by bladder neck closure along with a Mitrofanoff procedure.

Key points

- Incomplete duplication is relatively common and is often of little or no clinical significance. By contrast, complete duplication is rarer and is more frequently associated with symptoms, impaired function or both.
- Complete duplication anomalies can be divided, on the basis of their embryology, into those affecting principally the upper renal pole (ureterocoele, suprasphincteric or infrasphincteric ectopic ureter) or those affecting the lower renal pole (vesicoureteric reflux, pelviureteric junction obstruction).
- Renal dysplasia of the upper or lower pole is common in all forms of complete duplication.
- Infrasphincteric ectopic ureter in girls, leading to urinary incontinence, often presents problems with diagnostic imaging because the affected upper renal pole tends to be severely dysplastic. However, MRI is becoming a valuable imaging technique for investigating cryptic or complex duplex systems.
- Experience with laparoscopic heminephrectomy is limited at present but this approach has the advantage of permitting access to most or all of the upper pole ureter, thus avoiding the need for a suprapubic incision.
- Open bladder surgery may still be required for large ureterocoeles. Although the endoscopic puncture of ureterocoeles is simple and relatively non-invasive, the long-term results have yet to be fully evaluated.

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Posterior urethral valves and other urethral abnormalities

8

Divyesh Y Desai and Patrick G Duffy

Topics covered

Introduction

With the exception of strictures, urethral obstruction in childhood is congenital in origin and of the various causes of urethral obstruction only posterior urethral valves commonly give rise to secondary changes in the upper renal tracts – sometimes with devastating consequences. There is increasing evidence to indicate that the consequences of outflow obstruction are due as much to secondary effects upon bladder function as to the underlying obstruction itself. Moreover, the earlier the obstruction develops the worse the impact on the upper tracts, to the extent that obstruction dating from early fetal life is commonly complicated by renal dysplasia.

Posterior urethral valves

Hugh Hampton Young in 1919 described the first classification of this condition based on postmortem dissection studies. Posterior urethral valves carried a mortality rate of almost 100% during the early years of the 20th century and remained as high as 50% until the 1950s.

By contrast, the mortality reported in one recent series was only 0.3%, but this improvement has come at the expense of a greater proportion of young patients in chronic renal failure.

Posterior urethral valves occur only in males, in whom the incidence is of the order of 1 in 4000–6000. Although a few familial cases have been recorded, including in siblings, there is no established genetic predisposition.

Anatomy

Recent studies have challenged Young's classification, based on postmortem studies, which identified three types of valvular obstruction. Dewan and Ransley's anatomical and endoscopic studies point to a single configuration comprising an obliquely orientated congenital obstructive posterior urethral membrane (COPUM) with a variably sized eccentric aperture located within it (Figure 8.1), arising from the verumontanum, extending through the region of the external urethral sphincter to attach to the anterior urethral wall. Following urethral instrumentation, including catheterisation, the membrane is disrupted in the midline to result in the appearance of two separate, side-by-side valve leaflets described as the classical type I valves by Young. Type III valves are uncommon (5%) and are best described as a transverse perforated membrane in the bulbar urethra

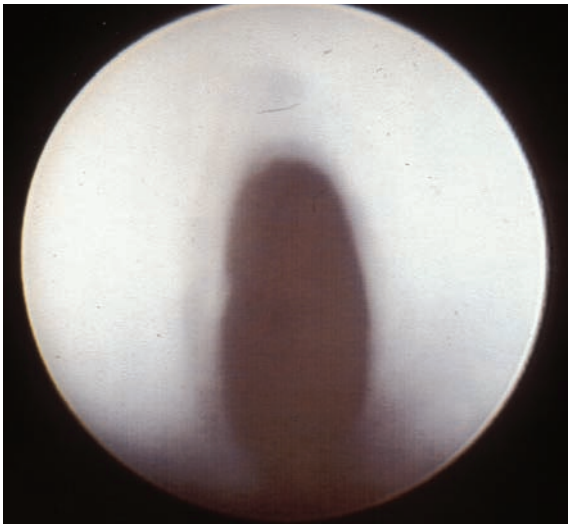

Figure 8.1 Endoscopic appearance of intact valve membrane prior to endoscopic ablation.

with no attachment to the verumontanum. Moreover, type II valves, which are described as leaflets that extend upwards from the verumontanum, are non-obstructive folds of mucosa of no clinical significance.

Pathophysiology

The valvular obstruction develops at approximately 7 weeks' gestation as a result of abnormal embryogenesis at the confluence of mesonephric ducts and the urogenital sinus membrane. The consequent dilatation of the fetal urinary tract may be detectable by ultrasonography as early as the 14th week of gestation.

Studies of experimentally induced fetal bladder outflow obstruction in animals have established the following:

- Early outflow obstruction leads to abnormalities in bladder wall components with an increase in the collagen element, aberrations in the nerve supply and renal dysplasia (which is characterised on histology by the presence of primitive tubules and the persistence of abnormal mesenchymal derivatives such as cartilage interspersed between normal renal tissue).
- Obstruction in later gestation results in the typical sequelae of chronic bladder outflow obstruction and raised intravesical pressure, without the occurrence of renal dysplasia.

Clinical experience indicates that the consequences of obstruction by posterior urethral valves in man may exist at these extremes or at any point between them. Thus, the long-term prognosis in an individual with this disorder is determined by a combination of the degree of early abnormal development, involving the urethra, bladder, kidneys and the ureters, and the severity of late secondary effects of outflow obstruction on the bladder and the upper urinary tract.

The relative contributions made by these different factors to the functional outcome of bladder as well as renal function is often difficult to determine, and therefore predicting long-term outcomes is usually difficult. The urinary tracts of boys with posterior urethral valves must therefore be monitored through childhood, particularly during teenage and adolescent years.

Presentation

The fetus

Currently more than 80% of cases are detected on prenatal ultrasound. Although the underlying urethral anomaly dates from the seventh to the ninth week of gestation, dilatation of the urinary tract may not develop until much later in pregnancy. Fifty five per cent of cases of prenatally detected posterior urethral valves are picked up on routine maternal ultrasound performed between 16 and 20 weeks. In the remaining cases, the appearances of the fetal urinary tract are normal in the second trimester, and the condition is detected in later pregnancy as a result of scans performed for obstetric indications.

Functional outcome is closely linked to the gestational age at which dilatation becomes apparent, and studies have shown that when the condition is detected at 16–20 weeks the prognosis is likely to be poor, especially if oligohydramnios is

also present. In pregnancies which proceed to term, a severely affected infant often demonstrates features of Potter's syndrome at birth (characteristic facies – Potter's, skeletal 'moulding' deformities), and death supervenes in the early newborn period as a result of pulmonary hypoplasia.

In the absence of second-trimester oligohydramnios the functional prognosis is linked to the severity of dilatation and other prognostic features on second-trimester ultrasound (Table 8.1).

Various biochemical constituents of fetal urine (sodium, calcium, B_2-microglobulin, osmolality) have been studied as possible prognostic markers, but there is considerable overlap with normal values and predictive sensitivity is poor (see Chapter 10).

In cases where dilatation develops later in gestation, the prognosis is generally good. In addition to dilatation and renal dysplasia (bright kidneys), other findings detected by fetal ultrasound include lung hypoplasia, urinary ascites and perinephric urinomas.

The neonate

Symptoms usually relate to bladder outflow obstruction or, less often, to the effects of impaired renal function. Listlessness, poor feeding, irritability and failure to thrive are common. The urinary stream, if witnessed, is usually poor. The bladder is palpable in most instances; the kidneys may also be palpated. Urinary ascites occurs as an occasional complication.

The infant

Presentation in infancy is generally with a urinary infection (Chapter 4) and in the majority of cases physical signs are absent.

Gram-negative sepsis and renal failure with gross electrolyte disturbance were common forms of presentation but with increasing detection by prenatal ultrasound and heightened awareness of urinary infection among infants they have become unusual. Chronically impaired renal function is usually manifest as poor growth.

Table 8.1 Ultrasound features of posterior urethral valves in the fetus

Male fetus
Bilateral upper tract dilatation
Persistently distended full bladder
Predictors of poor functional outcome and early-onset renal failure
Detection before 24 weeks' gestation
Bladder wall thickening
Echo-bright kidneys (renal dysplasia)
Oligohydramnios

The older child

Presenting features may include manifestations of renal failure such as growth retardation, urinary infections or voiding symptoms (typically prolonged voiding, rather than a poor urinary stream as such). In addition, the diagnosis of posterior urethral valves is occasionally made during the investigation of diurnal or nocturnal enuresis.

Investigations

Prenatal

The presence of posterior urethral valves can only be inferred from the ultrasound appearances of a distended fetal bladder and dilated upper tracts (Figure 8.2), as the alternative diagnoses include urethral atresia (always lethal), prune-belly syndrome, megacystis–microcolon intestinal hypoperistalsis syndrome, and marked primary vesicoureteric reflux. However, the diagnosis can be made with more certainty if there is dilatation of the posterior urethra – the so-called 'keyhole sign' (Figure 8.3).

Postnatal

Ultrasonography is the initial investigation, the relevant findings comprising upper tract dilatation (which is sometimes only unilateral), perinephric urinoma (occasionally), thickening of the bladder wall, with or without residual urine, and, if

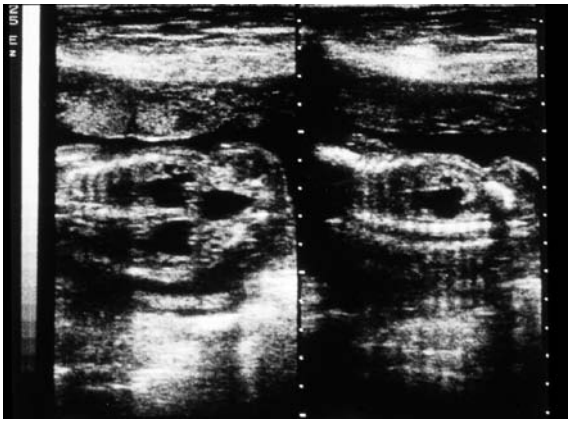

Figure 8.2 Prenatal ultrasound demonstrating marked dilatation of both fetal kidneys and the fetal bladder. The fetal spine and thorax are clearly visible in both these longitudinal images.

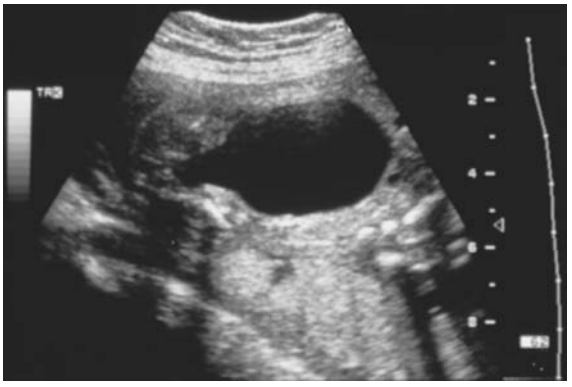

Figure 8.3 Ultrasound appearances illustrating the diagnostic 'keyhole sign'. Dilated (thick-walled) bladder and dilated posterior urethra.

voiding views can be obtained, dilatation of the posterior urethra.

Micturating cystourethrography (MCU) provides the definitive diagnosis, with a range of findings, as illustrated in Figures 8.4–8.6. Vesicoureteric reflux is present in 40–60% of cases at the time of initial evaluation and is unilateral in approximately two-thirds of cases.

Initial assessment also includes measurement of electrolyte balance and renal function (it should be noted that in the first 48 hours of life serum creatinine levels are a reflection of maternal renal function).

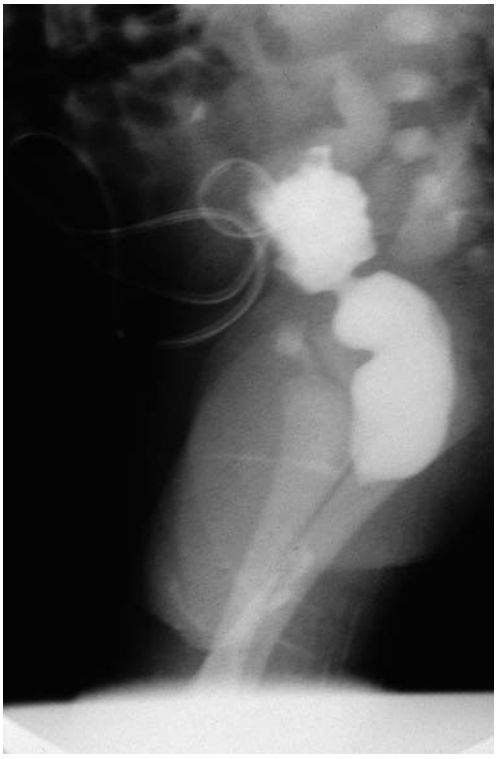

Figure 8.4 Newborn infant: micturating cystourethrogram (MCU) findings. Grossly dilated posterior urethra, indentation by prominent bladder neck, small trabeculated bladder.

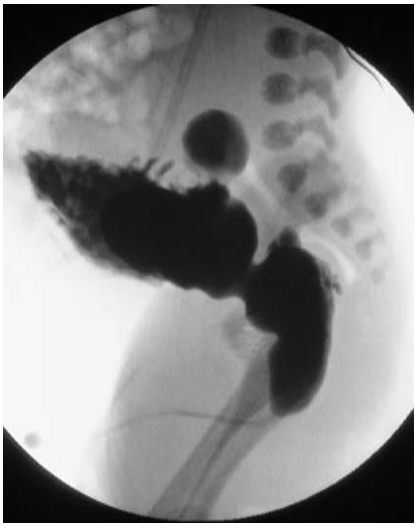

Figure 8.5 Newborn preterm infant, prenatal diagnosis. Heavily trabeculated bladder with diverticulum, prominent bladder neck, and demarcation between dilated posterior urethra and non-dilated distal urethra at the site of the valve membrane.

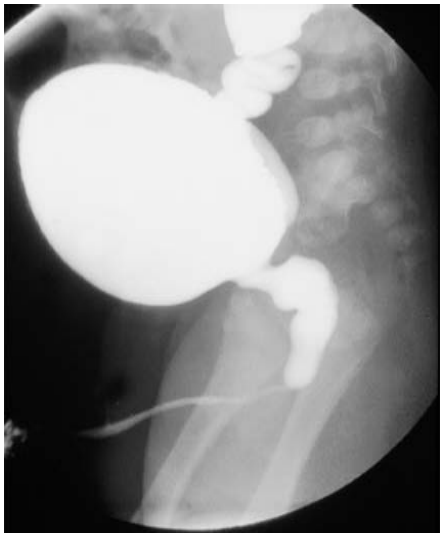

Figure 8.6 MCU in a boy presenting in the first year of life with urinary infection. Smooth-walled non-trabeculated bladder, unilateral grade IV reflux.

Treatment

The fetus

The rationale for fetal intervention derives from experimental studies, which demonstrated that experimentally induced obstructive renal damage could be ameliorated by intrauterine decompression of the obstructed fetal bladder. However, the extent to which these experimental findings can be translated to humans remains unclear. In clinical practice, prenatal intervention, in the form of vesicoamniotic shunting, has a chequered history and the weight of published experience indicates that it may have a limited role. Evaluating the possible benefits of vesicoamniotic shunting during pregnancy in the management of posterior urethral valves is subject to the following limitations:

- Posterior urethral valves can be difficult to diagnose with certainty.
- Renal failure may not supervene until late childhood or adolescence; thus it is difficult to assess the true impact of intervention.
- There are no controlled trials to compare the outcome in boys who were treated in utero against those who were not.

In order to address this very important issue, a UK-wide trial is currently underway (PLUTO). This is a multicentre trial, which will assess the effects of prenatal vesicoamniotic shunting on known outcomes of bladder and renal function in boys with posterior urethral valves. The results may enable us to address more clearly the role of intervention in bladder outflow obstruction.

Experience with intrauterine valve ablation was reported with enthusiasm and optimism, but no long-term outcomes are available.

Termination of pregnancy is the most common form of prenatal intervention, particularly when severe dilatation and associated oligohydramnios are detected in early pregnancy. In these circumstances decompression of the obstructed urinary tract is of little if any benefit for renal function, since irreversible renal dysplasia is almost invariably present. However, there is reasonable evidence of some beneficial effect on pulmonary hypoplasia.

Elective preterm delivery represents another form of intervention, and it may be beneficial in cases of rapidly progressing late-onset dilatation. It is important to balance lung maturity with the risk of progressive renal damage in deciding the optimum timing for preterm delivery.

Between these extremes, vesicoamniotic shunting may have a role in the presence of early obstruction and preserved renal function. However, the procedure carries an appreciable risk of fetal morbidity, which although only 5% in skilled hands is higher in some published series.

Two previous studies of the long-term outcome of shunting reported high intrauterine and neonatal mortality rates and an incidence of renal failure of more than 50% amongst survivors. A more recent study, however, reported that survivors experienced normal neurodevelopment, acceptable renal and bladder function and a satisfactory quality of life.

Although the role of fetal intervention remains controversial, there is universal agreement that prenatal diagnosis has been beneficial by ensuring that the treatment of posterior urethral valves can be undertaken promptly and the risk of serious sepsis minimised.

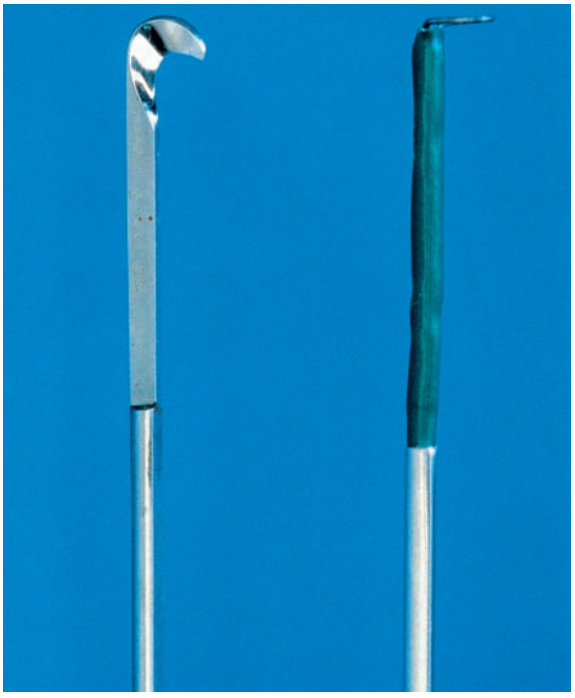

Figure 8.7 Cold knife and cutting resectoscope loop for use with neonatal resectoscope. The availability of instruments designed for neonatal use has simplified management and greatly reduced the incidence of instrumentation-induced urethral trauma.

The neonate

To minimise risk of electrolyte disturbances or of urinary infection the obstruction should be relieved promptly.

Urethral or suprapubic bladder drainage

The usual primary treatment, this will remain for 7–10 days to obtain baseline renal function.

Endoscopic valve ablation

Modern miniaturised endoscopes (Figure 8.7) are used even in small premature neonates. The valve leaflets are incised from margin to base (rather than fully resected), conventionally at the 4 and 8 o'clock positions (Figure 8.8). Unless significant intraoperative bleeding is encountered, postoperative catheterisation is unnecessary.

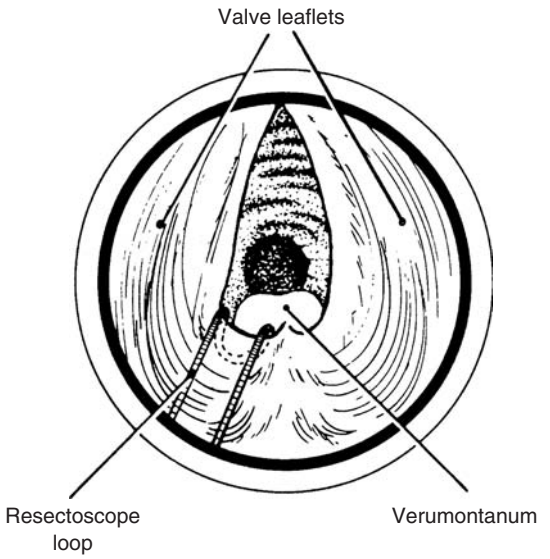

Figure 8.8 Position of the cutting loop prior to ablation of the valve membrane.

Vesicostomy

Vesicostomy drainage may be preferred in those with markedly impaired renal function, especially if deteriorating despite catheterisation, and/or in those with gross bilateral vesicoureteric reflux.

The stoma is created at the apex of the bladder to minimise the risk of prolapse. Closure is undertaken after subsequent valve ablation, within 6–18 months, depending on the initial indication for selecting vesicostomy and the child's level of renal function (Figure 8.9).

Supravesical diversion

Bilateral end ureterostomies or pyelostomies are now rarely performed because:

- defunctioning the bladder may adversely affect its later performance
- a vesicostomy usually provides equally effective drainage and is more easily managed by parents.

Refluxing ureterostomy

Refluxing ureterostomy is an innovative method of overcoming the high bladder pressures during

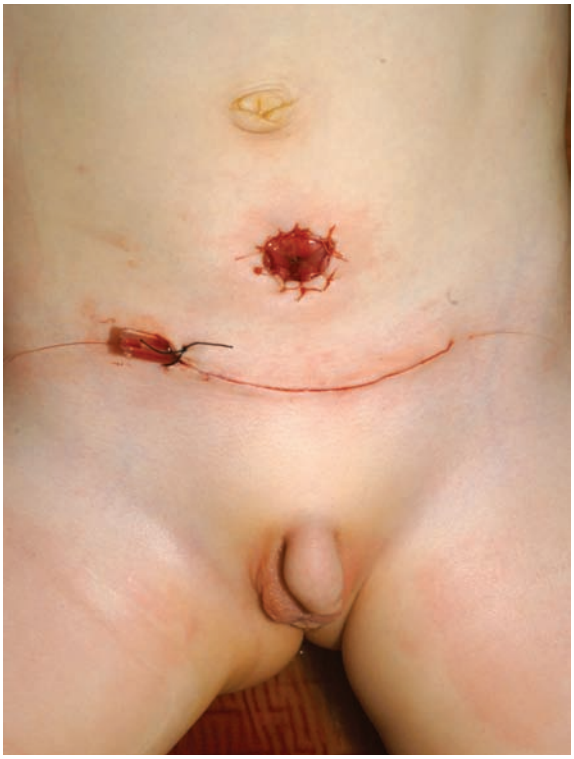

Figure 8.9 Cutaneous vesicostomy is the most commonly used form of temporary diversion.

storage and voiding which persist in infancy despite relief of obstruction. In addition, the procedure also maximises drainage from the ipsilateral kidney and at the same time maintains bladder cycling. The urinary tract is usually reconstituted between 2 and 3 years of age in preparation for potty training.

Urinary leaks

Urinary ascites and perinephric collections or 'urinomas' usually respond to a short period of bladder drainage. Large or persistent perirenal collections may require ultrasound-guided percutaneous aspiration or open drainage (in combination with open nephrostomy).

The infant

Urinary infection in infants with previously undiagnosed posterior urethral valves is often complicated by septicaemia and gross disturbances of electrolyte and acid–base balance, of which hyperkalaemic acidosis is the most serious form. The metabolic disturbances and underlying sepsis demand vigorous treatment, which should be undertaken in cooperation with a paediatric nephrologist. Surgical treatment of the bladder outflow obstruction is best deferred until the general condition has been stabilised, usually after 2–7 days. Vesicostomy may occasionally be required as the primary intervention.

The older child

With few exceptions, endoscopic ablation of the valves is the initial treatment.

Prognosis

Approximately one-third of individuals have impaired renal function in the long term, although this may not become manifest until adolescence. Factors implicated in the aetiology of chronic renal failure include:

- Primary renal dysplasia.
- Secondary damage resulting from bladder outflow obstruction; this occurs principally in utero, but may also occur postnatally if undiagnosed obstruction persists after birth.
- Urinary infection, often in association with vesicoureteric reflux.
- Secondary damage resulting from bladder dysfunction, which persists after relief of outflow obstruction.

The importance of this last component, which is manifest clinically as impaired continence, has only been fully recognised in recent years with the publication of studies demonstrating that patterns of bladder dysfunction change over time. Typically there is a tendency for detrusor overactivity to be replaced by detrusor failure, along with progressive enlargement of bladder capacity and increasing residual volumes of poorly concentrated urine.

Urodynamic studies undertaken in the authors' unit have shown a uniform pattern of bladder

function 1 year after satisfactory valve ablation. During the filling phase, the functional capacity of the bladder is reduced, there is evidence of detrusor overactivity but compliance is unimpaired. The voiding phase is characterised by a distinctive biphasic or polyphasic detrusor pressure profile, high voiding detrusor pressures and incomplete bladder emptying.

By the age of 5 years, bladder function has evolved and falls into three distinct patterns based on voiding bladder dynamics. There is a tendency for detrusor overactivity to diminish and for bladder capacity to increase over the course of time but a small proportion of cases show evidence of bladder decompensation as early as 5 years of age.

Predictors of a poor renal function

Prenatal

- Maternal oligohydramnios, regardless of the gestational age.
- Early detection on prenatal ultrasound of 'bright' kidneys and pelvicaliceal dilatation.

Postnatal

- Presentation in the first 12 months of life (if undetected prenatally).
- Proteinuria.
- Bilateral vesicoureteric reflux.
- Impaired continence at 5 years of age upwards.

Indicators of good renal function

- Presentation in later childhood.
- Protection of the upper tracts by a 'pop-off' phenomenon.

Of these, the most common is unilateral high-grade vesicoureteric reflux in which the affected ipsilateral kidney has negligible or zero function where the contralateral kidney is normal (VURD syndrome).

The protective value of the 'pop-off' phenomenon has probably been overstated, and recent evidence suggests that although this may impart some medium-term benefit, a proportion of boys nevertheless progress to renal failure. Other less common forms of 'pop-off' mechanism include urinary ascites, perinephric urinoma and a large bladder diverticulum.

Follow-up and long-term management

All boys with posterior urethral valves require long-term follow-up. A suggested protocol is given in Table 8.2. Differential renal function is monitored, by MAG3 (mercaptoacetyltriglycine) renography or by DMSA (dimercaptosuccinic acid) scintigraphy, once overall function has stabilised. Upper tract dilatation often improves following valve ablation, but usually persists either unilaterally or, more commonly, bilaterally. Possible explanations include:

- incomplete relief of bladder outflow obstruction
- persistent vesicoureteric reflux
- ureterovesical obstruction secondary to occlusion of the ureterovesical junction by a thick-walled bladder (rare)
- upper tract obstruction due to high-pressure bladder dysfunction (non-compliance, instability)
- ureteric decompensation, particularly in conjunction with polyuria.

Table 8.2 Follow-up protocol for patients with posterior urethral valves

Routine at every visit
Height and weight
Blood pressure
Urinary tract ultrasonography
Urine dipstick
Serum creatinine and electrolytes
As indicated
Isotope renography (MAG3 or DMSA)
Flow rate
Urodynamics
Formal estimation of GFR

A high obligatory output of dilute urine occurs when the concentrating ability of the kidneys declines with the onset of early chronic renal failure (tubular defect). The urinary tract may demonstrate increasing dilatation in response to this large urine output. Investigation should therefore be aimed at reassessing glomerular and tubular renal function.

Vesicoureteric reflux resolves in 30–60% of cases following valve ablation. However, resolution is less likely in the presence of bladder dysfunction or when function in the affected renal unit is poor.

Neonatal circumcision is performed routinely by some surgeons to minimise the risk of infection, although the benefits are largely anecdotal. Breakthrough urinary infections despite antibiotic prophylaxis may improve following circumcision and the need for antireflux surgery or nephroureterectomy is rare.

Bladder dysfunction

Diurnal enuresis secondary to bladder dysfunction often responds to detrusor antispasmodics such as oxybutynin or alternative anticholinergics. Intermittent catheterisation should be considered where incontinence is associated with an impaired voiding and a large volume of residual urine. In practice, urethral self-catheterisation rarely proves acceptable to boys with posterior urethral valves, because, in contrast to patients with neuropathic bladder, their urethral sensation is normal. For this reason, effective long-term intermittent catheterisation is usually dependent on the creation of a continent catheterisable (Mitrofanoff) channel.

Augmentation cystoplasty

The role of augmentation cystoplasty in boys with posterior urethral valves is controversial. Although continence is usually improved, this is at the expense of impaired voiding in at least 40% of individuals, which in turn calls for intermittent catheterisation. Whether the procedure also secures its more important objective of long-term preservation of renal function remains to be definitively established. Bladder function continues to evolve during childhood, with a tendency towards improvement as far as its storage dynamics are concerned. At the present time bladder augmentation would be considered for boys less than 3–4 years of age with severe renal dysfunction, for whom renal transplantation is on the horizon. In this situation one does not have the luxury of awaiting spontaneous improvements in bladder function and it is essential to ensure a safe lower urinary tract prior to renal transplantation. The long-term complications of enterocystoplasty (mucus stone formation, metabolic disturbance, etc.) can be avoided by augmenting the bladder with dilated ureter (ureterocystoplasty). This technique is often more applicable to boys with posterior urethral valves than children undergoing augmentation for neuropathic bladder since they are more likely to have a dilated ureter associated with a non-functioning ipsilateral kidney.

Other urethral abnormalities

Anterior urethral valves, diverticula and megalourethra

These anomalies, which are confined to males, are eight times less prevalent than posterior urethral valves. In many respects they constitute a continuum of urethral pathology while also being distinct entities in their own right. For example, it is difficult to define the point at which the urethral dilatation proximal to anterior urethral valves constitutes a diverticulum, and similarly the point at which an extensive diverticulum becomes a megalourethra.

Anterior urethral valves

As classically described, these take the form of either a fenestrated diaphragmatic membrane or a mucosal cusp arising from the ventral wall of the urethra. In 40% of cases the valve is sited at the bulbar urethra, whereas in 30% it is at the penoscrotal junction and in 30% in the penile

urethra. The presentation is with obstructive symptoms, such as a poor urinary stream, hesitancy or urinary retention. Secondary changes in the upper urinary tracts are rare. Micturating cystourethrography demonstrates the obstruction, and treatment is by endoscopic incision.

Urethral diverticulum

In the more common wide-mouthed form, usually located in the region of the penoscrotal junction, the distal lip may give rise to a form of valvular obstruction as the diverticulum undergoes progressive distension. Presentation is either with obstructive symptoms or with postmicturition dribbling. The rarer saccular lesions have a narrow neck and may occur anywhere along the length of the penile urethra, including in the fossa navicularis. Presentation is with urinary infection – rarely associated with stone formation within the diverticulum. Treatment is by endoscopic incision or resection of the obstructing lip or, rarely, by a perineal approach for the excision of a large diverticulum.

Megalourethra

This rare condition is characterised by marked dilatation of the penile urethra in the absence of any evident obstruction. Megalourethra may be associated with lack of corpus spongiosum or, in the extreme form, with complete absence of the corpora cavernosa. In such cases the penis amounts to little more than a floppy sac comprised of skin externally and urethral mucosa internally. An association exists between megalourethra and other congenital abnormalities, particularly prune-belly syndrome.

Cowper's gland cysts (syringocoele)

These paired structures, located on either side of the urethra at the level of the urogenital diaphragm, are each drained by a duct that courses distally through the corpus spongiosum to enter the bulbar urethra. Distension of the ducts, or of the glands themselves, may cause urethral compression or, if the anterior wall of the cyst ruptures into the urethra, may result in an obstructive membrane. Treatment is as for anterior diverticulum.

Urethral duplications

These rare anomalies may be sagittal or collateral. Of these, the sagittal pattern is more common and takes the form of two channels running one above the other in the sagittal plane, whereas in the collateral form the duplicate urethras run side by side. The most common sagittal configuration comprises an orthotopic principal urethral channel and an epispadiac accessory urethra lying dorsal to it.

In some cases both urethras leave the bladder separately and remain separate throughout their length, whereas in other cases the duplicate urethras unite distally to form a single channel. In the so-called 'spindle' variety the urethra separates into two components before reuniting again more distally, whereas in 'Y' duplications, an accessory urethra diverges from the main channel to emerge in the perianal region or the perineum. Reconstruction is dependent upon individual anatomy but nearly always entails excision of the narrower accessory urethra.

Posterior urethral polyps

These fibroendothelial lesions arise from the verumontanum. Small polyps are usually discovered incidentally during the course of endoscopy for some unrelated purpose, whereas the larger lesions, with a polypoid head floating freely on an extended stalk, tend to obtrude through the bladder neck to give rise to acute, transient episodes of urinary retention. Haematuria or frank urethral bleeding may also occur. Diagnosis is by cystourethroscopy or MCU (Figure 8.10). Most polyps can be excised endoscopically, although for large polyps an open transvesical approach may be required.

Urethral strictures

The aetiology, investigation and management of post-traumatic strictures is considered in Chapter 22. Occasionally, however, a urethral stricture is discovered in a boy with no antecedent history of

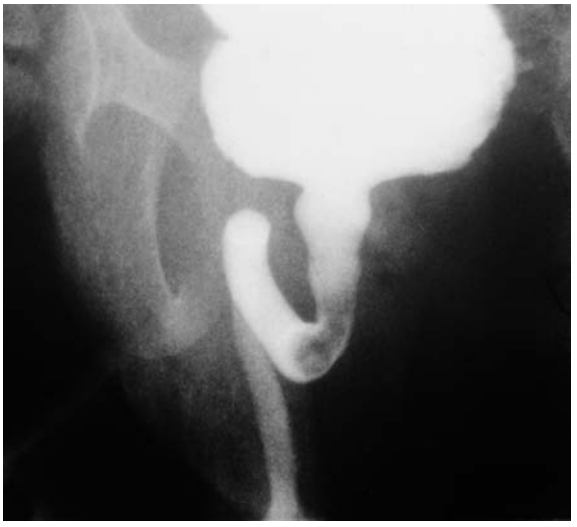

Figure 8.10 MCU outlining a posterior urethral polyp prolapsing from its point of origin into the membranous and bulbar urethra.

external injury, urethral instrumentation or catheterisation. In very young boys the aetiology can be assumed to be congenital, but in the older age group the possibility of previously unrecognised trauma must be entertained. Whether congenital or acquired, such strictures are generally mild and respond well to endoscopic urethrotomy. Formal urethroplasty is rarely required.

Cobb's collar

The clinical status of this anomaly is arguable and its principal significance is as an occasional radiological finding on MCU comprising a short, narrowed segment of urethra immediately distal to the urogenital membrane. On endoscopy, the findings consist of little more than a soft, non-obstructing concentric ring. Although Cobb's collar has sometimes been implicated as a possible cause of voiding disorders, notably enuresis, the consensus is that in children it is essentially a radiological or endoscopic finding without clinical significance.

Urethritis

Although the existence of this condition in boys is recognised by paediatric urologists, it has received little attention in the literature: the clinical features are non-specific and the aetiology is poorly understood. The condition is uncommon but occurs in boys aged 6 years and upward, with presenting features that include dysuria, penile discomfort and urethral discharge or urethral bleeding – usually consisting of no more than spotting on the underclothes. Attempts to culture a specific organism are unrewarding. In the absence of other features, cystourethroscopy is not indicated, as it rarely makes a practical contribution to clinical management. However, when urethroscopy is performed, the findings are characterised by erythema of the anterior and bulbar urethra, with a granular appearance and strands of fibrinous exudate. There is no specific treatment and the condition is self-limiting, although it sometimes runs a protracted course.

Key points

- The original classification devised by Young is outdated. Congenital urethral obstruction generally conforms to a uniform anatomical pattern, although there is considerable variability in the severity of obstruction and the degree of congenital damage to the upper tracts.
- The majority of cases are detected prenatally. The gestational age at diagnosis and the characteristics of the prenatal ultrasound findings provide a guide to prognosis. Prenatal intervention improves the outcome of lung function in the presence of severe oligohydramnios but there is little if any evidence that prenatal intervention benefits renal function.
- Despite relief of the urethral obstruction in early postnatal life, bladder function is abnormal in up to 70% of boys. The pattern evolves during childhood and if unaddressed may contribute to

deteriorating upper tract function and the onset of renal failure in late childhood or early adult life.

- Approximately one-third of individuals with posterior urethral valves are destined to develop chronic renal failure (as a consequence of dysplasia, obstruction, infection and bladder dysfunction). Careful follow-up should be maintained into adulthood.

Further reading

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Cystic renal disease 9

David FM Thomas

Topics covered
Prevalence of different forms of cystic renal diseases in childhood
Autosomal recessive polycystic kidney disease (ARPKD)
Autosomal dominant polycystic kidney disease (ADPKD)
Multicystic dysplastic kidney (MCDK)
Multilocular renal cyst
Simple renal cyst

Introduction

Cystic pathology of the kidney is relatively common across the age range from childhood into late adulthood. The pattern of renal cystic disease in infancy and childhood differs from that encountered in adults, with multicystic dysplastic kidney (MCDK) and the autosomal recessive form of polycystic kidney disease (ARPKD) assuming greater importance than autosomal dominant polycystic kidney disease (ADPKD).

The introduction of routine ultrasound imaging into obstetric practice has revealed that the true prevalence of asymptomatic unilateral multicystic dysplastic kidney is considerably higher than was previously suspected, but only a small percentage are clinically evident at birth and the majority of unilateral MCDKs clearly remained undetected in the past.

The terminology previously used to describe the different clinical and pathological forms of cystic renal disease has given rise to understandable confusion. In particular, terms such as 'dysplastic', 'hypoplastic', 'shrunken', 'polycystic' and 'multicystic' have often been used loosely or interchangeably in the literature with little regard to differences in histology and developmental biology. In clinical practice, confusion most commonly arises from the failure to distinguish between multicystic dysplastic kidney, a sporadic structural abnormality which, when unilateral, carries a good prognosis, and polycystic kidney disease, an inherited disorder characterised by diffuse pathology of the parenchyma of both kidneys.

Embryology and pathology

The different types of cystic renal disease encountered in childhood are so diverse that their embryology, inheritance and pathology are more conveniently summarised under the relevant headings. The Potter classification represented the first systematic attempt to categorise the differing forms of cystic renal pathology, but has been rendered obsolete by advances in molecular biology and genetics which have found little scientific justification for the groupings devised by Potter.

Polycystic renal disease

This important group of disorders is characterised by the presence of microscopic or macroscopic cystic tissue distributed diffusely throughout the parenchyma of both kidneys. There are no histological features of dysplasia.

Two major forms of polycystic renal disease are encountered: i.e. autosomal recessive (the type most commonly encountered in children) and autosomal dominant, which, although sometimes evident on renal ultrasound in childhood, is of little clinical impact until adult life.

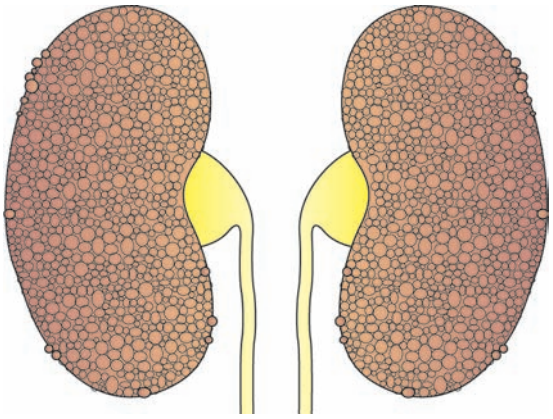


Figure 9.1 Autosomal recessive polycystic renal disease. Diffuse bilateral renal enlargement.

Autosomal recessive polycystic kidney disease (ARPKD) (Figure 9.1)

Incidence

1:10 000–1:40 000.

Pathology

Typically the kidneys retain their normal outline but are considerably enlarged. The pelves, calyces and ureter are normal in morphology. The renal parenchyma is extensively replaced by cylindrical, radially orientated cysts which are usually less than 2 mm in diameter. Liver involvement is almost invariable, with a pattern of bile duct abnormalities termed 'biliary dysgenesis'.

Genetics

ARPKD arises as a result of mutations of the polycystic kidney and hepatic disease 1 gene (*PKHD1*). The less severe mutations are compatible with survival and are thought to permit some expression of the gene product – a protein fibrocystin. Major mutations, however, are associated with lethal forms of the disorder.

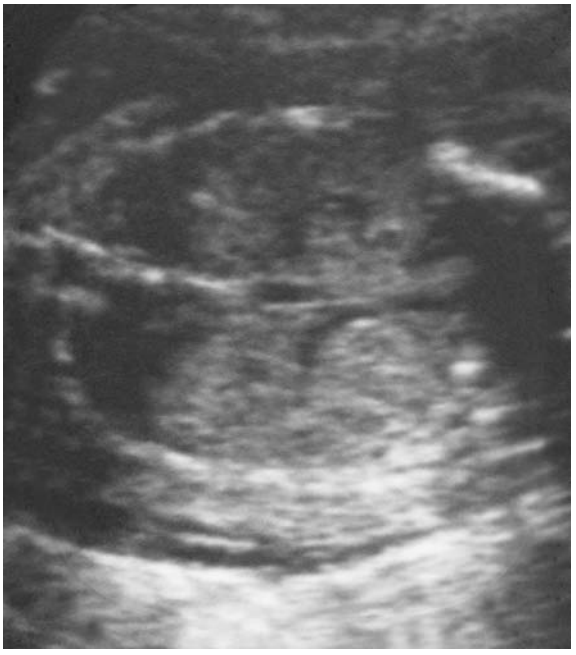


Figure 9.2 Prenatal ultrasound appearances of autosomal recessive polycystic kidney disease.

Presentation

ARPKD is associated with characteristic ultrasound appearances of diffuse bilateral renal enlargement (Figure 9.2). Ultrasound findings of oligohydramnios or reduced bladder volume are predictors of severe functional impairment. Termination of pregnancy is an option when the condition is detected in the second trimester, but ultrasound evidence of the disorder is not always apparent at this stage in gestation, or may not be sufficiently diagnostic until later in pregnancy.

Clinical features

In the neonatal period clinical features include readily palpable abdominal masses and, in more severe cases, pulmonary hypoplasia and 'moulding' deformities, e.g. Potter's facies, talipes, etc. Occasionally ARPKD does not come to light until later childhood, when it presents with hypertension or manifestations of hepatic fibrosis, such as portal hypertension or bleeding oesophageal varices.

Diagnosis is with ultrasound and, in some cases, computed tomography (CT). Renal biopsy may also be indicated.

Treatment

Initial ventilatory support may be required for the management of respiratory distress and pulmonary hypoplasia in severely affected infants. The requirement for ventilation does not carry the universally poor prognosis that was once the case. Medical management is directed at the treatment of hypertension, prevention of malnutrition and measures designed to minimise anaemia and renal bone disease. Children progressing to end-stage renal failure are managed by dialysis and transplantation, with native nephrectomy being indicated to control hypertension or create space for the transplanted kidney. Specific treatment may be required for the complications of hepatic disease.

Prognosis

Infants who do not have pulmonary hypoplasia have a high expectation of surviving beyond the neonatal period and, in those who do, the 5-year survival rate is 87%, with a 67% survival rate at 15 years.

Autosomal dominant polycystic kidney disease (ADPKD) (Figure 9.3)

Incidence

The most commonly inherited form of renal disease, ADPKD has a reported prevalence ranging from 1:200 to 1:1000. It is essentially a disorder of adult life, accounting for approximately 5–10% of adults on end-stage renal replacement programmes.

Pathology

Histologically, the cysts are lined by tubular epithelium and the intervening renal parenchyma may be normal or show evidence of glomerulosclerosis. Extrarenal manifestations include hepatic cysts and cerebral aneurysms.

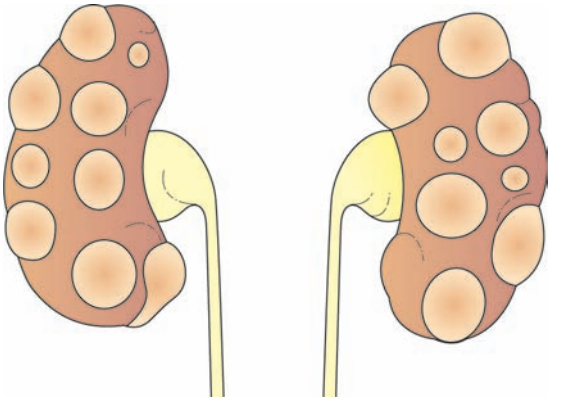


Figure 9.3 Autosomal dominant polycystic kidney disease. Discrete cysts of varying size interspersed between areas of normal renal parenchyma.

Genetics

Mutations of the *PKD1* gene, which is located on chromsome 16, account for 85% of cases. This gene encodes for a glycoprotein which is believed to play an important role in cell matrix interaction. A second gene defect caused by mutations of the *PKD2* gene on chromosome 4 accounts for the majority of the remaining cases. One study found that the mean age of death or onset of end-stage renal failure was 53 years in patients with the *PKD1* mutation, as opposed to 69 years in those with the *PKD2* mutation. The variability of the phenotype, sometimes in members of a single family, suggests that genetic factors are subject to considerable heterogeneity.

Presentation

ADPKD is occasionally identified during routine prenatal ultrasound examination. In addition, asymptomatic individuals can sometimes be diagnosed on ultrasound screening of the offspring or other young family members of patients known to have the disorder.

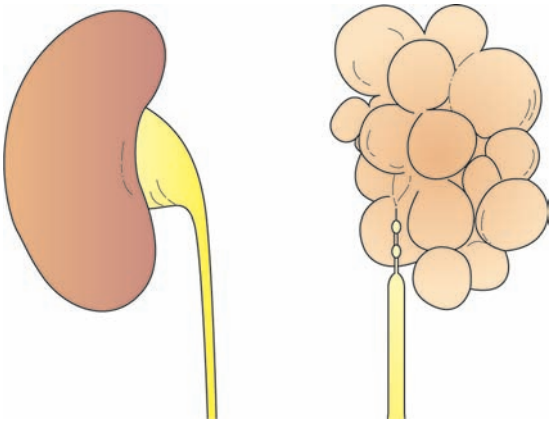


Figure 9.4 Multicystic dysplastic kidney. Kidney replaced by collection of cysts of varying size. Ureteric atresia.

In the majority of cases, however, clinical presentation is in adult life with hypertension, abdominal pain, palpable abdominal masses, haematuria or other urinary symptoms.

Management

The condition is managed expectantly, with follow-up aimed at the detection and early treatment of complications, notably hypertension. Cyst drainage or nephrectomy are occasionally indicated in the management of severe hypertension, or to control pain or urinary infection.

Prognosis

When the autosomal dominant form of polycystic kidney disease is diagnosed on ultrasound in childhood, either incidentally or during family screening, the prognosis for renal function is generally good, with 80% of children maintaining normal levels of renal function into adult life. In contrast, when detected prenatally or in the neonatal period, ADPKD disease carries a poor prognosis.

Multicystic dysplastic kidney (MCDK) (Figure 9.4)

Prior to the introduction of routine antenatal ultrasound, MCDK was regarded as a relatively rare anomaly which generally presented as an abdominal mass in the neonatal period. Nephrectomy was routinely undertaken in such cases. It is now evident, however, that the true prevalence of MCDK is far higher than was previously suspected, but in the majority of cases the lesion is clinically undetectable and the affected infant is entirely asymptomatic and outwardly normal. The management of prenatally detected MCDK and the arguments surrounding 'prophylactic' removal of asymptomatic kidneys remain a source of controversy.

Incidence

Current evidence from a number of sources indicates a prevalence for unilateral MCDK in the range 1:2500–1:4000 live births. Bilateral MCDK, a lethal anomaly, has an estimated incidence of 1:20 000 pregnancies.

Aetiology/embryology

Proximal ureteric atresia (or, more rarely, distal ureteric obstruction) is almost invariably found in association with MCDK (Figure 9.5). Complete ureteric obstruction at an early stage in embryonic development has therefore been invoked as the cause of the MCDK malformation.

Faulty development of the ureteric bud and metanephric mesenchyme may also be implicated (see Chapter 1). Familial occurrence of MCDK has been reported, and although MCDK generally appears to behave as a sporadic anomaly, in some families it may rarely be inherited as an autosomal dominant trait with variable penetrance (Figure 9.6). Nevertheless, the overall risk of familial occurrence is extremely low and routine screening of siblings and other first-degree relatives for MCDK is not justified.

Pathology

MCDK comprises an irregular collection of tense non-communicating cysts of varying size lined by cuboidal or flattened tubular epithelium. Renal parenchyma, where present, is dysplastic and

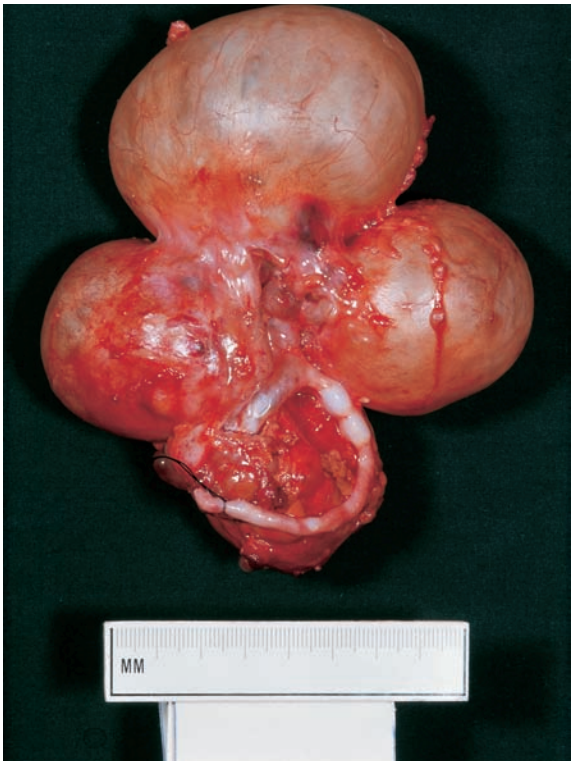


Figure 9.5 Nephrectomy specimen. Multicystic dysplastic kidney. (Courtesy of Mr PG Ransley.)

consists of small islands or flattened plates of abnormal tissue interposed between cysts.

Although the entire kidney is usually affected, there have been case reports of segmental MCDK in which the cystic changes and characteristic histology are confined to a segment of an otherwise, relatively normal kidney.

Presentation

MCDKs present in one of three ways:

- **Clinically** – usually as an abdominal mass in the neonatal period. Only a small proportion of all MCDKs now present in this fashion. Typically the surface of a palpable MCDK is 'knobbly' and irregular in contour, contrasting with other neonatal renal masses, e.g. hydronephrosis or polycystic kidney, which have a smoother surface on palpation.
- **Incidental postnatal ultrasound finding** in an infant with coexisting congenital anomalies, e.g. oesophageal atresia.
- **Prenatal ultrasound**. The majority of prenatally diagnosed MCDKs (> 80%) are small and clinically undetectable at birth.

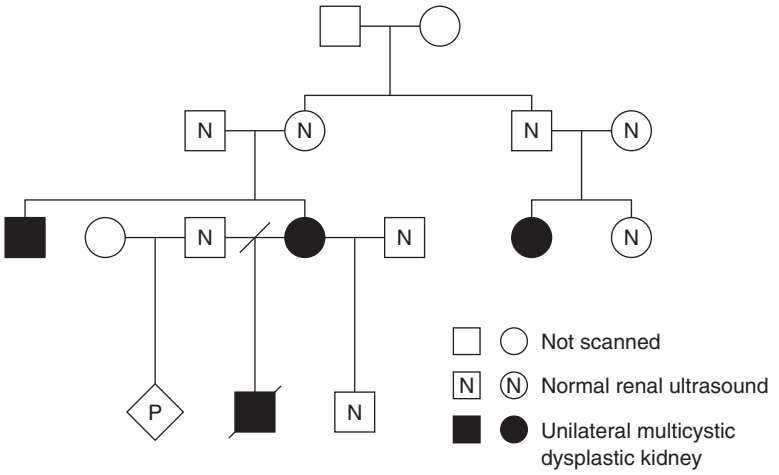


Figure 9.6 Familial occurrence of MCDK. Pedigree of affected family. Probable autosomal dominant pattern of inheritance. Most MCDKs occur as a sporadic anomaly.

Diagnosis

Although the prenatal ultrasound appearances of MCDK can occasionally be difficult to distinguish from those of marked hydronephrosis, most experienced radiologists can make the diagnosis with a high degree of accuracy. Postnatally the diagnosis is confirmed by a combination of ultrasound and isotope imaging. MCDKs are characterised by a total absence of isotope uptake (0% differential function) on DMSA (dimethylsuccinic acid). In some centres MAG3 (mercaptoacetyltriglycine) is favoured, as this yields additional information on drainage in the contralateral kidney.

The role of the micturating cystourethrogram (MCU) in the evaluation of infants with prenatally detected MCDK is controversial. When performed routinely, it reveals a 20–30% incidence of low-grade contralateral or ipsilateral vesicoureteric reflux (VUR). However, the clinical significance of this finding is arguably often low, since this low-grade VUR usually resolves in early life and rarely gives rise to infection. In the author's experience less than 3% of children with MCDK required surgical correction of reflux, and it is therefore the author's preference to reserve MCU for those infants in whom there is ultrasound evidence of ureteric or contralateral renal dilatation. This selective approach to the use of micturating cystourethrography is endorsed by recently reported studies. However, it is important that parents and general practitioners are aware that otherwise normal ultrasound appearances do not exclude the possibility of low-grade VUR, and the occurrence of a documented urinary tract infection (UTI) or an unexplained febrile illness is an indication to proceed to MCU.

Natural history

A number of studies have documented the potential for prenatally detected MCDKs to involute – i.e. to disappear on ultrasound – both prenatally and postnatally. In the cases recorded on the US National Multicystic Kidney registry, only 14% disappeared completely on ultrasound, whereas 45% demonstrated reduction in size, 35% remained unchanged in size and 5% demonstrated enlargement. However, the duration of follow-up was not specified. In a study in the author's unit, involution was observed in 52% of prenatally detected MCDKs at median follow-up of 66 months (range 24–144 months), with approximately 30% of MCDKs having involuted (disappeared) in the first 12 months of life. This experience is endorsed by the findings of another UK study which reported complete involution of 33% of MCDKs by 2 years of age, increasing to 47% at 5 years and 59% at 10 years.

The documented tendency for MCDKs to involute spontaneously, coupled with the relative rarity with which unilateral renal agenesis is diagnosed in utero, has been interpreted as evidence that a proportion of cases of apparent renal agenesis diagnosed in adult life or at postmortem may in fact represent involuted MCDKs.

Complications

Hypertension is a rare but well-documented complication of MCDK and nephrectomy is undoubtedly warranted when it occurs. But how common is this complication?

In 1988, the authors of an early study of prenatally detected MCDK reported the findings of a literature search which had identified only nine cases of hypertension responding to nephrectomy in the preceding 20-year period. A recent (2006) review of reported cases over the previous decade identified a total of 31 cases of hypertension, of which at least six definitely responded to nephrectomy. Nevertheless, when viewed in the context of the prevalence of MCDK (1:2500–1:4000), the number of published case reports represents a low order of risk for developing hypertension.

In the US registry, 426 children were managed conservatively, of whom five (1%) developed hypertension. In a UK prospective study of 165 patients (of whom 43 were followed for 10 years), none developed hypertension.

The possible link between MCDK and hypertension can be studied from a different angle. If

hypertension occurs on an appreciable scale this should be reflected in the published literature on renal hypertension in childhood, but this is not the case. No cases of MCDK were encountered in 454 children with hypertension presenting to the paediatric nephrology unit at the Hospital for Sick Children, Great Ormond Street, London. Similarly, two published series of children in other centres with 'surgical' causes of renal hypertension undergoing nephrectomy did not include a single MCDK.

In summary, from the evidence currently available, it appears that the risk of hypertension associated with MCDK is very low (of the order of 1% or less) and is not sufficient to justify 'prophylactic' nephrectomy in asymptomatic infants and children.

It is also important to note that removal of the kidney does not necessarily obviate the risk of hypertension and the need for blood pressure monitoring, since there have been reports of hypertension associated with pathology in the remaining contralateral kidney.

Malignant potential

In a review of 26 published series totalling 1041 children with MCDKs no cases of malignancy were reported over periods of follow-up extending up to 23 years. Moreover, no instances of malignancy were encountered amongst the children recorded on the US MCDK registry. As with hypertension it is also possible to view the question from a different angle by asking, 'How commonly does MCDK figure in published series of Wilms' tumours?' In the United States, detailed data on 7500 Wilms' tumours were collected over an 18-year period as part of the National Wilms' Tumor Study. Out of these 7500 tumours, only five arose in MCDKs.

On current estimates of the true prevalence of MCDK this represents an individual lifetime risk of the order 1:2500. Given that Wilms' tumour is now largely curable, the lifetime risk of dying from a Wilms' tumour arising in an MCDK has been calculated to be comparable to the risk of mortality associated with general anaesthesia. Although opinion remains divided, the available evidence does not justify submitting asymptomatic infants or children to nephrectomy as a prophylactic measure.

Other complications

Symptoms such as pain or haematuria have been ascribed to MCDKs in rare cases reported in the adult literature. These symptoms are seldom, if ever, seen in association with MCDK in the paediatric age group. When urinary infection occurs in children with MCDK it is more likely to be due to underlying VUR or some coexistent anomaly rather than the MCDK itself (which does not communicate with the rest of the urinary tract because of the presence of ureteric atresia).

Management

Coexisting anomalies

Contralateral pelviureteric junction (PUJ) obstruction is present in 5–10% of cases and is managed conservatively or surgically according to its severity. Vesicoureteric reflux is generally low grade and is usually managed conservatively by antibiotic prophylaxis and urine surveillance or by endoscopic correction if appropriate.

Multicystic dysplastic kidney

Nephrectomy is undoubtedly justified for those rare instances when MCDK presents in the neonatal period as a large, clinically evident abdominal mass. Depending on factors such as the size of the mass and the presence or absence of other anomalies, surgery can usually be deferred until 4–6 weeks of age or later.

The arguments for the 'prophylactic' removal of asymptomatic MCDKs centre principally on the perceived risks of malignancy and hypertension, and have already been considered above. Specialist opinion in the UK generally favours conservative management. Nevertheless it is widely accepted

that hypertension, increasing size or the appearance of unusual or worrying features on ultrasound follow-up are indications to proceed to nephrectomy.

Ultrasound follow-up is maintained on an annual basis until 5 or 6 years of age. Although some paediatric urologists insist on the disappearance of the MCDK before discharging the child, this has not been the author's practice. Measurement of blood pressure in infants or fractious young children can be difficult but becomes easier as the child gets older. At the time of discharge from surgical follow-up, it is prudent to arrange for blood pressure to be checked by a paediatrician or GP on an annual basis thereafter, continuing into adult life.

Nephrectomy

The traditional approach to removal of an MCDK entails the use of a small incision anterior to the tip of the 12th rib or a posterior lumbotomy incision. Aspiration of cyst fluid facilitates removal through a limited incision. More recently, laparoscopic nephrectomy has gained popularity as the procedure of choice. Ideally, this should be performed retroperitoneally rather than via a transperitoneal approach because of the potential risk of intraperitoneal complications (see Chapter 23). The benefits of laparoscopic nephrectomy may be fairly marginal in view of the simplicity and low morbidity with which MCDKs can be removed via a small incision.

Multilocular renal cyst (Figure 9.7)

This rare renal lesion, also described as cystic nephroma, benign multilocular cystic nephroma, etc., may give rise to diagnostic difficulty, typically being misdiagnosed as a cystic Wilms' tumour.

Aetiology

It remains unclear whether multilocular renal cyst should be regarded as a neoplasm or a developmental anomaly. Although malignancy ascribed to this lesion has been reported in adult life, multilocular renal cyst is not generally considered a premalignant lesion. It occurs sporadically with no evidence of an inherited basis.

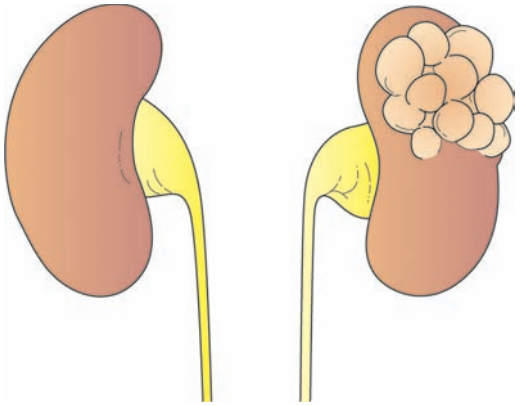


Figure 9.7 Multilocular renal cyst.

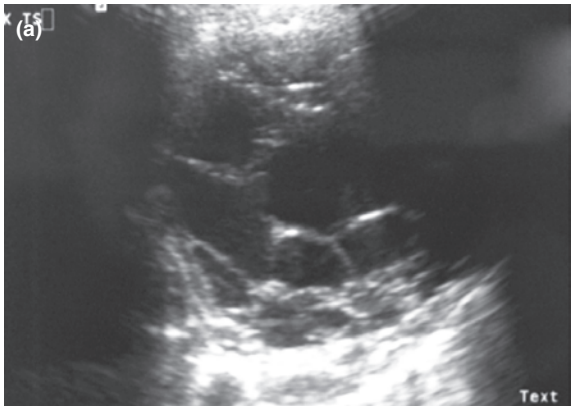
Incidence

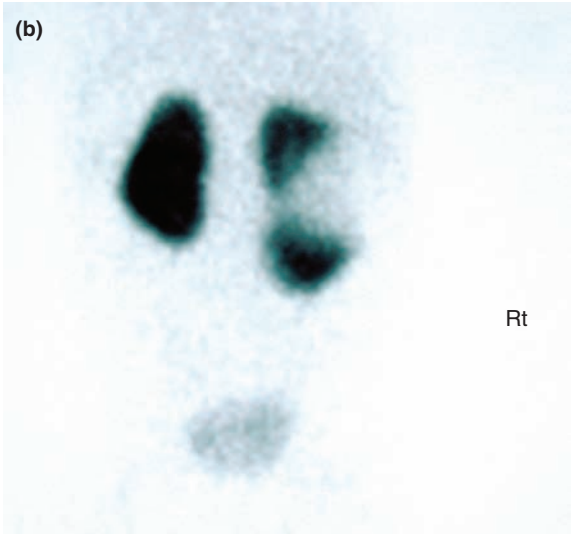
Experience in the Yorkshire region of the UK suggests that the incidence is approximately 1:200 000–1:250 000. The condition demonstrates a bimodal age distribution, with one peak in infancy and a second peak in early adult life, separated by an unexplained hiatus in distribution. Children account for 30–50% of cases.

Presentation

Most cases present with haematuria, loin pain or an abdominal mass, although multilocular cyst can occasionally come to light as an incidental finding on ultrasound during the investigation of unrelated symptoms.

Diagnosis is by ultrasound complemented by CT and possibly magnetic resonance imaging (MRI). DMSA is also helpful to delineate functional tissue if nephron-sparing surgery is under consideration (Figure 9.8). Typically the multilocular cystic lesion is localised within the renal parenchyma, but may extend into the collecting system or distort the renal capsules. An experienced paediatric radiologist should be able to distinguish multilocular renal cyst from other forms of renal pathology, but even with sophisticated imaging it may be difficult to distinguish from a cystic variant of Wilms' tumour.





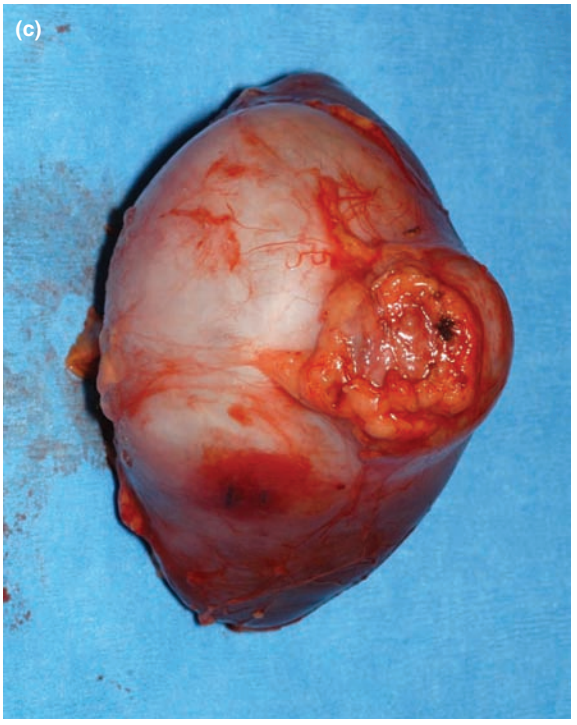


Figure 9.8 (a) Ultrasound scan. Multilocular cystic lesion in the right kidney of a 2-year-old girl presenting with haematuria. (b) Non-functioning lesion in the midzone of the right kidney demonstrated on DMSA, not amenable to nephron-sparing surgery. (c) Nephrectomy specimen. Distortion of the renal outline by the tense intrarenal lesion. Histology confirmed benign multilocular cyst.

Management

Nephrectomy is the accepted form of treatment. In view of the benign nature of the lesion nephron-sparing surgery, i.e. partial nephrectomy, might be considered in certain circumstances, such as a multilocular renal cyst in a solitary kidney.

Simple renal cyst (Figure 9.9)

Although a common finding in adults, simple or 'solitary' renal cysts are only occasionally encountered in childhood and are thus likely to be acquired rather than congenital in aetiology. Although it has been stated that simple cysts do not give rise to problems, this is not invariably the case and the author has treated a number of children with pain arising in simple renal cysts which has responded to

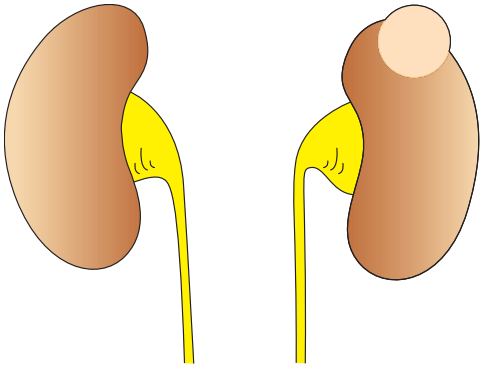


Figure 9.9 Simple renal cyst – rare in childhood.

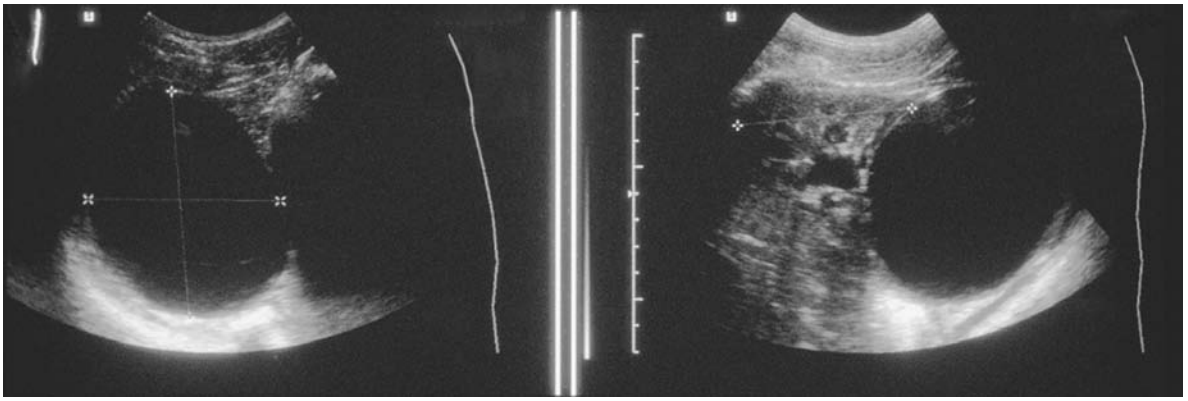


Figure 9.10 Ultrasound appearances of large simple cyst in the lower pole of the left kidney of a 7-year-old boy presenting with abdominal pain and a palpable mass. The condition was successfully managed by laparoscopic partial excision/deroofing.

surgical removal or deroofing of the cyst. Nevertheless, it is also important to note that a simple cyst may be an incidental unrelated finding in a child with non-specific abdominal pain. Dilatation of the upper pole of a duplex kidney is sometimes mistaken on ultrasound for a simple cyst by radiologists unfamiliar with paediatric urology. Rarely a child may present with abdominal pain or other symptoms which are genuinely attributable to the presence of a large, tense simple renal cyst (Figure 9.10). Management is the same as for symptomatic renal cysts in adults, and comprises percutaneous cyst aspiration and injection of alcohol, or laparoscopic or open deroofing and subtotal excision of the cyst wall. Recurrence is uncommon.

Key points

- Despite the potentially confusing terminology it is important to have a clear understanding of the various patterns of cystic renal disease in view of the important differences in clinical significance and prognosis.
- Autosomal recessive polycystic kidney disease is detected prenatally or presents in the newborn period.
- Autosomal dominant polycystic kidney disease does not generally come to light with symptoms until adulthood and is generally asymptomatic in those children in whom the condition has been identified by ultrasound screening.
- Multicystic dysplastic kidney (MCDK) is a developmental abnormality of the kidney which is more prevalent in the general population than was previously recognised.
- Current evidence suggests that the risk of malignancy associated with MCDK is not significantly increased over the normal paediatric population. The risk of hypertension appears to be of the order of 1% in childhood. This low order of risk does not justify routine 'prophylactic' nephrectomy.
- A lifelong annual blood pressure check is advisable. Removal of the MCDK does not obviate the need for this precaution in view of reported cases of hypertension arising from the remaining contralateral kidney.

Further reading

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Prenatal diagnosis

10

HK Dhillon

Topics covered

Obstetric ultrasound: current practice
Prenatal management
  Counselling
  Fetal intervention
Postnatal management
  Diagnostic imaging
  Protocols and guidelines

Introduction

The first case reports of the detection of urinary tract malformations by prenatal (antenatal) ultrasound first appeared in the literature in the mid 1970s, but it was not until the early to mid 1980s that maternal ultrasound was routinely incorporated into obstetric practice in the UK. Since then, a substantial body of experience has accumulated and the management of infants with prenatally detected uropathies constitutes a major component of paediatric urological practice. Abnormalities of the genitourinary tract are amongst the commonest anomalies detected in utero. This partly reflects the relatively high incidence of congenital anomalies within the genitourinary system, but is also because the common anomalies are usually associated with dilatation or cystic pathology which is relatively easy to visualize on ultrasound. Unfortunately, relatively few long-term studies have been undertaken to document the late outcome of prenatally detected uropathies. As a consequence, there are still some unresolved controversies surrounding early surgical intervention or conservative management of conditions such as prenatally detected pelviureteric junction (PUJ) obstruction, multicystic dysplastic kidney, and vesicoureteric reflux (VUR). Whereas progress has been made in identifying criteria to identify subpopulations at greatest risk of later functional deterioration or clinical complications, research has tended to focus on short- to medium-term outcomes. Further evidence of long-term follow-up studies would be particularly valuable in helping to establish which prenatally detected uropathies are not destined to pose any threat of morbidity and which, indeed, may not warrant any investigation.

The investigation and management of infants with prenatally detected urinary tract abnormalities is guided by three important considerations:

- The majority of infants with prenatally detected urinary tract abnormalities are outwardly normal and healthy at birth. As such, they cannot be considered as patients in the conventional sense. This is particularly true of infants with isolated unilateral anomalies in whom relevant clinical findings are present in fewer than 5% of cases. Bilateral renal pathology is more likely to be associated with relevant physical signs or coexisting syndromes, but, nevertheless, the majority of infants with prenatally detected bilateral uropathy are asymptomatic and outwardly normal at birth.
- Only a very small proportion of infants with prenatally detected uropathies (<5%) have renal insufficiency of sufficient severity to require nephrological support and, overall, the majority of affected infants do not require any form of early surgical intervention.
- The prenatal detection of a fetal urinary tract abnormality often generates disproportionate

parental anxiety during the pregnancy. Parents who have been told that their unborn child has a kidney abnormality tend to assume the worst, including a scenario involving dialysis and renal transplantation. In our experience, only a minority of parents receive accurate counselling on the prognosis of the urological abnormality diagnosed in utero. Paediatric urologists should, ideally, play a far greater role in prenatal counselling but the pressure of heavy clinical workloads can make this difficult to achieve.

Obstetric ultrasound – current practice

Nuchal pad translucency was developed as an ultrasound screening test at 10–12 weeks' gestation in high-risk pregnancies, particularly for Down's syndrome. Although this early scan is being extended into the lower-risk obstetric population, its sensitivity for the detection of urinary tract abnormalities is poor.

Routine fetal anomaly scanning is undertaken between 15 and 20 weeks, at a time when the diagnostic sensitivity of ultrasound has greatly increased. This timing enables severe congenital malformations to be diagnosed with sufficient accuracy to permit an informed decision on termination of pregnancy. In one study of 560 terminated pregnancies, neonatal and infant deaths, abnormalities of the urinary tract were incriminated as the sole or contributory cause of death in 323 instances, of which 221 occurred in utero as a result of termination of pregnancy, intrauterine death or stillbirth, while 102 occurred postnatally, usually from pulmonary hypoplasia.

The **sensitivity and specificity of ultrasonography** for the detection of urinary tract abnormalities is influenced by the quality of the equipment used, the experience of the ultrasonographer or radiologist performing and interpreting the scan and by maternal size and obesity.

Anomalies such as renal ectopia or renal agenesis which are not accompanied by dilatation are considerably more difficult to detect than those characterised by dilatation or cystic disease. Although virtually every major, potentially lethal urinary tract abnormality is detectable in the second trimester, non-lethal abnormalities, including most cases of PUJ obstruction, VUR and duplication, are not necessarily associated with detectable dilatation at this stage in gestation. The prenatal detection of anomalies at the milder end of the pathological spectrum is therefore dependent upon scans being performed later in pregnancy. If prenatal scanning is limited to a single fetal anomaly scan in the second trimester, many anomalies are destined to remain undetected in pregnancy. Gestational age at the time of scanning is, therefore, the most important factor determining the sensitivity of prenatal urological diagnosis. Figures 10.1–10.3 illustrate the appearances of some common upper tract abnormalities on prenatal ultrasound scans at 22 weeks' gestation.

Incidence

The incidence of prenatally detected urinary tract anomalies reported from different centres varies considerably, depending on the gestational age at which ultrasound screening is routinely performed. However, the incidence of significant prenatally detected uropathies averages around 1:500 to 1:600 pregnancies. By contrast, mild dilatation is a common prenatal finding, being identified at

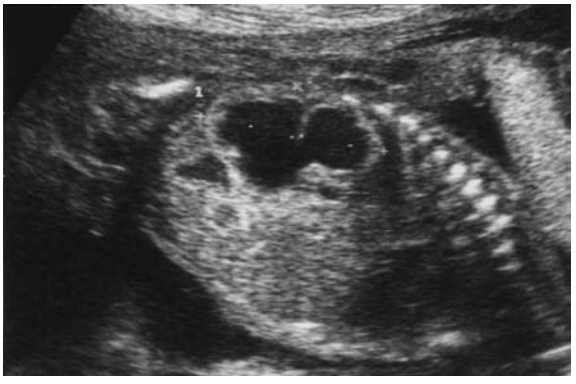

Figure 10.1 Unilateral severe hydronephrosis with clubbed calyces and echogenic cortex at 22/40 weeks.

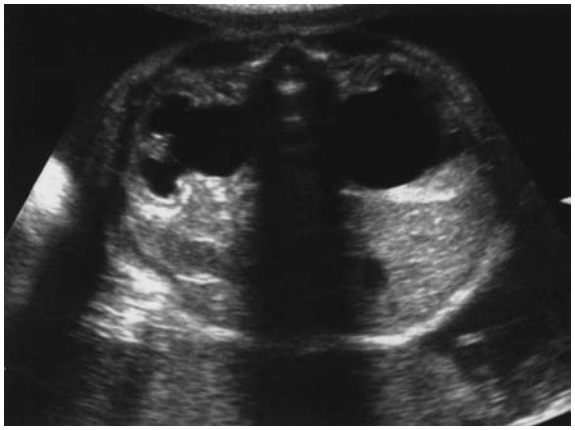

Figure 10.2 Bilateral severe hydronephrosis at 22/40 weeks.

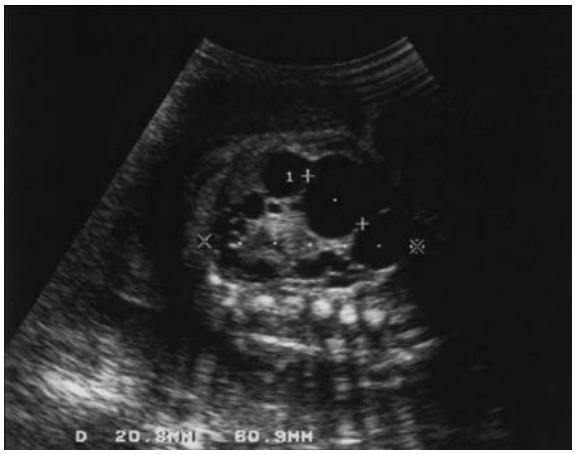

Figure 10.3 Multicystic dysplastic kidney at 22/40 weeks.

some stage in approximately 1:100 pregnancies. However, it is often a transient finding with a tendency to resolve spontaneously during the course of pregnancy.

Management

Prenatal management

The potential to influence the clinical outcome of a prenatally detected uropathy by active intervention during pregnancy is limited to the severe end of the spectrum of obstructive pathology and comprises fetal surgery (generally vesicoamniotic shunting) or termination. Although there has been a suggestion that preterm delivery and early postnatal treatment may improve the outcome for some boys with posterior urethral valves, there is insufficient evidence to justify elective preterm delivery.

When the urinary tract anomaly has been detected prenatally, there are several options.

Counselling

Counselling should ideally encompass:

- the differential diagnosis, insofar as this can be established with the ultrasound information available
- an explanation of the investigations that are likely to be advised following delivery
- a broad outline of prognosis.

If the need for postnatal surgery is envisaged, parents should be reassured that this is rarely of a serious or life-threatening nature. Unfortunately, it is often impossible to provide a detailed prediction of what the future holds since the prenatal ultrasound findings are non-specific in approximately 70% of cases. For example, the discovery of unilateral ureteric and renal dilatation at 34 weeks' gestation would involve a discussion covering megaureters, VUR and duplex kidneys.

For logistical reasons, counselling for prenatally detected uropathies of mild or moderate severity, particularly those detected in later pregnancy, is mostly undertaken in the hospital where the mother is receiving her routine obstetric care. When the anomaly is at the more severe end of the spectrum, particularly when detected on second-trimester fetal anomaly scanning, the options may include termination of pregnancy and, possibly, fetal intervention. In this situation, prompt referral to a fetal medicine centre is indicated for more detailed investigation and counselling.

Fetal intervention

The indications for possible intervention during pregnancy are limited to the severe end of the pathological spectrum where the ultrasound findings and

the results of additional investigations point to a strong probability of intrauterine death or early postnatal demise. Termination of pregnancy may also be included in the options following the discovery of a major, non-lethal malformation, which, nevertheless, carries grave implications for quality of life.

Bilateral renal agenesis or bilateral multicystic dysplastic kidneys are examples of anomalies which are clearly incompatible with survival. In one study renal agenesis and multicystic dysplasia (or a combination of pathologies) accounted for more than 60% of terminations of pregnancy for urological anomalies. By contrast, the prognosis of urethral obstruction (typically posterior urethral valves), is more difficult to predict, since there is a broad spectrum of severity ranging from urethral atresia with oligohydramnios and pulmonary hypoplasia to mild degrees of urethral valve obstruction in which renal function is largely unimpaired. Nevertheless, the high overall level of morbidity due to congenital urethral obstruction is reflected in the statistic that males constitute 90% of children undergoing treatment for renal failure in the first 4 years of life.

Fetal intervention is subdivided into:

- diagnostic procedures intended to assess functional prognosis and detect chromosomal abnormalities
- termination of pregnancy
- therapeutic intervention, usually in the form of vesicoamniotic shunting.

Karyotype

Chromosomal analysis can be performed by examining exfoliated cells in amniotic fluid, by sampling blood from the umbilical cord (cordocentesis) or by chorionic villus sampling.

Fetal urine sampling

Conventional tests of renal function such as creatinine clearance or measurement of plasma creatinine and urea have no validity in intrauterine life since the fetus is effectively 'dialysed' by the placenta, with the result that levels of creatinine, urea, etc., in fetal plasma mirror those in the maternal circulation. However, the composition of fetal urine has been studied with the aim of developing a more selective approach to fetal intervention. Ideally, the measurement of urinary constituents as indicators of renal function would be used to select fetuses with potentially recoverable function for treatment, as opposed to those with irreversible renal dysplasia. Since urine sampling is an invasive procedure, data derived from normal fetuses without urinary tract anomalies are relatively scanty.

Biochemical parameters which have been identified as predictors of poor functional outcome include:

- fetal urinary sodium of >100 mEq/l after 20 weeks' gestation
- elevated urinary calcium (>1.2 mmol/l)
- increased levels of urinary and serum β_2-microglobulin.

Unfortunately, there is a considerable overlap between pathological and normal values. The difficulty is compounded by the limited data derived for normal fetuses at different gestational ages. In the hope of developing more sensitive prognostic tests, attention has recently switched from markers of excretory renal function to molecules which are expressed during renal differentiation and which may be implicated in renal dysplasia, e.g. TGF-β_1 (transforming growth factor beta-1).

Vesicoamniotic shunting

The rationale for this therapeutic intervention is derived from the premise that decompression of the obstructed urinary tract in utero will avert progressive renal damage and functional deterioration. Although open fetal surgery via hysterotomy and fetoscopy and valve ablation have been reported, the method which has been most widely practised comprises ultrasound-guided percutaneous insertion of a pigtail shunt catheter into the

fetal bladder to drain urine into the amniotic fluid (Figure 10.4). With few exceptions, the published results of fetal intervention (either open fetal surgery or vesicoamniotic shunting) have been disappointing. Results reported by the Fetal Surgery Register in the mid 1980s documented an overall mortality rate of 59% in a series of 73 fetuses. A subsequent review of the literature noted a 45% incidence of procedure-related morbidity, including premature labour. Two long-term outcome studies have been published – from Detroit and San Francisco. In the Detroit series, 34 fetuses underwent intrauterine decompression – of whom 13 (38%) nevertheless died in utero or postnatally. Fifty-seven per cent of those children who survived more than 2 years developed renal insufficiency – of whom the majority required early renal transplantation. The San Francisco group analysed the late outcome date for 36 fetuses treated between 1981 and 1999 – all of whom had been selected for treatment on the basis of favourable urinary biochemistry. In 14 fetuses the diagnosis was posterior urethral valves: of these, six did not survive to term, but eight survivors were assessed at the mean age of 11.6 years. By this stage, five were in renal failure and only three (21% of the total number of fetuses with posterior urethral valves) were alive with normal renal function.

Whereas the published results of vesicoamniotic shunting do not lend support to its use in routine clinical practice, it is important to note that shunting has generally been confined to fetuses at the severe end of the obstructed spectrum, typically with oligohydramnios. In these fetuses, renal dysplasia and damage is already well established by the time treatment is undertaken and the potential to improve the prognosis by this stage is very limited. One cannot, therefore, dismiss the possibility that shunting might be beneficial in less severely affected fetuses where bladder distension and bilateral upper tract dilatation is not accompanied by oligohydramnios or severely deranged urine biochemistry. Ideally, a controlled trial could have resolved this question, but, for a number of practical and ethical reasons, a statistically meaningful controlled trial is now no longer possible.

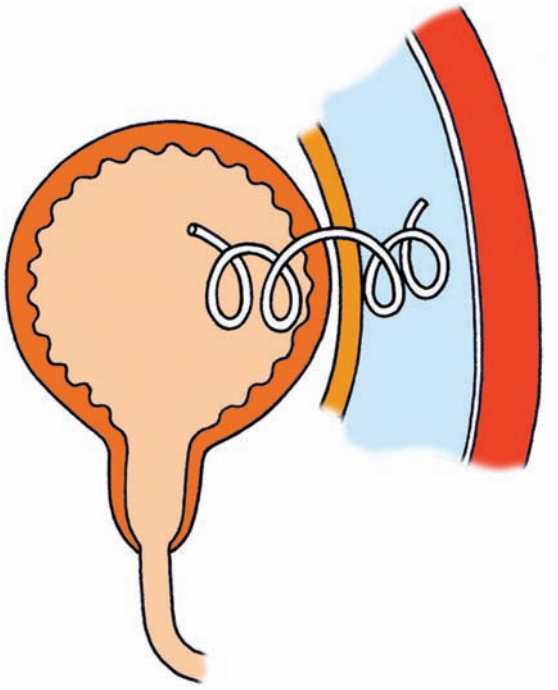

Figure 10.4 Vesicoamniotic shunt. A double pigtail catheter is inserted percutaneously via trochar and positioned to drain urine from the obstructed fetal bladder into the amniotic fluid.

Termination of pregnancy

With the increasing prevalence and accuracy of prenatal diagnosis, there is a growing tendency for parents in the UK to opt for termination of pregnancy following the discovery of a urological abnormality which is inconsistent with survival – or which carries a poor prognosis for quality of life. Sympathetic and informed counselling is essential to ensure that parents have access to the information they need to reach an informed (and often very difficult) decision about their unborn child. It is important, for example, that they have a realistic picture of what is entailed in the management of renal failure in childhood, in terms of hospitalisation, medication, surgery and the difficulties inherent in dialysis and transplantation.

Termination of pregnancy is being increasingly requested following the prenatal diagnosis of major anomalies such as cloacal and 'classic' bladder exstrophy. As a consequence, the number of infants being born with these anomalies is declining and only two referral centres in England and Wales are recognised by the government for the management of new cases of the exstrophy epispadias complex.

There are considerable variations in the attitudes to termination of pregnancy in different countries. Nevertheless, even in the United States, a study in Boston found that elective termination of pregnancy had been performed in 65% of pregnancies following the detection of spina bifida, 46% of pregnancies following the prenatal diagnosis of posterior urethral valves, 31% for prune-belly syndrome and 25% for bladder exstrophy.

Postnatal management

Antibiotic prophylaxis

This should generally be commenced for all newborn infants with prenatally detected uropathies pending the outcome of postnatal investigation, notably a micturating cystogram. Exceptions include:

- infants with mild isolated renal dilatation with an anteroposterier (AP) diameter of ≤10 mm and normal calyces
- multicystic dysplastic kidney with an entirely normal contralateral kidney
- ectopic kidney without evidence of dilatation.

The antibiotic most widely used is trimethoprim in a single daily dose of 2 mg/kg, usually administered at night.

Postnatal ultrasound

Urinary output is often reduced in the first day of life, with the result that an abnormal urinary tract may appear less dilated when not subjected to a representative diuretic load. For this reason, the initial postnatal scan should ideally be deferred until after 48 hours of age, i.e. when normal urinary output has been established. However, this optimal timing may be difficult to achieve, since many mothers now opt for early discharge from hospital. **The timing of the initial ultrasound scan is, therefore, best guided by the prenatal findings.**

Prompt postnatal ultrasound and referral to a specialist unit are essential for fetuses with suspected lower urinary tract obstruction, as signified by bilateral upper tract dilatation, thick-walled bladder, ureteric dilatation, etc.

Bilateral dilatation without bladder or ureteric involvement also merits early ultrasound – ideally between 3 and 7 days of age. In contrast, unilateral dilatation with a normal contralateral kidney carries a low risk of early morbidity and the initial postnatal scan can reasonably be deferred and performed on an outpatient basis at some point in the first 10–14 days of life.

In most specialist centres, the AP diameter of the renal pelvis in the transverse plane is now routinely measured. Although this measurement is subject to factors such as operator variability and the degree of hydration, the measurement of renal pelvic diameter is nevertheless preferable to subjective descriptions such as 'mild', 'moderate', 'gross' hydronephrosis, 'full', or 'baggy' renal pelvis. In addition to documenting the AP diameter of the renal pelvis, it is important to record the appearances of the calyces and renal parenchyma.

Micturating cystourethrogram (MCU)

The role of the MCU in the routine postnatal evaluation of infants with prenatally detected dilatation remains controversial, with practice varying considerably between different centres.

However, the **following conditions are generally regarded as being definite indications for a postnatal MCU:**

- abnormal bladder (particularly a thick-walled bladder or other evidence of outflow obstruction)

- bilateral upper tract dilatation
- dilatation of one or both ureters seen on either on pre- or postnatal ultrasound
- duplex kidneys (in view of the high incidence of lower pole reflux).

The question of whether infants with mild dilatation (<15 mm AP diameter) should routinely be investigated by MCU remains controversial.

The available evidence suggests that the incidence of underlying reflux associated with mild renal pelvic dilatation is of the order of 10–15%. In most instances, however, it is low-grade VUR which occurs more commonly in males and carries a high probability of spontaneous resolution in the presence of two normal kidneys on a DMSA (dimercaptosuccinic acid) scan. In practical terms, the information provided by an MCU is only likely to influence the clinical outcome in a very small percentage of infants with prenatally detected mild dilatation. Moreover, the MCU is an invasive and potentially distressing procedure which carries some risk of morbidity in its own right (predominantly infection). For these reasons, many paediatric urologists no longer advocate routine MCU if dilatation is confined to the renal pelvis (i.e. no evidence of ureteric and/or calyceal dilatation), and the AP diameter of the pelvis is <15 mm. Some cases of low-grade VUR will be missed by this approach, but this is outweighed by the benefit of a greatly reduced burden of unnecessary investigation into healthy infants.

If an MCU is not undertaken, the child's parents and general practitioner should, nevertheless, be alerted to the importance of having the urine checked for possible infection in the event of an unexplained febrile illness or more specific features of urinary infection.

Isotope imaging

The choice of imaging modality is determined largely by the findings on postnatal ultrasonography and MCU (when this has been performed). The principal role of ^{99m}Tc DMSA lies in confirming total absence of function in a multicystic kidney and for studying differential function and renal damage associated with congenital VUR.

^{99m}Tc MAG3 (mercaptoacetyltriglycine) is the isotope most widely used for the diagnosis of obstruction. It is important to note, however, that drainage curve data cannot be relied upon in young infants, even following the administration of diuretic. Since the information derived from DMSA scintigraphy or diuretic renography rarely influences practical management in the first few weeks or months of life, isotope imaging is best deferred until 1–3 months of age.

A rational approach to diagnosis and management

Diagnostic pathways

Suggested diagnostic pathways for the postnatal investigation of different prenatally detected urinary tract abnormalities are illustrated in Figures 10.5–10.8. These are suggested as broad guidelines, but it may be necessary to take additional factors into account when planning the timing and nature of postnatal investigation in individual cases.

Mild dilatation (pyelectasis)

Dilatation of the renal pelvis in the range AP diameter 5–10 mm is a common finding, being present at some stage in approximately 1 in 100 pregnancies. As already stated, however, this is often a transient finding which has resolved or improved in more than 50% of cases by the third trimester. Mild dilatation has been studied as a possible marker of chromosome abnormalities. When this is an isolated finding, the risk of chromosomal abnormalities is no higher than for the general fetal population. Mild dilatation does, however, carry a higher association with chromosomal abnormalities if it occurs in conjunction with other congenital abnormalities. The significance of mild dilatation as a possible marker of underlying VUR has already been considered above. Regardless of its cause, the morbidity

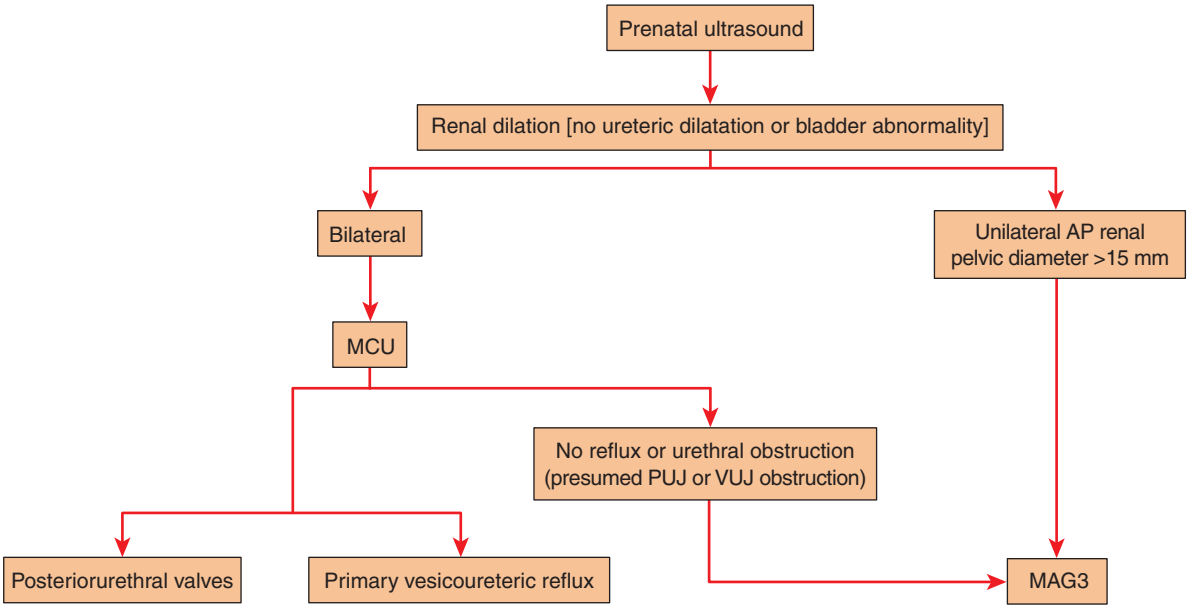

Figure 10.5 Diagnostic pathway for postnatal investigation of prenatally detected dilatation confined to the renal collecting system(s).

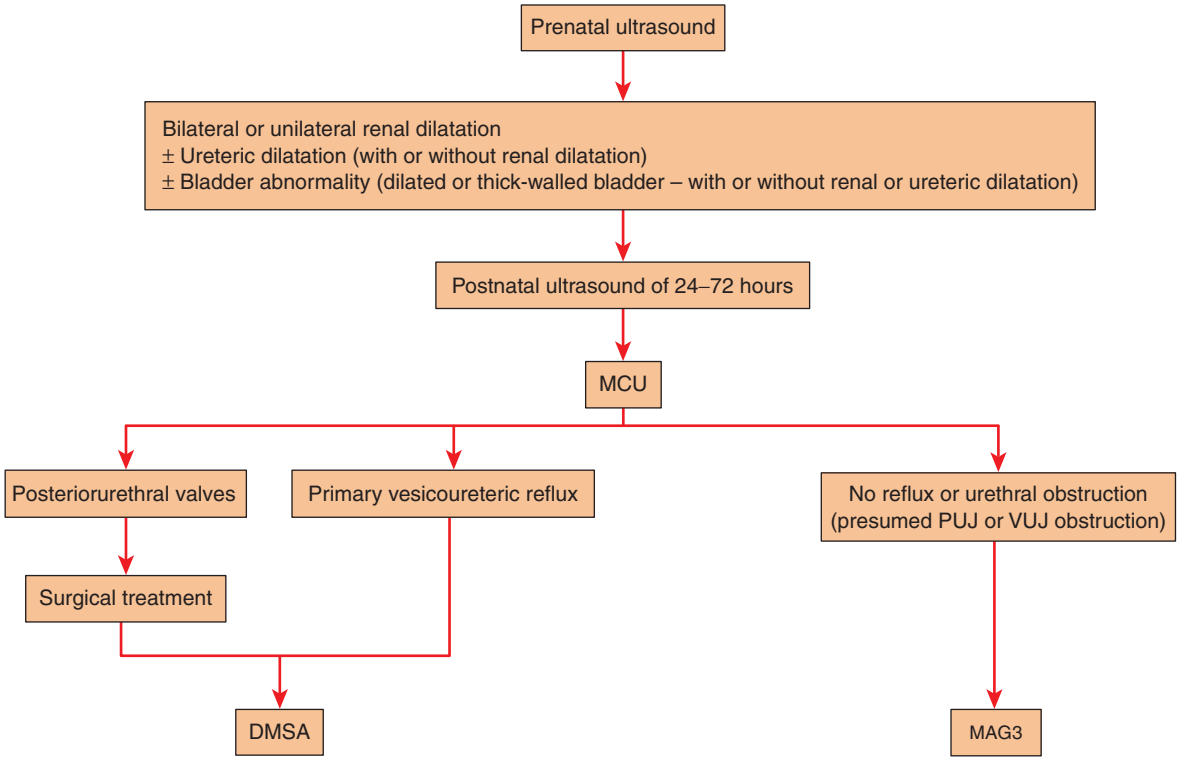

Figure 10.6 Diagnostic pathway for postnatal investigation of renal dilatation which is accompanied by ureteric dilatation and/or a bladder abnormality.

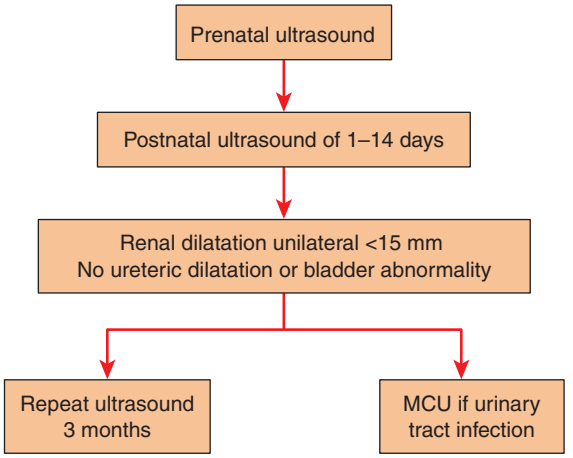

Figure 10.7 Diagnostic pathway for postnatal investigation of mild unilateral dilatation (renal pelvic anteroposterior diameter <15 mm), without coexisting ureteric dilatation or bladder abnormality.

generated by mild dilatation appears to be minimal. In a follow-up study, totalling 122 child-years of follow-up, there were only two episodes of morbidity related to the urinary tract, neither of which were due to reflux. In a questionnaire case–control study reported from the Netherlands, the incidence of urinary tract symptoms in children with a history of prenatally detected mild dilatation was compared with normal controls in the age range 4–9 years. No difference was found in the incidence of either urinary tract infection or incontinence between the two groups.

It is important to alleviate the anxiety which may inevitably be created in the minds of parents following the discovery of mild dilatation and to ensure that infants are not overinvestigated.

Key points

- The sensitivity of ultrasound for the prenatal detection of urinary anomalies is dependent upon a number of factors, most importantly gestational age at scanning.

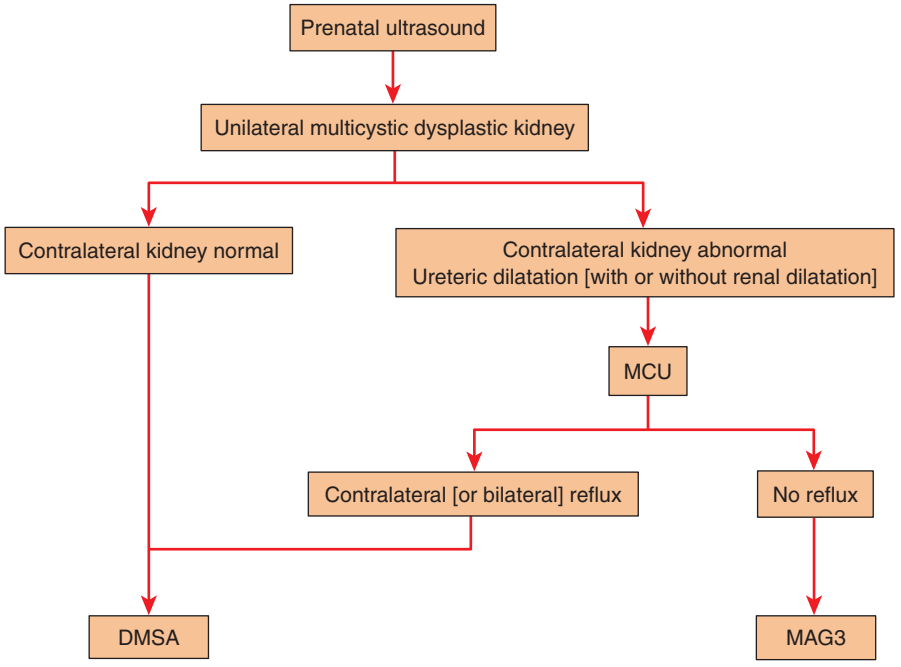

Figure 10.8 Diagnostic pathway for the investigation of prenatal ultrasound appearances suggesting multicystic dysplastic kidney (see also Chapter 9).

- The majority of infants with prenatally detected uropathies are entirely asymptomatic and outwardly normal at birth.
- Although information on the long-term outcome and natural history of asymptomatic prenatally detected uropathies is being acquired, much is still unknown. Surgical intervention is generally unwarranted unless there are clear-cut indications.
- The published results of vesicoamniotic shunting relate largely to fetuses with severe degrees of renal impairment. A possible benefit from fetal intervention in less severely affected cases (where there is a better prospect of improving the functional outcome) cannot be discounted.
- The combination of prenatal diagnosis and termination of pregnancy is resulting in declining numbers of referrals of severe but non-lethal urological malformations such as prune-belly syndrome and cloacal and classic bladder exstrophy.
- Mild dilatation (pyelectosis) is a common finding of minimal clinical significance. The role of micturating cystography is controversial, but the available evidence suggests that this is no longer justified on a routine basis.

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Stone disease in children 11

Patrick G Duffy, David FM Thomas and Martyn E Flett

Topics covered
Incidence and epidemiology
Pathology/aetiology
Clinical presentation
Diagnostic imaging, metabolic screening
Open stone surgery
Minimally invasive modalities
Stone recurrence

Introduction

Urinary calculi (stones) are rare in children, who are estimated to account for only 2–3% of all patients with stone disease. Infection remains a major aetiological factor, particularly in boys, but the proportion of affected children with an underlying biochemical predisposition appears to be increasing. For this reason, metabolic evaluation is essential for every child. The rate of stone recurrence is lower in children compared with adults. The majority of stone disease is now managed, as in adults, by lithotripsy or endourological techniques and, as a consequence, the incidence of open surgery has decreased dramatically.

Incidence and epidemiology

Geographical variations in the incidence of stone disease in children reflect differences in the prevalence of environmental, dietary and genetic factors. In the UK the estimated incidence of urinary calculi in children is approximately 3 new cases per million of the population per year. A recent review suggests that although infective calculi are more common in boys under 5 years of age there is also an increased incidence of metabolic abnormalities. The greater frequency of infection in uncircumcised infants and differing cultural attitudes to neonatal circumcision may help to explain the higher incidence of stone disease in certain European countries compared with the United States where neonatal circumcision remains commonplace.

The incidence of stones is twice as high in boys as it is in girls. Moreover, the peak age of presentation is younger in boys, being 3 years vs 4 years in girls. This gender difference reflects in part the role of bacterial colonisation and subsequent urinary infection in uncircumcised boys.

A geographical 'stone belt' extending from the Balkans across Turkey, Pakistan and northern India is characterised by a high incidence of endemic bladder stones in children. Chronically inadequate dietary intake of protein has been implicated, but relative dehydration associated with the climate and diarrhoeal illness may also be a contributory factor.

A study reported from London found that the proportion of paediatric stones secondary to infection has fallen from 60% to 30% over a 30-year period. This decrease parallels other series from around the world, with an increased relative proportion of metabolic abnormalities in richer developed countries and a corresponding decrease in infective and endemic stones.

Pathology/aetiology

Urinary calculi are composed of crystalline and matrix components in varying proportions. Matrix, a gelatinous glycoprotein, is a particular feature of infective stones, which are typically soft and crumbly

in composition. Metabolic stones, e.g. cystine and xanthine, are predominantly crystalline and correspondingly harder. The terminology historically used to describe the crystalline structure of urinary calculi ('struvite', 'brushite', 'weddellite', etc.) is uninformative, and in this chapter stones are categorised by reference to their chemical composition.

Factors involved in stone formation

- **Urinary concentration, ionic activity and solubility of stone-forming constituents.** Stone formation is initiated by the precipitation of urinary constituents from solution, followed by crystal formation. In turn, this process is influenced by the urinary excretion rate of the stone-forming substance, the level of hydration and the urinary pH.
- **Presence of abnormal urinary metabolites or pathologically elevated concentration of normal urinary constituents.** When a metabolite is excreted in high concentrations its saturation point in the urine is exceeded and crystal deposition occurs, progressing to stone formation. Reduced urinary output, leading to a higher urinary concentration of the metabolite and unfavourable urinary pH, will accelerate this process.
- **Urinary infection.** Certain bacterial species, notably *Proteus*, *Klebsiella* and *Pseudomonas,* are capable of the enzymatic splitting of urea to produce NH_3, with consequent elevation of the urinary pH and precipitation of ammonium salts. Infection is also a key factor in the production of the proteinaceous matrix component of calculi.
- **Anatomical abnormalities of the urinary tract.** Urinary infection associated with underlying urological abnormalities predisposes to stone formation by the mechanisms outlined above. Stasis of urine within an obstructed or dilated urinary tract creates an environment in which stone-forming substances are more likely to precipitate out of solution and thus initiate stone formation. This process can occur in sterile urine, but not uncommonly infection and stasis coexist.
- **Foreign materials.** Non-absorbable foreign bodies, usually surgical in origin (stents, fragments of catheters, non-absorbable sutures or staples) act as a nidus of encrustation and stone formation.
- **Prematurity.** Ex-premature children (born at less than 37 completed weeks' gestation) are at much greater risk of nephrocalcinosis and nephrolithiasis. Approximately 20% of babies born under 32 weeks' gestation develop nephrocalcinosis and 5–9% have calculi. The risks are increased with increasing prematurity of birth, decreasing birth weight, co-morbidity and the use of furosemide, thiazides and other drugs. Premature and formula-fed babies have increased solute excretion (e.g. oxalate). Babies receiving parenteral nutrition have a higher oxalate and calcium but lower citrate excretion, contributing to higher calcium oxalate saturation.

Aetiology: clinical aspects

Infective calculi

Infective stones initially comprise a combination of magnesium, ammonium phosphate and glycoprotein matrix in varying proportions. Calcium phosphate and other inorganic constituents then become incorporated into the expanding stone mass. Their consistency is variable, with areas of hard calcified material embedded within softer, less densely calcified matrix. Calcified areas are radioopaque but the softer matrix component, which may extend throughout much of the collecting system, is radiolucent or only faintly apparent on plain X-ray. The descriptive term 'staghorn' refers to an infective calculus that has adopted the configuration of the renal pelvis and calyces (fancifully likened to the antlers of a stag). Rarely, the infective process progresses to involve the entire renal parenchyma in a chronic inflammatory mass – xanthogranulomatous pyelonephritis (see below).

Metabolic calculi

Calcium

Hypercalciuria is the commonest metabolic abnormality found in children with calculi, occurring in up to 25% of patient in some series. Urinary calcium excretion is much higher in infants than in older children. In children, hypercalciuria is very rarely associated with hypercalcaemia. The majority of children have no identifiable underlying tubulopathy or other disorder. Elevated urinary calcium levels are, however, more frequent in certain groups: ex-premature infants, children with significant neurological defects impairing mobility and as a side effect of drugs (furosemide). In newborn infants, the combination of hypercalciuria and nephrocalcinosis points to the presence of a renal tubular defect – a major disorder of calcium metabolism.

Oxalate

Hyperoxaluria is found in 10–20% of children with stones and half of these have primary hyperoxaluria. Secondary hyperoxaluria can occur as a result of congenital enteropathies and after surgical small bowel resection. Children with cystic fibrosis have a higher incidence of renal stones and commonly have hyperoxaluria. Two rare genetically determined metabolic disorders are expressed as excessive production of oxalic acid: urolithiasis and nephrocalcinosis. The infantile form of primary hyperoxaluria is rapidly progressive and is characterised by the deposition of oxalate throughout the tissues. A second form presents with calculi in adult life. A combination of renal and orthotopic liver transplantation has been advocated for severe forms, with the aim of treating not simply the renal complications but also the underlying hepatic enzyme deficiency.

Cystine

Cystine is one of four amino acids affected by a recessive inherited disorder of renal tubular reabsorption (the others being lysine, arginine and ornithine). The solubility of cystine is relatively poor and its elevated concentration within the collecting system results in crystal deposition and stone formation. Although cystine itself is only weakly radioopaque, the incorporation of calcium within the aggregation of amino acid crystals forms hard stones, which are clearly visualised on plain X-ray.

Uric acid

Metabolic disorders of uric acid metabolism are rare in children, but acute deposition of uric acid crystals within the urinary tract can occur as a result of massive cell breakdown, e.g. following the introduction of cytotoxic treatment for leukaemia or lymphoma. In these conditions uric acid crystalline debris 'silts up' the collecting systems, leading to anuric renal failure. Uric acid is radiolucent and thus cannot be directly visualised on plain X-ray.

Xanthine

Xanthine oxidase deficiency, a rare autosomal recessive disorder, results in the deposition of insoluble non-opaque xanthine stones within the urinary tract.

Underlying urological conditions

Predisposing urological abnormalities can be identified in approximately 20–30% of children with urinary calculi, a far higher figure than in adults. Although vesicoureteric reflux (VUR) may play an aetiological role by promoting urinary infection, it may represent a secondary phenomenon, particularly following the passage of ureteric calculi. Reflux should therefore be reassessed some months after stone clearance if antireflux surgery is envisaged.

The role of obstruction and stasis is generally easier to establish. Although uncommon, stones associated with primary pelviureteric junction (PUJ) obstruction are characteristically small and multiple (fancifully likened to melon seeds). Stones forming within megaureters can occasionally present acutely with complete upper tract obstruction following impaction at the vesical junction.

The use of intestinal segments for bladder reconstruction (enterocystoplasty) is accompanied by a

significant risk of stones, amounting to 30–40% in some series. A combination of factors includes stasis, the presence of intestinal mucus within the urine acting as a nidus for crystalline deposition, and chronic low-grade bacteriuria. Regular bladder washouts reduce the risk, principally by ensuring more effective clearance of urinary mucus than intermittent catheterisation alone.

Clinical presentation

Age

Stones may develop from as early as 2–3 months of life. In children there is a higher prevalence in early childhood (less than 5 years), predominantly due to an excess of infective stones secondary to urinary tract infection.

Urinary infection

Although older children may present with recognisable symptoms of urinary infection, the clinical picture in infants may be deceptively non-specific, consisting of vague ill health, low-grade fever and failure to thrive. The isolation of *Proteus* from a child's urine should always prompt investigation for possible underlying stone disease.

Haematuria

Macroscopic or microscopic haematuria is a common feature of calculi, but there is only a poor correlation between the severity of haematuria and the extent and distribution of stones within the urinary tract. Absence of blood on microscopy or reagent strip testing does not exclude the possibility of stones.

Passage of stone material per urethram

Occasionally stones come to light when a fragment or some softer matrix material is passed per urethram. In infants the presence of unusual material and streaks of blood in the nappy may be incorrectly ascribed to balanitis.

Pain

Acute renal colic of the pattern and severity encountered in adults is not a prominent feature of the symptomology in children. When pain does occur it is often a poorly localised symptom in a fractious, unwell child.

Abdominal mass

Xanthogranulomatous pyelonephritis (see below) presents with general ill health which may be accompanied by a palpable abdominal mass – a clinical picture resembling Wilms' tumour.

Diagnosis

The role of diagnostic imaging can be considered at two levels.

Initial screening for possible calculi

Ultrasound

In experienced hands ultrasound is a sensitive modality for the detection of renal calculi. Depending on their physical characteristics (chemical composition, hardness, etc.), calculi can be directly visualised on ultrasound. In addition, solid stones cast an 'acoustic shadow', which serves to distinguish calculi from other echogenic lesions within the renal collecting system (Figure 11.1). Ureteric calculi and small bladder calculi may sometimes be difficult to detect on ultrasound.

Abdominal X-ray

Until recently a plain abdominal radiograph has been considered mandatory to look for possible calculi in any child undergoing investigation for haematuria. Similarly, the investigation of urinary infection in boys less than 5 years of age has previously included a routine plain abdominal X-ray (Figure 11.2). Likewise, a documented *Proteus* urinary infection at any age was thought to merit a plain abdominal X-ray, except in older girls with

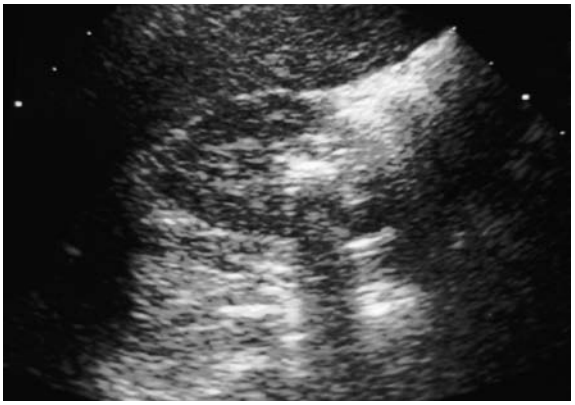


Figure 11.1 Ultrasound appearances of renal calculi, illustrating 'acoustic shadow'.

uncomplicated urinary infection of mild or moderate severity. However, the sensitivity of ultrasound for the detection of calculi is now such that this can be employed as the first-line investigation in the majority of instances, with abdominal X-ray being undertaken on a selected basis (see Chapter 3).

Unenhanced spiral computed tomography

This procedure is rapidly being adopted as the initial investigation of choice for adults with suspected stone disease. Spiral computed tomography (CT) provides an accurate diagnosis within minutes, avoids the potential risk of adverse reaction to contrast media and will positively demonstrate the presence of radiolucent calculi that cannot be directly visualised by conventional radiology. However, the radiation dosage is estimated to be three to five times greater than that of an intravenous urography (IVU), although this nevertheless amounts to only a quarter of the recommended limit of medical radiation exposure for a child in a year. Other drawbacks include the requirement for more complex equipment than IVU and greater difficulty in interpreting the images of the collecting system. The role of spiral CT as front-line diagnostic modality in children requires further evaluation.

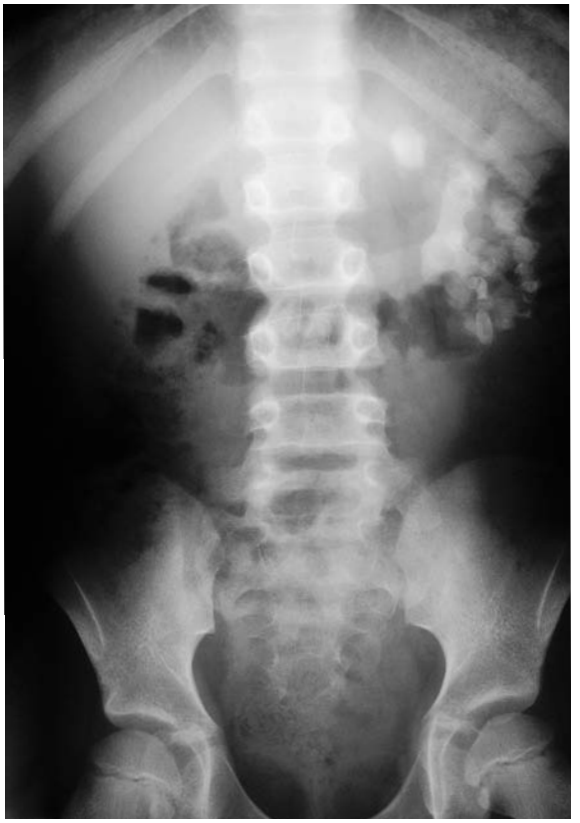


Figure 11.2 Plain X-ray revealing multiple infective calculi in the left kidney.

Evaluation prior to treatment of proven stone disease

DMSA

Regardless of whether open surgery or minimally invasive treatment is planned, differential function in the affected kidney(s) should be documented on DMSA (dimercaptosuccinic acid), and re-evaluated after treatment.

Intravenous urography

For a number of reasons the IVU retains a valuable, if limited, role in the diagnostic evaluation of stones – for example, by permitting visualisation of non-opaque stones and the matrix component of infective staghorn calculi. Information on calyceal anatomy is important in planning percutaneous nephrolithotomy (PCNL) and external shockwave lithotripsy

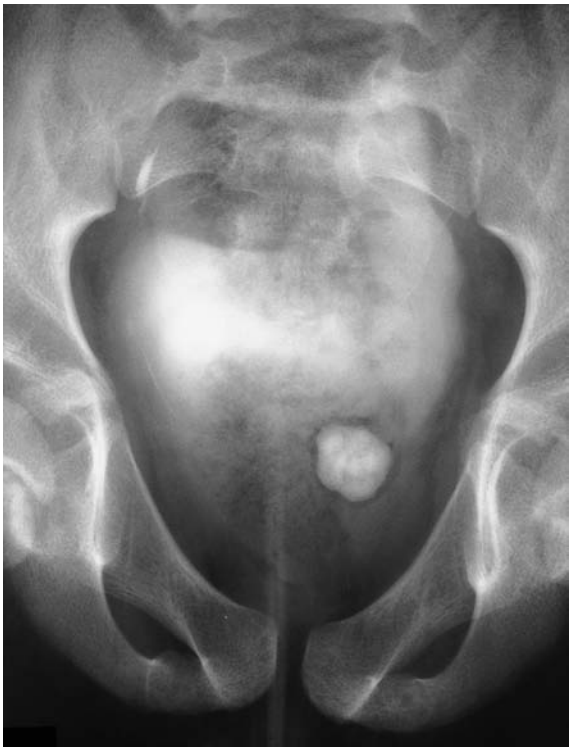


Figure 11.3 Intravenous urogram demonstrating a calculus in a single (orthotopic) ureterocoele. The IVU is also useful in helping to establish the nature of the predisposing anatomical abnormality.

(ESWL). Ureteric calculi are best localised by intravenous urography (Figure 11.3). Finally, the IVU may be helpful in identifying any underlying anatomical abnormality predisposing to urolithiasis.

Additional investigations

Micturating cystography

Micturating cystography (MCU) is not routinely required. Infection and the passage of stone material to the bladder may result in transient VUR, which resolves once the infection has been treated and stone clearance achieved. However, when ureteric dilatation persists postoperatively, or in the event of further infection, an MCU should be performed.

Dynamic renography

Dynamic renography, e.g. MAG3 (mercaptoacetyltriglycine), DTPA (diethylenetriamine pentaacetic acid), is undertaken if obstruction is suspected. However, the diagnosis of obstruction should not be made in the presence of a large calculus within the renal pelvis. Assessment of a possible pelviureteric junction (PUJ) obstruction can only be made after a period of time following the complete removal of the stone.

Computed tomography

As already indicated, the potential role of unenhanced spiral CT in the initial diagnosis of stone disease is still undergoing evaluation in children. However, CT has a well-established role in the diagnosis of xanthogranulomatous pyelonephritis and for visualising non-opaque calculi.

Metabolic investigations

Underlying metabolic disorders are not always reliably reflected in the chemical composition of the stones they give rise to. For this reason urinary biochemistry is more useful than the time-honoured practice of sending stones for laboratory investigation. The presence of urinary infection does not exclude the possibility of metabolic stones, as the two aetiologies may coexist. Every child with stone disease, regardless of the perceived aetiology, should therefore undergo metabolic screening after the eradication of infection (Table 11.1).

Stone screening

Stone screening can be reliably undertaken on a random 'spot' sample of 2–5 ml of urine, although an early morning specimen may be preferable for some studies. Twenty-four hour urine collections are impracticable in children and are only required for the specific investigation of rare metabolic disorders.

Table 11.1 Metabolic screening protocol

Fasting blood sample for plasma levels of urea, electrolytes, creatinine, calcium, phosphate, uric acid
Early morning urine sample (pH to exclude renal tubular acidosis)
'Spot', i.e. untimed, urine sample 2–5 ml (divided in the laboratory into two aliquots)
First aliquot acidified and analysed for creatinine, calcium, magnesium, cystine, oxalate
Second aliquot alkalinised and analysed for creatinine and uric acid

Management

Some form of intervention is almost invariably required to physically remove the stone(s) or reduce them to fragments, which can then be passed spontaneously. In adult practice minimally invasive modalities have become the mainstay of treatment. With improvements in the technology and increasing experience these techniques are now effectively used in paediatric practice, making the need for open surgery significantly less common. However, there are aspects of treatment unique to paediatric stone disease that need specific consideration:

- Sixty per cent of stones in children are infective in origin and often bulky; as such, they may not be amenable to ESWL. However, some authors have published evidence to support the contention that even large calculi in infants under 1 year of age respond well to ESWL.
- General anaesthesia is necessary for younger children in view of the discomfort and to ensure they remain still. The majority of ESWL procedures in adults are performed without general anaesthesia.
- PCNL and ureteroscopy can now be performed with suitable instruments in children; however, the instruments used in children are, nevertheless, relatively large in relation to body size because of the need to insert probes for stone disintegration of large calculi.

Open stone surgery

Kidney

Following exposure and mobilisation of the kidney, isolated stones within the collecting system can usually be removed with stone forceps via an incision in the renal pelvis without undue difficulty (Figure 11.4). The bulk of a staghorn calculus can also be removed by this approach, but the subsequent removal of fragments impacted in the calyces, necessary to achieve total stone clearance, often proves time-consuming and frustrating. Some of the manoeuvres that can facilitate this task are illustrated in (Figure 11.5). With the advent of ESWL it is often preferable to treat any small residual fragments by ESWL at a later date, rather than incur the haemorrhage and parenchymal damage associated with multiple incisions in the renal cortex.

Techniques dating from the days of extensive open stone surgery in adults (anatrophic nephrolithotomy, renal cooling, etc.) have only a very limited application in paediatric practice. To minimise the risk of unsuspected retained fragments, intraoperative 'on-table' X-rays of the kidney are mandatory to confirm that stone clearance has been achieved (Figure 11.6). Intraoperative X-rays may also help the surgeon decide when to abandon nephrolithotomy in favour of postoperative ESWL.

Extrarenal drainage is essential in view of the considerable leakage of urine that may occur from the incision sites in the kidney postoperatively. Following extensive renal surgery a short period of nephrostomy or indwelling JJ stent drainage may also be indicated (Figures 11.7 and 11.8).

Ureter

In the absence of obstruction, severe pain or infection, a small stone (e.g. <5 mm) can be managed

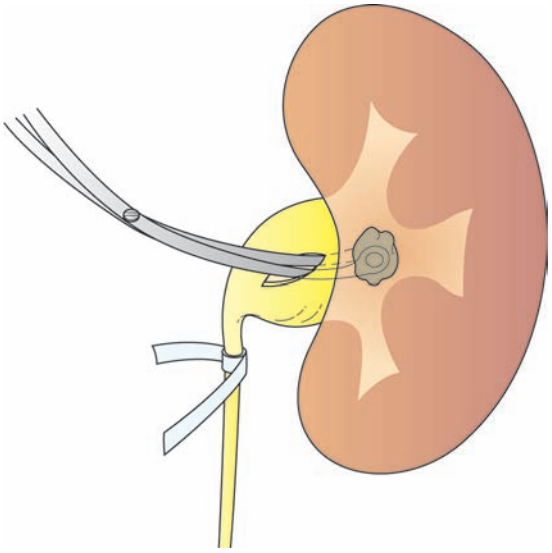


Figure 11.4 Pyelolithotomy. Open removal of a calculus from the renal pelvis.

expectantly in the hope that it will pass spontaneously into the bladder, from where it will be passed by voiding or will be accessible to endoscopic removal. If the stone fails to pass or is accompanied by symptoms or obstruction, the following options are considered.

Ureteroscopy

This procedure can be performed in any age group. The stone is disintegrated with a laser probe – see below.

Stone basket

Stone extraction using a basket is not of practical use in paediatric practice. After disintegration, most fragments pass spontaneously.

Ureterolithotomy

Stones in the distal ureter can be removed via a Pfannenstiel incision. Midureteric stones are best approached transperitoneally via an oblique muscle-cutting incision. The ureter is closed loosely with a few interrupted absorbable sutures to minimise the risk of stricture formation.

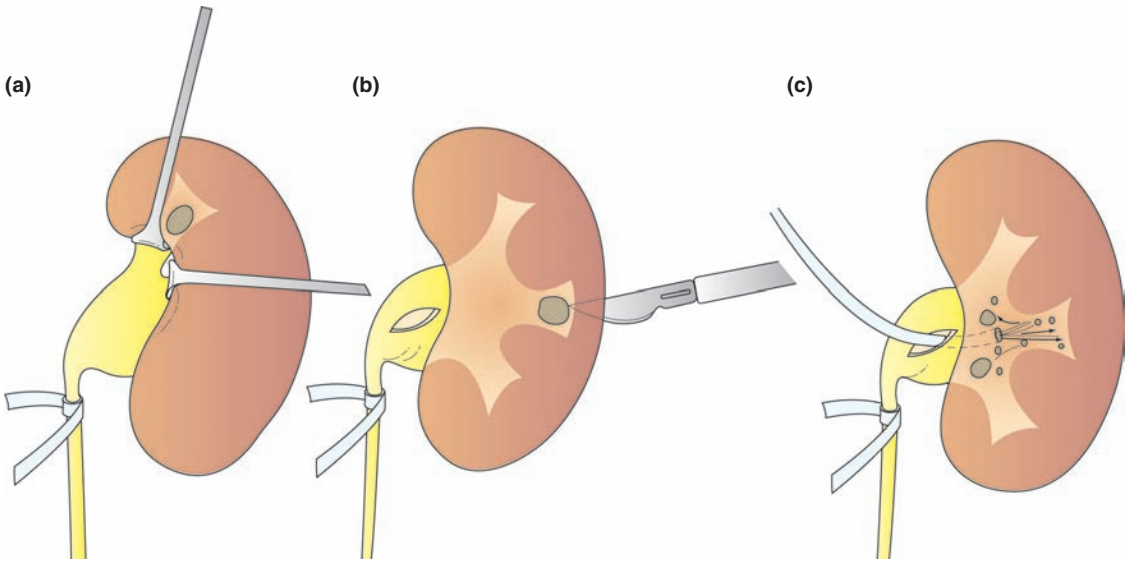


Figure 11.5 Additional intraoperative manoeuvres for the clearance of calyceal calculi or fragments. (a) Surgical exposure of calyceal neck by dissection at the renal hilum. (b) Nephrolithotomy. (c) High-pressure saline irrigation.

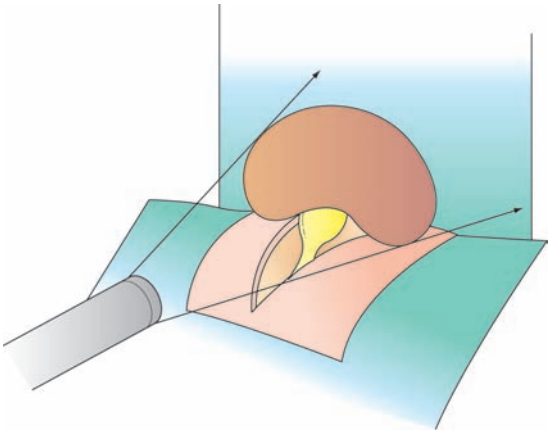


Figure 11.6 Intraoperative 'on-table' X-ray to confirm stone clearance.

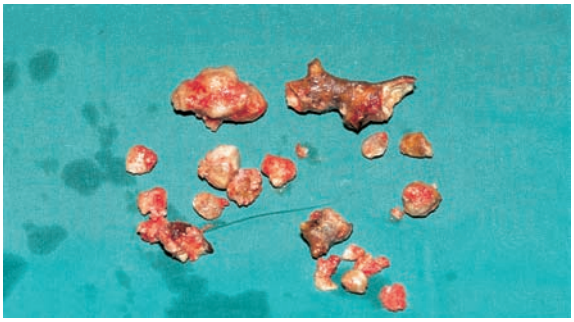


Figure 11.7 Multiple infective calculi, removed by pyelonephrolithotomy from the patient illustrated in Figure 11.2.

Bladder

Stones which have recently passed into the bladder from the upper tracts can be managed conservatively in the expectation that they will be passed from the bladder by voiding, but stones arising de novo within the bladder, or bladder stones forming around the nidus of an upper tract fragment, are often too large to pass spontaneously by the time they are diagnosed.

Open surgery (cystolithotomy) remains the preferred option for very large stones, particularly those forming within augmented bladders. Where the bladder neck has been formally closed in conjunction with augmentation and the creation of a Mitrofanoff stoma, open cystolithotomy is the simplest and most effective surgical option.

Urethra

Urethral calculi are rare in children and result from impaction of a calculus (or post-ESWL fragments) during its passage through the urethra, or in situ stone formation within an anatomical abnormality, such as a müllerian remnant or the urethral stump of a rectourethral fistula following surgery for an anorectal anomaly.

Urethral calculi can be removed or crushed using rigid endoscopic biopsy forceps. Meatotomy

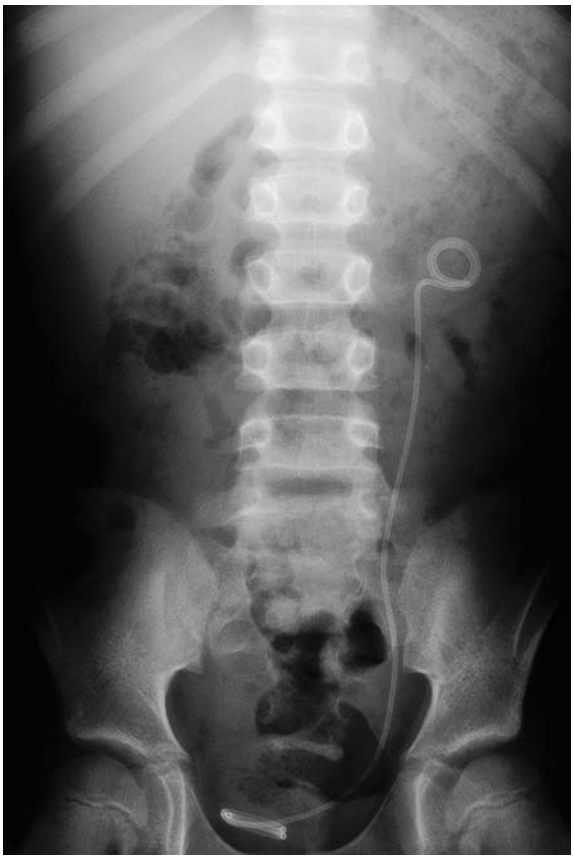


Figure 11.8 Plain abdominal X-ray of the patient illustrated in Figures 11.2 and 11.7. Total stone clearance achieved, indwelling JJ stent in situ.

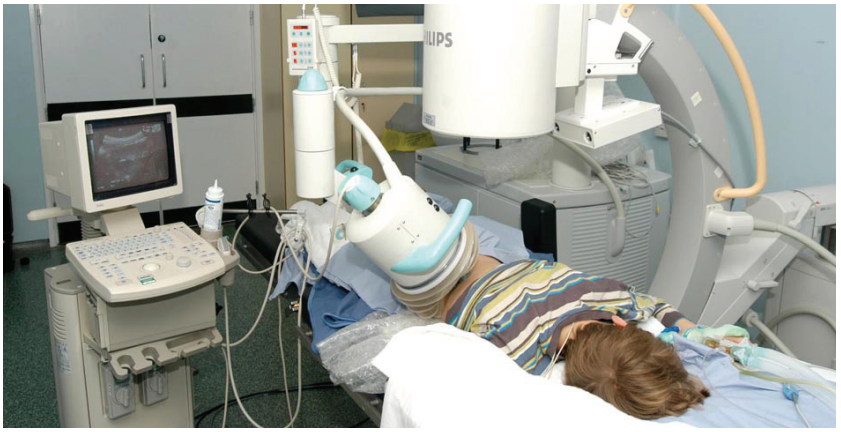


Figure 11.9 Child being treated under general anaesthesia by a current generation Storz lithotripter. Stone localisation and imaging during the treatment is achieved by a combination of X-Ray C arm and ultrasound.

may be required to release a stone impacted within the fossa navicularis.

Minimally invasive treatment

Kidney

External shockwave lithotripsy (Figure 11.9)

Shockwaves generated either by high-tension spark or by piezoelectric energy are transmitted through a fluid to the patient. Using ultrasound or X-ray linked to the shockwave generator, this energy is focused on the renal stone(s). Unlike adults, in the paediatric age group general anaesthesia is frequently required to ensure that a suitable position is maintained throughout the duration of treatment, to provide analgesia and ensure cooperation with the procedure. Repeated general anaesthetics may be required to achieve stone clearance.

ESWL has been demonstrated to be valuable for the treatment of small or non-infective stones in older children, and also for 'mopping up' residual fragments following PCNL or open stone surgery.

Percutaneous nephrolithotomy

A percutaneous track is established to permit the introduction of an endoscope into the renal collecting system. Under direct vision the stone is removed or disintegrated most commonly with an ultrasonic probe (Figure 11.10). Although PCNL has so far been largely limited to older children and adolescents, the availability of instruments designed specifically for paediatric use will extend the role of this modality.

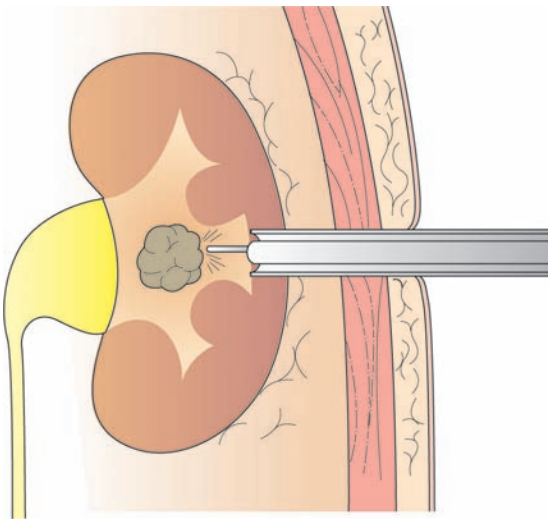
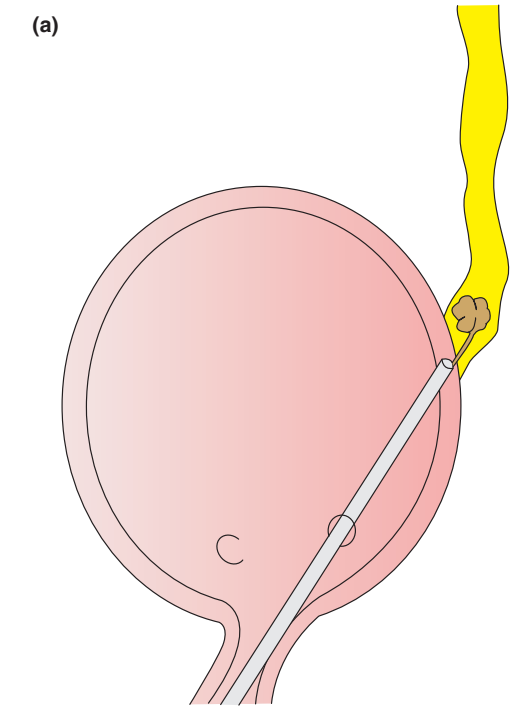


Figure 11.10 Percutaneous nephrolithotomy (PCNL).

Ureter

Ureteric stones, once visualised by semirigid or flexible ureteroscopy (Figure 11.11a and b), are fragmented by laser (pulse dye laser or holmium). Infrequently, where large fragments remain, a JJ stent may be required.



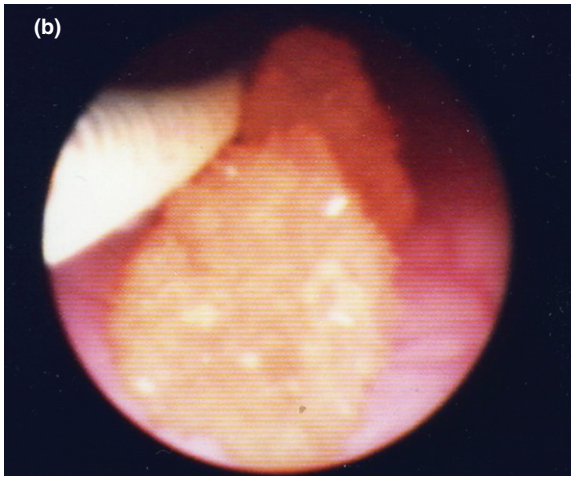


Figure 11.11 (a) Ureteroscopy and laser lithotripsy. (b) Ureteroscopic view demonstrating two individual 5 mm calculi prior to laser fragmentation. Note guide wire running in 11 o'clock position.

Bladder

Endoscopic treatment is now feasible for the majority of bladder stones. The stone is shattered using a lithoclast (employing the principle of a pneumatic drill) passed down the channel of a paediatric cystoscope (Figure 11.12). Larger fragments are removed by vigorous irrigation and suction, whereas small fragments can be left to pass spontaneously.

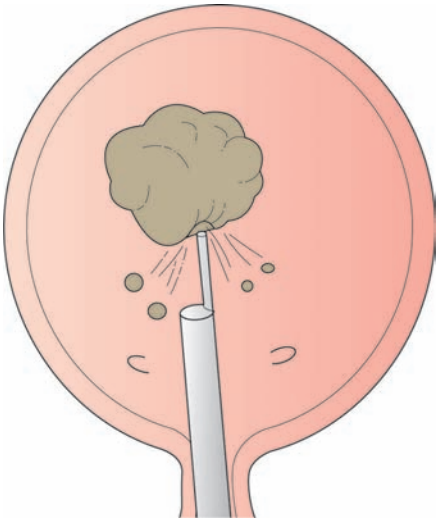


Figure 11.12 Endoscopic fragmentation of bladder calculus by lithoclast.

Complications

Open stone surgery

Complications include haemorrhage, particularly after multiple nephrotomies, retained or displaced stone fragments, prolonged urinary leakage and parenchymal damage resulting in loss of renal function.

Open ureterolithotomy carries a risk of ureteric stricture. Ureteric damage (perforation, avulsion) may also result from injudicious attempts at ureteric basket extraction.

Minimally invasive modalities

Initial concerns regarding the safety of these techniques in children, particularly the risk of parenchymal damage and subsequent hypertension, have not been borne out in practice, although the long-term outcomes have yet to be fully documented.

Parenchymal damage is an anticipated risk associated with PCNL, but, as with ESWL in this age group, the findings of postoperative DMSA scans have generally shown very little evidence of significant scarring. Ureteroscopy may result in transient reflux and carries a possible risk of fibrosis and vesicoureteric junction obstruction, but in the hands of an experienced endourologist the risk of complications appears to be low.

Results

A recent review of 15 years of paediatric experience confirmed that the minimally invasive management of calculi is both safe and effective. In this series 218 renal units were managed by ESWL (140 renal units), PCNL (43 renal units) or ureteroscopy (35 renal units). The incidence of underlying urological abnormalities was around 20%. The overall success rate in clearing stones <20 mm by ESWL was 85% (comparable with other recent published studies). However, in cases of larger or staghorn calculi, the results were significantly worse. For these and certain other stones there has therefore been a gradual shift to the use of PCNL – for which a clearance rate of 79% was achieved in this series. PCNL had a 7% retreatment rate (although 37% of children required some additional procedures), albeit with a complication rate of only 6%. For ureteric stones, ureteroscopy and laser lithotripsy with the holmium laser was highly effective, achieving 100% clearance.

Conclusions based on the published literature can be briefly summarised as follows: renal calculi which are <20 mm are most effectively treated by ESWL, whereas larger stones and especially staghorn calculi are better treated by PCNL. For ureteric stones, ureteroscopy and lithotripsy with the holmium laser is now the modality of choice. In addition, there is still an occasional place for open surgery.

Recurrence

Infective calculi

The recurrence risk can be minimised by correcting any underlying predisposing anatomical abnormality and by maintaining infection-free urine with antibiotic prophylaxis for 12 months following surgery.

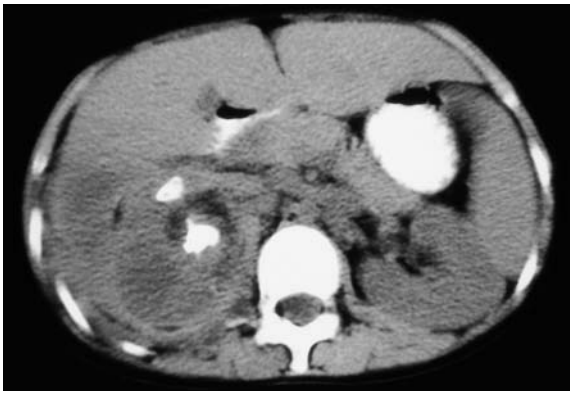


Figure 11.13 CT scan. Xanthogranulomatous pyelonephritis of the right kidney, illustrating calculi embedded within a non-functioning inflammatory renal mass. Normal left kidney.

Metabolic calculi

A high fluid intake is essential. In addition, a number of specific measures can be employed, e.g. pyridoxine in primary hyperoxaluria, D-penicillamine in cystinuria, and allopurinol in conjunction with a low-purine diet for xanthinuria.

Xanthogranulomatous pyelonephritis

This rare manifestation of stone disease is characterised by features of chronic sepsis – weight loss, anaemia, elevated erythrocyte sedimentation rate (ESR) – and the presence of an inflammatory mass which may extend to involve adjacent viscera. The diagnosis is confirmed by a combination of ultrasound, CT (Figure 11.13) and DMSA, which reveals absent or minimal function in the affected kidney. Treatment consists of nephrectomy. Although open nephrectomy is generally preferable in view of the dense inflammatory adhesions and risk of damage to adjacent organs, the use of laparoscopic nephrectomy for this condition has also been reported.

Key points

- Urinary calculi are rare in childhood. Urinary infection is an important aetiological factor, but underlying metabolic predisposition is being increasingly recognised as a major cause.
- Every child presenting with calculi should be thoroughly evaluated to identify any underlying metabolic disorder or urological malformation.
- Urine biochemistry should be combined with stone analysis to diagnose metabolic disorders.
- Minimally invasive modalities such as ESWL, PCNL and endoscopic lithotripsy have now largely superseded open techniques in the treatment of children's stones.
- Careful follow-up, with maintenance of sterile urine and appropriate treatment of any metabolic disorder, is essential to minimise the risk of stone recurrence.

Further reading

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Urinary incontinence 12

Henrik A Steinbrecher, Padraig S Malone and Anthony MK Rickwood

Topics covered
Development of bladder control
Patient assessment
Organic urinary incontinence
Functional diurnal incontinence
Nocturnal enuresis

Introduction

Urinary incontinence by day (diurnal), night (nocturnal) or both day and night is common during childhood. It can be defined as the 'involuntary loss of urine from the urinary tract'. It is often a cause of major social morbidity in affected individuals: it causes children to be stigmatised by their peers and has a disruptive impact within their families. Children who wet, therefore, deserve as much attention as children with other urological disorders.

The terminology currently recommended by the International Children's Continence Society will be employed throughout this chapter. A simple classification used in this chapter is shown in Figure 12.1. Although organic (anatomical) causes of incontinence are rare (accounting for well under 1% of referrals from general practice), it is essential that they are excluded in the first instance since they almost always require active treatment (often surgical) and, in some instances, pose a threat to renal function. Only when an organic cause has been excluded can the complaint be assumed to be functional in aetiology. The problem then essentially becomes social rather than medical, and because the natural history of almost all these disorders is benign, any decision regarding active management should rest principally with parents and the young patient.

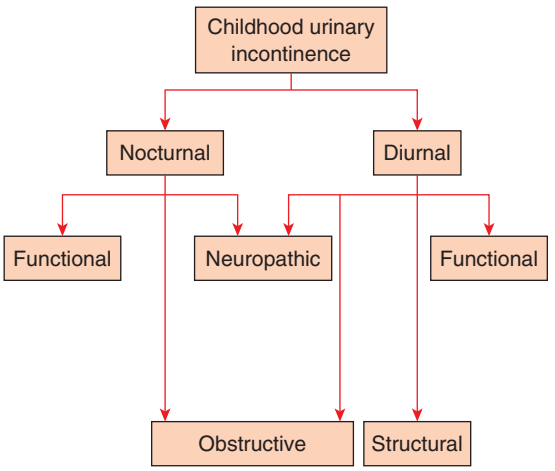

Figure 12.1 Simple classification of childhood urinary incontinence.

Development of bladder control

During infancy, voiding is a reflex act which is mediated and coordinated at brainstem level. Nevertheless, the arousal characteristically occurring premicturition indicates the existence of sensory input to higher centres. As a result, for example, voiding rarely, if ever, occurs during sleep. Although reflex voiding contractions are not under any voluntary control, they are nonetheless accompanied by relaxation of the sphincter complex (detrusor–sphincter synergia) and detrusor contractions are

sustained until the bladder is empty. This pattern of normal reflex voiding is sometimes disturbed in infants with organic bladder outflow obstruction (e.g. posterior urethral valves), while studies of boys with gross vesicoureteric reflux have shown high-pressure dysfunctional voiding even in the absence of demonstrable urethral obstruction.

During the first year of life the frequency of voiding remains fairly constant, at approximately 20 times per day, declining over the next 2 years to around 11 times per day, and by the age of 7 years settling to an average of five times per day. This decreased frequency is associated with a growth-related increase in bladder capacity that is disproportionately greater than the volume of urine produced.

Successful toilet training is dependent upon several factors, the most important being the development of voluntary inhibition of the voiding reflex. Following successful toilet training, the normal bladder cycle consists of the following stages, each under neurological modulation:

1. As the bladder fills, the urethral sphincter contracts via modulation from T10–12 lumbar sympathetic pathways and S2–4 voluntary somatic control.
2. The urethral sphincter relaxes via S2–4 voluntary somatic control.
3. The pelvic floor relaxes via S2–4 voluntary somatic control.
4. The detrusor contracts in response to stimulation via parasympathetic S2–4 pathways.
5. Urinary flow occurs to completion.
6. The urethral sphincter contracts via S2–4 voluntary somatic control.

In some young children – perhaps even the majority – there is a transitional phase where this ability to inhibit the voiding reflex is related to filling volume, so that once this is reached there is only a short interval between the first perception of a desire to void and the necessity to do so. Usually by 5 years of age, a mature filling/voiding cycle exists, with maintenance of detrusor stability despite a strong desire to void. At the appropriate time, voiding to completion occurs by sustained detrusor contractions accompanied by synergistic sphincter relaxation.

Table 12.1 Organic causes of childhood urinary incontinence

Urinary infection (Intermittent leakage)
Neuropathic (Continuous/intermittent leakage)
Bladder outflow obstruction (Intermittent leakage)
Structural (Continuous leakage)
Exstrophy/epispadias
Ureteric ectopia (girls)
Congenital short urethra (girls)
Urovaginal confluence (girls)

Patient assessment

Clinical

Exclusion of organic disease (Table 12.1) always represents the first priority and is usually possible on the basis of history, physical examination and, when appropriate, ultrasonography of the urinary tracts. More invasive investigations, including urodynamics, are only required occasionally.

History

Whenever dealing with a child with urinary incontinence, the three fundamental questions to be addressed are:

- **Does the wetting occur principally or entirely by night, principally or entirely by day, or both by day and night?**
- **Is the problem *primary* (i.e. lifelong) or *secondary* (i.e. of onset following toilet training and after a period when the child was dry)?**
- **In the case of daytime wetting, does this occur continuously or only intermittently?**

For practical purposes, purely night-time wetting that is primary and unaccompanied by any daytime symptoms (primary monosymptomatic nocturnal enuresis) *never* has an underlying organic basis. Bedwetting that is of secondary onset or is associated with daytime symptoms, by contrast, can very

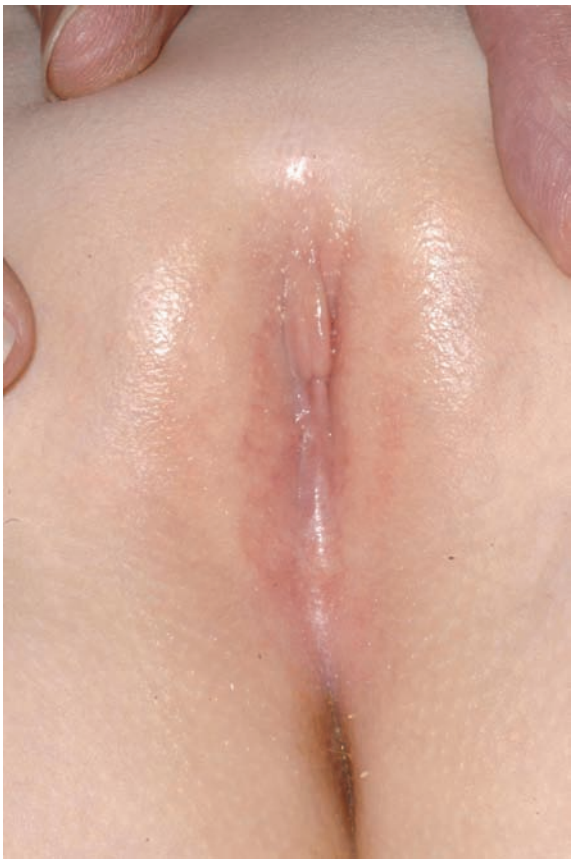

Figure 12.2 Six-year-old girl presenting with dribbling upon standing up after voiding. Examination revealed extensive occlusion of the introitus by labial adhesions, resulting in retrograde filling of the vagina during voiding. Symptoms were cured by separation of the labial adhesions.

occasionally result from bladder outflow obstruction or neurological disease. It should be noted that polyuric states (e.g. diabetes mellitus or insipidus) typically cause nocturia, not bedwetting.

Although wetting confined *solely* to the daytime is usually functional, in girls there are two other anatomical possibilities deserving consideration, one being retrograde filling of the vagina during voiding that leads to slight urinary leakage for the first half hour or so thereafter. Typically this occurs in girls with partial occlusion of the introitus due to extensive labial adhesions (Figure 12.2). The other possibility is that of an ectopic ureter. Urine may pool within the dilated ureter or vagina, leaking out only when the child is active and upright but not while the child is asleep and lying flat. A number of key considerations are helpful when evaluating the history:

- **Both primary and secondary wetting are compatible with either a functional disorder or organic disease.**
- **Although secondary wetting is usually functional in aetiology, it can also occur as a result of bladder outflow obstruction or neurological disease.**
- **A congenital structural anomaly can be virtually discounted as a cause of wetting in a child who was previously dry.**
- **Daytime wetting that is truly continuous *always* has an underlying organic cause, either structural or neurological.**
- **Although intermittent daytime wetting is very occasionally indicative of bladder outflow obstruction or neurological disease, it is of functional origin in the great majority of cases, particularly when the wetting occurs infrequently.**

Typical information to be obtained in a history of a child with wetting is listed in Table 12.2.

Physical examination

The examination of a child with incontinence should include the abdomen, spine and genitalia, along with assessment of the lower limbs and gait and a simple lower limb neurological examination. Salient features on examination include:

- **A palpably enlarged bladder**, with or without palpable kidneys, is indicative of outflow obstruction, whether organic or neurological. A palpable bladder that is also expressible is virtually pathognomonic of neurological disease: this is all the more likely in the presence of gross constipation.
- Examination of the **male genitalia** will identify **primary epispadias, pathological phimosis** (balanitis xerotica obliterans) and **meatal stenosis**

Table 12.2 History of a child with wetting

	Example	Comment
Number of episodes of wetting/day and or nights/week	Day = 5/7, 3×/day Night = 7/7, 1×/night (early morning)	Accurate data should be obtained for ease of follow-up assessment. Terms such as 'occasional' and 'sometimes' are unhelpful
Frequency of voiding/day and voiding/night	Day/night = 7/1	
Presence of urgency/ Vincent's curtsey sign Urge incontinence		Child crouches down on heel, pushing on perineum to prevent leakage
Stress incontinence	Laugh, exercise, cough	
Stream – onset, presence of hesitancy		Hesitancy may be caused by obstruction. A normal stream does not exclude obstruction
Stream characteristic	Stop/start, continuous	Sign of obstruction or detrusor instability
Fluid intake, last drink taken, type of drink taken	ml/day of cola, blackcurrant, water	Cola drinks and blackcurrant juice have been incriminated as possible causes of bladder instability
Bowel habit	Bowels open 1–2×/day, no pain, no blood, normal motions	It is vital to get a bowel history in children with incontinence
Use of shampoos, soaps, etc.	Hair wash in bath, child sits in soapy water, etc.	It has been speculated that changes in perineal bacterial flora can predispose to urinary infections and secondary bladder instability
Family history of wetting	Parents wet until teens, siblings wet	This aspect of the history is only relevant to night-time wetting
Drug history, other health history	Asthma, cystic fibrosis, ADHD	Some medical illnesses and their treatment affect bladder function

ADHD, attention-deficit hyperactivity disorder.

(including, occasionally, stenosis of a hypospadiac orifice). Examination of the **female genitalia** will identify **primary epispadias** (Figure 12.3) a **urogenital sinus anomaly** (Figure 12.4), **fused labia minora** and **imperforate hymen**. An **ectopic ureteric orifice** is only very rarely evident on gross inspection, although in some affected individuals urine may be seen leaking from the introitus. To avoid distress in older girls and adolescents, it is generally more appropriate to undertake the examination under sedation or anaesthesia. Regardless of the setting, examination of the genitalia should always be carried out in the presence of a chaperon.

- Hairy patches, swellings, cutaneous haemangiomata and sinuses of the **spine** are strongly indicative of underlying spinal dysraphism (although blind-ending pits overlying the tip of the coccyx are of no neurological significance). **Sacral agenesis** is detectable clinically by palpable absence of the lowermost sacral segments and, in most cases, by the appearance of flattening of the upper buttocks.
- **Neurological disease** is suggested by exaggerated lower limb reflexes (or frank clonus) or by wasting of the calves or deformities of the feet, especially if asymmetrical. The lowermost sacral segments should be examined for

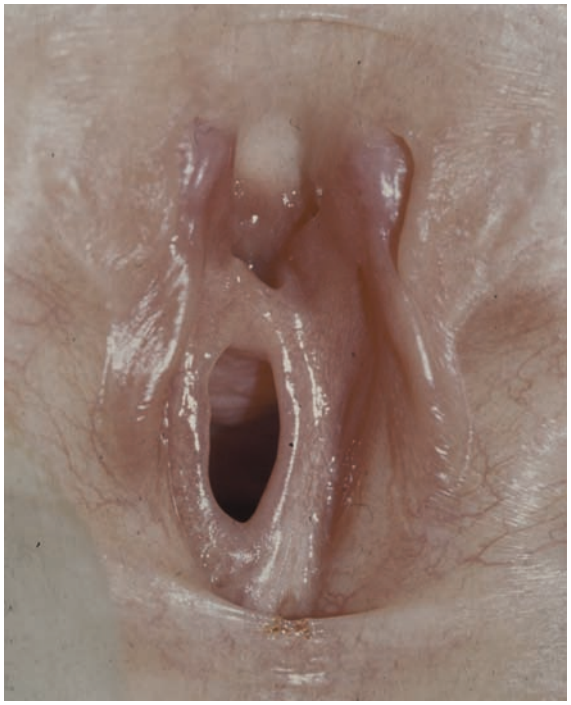

Figure 12.3 Female epispadias. Bifid clitoris with wide urethral meatus. This anomaly in females is invariably associated with sphincter weakness incontinence.

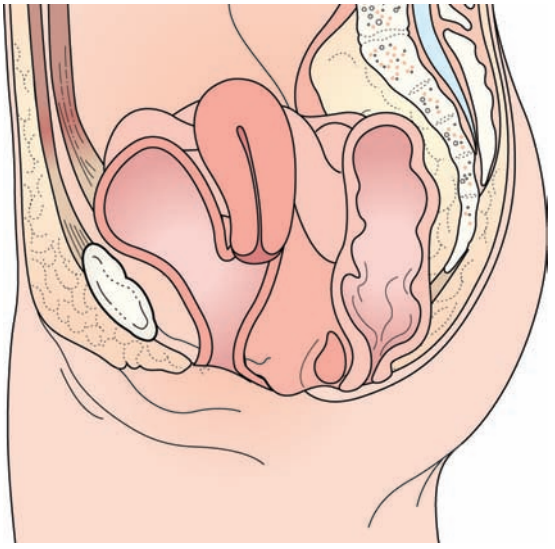

Figure 12.4 Anatomy of common urogenital sinus with urovaginal confluence. (See also Chapter 14, Cloacal anomalies.)

motor and sensory integrity. An abnormal gait should also arouse suspicion of neurological disease.

Investigations

An **ultrasound scan** of the abdomen and urinary tract is advisable for all children referred with daytime wetting and should, whenever practicable, include estimation of postvoid residual urine in addition to measurement of bladder wall thickness and visualisation of the upper tracts. Findings of possible significance include:

- **Duplication anomalies** are of relevance to wetting only in girls. Uncomplicated duplication is unlikely to be significant, whereas the identification of hydronephrosis or dysplasia in the upper pole of a duplex kidney is strongly suggestive of an ectopic ureter. It should be noted, however, that the ultrasound appearances of the kidney may be normal, in which event the demonstration of a dilated ureter behind the bladder may provide the clue to the presence of an ectopic ureter.
- **Upper tract dilatation** may be indicative of organic bladder outflow obstruction or neuropathic bladder and while these conditions usually give rise to bilateral dilatation, they are not excluded by the finding of unilateral dilatation.
- **Bladder wall thickening**, although suggestive of bladder outflow obstruction or neuropathy, is also commonly found, albeit to a minor extent, in children with functional detrusor overactivity and/or detrusor–sphincter dyssynergia.
- The presence of **residual urine** within the bladder after voiding is suggestive of bladder outflow obstruction or neuropathy. However, this finding should be interpreted with caution, especially in younger children who commonly have a significant residual urine (exceeding 10% of expected bladder capacity) on some occasions but not others. Hence, whenever there is doubt, the examination should be repeated.

A **urinary flowmeter** is often helpful in providing additional information, albeit with the proviso that flow rate needs to be carefully interpreted depending on the volume of urine voided. However, a flow rate of less than 15 ml/s or a urinary flow with a stop/start 'staccato' pattern is suggestive of anatomical or functional bladder outflow obstruction.

Although **urine culture** is usually negative, girls with asymptomatic bacteriuria represent a notable exception. In these patients the bacteriuria and the wetting may be separate manifestations of a common, single underlying pathology, typically characterised by incomplete bladder emptying from whatever cause.

Urodynamic examinations should be employed sparingly and selectively in children because they are invasive and potentially distressing. The indications include:

- suspicion of neuropathic bladder
- suspicion of genuine stress incontinence
- severe wetting that fails to respond to empirical treatment based upon a clinical diagnosis.

Magnetic resonance imaging (MRI) of the spinal cord, cauda equina and sacrum is indicated should there be suspicion of neurological disease.

Cystourethroscopy may be indicated, particularly for boys, when some form of anatomical bladder outflow obstruction is suspected. This examination may also be of occasional therapeutic benefit, e.g. endoscopic resection of late presenting urethral valves.

Additional investigations are occasionally necessary to confirm or exclude the presence of an ectopic ureter and these usually take the form of MRI (ideally MR urography) or laparoscopy. In the methylene blue test, the dye is instilled into the bladder via a catheter, which is then removed and a pad placed over the vulva. Subsequent leakage of clear urine onto the pad confirms the presence of an ectopic ureter: 'blue' leakage, by contrast, indicates that the wetting problem is of bladder origin.

Organic urinary incontinence in children (see Table 12.1)

Urinary infection

Acute lower urinary tract infection commonly causes wetting in children (usually girls) whose bladder control is quite normal at other times. Once the infection is treated, the wetting usually rapidly resolves, although in a few cases, it persists for some time afterwards. The indications for investigation are essentially the same as for the investigation of any child of comparable age presenting with urinary infection of similar severity.

Spinal neurological disease

Clinical features suggestive of underlying neurological disease comprise:

- urinary incontinence of unusual severity, especially if accompanied by constant dribbling of urine
- marked disturbance of bowel habit, particularly if associated with faecal soiling
- an expressible bladder
- any suggestion of lower limb locomotor problems, clumsy gait, etc.

A **spinal X-ray**, traditionally undertaken as the first-line investigation in the presence of one or more of the features listed above, is of limited value as a normal examination does not exclude the presence of neurological pathology, while the isolated laminal defects at L5 or S1 that are commonly found are only very rarely of any significance (unlike the occasional discovery of laminal or vertebral defects at two or more levels). For these and other reasons, **MRI** of the spine has become the investigation of first choice in such cases and, in the event of a positive finding or continuing suspicion of neurological disease, the opinion of a paediatric neurologist should be sought at an early stage.

Ultrasound may disclose upper tract dilatation (bilateral or unilateral), marked thickening of the bladder wall or a large residual urine volume.

Exstrophy/epispadias

See Chapter 15.

Congenital short urethra

As with epispadias, the history is one of continuous urinary leakage and the urethral meatus is typically both wide and patulous. The diagnosis is confirmed by endoscopy. It has been suggested that this anomaly is a variant of primary epispadias.

Urogenital sinus anomalies

Isolated lesions that are not associated with anorectal or cloacal anomalies sometimes present with urinary incontinence, due either to neuropathic bladder resulting from an associated spinal anomaly, or to a form of urogenital sinus anomaly (urovaginal confluence) associated with an incompetent sphincteric mechanism (see Figure 12.4). In the latter case there is always continuous daytime urinary leakage. All urogenital sinus anomalies are characterised by a single vulval orifice that resembles neither vagina nor urethra.

Labial adhesions

Labial adhesions may contribute to retrograde filling of the vagina on voiding and subsequent dribbling when the girl stands up from the toilet. While it is important to consider the diagnosis of labial adhesions in girls with postvoid dribbling, this phenomenon can also occur in the absence of labial adhesions.

Bladder outflow obstruction

This condition occurs far more commonly in boys than in girls. Causes in boys include **posterior urethral valves**, **urethral stricture** (including post hypospadias repair), **syringocele**, **meatal stenosis** (e.g. following circumcision) and pathological phimosis due to **balanitis xerotica obliterans**. In girls, **haematocolpos** or **hydrocolpos** due to imperforate hymen or vaginal atresia may present with bladder outflow obstruction, generally at or after puberty and with an accompanying history of primary amenorrhoea. Causes affecting both sexes are **pelvic tumours** and **severe constipation**, although these conditions more often present with urinary retention than incontinence.

The urinary stream is usually impaired but many boys are unaware of this (as are their parents). If there is suspicion of bladder outflow obstruction, it is often helpful to observe the child voiding, where this is possible, or alternatively obtain a measurement of flow rate. With few exceptions, incontinent episodes are associated with urgent micturition, which in turn is the consequence of obstructive detrusor overactivity. Residual urine, if not detectable clinically, is nearly always found on ultrasonography, often in conjunction with thickening of the bladder wall. The upper renal tracts, however, usually remain undilated, even in some cases of posterior urethral valves. In girls, hydrocolpos or haematocolpos is always demonstrable by ultrasonography.

All patients suspected of having bladder outflow obstruction deserve examination under anaesthetic, cystoscopy, or both. It is important to be aware that the clinical picture may resemble primary detrusor overactivity and, for a while at least, there may be a symptomatic response to detrusor antispasmodics. The speed at which wetting symptoms resolve following relief of obstruction is very variable and, while some children become dry within a matter of weeks or months, it is not uncommon for the incontinence to persist for longer, occasionally even for years. In that event, the use of antispasmodics is entirely appropriate.

Genuine stress incontinence and the wide bladder neck anomaly

Among girls presenting with urinary incontinence, only a very small proportion are found to have genuine stress incontinence, typically with a characteristic clinical history and appropriate urodynamic findings. The 'wide bladder neck anomaly' is periodically described in the literature, although whether this is a genuine entity remains open to doubt. It has recently been shown that girls

involved in strenuous sporting activity such as gymnastics can demonstrate stress incontinence and that patients with cystic fibrosis have up to a 30% incidence of this complaint. During videourodynamic examination of girls, it is not uncommon to find the bladder neck slightly open, but rarely, if ever, is it possible to demonstrate stress urinary leakage. In doubtful cases, an empirical trial of an α-adrenergic agonist (e.g. ephedrine) may be employed, and in the event of a clear-cut clinical response, genuine stress incontinence may be assumed even if this has not been confirmed urodynamically. In exceptional cases, it may be necessary to consider a bladder neck sling procedure for patients who have reached adolescence.

Ureteric ectopia

See Chapter 7.

Non-neuropathic neuropathic bladder

See below under 'Functional diurnal urinary incontinence'.

Functional diurnal urinary incontinence

Among 7 year olds, some 3% of girls and 2% of boys experience functional daytime wetting at least once a week. Some 30% of the former and 50% of the latter also have nocturnal incontinence. Functional diurnal enuresis in children is distinguishable in several forms (Table 12.3), almost all of them with a benign natural history and with detrusor overactivity as the underlying common cause.

Table 12.3 Functional diurnal enuresis

Detrusor instability
Urge syndrome
uncomplicated
dysfunctional voiding
Deferred voiding
Lazy bladder
Occult neuropathic bladder
?Detrusor instability or central (CNS)
Giggle incontinence
Non-detrusor instability
Diurnal frequency syndrome
Sensory urgency

The overactive bladder

Aetiology

More than of 80% of children with daytime wetting have urgency and in the great majority this is due to an overactive bladder, typically at the endstage of filling. The cause is unknown and may be multifactorial. It is, however, likely that in many instances the phenomenon represents no more than delayed maturity of bladder control and that affected children remain at that transition phase wherein detrusor inhibition is still volume related. Why this should occur is seldom obvious, as with few exceptions they are otherwise well-adjusted individuals who have experienced nothing out of the ordinary by way of toilet training. There is no familial predisposition to this complaint. Urgency may also feature prominently among the symptoms of children whose detrusor overactivity is a secondary response to functional outflow obstruction associated with dyssynergia.

Clinical features

The majority of affected children experience incontinence associated with urgency of micturition, and experience only a transient interval between the first desire to void and the necessity of doing so. Indeed some children claim that they do not realise they are voiding at all. Children attempt to counter urgent urinary leakage by contraction of the striated urethral sphincter and pelvic floor muscles and may reinforce this process by various manoeuvres, characteristically by crouching with the heel pressed into the perineum (Vincent's curtsey sign). Sometimes urinary leakage is considerable (flooding), but is mostly relatively slight,

consisting of damp patches only. However, leakage of as little as 2 ml is sufficient to stain boys' trousers and a similar volume may embarrass girls by the resulting urinary malodour. Some children find their problem worse in cold weather, while in others overactivity may be precipitated by certain drinks, particularly fizzy drinks. An element of daytime frequency exists in a majority of cases and a proportion – more boys than girls – are also troubled by nocturnal enuresis.

The urge syndrome has two subcategories:

- **Uncomplicated urgency** is clinically distinguishable by a normal, smooth, uninterrupted urinary stream, and is urodynamically characterised by detrusor–sphincter synergia and, usually, by voiding to completion. Girls and boys are almost equally affected. Only seldom is there a history of urinary infection. Minor degrees of constipation are common. It has been suggested that an appreciable proportion of these children exhibit features of the attention-deficit hyperactivity disorder (ADHD).
- **Dysfunctional voiding** is clinically recognisable by a urinary stream that is fluctuant or interrupted ('staccato' voiding), and the urodynamic picture during intentional micturition is one of detrusor–sphincter dyssynergia, either with incomplete relaxation of the sphincter or with alternating phases of contraction and relaxation. Incomplete voiding is common. It is thought that these children, having learned to ameliorate the consequences of detrusor instability by voluntary contraction of the urethral sphincter, subsequently and behaviourally come to lack sphincter inhibition during deliberate voiding. Girls are affected almost exclusively and upwards of 90% experience recurrent urinary infections. Some 30% have vesicoureteric reflux, with or without associated renal scarring, and there is evidence that such reflux develops *secondarily* as a result of repetitive episodes of abnormally high intravesical pressure consequent upon a combination of detrusor overactivity and detrusor–sphincter dyssynergia. Although degrees of constipation are sometimes found, these children only rarely exhibit features of any psychological disorder (see Hinman's syndrome below).

Prognosis

Spontaneous resolution is the rule, with only 2–3% of patients troubled into adult life. Among those more intractably affected, moving to live independently away from home often tends to effect the final cure. The chance of spontaneous resolution during any 1 year is of the order of 1 in 6.

Investigation

A positive urine culture merits other appropriate investigations (Chapters 3 and 4).

Ultrasonography commonly demonstrates minor thickening of the bladder wall, while significant residual urine (>10% of expected bladder capacity) is suggestive of dysfunctional voiding. If necessary, uncomplicated urgency can be distinguished from dysfunctional voiding by **flowmetry**.

Urodynamic examination is seldom needed for diagnostic purposes: unlike in adult men, bladder outflow obstruction is only a very rare cause of urgency in boys, while in girls, unlike in adult women, it is only very rarely necessary to distinguish detrusor overactivity from genuine stress incontinence.

Management

Active measures are seldom effective before 5 years of age. Thereafter, there are several options.

Ameliorative measures

School authorities should be made aware of the problem so that the child is allowed to go to the toilet as necessary. Inconspicuous incontinence pads are available in children's sizes.

Simple bladder retraining

Strategies include a fluid intake evenly distributed throughout the day, the avoidance of drinks known to precipitate bladder overactivity, and a regimen of

timed voiding, beginning at hourly intervals and, if successful, slowly extending these by degrees. During the course of history taking, it will often emerge that the affected child voids rarely, if at all, during the course of a normal school day, an admission that may come as a surprise to the parents. It is important, therefore, for the child to try and establish a regular voiding routine based around breaks and lunchtime. Significant constipation should be treated.

Detrusor antispasmodics

Oxybutynin is immediately and unequivocally effective in 60–70% of cases and troublesome side effects are less common than in adults. As a rule, treatment must be continued for at least 3 months, although in a few instances for rather longer than that and occasionally for more than a year. Many patients find slow-release oxybutynin more effective than the conventional preparation, while tolterodine represents an alternative agent for those unable to tolerate oxybutynin in any form.

Cognitive bladder retraining

Although effective in as many as 80% of cases, including those unresponsive to detrusor antispasmodics, this technique, because it is more demanding than simple retraining, is unsuitable for children under 8 years of age. As it is also both time-consuming and expensive, it is best employed on a selective basis, being most useful in well-motivated girls troubled by dysfunctional voiding. Conducted by a trained urotherapist, children in age- and sex-matched pairs undergo a structured programme that first introduces them to the elements of bladder anatomy and physiology and thereafter, using non-invasive biofeedback techniques, teaches them to recognise and then control their bladder signals.

Botulinum toxin A

There is increasing evidence from adult practice that the injection of up to 400 units of botulinum toxin A into the bladder produces a dramatic improvement in symptoms and objective urodynamic parameters, a therapeutic effect that can last for up to 7 months, including in patients unresponsive to first-line treatments. Similar results have lately been reported from a small number of paediatric trials. The toxin is injected at about 30 sites using a rigid cystoscope under general anaesthesia and, although injection into the trigonal area is usually avoided, it has recently been suggested that this trigonal sparing is unnecessary. According to some authorities, this form of treatment should nowadays be employed as the next step, should anticholinergic medication fail.

Neuromodulation

This is a well-established technique in adults, but because it is invasive and involves the implantation of sacral nerve electrodes, it is rarely used in children. However, the use of transcutaneous electrical nerve stimulation (TENS) is worth considering. Two electrodes are placed over S4 dermatomes on the buttocks and lower limbs and used for a number of hours. Some patients respond very well to this and the improvement may be incremental with successive cycles of treatment.

Sensory urgency

A few children, mostly girls, who exhibit symptoms typical of the urge syndrome yet are wholly unresponsive to treatment, are found on urodynamic examination to have sensory rather than motor urgency. Apart from a very small number of cases with chronic or interstitial cystitis, the aetiology of this complaint is no less obscure than that of its adult counterpart. Bladder overdistension under general anaesthesia produces symptomatic relief in some individuals and the use of intravesical oxybutynin has also been described.

Diurnal urinary frequency of childhood

More commonly affecting boys than girls, and principally those aged 4–7 years old, this complaint is characterised by the sudden onset of gross daytime urinary frequency, as often as every 10–15 minutes. It is pathognomonic of this disorder that the daytime frequency is *not* accompanied by any corresponding degree of nocturia: night-time voiding seldom

occurs more than twice and typically not at all. Bedwetting may happen during the first few days, and occasionally diurnal enuresis also, but otherwise incontinence is not a feature of the condition and other urinary symptoms are conspicuously absent. Urine culture and ultrasonography are normal and the frequency is wholly unresponsive to detrusor antispasmodics. The aetiology is unknown, although the discrepancy between bladder behaviour awake and asleep is compatible with a behavioural origin. The complaint is always self-limiting, usually over 3–12 weeks. A handful of children experience recurrent cycles over a period of 1–2 years.

Deferred voiding

This problem is common in 4–6 year olds of both sexes, but only occasionally in older individuals, many of whom have a behavioural disorder. Urgent micturition, owing to presumed detrusor instability, is a consistent feature, but the wetting arises principally because the child defers micturition until it is too late. In most cases, it is apparent that other activities, e.g. playing outdoors, take precedence over the social desirability of continence. Treatment is unnecessary for youngsters as the condition is self-limiting. Older children with behavioural disorders deserve the attentions of a clinical psychologist.

Lazy bladder

This condition, virtually confined to girls, typically comes to light at 8–10 years of age and may present with daytime incontinence, urinary infection or incidental detection of a palpable and usually visibly distended bladder postmicturition. The upper renal tracts are always undilated and the urodynamic picture is one of low-pressure retention with detrusor–sphincter dyssynergia and non-sustained detrusor contractions. Detrusor overactivity is a further feature in most cases. Lazy bladders are almost certainly behavioural in origin, resulting from excessive reliance on hold manoeuvres over a prolonged period of time. It is usually self-limiting, characteristically resolving quite suddenly during the course of puberty. Only symptomatic children need treatment, supplemented by antibiotic prophylaxis in the event of urinary infection. Daytime incontinence represents a difficult problem in these cases as detrusor antispasmodics must obviously be used with caution. Intermittent catheterisation works well if tolerated. Cognitive bladder retraining represents the most effective remedy.

Giggle incontinence

Largely confined to girls, this complaint typically presents around 9–12 years of age. The history is unmistakably one of urinary leakage occurring with giggling or laughing but at no other time. In most instances there is an otherwise entirely normal pattern of micturition. Urodynamic examination may disclose detrusor instability, either spontaneous or provoked, but is more often wholly unremarkable, even during giggling. The aetiology is unknown, although there is often a family history. Whether the complaint is truly self-limiting is open to doubt and the apparent improvement that usually occurs through puberty and into adult life may, in reality, represent no more than adaptation to avoid the precipitating circumstances.

Frequent episodes call for treatment. Oxybutynin is helpful in some cases and imipramine in others. Ritalin (methylphedinate) is the most consistently effective agent. Because it is mostly used in the treatment of ADHD, the parents of children with giggle incontinence may reject its use on account of the perceived stigma attached to ADHD and unfavourable media coverage. Nevertheless, it can prove dramatically effective in girls for whom severe giggle incontinence has a major impact on their school and social life.

Non-neuropathic neuropathic bladder

In children with this rare disorder the bladder behaves as though ‘neuropathic’ yet there is no identifiable neurological disease. The condition is distinguishable from severe dysfunctional voiding or lazy bladder by the radiological features of sacculation and elongation of the bladder (‘fir-tree’ bladder), which, in most instances, are accompanied by secondary changes in the upper renal tracts.

In the classic form, **Hinman's syndrome**, there is almost always a background of domestic turmoil or a history of severe physical or psychological upset occurring at, or shortly after, the time of toilet training. It is likely that affected children, because they are profoundly fearful of wetting themselves, grossly overuse their external urethral sphincter to counteract unstable detrusor contractions in a desperate attempt to stay dry. This leads to excessive intravesical pressures, to detrusor hypertrophy and, ultimately, to detrusor non-compliance, with consequent secondary upper renal tract complications. Presentation, typically at 5–8 years of age, is with unusually severe urinary incontinence, compounded in most cases by urinary infections and marked disturbance of bowel habit. A few children have evidence of renal insufficiency. The natural history is variable, with a tendency towards spontaneous resolution postpubertally. However, because of the risk to the upper renal tracts in the absence of treatment, an expectant approach is not a safe option and management should be instituted along the lines described for the true neuropathic bladder (Chapter 13).

In the **other form of this complaint** it would appear that there is some genuine but unidentifiable neurological lesion. There is never any background of psychological disturbance and presentation is often with episodic urinary retention, sometimes dating back to early infancy. Somewhat curiously, bowel habit is usually normal. So far as treatment is concerned, any distinction between these two categories of non-neuropathic bladder is academic.

Primary monosymptomatic nocturnal enuresis

Some 5–10% of 7 year olds wet the bed three or more times a week, a figure that does include a few children with secondary nocturnal enuresis and a slightly higher proportion who also have daytime symptoms, with or without actual wetting. However, the substantial majority who wet the bed have primary monosymptomatic nocturnal enuresis and, of these, two-thirds are boys.

The aetiology of this complaint is multifactorial and in any individual one or more factors may apply. Established aetiological factors comprise:

- A positive family history (upwards of 75% of cases).
- Impaired functional bladder capacity, clinically manifest by a degree of daytime frequency.
- Uninhibited nocturnal detrusor contractions. Although demonstrable in approximately a third of patients, these also occur in asymptomatic children. Diurnal urgency of micturition is a clinical indicator of such detrusor activity.
- Sleep arousal difficulty. Nocturnal enuresis does not, as is commonly supposed, result from deep sleep, as bedwetting occurs at all stages of the sleep cycle, but many affected children lack the normal arousal from sleep that should occur as functional bladder capacity is approached.
- Absence of a circadian rhythm of vasopressin release. Levels of vasopressin normally increase at night, but in as many as 75% of bedwetters (and a still higher proportion of those with a positive family history) such an increase is absent or diminished and leads to a nocturnal urinary output exceeding the functional bladder capacity.

Although nocturnal enuresis is sometimes a manifestation of psychosocial problems or of behavioural disorders, the great majority of bedwetters are normally adjusted children. The clinical features vary from one patient to another. Some children wet every night or almost so, whereas others are troubled less often and tend to experience alternating spells of wet and dry nights. Some children wet more than once a night, and the time of wetting varies between individuals. With only occasional exceptions, the wetting does not wake the child. As indicated previously in this chapter, secondary enuresis should prompt suspicion of organic disease. However, this is an unlikely explanation if, as is often the case, the onset has coincided with some physical or emotional upset. Except for those children with coexisting daytime symptoms and those with 'suspicious' secondary enuresis, investigation is unnecessary, with the exception of excluding infection. The prognosis

is excellent, with spontaneous resolution by the time of physical maturity occurring in 97–99% of affected individuals. The probability of cessation in any 1 year is approximately 1 in 6.

Treatment, if sought, should not commence before 5 years of age. The type of treatment depends in some measure on the clinical features, while its likelihood of success is heavily dependent on the motivation of the child and the family. It should be emphasised that all medications represent treatment rather than cure, although symptomatic treatment may help to expedite cessation of the underlying problem earlier than would otherwise have been the case. The parents should be encouraged to take a positive attitude towards the problem and scolding and punishment are to be condemned. Possible active measures are as follows:

- Star charts, combined with rewards, are particularly suited to the younger patient.
- Enuretic alarms, which alert and sensitise the child to respond appropriately to a full bladder during sleep, serve to convert this signal from one of micturition to one of inhibition of micturition and waking (Figure 12.5a and b). This measure, best deferred until at least 7 years of age, achieves a successful outcome in 60–75% of cases and, unlike treatment with medication, such success is only seldom followed by relapse. Failures tend to occur in least-motivated children and in those with a background of domestic disharmony or a history of daytime symptoms.
- Desmopressin has a vasopressin-like action and, whether administered intranasally (Desmospray) or orally (Desmotabs, Desmomelt), is effective in upwards of 70% of patients. The relapse rate after cessation of treatment is high (30–50%) and is to some extent dependent on the duration of treatment. Desmopressin may be used for short periods, to cover special occasions, or for a more extended duration, up to 12 months. Whenever used over a prolonged period, the dosage should be periodically reduced or stopped in order to determine whether the treatment needs be continued. Predictors of success include a positive family history or wetting soon after going to sleep, whereas predictors of failure are concurrent daytime symptoms.
- Detrusor antispasmodics, such as oxybutynin, are principally of value in children who are also troubled by daytime urgency and frequency. When given on this selective basis, these drugs are effective in up to two-thirds of cases.
- Imipramine is nowadays considered an unfashionable treatment of last resort. Nevertheless, its efficacy has been confirmed in several well-conducted trials. Its mode of action is unknown.
- Combination of treatments. In some patients, treatments that are unsuccessful individually may prove to be effective when used in combination. Examples are desmopressin with oxybutynin and desmopressin with an enuretic alarm. However, imipramine should *never* be prescribed in conjunction with desmopressin.

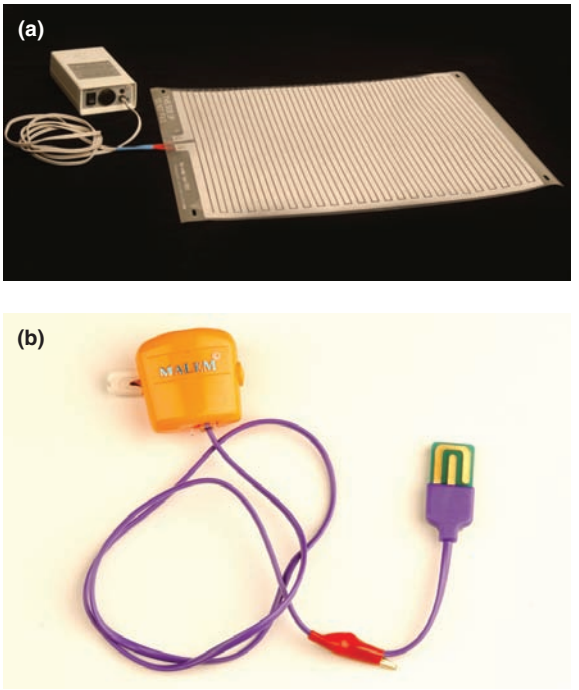

Figure 12.5 (a) Enuresis alarm. The pad is placed under the bed sheet, with bedside battery-powered buzzer. (b) Compact enuresis alarm suitable for the treatment of nocturnal enuresis or ambulatory treatment of diurnal enuresis. The buzzer device is pinned to the pyjamas (or clothes when used in the daytime) and the sensor worn between two pairs of underclothes.

Key points

- The initial priority is to exclude organic causes of urinary incontinence, although these are rare.
- Primary monosymptomatic nocturnal enuresis seldom, if ever, has an underlying organic basis.
- Most organic (anatomical or neurological) causes of daytime wetting can be excluded on the basis of history, examination and ultrasonography.
- Organic causes of daytime wetting are classifiable as neurological, obstructive and structural, the last category being confined almost exclusively to girls.
- Functional diurnal enuresis is due to detrusor instability in the great majority of cases, and the natural history of this complaint in children is one of spontaneous resolution.

Further reading

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Neuropathic bladder

13

Henrik A Steinbrecher, Padraig S Malone and Anthony MK Rickwood

Topics covered
Aetiology
Pathophysiology
Patient assessment
Investigation
Management
Bowel management

Introduction

Until the late 1950s, when the development of shunting devices to treat hydrocephalus led to the survival of large numbers of patients born with myelomeningocoele, neuropathic bladder was a rare disorder in children and received correspondingly little attention. Thereafter, unfortunately, it soon became apparent that children with myelomeningocoele presented with urological problems, as well as others, over and above those experienced by adults with spinal cord injury. The particular difficulties were:

- a preponderance of female patients, with evident implications for the management of incontinence
- a high incidence of secondary upper renal tract complications in patients of both sexes, although in boys more commonly.

Conduit urinary diversion quickly became established as the means of overcoming both problems in children with spina bifida and remained in vogue until the mid-1970s, by which time its limitations were apparent and alternative strategies had become available. The first of these, clean intermittent self-catheterisation (CISC), remains the mainstay of treatment today. Employed as the sole means of treatment, however, CISC, even when practicable, achieves continence in only a minority of patients (10–20%) and does not always protect the upper renal tracts. Subsequent developments, addressing these drawbacks, have comprised more effective medication, augmentation cystoplasty, sphincter-enhancing procedures and the Mitrofanoff principle.

Aetiology (Table 13.1)

Myelomeningocoele

Despite a markedly declining incidence during recent years, myelomeningocoele remains the most common cause of congenital neuropathic bladder. The condition results from partial failure of tubularisation of the neural crest and, because the normal process proceeds caudally, the conus medullaris is almost always involved, with only some 6% of patients escaping neuropathic bladder and bowel. The untubularised neural crest (neural plaque) contains grossly disorganised tissue and, consequently, the extent of the plaque determines the degree of paralysis. Regardless of the neurological deficit, 25–30% of patients retain positive conus reflexes (anocutaneous, glans-bulbar), and among these a minority with low-level sacral or lumbosacral myelomeningocoele have incomplete cord lesions with sensory sparing and, occasionally,

Table 13.1 Aetiology of childhood neuropathic bladder

Congenital	Acquired
Myelomeningocoele	Cord trauma
Spina bifida occulta Diastematomyelia Lumbosacral lipoma Intraspinal cysts Tethered cord	Cord infarction Prematurity Cardiac and aortic surgery
Sacral agenesis	Tumours Sacrococcygeal teratoma Neuroblastoma
	Transverse myelitis

motor sparing also. Other features of relevance to urological management include:

- **Hydrocephalus** – although almost invariably present, this does not always require shunting. The severity of hydrocephalus broadly matches the extent of the neural plaque and because, with some exceptions, the severity of hydrocephalus also reflects the level of intelligence, myelomeningocoele patients are unique in that increasing physical and intellectual disabilities tend to go hand-in-hand. In some patients CISC, or the manipulation required to handle an artificial urinary sphincter, may be precluded by the impaired manual dexterity often associated with hydrocephalus.
- **Mobility** – almost all patients with a neurological level above L3 (i.e. lacking normal quadriceps function) ultimately come to lead a wheelchair existence, no matter what degree of mobility they may have achieved during childhood. For someone with reasonably good mobility a bladder capacity sufficient for 2-hourly intervals between voiding is (just about) adequate, whereas for a wheelchair-bound patient at least twice that capacity is desirable.
- **Spinal deformity** – the incidence and severity of these deformities relates to the extent of the neural plaque. Kyphoscoliosis, the most severe deformity, is largely limited to thoracolumbar lesions and in some instances may make it physically impossible for patients of either sex to perform urethral self-catheterisation.
- **Congenital upper urinary tract anomalies** – although more prevalent than among the population at large, the nature of these anomalies (typically unilateral renal agenesis, or anomalies of position or fusion) is such that only rarely do they affect practical management.

Other congenital cord lesions

Because these lesions are not associated with hydrocephalus nor, as a rule, with major neurological deficits or spinal deformities, urological management is seldom influenced by factors other than the bladder dysfunction itself. Most affected patients, including those with incomplete cord lesions, have negative conus reflexes. The commonest of these lesions is lumbosacral lipoma.

Sacral agenesis (Figure 13.1)

Sacral agenesis may occur as a feature of anorectal anomalies or as an isolated lesion: in the latter instance, the mother is often an insulin-dependent diabetic. The implications of sacral agenesis in children with anorectal malformations are considered in Chapter 14. Regardless of whether it is an isolated or a coexisting anomaly, the cord lesion associated with sacral agenesis is invariably incom-

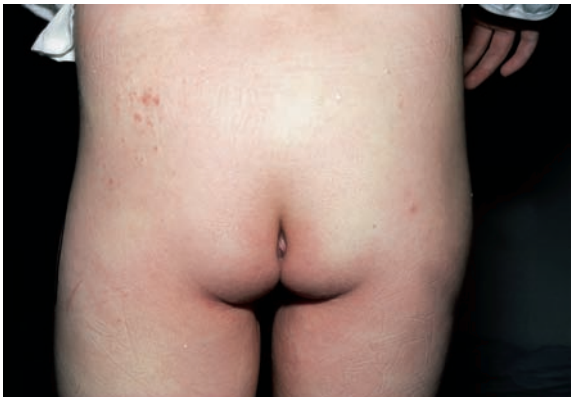

Figure 13.1 Sacral agenesis – characteristic wasting of the buttocks.

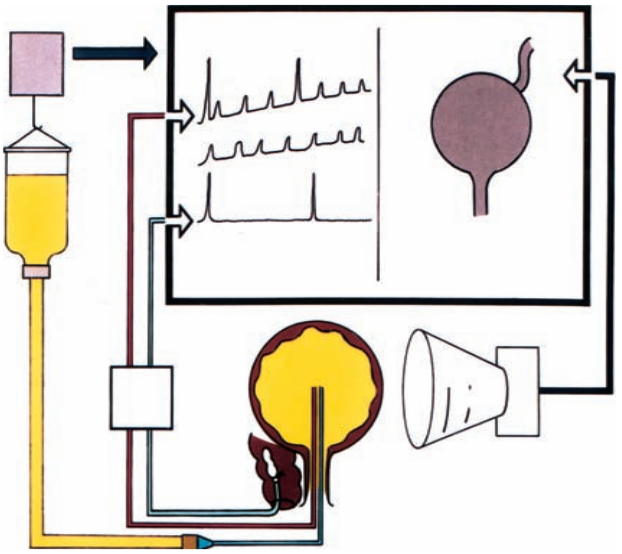

Figure 13.2 Videourodynamic equipment (videocystometry). Two catheters (or a single double-lumen catheter) are inserted into the bladder urethrally or suprapubically to permit filling and simultaneous intravesical pressure recording (TBP = total bladder pressure on the traces illustrated below). Electronic subtraction of intra-abdominal pressure, measured by a rectal balloon catheter (RP = rectal pressure), provides a measurement of true detrusor pressure (IDP = intrinsic detrusor pressure). Anatomical information is obtained by using radiographic contrast for the study, although X-ray screening time should be kept to a minimum.

plete and, uniquely, any peripheral neurological deficit bears no predictable relation to bladder or sphincter dysfunction.

Acquired cord lesions

These are rare. Cord trauma may occur at any level but is most common in the mid-dorsal region. Patients affected by transverse myelitis usually make an excellent recovery except for the bladder, which remains affected in upwards of 50% of cases. Other causes include spinal artery thrombosis (occurring in sick or premature infants) and spinal tumours.

Because of the small numbers, the risk of secondary upper renal tract complications is unquantifiable, although they undoubtedly occur more commonly than in adults with spinal cord injury. Girls and boys appear to be at roughly equal risk.

Pathophysiology

Basic considerations

In essence, clinical management aims to replicate, so far as possible, normal bladder function, namely:

- **filling and storage**, i.e. by ensuring adequate low-pressure functional capacity
- **emptying**, i.e. to maximise effective bladder capacity and minimise the risk of stasis-related infection
- **voiding at will** – in patients with neuropathic bladder, normal voluntary control of voiding is absent and some unphysiological or artificial means must be employed, either by abdominal compression or straining (possible only when there is some element of sphincteric incompetence) or by CISC, whether per-urethrally or via a Mitrofanoff channel.

Classification

As with acquired forms, congenital neuropathic bladder dysfunction is largely determined by the site of the cord lesion, albeit with the difference that an intermediate pattern of dysfunction is commonly seen. Urodynamic investigation, essential for elucidating the several patterns of bladder dysfunction associated with neuropathic bladder, should always consider the bladder–sphincter complex together rather than as separate entities. Basic features of the equipment used for videourodynamic investigation (also termed videocystometry) are illustrated in Figure 13.2. In some instances, electromyography (EMG) recordings of pelvic floor musculature are also measured using surface or needle electrodes.

Important practical considerations when conducting a urodynamic examination are that:

- It is best performed by the clinician also responsible for the patient's management.
- It should, if at all possible, be combined with simultaneous cystography.
- Slow filling is employed, at no more than 10% of expected bladder capacity per minute (expected functional capacity in ml is calculated as follows: 0–2 years, capacity = weight (kg) × 7; 2–12 years, capacity = (age + 2) × 30).
- The presence or absence of sphincteric incompetence should be assessed periodically during filling by manoeuvres that raise intra-abdominal pressure (standing, coughing, application of suprapubic pressure).
- In the presence of gross sphincteric incompetence it may be necessary to occlude the bladder neck by a Foley balloon catheter in order to fill the bladder to expected capacity.

A number of different classifications of the pathophysiology of neuropathic bladder have been described. The one adopted here is founded upon the three basic patterns revealed by urodynamic examinations, along with the ways in which these influence both bladder filling and emptying.

In suprasacral cord lesions (contractile bladder) the conus medullaris is intact (Figure 13.3) and so too, although isolated from higher centres, is the innervation of both detrusor and external urethral sphincter. Conus reflexes are positive. Detrusor contractility is enhanced. The sphincteric mechanism, usually including the bladder neck (Figure 13.4), is intact and voiding occurs *solely* by detrusor contractions, almost always accompanied by detrusor–sphincter dyssynergia (i.e. loss of the usual coordination between detrusor contraction and sphincter relaxation). This may be termed **dynamic sphincteric obstruction**. Repetitive high-pressure detrusor overactivity may ultimately lead to secondary changes in the detrusor itself and, in turn, to detrusor non-compliance and/or upper renal tract complications.

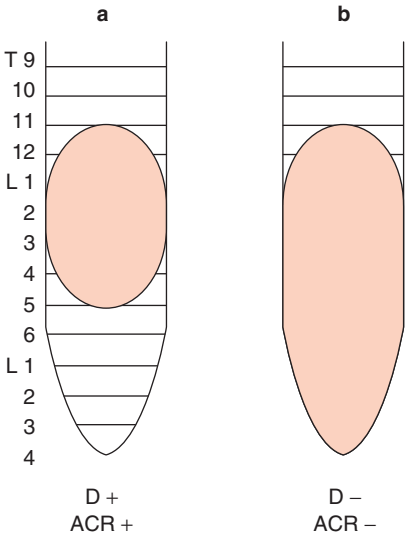

Figure 13.3 Suprasacral (a) and sacral (b) cord lesions: note that bladder innervation is determined by the distal, not the proximal, extent of the lesion (D = reflex detrusor activity, ACR = anocutaneous reflex).

In sacral cord lesions (acontractile bladder) the conus medullaris is destroyed (see Figure 13.3), as is the innervation of both detrusor and external urethral sphincter. Conus reflexes are negative and detrusor contractility is absent. Some degree of sphincteric incompetence is always present so that voiding occurs either by overflow or by raising intra-abdominal pressure. During such voiding, any obstruction is located at the level of the external urethral sphincter (Figure 13.5), and is termed **static sphincteric obstruction**. Unlike detrusor–sphincter dyssynergia, static sphincteric obstruction represents a fixed urethral resistance, constant in any individual patient but varying unpredictably from one patient to another.

More severe degrees of obstruction result in good functional capacity at the expense of large volumes of residual urine (see Figure 13.5), whereas minimal obstruction, equating to gross sphincteric incompetence, is associated with greatly reduced functional capacity and negligible residual urine (Figure 13.6). An inevitable consequence of voiding by abdominal straining against a fixed urethral resistance is that functional

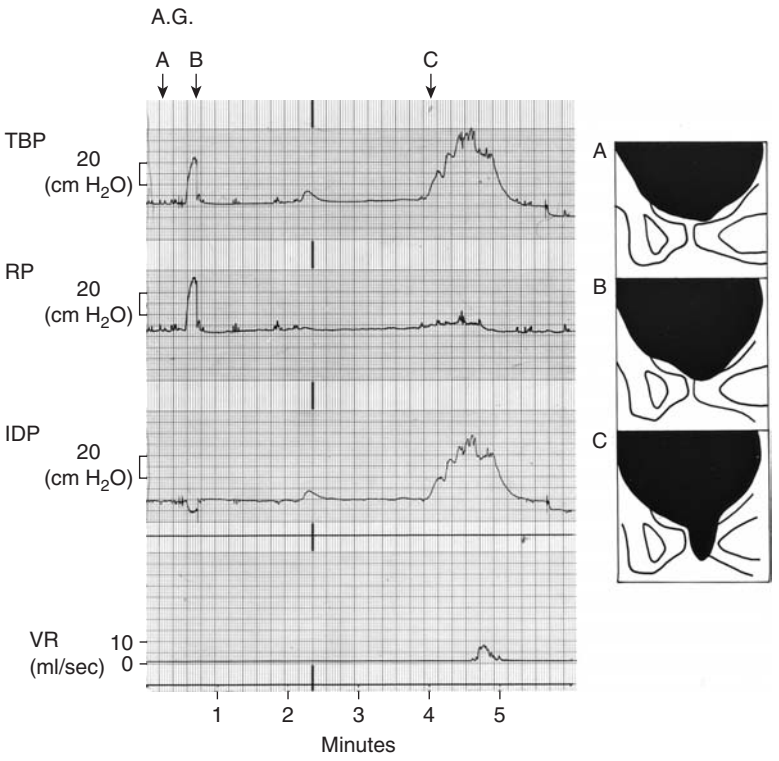

Figure 13.4 Contractile bladder. The bladder neck is closed at rest (A) and remains so despite a rise in intra-abdominal pressure (B). A reflex detrusor voiding contraction is accompanied by detrusor–sphincter dyssynergia and which is initially complete (C) (TBP = total bladder pressure, RP = rectal pressure, IDP = intrinsic detrusor pressure).

capacity scarcely exceeds residual urine, and hence that effective capacity is virtually zero. Acontractile bladders may be smooth or sacculated. A degree of detrusor non-compliance is common and, when present, serves to further limit functional capacity where urethral resistance is low, or results in excessively raised intravesical pressure where the resistance is high.

Intermediate bladder dysfunction is characterised by a combination of detrusor hyperreflexia, typically generating low pressures, and some degree of sphincteric incompetence (Figure 13.7). Conus reflexes are negative. Sacculation (Figure 13.8) is common, as is detrusor non-compliance. During voiding the appearance of any urethral obstruction more closely resembles that of static sphincteric obstruction than detrusor–sphincter dyssynergia.

The factors responsible for impaired bladder capacity are summarised in Table 13.2. In patients with myelomeningocoele the patterns of dysfunction are: contractile 25%, acontractile 15% and intermediate 60%. Contractile dysfunction is appreciably rarer with all other forms of congenital cord lesion.

Incomplete cord lesions

Incomplete cord lesions, with sacral sensory sparing (and sometimes motor sparing also), are of clinical significance principally when associated with contractile bladder dysfunction (conus reflexes positive). Such patients retain some sensation of bladder fullness and typically experience gross urgency of micturition. A proportion achieve spontaneous, if precarious, urinary continence. It is, however, important to note that despite acquiring continence these patients may nevertheless have urodynamic abnormalities predisposing to upper tract complications. Urethral sensation is usually largely intact with incomplete cord lesions and in some instances to the extent that the discomfort experienced during CISC precludes per-urethral self-catheterisation.

Secondary upper renal tract complications

Such complications, typically as obstruction or reflux, are prevalent in all children with neuropathic

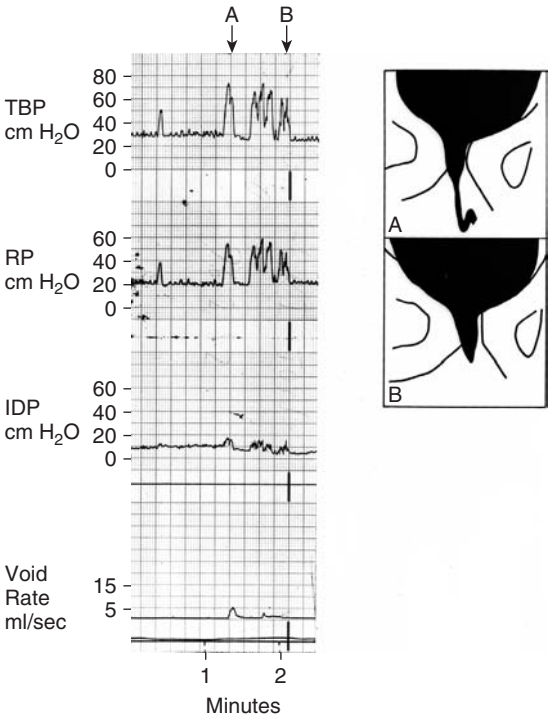

Figure 13.5 Acontractile bladder. During abdominal straining there is persistent narrowing at the level of the external urethral sphincter (A), which ultimately becomes complete (static sphincteric obstruction) despite continued straining (B): baseline intravesical pressure falls following this partial voiding.

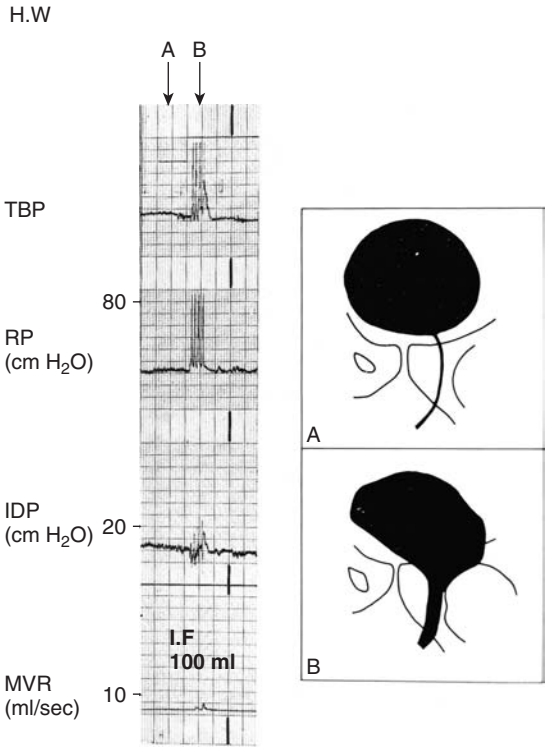

Figure 13.6 Acontractile bladder. The bladder neck is closed at rest (A) but the sphincteric mechanism becomes totally incompetent with a rise in intra-abdominal pressure (B).

bladder, whatever the cause. Twenty per cent of children with myelomeningocoele are affected by the age of 2 years. The incidence thereafter is difficult to determine and may be influenced (for better or for worse) by the effects of treatment. At an estimate, however, 50% of boys are at risk of upper tract complications by the time they complete puberty; the percentage in girls is somewhat smaller.

Factors responsible for secondary complications are summarised in Table 13.3.

- **Urinary infection** is extremely common and, in the very young, may lead to renal scarring even in the absence of vesicoureteric reflux. Most infections result from bladder dysfunction, and their treatment consequently hinges more upon improving bladder function rather than repetitive courses of antibiotics.
- **Vesicoureteric reflux** may be primary or, more often, secondary. In the case of secondary reflux, treatment is aimed principally at correcting the underlying abnormality of bladder function.
- **Bladder outflow obstruction**, whether in the form of detrusor–sphincter dyssynergia or static sphincteric obstruction, is an invariable precursor to secondary upper urinary tract obstruction or reflux. However, it leads to these complications *only* when associated with raised intravesical pressure due to detrusor overactivity, detrusor non-compliance, or a combination of both. The relative importance of these two factors is debatable, with conventional urodynamics pointing to detrusor non-compliance as the more important factor whereas ambulatory studies have tended to implicate detrusor overactivity. When considering detrusor non-compliance,

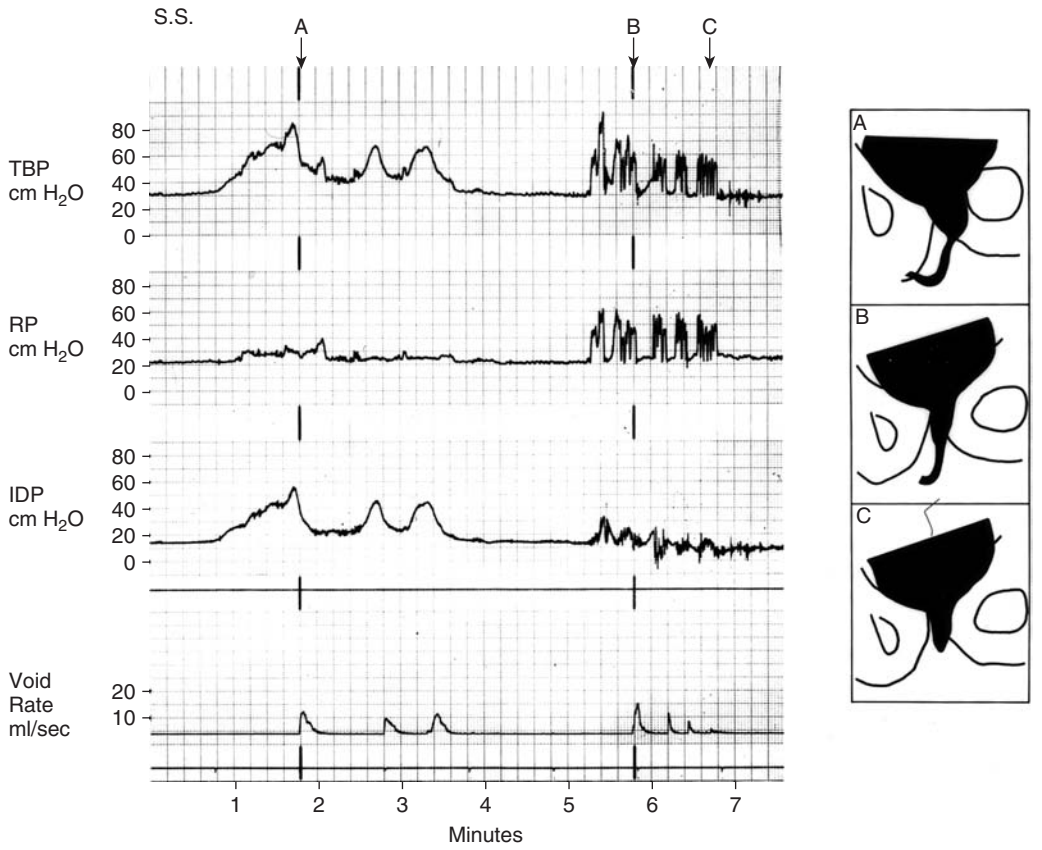

Figure 13.7 Intermediate bladder. Voiding occurs both by detrusor hyperreflexia (A) and by raising extra-abdominal pressure (B).

baseline pressures exceeding 20 cmH_2O within the physiological range of capacity on conventional slow-fill urodynamics should be regarded as being 'unsafe'. Whatever the detrusor behaviour, secondary upper renal tract complications never occur in the presence of gross sphincteric incompetence and a permanently empty bladder. This happy state may, of course, be reversed if sphincteric incompetence is treated without considering the possible subsequent effects of detrusor malfunction.

Natural history of neuropathic bladder malfunction

Neuropathic bladder dysfunction can change over the course of time, in terms of both severity or, less often, the particular pattern of dysfunction. Whatever change occurs, however, is almost invariably for the worse. Although no time of life is free of this problem, the periods of greatest risk are during the first 2 years, when some 30% of neonatally 'safe' bladders become 'unsafe', and subsequently during the course of puberty. In this latter age group, boys are at greater risk than girls, possibly because prostatic growth increases urethral resistance.

Patient assessment

History

General features to be ascertained from the history comprise mobility, intelligence and social

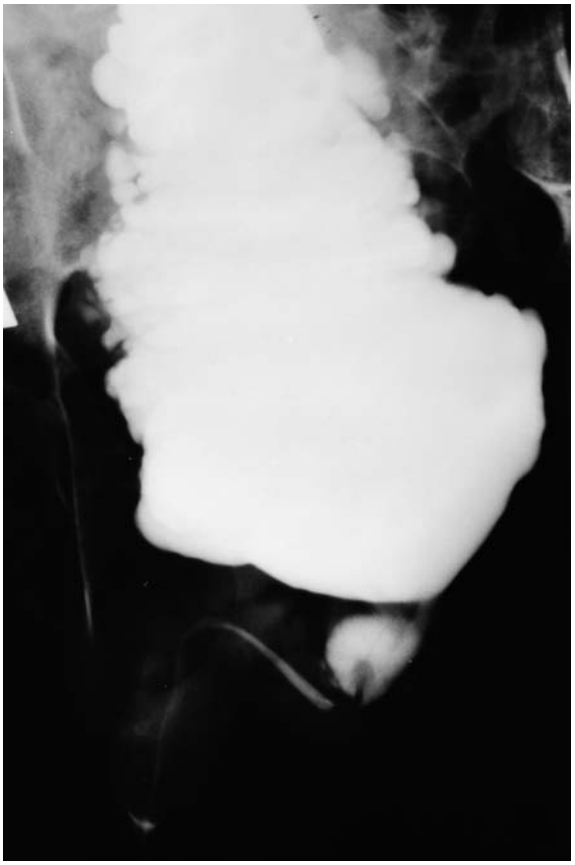

Figure 13.8 Cystographic appearances of neuropathic bladder (intermediate type) showing both sacculation and static sphincteric obstruction.

background, plus the nature and effectiveness of any bowel management. With regard to the urinary tract:

- **Continuous dribbling**, particularly if exacerbated by coughing, crying or standing, is almost pathognomonic of some degree of sphincteric incompetence.
- **A discrete, spontaneous urinary stream** is typical of a contractile bladder, whereas a stream that is also interrupted is typical of detrusor–sphincter dyssynergia.
- **Urinary infections**, especially if febrile, are strongly suggestive of upper renal tract complications, actual or impending.

Examination

The relevant features are that:

- **Bladder distension** is indicative of outflow obstruction.
- **An expressible bladder** is pathognomonic of bladder neuropathy with some measure of sphincteric incompetence.
- **A bladder that cannot be expressed**, by contrast, implies either sphincteric competence or a bladder that is virtually empty by reason of gross sphincteric incompetence.
- **Neurological examination**, which can be limited to the lowermost sacral segments, is aimed at demonstrating the presence or absence of conus reflexes and the existence of any sacral sensory or motor sparing. It should be borne in mind that because they are associated with sphincteric competence, positive conus reflexes carry an excellent prognosis for continence. Most patients with positive reflexes become dry on CISC alone or in combination with an anticholinergic drug; few patients come to augmentation cystoplasty and none to sphincter enhancement procedures.

Table 13.2 Causes of impaired bladder capacity

Contractile bladder	Acontractile bladder	Intermediate bladder
Detrusor overactivity	Sphincteric incompetence Detrusor non-compliance Combinations	Sphincteric incompetence Detrusor overactivity Detrusor non-compliance Combinations

Table 13.3 Causes of secondary upper renal tract complications

Urinary infection
Vesicoureteric reflux
Bladder outflow obstruction *plus* detrusor overactivity and/or non-compliance

Neonatal assessment

The expressibility (or otherwise) of the bladder is readily determinable neonatally, similarly the presence or absence of conus reflexes and, as judged by general arousal to perianal pinprick, the existence of sacral sensory sparing. No matter how slight the neurological deficit, a neuropathic bladder is certain if the bladder can be readily expressed, if the conus reflexes are negative, or if there is no sensory sparing. By contrast, bladder function *may* prove to be normal if the bladder cannot be expressed *and* conus reflexes are positive *and* there is sacral sensory sparing, a combination of findings that is sadly rare.

Investigations

Imaging studies

Ultrasonography of the urinary tracts, with estimation of the volume of residual urine where practicable and relevant, represents the best means of both initial assessment and follow-up. The frequency of ultrasound examinations for the latter purpose is determined by what is known of bladder dysfunction and hence the perceived risk of upper tract complications. Among other imaging studies, **DMSA scintigraphy** is of value in patients with vesicoureteric reflux or those experiencing febrile urinary infection. **Micturating cystography**, to confirm or exclude vesicoureteric reflux or bladder outflow obstruction, is best combined with simultaneous urodynamic examination.

Urodynamics

Some of the technical aspects of urodynamics have been considered above and are illustrated in Figure 13.2. The principal indications for this examination are to:

- identify the 'unsafe' bladder in neonates and plan for its immediate treatment
- determine the cause(s) of secondary upper urinary tract complications
- plan the treatment of incontinence.

Management

Basic considerations

In order of priority, the aims of management are:

- to preserve renal function
- to prevent progressive bladder damage (fibrosis as a result of high-pressure storage and emptying)
- to achieve social continence (ideally without dependence on appliances and in a manner the patient may practise independently).

Consequently, all schemes of management incorporate the following basic principles:

- Renal function always takes precedence over continence.
- Treatment must relate realistically to the patient's other characteristics and abilities as a whole (i.e. age, sex, mobility, intelligence, dexterity, deformity, social circumstances).
- Treatment must also relate to the nature of the bladder dysfunction.
- When bladder dysfunction is complex its treatment may also need to be more complex (e.g. CISC combined with a measure to improve bladder capacity, or with more than one measure when the reduced capacity is the outcome of two or more factors).
- Measures that are non-invasive and/or reversible take priority over those that are neither (i.e. medical management should always be tried before surgery is considered).

In practice, when CISC proves to be ineffective on its own, any additional measures are invariably directed at securing adequate low-pressure functional bladder capacity.

General management of impaired/high-pressure bladder capacity

Detrusor overactivity

- Medication (anticholinergics).
- Botulinum toxin A injection (repetitive).
- Augmentation cystoplasty.

Medical management of detrusor overactivity usually comprises treatment with **oxybutynin** and, because this agent is effective in most cases, augmentation cystoplasty is rarely required for this indication alone. For patients in whom side effects are not tolerated, oxybutynin may be administered, in the same dosage, by the intravesical route.

Tolterodine, an alternative anticholinergic agent, is probably equally efficacious and is claimed to have a lower incidence of side effects. There are now a number of extended-release preparations available and these appear to be more effective with fewer side effects: extended-release oxybutynin is probably the best. Oxybutynin is also now produced in dermal patch form. Newer, more selective, anticholinergic agents are being developed and are currently undergoing clinical trials.

Botulinum toxin A injection is usually employed as a temporising measure until young patients acquire the maturity and compliance with management that is needed before proceeding to augmentation cystoplasty. The duration of action of botulinum toxin injection is approximately 7 months.

Detrusor non-compliance

- Augmentation cystoplasty.

Although the cause of detrusor non-compliance remains disputed, there is general agreement that the phenomenon is unresponsive to any currently available medication.

Sphincteric incompetence

- Medication (α-adrenergic agonists).
- Periurethral/bladder neck injections with a bulking agent.
- Bladder neck suspension.
- Bladder neck sling.
- Urethral lengthening procedures (Kropp or Pippi Salle procedures).
- Artificial urinary sphincter.
- Periurethral inflatable constrictor (Lima).
- Bladder neck closure.

The treatment of sphincteric incompetence remains less than satisfactory. Marginal degrees of incompetence may respond to α-adrenergic agonists (e.g. ephedrine), but anything more major calls for surgery. As is evident from the length of the list above, there is as yet no single procedure that guarantees success. It must also be re-emphasised that a safe and successful outcome from treating sphincteric incompetence is dependent on measures to ensure adequate management of any coexisting detrusor overactivity and/or detrusor non-compliance.

Surgery for impaired/high-pressure bladder capacity

Augmentation cystoplasty

Enterocystoplasty

Despite the morbidity inherent in prolonged exposure of intestinal epithelium to urine (Table 13.4), enterocystoplasty remains the principal means of bladder augmentation as it employs a material that is universally available and, with a few exceptions, secures consistent and satisfactory urodynamic outcomes. Intestinal segments in common usage are ileum, ileocaecum, sigmoid colon and stomach. With the exception of stomach, all require detubularisation to obviate high-pressure peristaltic activity. As a rule, a clam-patch cystoplasty (Figures 13.9 and 13.10) is used when the urodynamic problem is principally detrusor overactivity, and a pouched augmentation (Figure 13.11) when the bladder is small and non-compliant. Despite detubularisation,

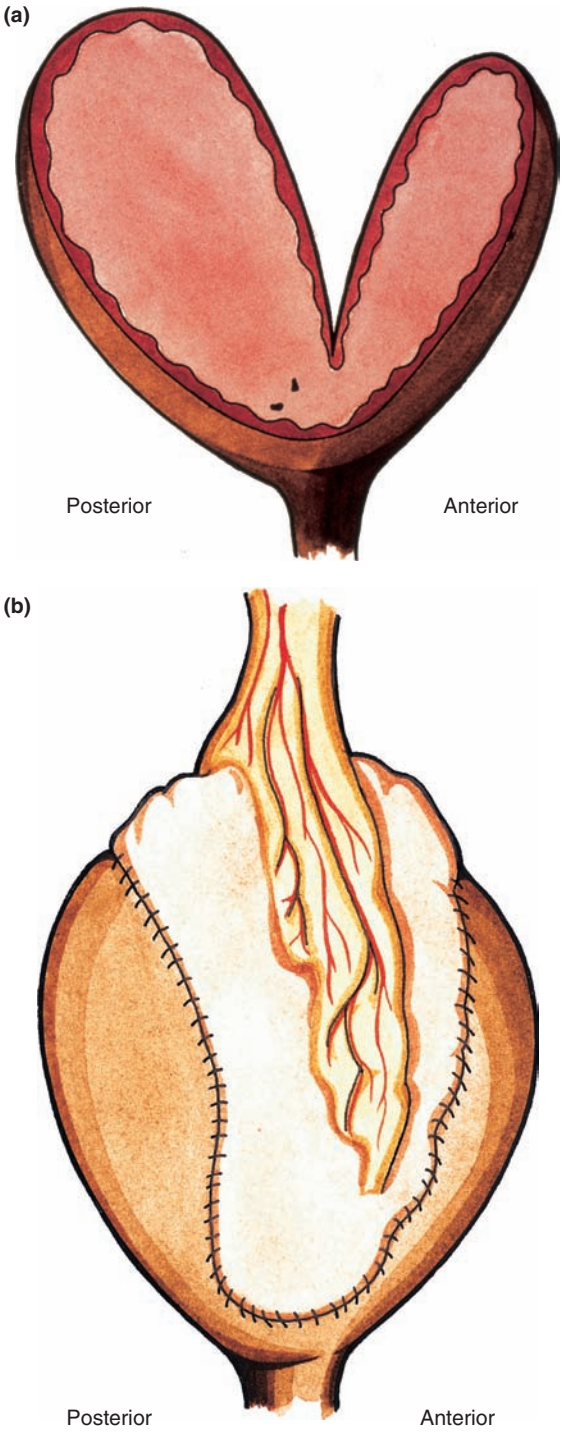

Figure 13.9 Clam ileocystoplasty viewed laterally. (a) Bladder opened and incised down to the trigone to create a 'clam' configuration. (b) Segment of ileum isolated on its mesentery, opened (detubularised) and sutured on to the bladder.

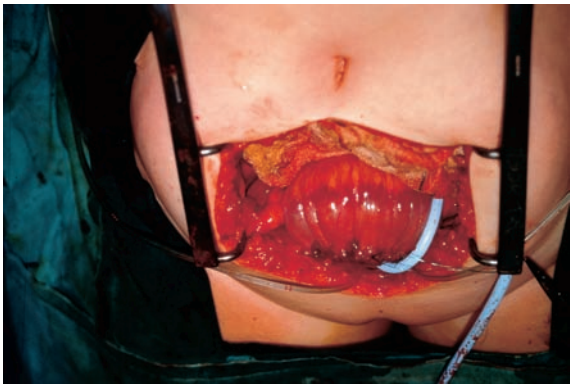

Figure 13.10 Operative photograph showing completed clam ileocystoplasty.

troublesome peristaltic activity may still occur, even to the extent of necessitating further augmentation. As this occurs most commonly following sigmoid cystoplasty, the use of this bowel segment is best avoided where possible.

Autoaugmentation

Excision or incision of the detrusor muscle over the bladder dome creates, in effect, a large, broad-mouthed diverticulum. Although avoiding the potential complications of enterocystoplasty, the urodynamic outcome in terms of increased capacity and reduction of overactivity is rather less impressive or predictable. Moreover, the long-term results are not encouraging as fibrosis and contraction of the diverticulum occurs. However, for isolated overactivity, satisfactory outcomes are reported from some units.

Ureterocystoplasty (Figure 13.12)

The dilated ureter, once opened along its full length, is usually anastomosed to the bladder as a clam patch; the overlying kidney is removed if having no useful function or, if otherwise, is drained by transureteroureterostomy. Because it furnishes a urodynamic outcome the equal of enterocystoplasty, ureterocystoplasy is the procedure of choice whenever a suitably dilated ureter is available. Unfortunately, this is rarely the case.

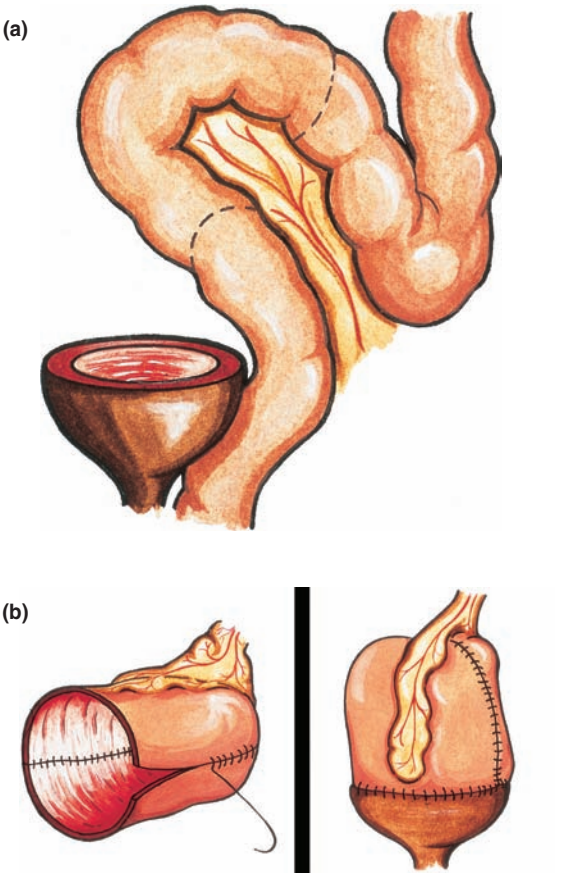

Figure 13.11 Sigmoid pouch cystoplasty. (a) Segment of sigmoid colon isolated on its mesentery. (b) Colonic segment detubularised, then reconfigured as a pouch. The use of this form of enterocystoplasty is generally limited to small, non-compliant bladders.

Table 13.4 Complications of enterocystoplasty

Mucus production
Catheter blockage
Infection
Bladder stone
Metabolic changes
Hyperchloraemic alkalosis
Electrolyte disturbance
Systemic alkalosis (gastrocystoplasty)
Spontaneous perforation
Metaplasia/malignancy
Bowel problems
Diarrhoea
Vitamin B_{12} deficiency
Dysuria/haematuria (gastrocystoplasty only)

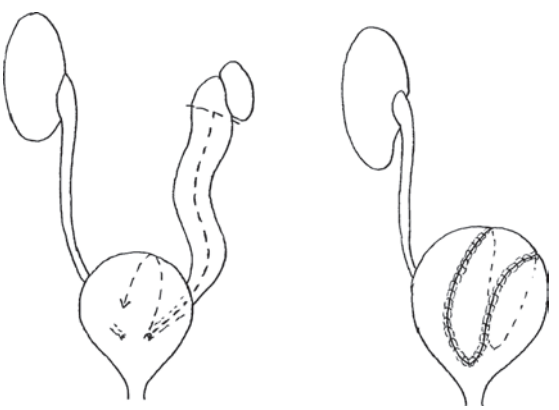

Figure 13.12 Ureterocystoplasty.

Autoaugmentation plus demucosalised enterocystoplasty

The epithelial diverticulum created by a standard autoaugmentation is covered by a demucosalised enteric patch, usually of stomach or colon. Although this technique enjoys the theoretical advantage of creating an augmentation lined by urothelium rather than intestinal epithelium, the long-term outcome has yet to be assessed. Fibrosis and contraction of the patch is still a problem.

Augmentation with tissue-engineered neobladder

Only very recently developed for human use, this technique entails replacing much of the neuropathic bladder with a cup-like Vicryl 'construct' into which the patient's own urothelial and detrusor cells have been seeded and grown in vitro prior to reconstructive surgery. Although the results obtained in the first seven patients treated by this means confirmed its feasibility, the functional

outcomes were disappointing, with little, if any, increase in bladder capacity. Presently, then, this approach must be regarded as being in the experimental phase.

Sphincter-enhancement procedures

These are two general categories of sphincter-enhancement procedure:

- The artificial sphincter, which, because it can be turned 'on' and 'off' at will, theoretically enables voiding by abdominal straining alone.
- Other procedures, which, in creating or enhancing a fixed urethral resistance, necessitate voiding by CISC.

Artificial urinary sphincter (Figure 13.13)

This device has several drawbacks:

- Cost.
- Infection and/or urethral erosion, necessitating device removal.
- Need for revisionary procedures. When the entire device has been inserted, revision is almost always required within 12 years of implantation.

Although voiding is ideally achieved by abdominal straining alone, in practice some 80% of patients use CISC as the sole or a supplementary means of voiding. This proportion is less if preliminary transurethral sphincterotomy is undertaken, but the effect of this procedure is not always permanent. Additionally, very few patients who have also undergone augmentation can achieve adequate emptying without CISC.

Despite these disadvantages, the artificial urinary sphincter remains the best option for boys and renders upwards of 80% reliably dry. Because the device is designed for adults, it is not suitable for children under 8 years of age. The sphincter cuff is usually implanted at the bladder neck, although the bulbar urethra is an alternative site after puberty. When augmentation cystoplasty is undertaken simultaneously, it is preferable to implant the sphincter cuff alone, as this combination will be sufficient in itself to secure continence in some patients, thereby obviating any need to implant the other components of the system.

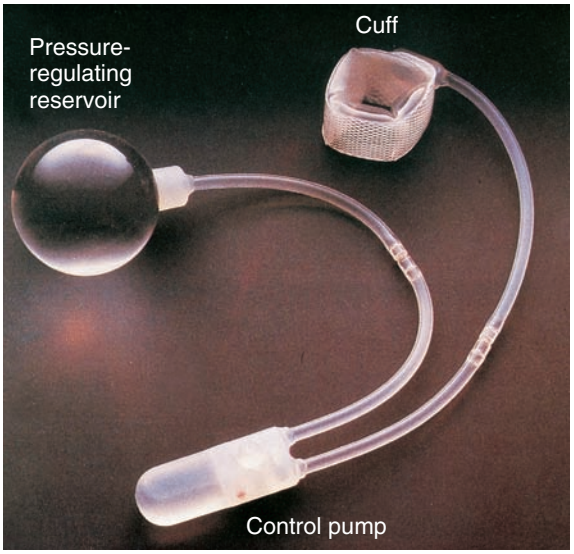

Figure 13.13 American Medical Systems AMS 800 artificial urinary sphincter. Components comprise the cuff, which is implanted around the urethra; the pump, which is implanted in the scrotum; and the pressure-regulating balloon, which is sited in a plane between the peritoneum and the abdominal wall musculature. (Reproduced with permission from American Medical Systems UK Ltd, Hanwell, Middlesex, UK.)

Inflatable periurethral constrictor (Figure 13.14)

This new device is cheaper and has fewer components than the artificial sphincter. Three cuff sizes are available and these can also be adjusted at the time of surgery. As with the artificial sphincter, the cuff is implanted around the bladder neck or bulbar urethra, while the reservoir is positioned subcutaneously in the iliac fossa, the inguinal

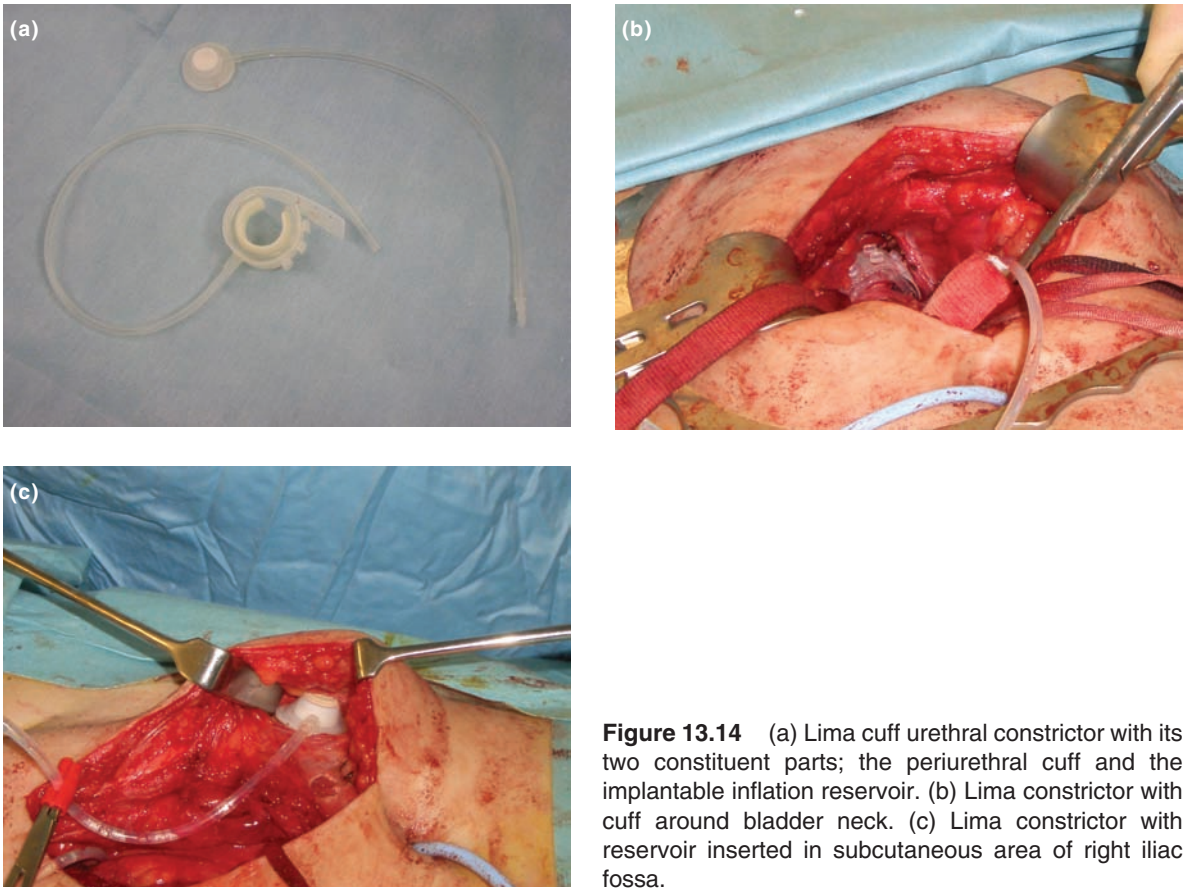

Figure 13.14 (a) Lima cuff urethral constrictor with its two constituent parts; the periurethral cuff and the implantable inflation reservoir. (b) Lima constrictor with cuff around bladder neck. (c) Lima constrictor with reservoir inserted in subcutaneous area of right iliac fossa.

region or the scrotum. Accessible by means of percutaneous puncture, the reservoir is subsequently filled under manometric control to the pressure required to achieve continence in an upright position. Voiding or CISC can be achieved without need to empty the cuff, although it can be deactivated or reactivated at any time by emptying or refilling the reservoir.

Injection of periurethral bulking agents (collagen, silicone, Deflux)

Such agents are of limited value, and secure complete continence only in those patients with inherently marginal sphincteric incompetence or those who are virtually dry as a result of previous surgery but require a minor degree of additional outflow resistance to achieve an ideal result.

Bladder neck suspension and slings

If combined with simultaneous augmentation cystoplasty, a Marshall–Marchetti bladder neck suspension achieves success in upwards of 80% of girls. The results of bladder neck slings may prove to be marginally superior.

Pippi Salle procedure (Figure 13.15)

This urethral lengthening procedure is suitable for girls but not for boys.

Bladder neck closure

Bladder neck closure necessitates a simultaneous Mitrofanoff procedure and, in many cases, an augmentation cystoplasty. Although successful in more than 90% of cases, both boys and girls, bladder neck closure should be considered a

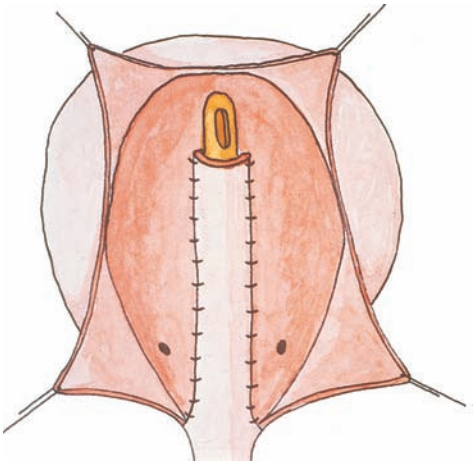

Figure 13.15 The Pippi Salle procedure.

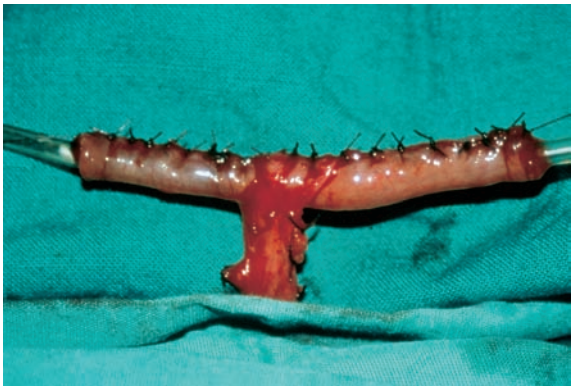

Figure 13.16 Monti tube fashioned from ileum. This is the most satisfactory alternative to the appendix for the creation of a continent catheterisable conduit (Mitrofanoff procedure).

procedure of last resort, to be employed only when alternatives have failed or are impracticable. Once the bladder neck has been closed there remains only one, limited, means of endoscopic access to the bladder, an important consideration in view of the incidence of bladder stones following Mitrofanoff procedures and enterocystoplasties.

Other surgical procedures employed with neuropathic bladder

Mitrofanoff procedure

The principal indications are:

- patients undergoing bladder neck closure
- patients in whom urethral CISC is impracticable by reason of deformity, or is unacceptable because of urethral sensation.

The appendix, if available and of sufficient length, is the conduit of first choice. The best alternative is a Monti tube (Figure 13.16), which, if constructed of ileum, provides an easily catheterisable conduit some 7 cm long. When necessary, a greater length can be obtained by end-to-end anastomosis of two or more such tubes or by the so-called spiral Monti. Stomal stenosis at the junction between the conduit and skin of the abdominal wall is the most common complication and the risk can be minimised by the use of multiple skin flaps or by siting the stoma in the umbilicus. In obese patients or those with spinal deformities, it is important that the stoma be visible and readily accessible in the sitting position.

Cutaneous vesicostomy

This simple and effective temporising means of reversing established upper renal tract complications is mainly employed in infants. To reduce the risk of prolapse the stoma should be sited as near the apex of the bladder as possible.

Endoscopic urethral sphincterotomy

For boys, sphincterotomy is equally effective in treating detrusor–sphincter dyssynergia and static sphincteric obstruction but inevitably leads to incontinence if the bladder neck is incompetent. Hence this procedure is of only limited use, either as a preliminary manoeuvre prior to the insertion of an artificial urinary sphincter or, occasionally, for infants and severely disabled patients.

Conduit urinary diversion

Once the mainstay of treatment, this procedure is nowadays almost exclusively reserved for severely disabled patients. Careful siting of the stoma is critical in patients with spinal deformities. When

the ureters are undilated, the upper renal tracts are best preserved by constructing a sigmoid conduit with antirefluxing ureterocolic anastomoses.

Management in neonates and infants

Although the upper renal tracts represent the immediate concern, any active treatment should avoid compromising later continence. Neonates identified as having an 'unsafe' bladder are best commenced on intermittent catheterisation at this stage, and oxybutynin (or botulinum toxin A) may also be considered if there is marked detrusor overactivity. In other circumstances, regular (4-monthly) ultrasound surveillance during the first 2 years of life is usually sufficient.

Despite every effort, major upper renal tract complications may still occur and are usually best managed by a temporising cutaneous vesicostomy. Endoscopic sphincterotomy represents an alternative for male infants with a contractile bladder and a competent bladder neck.

Management of the severely disabled

Less ambitious management, limited to protecting the upper renal tracts and securing dryness with a minimum dependence on others, is advisable for patients with impaired intellect, poor dexterity or, most commonly, an inability to balance without support when sitting. A penile appliance is appropriate for boys and endoscopic sphincterotomy should be undertaken if there is any element of bladder outflow obstruction. An indwelling urethral catheter, if properly handled, is suitable for long-term management of girls. Where these measures fail or are considered socially unacceptable, a conduit urinary diversion may be offered to patients of either sex.

Bowel management

It is self-evidently highly desirable that faecal incontinence is not neglected at the expense of dealing with its urinary equivalent: all children deserve to be clean as well as dry. Assessment and treatment should begin at the same time as urological management.

The effects of spinal cord lesions on the rectum and anal sphincter are similar to those on the bladder/sphincter mechanism and faecal incontinence may result from constipation, overflow incontinence, sphincteric incompetence or any combination of these mechanisms. As a rule, initial treatment involves avoiding gross constipation by means of an appropriate diet or laxative medication, and ensuring regular colonic emptying by a variety of methods that include abdominal straining, manual evacuation, purgatives, suppositories or retrograde enemas.

If these measures fail, or if an older child becomes unwilling to continue treatment with enemas or suppositories, an antegrade continence enema (ACE) procedure should be considered. Utilising the Mitrofanoff principle to provide continent catheter access to the proximal or distal colon, the ACE procedure enables the colon to be regularly and fully evacuated by means of a variety of solutions ranging from tap water to phosphate. If, as is often the case, the appendix is not available for this purpose, a Monti ileal tube may be used instead, or, alternatively (and especially if no major urological surgery is to be undertaken at the same time) a percutaneous endoscopically guided tube postitioned in the caecum under colonoscopic vision. Measurement of the colonic transit time is often helpful in determining where an ACE procedure should be positioned. If the transit time is prolonged, a left-sided ACE is the preferred site as it is associated with fewer problems (e.g. pain and colonic distension) following introduction of antegrade enema fluid. Where practicable and if wished, an ACE procedure can be performed at the same time as bladder reconstruction, thereby achieving faecal and urinary continence at the one operation.

Since its introduction in 1989, over 1000 ACE procedures have been performed, and for patients with a neuropathy a high success rate (exceeding 80%) is coupled with a significant increase in the 'quality of life' score. The commonest long-term

complication is stomal stenosis. If the ACE fails or is deemed not suitable, a permanent colostomy remains an acceptable option.

Key points

- Secondary upper renal tract complications are far more prevalent among children with congenital neuropathic bladder than among adults with acquired lesions, and occur in both boys and girls.
- Bladder function is determined by whether the conus medullaris is intact or destroyed: in the former instance, conus reflexes are positive and the sphincteric mechanism is almost always competent. Positive conus reflexes carry a good prognosis for continence.
- Especially among myelomeningocoele patients, management may be influenced by non-urological considerations (intelligence, mobility, spinal deformity).
- Intermittent catheterisation represents effective management only when there is adequate low-pressure functional bladder capacity. In 80–90% of patients this is lacking.
- Impaired bladder capacity may be the result of detrusor overactivity, detrusor non-compliance or sphincteric incompetence, either singly or in some combination. Of these, sphincteric incompetence is the most difficult to treat.
- Secondary upper renal tract complications occur only when intravesical pressure becomes raised as a result of detrusor hyperreflexia and/or detrusor non-compliance and never occur when gross sphincteric incompetence leads to a permanently empty bladder.

Further reading

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The urinary tract in anorectal malformations, multisystem disorders and syndromes

14

Duncan T Wilcox

Topics covered

Anorectal anomalies
- Associated anomalies – urogenital/spinal
- Lower urinary tract dysfunction
- Surgical management

VACTERL and CHARGE associations
Ectopic/horseshoe kidney

Anorectal anomalies

Anorectal anomalies comprise a spectrum of congenital malformations in which the anus fails to open normally on to the perineum. At one end of this spectrum are the minor anomalies in which the anal canal is present but the anus is covered by perineal skin (Figure 14.1). The severe forms of anomaly are characterised by a high termination of the rectum and the presence of a congenital fistula connecting the rectum to the lower urinary tract (Figure 14.2a and b). In females the most severe expression of the anomaly is the cloacal malformation, in which the rectum, urethra and vagina join to form a single confluent channel draining by a common opening on the perineum (Figure 14.3).

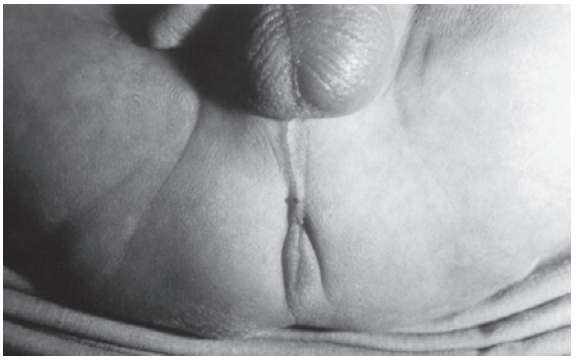


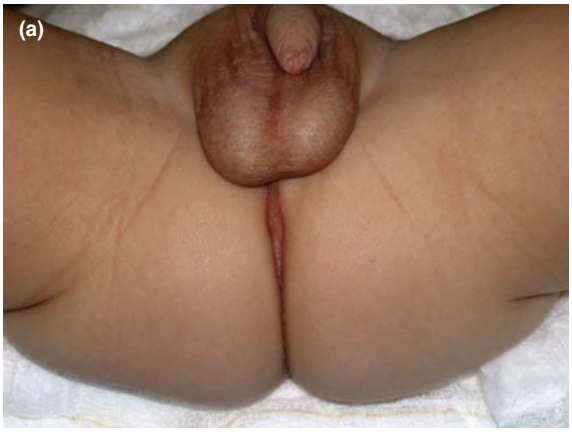
Figure 14.1 Characteristic appearances of the perineum in an infant with low anorectal anomaly.

Incidence and aetiology

The incidence of anorectal malformations is approximately 1 in 5000 live births, with a slight male to female preponderance of 3 to 2. The embryological defect resulting in congenital cloacal anomalies can be ascribed to a failure of the normal 'compartmentalisation' of the primitive cloaca by the urorectal septum and Rathke's folds. At a more fundamental level, the aetiology of anorectal anomalies, including persistent cloaca, remains poorly understood. Although the observed association with genetically determined conditions such as Down's syndrome points to a genetic component in some cases, it is most unlikely that the complex spectrum of anorectal malformations will prove to be the outcome of a simple gene mutation, although knockouts of certain genes including *ephrin B* and *Sonic Hedgehog* do lead to anorectal anomalies in mice.

Classification

A simple classification system is given in Table 14.1. Approximately two-thirds of girls have the 'low'



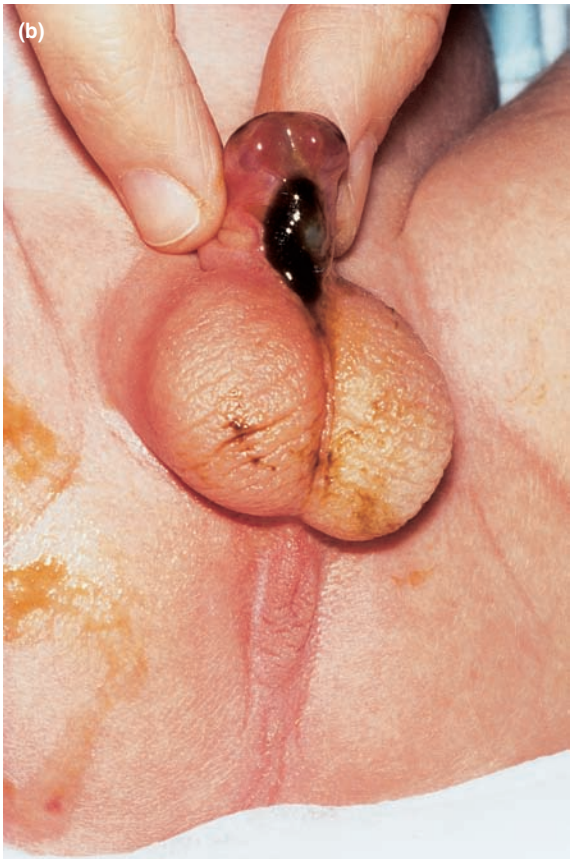


Figure 14.2b (a) Perineum of male infant with buttocks parted. High anorectal malformation with absent anus. Note area of decreased pigmentation at the site of where the anus should be. (b) Meconium discharging from the urethral meatus of a male infant with rectourethral fistula associated with high anorectal anomaly. Note also the presence of hypospadias.

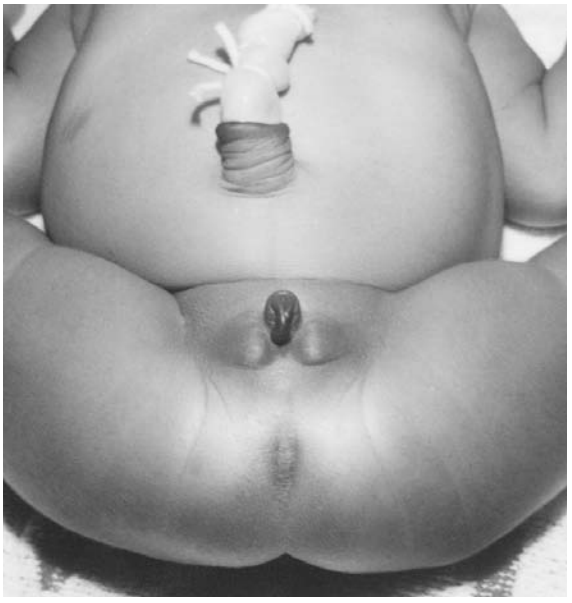


Figure 14.3 Cloacal anomaly. Single perineal orifice draining the urinary, genital and lower gastrointestinal tracts in a female infant.

form of the anomaly, in which the anorectal canal descends through the pelvic floor to terminate at the level of the perineum. Although the anus may end blindly, there is frequently a perineal fistula between it and the vaginal vestibule. By contrast, two-thirds of boys have a 'high' anomaly, with the rectum ending above the levator musculature and terminating via a rectourinary fistula. Consequently, the functional outlook for boys is worse. However, cloacal anomalies in girls represent an exception to this general rule and for this reason must be considered separately.

Table 14.1 Simple classification of anorectal malformations

Male	Female
Anorectal anomaly without fistula	Anorectal anomaly without fistula
Perineal fistula	Perineal fistula
Rectourethral fistula	Vestibular fistula
Rectovesical fistula	Cloaca

Table 14.2 Other anomalies associated with anorectal malformations

Anomaly	Incidence (%)
Vertebral	25–40
Cardiac	20
Tetralogy of Fallot	
ASD/VSD	
Gastrointestinal	15
Tracheo-oesophageal fistula	
Duodenal atresia	
Hirschsprung's disease	
Genitourinary	60

Associated anomalies (Table 14.2)

Anorectal malformations are frequently associated with abnormalities in other systems, with most published series reporting a 50–60% rate of coexisting anomalies. Of these, the most common is the VACTERL association (previously termed the VATER syndrome), which comprises vertebral, anorectal, cardiac, tracheo-oesophageal, renal and limb (typically radial) anomalies. Not all components of the VACTERL association are expressed in every patient, the most common being vertebral, anorectal and renal abnormalities. The anomalies of most relevance to urologists are those affecting the genitourinary tract and spine.

Urinary tract anomalies

Coexisting anatomical anomalies of the upper and lower urinary tract occur in approximately 60% of patients with anorectal malformations. Of these, the most common is vesicoureteric reflux (Figure 14.4), which in some series has been reported to be present in more than half the patients studied. The pattern of urinary anomalies identified is illustrated in Table 14.3. In addition to structural anomalies, up to 6% of children develop renal impairment, an incidence which increases to nearly 50% of girls with cloacal anomalies. Consequently, early detection of renal impairment is an important aspect of management.

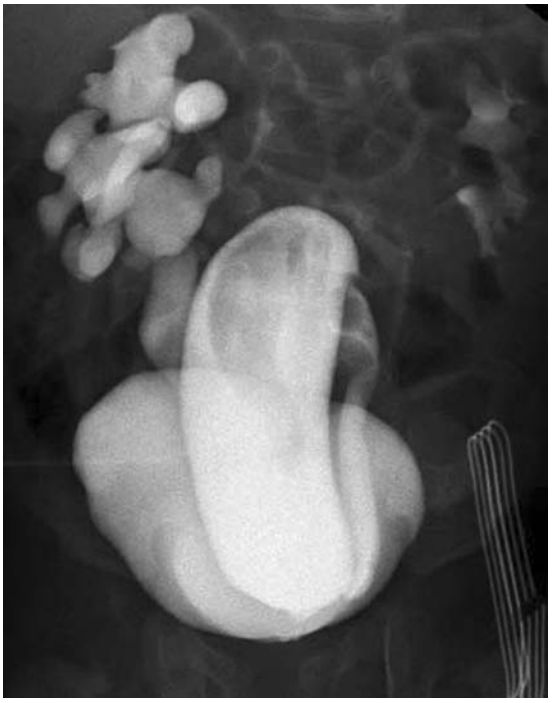


Figure 14.4 Coronal view of a distal loopagram. Contrast shows bilateral vesicoureteric reflux (grade IV on right).

Table 14.3 Pattern of structural anomalies of the urinary tract in 45 children with anorectal malformations treated at the Hospital for Sick Children, Great Ormond Street

Urinary anomaly	Patients (n = 45)
Vesicoureteric reflux	16
Hydronephrosis	6
Crossed fused ectopia	3
Dysplastic kidney	3
Bladder diverticulum	2
Renal agenesis	1
Horseshoe kidney	1
Megaureter	1
Prune-belly syndrome	1

Genital anomalies

Abnormalities of the male external genitalia are commonly present, including undescended testes (20%), bifid scrotum (15%), hypospadias (18%)

and (rarely) absence of the vas deferens. Anomalies of the female genital tract are less readily apparent, but vaginal and uterine duplications, as well as vaginal septae, are well documented and may be present in up to 30% of girls with anorectal anomalies. Cloacal malformations are associated with an even higher incidence of anomalies of the internal genitalia. In addition, clitoral hypertrophy has been reported.

Spinal anomalies

The incidence of vertebral anomalies in children with anorectal malformations has been reported to be as high as 40%. Many of these children have associated intraspinal pathology, carrying a risk of tethered cord syndrome and, in turn, urological, neurological and orthopaedic complications. Because early neurosurgical intervention may be effective in averting progressive neurological deterioration in some patients, it is important to identify possible cord tethering at an early stage. Investigation of the spine should therefore be undertaken routinely in all children with anorectal anomalies, with more detailed investigation of the spinal cord in those in whom a problem is identified.

Initial imaging should include both anteroposterior and lateral radiological views of the sacrum to identify sacral anomalies. The most commonly identified lesions are partial and complete sacral agenesis (Figure 14.5). If the sacrum is radiologically normal, intraspinal pathology is unlikely to be present although it has been reported. Consequently, most centres usually undertake further investigations. In infants under 4 months of age spinal ultrasound has proved to be very sensitive in identifying intraspinal anomalies, although it is less accurate than magnetic resonance imaging (MRI) for visualising the specific intraspinal pathology. In one recently published series no spinal anomalies were missed on ultrasound. It is therefore currently recommended that neonates with anorectal malformations should be investigated initially with sacral radiographs and spinal ultrasound, with MRI being reserved for those in whom neurosurgery is being considered.

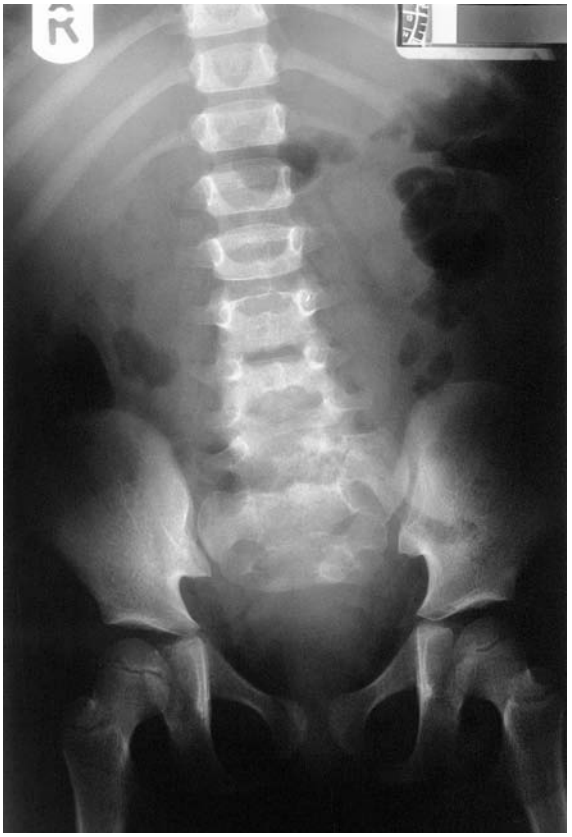


Figure 14.5 Plain radiograph demonstrating sacral agenesis.

Lower urinary tract dysfunction

Bladder dysfunction may be the result of a congenital neuropathy associated with a coexisting spinal anomaly, or it may represent neurological damage acquired during surgical repair of the anorectal malformation. In one series, 25% of children with anorectal anomalies were found to have severe lower urinary tract dysfunction, which in every instance was associated with a demonstrable sacral abnormality. The majority of children with severe bladder dysfunction were incontinent, and a third had reflux nephropathy, highlighting the importance of investigating the lower urinary tract in children whose anorectal anomaly is accompanied by a sacral abnormality. In addition to those children with bladder neuropathy associated with a congenital spinal anomaly, a further 20% of children

experienced deterioration of bladder function following surgical repair of their anorectal malformation; in half of them this proved to be permanent. In summary, up to 20% of patients with anorectal malformations suffer from urinary incontinence. Moreover, bladder dysfunction, when present, can lead to renal damage in a third of patients. Consequently, awareness and appropriate investigation of these children is necessary to minimise the risk of ongoing renal damage.

Urological investigation of children with anorectal anomalies

The radiological investigations of the spine and urinary tract in children with anorectal malformations are summarised in (Figures 14.6 and 14.7). Whether all children should also be routinely investigated by urodynamics is debatable, although, as might be expected, there is a high incidence of abnormal urodynamic findings in those with sacral abnormalities. In addition, despite the use of a midline posterior approach for surgical correction of the anorectal anomaly, up to 10% of children develop demonstrable and permanent bladder dysfunction following surgery. Initial urodynamic assessment and urodynamic follow-up are advisable for all children with sacral anomalies, and/or signs of bladder dysfunction. Routine clinical follow-up should be continued (including renal and bladder ultrasound) until urinary continence has become established. The onset of new symptoms or a change in the pattern of existing symptoms, both of which might indicate the onset of neurological deterioration, merits formal urodynamic assessment.

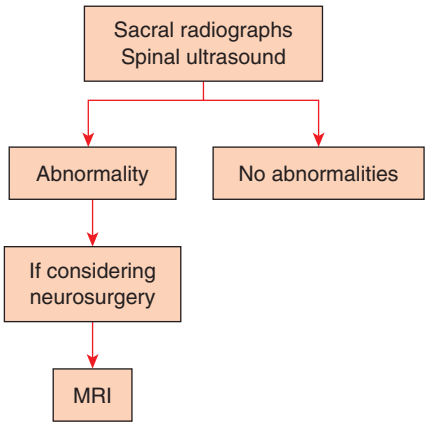


Figure 14.6 Diagnostic algorithm for the investigation of the spine in an infant with an anorectal anomaly.

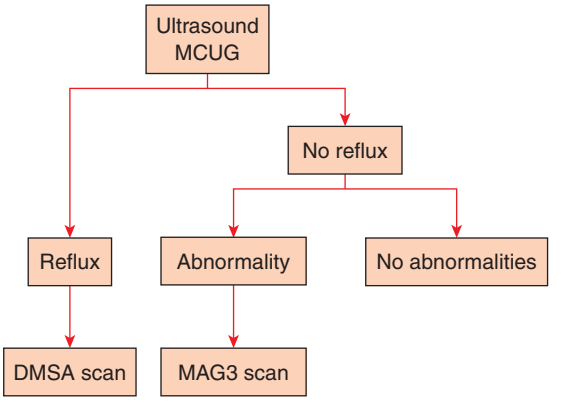


Figure 14.7 Diagnostic algorithm for the investigation of the urinary tract in an infant with an anorectal anomaly.

Surgical management of anorectal anomalies

A detailed account of the surgical management of anorectal anomalies is beyond the scope of this chapter. In general, these children undergo colostomy shortly after birth, followed by formal repair at approximately 3 months of age. The technique most widely employed is the posterior sagittal anorectoplasty originally described and popularised by Peña (Figure 14.8).

Urological complications of surgery

Although the introduction of the midline posterior sagittal approach has reduced the incidence of neuropathic bladder, approximately 10% of children develop new or increased bladder dysfunction following this procedure. Mobilisation and

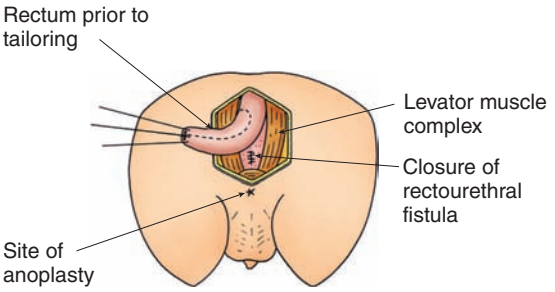


Figure 14.8 Posterior sagittal anorectoplasty. With the patient prone, the rectum is approached via a sagittal incision. The rectourethral fistula is divided and the rectum tailored before being positioned through the levator complex and external sphincter and brought down onto the perineum.

division of the rectourethral fistula is an integral step in the operation and, as such, may inevitably cause some damage to the immediately adjacent autonomic pelvic nerves. The urethra itself is also at risk during this dissection. Urethral damage occurred in 12% of patients during the older abdominoperineal operations for anorectal anomalies, but this complication is much rarer with posterior sagittal anorectoplasty. Injuries to the vas deferens have also been reported. The complexity of the surgery, and hence the risk of complications, is greatest in children with severe anorectal anomalies associated with the presence of a fistula between the rectum and the urinary tract.

Cloacal anomalies

Cloacal anomalies account for approximately 10% of anorectal malformations in girls. The cloacal malformation is characterised by confluence of the urethra, rectum and vagina to form a common channel draining by a single opening on the perineum (see Figure 14.3). Cloacal anomalies are currently classified according to whether the common channel is less or greater than 3 cm in length, as measured on cystoscopy. In addition to the renal anomalies seen with anorectal anomalies, cloacal malformations are accompanied by a high incidence of vaginal abnormalities. Septate vagina and/or bicornuate uterus have been reported in 45% of cases, and up to 5% have an absent vagina.

The initial management of a child with a cloacal anomaly requires not only diversion of the faecal stream, usually by a colostomy, but also drainage of the urinary tract and, where necessary, decompression of hydrocolpos. In some patients satisfactory bladder drainage can be achieved by intermittent catheterisation of the common channel, but it may be necessary to place a suprapubic catheter. Rarely, both vesicostomy and vaginostomy are required to secure adequate infection-free drainage. However, this approach is best avoided as it can complicate the definitive repair. Cloacal malformations are now mostly corrected using the posterior sagittal approach, particularly in cases where the common channel exceeds 3 cm in length. Where the common channel is short (<3 cm) it may be feasible to use a perineal approach to relocate all three orifices on to the perineum by mobilisation of the urogenital sinus.

The functional results of surgery for these children reflect the length of the common channel. In the 'low' confluence anomalies, where the common channel is less than 3 cm, 70% of children will be continent of urine and 50% continent of faeces. In contrast, only 30% of children with a channel length greater than 3 cm will be continent of urine and faeces. The sexual outcome is not well documented, although some women are known to be sexually active and there are reports of successful pregnancy following cloacal repair.

Syndromes and associations involving the urinary tract

Abnormalities of the genitourinary tract are often seen in association with or as part of a clinical syndrome. Two of the most important associations are:

- **VACTERL association**, which comprises **v**ertebral, **a**norectal, **c**ardiac, **t**racheal, oesophageal (***esophageal***), **r**enal and **l**imb anomalies. Those aspects of greatest relevance to the urologist have already been considered above.
- **CHARGE association,** which consists of **c**oloboma of the eye, **h**eart anomalies, choanal

Table 14.4 Genitourinary malformations in the CHARGE association

	Incidence (%)
Genital anomalies	56
Hypospadias	
Micropenis	
Undescended testicle	
Vaginal and uterine atresia	
Urinary tract anomalies	42
Duplex kidney	
Vesicoureteric reflux	
Renal agenesis	
Hydronephrosis	

atresia, mental **r**etardation, **g**enital and **e**ar anomalies. In one series of 32 children with CHARGE, the overall incidence of genitourinary tract abnormalities was 69% (Table 14.4).

Abnormal migration and fusion of the kidney

Ectopic kidney

Ectopic kidneys can be divided into simple, horseshoe and crossed renal ectopia.

Simple ectopic kidney

The ectopically sited kidney may be located anywhere along the embryological path of ascent from the pelvis to the renal fossa. Pelvic kidneys are the most common of renal ectopias, accounting for 60% of all cases. In 90% the anomaly is unilateral and with a slight left-sided preponderance. In addition to its abnormal location, a pelvic kidney is frequently hypoplastic and irregular in shape (Figure 14.9). Other ectopic kidneys lie at some point between the pelvis and the normal position or, very rarely, within the thorax.

Genital and contralateral urinary abnormalities are often associated with ectopic kidneys and include absence of the vagina, retrocaval ureter, bicornuate uterus, supernumerary kidney and ipsilateral ectopic ureter. The ectopic kidney can be a component of more complex syndromes, such as the Mayer–Rokitansky–Küster–Hauser syndrome, Fanconi's anaemia or conjoined twins.

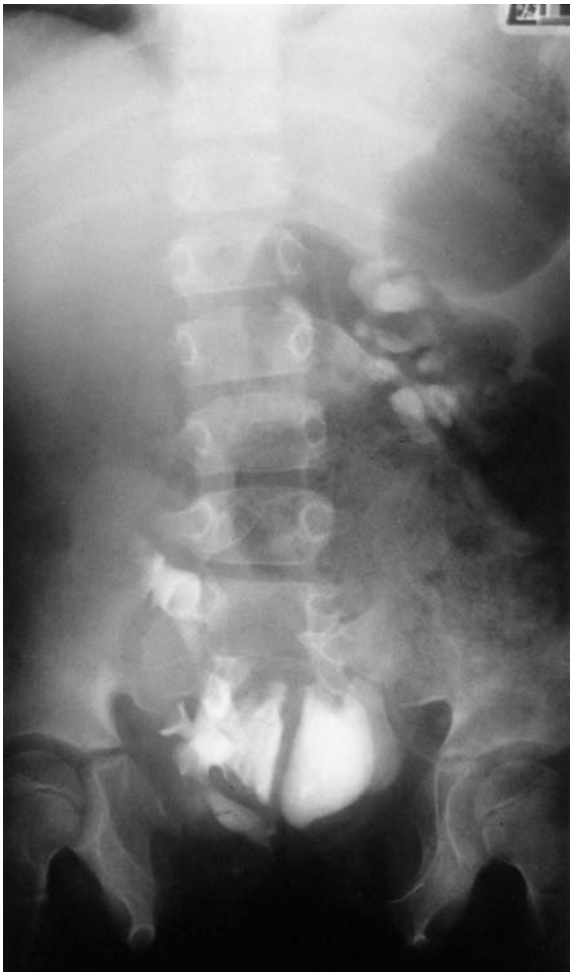


Figure 14.9 Intravenous urogram demonstrating ectopic kidney – pelvic right kidney.

Horseshoe kidney

Horseshoe kidneys are encountered in 1:400 and 1:1800 autopsies and the anomaly is more common in males. In 95% of cases the lower poles of the two kidneys are joined by an isthmus of renal tissue which may consist of normal

parenchyma or dysplastic or fibrous tissue. In about 40% of cases the isthmus lies at the level of L4, just beneath the origin of the inferior mesenteric artery, in 20% in the pelvis (Figure 14.10) and in the remaining 40% at the level of the lower poles of normally placed kidneys. A small proportion of horseshoe kidneys are fused at their upper poles. The ureters arch anteriorly to pass over the isthmus, thus explaining the relatively high incidence of pyeloureteric anomalies (20%) associated with horseshoe kidney (Figure 14.11a and b). Horseshoe kidney is commonly found in association with other abnormalities or syndromes, notably Turner's syndrome and abnormalities of the central nervous system, the gastrointestinal tract and the skeletal and cardiovascular systems.

Crossed renal ectopia

There are four varieties of crossed renal ectopia:

- with renal fusion (85% of cases)
- without fusion (<10%)
- solitary
- bilateral.

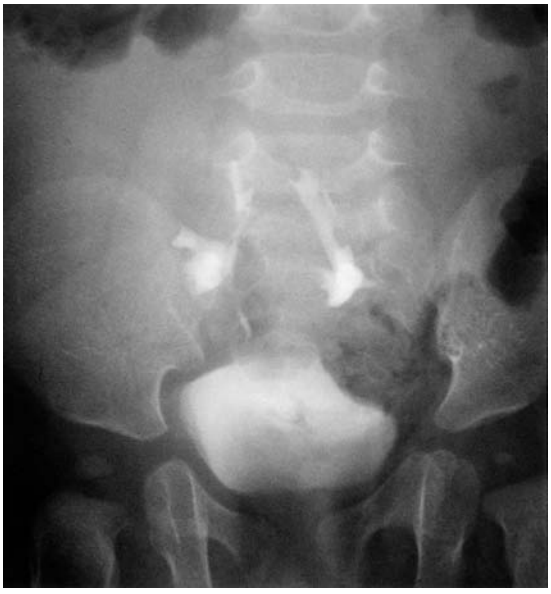
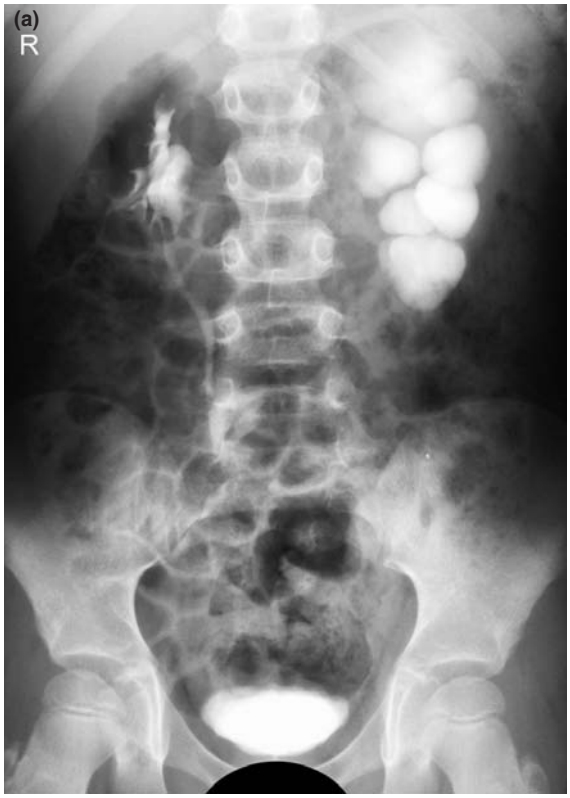


Figure 14.10 Intravenous urogram – horseshoe kidney.



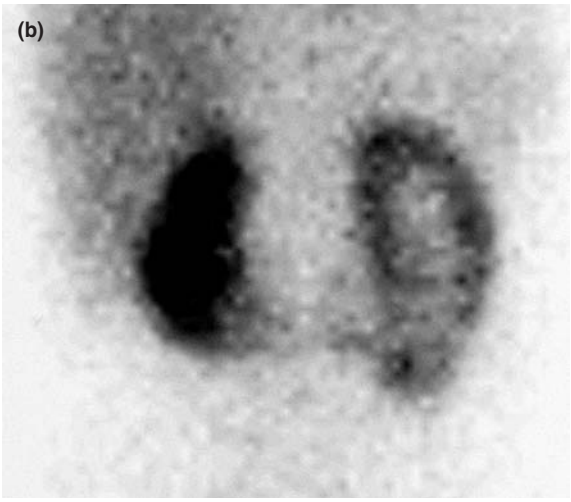


Figure 14.11 (a) Intravenous urogram demonstrating dilatation due to obstruction in the left side of a horseshoe kidney. (b) DMSA scan in the same patient demonstrating reduced isotope uptake in the central part of the left kidney (dilated collecting system) and functioning tissue outlining the isthmus connecting the right and left kidneys.

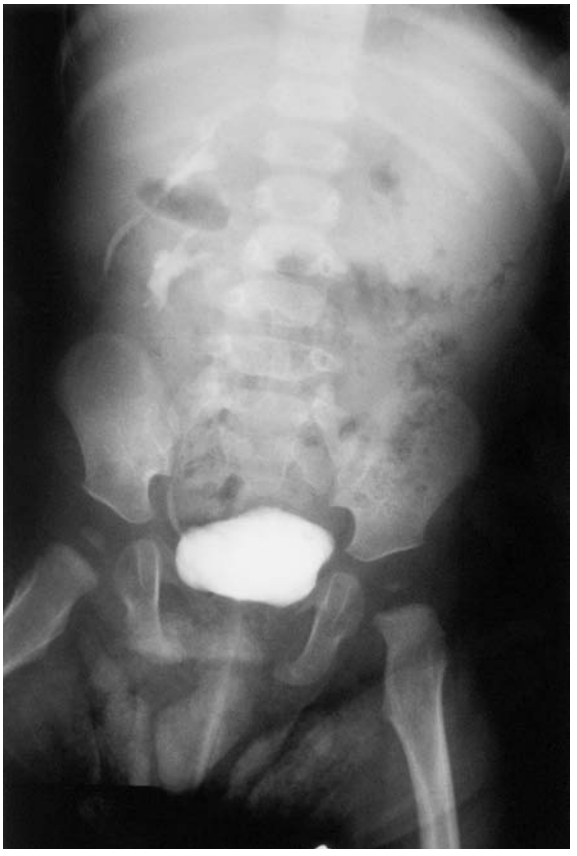


Figure 14.12 Intravenous urogram – crossed fused renal ectopia.

There is a slight male predominance, and crossing from left to right occurs more frequently than from right to left. The point of fusion is usually between the upper pole of the crossed kidney and the lower pole of the normally positioned kidney (unilateral fused type) (Figure 14.12). Associated anomalies are commonly found with renal ectopia. In addition, renal ectopia may also be a component of more complex syndromes, such as VACTERL and agenesis of the corpus callosum.

Presentation and investigation of abnormalities of ascent and fusion

Abnormalities of ascent and fusion are most commonly incidental findings, typically on prenatal or postnatal ultrasound examinations. Conversely, non-dilated pelvic ectopic kidneys may be difficult to visualise on ultrasound, and absence of the kidney in the renal fossa may be misinterpreted as renal agenesis. In such cases the presence of ectopic functioning renal tissue is best demonstrated by DMSA (dimercaptosuccinic acid) renography. Crossed fused renal ectopia may sometimes present clinically as an incidentally discovered mass during the course of abdominal examination. The occurrence of pain or symptoms associated with urinary infection generally denotes additional pathology, such as vesicoureteric reflux or pelviureteric junction obstruction. Investigation of an uncomplicated ectopic or horseshoe kidney can reasonably be limited to ultrasound and a DMSA scintigram. Additional investigations are indicated if there is hydronephrosis or a history of documented infection raising the possibility of reflux. However, it is important to stress that the majority of patients are untroubled by their abnormally placed kidney, and surgical intervention should be confined to correcting coexisting pathology, obstruction or reflux. When surgery is warranted it should be borne in mind that the anatomy may be abnormal and that the blood supply can have an aberrant course.

Key points

- Children with anorectal anomalies have a high incidence of urinary tract abnormalities and functional urinary problems. In addition to urinary incontinence, the bladder dysfunction in children with anorectal malformations poses a potential threat of urinary tract infection, renal damage and chronic renal failure.
- Early recognition and effective management of urological problems in children with anorectal malformations is essential to minimise these risks.

- In view of the high incidence of genitourinary tract anomalies in the CHARGE association all affected infants should be screened appropriately, initially by urinary tract ultrasound, and then with additional modalities such as renography where indicated.
- Anomalies of ascent and fusion, including pelvic kidney, horseshoe kidney and crossed ectopia, are mainly asymptomatic incidental findings. Surgical intervention is only required when there is complicating pathology such an obstruction or reflux.

Further reading

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Bladder exstrophy and epispadias

15

Peter Cuckow

Topics covered
Embryology and anatomy
Bladder exstrophy: management and outcomes
Cloacal exstrophy: management and outcomes
Primary epispadias: management and outcomes

Introduction

This chapter covers one of the most challenging conditions in paediatric urology. In addition to the complex surgery needed to correct the severe bladder abnormalities and genital deformities, there may be secondary problems relating to renal function and fertility. Because of the low incidence of bladder exstrophy and related conditions (Table 15.1), very few individual surgeons have had the opportunity to acquire sizeable series of patients. Even those working in major centres serving large populations may see only one or two new patients each year. In the UK it was therefore decided to concentrate bladder exstrophy surgery in two supraregional centres, thus enabling a smaller number of paediatric urologists to develop and maintain higher levels of expertise than was possible when cases were distributed between more centres. Concentrating exstrophy management in two supraregional centres has had the added benefit of facilitating the development of new treatment strategies and new clinical and laboratory research initiatives which will hopefully contribute to improved outcomes for children born with this complex of severe anomalies.

Embryology and anatomy

The three distinct anomalies which constitute the exstrophy–epispadias complex are believed to represent a spectrum of abnormalities arising from failure of development of the lower abdominal wall during the early weeks of gestation.

Bladder exstrophy

Failure of migration of mesoderm to the area of the cloacal membrane, and subsequent lack of development of an intermediate layer between its inner (endodermal) and outer (ectodermal) layers, leads to rupture and exposure of an open bladder plate and urethra. These structures occupy a triangular space between a low-set umbilicus superiorly, split rectus abdominis muscles on each side and an open pelvic

Table 15.1 Incidence and sex distribution of the exstrophy–epispadias complex

	Incidence per live births	Male to female ratio
Bladder exstrophy	1:50 000	3:1
Primary epispadias	1:120 000	5:1
Cloacal exstrophy	1:300 000	6:1

ring inferiorly. The penile root remains attached to the inferior border of the inferior pubic rami on either side so that each hemicorpus has to traverse the intervening gap (known as the pubic diastasis) to unite with the contralateral corporeal body in the midline. The result is a foreshortened penis in males. The bladder plate is continuous with the urethral plate, on which are sited the openings of the ejaculatory ducts at the level of the prostate (the verumontanum). The exposed urethral plate covers the dorsal surface of the corporeal bodies and glans (Figure 15.1). The testes are usually descended. Failure of development of the lower anterior abdominal wall and pelvic ring also imparts a relatively anterior position to the anus. In females the bladder component is identical, the clitoral corpora are separated and a short urethral plate runs between the open bladder and the vagina (Figure 15.2).

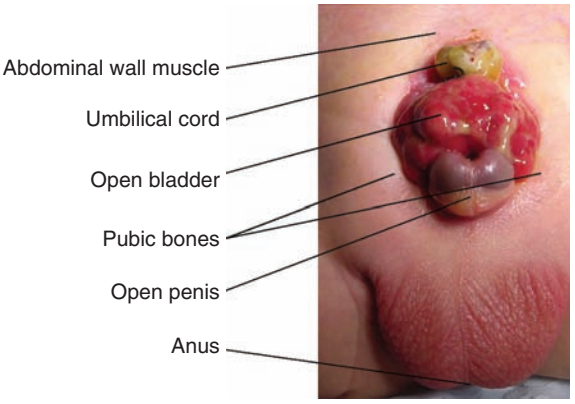

Figure 15.1 Newborn male infant with bladder exstrophy.

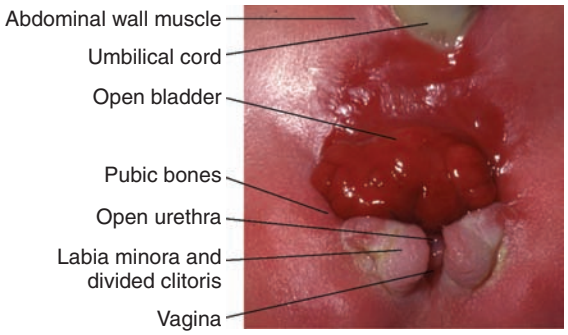

Figure 15.2 Newborn female infant with bladder exstrophy.

Cloacal exstrophy

Cloacal exstrophy is a more severe variant in which there is probably an additional failure of septation of the cloaca, so that the bladder anteriorly is not separated from the hindgut posteriorly. This has the effect of bringing both bladder and bowel components to the surface, with a central bowel field that lies in the midline between two separated halves of the bladder. There can be extensive prolapse of the proximal colon and ileum and one or two appendices may be seen on the bowel field. A second opening inferiorly indicates a rudimentary loop of distal hindgut. The anus is imperforate and the sacrum is shortened with a high incidence of myelomeningocoele and spinal dysraphism. The pubic diastasis in these patients may be so great that the penile corpora fail to meet in the midline and are completely separated. In addition, the testes are often undescended and absent from the scrotum or hemiscrotum. Superiorly there is usually an associated exomphalos (Figure 15.3).

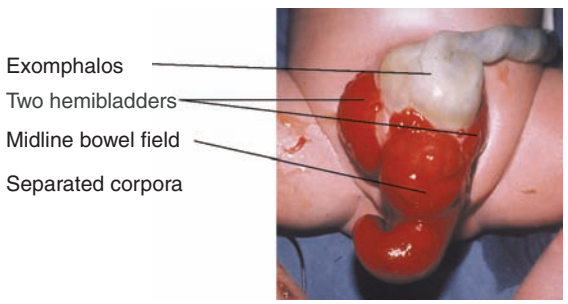

Figure 15.3 Newborn male infant with cloacal exstrophy.

Primary epispadias

The embryological origins of epispadias are poorly understood. In primary penile epispadias there is variable diastasis that tends to be less severe than in bladder exstrophy. The pelvic ring is often complete, with an apparently normal abdominal wall. As a result the anus is appropriately sited and the scrotum also appears normal. The urethra opens on the dorsal aspect of the penis. Depending on the severity of the epispadias, the urethra may open distally on the glans (glanular epispadias), on the shaft

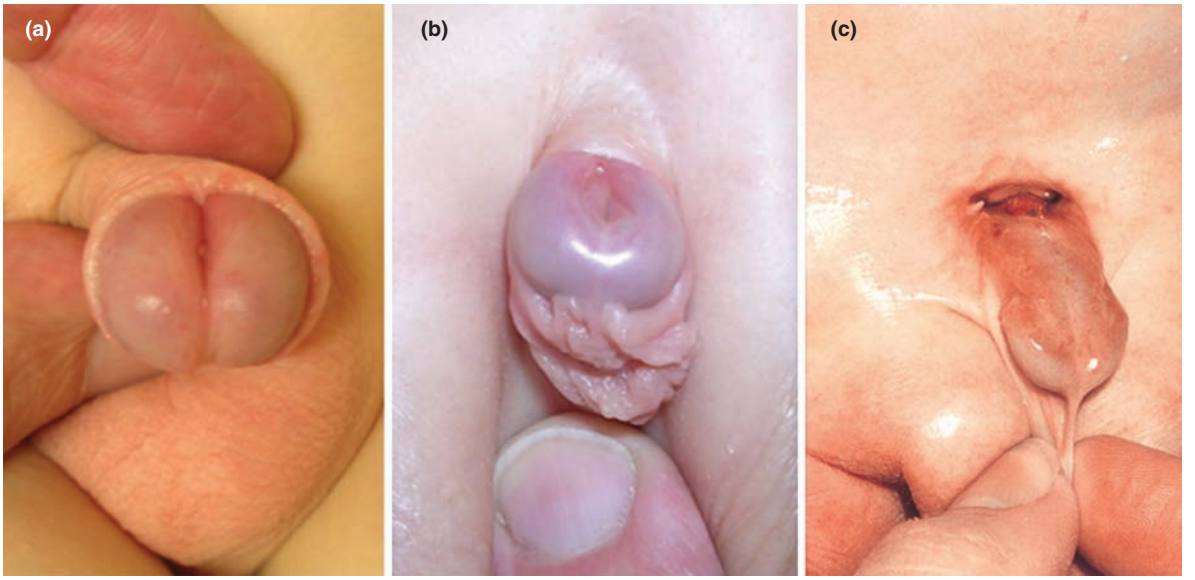

Figure 15.4 Male primary epispadias: (a) glanular; (b) penile; and (c) penopubic.

(penile epispadias) or proximally at the junction with the anterior abdominal wall (pubic or penopubic epispadias) (Figure 15.4). Underlying deficiencies of the bladder neck and proximal urethra and striated sphincter complex determine the degree of associated incontinence. As a general rule, however, the severity of incontinence correlates with the position of the urethral opening, being most severe in proximal epispadias. In these cases the posterior urethra merges with the bladder neck and the verumontanum may lie at the level of the bladder neck or even within the bladder itself. The ureteric orifices often lie close together and are normal or narrowed in calibre, contrasting with the wide refluxing orifices seen in exstrophy.

In female primary epispadias the urethra is wide open on its dorsal surface and the clitoris is separated on either side with its attached labium minorum. The urethra is short and wide and the bladder neck is deficient, leading to severe stress-type incontinence in all patients (Figure 15.5).

Antenatal diagnosis

The detection rate of cases of bladder exstrophy by antenatal ultrasound is currently around 40% at 18 weeks' gestation. Diagnostic features include inability to visualise urine in the fetal bladder; low-set umbilical cord; a short, wide penis; and a bulging bladder plate. Cloacal exstrophy may be confused with other abdominal wall defects such as gastroschisis, but is more likely to be detected because of the presence of other abnormalities such as myelomeningocoele and renal and cardiac anomalies. Antenatal diagnosis provides an opportunity for parents to consider termination of pregnancy, but counselling should take into account the improving outcomes of intervention, particularly in classic bladder exstrophy.

Classic bladder exstrophy

Presentation and clinical features

If not detected antenatally, classic bladder exstrophy presents at birth with a visible bladder plate below a low-set umbilical cord. The mucosa may become quite inflamed and polypoid, especially after a few hours' exposure following delivery. The shaft of the penis is usually short and thick with a good-sized glans. Although the genitalia are usually recognisably male or female, there may be some

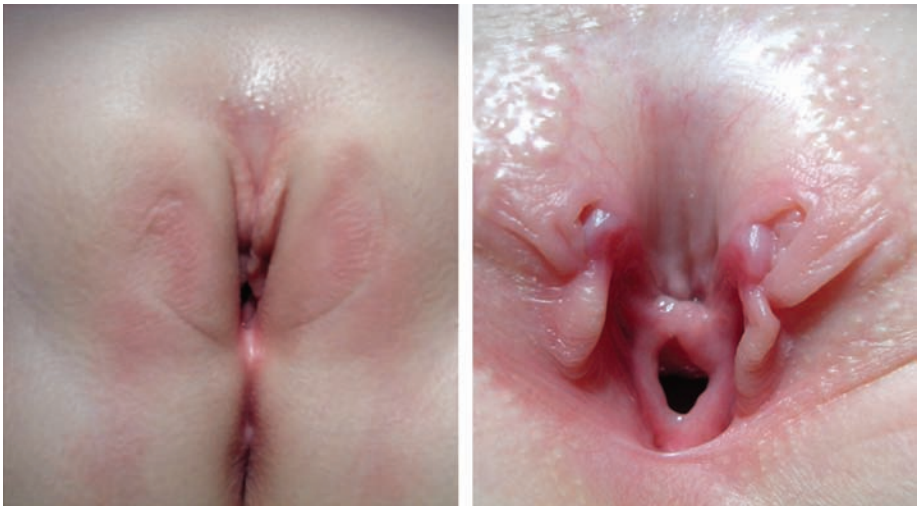

Figure 15.5 Female primary epispadias.

confusion over gender in the referring hospital. The scrotum is present in boys with the distinctive upwards direction of the rugae and the testes are usually palpable within it.

Classic bladder exstrophy has few associated anomalies and babies are usually born at or close to term and are otherwise well. Inguinal hernias are present in up to 80% of boys and 15% of girls but may not become apparent until after primary closure.

Initial neonatal management and primary closure

Because affected newborns are born at term and rarely have other medical problems, they can be put to the breast and require no medical intervention in the delivery suite. Vitamin K should be administered, particularly if surgery is anticipated in the next few hours. While transfer to an appropriate specialist centre is arranged, the exposed bladder plate is protected with a cling-film wrap inside the nappy. Antibiotics or intravenous access are not required at this stage unless indicated by the presence of other complications such as prematurity. If necessary, transfer can be delayed for a few hours to enable both parents to accompany the baby.

Following transfer, the child is assessed at the specialist centre, a baseline renal ultrasound is performed and oral antifungal prophylaxis is commenced as a prelude to surgery in the first 48 hours of life

Surgical technique (Figure 15.6)

An epidural catheter provides optimal postoperative analgesia, broad-spectrum antibiotics are administered and the abdomen and lower limbs are prepared and draped within the operative field. Ureteric catheters (usually 6 Fr feeding tubes) are inserted and the bladder plate is dissected free of the skin and rectus muscles on either side. Any large polyps are usually excised at this time and the mucosal defects repaired. In boys, exposure of the external inguinal ring enables the hernial sacs to be identified and ligated. The umbilical root is usually excised after dividing its vessels, as this is a source of infection postoperatively. It is usually possible to perform this dissection extraperitoneally and it is then continued inferiorly to the level of the verumontanum on either side of the proximal urethral plate. In girls, the dissection is continued to just above the vaginal opening. Deep dissection on either side of the bladder neck enables the bladder and proximal urethra to be closed in the

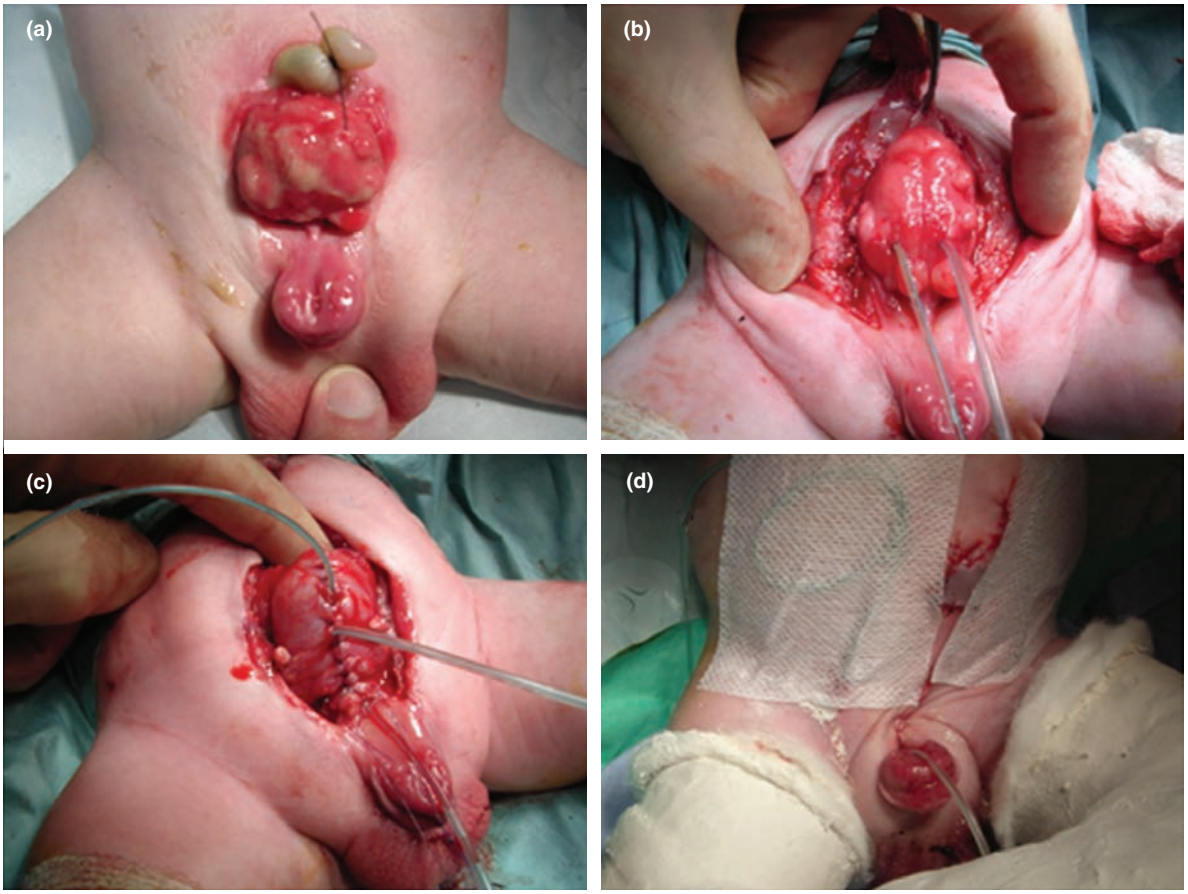

Figure 15.6 (a) Primary closure of a newborn male exstrophy. (b) Separation of the bladder plate. (c) Closure of bladder with ureteric catheters. (d) Appearance after abdominal wall closure with plaster cast.

midline with interrupted 4/0 absorbable sutures. The ureteric catheters are brought out through the bladder closure and then through separate punctures lateral to the rectus muscles and away from the midline muscle and skin closure. A fine silicone stent is used across the urethral opening and secured to the bladder plate with a fine absorbable suture. Unless the diastasis is wide, pressure on the iliac crests will bring the pubic rami together in front of the bladder neck, which drops back into the pelvis. Interrupted horizontal mattress sutures of heavy-gauge PDS (polydioxanone) are used to approximate the pubic rami and further interrupted sutures used to join the rectus muscles above it. The subcutaneous layers and skin are closed with interrupted absorbable sutures. Finally, a frog-leg plaster is applied to the lower limbs to immobilise them in the first few days.

Postoperatively, all tubes are left on free drainage and adequate analgesia maintained with the epidural catheter. Feeding is recommenced early, with expressed breast milk if necessary, and prophylactic antifungal agents are continued. The ureteric catheters are removed after 10 days and the urethral stent after 2–3 weeks, at which time the plaster cast is also removed. Ultrasound evaluation of the upper urinary tract is performed after all catheters have been removed to assess bladder emptying and the upper tracts before discharge. Regular follow-up with ultrasound is scheduled to evaluate progress and to help plan later interventions for continence and genital reconstruction.

Complications are relatively common after major reconstructive surgery of this nature, and may include wound breakdown and partial or complete dehiscence, which occurs in up to 10% of patients. Factors contributing to this dehiscence include pooling of urine at the new urinary meatus, the use of stents emerging through the midline closure and retention of the umbilical stump. All of these factors predispose to wound infection, which, in combination with tension (and ischaemia), leads to dehiscence. Partial dehiscence which does not expose the bladder may be left to heal by secondary intention. A more serious dehiscence comprising either exposure of the bladder plate or prolapse of the bladder will require reclosure, for which pelvic osteotomies may be indicated.

The ureters in classic bladder exstrophy dip into the pelvis and enter the bladder through wide orifices without the normal antireflux oblique tunnel. It is not surprising, therefore that vesicoureteric reflux is almost invariably present after primary bladder closure. Moreover, a tight urethral closure causing outflow obstruction can lead to upper tract dilatation and renal damage if infection supervenes. Close surveillance is required to identify upper tract dilatation and a period of intermittent catheterisation of the tight bladder outlet is sometimes required.

The role of pelvic osteotomy

The pelvis in newborn exstrophy patients is sufficiently flexible to allow closure of the bladder without osteotomy in the majority of cases. But where the pubic diastasis is wide or when closure is delayed, division of the bony pelvis between the anterior superior iliac spine and the greater sciatic notch creates great pelvic mobility and allows a tension-free closure of the pubis. When used routinely, osteotomy extends the operating time by up to 2 hours, increases blood loss and prolongs postoperative immobility. Nowadays it is therefore reserved for revision cases and cloacal exstrophy. Postoperative fixation of the bony pelvis is achieved with frog-leg plasters in babies and external fixators in older children.

Secondary procedures for continence and genital reconstruction

In girls, primary closure can occasionally be sufficient to impart continence and create a satisfactory cosmetic appearance. In the overwhelming majority of exstrophy patients, however, further procedures will be required to achieve continence and for the reconstruction of functionally and cosmetically acceptable genitalia. Until further continence procedures are performed, the inadequate outlet resistance results in dribbling incontinence. Although urinary tract infections are uncommon, some surgeons place patients on prophylactic antibiotics.

Continence surgery

There are currently three accepted strategies in bladder exstrophy management. The first approach, popularised by Mitchell, aims to create continence by complete anatomical reconstruction carried out at the time of initial bladder closure. The bladder plate is fully mobilised and the penile corpora and urethral plate completely separated before closure of the bladder and reconstruction of the urethra and penis. Although good results have been reported by the proponents of this complex single-stage reconstruction, it nevertheless represents a daunting surgical challenge in a newborn infant and major complications have been reported.

The more traditional staged reconstruction, popularised by Jeffs and Gearhart, has been the standard approach for many years. Following conventional bladder closure at birth, epispadias repair is subsequently performed in the first 2 years of life. This is then followed by a bladder neck reconstruction when the required bladder capacity has been attained, usually by 5 years of age. If incontinence persists because bladder capacity fails to increase sufficiently after the bladder neck repair, a further bladder neck reconstruction may be undertaken in conjunction with augmentation enterocystoplasty and the formation of a Mitrofanoff catheterisable conduit.

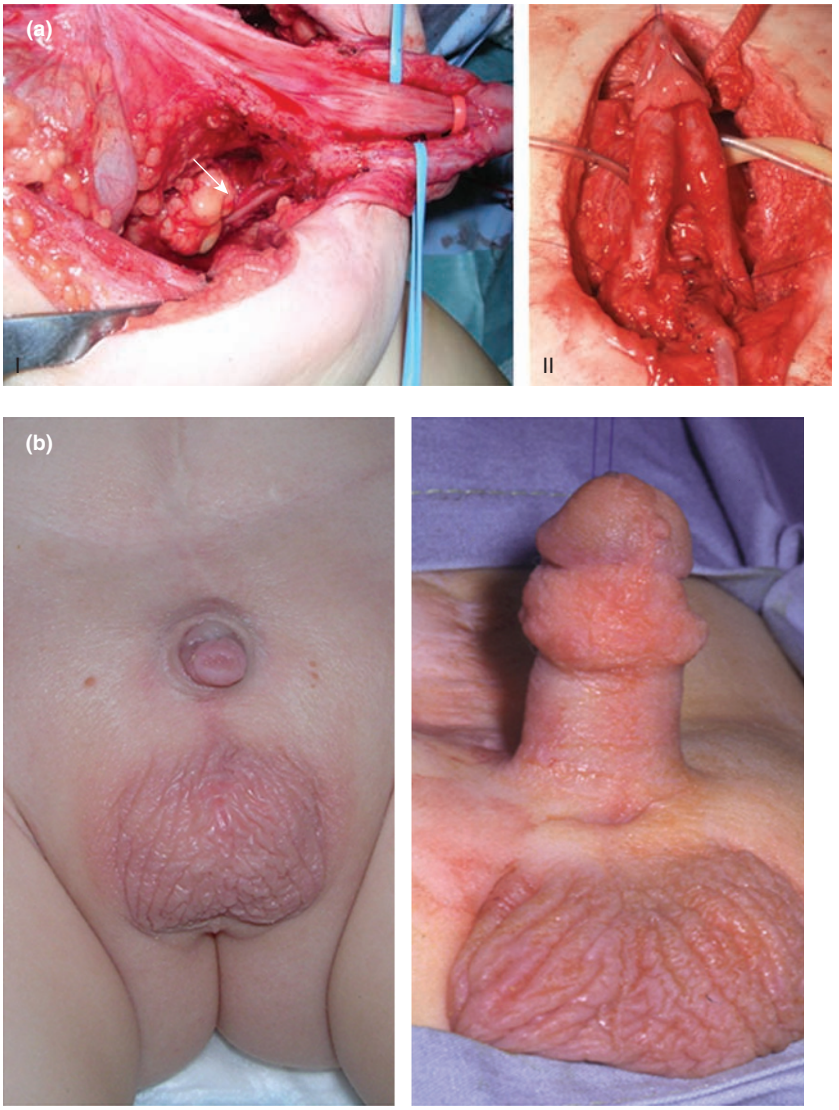

Figure 15.7 (a) The Kelly operation. (I) From the right of the patient, the penile corpora and urethral plate are dissected and the bladder is held to the left, the base of the corpus is separated from the pubis and moves medially, the pelvic floor has been released and the pudendal pedicle is seen (arrowed). (II) From below the penis, the urethra has now been detached, tubularised and brought between the mobile corpora; muscle is being wrapped around it. (b) Kelly operation: postoperative appearances.

The third option is the Kelly operation, which is now the procedure of choice at Great Ormond Street Children's Hospital. After successful neonatal closure of the bladder, an examination under anaesthetic is performed at 3 months to check the bladder and its outlet. Irrespective of bladder size, the operation is performed from 6 months of age. Initially, the bladder is reopened in the midline and both ureters reimplanted using the Cohen technique. The soft tissues, including the urethra, penile corpora and pelvic floor, are then fully mobilised before reconstructing the bladder outlet, urethra, sphincter and penis.

Detachment of the penile corpora from the lower border of the inferior pubic rami must be combined with release of the pudendal pedicle which runs from the greater sciatic notch to the base of the penis in Alcock's canal and lies on the internal obturator fascia, beneath the pelvic floor muscles. Following this manoeuvre, the base of the penis can move freely towards the midline and lie next to the contralateral corpus. This eliminates the effect of the pubic diastasis and increases penile protrusion and apparent length (Figure 15.7a).

Dissection of the urethral plate from the corpora and the glans enables it to be tubularised around

an 8 Fr stent. The level of the bladder neck is defined between the verumontanum and the ureteric orifices and mucosal triangles removed on either side, before closing it and then the bladder above. In the majority of boys the length of the urethral plate is inadequate and would limit the final penile length. For this reason the urethral plate is separated form the corpora, allowing it to be brought down between the penile corpora to a hypospadiac position. At this point, it lies anterior to the muscles running between the bases of the corpora, which are loosened by the corporal mobility. These can then be wrapped around the urethra with loose sutures, in a position that will be just below the verumontanum and where the physiological sphincter is sited in normal males.

The corporeal bodies are joined in the midline with external rotation to eliminate the dorsal chordee and to secure the position of the urethra below them. The new urinary meatus is secured on the ventral surface and the dorsal glans is reconstructed before replacing the shaft skin. The abdominal wall is reclosed with strong absorbable sutures and at this stage an umbilicoplasty is usually performed. A two-stage distal urethral reconstruction (analogous to hypospadias repair), using posterior auricular skin grafts, is completed during the next year. In the author's practice the Kelly operation undoubtedly offers a superior cosmetic result to the conventional staged repair (Figure 15.7b).

The Kelly procedure can also be performed in girls. The two components of the bifid clitoris are mobilised, with the labia minora left attached and their pudendal pedicles are also identified and preserved. Reconstruction of the bladder neck and urethra is undertaken in a similar fashion to males. The mobility of the hemiclitori enables them to be brought together in the midline. No further procedures will be needed in girls, as genital reconstruction is completed in a single stage.

Continence outcomes

The published continence rates following surgical reconstruction of bladder exstrophy have generated considerable confusion, and some controversy. Although continence rates as high as 70% have been reported by some centres, very few surgeons have been able to match them and there is a perception that selection according to bladder capacity and other factors may have played a role in some reported results. In practice, fewer than 25% of boys are likely to achieve both continence and voiding without the need of catheterisation following a traditional staged reconstruction.

Table 15.2 Grading system for continence

Grade	Description
0	Dribbles urine all the time with no control
I	Able to retain urine with a 'dry interval'; some control but still wearing protection
II	Sufficient dry intervals by day; in underwear and not needing protection; wet at night
III	Dry by day and night; no protection or accidents; 'normal child'

In the assessment and reporting of functional outcomes it would be helpful if a standardised definition of what constitutes 'continence' could be agreed and applied equally to all patients and treatment modalities. Only in this way can meaningful comparisons be made. The author has proposed the simple grading system shown in Table 15.2 for continence.

Using this schema, the author has assessed the outcome of 50 patients who have undergone the Kelly procedure. Of those patients followed for over 2 years, the majority (92%) have a significant dry interval during the daytime. However, some of these patients still need to wear pads because of incontinence related to reduced bladder capacity. Nevertheless, 71% of children are in normal underwear and are dry by day. Night-time continence requires a larger bladder capacity and, for this

reason, only 25% of children are currently dry at night. Experience has shown that the Kelly procedure provides a relatively predictable degree of outflow resistance and that the subsequent degree of continence depends upon the potential of the bladder to enlarge in response to the increased outflow resistance.

Persisting incontinence is due either to inadequate outflow resistance and/or inadequate bladder capacity. Further surgery is usually required, although if residual incontinence is mild some degree of further improvement can be expected with increasing age, particularly around puberty. For more severe persisting incontinence a repeat bladder neck reconstruction is performed in combination with ileocystoplasty and the formation of a Mitrofanoff catheterisable conduit. Ideally this should be timed to provide continence by the age of 6 years. If wetting persists despite this form of reconstruction, urodynamics are indicated and, depending on the findings, cystoscopic injection of a bulking agent such as Deflux (dextranomer/hyaluronic acid copolymer) into the region of the bladder outlet may sometimes improve continence. When incontinence persists despite all these measures, there may be no option other than to proceed to surgical closure of the bladder neck.

Late outcomes

Woodhouse has documented the late outcomes of sizeable numbers of patients born with bladder exstrophy. Although these results may reflect the results of outdated surgical approaches, such as ureterosigmoidostomy, the findings highlight the importance of careful long-term follow-up for all patients. Renal damage can be demonstrated in 25% of patients, due to a combination of lower tract obstruction, vesicoureteric reflux and urinary infection. Evidence of renal insufficiency is present in up to 10% of patients. For those patients who have achieved continence following a tight bladder neck procedure in childhood, there is a risk of decompensation and detrusor failure in the late teens. When this occurs, intermittent catheterisation via urethra or a cystoplasty with a Mitrofanoff conduit is necessary. Stone formation is relatively common and occurs in up to 25% of patients. The risk of malignancy in the reconstructed exstrophy bladder has been estimated to be in the region of 4% at 30 years follow-up.

Males experience normal libido and 90% of patients can achieve erections, although some require corrective surgery for severe persistent chordee to allow penetration. The majority can experience orgasm but have slow or retrograde ejaculation, reflecting the abnormalities of proximal urethral anatomy. Fertility is significantly reduced, probably as a result of disruption of the ejaculatory ducts during bladder neck surgery. Fertility may also be affected by episodes of epididymo-orchitis which occur in up to one-third of men. The potential to achieve paternity by normal means is as low as 5%.

For females the prospects for fertility are normal but surgery to the introitus may be required to facilitate intercourse. Pregnancy is often complicated by vaginal prolapse although, in future, this may prove to be less problematic after modern surgical procedures. Delivery by Caesarean section is recommended and it is prudent to have a urologist in attendance for patients who have previously undergone bladder augmentation.

Unfortunately some patients are still encountered who have experienced multiple failed operations for bladder exstrophy, perhaps with loss of penile corpora and compromise of their renal function. In these situations major and complex revisional surgery is required.

Cloacal exstrophy

Initial presentation and management

Cloacal exstrophy is more often diagnosed prenatally than bladder exstrophy because of the associated anomalies, which are listed in Table 15.3. Affected babies are frequently born prematurely and initially the cloacal exstrophy may be only one

Table 15.3 Associated anomalies in cloacal exstrophy

Anomaly	Cases affected (%)
Renal anomalies Ectopic kidney, agenesis, hydronephrosis	7
Sacral agenesis	60
Spinal dysraphism Myelomeningocoele, lipoma, tethered cord	50
Orthopaedic deformity Club foot, hip and pelvic deformity	40
Small bowel defects Malrotation, duodenal atresia, short gut	65
Cyanotic heart disease	<10

of many problems. It is usual to delay primary closure while other medical problems affecting the gastrointestinal tract and cardiorespiratory systems are evaluated and treated if necessary. Occasionally, surgical reconstruction may have to be delayed for several months. During this time the exstrophied bladder/bowel plate is protected with cling film and barrier creams applied to the surrounding skin. In the case of very low birth weight babies, enteral feeding is established, a target weight of 2.5–3 kg is set and closure deferred until this has been attained. When an exomphalos is present, this usually contracts spontaneously without the need for surgical intervention.

Routine preoperative evaluation includes urinary tract and spinal cord ultrasound examinations. Iliac osteotomies are routinely performed at the time of closure because of the surgical delay and because of the wider diastasis invariably present in these patients. The use of osteotomies usually permits a tension-free abdominal wall closure but when it is not possible to reduce the abdominal contents and close the abdominal wall, a silo is attached over the upper abdomen to reduce tension. This is then reduced and removed over the ensuing days. The bladder/bowel plate is dissected free from the skin and rectus muscles superolaterally and the abdominal cavity is entered. The proximal and distal bowel loops of bowel joining the midline bowel plate are identified and separated from the two hemibladders. A tubularised distal hindgut tube is created which is usually brought out in the left iliac fossa as an end colostomy (in preference to an incontinent anal canal). The hemibladders are joined and closed, reconstructing a bladder outlet and proximal urethra (Figure 15.8).

Gender of rearing

In the past, males with cloacal exstrophy were often assigned to female gender because of the severity of their genital anomaly and difficulty in reconstructing male genitalia in the presence of wide diastasis and short, widely separated corpora. Gender reassignment also necessitated early bilateral orchidectomy and a later ileovaginoplasty, usually at the time of definitive continent reconstruction. With the introduction of the Kelly operation, however, it is now possible to perform full corporeal mobilisation and achieve a more satisfactory penile reconstruction. It is hoped that this will avoid the need for gender reassignment in the majority of cases.

Initial outcomes

Prematurity and severe cardiac anomalies are a significant threat to early survival, together with complications of a short bowel and parenteral nutrition. Nonetheless, the majority of affected newborns now survive to childhood. Careful surveillance of the upper urinary tracts helps to optimise renal function and prevent progression to renal failure. Magnetic resonance imaging (MRI) is used by neurosurgeons to assess the need for cord surgery and orthopaedic surgeons are involved to correct any limb problems. Colostomy complications occur in around 50% of patients and it is occasionally necessary to remove the reconstructed hindgut and create an ileostomy in its place.

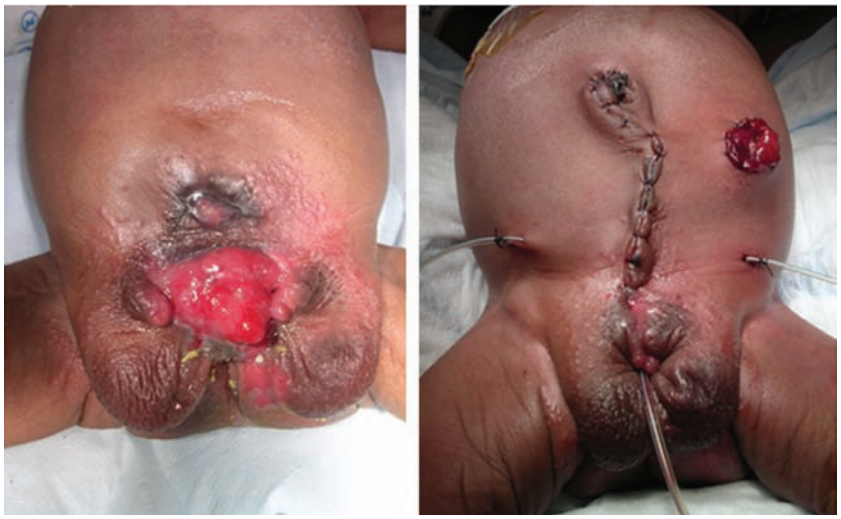

Figure 15.8 Male cloacal exstrophy, closed at 3 months. Osteotomies enable the bladder plates and hemiphalli to be brought together in the midline. In addition, there has been an end colostomy and umbilicoplasty.

Continence and long-term outcomes

The dual insult of exstrophy and neuropathy means all of these patients will need an enterocystoplasty to achieve continence and to ensure storage of urine at safe pressures. Augmentation of the bladder may be a challenge when there is only a short length of small bowel. In addition, the absence of a usable appendix requires the use of some alternative to create a catheterisable conduit. However, most patients can be successfully managed by a combination of ileocystoplasty and the formation of a Monti or small bowel catheterisable conduit. If there is insufficient small intestine, the alternatives for augmentation include a patch of stomach or a hindgut segment. The more complicated forms of reconstruction carry a greater risk of failure and any coexisting renal insufficiency will increase it further and add to overall morbidity.

Despite advances in reconstructive surgery some patients with severe forms of this anomaly may be left with lifelong urinary incontinence.

Patients who have been reared as males and who survive to adulthood are then confronted with serious issues regarding their sexual function. Moreover, the combination of small penile size and surgical damage to vasa deferentia and ejaculatory mechanisms result in very high rates of infertility.

Males who have undergone gender reassignment do not appear to experience gender dysphoria, providing their testes have been removed in early childhood. For these patients the surgical considerations relate mainly to vaginal reconstruction.

Primary epispadias

Presentation

Boys with primary epispadias are rarely identified prenatally but the anomaly is almost invariably detected at birth. In less severe (glanular) forms of the anomaly the prepuce is intact and the condition may not become apparent until the prepuce becomes retractile.

In girls, by contrast, the diagnosis may be considerably delayed, particularly as most paediatricians have not seen this rare anomaly and miss it at the postnatal check. The anomaly classically presents in childhood with a failure of potty training or a history of dribbling or stress incontinence. In some cases there is a long history of attendance at wetting clinics. To an experienced examiner or someone who has knowledge of this rare anomaly the appearances of the genitalia are diagnostic see Figure 15.5.

Management

Males

The Cantwell–Ransley epispadias repair is favoured by many surgeons and can be performed in the first year of life. In this procedure the urethral plate is fully mobilised off the penile corpora from the proximal urinary outlet and corporeal bodies but is left attached to the glans. The urethral plate is then tubularised and brought to a ventral position, below the corpora cavernosa, which are then approximated dorsal to the urethra. Rotation of the corpora eliminates the dorsal curvature of the penis and a distal Heineke–Mikulicz procedure in the glans with dorsal glans reconstruction brings the meatus into a more ventral position.

This operation is best suited to patients with good penile length in whom it is usually successful in creating a terminal urethral orifice and good cosmesis of the glans. Where the penis is smaller, however, the outcome may be a short phallus with a rather buried appearance. In these patients a more radical penile mobilisation such as that provided by the Kelly operation enables length to be enhanced, particularly if there is a pubic diastasis.

Epispadias is commonly associated with incontinence and on cystoscopy there is demonstrable weakness of the bladder outlet with the verumontanum lying close to the bladder neck or even within the bladder.

Although it is not possible to reliably assess continence in infants who are still in nappies, some indication is provided by the penile anatomy (severity of epispadias) and the cystoscopic findings. Patients with distal anomalies and good penile size, whose verumontanum is below the bladder neck and who appear to void without dribbling, are best managed by the Cantwell–Ransley repair. For those with a more severe form of the anomaly, the Kelly procedure is more appropriate and is analogous to technique employed in bladder exstrophy.

Outcome

The long-term outcome for sexual function is usually good, and normal fertility is retained unless there have been urethral complications or epididymo-orchitis. However, ejaculation may be slow or even retrograde. Patients who have only undergone penile reconstruction (the majority) will require additional bladder neck/sphincter surgery if their continence is impaired. Injection of a bulking agent into the bladder neck may improve short-term continence but its effect is not long-lived. The surgical options include a bladder neck repair or artificial urinary sphincter. In practice, it is difficult to reproduce a physiological bladder neck and sphincter mechanism and for some patients it may be necessary to progress to bladder augmentation and a Mitrofanoff conduit. Although the Kelly operation offers enhanced penile length, it remains to be seen whether the more aggressive approach to sphincteric reconstruction will translate into improved continence in due course.

Girls

Since the majority of girls with epispadias are incontinent, reconstructive surgery must be directed to correction of the incontinence as well as the genital abnormality. Good results have been reported for distal urethral reconstruction, but more proximal bladder neck surgery may also be required. The Kelly procedure offers good prospects of continence coupled with an improved external cosmetic appearance. There should be few implications for sexual function or fertility, although delivery should be by elective Caesarean section.

Key points

- The exstrophy–epispadias complex encompasses a group of rare anomalies which occur more commonly in males.
- Cloacal exstrophy is now usually detected antenatally, as are approximately 40% of cases of bladder exstrophy. Epispadias, however, is almost invariably diagnosed at birth.

- Most infants with uncomplicated or classic bladder exstrophy are otherwise healthy, and surgical correction can be undertaken safely within the first few days of life. The cosmetic and functional results obtained with the one-stage Kelly operation may prove to be superior to those achieved with conventional staged repair.
- Late morbidity is common in exstrophy patients and may include incontinence, sexual dysfunction and renal impairment. It is hoped that newer techniques will offer better long-term results.
- Cloacal exstrophy is often associated with prematurity or other medical problems which take priority over early surgical correction. Reconstruction presents a formidable challenge. Although it is usually possible to create a urinary reservoir, most patients are left with a permanent colostomy. It may be necessary to consider gender reassignment in severely affected males.
- Primary epispadias is commonly associated with incontinence due to deficiency of the bladder neck and sphincter complex.

Further reading

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Hypospadias 16

Duncan T Wilcox and Pierre DE Mouriquand

Topics covered

Introduction

Hypospadias is an association of three anatomical anomalies:

- an abnormal ventral opening of the urethral meatus
- ventral curvature (chordee) of the penis
- a hooded foreskin, which is deficient ventrally.

However, not all three of these features are present in every case.

Hypospadias is better defined as a hypoplasia of the tissues forming the ventral aspect of the penis beyond the division of the corpus spongiosum. It is characterised by a ventral triangular defect whose apex is the division of the corpus spongiosum; the sides are represented by the two pillars of atretic spongiosum and the base is the glans.

History

In the second century Galen described the problem of infertility associated with a proximal meatus and penile chordee, and was the first to use the term hypospadias. The modern treatment of hypospadias dates from the second half of the 19th century, when the techniques in current use were first described. For example, Thiersch and Duplay described tubularisation of the urethral plate, whereas Duplay also described a technique very similar to the meatal advancement and glanuloplasty later popularised by Duckett in the 1970s. In 1860, Poisson reported a meatal-based flip-flap repair which was later popularised with great success by Mathieu. Although techniques for the correction of hypospadias have continued to evolve, these advances have been largely built on the foundations laid by the pioneers of hypospadias surgery in the late 19th century.

Aetiology and incidence

The incidence of hypospadias is generally quoted at 1 in 300 live male births (0.33%). However, data from different countries show considerable variation, with reported incidences ranging from 0.2% in Sweden to 0.7% in the Netherlands. There has been a growing perception that hypospadias is becoming more common and, while this may be explained in part by better reporting of minor forms, evidence is mounting to a genuine increase in the underlying incidence. The apparent increase in the incidence of hypospadias, coupled with the increasing incidence of testicular cancer

and declining semen quality, have been cited as examples of the possible impact of oestrogenic environmental pollutants ('endocrine disruptors') on normal virilisation of the male fetus. In addition, endocrinopathy, low birth weight and higher maternal age (possibly mediated by placental insufficiency) have been identified by some studies as possible aetiological factors. Hypospadias is more common in monozygotic twins and in the offspring of fathers who have hypospadias, indicating that there may be a polygenic inheritance. The concept of a genetic component has been strengthened by the finding of hypospadias associated with specific gene (*Ins l3*) knockout mice. The overall incidence of hypospadias in first-degree male relatives of affected boys is 7–10%, rising to 10–20% in brothers of boys with severe forms of the condition.

Intersex and associated anomalies

Severe forms of hypospadias can present with similar appearances to disorders of sex development (DSD), especially when severe hypospadias is associated with undescended testicles and a prostatic utricle. In some series up to 50% of patients with both hypospadias and cryptorchidism have been found to have an underlying genetic, gonadal or phenotypic sexual abnormality. It is essential that patients with hypospadias and undescended testicles are fully investigated so that DSD can be excluded. With the exception of an increased overall incidence of undescended testis, other anomalies in patients with isolated hypospadias are rare. Abnormalities of the urinary tract are unusual, occurring in approximately 2% of patients; consequently, routine ultrasound of these children is unnecessary. The overall incidence of undescended testis is in the range 5–10%, rising to 50% in those with the severe perineal or penoscrotal forms. These severe forms are also associated with a persistent prostatic utricle in 20% of cases, which on occasions can make urethral catheterisation of the bladder difficult. But since it is rarely necessary to remove the utricle, routine cystography or cystoscopy to identify a utricle is not required unless the child is symptomatic.

Classification

Although many classifications have been described based on the position of the ectopic urethral meatus (Figure 16.1), the level of division of the corpus spongiosum may provide a more accurate means of distinguishing anterior hypospadias with little or no chordee from posterior hypospadias with chordee and hypoplasia of the tissues forming the ventral aspect of the penis (Figure 16.2).

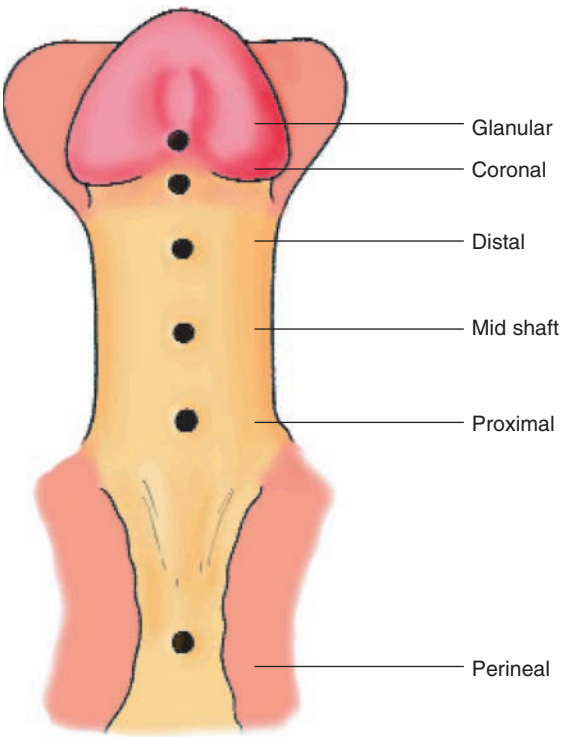


Figure 16.1 Standard classification of hypospadias.

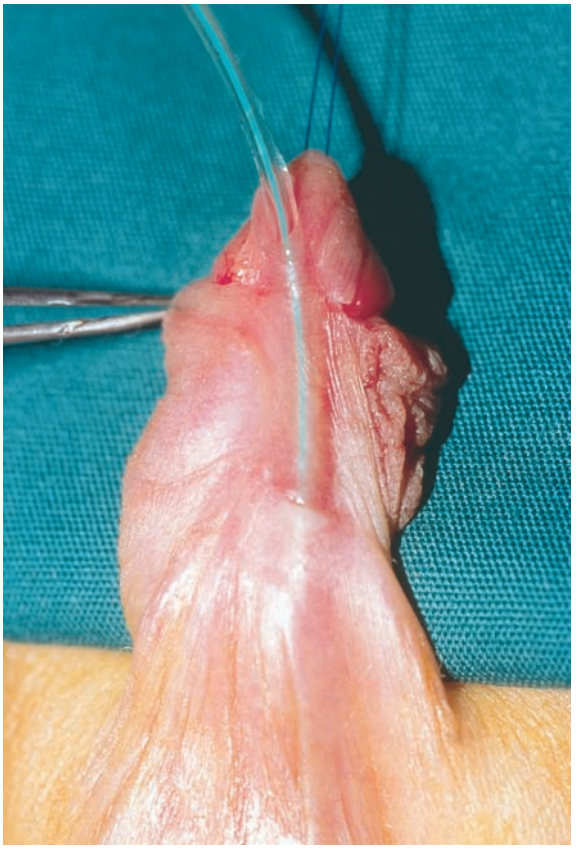


Figure 16.2 Deceptively severe case illustrating the potential pitfalls of classification based on the position of the urethral meatus. The urethra terminates with an opening on the glans but the entire urethra is 'paper thin', and this case is, in effect, a proximal form of hypospadias with chordee.

The authors' classification therefore recognises three main types of hypospadias:

1. Hypospadias with a distal division of the corpus spongiosum with little or no chordee.
2. Hypospadias with a proximal division of the corpus spongiosum with a marked degree of hypoplasia of the ventral tissue and a significant degree of chordee.
3. Patients with hypospadias despite multiple previous operations (previously termed 'hypospadias cripples').

Specific surgical principles

Although more than 300 different techniques have been described for the repair of hypospadias, the last decade has seen the emergence of a growing consensus amongst specialist hypospadias surgeons. For the majority of patients this comprises either tubularisation of the urethral plate or a two-stage repair usually involving a free flap. This chapter will concentrate on these two techniques, but other methods which are still in current use will also be described.

Regardless of the particular type of repair, there are three specific components to the surgical correction of hypospadias:

- correction of the penile chordee
- reconstruction of the urethra (urethroplasty)
- skin coverage of the penis aimed at achieving a normal cosmetic appearance.

Correction of penile chordee

Penile chordee can result from a number of factors, including abnormal tethering of the penile shaft skin on to the underlying structures, tethering of the urethral plate to the corpora cavernosa, or atretic corpora spongiosum tissue extending from the abnormal meatus to the glans. Finally, chordee may be due to an intrinsic flexion deformity of the corpora cavernosa (Figure 16.3). Correction of penile chordee can involve a number of steps, which should be addressed in the following order:

1. Degloving the penis by fully mobilizing the overlying skin. In the majority of patients (80%), this is all that is required to correct the chordee.
2. Excision of the atretic and fibrous corpora spongiosum proximally and distally to the abnormal meatus.
3. Dissection of the urethral plate, which is carefully elevated off the corpora cavernosa. (Not all surgeons perform this step, opting instead to go straight to a dorsal plication.)

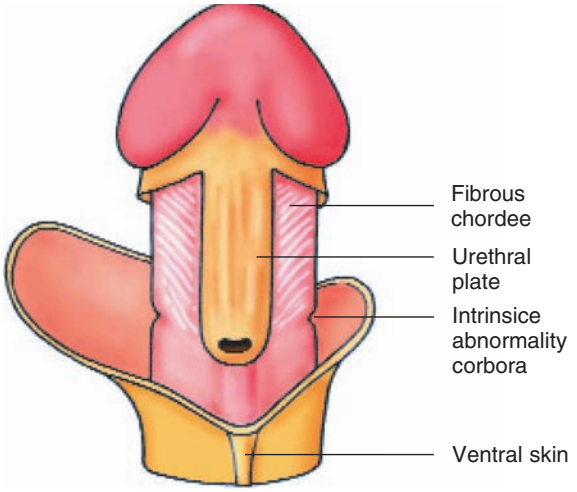


Figure 16.3 Causes of penile curvature associated with hypospadias.

Figure 16.4 Correction of intrinsic chordee by plication on the dorsal aspect of the corpora, following mobilisation of the overlying neurovascular bundles (as described by Baskin).

In some patients ventral curvature of the penis persists despite these steps, in which case it is necessary to plicate the dorsal aspect of the tunica albuginea (Nesbit procedure; Figure 16.4). The correction of penile chordee is controversial, with some surgeons preferring to plicate the tunica albuginea if chordee persists once the penis has been degloved. We prefer to avoid plication, as the long-term results are unknown and the manoeuvre may affect penile growth, leading to secondary deformities. When correction of the penile chordee is completed and confirmed with an artificial saline erection test, it is necessary to reconstruct the urethra.

Urethroplasty

Reconstruction of the urethra can be performed in a single stage or in a two-stage procedure. Most surgeons now opt for a single-stage repair whenever this is possible. As a general rule, a single-stage repair is appropriate for distal, mid shaft and proximal hypospadias without significant chordee. A two-stage repair is generally reserved for perineal hypospadias with chordee and for 'hypospadias cripples'. The majority of surgeons now perform tubularisation of the urethral plate as their preferred one-stage method.

Tubularising the urethral plate (Figure 16.5)

Currently the most widely used single-stage repair is a Duplay-type tubularisation incorporating a vertical incision in the urethral plate, as described by Snodgrass. This modification allows the urethral plate to be tubularised without tension. In addition, it is has been asserted that epithelialisation of the urethral plate incision may contribute to the circumference of the neourethra.

In this procedure the urethral plate is marked and then incised (Figure 16.5a); its width is then assessed. The urethral plate is incised and then rolled into a tube once any chordee has been corrected (Figures 16.5b). Some surgeons also favour a modification in which a free graft of preputial skin is inlaid into an incision in the urethral plate to reduce the risk of contraction and stenosis of the neourethra (Figures 16.5b,c). If the

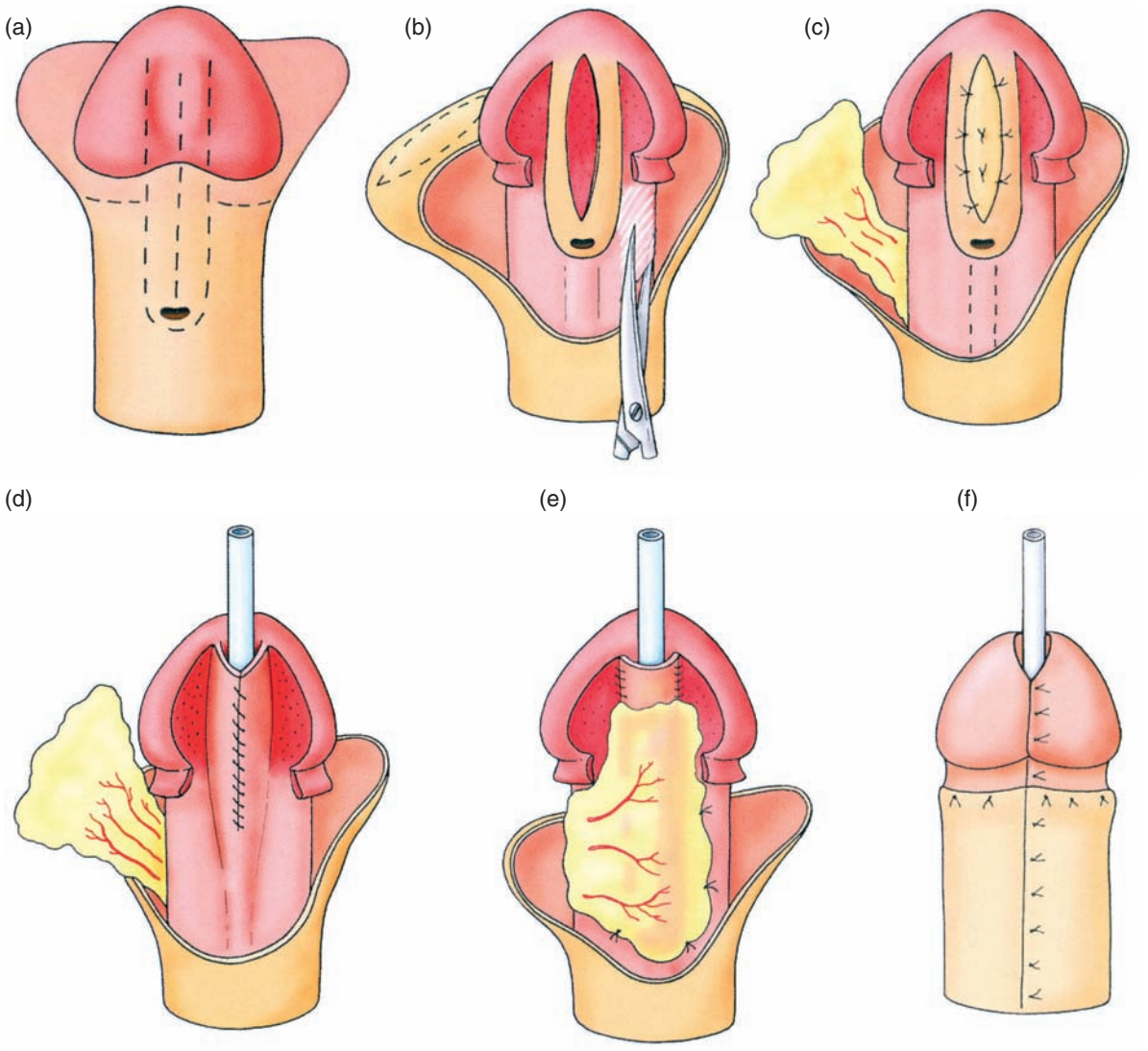


Figure 16.5 Key steps in the tubularised incised plate (Snodgrass) repair (see text for explanation).

urethral plate is wide and sufficiently supple to be tubularised over an 8 Fr catheter, it can be rolled into a tube without the need for a urethral plate incision (Duplay procedure) (Figure 16.5d). Once the neourethra is formed, a vascularised de-epithelialised pedicle of tissue is placed over the anastomosis to reduce fistula formation (Figure 16.5e). The glanuloplasty is performed by reapproximating the glans wings in two layers. The skin is then reconfigured, ensuring that there is

adequate coverage on the ventral surface so that penile chordee does not recur (Figure 16.5f). A dripping stent or urethral catheter is usually left draining for 7 days.

Two-stage repair (Figures 16.6 and 16.7)

The first stage of the operation involves correcting the chordee as described above (Figure 16.7a,b), preparing the glans and harvesting the free flap (Figure 16.7c). Once the chordee has been corrected a midline ventral incision is made from the most dorsal part of the new meatus on the glans to the current meatus. Glans wings are created so that the glans opens widely ('like a book'). The ideal material for the flap should be easy to harvest, without leaving a long-standing cosmetic defect. It should be supple and non-hair bearing. The most commonly used graft material is inner preputial skin. However, postauricular Wolfe skin grafts can also be used for primary repair. Buccal skin and bladder mucosa are less frequently used for standard two-stage repairs, but do have a role in 'salvage' hypospadias.

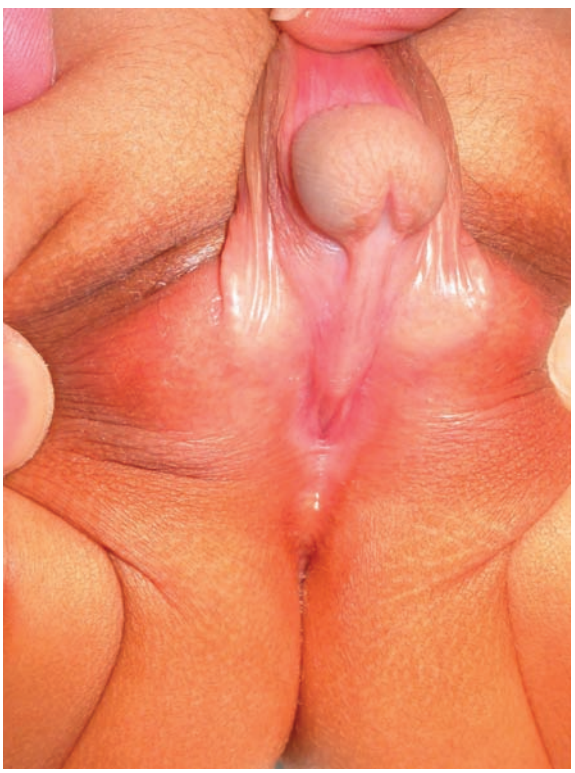


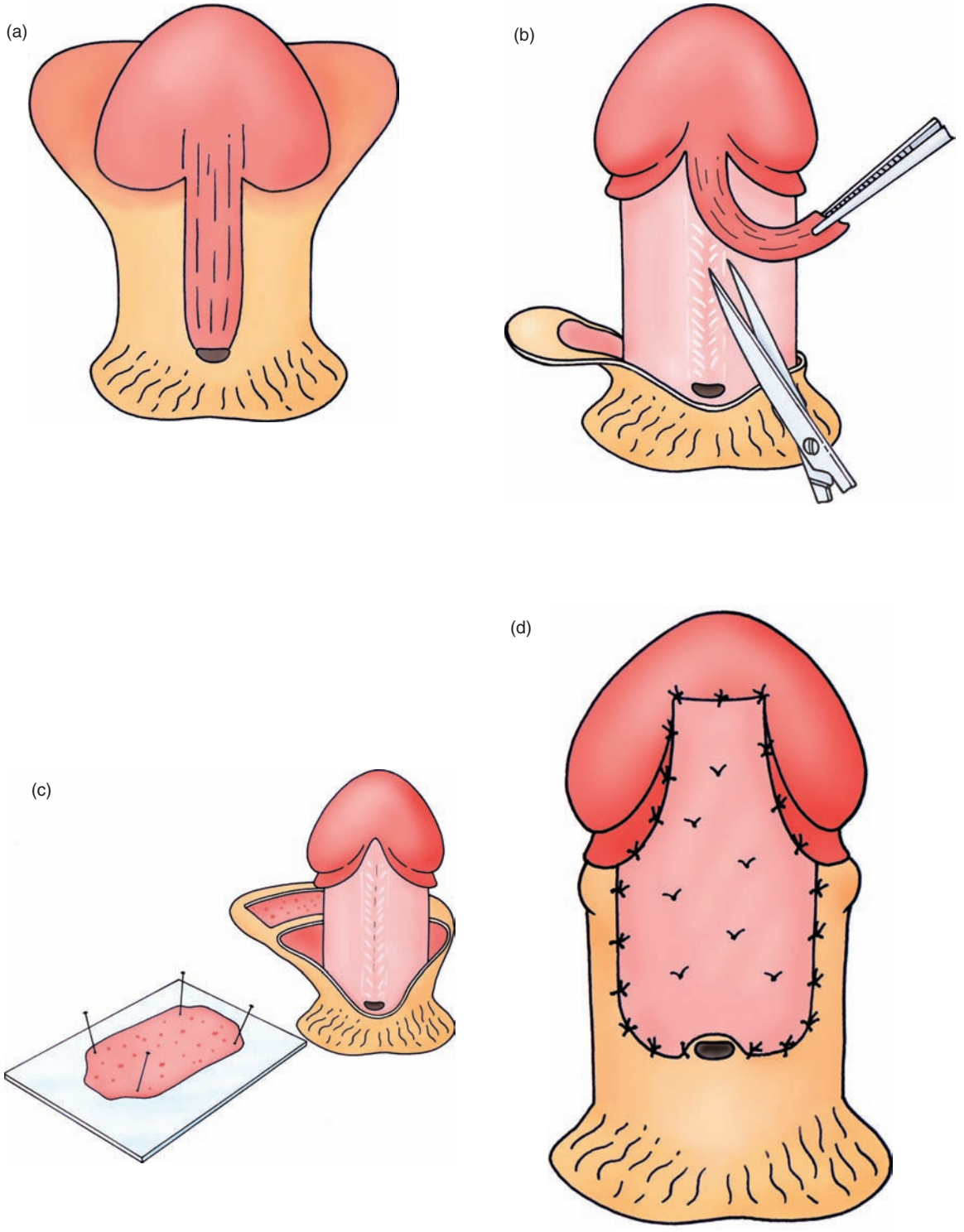
Figure 16.6 Severe proximal hypospadias, unsuited to a single-stage repair.

When the donor graft has been taken, the fat and subepithelial tissue are removed to enhance graft revascularisation (Figure 16.7c). The graft is then placed into the glans and tacked with absorbable sutures; 'windows' are made in the graft to allow haematomas to escape, and a few midline quilting sutures are placed to anchor the graft to on its base (Figure 16.7d,e). A firm dressing is applied, with a catheter, which holds the graft in place and minimises haematoma formation. After 1 week the dressing and catheter are removed. The second stage of the repair is usually performed after 6 months. This step involves tubularisation of the graft into the neourethra (Figure 16.7f,g) and then placing a second vascularised layer over the anastomosis (Figure 16.7h). Once this is completed the glans is recreated and the penile skin closed (Figure 16.7i). This second stage is very similar to one-stage tubularisation of the urethral plate already described.

Other techniques which are still in current usage are described below.

Urethral repositioning

The MAGPI procedure (Figure 16.8), an acronym of '**m**eatal **a**dvancement and **g**lanulo**p**lasty **i**ncorporated' was originally described by Duckett. It is more accurately described as a refashioning of the glans penis, with only minor meatal advancement. It is only suitable for cases in which the urethra is mobile – which can be confirmed if simple traction can move the meatus to the tip of the glans. A vertical incision between the tip of the glans and the meatus is created (Figure 16.8a,b) and then closed transversely, thereby advancing the meatus. A circumferential incision is made in the skin below the corona and the meatus. The glanuloplasty is then performed in two layers (Figure 16.8c,d), and finally the penis is circumcised and the skin closed. It is not normally necessary to



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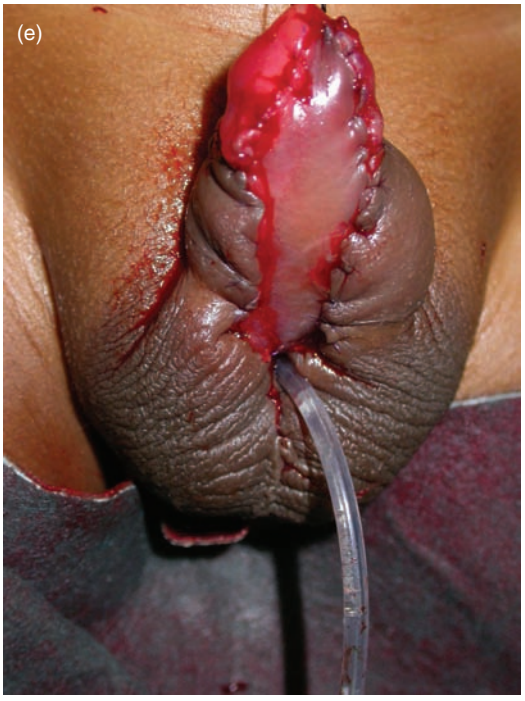

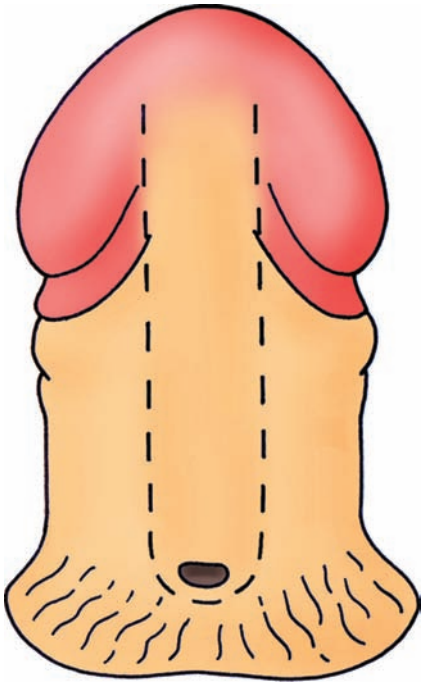

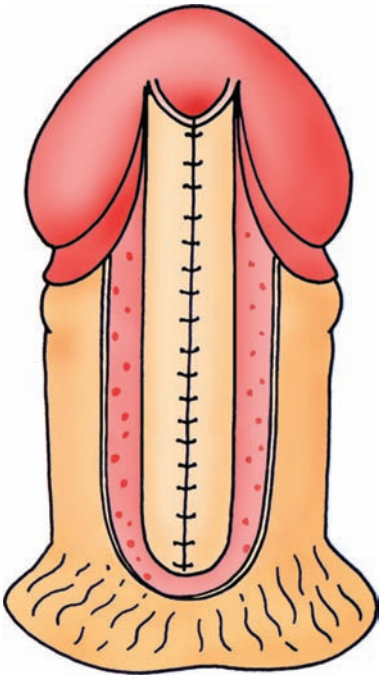

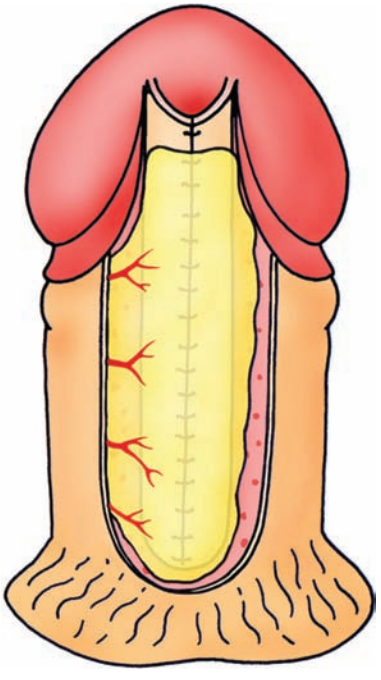

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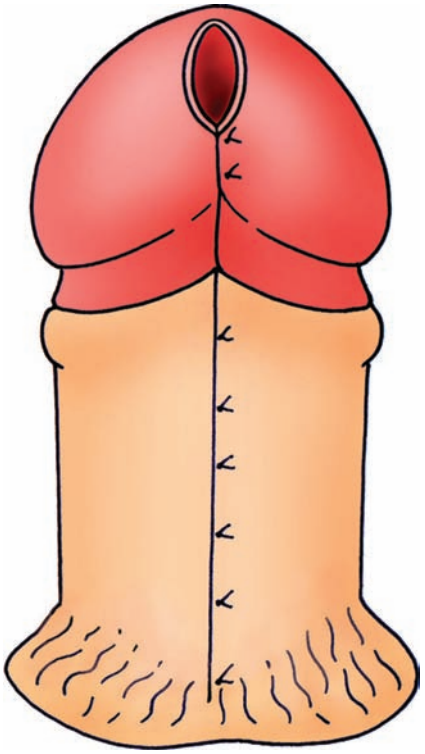

Figure 16.7 Key steps in the two-stage repair (see text for explanation).

leave a urinary catheter in for this procedure. Many authors have described alternative techniques in which the urethra is mobilised and repositioned at the tip of the glans. Urethral mobilisation was reported over 100 years ago, but has recently been repopularised by Koff and colleagues. The technique requires mobilisation of the urethra to the scrotum and has not gained widespread acceptance.

Pedicle flaps

Two types of pedicle flap are commonly used, the meatal-based flap and the preputial flap. Both of these procedures utilise skin flaps which remain attached at some point to the urethral plate.

Meatal-based flap (Mathieu procedure) (Figure 16.9)

The urethral plate is incised (Figure 16.9a) and the glans flaps developed. A flap of proximal penile skin is created using the meatus as the base (Figure 16.9b). The flap is then placed on to the urethral plate and both lateral edges are sutured to it. Adjacent subcutaneous tissue is used to cover ('waterproof') the suture line (Figure 16.9c). Once the neourethra is created, the glanuloplasty is performed (Figure 16.9d). A urinary catheter is left in for 4–7 days, although some authors have reported that no drainage is necessary. As a rule the maximum length of this flap should be no more than three times the width of the base and in practice this technique is unsuited for a urethroplasty exceeding 1.5 cm.

Preputial flap (onlay island flap procedure) (Figure 16.10)

The urethral plate is incised vertically using two parallel incisions. The penis is then degloved back to its base using a circumferential subcoronal incision. Once this is complete, the penile chordee, if present, is corrected. The glans flaps are then created and the proximal thin urethra is cut back until normal urethral tissue is found. A pedicle flap is then created out of the inner prepuce, as shown in Figure 16.10a. The preputial flap is brought around the side of the penis to its ventral surface and sutured to the urethral plate (Figure 16.10b,c). Once the neourethra has been created in this fashion, the subcutaneous pedicle is anchored to the tunica albuginea lateral to the urethral anastomosis (Figure 16.10d). This 'waterproofing' subcutaneous flap covers the anastomosis and provides support for the neourethra. Occasionally it is necessary to divide the urethral plate in order to correct the chordee. In these rare cases the preputial flap can be tubularised, thereby creating the neourethra alone. The lateral glans wings are then approximated in two layers to recreate the glans, and the skin is closed (Figure 16.10e).

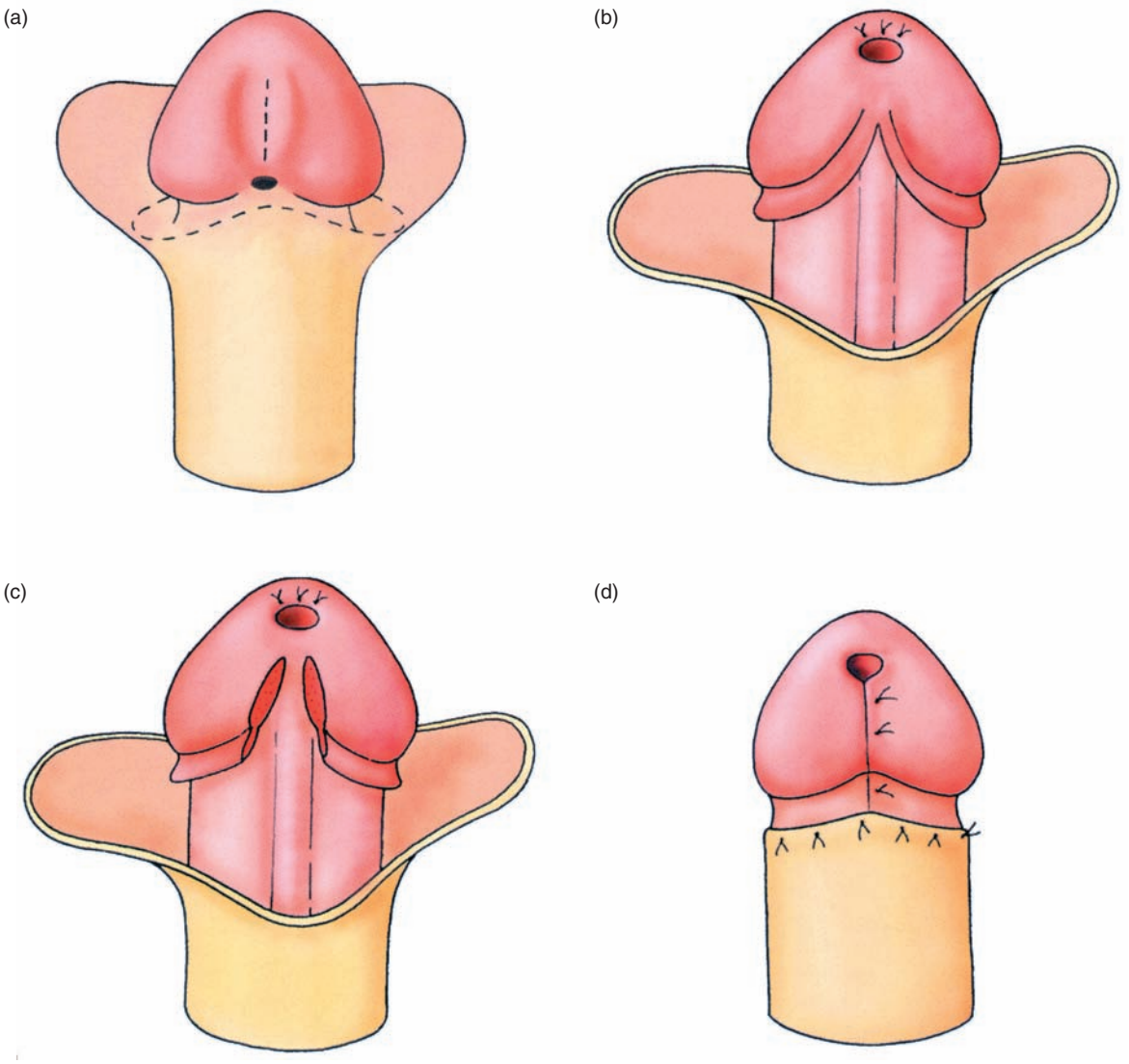

Figure 16.8 Urethral repositioning, key steps in the MAGPI repair (see text for explanation).

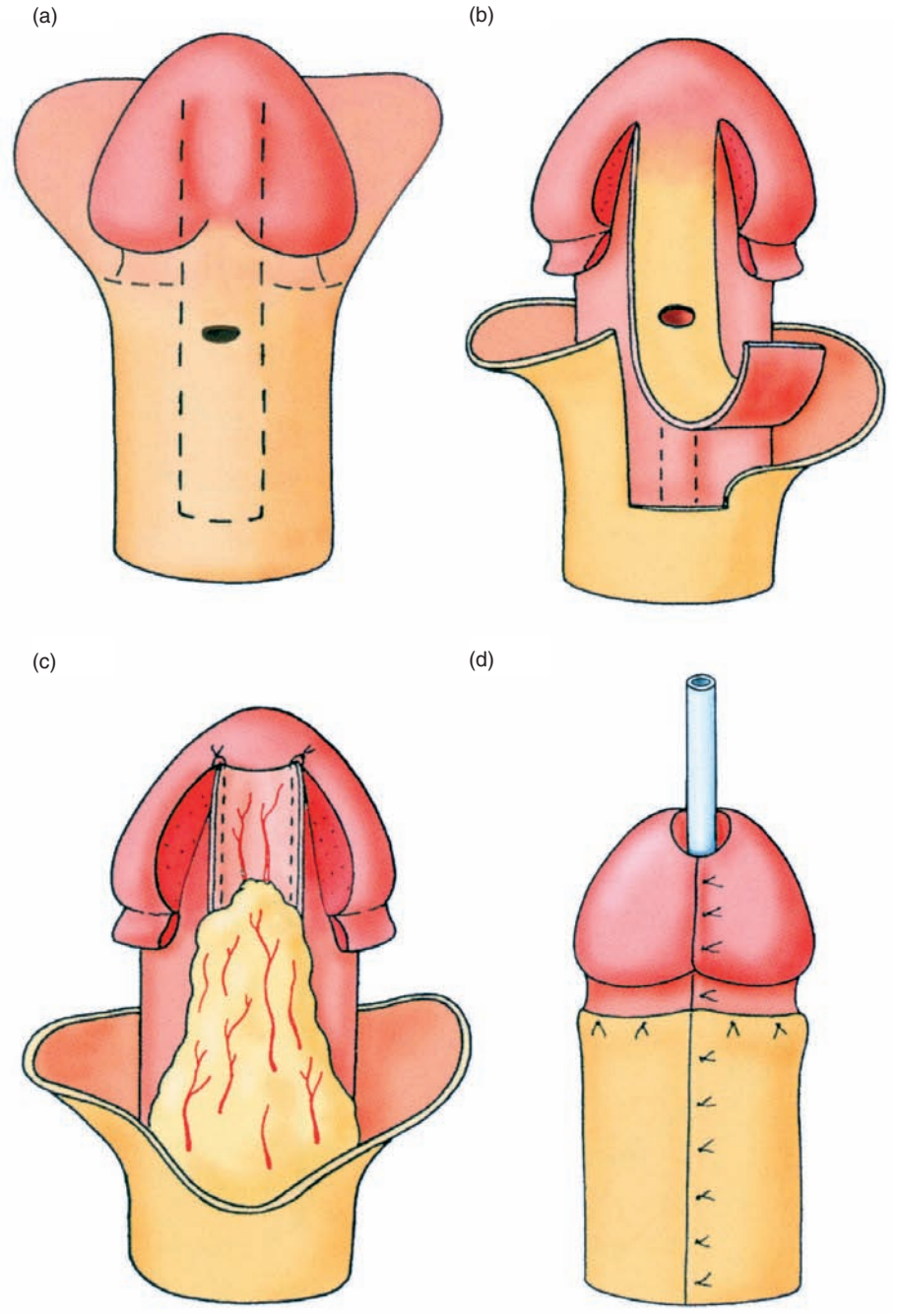

Figure 16.9 Key steps in a perimeatal-based flap (Mathieu) repair (see text for explanation).

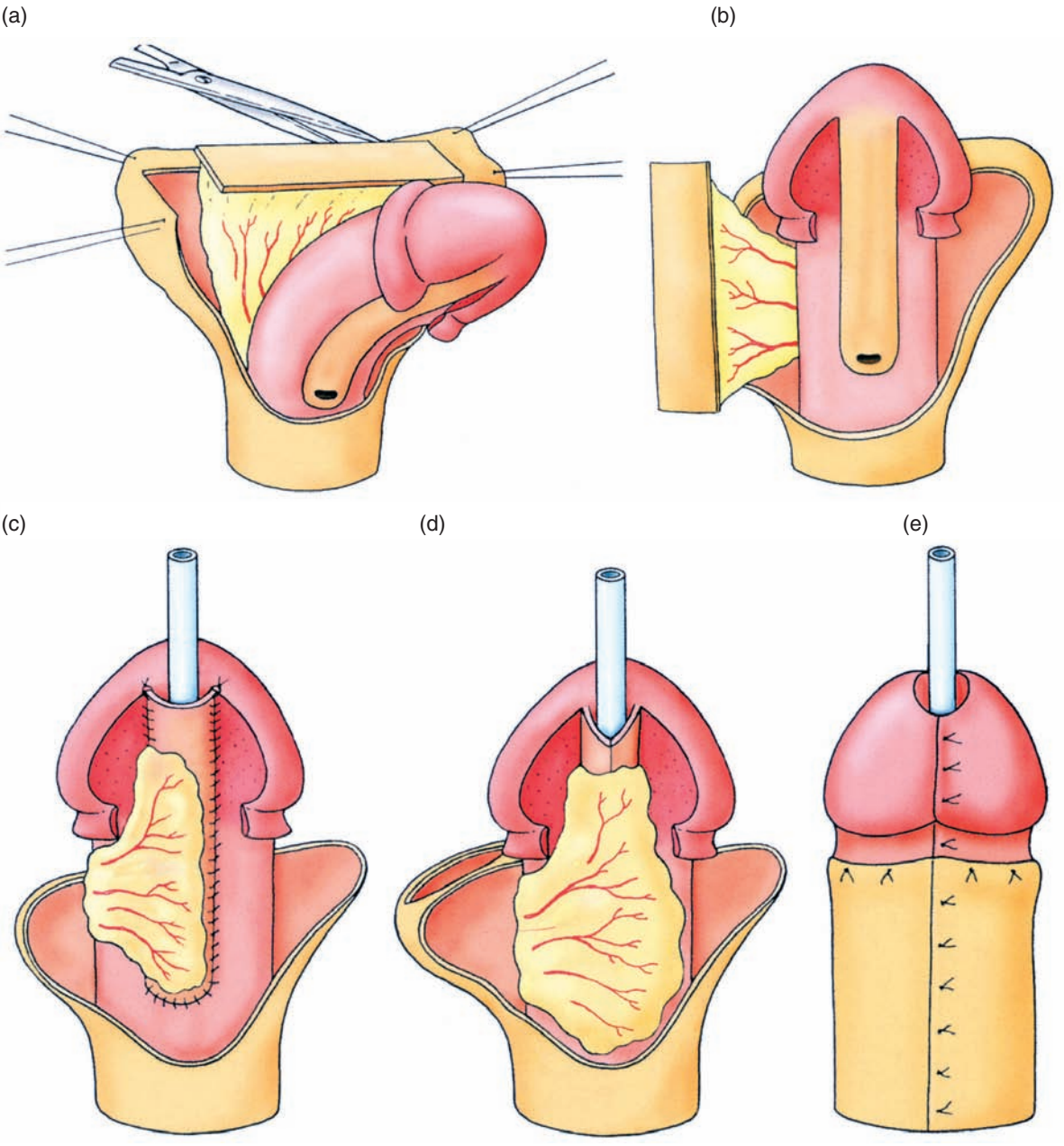

Figure 16.10 Key steps in pedicle flap repair (see text for explanation).

The **Koyanagi procedure** and its variants are alternative procedures for severe proximal hypospadias. It aims at using the urethral plate and the neighbouring strip of ventral tissues along with the inner aspect of the preputial hood, which is transferred ventrally with its pedicle. This large and well-vascularised material is freed from the ventral aspect of the corpus spongiosum down to the base of the penis. This allows the penis to straighten and to build an extended plate which is subsequently tubularised.

Covering the penis

When the urethra has been reconstructed, it is necessary to recreate the meatus and glans. Glanuloplasty is performed by bringing the two wings of the glans around to cover the urethra; the glans is then closed in two layers. The distal end of the neourethra is sutured to the new meatus, thereby creating a slit-like meatus. Once this is complete, the residual inner preputial skin adjacent to the coronal sulcus is brought around the ventral side of the penis to create a circumferential mucosal 'cuff' or 'collar' surrounding the glans. Skin cover is provided by moving the excess skin from the dorsal side to the ventral side: this gives a good cosmetic result that is superior to the Byars flaps previously used. The following techniques are common variants.

Chordee without hypospadias (Figure 16.11)

In most cases this is a misnomer since they do in fact represent a form of hypospadias in which the distal penile urethra is flimsy, despite the presence of a glanular meatus and circumferential prepuce. It may be possible to achieve good correction by degloving the shaft and excising chordee tissue while preserving an intact urethra. At the time of operation, however, it may prove necessary to excise the abnormal urethra back to healthy spongiosum-supported urethra and proceed to urethroplasty as if it were the corresponding degree of true hypospadias.

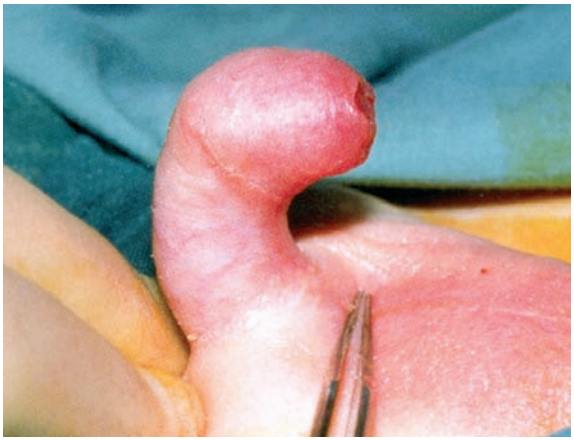

Figure 16.11 Chordee without hypospadias.

Megameatus intact prepuce (Figure 16.12)

Because there is no external clue to the presence of this variant, it sometimes comes to light for the first time in a boy who is about to undergo circumcision. In this situation the planned circumcision should be abandoned, the child returned to the ward and the findings discussed with the parents. If the parents opt for surgical correction of the glanular defect, referral to a specialist is advisable. A suitable technique has been described by Duckett, who also specifically cautioned against the use of the MAGPI repair in view of its high failure rate when used for the attempted repair of this variant.

'Salvage' or 'redo' surgery often calls for ingenuity and familiarity with a number of different techniques. Where the neourethra is largely intact and the surrounding skin is healthy, a procedure using locally available skin may suffice, but where there is extensive scarring and, particularly in the presence of residual chordee, it is usually preferable to abandon the unhealthy existing neourethra and perform a substitution procedure with an onlay or tubularised free graft. Postauricular skin is suitable, but buccal skin, harvested from the lower lip (Figure 16.13) or cheek, is more widely used for this purpose.

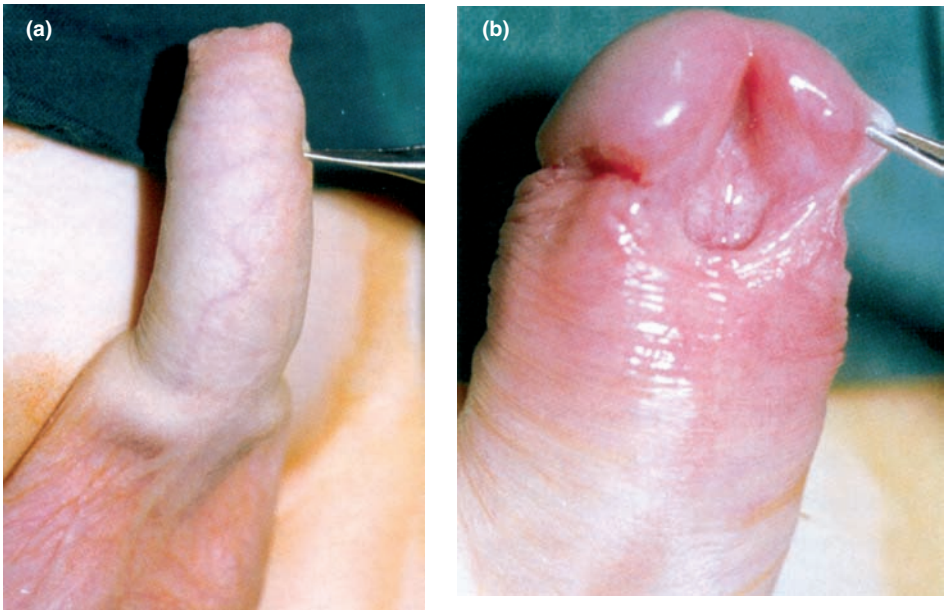

Figure 16.12 Megameatus intact prepuce variant. (a) Normal external appearances before the prepuce is retracted. (b) Glanular anomaly revealed by retraction of the prepuce; deep glans groove with 'fish mouth' megameatus.

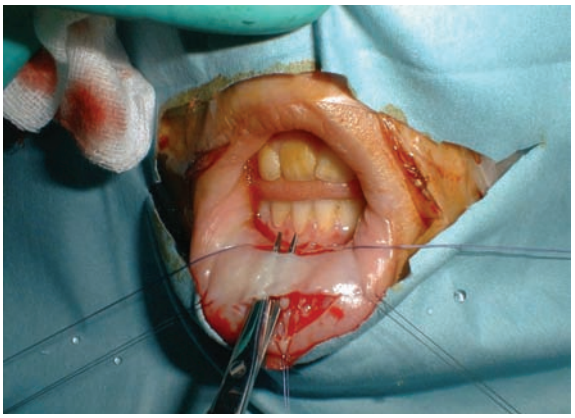

Figure 16.13 Buccal mucosa graft – site on buccal aspect of the lower lip marked out prior to harvesting of the buccal skin graft for salvage repair.

General surgical principles

Magnification

The precision needed to perform this delicate surgery means that most surgeons use some form of optical magnification. Operating microscopes have almost unlimited magnification power, but they are cumbersome and often too powerful for most cases of hypospadias. Most surgeons therefore use standard operating loupes which are easy to use and provide magnification in the range 2.5–4.3×. The most important consideration, however, is that the surgeon should feel comfortable using the optical magnification.

Sutures

The suture material used needs to be fine gauge, absorbable and easy to use. Historically chromic catgut was the most commonly used suture, but with developments in suture technology others are now available. We prefer 7-0 or 6-0 polydioxanone (PDS): these fine absorbable monofilament sutures provide excellent strength and disappear before suture tracts are formed.

Haemostasis

A bloodless operating field is essential for this surgery. It can be obtained by using one of the three following techniques:

- A tourniquet at the base of the penis provides an excellent bloodless operating field. Care must be taken not to leave the tourniquet for long because of the theoretical risk of reperfusion injury.
- Adrenaline 1:100 000 can also be used, up to a maximum dose of 10 mg/kg. Although there is a theoretical risk that excessive vasoconstriction might compromise the vascularity of skin flaps, there is no evidence that this occurs in practice.
- Bipolar diathermy is generally preferred, but the safe use of monopolar diathermy has been described. Diathermy may be inadequate to control bleeding from the glans. It is currently our policy to use a tourniquet followed by a compressive dressing at the end of the operation.

Antibiotics

Practice varies with respect to the use of prophylactic antibiotics, ranging from none to a course of antibiotics while the catheter is in situ. A recent trial suggests that antibiotic coverage of the operation is beneficial.

Urinary drainage

The indications for postoperative urinary diversion depend upon the type of reconstruction. Some forms of distal hypospadias repair may not require any form of urethral catheter drainage. We use transurethral catheter drainage for all but the most minor repairs. In general this takes the form of a 6–8 Fr dripping stent. Use of a standard Foley indwelling urinary catheter carries the concern that the deflated balloon might distend or disrupt the delicate suture lines of the anastomosis when the catheter is withdrawn. Some surgeons favour the use of a suprapubic catheter, but we do not feel this is necessary, except perhaps after complex or 'salvage' redo surgery.

Dressing

The dressing serves many purposes, which ideally include gentle compression of the penis to reduce haemorrhage and oedema, immobilisation and protection from contact to reduce postoperative pain. Many dressings are available and are subject to preference of the surgeon. These include silastic foam, a clean bandage and bio-occlusive dressings (Tegaderm). The dressings stay in place for between 2 and 7 days, depending on the complexity of the repair.

Outcome

The results of hypospadias repair reflect the severity of the original defect and the type of operation performed.

Tubularisation of the urethral plate

The technique of tubularisation, as originally described by Duplay, has a secondary operation rate of around 10%, principally for urethral fistulae. This technique does have the advantage of creating a slit-like meatus, which is more cosmetically appealing. The outcome following the Snodgrass repair (tubularised incised plate) appears to be at least as good. In an early multicentre experience with the tubularised incised plate hypospadias repair, the results in 148 boys were reported from 6 paediatric urology centres. Complications included fistulae in 5%, meatal stenosis in 2% and partial glans dehiscence in 5%. Comparable results have been confirmed in later studies for the use of the tubularised incised plate (Snodgrass) repair for both proximal and distal hypospadias, with approximately 10% of patients requiring reoperation. Concerns have been expressed about the potential long-term risk of stenosis as a consequence of scarring in the incised portion of the urethral plate. However, in a long-term follow-up study only a small percentage required dilatation. Moreover, measurement of voiding flow rates showed that 33/48 patients had normal peak flow rates when corrected for age and 46/48 patients had a postvoid residual of less than 10%.

Two-stage repair

Bracka has reviewed his personal series of 600 patients managed by two-stage repair. In the majority of cases

the neourethra had been fashioned from a free graft derived from inner preputial skin. The first-stage operation required revision in 4% of patients for persistent chordee or to increase the area of meatal skin, whereas the complications of the second stage were fistulae in 6% of patients, with 'redo' or 'salvage' repairs having a higher fistula rate of 10% (compared with 3% for primary procedures). A higher fistula rate was encountered in patients operated on in the earlier part of the series before the introduction of a vascularised dartos flap between neourethra and the skin. Urethral stenoses occurred in 7% of patients. This figure was attributable, in part, to balanitis xerotica obliterans. Long-term functional outcomes in patients following a two-stage repair have recently been reported by a number of centres. Up to 40% of patients report spraying of the urinary stream and some described having to 'milk' the penis following voiding to empty the neourethra to avoid postvoid dribbling. In one study of the functional outcome in 43 adults following reconstruction with buccal mucosal grafts, seven patients (16%) had urinary symptoms, of whom two had experienced severe urinary symptoms. In all, 26% of patients described problems with urinary spraying. This technique does, however, give an excellent cosmetic result.

Urethral advancement

Duckett reported his experience with the MAGPI procedure for the correction of glanular hypospadias in his series of over 1000 patients. Of these, only 1.2% required a secondary procedure. Partial meatal regression is, however, a relatively common problem with this procedure and leads to an inferior cosmetic result.

Pedicle flaps

In the Mathieu repair distal strictures are rare (1%) and fistulae occur in approximately 4% of cases. However, the meatus is often crescentic in appearance, giving a poor cosmetic result. Wide glans mobilisation and a midline dorsal incision of the urethral plate may reduce this problem.

Preputial flaps

This method of repair is often reserved for the more complex cases of hypospadias: consequently, the rate of complications is higher. There is wide variability in the published fistula rate, from 4% to 69%.

Psychosexual outcome

Sexual function following successful hypospadias correction should be unaffected, with normal erectile function and normal prospects of fertility, providing the patient does not have coexisting undescended testicles. The long-term psychosocial and psychosexual outcome of men who have undergone hypospadias surgery is not well documented and those studies that have been undertaken have arrived at differing conclusions. Moreover, because these are long-term retrospective studies, their findings reflect the outcome of techniques which have been superseded by newer operations in the intervening decades. One recent study found that men who had been operated on for hypospadias had similar psychosocial outcomes to age-matched controls who had undergone inguinal herniotomy.

Complications

Early

Operations to correct hypospadias carry the risk of complications that are common to all surgical interventions, but which can severely affect the outcome of the procedure. Because of the vascularity of the penis, **haemorrhage** can often be a concern. Intraoperatively, bleeding can usually be controlled by one of the methods previously discussed. Postoperatively, most surgeons prevent delayed haemorrhage with a compressive bandage; this also acts to reduce the postoperative oedema that occurs following most hypospadias repairs. It is essential to minimise **haematoma** formation, as this can act as a focus for infection and subsequent fistula formation. Care needs to be taken to avoid

wound infections and the need for meticulous haemostasis and tissue handling is paramount. Infection, haematoma formation and ischaemic tissue flaps can all lead to poor wound healing, resulting in fistulae and/or complete breakdown of the repair. Complete dehiscence of the repair is fortunately rare, but when it does occur the subsequent secondary or 'salvage' repair is a daunting task.

Late

The long-term complications of hypospadias surgery are well known and, sadly, all too common. Their incidence rate depends on the initial severity of the hypospadias, the choice of procedure and the skill and experience of the surgeon.

Fistulae

Fistulae are the most common complications following hypospadias surgery, and can occur in up to 30% of patients. A fistula can present acutely immediately after the catheter is removed, or many years after the repair. If the fistula appears acutely many surgeons would replace the catheter for 14 further days with the aim of allowing it to close spontaneously. Although this approach may be effective, many early fistulae persist and require further treatment. The location of a hypospadias fistula varies, but it is often just proximal to the junction of the glans and penile shaft. Occasionally large or multiple fistulae occur, usually indicating that the original urethroplasty was unsatisfactory and needs to be repeated.

Before attempting to repair a fistula it is imperative to exclude meatal and/or distal urethral strictures, as this will predispose to recurrence of the fistula. Fistulae are sometimes associated with urethral diverticula, which need to be excised at the time of the fistula repair.

Repair of hypospadias fistulae should not be dismissed lightly and in some series there has been a 50% recurrence rate. The timing of the closure is important. Although early closure was favoured in the past, it is now recommended that an interval of at least 6 months should elapse after the original repair before fistula closure is attempted. Many techniques have been described. Simple closure, consisting of freshening and then closing the fistula edges and the overlying skin, is associated with a high recurrence rate and is not recommended by the authors. A flap-based repair has also been described, in which the fistula is dissected down to the urethra and the urethral defect closed by inserting absorbable sutures. A flap of skin is then formed from which a vascularised subcutaneous layer is created and placed over the urethral repair. Once the urethra is covered, the skin flap is advanced to close the skin defect. Although more complex, this technique is more effective, with Duckett reporting a 90% success rate.

In some cases the fistula is very large and represents a failure of the original urethroplasty. Surgery that is limited to fistula closure in these cases is generally doomed to failure, and in these circumstances a repeat urethroplasty is invariably required. The use of a urinary catheter following fistula repair is much debated and the success rate in those diverted or left undiverted seems very similar in most series. Therefore, unless there is some doubt about postoperative voiding it is possible to perform a fistula repair without draining the bladder.

Meatal stenosis

Meatal stenosis results from either ischaemia of glans flaps or an inadequately mobilised glans wrap. It can present with difficulty voiding, a narrowed urinary stream, spraying or, in some patients, with urinary tract infections secondary to incomplete bladder emptying. Meatal stenosis can be treated initially with gentle dilatation of the meatus. Although this can be accomplished as an outpatient procedure using a fine-tipped catheter in minor degrees of stenosis, dilatation under general anaesthesia is required for moderate or severe degrees of stenosis. When dilatation alone will not suffice, formal meatotomy is a simple procedure that is generally successful.

Urethral stenosis

Urethral stenosis is a rare problem with modern procedures, which avoid a circular anastomosis. Although strictures can occur at any point along the urethroplasty, they most commonly occur at the distal and proximal ends of the neourethra. Distal stenosis is often associated with a fistula and can usually be treated with regular dilatation but in severe cases a formal surgical repair is necessary. Proximal stenosis is a serious complication which, if severe, often requires complete reconstruction of the urethra.

Persistent chordee

The persistence of penile chordee after hypospadias repair is usually due to inadequate correction at the time of the original repair. In rare cases, however, it may be the consequence of postoperative fibrosis. This complication is easier to avoid – by a good repair and confirmation of correction with an intraoperative artificial erection test – than to treat. In the correction of persistent chordee it is first necessary to deglove the penis completely to exclude skin tethering as the cause. If true chordee is found to be present after this manoeuvre, dorsal plication of the tunica albuginea is usually sufficient to correct it.

Balanitis xerotica obliterans

This rare complication caused by chronic inflammation and fibrosis of the glans and meatus results in scarring and meatal stenosis. Topical steroids help in some patients, but the majority require a formal meatoplasty to correct the stenosis.

Hairy urethra

The presence of hairs within the lumen of the neourethra is a consequence of using hair-bearing skin for the urethroplasty. Its significance lies principally in the potential for hairs to act as a nidus for the formation of urethral calculi. This is largely a historical complication that has been overcome by the introduction of operations utilising non-hair-bearing skin. For patients with a hairy urethra causing symptoms the only effective option is a repeat non-hair-bearing urethroplasty.

Urethrocoele

This term refers to a dilated, 'baggy' section of neourethra, often resulting from distal obstruction that gives rise to 'back pressure' distension of the proximal neourethra. It may also be secondary to an absence or deficiency of supportive corpus spongiosum tissue. A urethrocoele can present with a poor urinary stream, postvoid dribbling, urinary tract infections, swelling of the ventral aspect of the penis at the time of voiding and urethral calculi secondary to stasis. Surgical treatment requires excision of the redundant urethral tissue and treatment of any distal stenosis as necessary.

Key points

- Despite advances in technique, instrumentation and aftercare, the correction of hypospadias remains one of the most technically challenging aspects of paediatric urology.
- There is no place for the 'occasional' hypospadias surgeon, even in the correction of so-called 'minor' hypospadias. Surgeons should have a detailed understanding of the various concepts and surgical techniques and maintain a clinical workload that is sufficient to obtain consistently good results.
- Preservation of the urethral plate is the keystone of modern single-stage procedures; however, there has been a recent revival of the two-stage free flap technique for more complex patients.
- With improving functional results the challenge is now to obtain the optimal cosmetic result to provide patients with a penis of normal appearance regardless of the severity of the original abnormality.

Further reading

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The prepuce

17

Kim AR Hutton

Topics covered

Development and function of the prepuce
Preputial disorders and abnormalities
  Pathological phimosis
  Balanoposthitis
  Paraphimosis, preputial cysts, megaprepuce
Circumcision
Alternatives to circumcision
  Topical steroids
  Preputioplasty

Introduction

The history of circumcision has been well documented, with evidence of the practice dating back to ancient Egypt during the Sixth Dynasty of the Old Kingdom (2345–2181 BC). Although approximately one-third of English boys underwent 'routine' circumcision in infancy in the 1930s, this number has since dwindled to negligible proportions. In the UK, circumcision for non-medical reasons is now virtually confined to those faiths in which ritual circumcision is required to comply with religious beliefs. By contrast, newborn circumcision remains culturally entrenched, regardless of religious faith in the United States, although the legitimacy of this practice is being increasingly challenged. The number of 'medical' circumcisions in children performed in the UK's National Health Service (NHS) has declined progressively over the last three decades. For example, whereas NHS data for England recorded that 18 500 circumcisions were performed in boys aged 0–16 in 1994/1995, the figure fell over the ensuing decade to 10 000 in 2004/2005. This striking reduction in the number of circumcisions occurred almost entirely in district general hospitals and almost certainly reflects fewer unnecessary circumcisions being undertaken by adult surgeons.

An understanding of the valid medical indications for circumcision (or alternative procedures) calls for a knowledge of preputial development before and after birth, and of preputial pathology.

Development and function of the prepuce

Prenatally

First appearing at 8 weeks' gestation as a ridge of thickened epithelium, the prepuce grows forward over the developing glans so that preputial construction is complete by 16 weeks' gestation. At this stage, however, the epithelia lining the prepuce and surfacing the glans are contiguous, with no plane of separation between them, so that 'preputial adhesions' represent a feature of normal development, not a pathological process. Spontaneous separation, commencing late in gestation and usually proceeding proximally, occurs by desquamation, with areas of cell nests degenerating to form a series of spaces that ultimately enlarge and coalesce to form a continuous preputial sac.

Postnatally

Preputial separation after birth proceeds at a rate varying from one individual to another and is uninfluenced by environmental or genetic factors: even at 5 years of age some degree of preputial adherence persists in upwards of 70% of boys. This

process may be accompanied by mild inflammatory episodes, possibly due to infection of retained smegma. At birth the prepuce is almost always non-retractable and usually remains so for a variable period thereafter, during which time attempted retraction results in the appearance of a blanched and apparently constricting ring of skin proximal to the preputial meatus (Figure 17.1). Viewed end-on, the preputial orifice is supple and unscarred, with an opening likened to a flower as the foreskin is pulled back (Figure 17.2).

Although normal, developmental, non-retractility of the foreskin is often termed 'phimosis' (Ψιμοσισ 'muzzling' in Greek). This is misleading as it implies the existence of pathology when in reality there is none. 'Non-retractile foreskin' or 'physiological phimosis' are thus more appropriate terms.

In younger boys the natural history of non-retractile foreskin and preputial adhesions was documented by Gairdner in 1949 and in older boys by Øster in 1968. Their findings, summarised in Figure 17.3, show unequivocally that the foreskin, if left alone, becomes fully and easily retractable by physical maturity in all but a tiny minority of boys (probably around 1%).

'Ballooning' of the foreskin during micturition is a common phenomenon in the period of early childhood when the foreskin is still non-retractile, but when substantial preputial separation has taken place. Typically occurring between 2 and 4 years of age ballooning calls for no treatment as it is both transient and self-limiting, resolving as the prepuce becomes more retractable. Concerned parents can be confidently reassured that neither non-retractility nor ballooning are indicative of obstructed voiding, as non-invasive studies have established that urine flow rates (Figure 17.4), postvoid residual bladder volumes and bladder wall thickness are unaffected by physiological phimosis.

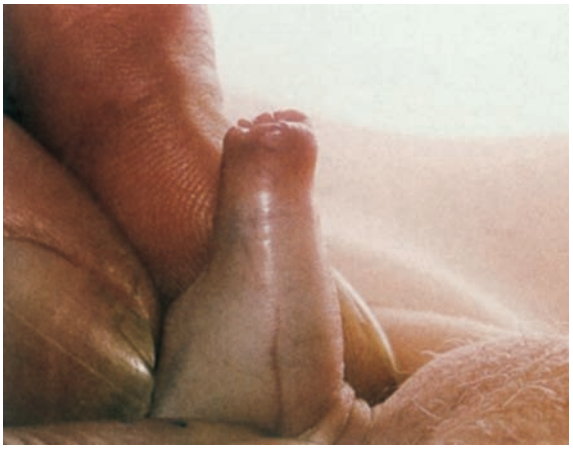

Figure 17.1 Developmentally non-retractile foreskin: attempted retraction reveals an apparent constriction ring a few millimetres proximal to the preputial orifice.

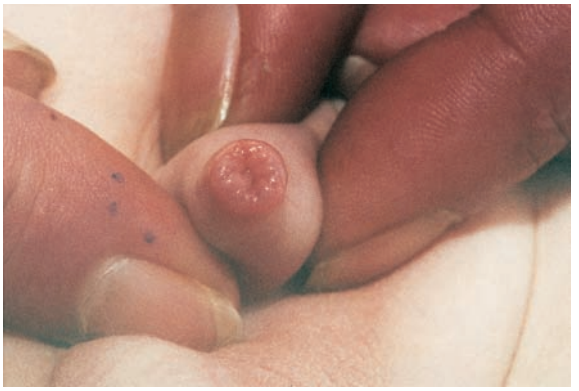

Figure 17.2 Developmentally non-retractile foreskin: on attempted retraction, the preputial orifice opens as a flower with a moist, supple and unscarred appearance to the pouting inner preputial mucosa.

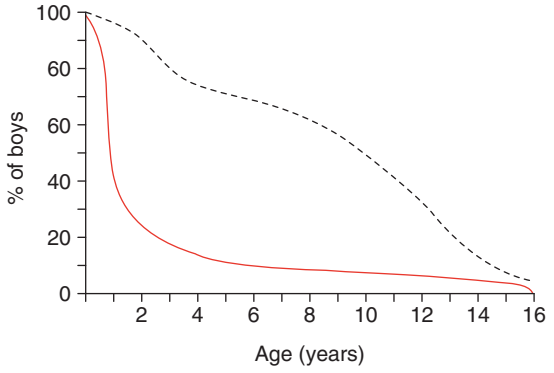

Figure 17.3 Natural history of non-retractile foreskin (red) and of preputial adhesions (black) (from Gairdner (1949) and Øster (1968)).

Preputial function

Although the prepuce serves no essential physiological function, it is not wholly without purpose. In the first instance, the foreskin typically remains non-retractable prior to toilet training, thereby – perhaps coincidentally, perhaps not – protecting the glans penis and its meatus from ammoniacal inflammation and hence meatal ulceration or subsequent stenosis.

The other consideration is that of sexual satisfaction. In contrast to the glans, which is innervated principally by free nerve endings mediating poorly localised sensations, the prepuce has a rich somatosensory innervation forming an important component of the normal complement of penile erogenous tissue. Amputation neuromas may follow circumcision. Moreover, this procedure not only removes some 30% of the penile skin, plus the greater part of the muscular component of the dartos layer, but also leaves the surface of the glans to undergo keratinisation. However, because of the highly subjective nature of sexual pleasure it is impossible to draw meaningful comparisons between the circumcised and the uncircumcised state other than on a purely anecdotal basis.

Preputial disorders and abnormalities

Balanitis xerotica obliterans

True pathological phimosis with scarring of the preputial orifice (Figures 17.5 and 17.6) is caused by the chronic cicatrising skin condition **balanitis xerotica obliterans** (BXO). The disease process is histologically identical to lichen sclerosis et atrophicus of the vulva and affects the prepuce, glans and occasionally the urethra. Histological findings are characterised by the following features – hyperkeratosis with follicular plugging, atrophy of the stratum spinosum Malphigi with hydropic degeneration of basal cells, lymphoedema, hyalinosis, homogenisation of collagen in the dermis and an associated band-like chronic inflammatory cell infiltrate (Figure 17.7). The disorder typically presents with irritation, local infection, dysuria, bleeding, secondary non-retractability of the foreskin or a deteriorating urinary stream. On rare occasions it can progress to the point of presenting with acute urinary retention or secondary diurnal or nocturnal enuresis resulting from chronic outflow obstruction.

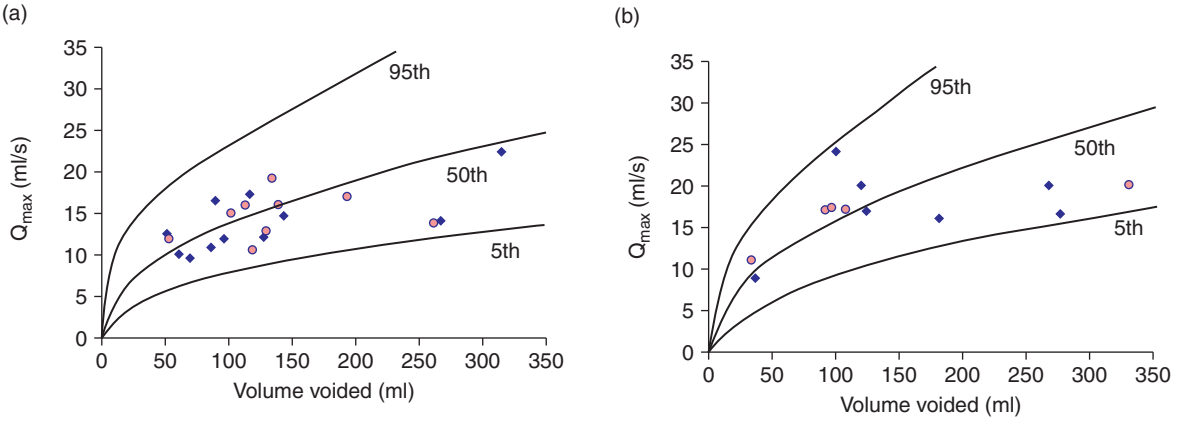

Figure 17.4 Uroflow age-related nomograms plotted with the Q_{max} and voided volume data for 32 boys with physiological phimosis: (a) nomogram for 3–7 year olds; (b) nomogram for 8–12 year olds. The blue diamonds represent flow data from patients with, and pink circles from boys without, ballooning of the foreskin. The two groups have a similar distribution of flow rate values and all points are within the normal range. (Reprinted with permission.)

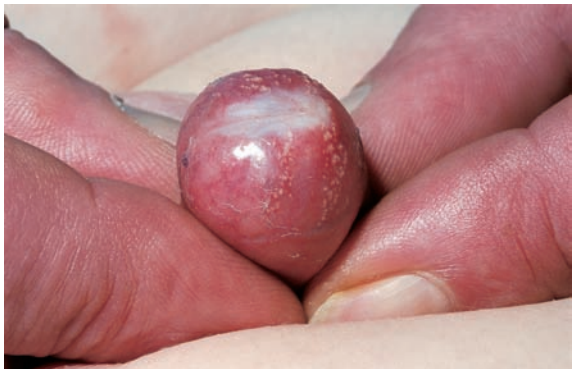

Figure 17.5 Pathological phimosis due to balanitis xerotica obliterans. Characteristic pallor, scarring and stenosis of the prepuce.

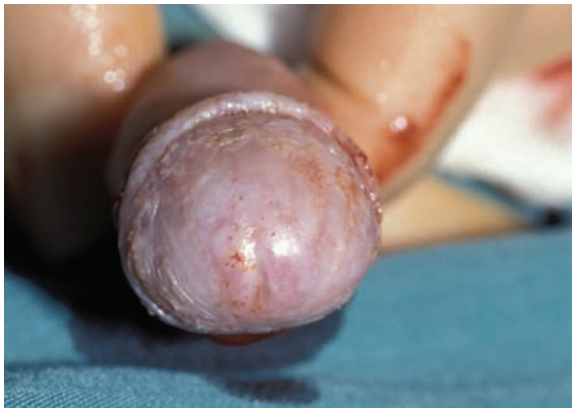

Figure 17.6 BXO, extensive glanular involvement and meatal stenosis.

Ultrasonography in cases with obstructive symptoms may disclose thickening of the bladder wall and/or significant residual urine, although only very rarely secondary dilatation of the upper renal tracts.

BXO is rare under the age of 5 years old, with a peak incidence in boys aged 9–11 years old (76%), and is estimated to have affected 0.6% of boys by their 15th birthday. Glanular involvement occurs in 49% of cases, although the meatus is affected in only a small proportion.

The **aetiology of BXO** is unknown, with no familial predisposition, or any identifiable causative bacterial or viral agent. There is no association

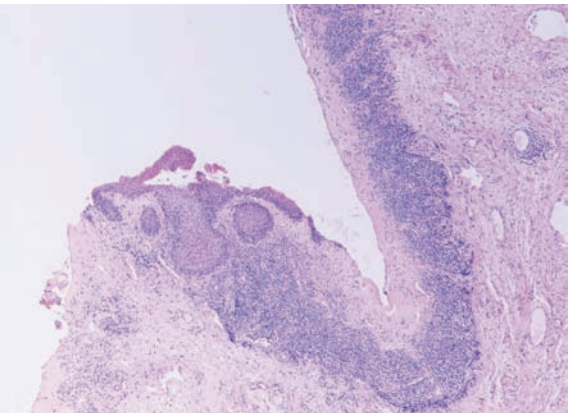

Figure 17.7 Characteristic histological features of BXO, including an acellular band/layer between the epithelium and deeper dermis and a band-like chronic inflammatory cell infiltrate.

with puberty and, contrary to widespread belief, BXO does not result from recurrent balanoposthitis (Figure 17.8).

The preferred **treatment** is circumcision: indeed, pathological phimosis constitutes the only absolute indication for this procedure in boys. Preputioplasty is not an option as the continuing inflammatory process results in recurrent stenosis of the preputial orifice. Glanular involvement nearly always resolves following circumcision. However, meatal involvement calls for simultaneous meatotomy or meatoplasty in approximately 5% of cases and postoperative application of topical steroid creams may lessen the risk of subsequent restenosis. Parents should be notified of the risk of recurrent meatal stenosis and follow-up is also advisable for this reason.

In boys presenting with milder forms of BXO, the application of a potent topical steroid (e.g. 0.05% mometasone furoate, 0.05% clobetasol propionate or 0.05% betamethasone cream) may ameliorate local symptoms and result in an improvement in the appearances of the foreskin. But while this approach may afford symptomatic relief, it is rarely curative and delays rather than avoids the need for circumcision. Misguided attempts to persist with medical management despite progressive BXO carry the risk that the

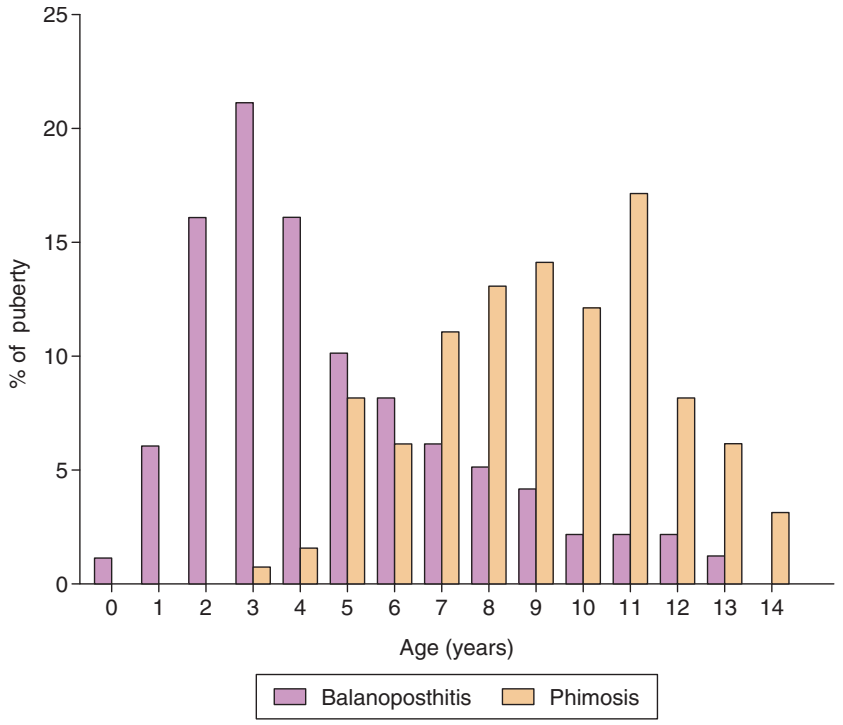

Figure 17.8 Age distributions of pathological phimosis (orange) and of balanoposthitis (purple) (Urology Department, Alder Hey Children's Hospital, 1984–99).

partially treated sclerotic process may extend to involve the meatus and distal urethra.

In adults there is an association between BXO and penile cancer (28% of patients with penile malignancy have BXO), although a specific causal relationship is uncertain. The relevance of this association to paediatric patients is unknown since there are no data documenting the long-term outcome for boys with BXO followed into adulthood.

Acute balanoposthitis

In its full-blown form, acute balanoposthitis consists of purulent, pyogenic, infection of the entire preputial sac. Typically this is accompanied by purulent discharge and overlying oedema of the prepuce that may, on occasion, spread to involve the skin of the entire penile shaft. In the lesser severe forms of the condition, more properly termed posthitis, the inflammatory process is limited to the preputial orifice and the outer reaches of the lining of the foreskin, resulting in localised erythema and oedema, along with corresponding irritation, but not purulent discharge. Dysuria is a common complaint and minor bleeding from the preputial orifice may also occur. Urinary infection is the only **differential diagnosis** and may be distinguished from balanoposthitis by the absence of preputial symptoms and signs.

Balanoposthitis is comparatively infrequent prior to toilet training, perhaps because ammonia inhibits the growth of pathogens. Common causative organisms are *Staphylococcus aureus*, *Escherichia coli* and *Proteus* spp., although in a third of cases the preputial discharge is sterile on culture. Balanoposthitis occurring when the prepuce is fully and easily retractable should arouse suspicion in older boys, as it may be the presenting feature of diabetes mellitus.

Treatment comprises antibiotic therapy for acute episodes, where indicated, and attention to hygiene. Beyond the acute episode, therapeutic intervention should be restricted to boys who suffer recurrent episodes. Because the complaint is typically associated with complete or partial non-retractility of the foreskin, preputioplasty or preputiolysis (according to individual circumstances) should be considered as surgical alternatives to circumcision. Topical steroid creams represent another option.

Schönlein–Henoch purpura involving the penis

The preputial and penile swelling and oedema sometimes associated with this condition may be confused with balanoposthitis if these features appear before the characteristic purpuric rash on the legs, lower abdomen and buttocks. Likewise, idiopathic scrotal oedema can occasionally extend up from the perineum to involve the penile shaft, although this is unlikely to cause diagnostic uncertainty.

Paraphimosis

This is a rare condition in boys which is related to manipulations of the foreskin and a failure to draw the prepuce forward again following retraction, with resultant congestion and oedema of the prepuce and glans (Figure 17.9). Often the boy has been encouraged to retract the foreskin for physiological phimosis by parents or medical staff. Iatrogenic paraphimosis can occur following catheterisation if the foreskin is not reduced. Paraphimosis does not signify underlying foreskin disease and an isolated episode is not an indication for circumcision. It is only seldom necessary to resort to a dorsal slit and in most instances reduction can be achieved by reducing the preputial oedema by manual compression, multiple needle puncture or topical cooling then drawing the foreskin forwards over the glans employing EMLA cream as a topical local anaesthetic. Recurrent episodes are exceptional and constitute the only indication for circumcision with this complaint.

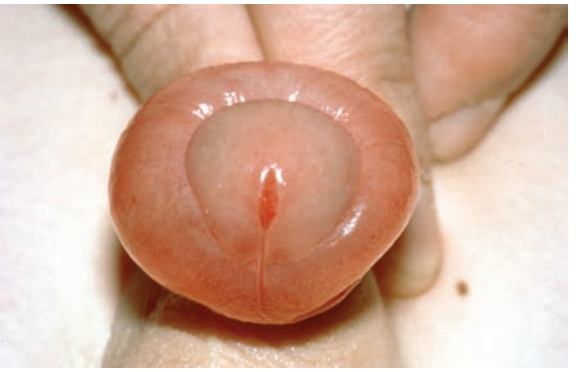

Figure 17.9 Paraphimosis. There is oedema of the foreskin and glans due to a constriction ring at the subcoronal level.

Preputial cysts and adhesions

Depending on age, preputial adhesions are a normal phenomenon and resolve spontaneously through childhood, as described by Gairdner in 1949. Some boys present with one or more yellowish lumps on the penis that are often diagnosed by the general practitioner as sebaceous cysts or lipoma of the penile shaft. Invariably, on outpatient assessment, these prove to be collections of retained **smegma** trapped by surrounding preputial adhesions (Figure 17.10). Reassurance is all that is required, as the smegma is released when the adhesions lyse spontaneously over time.

There is a very limited role for the surgical release of **preputial adhesions** in the management of recurrent balanoposthitis and such patients may be better served with a circumcision or preputioplasty (see later). Occasional examples are seen of **true retention cysts** of the prepuce. Localised retention cysts can be enucleated, but more diffuse lesions call for circumcision.

Congenital megaprepuce

This rare condition has only recently received recognition as an entity in its own right and it is possible that it represents a genuinely new pathology. On cursory inspection it resembles a buried penis, but closer examination reveals an

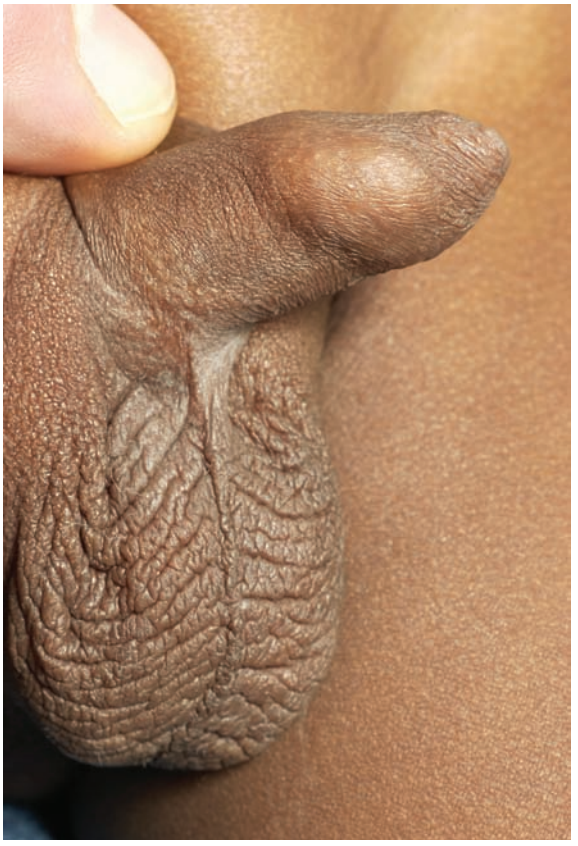

Figure 17.10 Smegma retention 'cyst'. The mobile, subcutaneous, firm lump at the coronal level has a yellowish appearance and is often misdiagnosed in primary care as a dermoid cyst or lipoma.

enormously capacious preputial sac, engulfing the whole penile shaft and upper scrotum (prompting the term 'preputial bladder'). Urine dribbles more or less continuously from the preputial orifice and, although the capacious urine-filled sac can be readily emptied by compression, there is never a normal urinary stream. Almost nothing is known of the natural history of the deformity and whether or not it tends to improve over time, since surgery is usually undertaken because of functional and cosmetic concerns (Figure 17.11). The correction of congenital megaprepuce can be a significant technical challenge and considerable experience is required to achieve a good cosmetic result. The main problems stem from a deficiency of penile shaft skin, an absence of defined penopubic and penoscrotal angles and a marked excess of inner preputial 'mucosa'. Various reconstructive procedures have been described which result in a circumcised penis. Revision surgery is not uncommon for redundant penile skin or recurrence of the buried appearance.

Circumcision

Religious circumcision

The ethical issues surrounding religious circumcision are beyond the scope of this chapter but centre principally on concerns that scarcely any boys being submitted to the procedure are in a position to give informed consent. Although there is some variation between different areas of the UK, religious circumcision is not generally funded within NHS hospitals. However, in some cities with a large Muslim population, circumcision services are provided under the auspices of local NHS organisations. Religious circumcisions in the Muslim faith are otherwise undertaken in the community by general practitioners and other medically qualified practitioners and in the Jewish community by mohels – trained circumcisers who may or may not be medically qualified.

'Routine' circumcision

Most medical arguments previously advanced in justification of newborn circumcision, including a reduced risk of venereal disease or carcinoma of the penis for the patient, or of carcinoma of the cervix in a prospective spouse, have largely been discounted. However, there is now good evidence from recent randomised trials in sub-Saharan Africa that circumcised adults are relatively protected from infection by the human immunodeficiency virus (HIV). Thus routine circumcision may become an important healthcare measure in developing countries with a high prevalence of **HIV infection**.

Otherwise, the only other possible justification relates to the risk of **urinary tract infection (UTI)**.

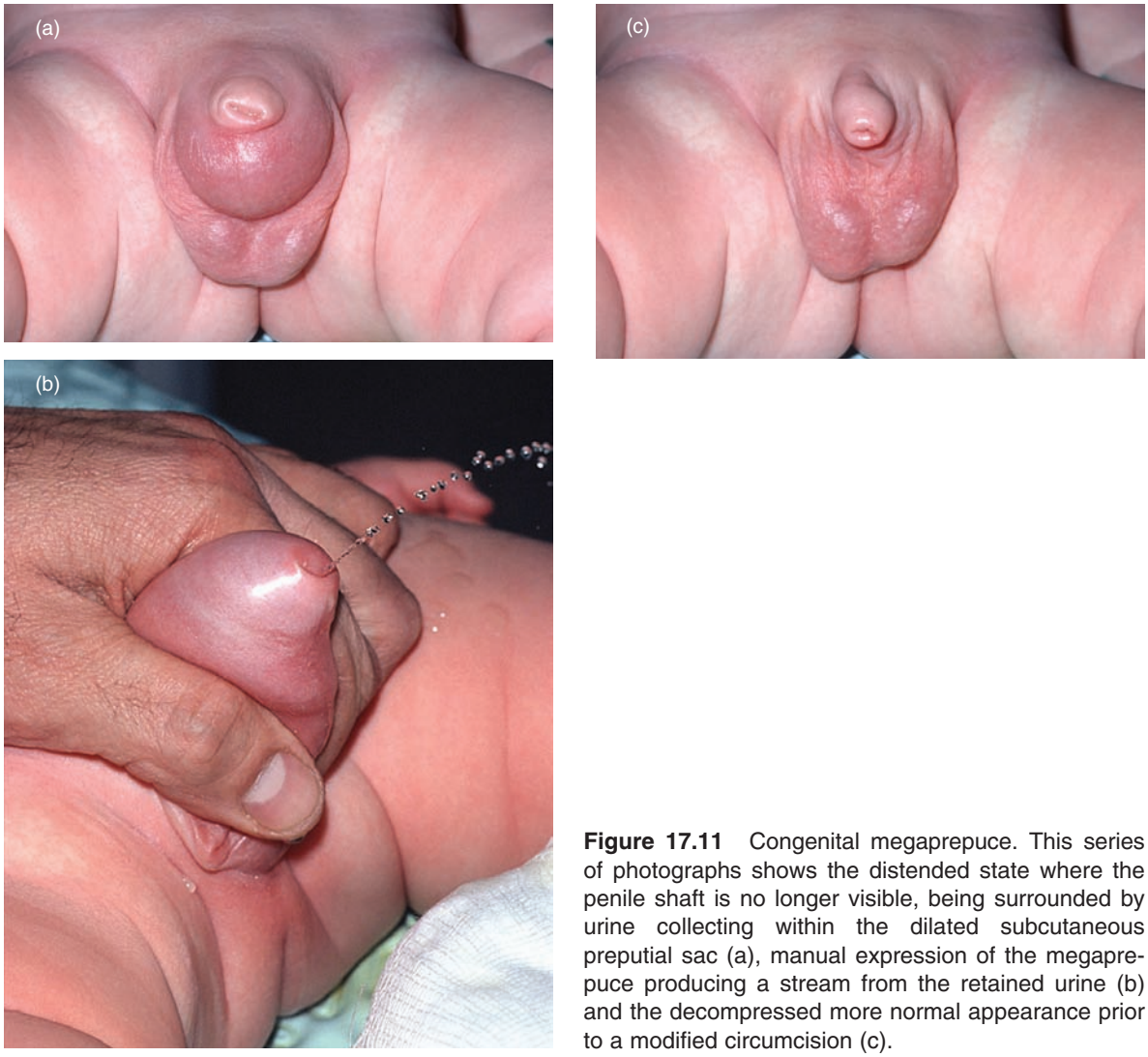

Figure 17.11 Congenital megaprepuce. This series of photographs shows the distended state where the penile shaft is no longer visible, being surrounded by urine collecting within the dilated subcutaneous preputial sac (a), manual expression of the megaprepuce producing a stream from the retained urine (b) and the decompressed more normal appearance prior to a modified circumcision (c).

It has long been recognised that during the first year of life UTI occurs more frequently in boys than in girls and, moreover, that the risk of a UTI is six to ten times higher in uncircumcised boys. Nevertheless, the absolute incidence of UTI is low, and it has been calculated from a systematic review of randomised trials and observational studies that the number needed-to-treat to prevent one UTI in normal boys is 111. Routine neonatal circumcision is clearly not justified as a routine prophylactic measure on this basis. However, there is more persuasive evidence that circumcision is beneficial in reducing the risk of UTI in male infants with predisposing urinary pathology, such as vesicoureteric reflux or urinary dilatation resulting from congenital urethral obstruction. In boys with recurrent UTI or high-grade vesicoureteric reflux, the risk of UTI recurrence is 10% and 30% and the numbers needed-to-treat are much less at 11 and 4, respectively. However, performing circumcision at the

time of antireflux surgery does not reduce further the incidence of postoperative UTI.

Circumcision for medical indications

The principal indications cited for medical circumcision in the UK are 'phimosis' and balanoposthitis. In Scandinavian countries approximately 2% of boys are circumcised for medical reasons and although the percentage has historically been considerably higher in the UK the percentage has almost fallen to the Scandinavian level over the last decade, currently standing at around 3% for boys aged 0–16 years old. Nevertheless, it is almost certainly the case that unnecessary circumcisions are still being performed, particularly for physiological phimosis in boys under 5 years old (an age at which BXO is virtually unheard of and non-retractility of the healthy prepuce is the norm).

Contraindications to circumcision

All parents of boys with hypospadias, as well as those with epispadias or ambiguous genitalia, should be advised not to have their son circumcised as the foreskin may be required for reconstructive purposes. Special considerations relating to buried penis are outlined below. A family history of bleeding disorder is a relative contraindication to circumcision. In this context, excessive postoperative haemorrhage after circumcision may be the first manifestation of a bleeding disorder such as factor VIII deficiency.

Surgical aspects

The techniques employed for neonatal circumcision will not be considered here. Circumcision performed for genuine medical indications should be undertaken as a formal surgical procedure under general anaesthesia, with additional local anaesthesia (caudal or penile block) to provide postoperative analgesia. The details of technique are a matter of individual surgical preference, but the following general points should be observed:

- Care should be taken to ensure that the prepuce is completely separated from the underlying glans and coronal sulcus prior to circumcision. Failure to do so may result in the formation of persistent skin bridges between the glans and the penile skin.
- The outer and inner layers of preputial skin should be excised separately and trimmed further if necessary to ensure the best cosmetic result. For this purpose some surgeons delineate the planned incisions with a marking pen. Failure to excise sufficient of the outer layer may leave redundant penile skin, resulting in an unsatisfactory cosmetic outcome (incomplete circumcision) and a requirement for secondary surgical revision.
- Conversely, removal of too much skin may leave insufficient to cover the penile shaft. This risk is greatest in boys with so-called 'buried penis', in whom even a standard circumcision may result in a denuded penile shaft and a requirement for skin grafting. A modified technique is required in such cases, to redistribute rather than remove preputial skin.
- Careful attention to haemostasis is important to minimise the risk of postoperative haemorrhage. Bipolar diathermy is more effective than ligation of individual vessels. Laser circumcision has been shown to have a low risk of postoperative haemorrhage.
- Sutures chosen for skin closure (e.g. Vicryl Rapide) should be rapidly absorbed to reduce the incidence of suture tract formation, whereas some surgeons employ subcuticular sutures to minimise this risk. The use of tissue glues instead of sutures is well documented in sizeable series and has been claimed to reduce operative times and improve cosmetic appearances.

The choice of postoperative dressing (if any) is also a matter of individual preference. Many surgeons

avoid dressings because of the distress caused by their removal.

Complications of circumcision

Parents should be made aware that there is an appreciable incidence of postoperative distress and morbidity following circumcision. Early complications include urinary retention and haemorrhage. The former can be prevented by adequate analgesia or intraoperative local block with levobupivacaine. As a rule, any subsequent difficulty with micturition can be relieved by sitting the boy in a warm bath and allowing him to urinate in the water, while on occasion oral diazepam can sufficiently relax the urethral sphincter to avoid a full-blown episode of acute retention. Haemorrhage of sufficient severity to necessitate early reoperation is reported to occur in 2–5% of boys. The most common postoperative problem is encrustation, scabbing and infection of the exposed glans. Meatal stenosis occurs in a small proportion after circumcision. Major complications such as severe sepsis, urethral fistula, injury to the glans and partial penile amputations are virtually confined to religious circumcisions performed in the community (Figures 17.12 and 17.13).

Alternatives to circumcision

These are designed not to treat pathological phimosis due to BXO but rather to render a normal foreskin fully retractable at an earlier age than would otherwise have been the case. Although such intervention is often well worthwhile for boys troubled by localised symptoms or recurrent balanoposthitis, it is not justifiable simply as a response to parental pressure prompted by concerns about non-retractility of the foreskin or 'ballooning'. Reassurance and an explanation of the natural history of the healthy non-retractile foreskin should be employed in this situation.

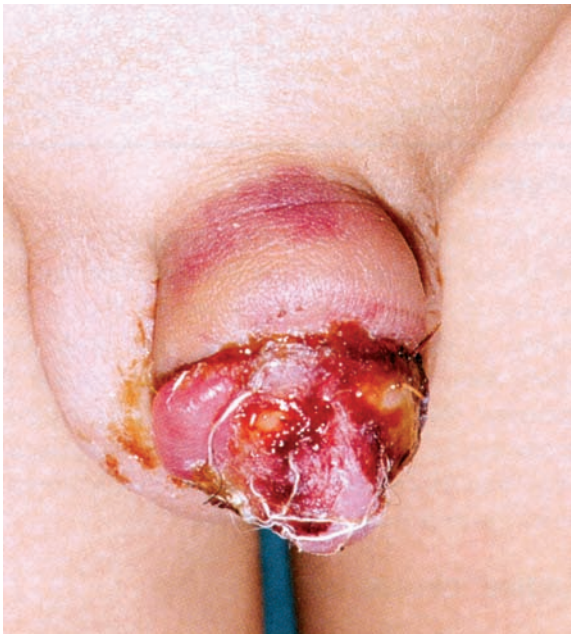

Figure 17.12 Complication of circumcision. Child admitted to hospital following religious circumcision. Excoriation and infection of the glans.

Topical steroids

There are now many retrospective and prospective studies unequivocally demonstrating that a range of steroid creams can alter the characteristics of the foreskin, rendering it retractable earlier than would naturally have been the case. Postulated modes of action relate to the anti-inflammatory and antiproliferative properties of topical steroids. There may also be effects on extracellular matrix composition.

Although the literature consists largely of observational and uncontrolled studies, it does include at least eight controlled studies – indicating that the beneficial effect is genuinely attributable to the steroid component, not simply a non-specific physical effect of the cream or ointment. Unfortunately the entry criteria into these studies are usually poorly defined and the extent, if any, to which they included cases of early BXO is unclear. It is difficult to escape the impression, however,

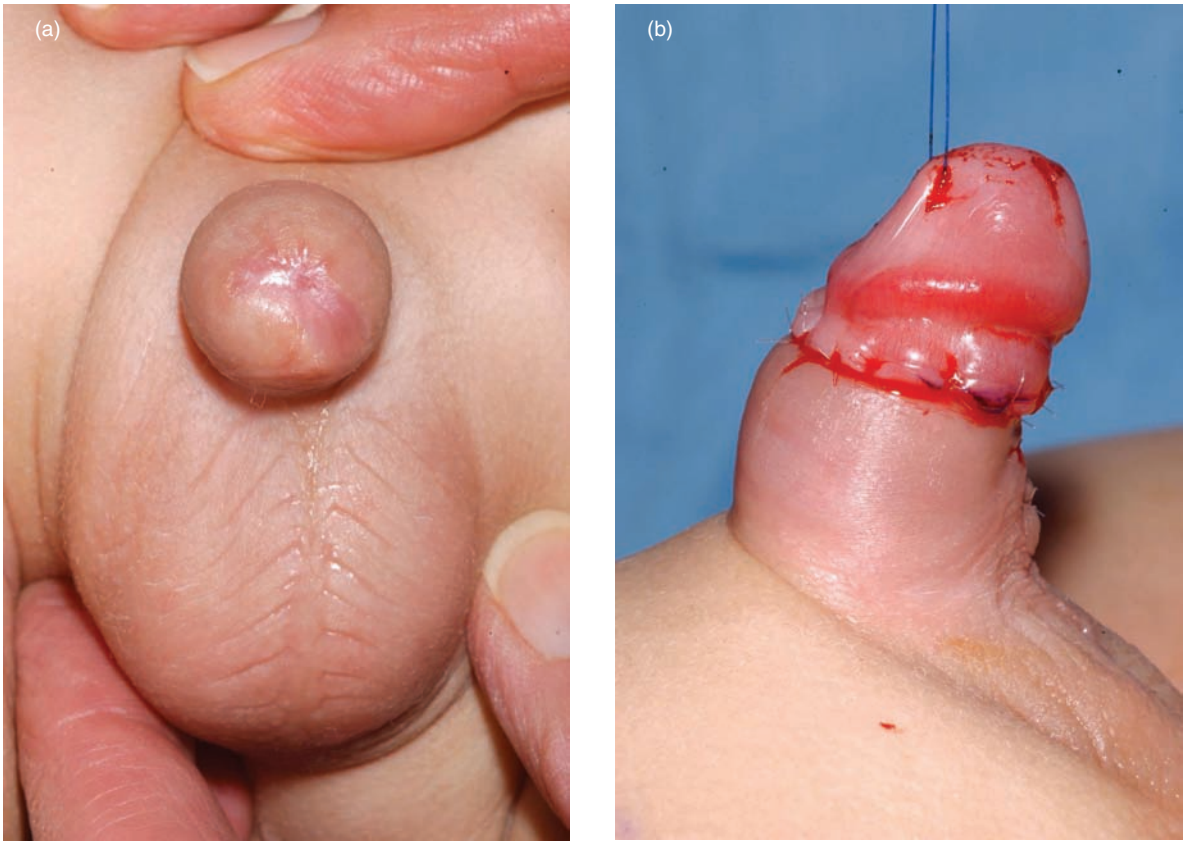

Figure 17.13 (a) Iatrogenic buried penis due to scarring and occlusion of the residual skin following ritual circumcision. (b) Appearances following surgical release and revision of circumcision.

that the favourable results reported by these studies were obtained predominantly in boys with healthy non-retractile foreskins. Various different steroid preparations have been used (including 0.05% betamethasone cream, 0.05% clobetasol propionate cream and 0.02% triamcinolone acetonide cream), usually with a twice daily application for 4–8 weeks and a repeat course if initial results are unsatisfactory. Although 'success rates' of 70–95% have been reported, 'success' is often loosely (and subjectively) defined, with some authors regarding it as full retraction whereas others extend the definition of 'success' to encompass partial responders or boys with retractability deemed 'appropriate for age' following treatment. Application of the steroid cream must be combined with regular attempts at retraction of the prepuce to achieve success. One consistent finding to emerge from all the studies is that this form of treatment is safe and free of complications.

Preputioplasty

In boys where intervention is felt necessary for a tight non-retractile foreskin, a preputioplasty may be a sensible option allowing foreskin preservation. Performed under general anaesthetic, this consists of incising the 'constriction ring' apparent on retracting the foreskin and closing the incision transversely with interrupted sutures

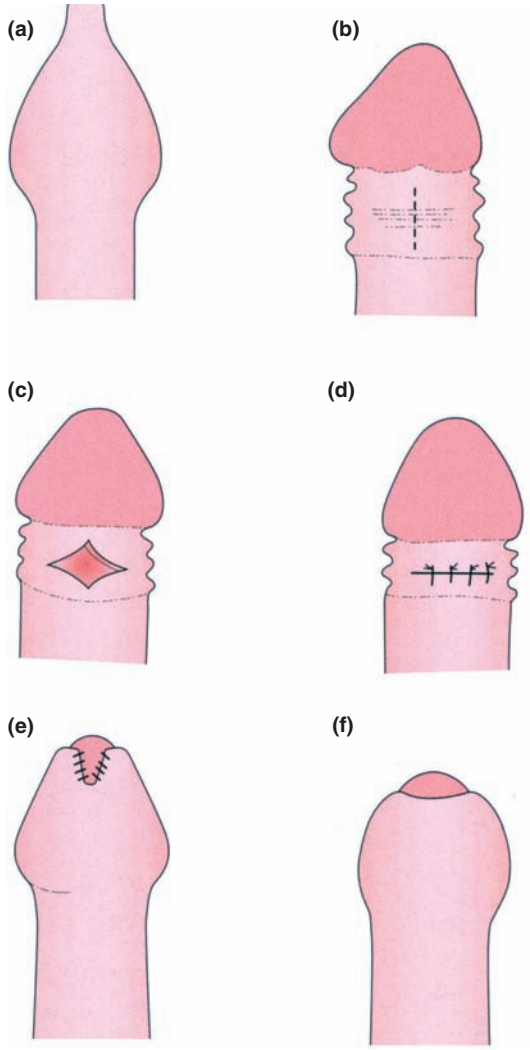

Figure 17.14 Technique of preputioplasty. (a) Adhesions divided, prepuce retracted. (b) Constricting ring incised and (c, d) incision closed transversely. (e) 'Dorsal slit' appearance on completion of the procedure evolves into normal retractile prepuce (f) if retraction is undertaken regularly in the ensuing weeks.

(Figure 17.14). A single incision has a tendency to leave an initial cleft-like deformity, resembling a limited dorsal slit, although this improves with time. For this reason various modifications have been described using multiple incisions or Y-V plasties. The procedure is contraindicated in the presence of BXO and success depends on early and frequent retraction of the prepuce postoperatively once oedema and pain have settled. It is a good alternative to circumcision when used selectively, ideally in older boys who are able to cooperate with the postoperative regimen of regular retraction.

Key points

- Although the foreskin is almost always unretractable at birth, it spontaneously becomes fully and easily retractable in approximately 99% of boys by 16 years of age.
- Conservative treatment of the non-retractable foreskin involves educating the parents on the natural fate of the foreskin.
- Effective alternative treatments for the non-retractable foreskin include the use of topical steroid therapy and, on occasion, preputioplasty.
- Surgical intervention for balanoposthitis can reasonably be considered for boys troubled by recurrent episodes and may take the form of preputioplasty and/or preputiolysis rather than circumcision.
- Pathological phimosis due to balanitis xerotica obliterans affects only 0.6% of boys and is rare under the age of 5.
- Balanitis xerotica obliterans is the one absolute indication for circumcision.

Further reading

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Testis, hydrocoele and varicocoele

18

Nicholas P Madden

Topics covered

Undescended testis
- Epidemiology
- Impalpable testis, retractile testis, ascending testis
- Fertility, malignancy

Hydrocoele

Varicocoele

Introduction

Orchidopexy and operations for hydrocoele (so-called 'groin surgery') are among the commonest elective surgical procedures of childhood, and the management of varicocoele is increasingly entering the sphere of paediatric urological practice. Despite the frequency of these conditions, several important aspects of the long-term functional outcome of orchidopexy and the treatment of varicocoele remain unresolved. The reasons lie partly in the lengthy interval between intervention and outcome (plus the difficulty of devising reliable prospective studies) and partly in the problems inherent in measuring fertility. The embryological basis of cryptorchidism and hydrocoele, the normal mechanism of testicular descent and the role of the processus vaginalis are described in Chapter 1.

The well-documented phenomenon of secondary testicular ascent is addressed below under the separate heading 'Ascending testis'. For ease of understanding throughout this chapter, the terms 'cryptorchidism' and 'undescended testis' will refer to congenital maldescent.

Incidence

The incidence of cryptorchidism appears to be increasing. An authoritative study in the 1950s put the figure at 0.8% at 1 year of age, whereas subsequent work in the 1980s based on similar criteria documented an incidence, of 1.55%. Hospital discharge data collected in England in the early 1990s indicated that at that time the orchidopexy rate for boys in England and Wales was considerably higher than either of these estimates of incidence, at approximately 3%. Over the period 1994–2004, however, the orchidopexy rate in England fell by a third, the most plausible explanation being a reduction in the number of inappropriate procedures performed on retractile testes. The calculations are now further complicated by the acceptance of the well-documented phenomenon of secondary testicular ascent. In summary, the best current estimate of the incidence of testicular maldescent (both congenital and acquired) is probably of the order 1.5–2%.

In boys born at term the testis should be in the scrotum and, where it is not, spontaneous descent thereafter is comparatively unusual. By contrast, premature infants have a significantly higher incidence of undescended testes, and in these infants spontaneous testicular descent frequently occurs during the first 3 months of life (Table 18.1).

Pathology

Congenitally undescended testes develop progressive histological changes during the first few years of life, with defective transformation of gonocytes and loss of germ cells. These changes are most

Table 18.1 Incidence of undescended testis in low birthweight premature infants

	Incidence of undescended testis (%)	
Birthweight (g)	At birth	At 3 months
<2000	45.4	7.7
2000–2499	13.4	2.5
>2500	3.8	1.4

apparent from 2 years of age onwards. In gonads not brought into the scrotum, this histological picture progresses to one in which there is complete loss of germ cells (so-called 'Sertoli cell only' appearances). Seminiferous tissue accounts for the bulk of testicular volume and its loss therefore results in atrophy of the testis and azoospermia. Eventually, carcinoma in situ may supervene, being present in up to 25% of testes retained in an intra-abdominal position into adult life. The histological changes observed in cryptorchidism probably represent the outcome of a combination of temperature-related damage, pituitary–gonadal dysfunction and underlying dysplasia. Undescended testes are also associated with an appreciable incidence of coexisting congenital abnormalities of the epididymis and vas which, in their own right, may further contribute to impaired fertility in later life.

It should be noted that congenitally maldescended testes are almost always associated with a completely patent processus vaginalis or, occasionally, a frank inguinal hernia. However, genuinely ectopic testes represent an exception to this rule, as these gonads have descended fully but to the wrong site.

Testicular dysgenesis syndrome has been proposed as a unifying concept to explain the association between undescended testes, testicular malignancy, reduced fertility and hypospadias. The limited biopsy data relating to ascending testes reveals similar histological changes to those associated with congenitally undescended testes retained into later childhood. If confirmed by further studies, this would provide further evidence of the role of elevated temperature as a major factor in degenerative damage.

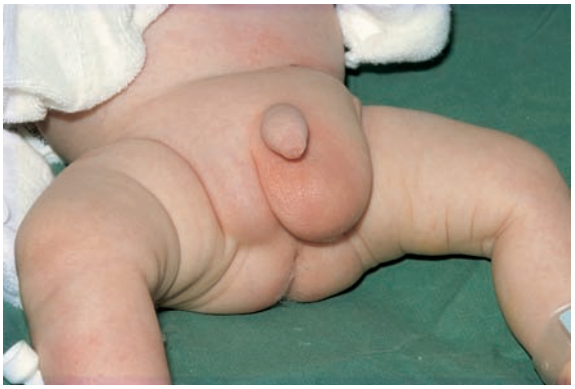


Figure 18.1 Right ectopic testis. Empty right hemiscrotum, and a visible swelling (ectopic testis) in the perineum lateral to the scrotum.

Classification

Because of the implications for clinical management, the most practical distinction lies between the palpable and the impalpable testis.

The anatomical classification of undescended testis can be further subdivided into maldescended testes, lying somewhere along the normal line of descent, and ectopic testes lying outside that line. Ectopic gonads are most commonly encountered in the perineum, lateral to the scrotum (Figure 18.1), occasionally in the thigh, and exceptionally, as crossed ectopia, in the contralateral hemiscrotum. Although undescended testes are often to be found within the 'superficial inguinal pouch', this location is no longer considered to be 'ectopic'.

Presentation

In the UK, undescended testes are most frequently diagnosed during the course of the examination routinely performed in all newborns. If at this stage the testis is not in the scrotum, its position should be reassessed at 3 months of age (or 52 weeks postconceptual age in premature infants). It should be noted that at birth, and for the first 3 months of life, the cremasteric reflex is absent, so that the true location of the gonad is easier to

assess than at other times in infancy and childhood. Testicular maldescent is also sometimes identified for the first time during routine developmental assessments at 6–8 months of age, or during subsequent school medical examinations.

The right testis is more commonly undescended than the left, and in approximately 25% of cases of cryptorchidism the condition is bilateral.

Older boys referred with 'undescended testis' more commonly prove to have a retractile or ascending gonad. The term 'retractile testis' should be confined to those where the testis, wherever sited initially, can nevertheless be brought fully to the floor of the scrotum without tension on the spermatic cord. It is important to note that a cremasteric reflex can sometimes also be elicited in congenitally maldescended testes, and hence the distinction between maldescent and retractility is not always so clear-cut as was once believed.

History

History is straightforward if referral is made directly from a maternity unit. When boys are referred at any later stage the information recorded in the neonatal notes regarding the location of the testes at birth can be helpful. However, these findings are not always reliable and in most instances this information is lacking, and so the history assumes importance. Occasionally, transient testicular descent has been observed, typically during a warm bath, in which case the diagnosis is almost certainly one of retractile testis. In the absence of such a history the parents should be asked whether the possibility of testicular maldescent was mentioned at birth, at subsequent routine checks during infancy or, in older boys, at any school medical examination. If the answer to these questions is 'no', there is strong presumptive evidence that the testis was, at some stage, fully descended.

Examination

Examination begins with scrotal inspection. Not infrequently, both gonads are to be seen at the base of the scrotum, in which case the diagnosis is evidently one of retractile testis. Sometimes there is obvious asymmetry of the scrotum, whereas in other instances, where bilateral maldescent is suspected, the scrotum appears to be 'small'. However, because the scrotal skin is highly sensitive to external temperature, a 'small' scrotum, or one exhibiting asymmetry, cannot be taken as reliable evidence of true testicular maldescent. The examiner's hands must not be cold and examination should be conducted in a relaxed, warm environment. Palpation may be facilitated by the application of talcum powder to minimise friction between the examiner's hands and the patient's skin. Starting laterally to the right internal ring, the left hand moves down the inguinal canal, 'milking' the testis towards the scrotum. Once the left hand reaches the pubic tubercle, the right hand is employed to locate the testis and to draw it downwards towards the scrotum.

A testis which can be readily manipulated from the groin to the floor of the scrotum, and which remains there, is evidently 'retractile' and, as such, normal (Figure 18.2). In other instances, although the testis can be brought to the base of the scrotum, this is only with some difficulty and is followed by immediate ascent once traction is released, a situation commonly termed 'high retractile testis'.

Thickening of the spermatic cord may be indicative of a persistent processus vaginalis, and very occasionally – usually in infants – there is an inguinal hernia. Care should be taken not to overlook ectopic gonads, which are most often to be found in the perineum immediately lateral to the scrotum. Where one testis is impalpable, hypertrophy of the contralateral testis (see below) suggests that the impalpable gonad is absent, although this finding is not sufficiently reliable to avoid the need for laparoscopy.

Management

Hormonal treatment

Although success rates in excess of 50% have been reported in uncontrolled studies, these almost

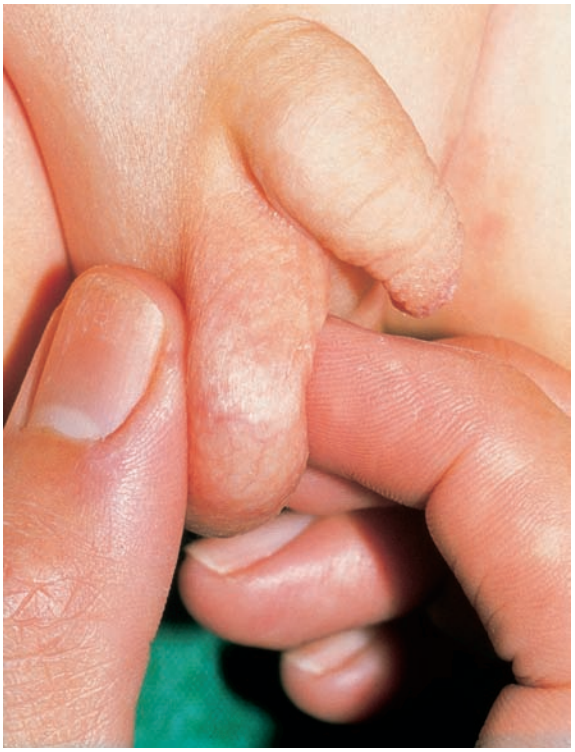


Figure 18.2 True retractile testis, brought easily to the floor of the scrotum without undue traction.

certainly reflect the inclusion of boys with retractile testes. When subjected to a double-blind placebo cross-over trial it was demonstrated conclusively that hormone therapy is ineffective in treating congenitally undescended testes. Nonetheless, hormonal manipulation does have its uses, sometimes when administered preoperatively to facilitate a potentially difficult orchidopexy, and otherwise to distinguish between true maldescent and 'high retractile testis'.

Hormonal treatment may consist of a 3-week course of intranasal luteinising hormone-releasing hormone administered four to six times daily or, more commonly, of human chorionic gonadotrophin given by intramuscular injection once or twice weekly for the same period.

Surgery

Palpable undescended testis

Standard single-stage orchidopexy is usually undertaken as a day-case procedure, ideally at some stage between 9 and 24 months of age. In experienced hands, the incidence of testicular atrophy following orchidopexy before 2 years of age is no greater than when the procedure is undertaken at a later stage.

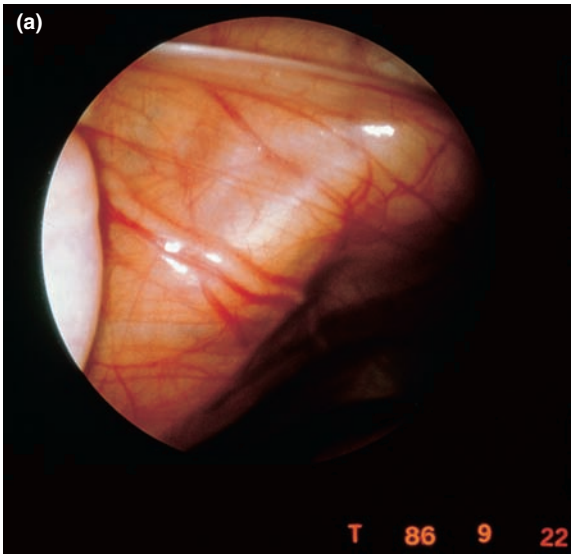
Impalpable testis

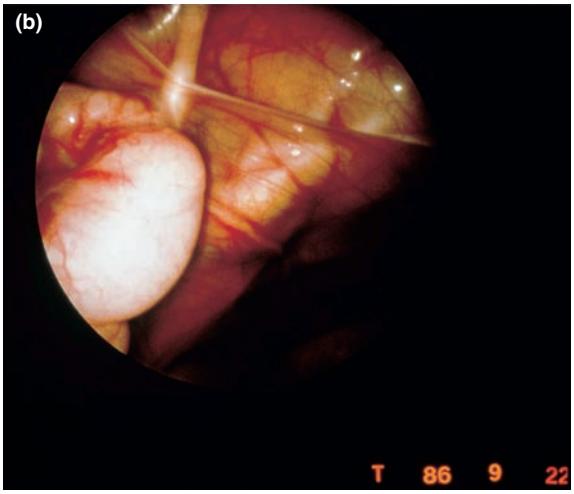
Some 10–20% of undescended testes are impalpable. Before embarking upon definitive surgery, it is necessary to establish whether the testis is absent (anorchia), is intra-abdominal, or is represented by an atrophic nubbin of tissue within the inguinal canal. In approximately 40% of cases of 'impalpable testis' the gonad lies intra-abdominally; in 30% it has 'vanished', with vas and vessels ending blindly deep to the internal inguinal ring; in 20% the vas and vessels end blindly within the inguinal canal; and in 10% the testis is normal but concealed within the inguinal canal.

Ultrasound is unreliable in distinguishing between anorchia and intra-abdominal testis, giving both false-positive and false-negative findings, but it is sometimes helpful in visualising a testis within the inguinal canal. Magnetic resonance imaging (MRI) is also unhelpful alone, although more reliable when combined with angiography, but this requires a general anaesthetic.

Consequently, laparoscopy remains the investigation of first choice in cases of impalpable testis, being both highly reliable and providing positive guidance for further management. In this regard, **there are five possible laparoscopic findings:**

- **Testis lying adjacent to the internal inguinal ring** – such gonads are usually amenable to a single-stage orchidopexy using a conventional or a preperitoneal approach. An experienced laparoscopist may be able to manipulate the testis towards the inguinal canal so as to assess the feasibility of a single-stage procedure.
- **Testis located on the posterior abdominal wall or ectopically within the pelvis** (Figure 18.3) – this calls for a decision as to whether to remove the gonad (either laparoscopically or as an open procedure) or whether to embark upon orchidopexy. Here the options lie between open





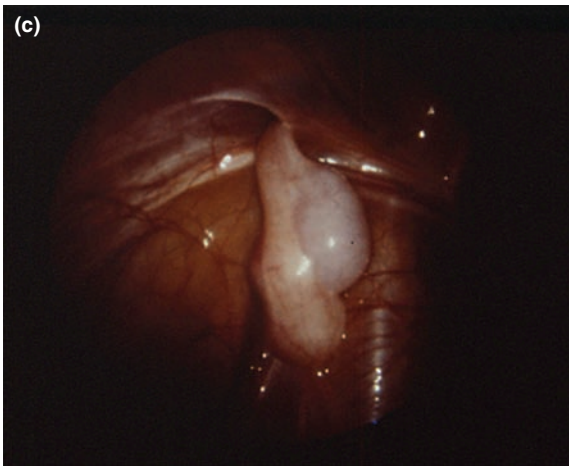


Figure 18.3 (a,b) Intra-abdominal testis and vas viewed laparoscopically. (c) Intra-abdominal testis lying above the entry to the inguinal canal.

or laparoscopically assisted orchidopexy, as either a single or a staged procedure.

- **Failure to visualise blind-ending vessels or testis** – in this rare situation, a limited laparotomy is indicated in view of the high risk of subsequent malignancy associated with an undetected intra-abdominal testes left in situ.
- **Vas and vessels ending blindly together at or above the internal ring** – such 'vanished' testes presumably result from intrauterine torsion and no further exploration is required.
- **Vas and vessels seen entering the inguinal canal** – here it is impossible to be certain whether the canal contains a normal testis or an atrophic nubbin of testicular tissue. Opinion varies on whether inguinal exploration is still mandatory in this situation. Alternatively it has been suggested that inguinal exploration is unnecessary if a nubbin is palpable and the contralateral testis is hypertrophied (>1.8 cm polar length or 2 ml in volume).

The last two situations are examples of testicular regression syndrome. Histological examination of the remnant shows a vascularised fibrous nodule with calcification, haemosiderin or spermatic cord elements. More extreme examples of this syndrome can present as disorders of sex development.

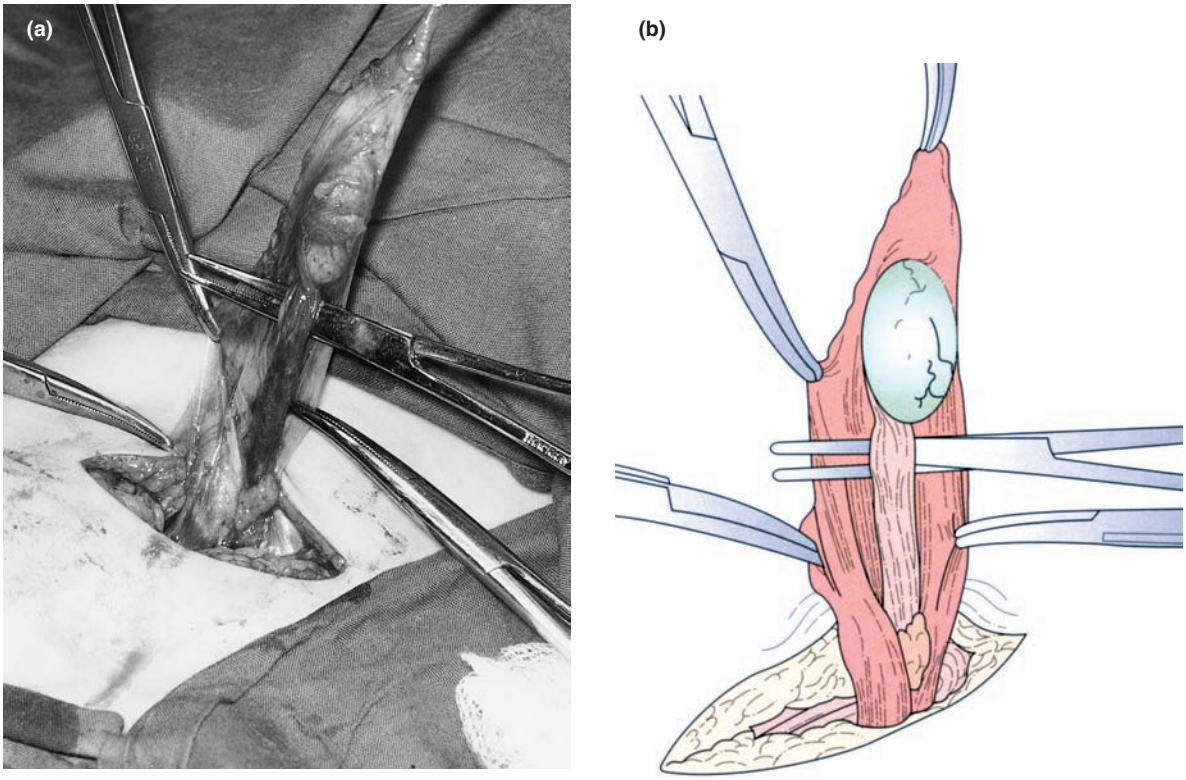


Figure 18.4 Conventional inguinal orchidopexy. (a) Intraoperative photograph. (b) Diagrammatic representation illustrating mobilisation of cord structures from the processus vaginalis.

Bilateral impalpable testes

Determination of karyotype is always worthwhile in this situation, looking for sex chromosome mosaicism or for chromosomal aberrations such as the Prader–Willi syndrome. A human chorionic gonadotrophin stimulation test may be undertaken to determine the presence or otherwise of functioning testicular tissue. However, although a positive result is encouraging for the parents, a negative result does not obviate the need for laparoscopy.

Orchidopexy – surgical considerations

For a detailed account of standard orchidopexy for a palpable testis, the reader is referred to one of the textbooks of operative paediatric surgery or urology listed under Further reading. In cases of true congenital maldescent the crucial step is clean separation of the patent processus vaginalis from the cord structures so as to facilitate full mobilisation of the testicular vessels, extended retroperitoneally if necessary (Figure 18.4).

In the absence of a patent processus vaginalis, orchidopexy is usually straightforward, with the gonad coming readily to the scrotum following separation of the cremasteric coverings from the cord structures.

More specialised techniques are required for testes lying high within the inguinal canal or within the abdomen: these options are listed below.

Preperitoneal approach (Jones)

A skin incision at or slightly higher than for a standard inguinal approach is employed and the oblique abdominal muscles are split to gain access to the peritoneum above the inguinal canal. Thereafter, the testis is mobilised transperitoneally and is passed to the scrotum through the inguinal canal or, if

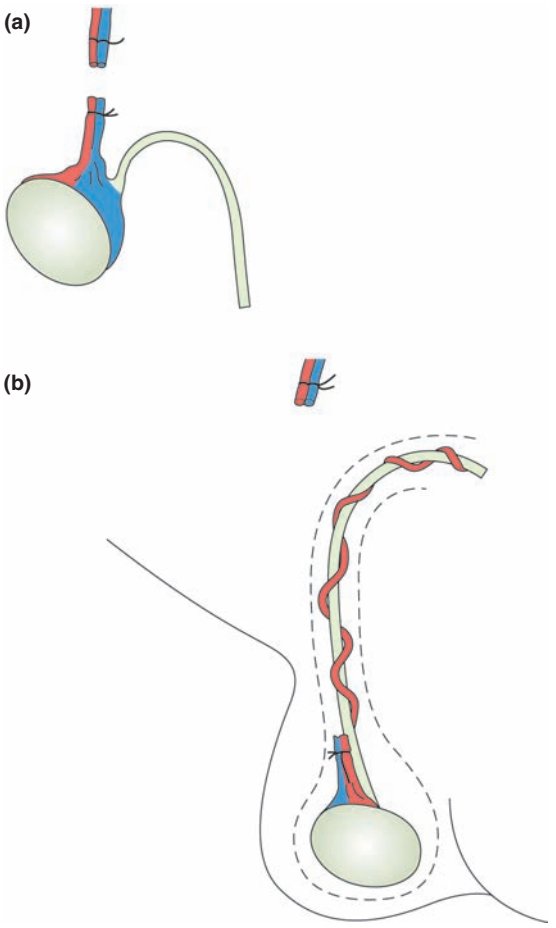


Figure 18.5 Fowler–Stephens orchidopexy. (a) Stage I, testicular vessels ligated or clipped in continuity. (b) Stage II, collateral vascularisation of the testis via the artery to the vas. After 6 months the testis is mobilised on the vas and a strip of surrounding peritoneum and brought to the scrotum by the most direct route.

necessary, more directly through the posterior wall of the canal medial to the inferior epigastric vessels.

Fowler–Stephens procedure (Figure 18.5)

With intra-abdominal testes, failure to mobilise the gonad to the scrotum is usually the result of inadequate length of the testicular vessels rather than of the vas deferens. The existence of a collateral blood supply to the testis via the artery to the vas represents the rationale for this procedure, and the results are better when it is conducted in two stages. At the first stage, undertaken either via an open approach or laparoscopically, the testicular vessels are isolated and divided, taking care not to disturb the vas and its important collateral vessels. The second stage is undertaken 6 months later, when this collateral supply has become more robust following ligation of the testicular vessels. The testis and vas are mobilised, along with a broad strip of overlying peritoneum, and brought transinguinally to the scrotum. This may be undertaken as an entirely open procedure or with laparoscopic assistance.

Microvascular orchidopexy

This procedure is appropriate for intra-abdominal testes, especially if the vas is too short for a Fowler–Stephens procedure or, rarely, if the vas is absent. The testicular vessels are mobilised and divided as high as possible, following which testis and vas are brought to the scrotum and the testicular vessels are anastomosed to the inferior epigastric vessels in the inguinal canal (Figure 18.6).

Laparoscopically assisted orchidopexy (Figure 18.7)

The intraperitoneal pedicle of testicular vessels is extensively mobilised laparoscopically, and when sufficient length has been obtained the testis is placed in the scrotum by either an open inguinal approach or an entirely laparoscopic procedure.

Difficult situations

Even an experienced surgeon may occasionally operate for what is thought to be a palpable testis, only to find – having opened the inguinal canal – that it is empty. This situation should not be managed by exploring retroperitoneally. First, if there is a patent processus vaginalis, this should be opened, and usually the ‘emergent’ testis will be easily delivered into the inguinal canal and a standard single-stage orchidopexy should be achievable, although there may be some tension when the testis is placed in the scrotum. If the testis is not

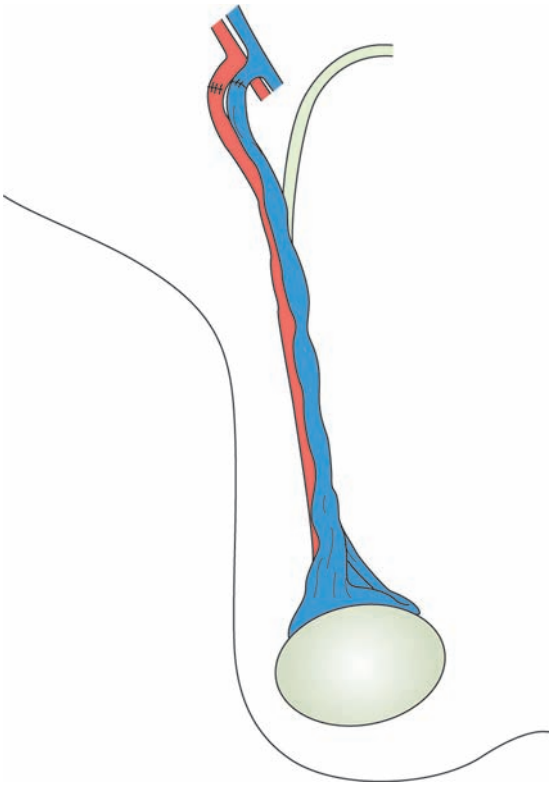


Figure 18.6 Microvascular orchidopexy. Testicular artery and single vein anastomosed to inferior epigastric vessels (or branches).

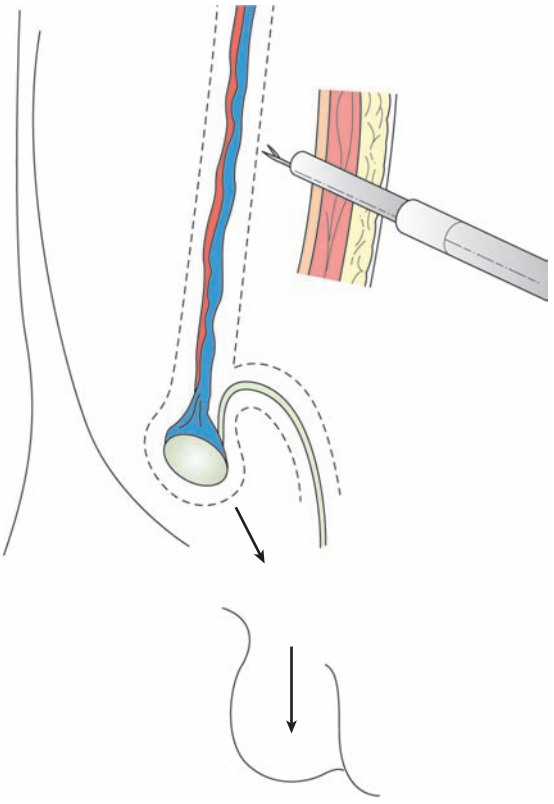


Figure 18.7 Laparoscopic or laparoscopically assisted orchidopexy. Extensive intraperitoneal mobilisation of testicular vessels enables the testis to be brought down to the scrotum with its vascular pedicle intact.

found by this approach, a preperitoneal (Jones approach – see above) should be used; this can easily be achieved through the same skin incision.

Management of retractile testis

In clear-cut cases parents may be reassured that retractile testes are common, particularly between the ages of 3 and 7 years, and that surgical intervention is rarely required. Moreover, one study has shown that men with bilateral retractile testes during childhood subsequently have normal testicular volume and fertility.

It is not possible to be so confident where the diagnosis lies between 'high retractile testis' and true congenital maldescent. In these circumstances the history may be more informative than the examination. Where any doubt exists, regular annual reassessment should be undertaken, and the parents should be advised that the need for surgery cannot be discounted.

If, during follow-up, it becomes apparent that a 'high retractile testis' is assuming an increasingly abnormal position, hormonal manipulation may be considered as both a diagnostic and a therapeutic trial. In practice, orchidopexy is generally favoured as the primary treatment of choice. In such cases it may be possible to perform this via a scrotal approach. Mobilisation of the cord structures, division of the remnant of the processus and complete separation

from the overlying cremasteric coverings is usually sufficient to allow the testis to be positioned satisfactorily in the scrotum.

Ascending testis

The concept of secondary ascent is now well documented by a number of credible studies dating from the 1980s, with recent reports suggesting that this phenomenon accounts for a relatively high percentage of boys undergoing orchidopexy in later childhood and up to 20% of all orchidopexies.

The aetiology of the condition is unknown, although obliteration of a patent processus vaginalis with contraction of the remnant has been advanced as a possible cause. A history of retractility has been identified as another contributory factor. In almost all series of 'secondary testicular ascent' orchidopexy was undertaken prior to puberty, so that it is impossible to be sure whether or not spontaneous descent would ultimately have occurred. However, in one large study reported from the Netherlands approximately 20% of ascending testes failed to revert to the scrotum at puberty. In view of some histological data suggesting that ascending testes are prone to similar degenerative changes to those found in undescended testes, there is a risk that those ascending testes which do return spontaneously to the scrotum may nevertheless have sustained damage during the period spent at a higher temperature in the groin. Further research is needed, but in the light of the limited available evidence, orchidopexy is the preferred treatment of ascending testes.

Complications of orchidopexy

The principal complications are postoperative testicular atrophy, injury to the vas and reascent of the testis. Among a total of 8425 procedures in 64 published studies, the failure rate, including atrophy, was 8% when the testis lay beyond the external inguinal ring, 13% when the testis was within the inguinal canal, and in the case of intra-abdominal testes 16% for microvascular procedures and 27% for two-stage Fowler–Stephens procedures. A 5% incidence of testicular atrophy following inguinal orchidopexy reported from one specialist paediatric surgical centre in the UK is probably representative of current practice.

However, atrophy is not an 'all or none' phenomenon and partial degrees of atrophy are probably more common than is generally recognised.

The incidence of injury to the vas is more difficult to determine, and although a figure of 1–2% is sometimes cited the true incidence is probably higher, as direct injury may go unnoticed or unreported. Postischaemic obliteration of the vas resulting from intraoperative damage to the delicate blood supply is likely to remain unrecognised except in individuals who undergo exploration or vasography in later life.

Long-term follow-up studies following prepubertal orchidopexy indicate that testicular volume is ultimately influenced by the initial position of the gonad, but not by the age at which the surgery was performed.

Long-term outcomes of orchidopexy

Fertility

Assessment of fertility is inexact, as almost all long-term studies have been retrospective, with the limitations inherent in such studies. In addition, the ability to father children does not consistently correlate with parameters of semen quality.

Although there is considerable variation in the results reported by different series, there is agreement that the prognosis for fertility is better when judged by paternity than by semen analysis. Moreover, all published series show that men with a history of unilateral undescended testis have

Table 18.2 Fertility (paternity) of men with a previous history of undescended testis (UDT)

Authors	Number of patients	Paternity rate of unilateral UDT (%)	Paternity rate of bilateral UDT (%)
Gilhooly et al	145	80	48
Kumar et al	56	84	60
Lee	467	88	59
Lee and Coughlin	408	90	65

Reviewed by Hutson (2006) see Further reading.

significantly better prospects of fertility than those with a history of bilateral undescended testes, regardless of how fertility is measured (Table 18.2). Indeed, one of the largest long-term studies found that the eventual paternity rates of men with a history of unilateral undescended testis were only marginally less than that for the normal population. However, men with a history of unilateral cryptorchidisim do demonstrate some degree of subfertility, as evidenced by the fact that 11% of those attempting paternity fail to achieve conception within 12 months, compared with only 5% of controls. Figures for both semen analysis and paternity are based upon men who underwent orchidopexy comparatively late in childhood. It seems reasonable to anticipate an improvement in fertility as a consequence of the recent trend toward earlier orchidopexy before the age of 2 years. Some evidence is emerging to this effect, but it will be some time before the presumed benefit of earlier orchidopexy can be confirmed by reliable long-term data.

The published evidence can be summarised briefly as follows:

- The long-term prognosis for fertility is better when judged by paternity than semen analysis.
- Published series report **paternity rates in the range 80–90%** for men with a history of **unilateral undescended testis** (percentage of men with normal semen analysis 55–95%).
- Published series report **paternity rates in the range 45–65%** for men with a history of **bilateral undescended testes** (percentage of men with normal semen analysis 25–30%).
- The evidence of biopsy studies supported by limited clinical data indicate that the prospects of fertility are enhanced by early orchidopexy (under 2 years of age).
- Testes arrested in a higher position of maldescent have a poorer prognosis for fertility.
- Ascending testes (secondary maldescent) share similar histological features to congenitally undescended testes and the impact on fertility may be comparable.

Malignancy

Men with a history of cryptorchidism are undoubtedly at increased risk of testicular malignancy. A large case–control study in the UK put the relative risk at 3.8 times greater than normal when orchidopexy had been performed after 9 years of age. However, the relative risk was not found to be significantly increased if the procedure was undertaken before that age. Other studies based on recent figures for the incidence of testicular cancer and cryptorchidism have generally placed the increased relative risk at between 5 and 10 times greater than that for the normal population. The lifetime risk of developing cancer in an undescended testis has been calculated to lie in the order of 1 in

100, compared with 1 in 500 in the population at large. However, this risk is somewhat less if maldescent is unilateral, and correspondingly somewhat greater if bilateral.

In adults the incidence of carcinoma in situ, a precursor of invasive malignancy, is strongly linked to the anatomical position of the testis, being found in 25% of gonads retained intra-abdominally into adult life. This and other evidence suggests that the original position of the testis may be a factor influencing the long-term risk of malignancy. During the first year of life undescended testes develop Leydig cell hypoplasia and delayed disappearance of gonocytes. There is some evidence that these gonocytes may degenerate into carcinoma in situ cells, thus providing further justification for the trend towards earlier orchidopexy in the belief that this will be accompanied by a reduction in the risk of malignancy.

Regardless of the age at which orchidopexy has been performed, men who have undergone the procedure should be encouraged to practise testicular self-examination.

Testicular microcalcification

This disorder, which is characterised by the presence of multiple small echogenic foci of calcification (Figure 18.8), has come to light as a result of the introduction of testicular ultrasound as a screening tool in adult urology. Two studies of healthy military personnel found prevalences of 2.4 and 5.6%, with marked differences between racial groups. Testicular ultrasound is performed far less frequently in children and adolescents but, nevertheless, cases of testicular microcalcification are being identified. Although it had been suggested that microcalcification might serve as a potential marker of premalignancy, this probably applies only when the finding is associated with other recognised risk factors, such as cryptorchidism, infertility, testicular asymmetry or atrophy. Increasingly, the evidence suggests that asymptomatic microcalcification is an innocent incidental finding in the majority of individuals and that prolonged ultrasound surveillance is not required unless other risk factors are present. In adolescents and young adults there is certainly no evidence to support testicular biopsy on the basis of this ultrasound finding.

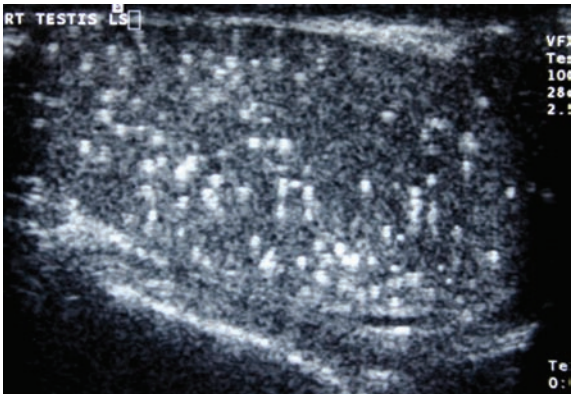


Figure 18.8 Testicular microcalcification. Ultrasound image demonstrating characteristic appearances.

Hydrocoele

With few exceptions, hydrocoeles in boys share a common underlying aetiology with indirect inguinal hernias: namely, failure of closure of the patent processus vaginalis following descent of the testis – see Chapter 1 (Figure 18.9). The difference between the two conditions lies in the diameter of the processus, which in communicating hydrocoeles is narrow and allows no more than the passage of intraperitoneal fluid (Figure 18.10). Non-communicating hydrocoeles are very rare in boys and occur principally around or after the time of puberty (Figure 18.11).

Communicating hydrocoeles are common in newborn males, with an incidence of 2–5%. Upwards of 90% of these congenital lesions resolve during the first year of life as a result of spontaneous closure of the processus. A hydrocoele, associated with a patent processus vaginalis, may present at some time later during childhood, although usually before the age of 5 years.

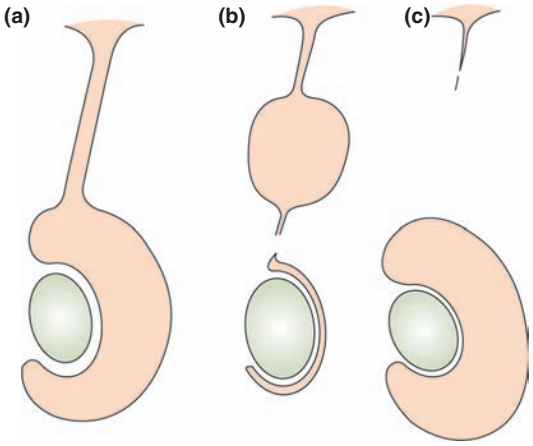


Figure 18.9 Anatomical classification of hydrocoele. (a) Communicating hydrocoele. (b) Hydrocoele of the cord ('encysted hydrocoele'). (c) Non-communicating hydrocoele.

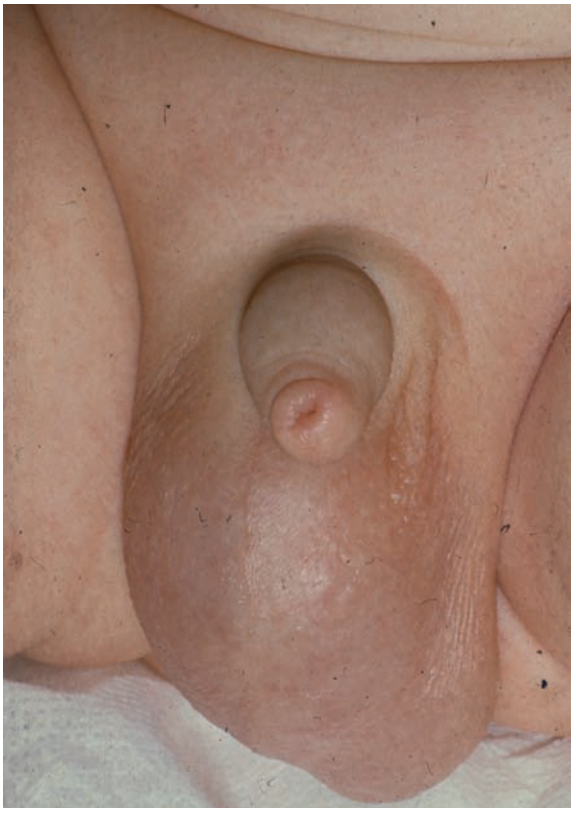


Figure 18.10 Congenital (communicating) hydrocoele.

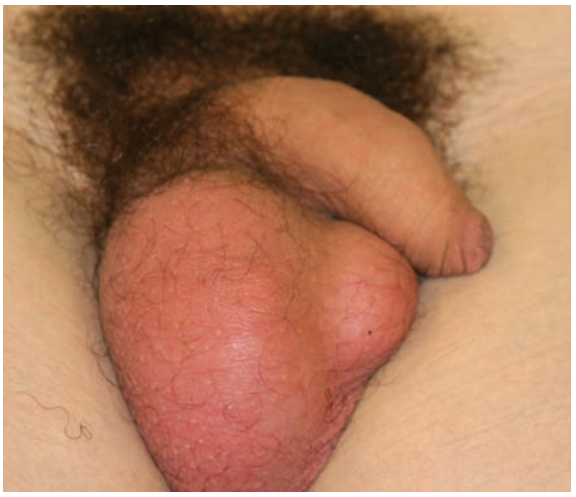


Figure 18.11 A 14-year-old boy presenting with 1-year history of increasing scrotal swelling. Non-communicating 'adult type' hydrocoele managed by scrotal approach and plicating hydrocoele sac.

Presentation

Most hydrocoeles present as a painless scrotal swelling which may vary in size throughout the day, being comparatively small first thing in the morning and enlarging during the course of the day. Sometimes hydrocoeles develop following the insertion of a ventriculoperitoneal shunt for hydrocephalus, whereas others present acutely in association with a viral illness. Although rare, it should always be remembered that hydrocoeles may be a secondary phenomenon associated with testicular tumours or omentum incarcerated in a hernial sac.

Encysted hydrocoeles of the cord typically present as a painless swelling in the groin and, being 'irreducible', are apt to be confused with an incarcerated inguinal hernia.

Examination

The principal differential diagnosis is one of an inguinoscrotal hernia, the latter being reducible whereas hydrocoeles are not. Transillumination, the classic physical sign of a hydrocoele, is not reliably

diagnostic as a scrotal hernia in infancy will also transilluminate in bright light. However, hydrocoeles impart a blue colour to the scrotum on inspection; in addition, hydrocoeles are mobile, whereas irreducible hernias are not. A hydrocoele of the cord is distinguished from an irreducible inguinal hernia, which does not extend to the scrotum, in that downward traction on the testis causes a corresponding movement in the hydrocoele.

Although investigation is usually unnecessary, ultrasonography is helpful whenever there is any suspicion of testicular tumour or incarcerated hernia.

Management

Congenital hydrocoeles should be managed conservatively, as almost all will resolve spontaneously during the first 12 months of life.

Surgical intervention is indicated for congenital hydrocoeles that persists beyond 1 year of age, and for those appearing for the first time in later childhood. Hydrocoeles of the cord are rarely present at birth and can present acutely. If the diagnosis is uncertain the combination of clinical examination (see above) and ultrasound may avoid unnecessary emergency operation.

Operative technique

The operation for communicating hydrocoeles is the same as for indirect inguinal hernia. Through a short skin-crease incision in the groin the spermatic cord is delivered, with or without opening the inguinal canal according to the surgeon's preference. The patent processus vaginalis is isolated from the testicular vessels and vas, traced back to its junction with the peritoneal cavity, and transfixed, ligated and divided at this point. The hydrocoele sac is then drained by incising the distal portion of the processus, or by percutaneous needle aspiration of the sac.

If the processus appears to be very narrow or of doubtful patency, suggesting a probable non-communicating variant, it is prudent to combine the groin procedure with a scrotal procedure to open, drain and evert the hydrocoele sac rather than run the risk of recurrence.

Varicocoele

Although the significance of varicocoeles lies principally in their association with subfertility, there is considerable variation in both the clinical characteristics of these lesions and their impact, if any, upon fertility. Opinion therefore remains divided on the indications for surgical intervention in childhood or adolescence. There is also debate as to the preferred surgical technique.

Incidence

Varicocoeles can be demonstrated in 6% of 10-year-old boys and 15% of 13 year olds, the latter figure being comparable to the prevalence among adult males generally. Among the male partners of infertile couples, the incidence of varicocoele is 30%.

Aetiology

The tortuosity and dilatation of the veins of the pampiniform plexus is the result of incompetence of the valvular mechanism that normally protects the spermatic veins from the hydrostatic pressure of the column of venous blood transmitted from the great veins. The fact that more than 90% of varicocoeles are left-sided reflects differences in venous anatomy, with the left testicular vein draining into the renal vein, whereas the right testicular vein drains into the vena cava. Several patterns of abnormal venous anatomy predisposing to varicocoele formation have been described:

- absence of valves within an otherwise normal single testicular vein
- anomalous venous drainage, for example between testicular and retroperitoneal veins
- bifurcation of the left renal vein, with an abnormal point of entry of the spermatic veins.

Although renal tumours account for less than 1% of varicocoeles during childhood, this possibility should never be overlooked.

Pathology

Studies involving the application of heat-sensitive strips to the scrotal skin have confirmed that the presence of a varicocoele elevates the temperature of the scrotal contents, leading to loss of the normal temperature differential necessary for spermatogenesis. The role, if any, of venous pressure-related damage to the testis is more difficult to assess. Testicular biopsies in the presence of a varicocoele show reduced spermatogonia, seminiferous tubal atrophy, endothelial cell proliferation and Leydig cell abnormalities. When found in patients under 18 years of age the changes are potentially reversible, but the more extensive histological changes found in older men are not – an observation that argues in favour of treating varicocoeles during adolescence rather than later.

Classification

The classification devised by Hudson is widely employed:

- Subclinical: neither palpable nor visible, but demonstrable by Doppler ultrasound.
- Grade I: palpable only on Valsalva manoeuvre.
- Grade II: palpable at rest but not visible.
- Grade III: visible and palpable at rest.

Presentation

Varicocoeles may be detected during the course of routine medical examination or may present symptomatically, either as a scrotal swelling, classically likened to a 'bag of worms', or by a dragging sensation within the scrotum, which is often worse during hot weather (Figure 18.12).

Diagnosis and investigation

The patient should be examined both lying and, more importantly, standing, the latter both with and without a Valsalva manoeuvre. Testicular size and volume should be assessed. The traditional method using a Prader orchiometer or callipers is prone to considerable observer variation. Ultrasound assessment of testicular volume is more reliable and can be combined with an abdominal ultrasound scan to exclude a renal tumour.

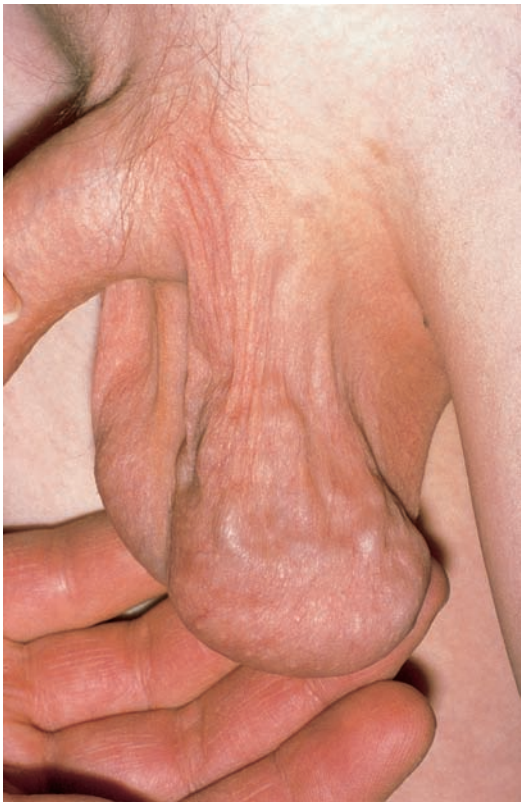


Figure 18.12 Grade III varicocoele. Visibly distended cremasteric veins ('bag of worms').

Indications for treatment

The presence of symptoms is generally accepted as an indication for surgical intervention, as is impairment of testicular growth. Among adolescent boys with asymptomatic lesions, however, the issue of 'prophylactic' intervention is altogether more controversial. The **arguments in favour of intervention** can be summarised as follows:

- Persistence of an untreated varicocoele into adult life leads to a demonstrable reduction in testicular volume, and there is evidence that surgical correction may partly reverse this process, leading to some degree of subsequent 'catch-up growth'.
- The incidence of varicocoele among men investigated for infertility is higher than in the male population at large.
- Some studies have found an improvement in semen quality and pregnancy rates following treatment of varicocoele in subfertile men.

Arguments against prophylactic intervention in adolescence are:

- Varicocoeles exist in some 15% of adult males, most of whom, as judged by paternity, have normal fertility.
- Although a link exists between varicocoele and infertility or subfertility, there is no consistent correlation between the presence or size of the lesion and semen quality or fertility.

Only time will ultimately resolve this controversy, but the present tendency is to advise 'prophylactic' intervention in the case of the larger, grade III, lesions, particularly if there is testicular asymmetry with a discrepancy in testicular volume of >20%. From the mid teens onwards the decision on whether to proceed to surgical correction of grade III varicoceles can also be guided by semen analysis.

Treatment options (Figure 18.13)

Embolisation

Embolisation may be carried out under sedation, although a general anaesthetic is usually used for prepubertal boys. A catheter introduced via the right femoral or internal jugular vein is screened into the left renal vein and thence into the spermatic vein. Venography is performed to identify collaterals. Embolisation is undertaken using coils inserted into the testicular vein or, less often, by the injection of a sclerosant.

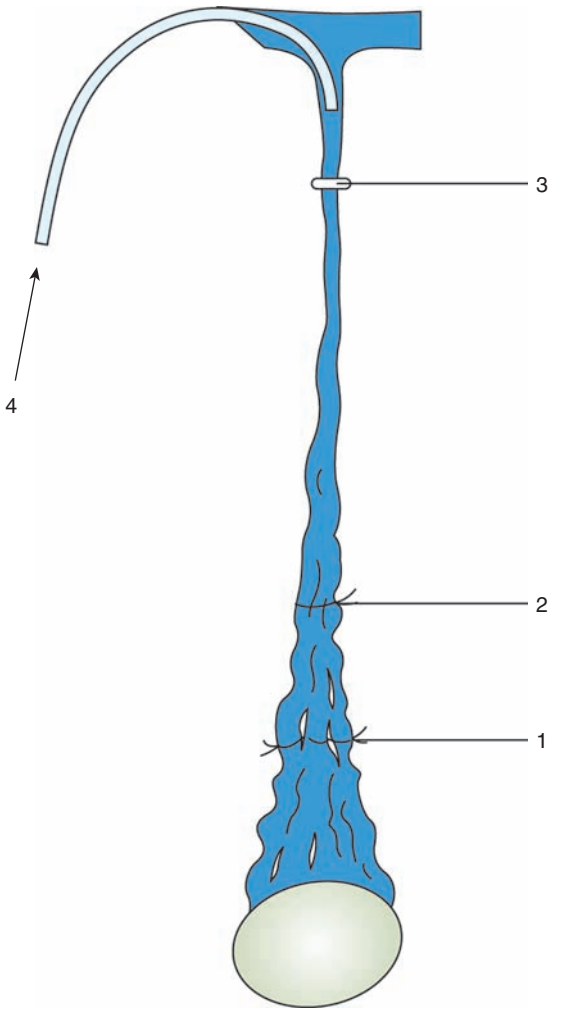


Figure 18.13 Varicocoele treatment options. (1) Surgical ligation of individual veins, inguinal approach. (2) Surgical ligation of veins and artery, high approach. (3) Laparoscopic clipping, all vessels or selective 'artery sparing'. (4) Embolisation.

Surgical ligation

Using the inguinal approach (Ivanissevich), the internal inguinal ring is exposed via the inguinal canal; the spermatic vein is exposed deep to the transversalis fascia and divided at this level.

Using the high approach (Palomo), a short transverse incision is performed lateral to the internal inguinal ring. The testicular vessels are

identified extraperitoneally above the point they diverge from the vas deferens. In Palomo's description, the testicular artery, vein and lymphatics are ligated and divided together but many surgeons ligate only the veins.

Microvascular procedures are nowadays sometimes performed for local ligation of varicocoeles. Although usually undertaken beyond the external inguinal ring, in prepubertal boys, the dissection is better performed within the inguinal canal. Magnification is employed and papaverine and intraoperative ultrasound are helpful in identifying and preserving the arteries. Care is taken to preserve the testicular and cremasteric arteries, the vas deferens and its artery, and also the lymphatics, as preservation of the lymphatics is believed to minimise the incidence of postoperative hydrocoele.

Other direct approaches to the dilated veins distal to the internal ring carry an unacceptably high risk of testicular atrophy and should be avoided.

With laparoscopic ligation three ports are placed and the testicular vessels identified. The veins can either be dissected and divided alone or clipped and ligated en bloc, along with the artery, as in the Palomo technique. This approach also allows easy identification and division of any abnormal veins, and is also especially applicable to the rare case of bilateral varicocoele. As with open techniques, lymphatic vessels should be preserved as far as possible in order to reduce the risk of postoperative hydrocele; this can be facilitated by injecting methylene blue into the scotum preoperatively, demonstrating the lymphatics more clearly at operation.

Complications and outcome

The fact that several surgical techniques continue to be employed for treating varicocoeles indicate that no single technique gives consistently satisfactory results. The failure rate for all procedures is up to 20%, although this figure appears to be rather lower when the testicular artery, as well as the veins, is occluded. The incidence of complications, notably hydrocoele and testicular atrophy, is in the region of 5%. Almost all published results relate principally to adult men, and there is insufficient information relating specifically to boys and adolescents from which to draw meaningful conclusions about the best form of treatment in this age group.

Improved fertility has been documented in subfertile men following varicocoele ligation, although these represent only a minority of all men with varicocoeles. Whether prophylactic treatment of asymptomatic varicocoeles in adolescents is beneficial for fertility has yet to be ascertained.

Key points

- The optimal age for orchidopexy remains uncertain. Paediatric urologists and paediatric surgeons favour the second year of life. For non-specialist surgeons it may be reasonable to defer orchidopexy until 3–4 years of age.
- The risk of testicular atrophy should be specifically discussed with parents when obtaining consent for orchidopexy.
- Laparoscopy is the investigation of choice for impalpable testes.
- In infants a clear diagnostic distinction must be made between an inguinal hernia (which requires prompt surgical intervention in this age group) and a communicating hydrocoele (which generally resolves as a result of spontaneous closure of the patent processus vaginalis in the first year of life).
- The available evidence suggests that treatment of varicocoeles in adolescence should be limited to boys with grade III varicocoeles, symptoms and/or evidence of impaired testicular growth.

Further reading

Barthold JS, Redman JF. Congenital anomalies of the testis and scrotum. In: Whitfield HN, Hendry WF, Kirby RS, Duckett JW (eds). Textbook of Genitourinary Surgery. Oxford: Blackwell Science, 1998; 254–260

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The acute scrotum

19

David FM Thomas

Topics covered
Epidemiology
Diagnostic features, symptoms and signs
Torsion of the testis
Torsion of testicular appendage
Epididymo-orchitis
Idiopathic scrotal oedema
Other acute scrotal pathology

Introduction

Acute scrotal pathology represents one of the few real emergencies encountered in paediatric urological practice. Testicular torsion accounts for 80–90% of cases of 'acute scrotum' in teenage boys and in view of the high probability of torsion in this age group immediate surgical exploration should be undertaken unless there is compelling evidence of an alternative diagnosis. By contrast, the differential diagnosis is more varied in prepubertal boys, but it is nevertheless important to recognise that testicular torsion figures prominently as a cause of acute scrotal pathology across the entire paediatric age range. Surgical intervention can sometimes be avoided if a reliable alternative diagnosis, such as torsion of a testicular appendage, can be established rapidly, but it is generally wiser to observe the time-honoured adage: 'Whenever doubt exists, it is safer to explore.'

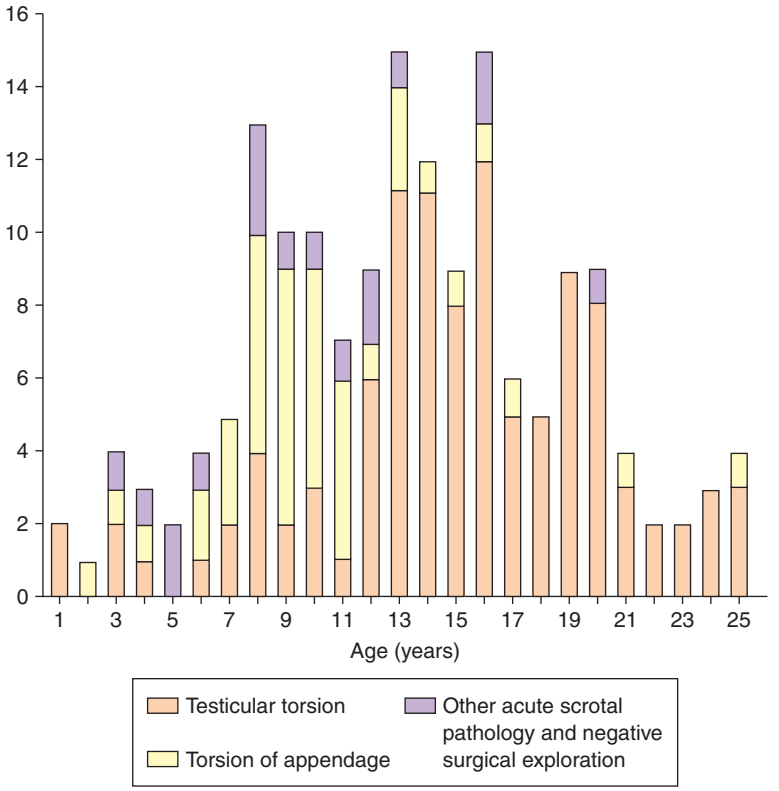

Figure 19.1 The relative frequency of different causes of acute scrotal pathology at different ages in childhood and early adult life (Ben-Chaim J, Leibovitch I, Ramon J et al – see 'Further reading').

Table 19.1 Relative frequency of different causes of 'acute scrotum' in 154 cases

	0–12 years		13–21 years	
Diagnosis	*n*	%	*n*	%
Torsion of testis	24	34	72	86
Torsion of appendix	33	47	8	9
Negative exploration	8	11	4	5
Epididymitis	3	4		
Acute scrotal oedema	1	2		
Acute haematocoele	1	2		
Total	70	100	84	100

Epidemiology

The relative frequency of the various causes of the 'acute scrotum' in the different age groups is illustrated in Figure 19.1. Between the ages of 13 and 21 years, testicular torsion accounts for nearly 90% of acutely presenting scrotal symptoms. However, in prepubertal boys torsion of a testicular appendage (hydatid of Morgagni) is more common, accounting for 45–50% of cases. Testicular torsion, nevertheless, accounts for approximately 35% of acutely presenting scrotal symptoms before puberty, with epididymo-orchitis, idiopathic scrotal oedema, acute hydrocoele and Henoch-Schönlein vasculitis constituting the remaining 15–20%.

Diagnosis

Clinical features

The differential diagnosis of the acute scrotum and the relative importance of the different pathologies in pre- and postpubertal boys in one sizeable series are detailed in Table 19.1. Although the diagnosis should be straightforward in the presence of a characteristic history and distinctive physical findings it should be noted that fewer than 50% of cases present with the classic 'full house' of signs and symptoms described in undergraduate textbooks. Frequently the history is less specific and examination simply reveals a swollen, reddened tender scrotum. In other instances the history or initial findings may be frankly misleading.

- Contrary to some textbook descriptions, pain is not always a prominent feature of testicular torsion and, indeed, in infants and young children pain may be virtually absent until changes secondary to established testicular infarction are apparent.
- Pain arising from a right-sided testicular torsion may radiate to the right iliac fossa, mimicking appendicitis.
- Examination of the scrotal contents should be routinely included as part of the clinical examination of any child or adolescent presenting with lower abdominal pain of sudden onset.
- Oedema and erythema of the scrotal skin are not apparent in the first few hours of testicular torsion. Absence of these physical signs should not be allowed to delay surgical exploration.
- The pathognomonic 'blue dot sign' associated with torsion of a testicular appendage (hydatid of Morgagni) is present in fewer than 20% of cases.
- Urinary symptoms (frequency, dysuria), which can sometimes feature in the clinical picture of testicular torsion, may be wrongly attributed to urinary infection and epididymo-orchitis.

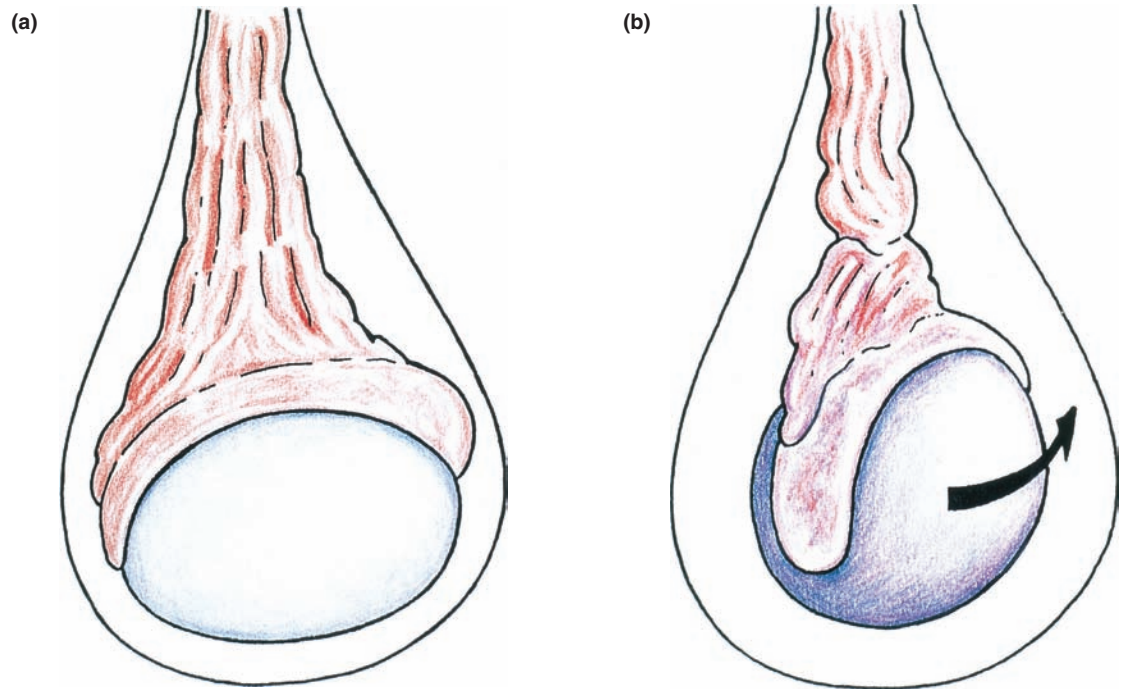

Figure 19.2 (a) Intravaginal torsion. 'Bell-clapper' testis suspended on an abnormally long leash of vessels (mesorchium) within the tunica vaginalis. (b) Undue mobility of the testis predisposes to torsion around the axis of the spermatic cord.

Diagnostic imaging

Colour Doppler ultrasound

Colour Doppler ultrasound provides simultaneous real-time anatomical imaging of the scrotal contents together with colour-encoded characteristics of blood flow. Perfusion of the testis is absent or dramatically reduced in testicular torsion. Drawbacks include operator dependency, limited out-of-hours availability and falsely reassuring findings in early or intermittent torsion.

Radionuclide testicular scanning (RTS)

This investigation – in which pertechnetate labelled with technetium-99m (^{99m}TC) is injected intravenously – is now rarely undertaken and is of largely historical interest. Testicular torsion is characterised by a central 'cold' area of poor isotope uptake, corresponding to the ischaemic testis, surrounded by a halo of vascular activity in hyperaemic scrotal tissue.

The role of diagnostic imaging, notably colour Doppler ultrasound, is largely confined to prepubertal boys in whom testicular torsion is thought to have been excluded on clinical grounds but where further confirmation is sought.

Testicular torsion

Although the peak incidence lies between the ages of 14 and 16 years (see Figure 19.1), the occurrence of torsion has been described across the entire age range extending from the neonatal period through to late adult life. NHS (National Health Service) hospital data for England indicate

that approximately 1000 boys aged 0–16 years undergo emergency scrotal exploration each year. Unfortunately, no information is available on operative findings or outcome. The left testis is affected more commonly than the right. Predisposing factors may include cold weather (precipitating activity of the cremasteric muscle) and testicular trauma. Maldescended testes account for 2–5% of cases.

Aetiology

Neonatal or intrauterine testicular torsion is of the extravaginal pattern, in which the testis and coverings twist in their entirety within the scrotum. In contrast, testicular torsion in all other age groups is generally intravaginal, i.e. the testis twists within the confines of the tunica vaginalis. It is generally accepted that an anatomical variant termed the 'bell clapper' testis, with a long mesentery-like leash of vessels (mesorchium), predisposes to torsion by permitting an abnormally mobile testis to twist around the axis of the spermatic cord (Figure 19.2). Although a rotational twist of 360–720° is commonly encountered at the time of surgical exploration, the degree of rotation required to produce testicular ischaemia is poorly documented.

Experimental studies, coupled with the findings of a limited number of clinical follow-up studies, indicate that the only prospect of salvaging a fully viable testis lies in restoring blood supply to the testis within 4–6 hours of the onset of ischaemia. However, it is too simplistic to regard atrophy as an 'all or none' phenomenon, and partial degrees of atrophy can occur even when exploration is undertaken in less than 6 hours. Atrophy of varying severity is virtually inevitable when surgical exploration is delayed by 6–8 hours after the onset of symptoms and ischaemic necrosis and atrophy are the rule after 8–10 hours.

Presentation

Unilateral scrotal pain and swelling of acute onset are the pathognomonic features of testicular torsion, but the clinical picture is variable and fewer than

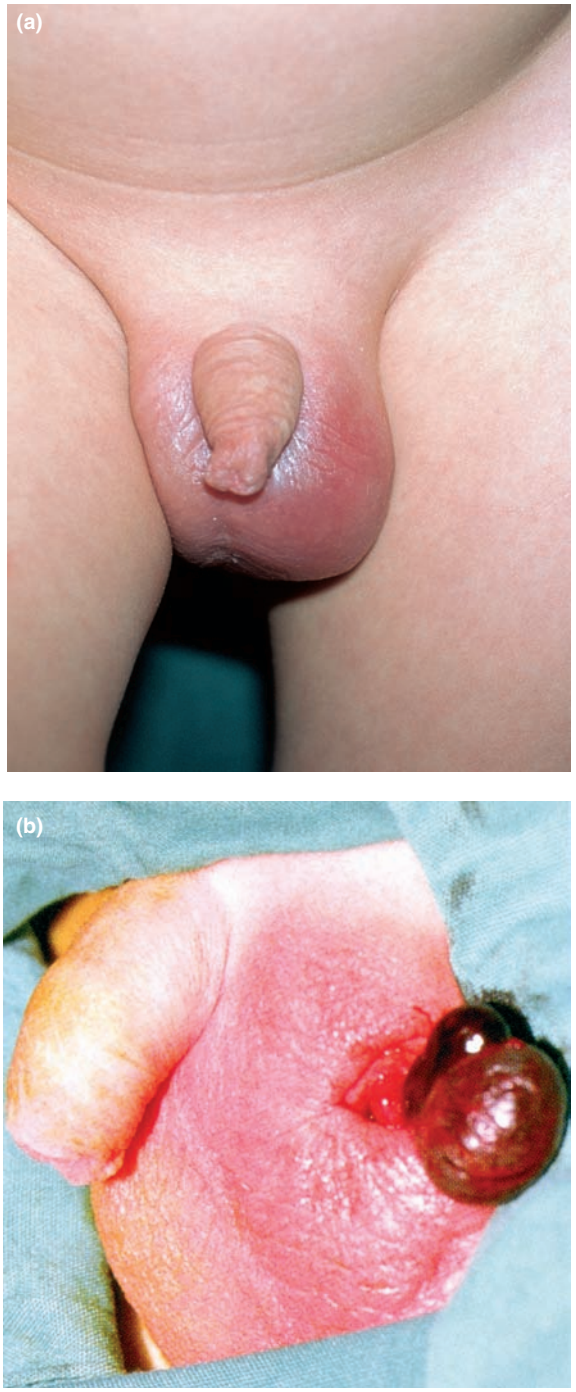

Figure 19.3 (a) Deceptively painless presentation of testicular torsion in an infant with a 3-day history of minimal symptoms. Discoloration of the scrotum prompted his parents to seek medical advice. (b) Prompt surgical exploration nevertheless revealed a necrotic testis.

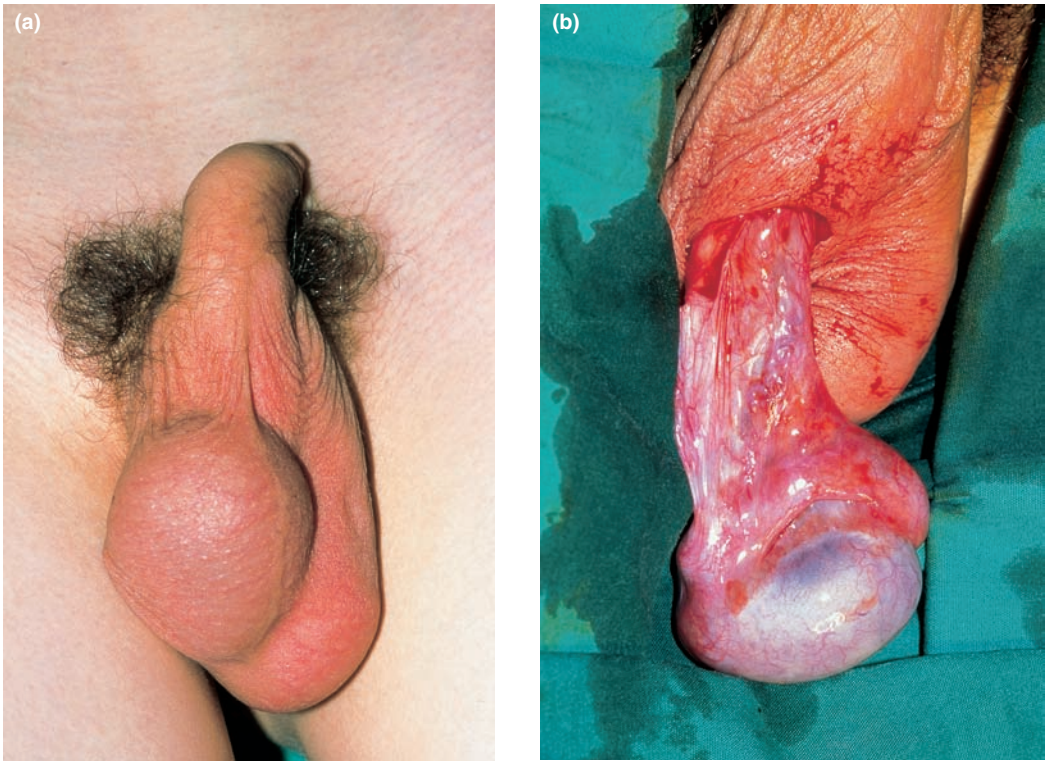

Figure 19.4 (a) Characteristic appearances of early torsion (3-hour history). The right testis is tender, mildly swollen and lies in an elevated position within the scrotum. (b) This testis was judged to be viable in view of the short history and operative findings indicating good return of perfusion following detorsion.

50% of cases present with a classic 'full house' of history and clinical findings. Pain is often referred to the groin or lower abdomen, and vomiting is a feature of approximately 40% of cases. The potentially misleading painless form of presentation is encountered more frequently in younger children (Figure 19.3) but may also give rise to diagnostic confusion in the postpubertal age group.

Management

External non-operative detorsion in the emergency department has been advocated, but although this may have a place in young adults it is not generally feasible in children.

Urgent surgical exploration is the keystone of management. Following exposure of the testis via a scrotal incision, the spermatic cord is untwisted and testicular viability assessed. Factors influencing the decision to conserve or remove the testis include the duration of the history, the appearance of the testis and arterial bleeding on incising the tunica albuginea (Figure 19.4). Surgical optimism (or wishful thinking) is often misplaced and unless the testis is clearly viable it is preferable to err in favour of orchidectomy (assuming the contralateral testis is healthy). When exploration has been undertaken within the first few hours and the testis is clearly viable it should be fixed to prevent recurrent torsion. Regardless of the outcome on the affected side, fixation of the contralateral testis is mandatory in view of the bilateral nature of the anatomy predisposing to torsion.

Technical aspects of fixation

Via a scrotal incision, the tunica vaginalis is opened and the testis anchored to the scrotal wall using two or three non-absorbable sutures, e.g. 4/0 or

5/0 Prolene (polypropylene), placed at the upper and lower poles of the testis and midzone. Cases of further torsion despite fixation have been reported following the use of catgut sutures. Sutureless fixation performed by placing the testis within a dartos pouch has been advocated by some surgeons on the basis of experimental evidence. However, this method cannot be guaranteed in clinical practice since the occurrence of torsion despite previous dartos pouch orchidopexy for cryptorchidism has been reported.

Although it has been suggested that puncture of the tunica albuginea by fixation sutures carries a risk of stimulating antisperm antibody production, there is no evidence to substantiate this hypothetical risk in prepubertal boys. By contrast, the presence of circulating autoantibodies has been demonstrated in a proportion of men following postpubertal torsion. The significance of this finding, and its relevance to fertility in these circumstances, remains uncertain. Moreover, it is not possible to determine the extent to which this finding might result from a breach in the blood/testis barrier sustained during suture fixation or, as seems more likely, exposure of antigens during detorsion or removal of the ischaemic testis.

In summary, the well-documented risks of recurrent or asynchronous contralateral torsion outweigh the theoretical risk of autoantibody formation. The recommended technique of fixation therefore consists of exposure of the testis and placement of three non-absorbable sutures between the tunica albuginea and the scrotal wall.

Implantation of a testicular prosthesis is an option available to young men following unilateral orchidectomy or testicular atrophy, but because of the risk of infection this should be a subsequent elective procedure via an inguinal incision, rather than at the time of acute surgical exploration.

Prognosis

Fertility

Follow-up studies in adults have revealed that semen quality is significantly reduced following unilateral torsion in adolescence. In one such study semen quality was reduced in 50% of men, and in another study of 36 patients only 16% had normal parameters of semen quality on follow-up. The mechanism is unclear, but possibilities include antisperm antibodies and pre-existing abnormalities of the spermatogenic tissue in the 'healthy' contralateral testis. Toxic free radicals released into the circulation as part of a reperfusion injury to the ischaemic testis at the time of exploration have also been implicated by some experimental studies. Follow-up studies have tended to rely upon parameters of semen quality as the measure of fertility but whether this is actually reflected in impaired rates of paternity is largely unknown.

Very little information exists on the prognosis for fertility following torsion in prepubertal boys, but the limited clinical data and some experimental evidence suggest that it does not have the same potential impact on fertility as torsion in adolescents and young adults.

Endocrine function

In contrast to the impaired spermatogenesis, endocrine function is unaffected and uniformly normal plasma levels of testosterone have been documented following unilateral torsion (regardless of the outcome for the twisted testis). Follicle stimulating hormone (FSH) levels may be elevated, reflecting impaired spermatogenesis in these patients.

The elective implantation of a testicular prosthesis should be offered patients who have undergone orchidectomy or in whom the salvaged testis has developed significant atrophy resulting in an obvious discrepancy in size. Ideally, implantation should be deferred until the mid teens to permit the use of an adult-sized prosthesis which best matches the volume of the contralateral testis (Figure 19.5).

Neonatal torsion

More strictly, neonatal torsion should be termed intrauterine or 'perinatal' torsion, since with very rare exceptions the event dates from the late stages

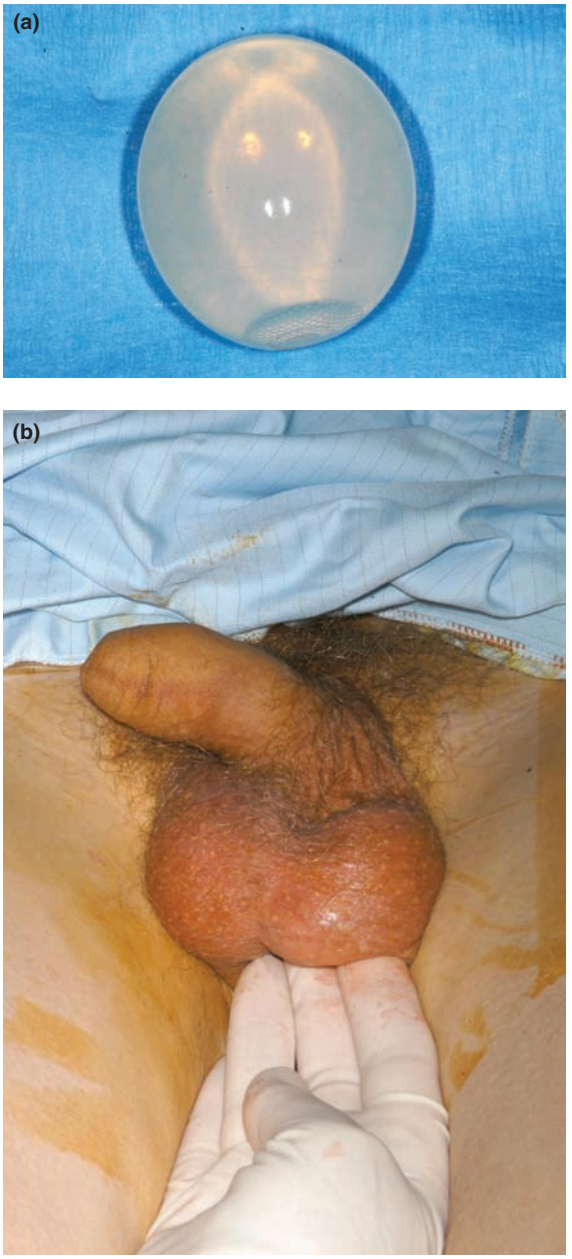

Figure 19.5 (a) Silicone gel testicular prosthesis. This is inserted via an inguinal incision and positioned in the most dependent part of the scrotum by inverting the scrotum and placing an anchoring suture in the reinforced disc at the lower pole of the prosthesis. (b) Postoperative appearances.

of intrauterine life. Indeed, cases of intrauterine testicular torsion have been documented on prenatal ultrasound. Typically, the surgeon is called to the postnatal ward to see an infant with scrotal discoloration and an indurated testis. In these circumstances the prospects of salvaging a viable testis are effectively zero. Reviewing the outcome of torsion in 30 neonates presenting over a 20-year period, Burge did not encounter a single viable testis. The almost invariably disappointing findings at surgical exploration, coupled with the belief that extravaginal torsion does carry the same risk to the contralateral testis, prompted a shift in policy.

As a result, many centres moved to conservative management of neonatal torsion, with regular ultrasound follow-up to monitor the process of testicular atrophy. One risk associated with non-operative management lies in the remote possibility of failing to recognise a congenital testicular tumour masquerading as 'neonatal' testicular torsion. If the ultrasound appearances are in any way suspicious, or the indurated testis fails to involute, surgical exploration and orchidectomy should be performed.

The assumption that torsion in the neonatal period does not carry a comparable risk of torsion to the contralateral testis as in other age groups is being challenged by recent reports suggesting that synchronous and asynchronous bilateral neonatal torsion is not as rare an event as was previously believed. Opinion may therefore swing back in favour of exploration and contralateral fixation.

Torsion of testicular appendage (hydatid of Morgagni)

Although children of any age can be affected, the peak incidence is between 10 and 12 years. In prepubertal boys torsion of a testicular appendage occurs more frequently than torsion of the testis itself (see Table 19.1).

Presentation

Although pain is the usual presenting symptom, it is typically less severe and more gradual in onset than that of testicular torsion. However, the two

conditions cannot always be distinguished reliably on clinical grounds, particularly in younger children. Haemorrhagic infarction of the hydatid of Morgagni, visible as a localised area of discoloration at the upper pole of the testis ('blue dot sign'), is pathognomonic of the condition but is only present in a minority of cases. Similarly, whereas examination may reveal tenderness confined to an indurated nodule, more generalised tenderness is often present and accompanied by oedema and erythema of the hemiscrotum.

Diagnosis

The clinical features may be sufficiently distinctive to enable an experienced clinician to make a firm diagnosis. Colour Doppler ultrasound can provide additional confirmation.

Management

Surgical intervention is indicated when testicular torsion cannot be excluded or when discomfort is severe. Treatment consists of simple excision of the infarcted hydatid of Morgagni. Prophylactic excision of the contralateral testicular appendage is not necessary. In cases where an unequivocal clinical diagnosis has been made, and where the pain is mild or resolving, conservative management is appropriate.

Epididymo-orchitis

Aetiology

Bacterial infection of the epididymis progressing to involve the testis occurs as a result of retrograde bacterial colonisation via the ejaculatory ducts and vas deferens. Vasal reflux of infected urine is usually present. Epididymo-orchitis (particularly when recurrent) may be linked to an underlying urological condition such as neuropathic bladder, persistent müllerian remnant ('prostatic utricle', 'vagina masculina') or ectopic ureter. However, it also occurs in infants with urinary infection associated with low-grade vesicoureteric reflux, or urinary infection for which there is no identifiable predisposing cause.

Presentation

Scrotal pain may be accompanied by evidence of urinary infection, e.g. dysuria or offensive urine. Examination typically reveals marked scrotal erythema and tenderness, and induration of the testis, often accompanied by fever and systemic upset.

Diagnosis

In boys of all ages testicular torsion is considerably more common than epididymo-orchitis, and this diagnosis should therefore be viewed with suspicion. Moreover, epididymo-orchitis cannot always be reliably distinguished from testicular torsion on clinical grounds alone. For these reasons surgical exploration should be performed, unless the child is known to have a predisposing urological abnormality and the clinical features point strongly to epidiymo-orchitis. Confirmatory investigations include:

- urine microscopy – pyuria, bacteriuria and positive urine culture
- Doppler ultrasound – hyperaemia and increased vascularity.

Management

Surgical

Surgical intervention is indicated:

- to exclude the diagnosis of testicular torsion
- to drain a scrotal or testicular abscess.

In cases of recurrent symptomatic epididymo-orchitis it may be necessary to consider vasectomy if the underlying urological abnormality is not amenable to surgical correction.

Excision of a large müllerian remnant has previously been performed using a transvesical, transtrigonal approach, but laparoscopic excision has been reported more recently. Little is known of

the late outcome for fertility following these procedures but risk of vasal injury is likely to be high.

Medical

Non-operative management comprises analgesia (epididymo-orchitis is an acutely painful condition) and an intravenous antibiotic, e.g. gentamicin or ciprofloxacin, pending the result of urine culture. Antibiotic treatment should be instituted postoperatively when the condition is discovered at exploration.

Prognosis

The fate of the testis cannot be reliably assessed until all the induration has resolved, which is generally a matter of several months. Following an isolated and promptly treated episode in a child without underlying urological abnormalities, the prognosis is generally good. However, after recurrent attacks of epididymo-orchitis varying degrees of testicular atrophy supervene.

Idiopathic scrotal oedema

This condition is virtually confined to the prepubertal age group, with a peak incidence between the ages of 5 and 6 years.

Aetiology

Although the condition is genuinely idiopathic, the association with anal pathology and the occasional finding of erythema extending from the perineum has been interpreted as evidence of reactive oedema secondary to localised lymphangitis.

Presentation

The clinical picture is characterised by marked oedema of the scrotum, which is usually unilateral in distribution but which may occur bilaterally and may also extend upwards to involve the subcutaneous tissues of the inguinal region (Figure 19.6). Pain is minimal or absent. The diagnosis presents few problems to those acquainted with the condition.

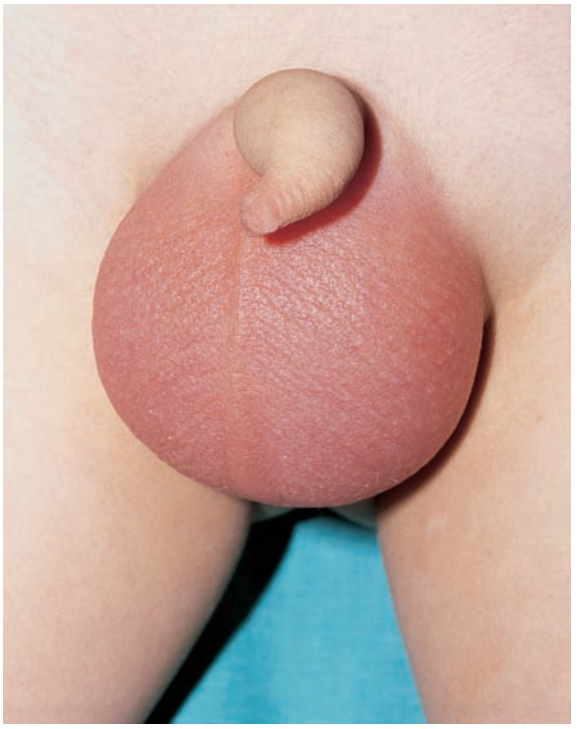

Figure 19.6 Idiopathic scrotal oedema.

Management

The swelling settles spontaneously, usually within 24–48 hours. Antihistamines or antibiotics are sometimes prescribed but there is no evidence of benefit, and in general no specific treatment is required.

Other acute scrotal conditions

Incarcerated hernia

In infancy, scrotal swelling may be the most striking visible manifestation of an inguinoscrotal hernia. Palpation will distinguish between an inguinoscrotal hernia (which extends from the inguinal region to the scrotum) and true intrascrotal pathology.

Acute hydrocoele

A tense, rapidly developing hydrocoele can give rise to diagnostic uncertainty. However, acute

hydrocoeles are rarely painful (unless associated with underlying pathology of the testis). Transillumination confirms the diagnosis.

Henoch–Schönlein vasculitis

Involvement of the testis, giving rise to tenderness, swelling and scrotal discoloration, is a well-documented complication of Henoch–Schönlein vasculitis. The presence of a purpuric rash should give the clue to the diagnosis and thus avert unnecessary surgical intervention.

Key points

- Torsion of the testis accounts for 90% of acutely presenting scrotal symptoms in postpubertal boys and adolescents. Urgent surgical exploration is mandatory unless there is compelling evidence of an alternative diagnosis.
- Regardless of the outcome on the affected side, it is mandatory to perform prophylactic open suture fixation of the contralateral testis.
- The recommended technique for fixation of the testis consists of opening the tunica vaginalis and placing three non-absorbable sutures between the tunica albuginea and scrotal wall.
- Most cases of so-called 'neonatal' torsion have actually occurred in utero and the affected testis is almost invariably non-viable.
- Torsion of a testicular appendage (hydatid of Morgagni) in a prepubertal boy can be managed conservatively provided a confident diagnosis has been made by an experienced clinician.
- Epididymo-orchitis is uncommon in childhood and, if proven, always merits investigation of the urinary tract.

Further reading

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Disorders of sex development 20

Henri Lottman and David FM Thomas

Topics covered
Embryological differentiation – normal and abnormal
Classification of disorders of sex development (DSD)
Investigation
Gender assignment
Surgical management of DSD
Gynaecological disorders of childhood and adolescence

Introduction

The nomenclature used to describe and classify this important group of disorders has undergone extensive revision since the first edition of this book was published. The changes adopted in this chapter reflect the recommendations of an international consensus conference on intersex held under the auspices of the North American and European Societies for Paediatric Endocrinology in 2006.

Wherever possible, potentially pejorative terms have been replaced. For example 'intersex' and 'true hermaphroditism' are now referred to as 'disorders of sex development (DSD)' and 'ovotesticular DSD', respectively. The old and new nomenclature are summarised in Table 20.1.

Because the acceptance and usage of the new terminology is likely to be a gradual process, the established terminology will also be included throughout this chapter, where it will appear as *italicised text*.

Table 20.1 Revised nomenclature

Previous	Proposed
Intersex	DSD
Male pseudohermaphrodite	46XY DSD
Female pseudohermaphrodite	46XX DSD
True hermaphrodite	Ovotesticular DSD
Mixed gonadal dysgenesis	Mixed gonadal dysgenesis (MGD) *(unchanged)*

Disorders of sex development originate from the following underlying mechanisms:

- chromosomal defects (chromosomal DSD)
- abnormalities of gonadal development (gonadal DSD)
- defects in the synthesis of sex hormones or relevant receptor (phenotypic/anatomical DSD).

Those aspects of sexual development which relate to behaviour and gender identity are less well understood and some areas, such as the concept of the 'male' or 'female' brain, remain highly controversial. The determinants of gender-related behaviour include neuroendocrine factors (notably the effects of testosterone on the developing brain) and complex sociocultural influences. Although some reference will be made to these important components of gender identity, a more detailed consideration of the psychological and behavioural manifestations of disorders of sex development is largely beyond the scope of this chapter.

A newborn infant with ambiguous genitalia presents the clinician with a rare and potentially urgent diagnostic problem. Congenital adrenal hyperplasia (CAH), numerically the most important condition, is associated with disorders of adrenal metabolism that may pose a threat to the survival of the affected infant. Even when the underlying condition does not carry this risk, it is important to investigate every infant with

ambiguous genitalia without delay. This is best achieved by involving a specialised multidisciplinary team comprising a paediatric endocrinologist, urologist, radiologist, biochemist and geneticist. Transfer to a specialist centre may be required if the relevant specialist expertise is not available locally.

Parents should be advised against registering the birth of a child with ambiguous genitalia until the diagnosis has been established and agreement reached on the assignment of gender.

Although the overall incidence of disorders of sex development is low, it is subject to geographical variation in population genetics: for example, there is a relatively high incidence of *true hermaphroditism* (ovotesticular DSD) in South Africa and of 5α-reductase deficiency in the Dominican Republic.

Normal sexual differentiation

A knowledge of the embryological development of the internal and external genital tracts is essential in understanding disorders of sex development (intersex states). The embryology of the genital tracts has already been considered in Chapter 1 but the key elements are summarised again as follows:

1. The precursors of the gonads, genital ducts and external genitalia are present in an identical undifferentiated state in both 46XX and 46XY embryos until around the 6th week of gestation.
2. The genital tract of the embryo and fetus is genetically programmed to develop by a process of passive differentiation down a female phenotypic pathway, unless positively switched into a pattern of male phenotypic differentiation by the influence of certain genetic and endocrine factors.
3. With the exception of those disorders characterised by the presence of both testicular and ovarian gonadal tissue (i.e. *true hermaphroditism* or ovotesticular DSD), disorders of sex development fall into two broad categories:
    - **inappropriate virilisation of a 46XX fetus as a result of intrauterine exposure to virilising agents** (46XX DSD or *female pseudohermaphroditism)*
    - **incomplete virilisation of a 46XY fetus** (46XY DSD or *male pseudohermaphroditism)*.

Differentiation of the male genital tract

Testis

Differentiation of the testis commences at around 6 weeks, when the gonadal primordium situated at the anterior aspect of the mesonephros is colonised by extraembryonic primordial germ cells. The process of differentiation is initiated during the 7th week, when the pre-Sertoli cells aggregate to form the seminiferous tubules secreting the glycoprotein müllerian inhibitory substance (MIS). Leydig cells appear at around 8–9 weeks, increasing until 12–14 weeks, when their number remains stable until 24 weeks before declining. At birth the testis contains relatively few Leydig cells, a state that persists until puberty, when there is proliferation of Leydig cells within the pubertal testis.

Internal genitalia

In the undifferentiated state the genital ducts of both XX and XY embryos comprise the mesonephric (wolffian) and paramesonephric (müllerian) ducts. Regression of the müllerian ducts in the male begins at 8 weeks in response to MIS and is complete by 10–12 weeks. Under the influence of androgens secreted by the fetal testis each mesonephric duct develops into epididymis, vas deferens and seminal vesicle. The prostatic bud develops around the distal end of the mesonephric ducts at approximately 11–13 weeks. The prostatic utricule forms at the junction of the paired mesonephric ducts and the urogenital sinus (Figure 20.1).

External genitalia

The undifferentiated state of the external genitalia in both XX and XY embryos comprises a genital tubercle, and a urogenital groove surrounded by urethral folds and labioscrotal swellings. Without

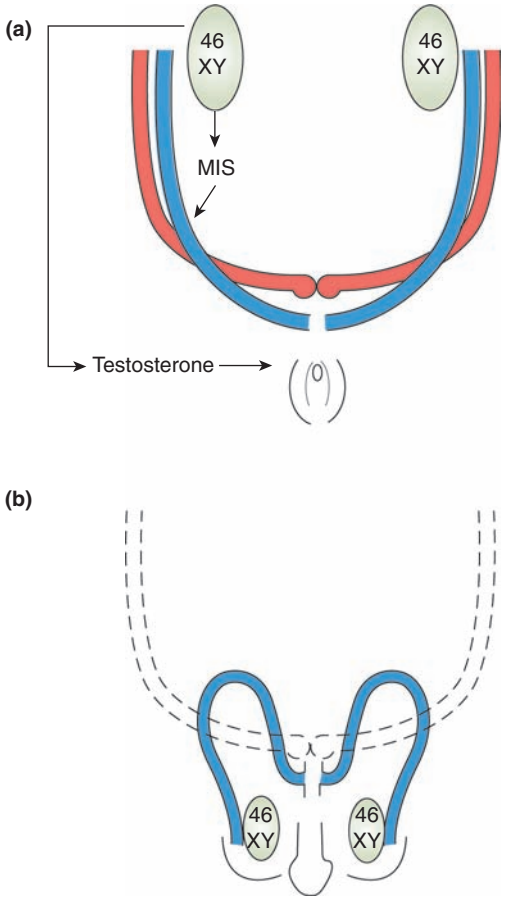

Figure 20.1 Normal male development. (a) Undifferentiated state. (b) Regression of paramesonephric ducts (red) under the influence of MIS, and persistence of mesonephric ducts (blue) in response to localised testosterone secretion by the fetal testis. Virilisation of external genitalia by circulating androgens.

androgenic stimulation the external genitalia of an XY fetus would be destined to retain these features and hence develop into the external genitalia of a female phenotype. Conversely, when exposed to circulating androgens the genital tubercle elongates and the urethral folds fuse over the urethral groove to create the penile urethra surrounded by the corpus spongiosus. Meanwhile, the genital swellings fuse posteriorly to form the scrotum. Male anatomical differentiation is essentially complete by the 13th week of gestation, except for testicular descent (see Chapter 1) and further penile growth and development, which continues from 20 weeks to term.

Differentiation of the female genital tract

Ovary

Differentiation is triggered around the 6th week of gestation by the interaction of the primordial germ cells and the mesenchymal tissue of the genital ridge. Oogonia enter the meiotic phase at 12–13 weeks, and all the germ cells have entered the meiotic prophase by 7 months. The oocytes then remain in a state of arrested division until the onset of puberty. From the 12th week of gestation the fetal granulosa cells produce oestrogens.

Internal genitalia

The mesonephric ducts undergo spontaneous degeneration at around 10 weeks, while the paramesonephric ducts develop into the fallopian tubes, the uterus and the upper vagina. The lower vagina is derived from urogenital sinus. Separation of the urethra and vagina results from downgrowth towards the perineum of the junction of the paired paramesonephric ducts and urogenital sinus at the level of the sinovaginal bulb (Figure 20.2).

External genitalia

Differentiation of the genitalia into the female phenotype occurs without any known requirement for endocrine stimulation, and begins with the formation of a dorsal commissure between the labioscrotal swellings. The genital tubercle persists as the clitoris, and the urethral folds become the labia minora and the labioscrotal swellings the labia majora.

The role of sex-determining genes

Determination of sexual differentiation in mammalian species is governed primarily by the presence of genes located on the Y chromosome. Of these, by far the most important is the testis-determining gene, which is located at the distal part of the short

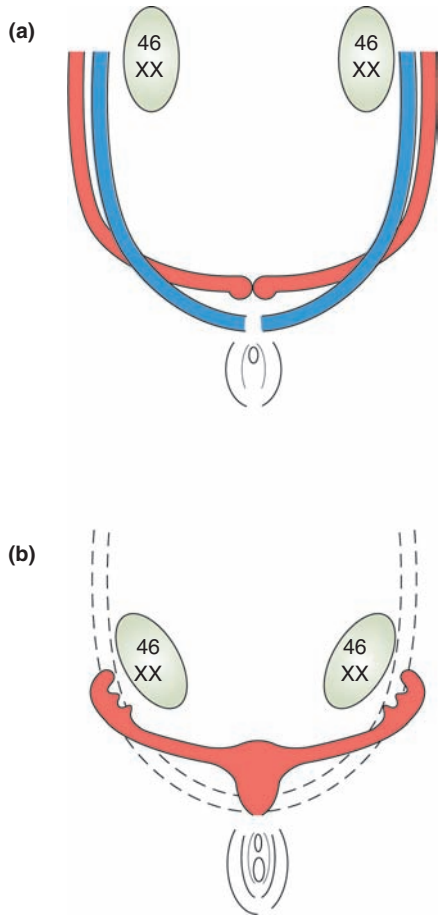

Figure 20.2 Normal female development. (a) Undifferentiated state. (b) Persistence of paramesonephric duct derivatives (no exposure to MIS). Spontaneous regression of mesonephric ducts. Passive differention of external genitalia to female phenotype.

arm of the Y chromosome and has been named *SRY* (sex-determining region Y). Although the *SRY* gene is ultimately responsible for initiating testicular differentiation, many downstream genes located on the sex chromosomes and autosomes are also involved in the complex sequence of subsequent events contributing to the embryological development of the genital tracts.

It had been thought that in the absence of the Y chromosome the gonad adopts a default pattern of differentiation to form an ovary. Evidence is emerging, however, that this is not an entirely passive process and that normal ovarian differentiation is dependent on the presence of the paired X chromosomes. In particular, survival of the germ cells requires the presence of two X chromosomes. In 45X female patients (Turner syndrome) the ovaries degenerate into fibrous streaks containing no surviving germ cells.

Phenotypic sex differentiation

Experimental studies conducted by Jost and Josso in animals such as the rabbit and rat have provided a detailed picture of the endocrine factors implicated in male sex differentiation.

As already indicated, müllerian inhibitory substance and androgens play key roles which are summarised below.

Müllerian inhibitory substance

Produced within the testis by the Sertoli cells, MIS is a glycopeptide that induces resorption of the müllerian (paramesonephric) ducts, stimulates the Leydig cells and is implicated in the initial phase of testicular descent. The genes coding for MIS and its receptor have been mapped on chomosomes 19 and 12, respectively.

Testosterone and dihydrotestosterone

Testosterone, secreted by the Leydig cells of the embryonic testis, is responsible for maintenance of the mesonephric ducts and virilisation of the urogenital sinus and external genitalia. The production of testosterone by the fetal testis is detectable at 9 weeks, with a peak around 15–18 weeks and then a sharp fall. Testosterone is released into the bloodstream, enters target cells and is converted to dihydrotestosterone (DHT) by the enzyme 5α-reductase. DHT binds to androgen receptors with a greater affinity than does testosterone. The androgen receptors are coded by genes located on the X chromosome. A local source of androgen is essential for mesonephric duct development, which does not

occur if testosterone is supplied only via the peripheral circulation, as in 46XX DSD (*female pseudohermaphroditism*) due to adrenal hyperplasia. The fetus is exposed to high levels of maternal and intrinsic gonadotrophins, and also to oestrogens of fetal and maternal origin. Their role in sexual differentiation is poorly understood.

Classification of disorders of sex development

As indicated above, disorders of sex development may have their origins in chromosomal defects, abnormalities of gonadal development or impaired endocrine function due to deficient sex hormone synthesis or receptor activity.

Despite full investigation, the cause cannot be established in some patients. This is particularly true in individuals whose ambiguous genital state is accompanied by the presence of a Y chromosome. Such cases presumably represent a defective component of sexual differentiation that has yet to be identified.

The most commonly encountered forms of DSD are:

- **46XX DSD** – virilisation of a 46XX female (previously termed *female pseudohermaphroditism)*. The majority of these patients have CAH.
- **46XY DSD** – inadequate virilisation of a 46XY male (previously termed *male pseudohermaphroditism)*. In contrast to 46XX DSD, there are several different causes, and in approximately 50% of cases no definitive diagnosis can be established.
- **Gonadal dysgenesis** – a spectrum of gonadal and genital abnormalities associated with absence of one of the pair of sex chromosomes, e.g. 45X, 45X/46XY, and often present in mosaic form (see Chapter 1).
- **Ovotesticular DSD** (previously termed *true hermaphroditism*) – both ovarian and testicular tissue are present in the same individual. The genotype and phenotype are variable.

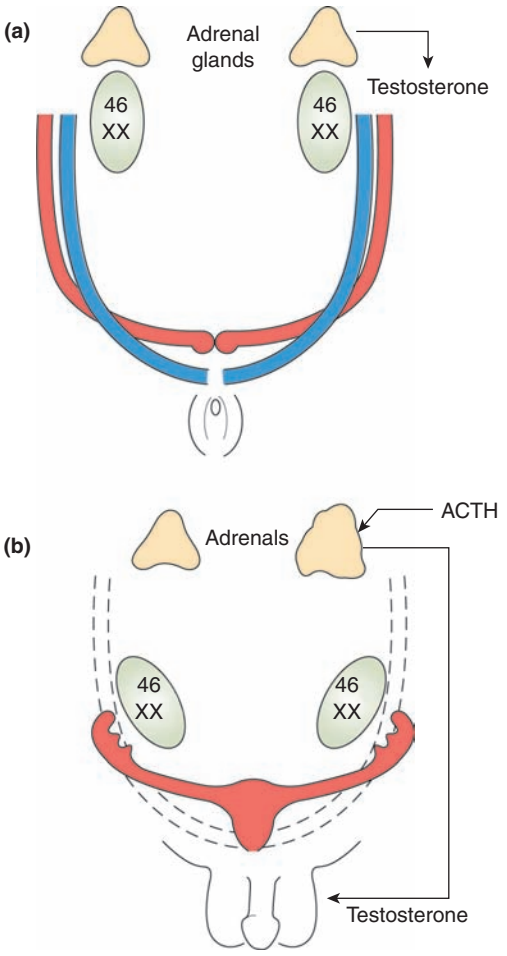

Figure 20.3 Congenital adrenal hyperplasia. (a) Undifferentiated state. (b) Persistence of paramesonephric duct derivatives (no exposure to MIS). Regression of mesonephric ducts (no localised secretion of testosterone by the gonad–ovary). Virilisation of external genitalia caused by circulating adrenal-derived testosterone.

46XX DSD (female pseudohermaphroditism)

Children with this group of abnormalities consist almost entirely of 46XX females whose external genitalia have been virilised by intrauterine exposure to androgens at a critical phase in differentiation (Figure 20.3). Affected individuals have ambiguous external genitalia but their ovaries and internal genitalia (fallopian tubes, uterus, upper vagina) are normal.

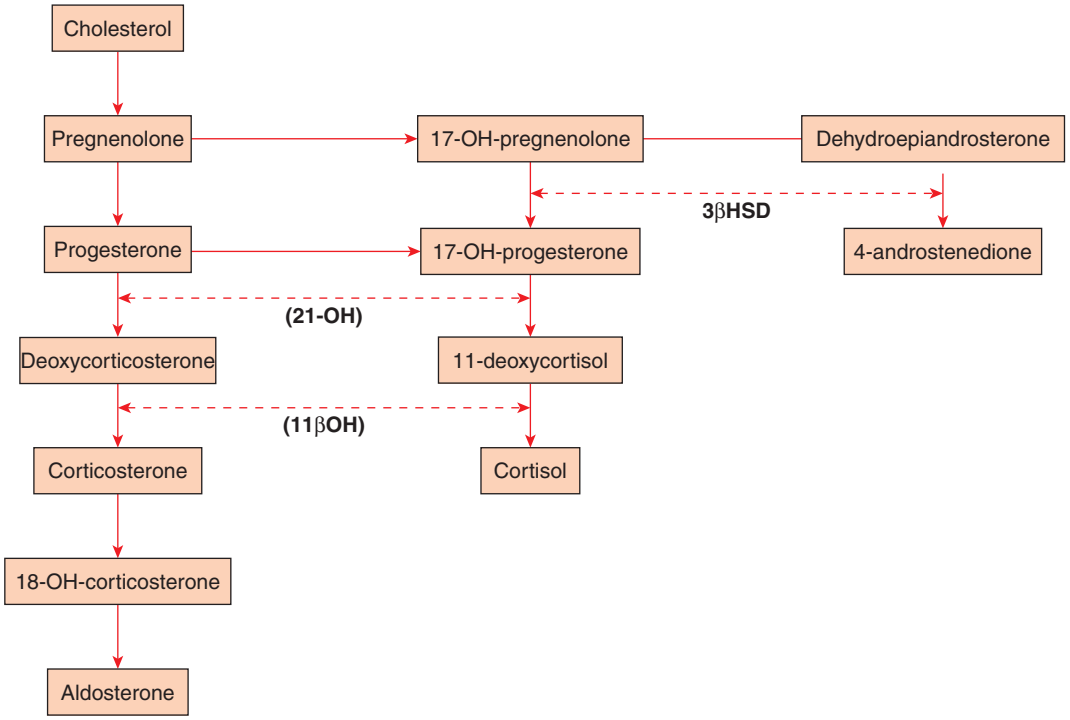

Figure 20.4 Congenital adrenal hyperplasia. Sites of enzyme block in metabolic pathway.

Congenital adrenal hyperplasia

CAH is not only the most common cause of 46XX DSD (*female pseudohermaphroditism)* but also accounts for approximately 85% of all infants with ambiguous genitalia in Western countries. The disorder can arise as a result of one of three enzymatic defects occurring at different points on the biosynthetic pathways for the production of cortisol and aldosterone in the adrenal gland. All three defects prompt overproduction of adrenocorticotrophic hormone (ACTH), which in turn stimulates overproduction of androgenic precursors by the adrenals (Figure 20.4).

21-Hydroxylase deficiency is the most common form of CAH (estimated incidence 1:15 000 births) and is an autosomal recessive disorder associated with a mutation of a gene located on chromosome 6. The diagnostic feature is elevation of plasma 17α-hydroxyprogesterone. Prenatal diagnosis is possible and treatment has been described using dexamethasone to suppress the fetal pituitary–adrenal axis from the 9th to the 17th weeks of gestation. Fifty per cent of cases are complicated by a salt-losing state which may pose a potentially life-threatening neonatal emergency. Management comprises gluco- and mineralocorticoid replacement therapy, female gender assignment and consideration of feminising genitoplasty.

11β-Hydroxylase deficiency is a rare cause of CAH associated with severe virilisation and leading to salt retention and potassium loss with, in some instances, hypoglycaemia and impaired stress response. The diagnosis is based on the elevation of plasma levels of 11-deoxycortisol. Prenatal diagnosis is feasible in the siblings and the offspring of affected individuals. Sex determination and a range of genetic studies with gene probes for CAH can be performed on fetal cells obtained by chorionic villus sampling or amniocentesis. In addition, the external genitalia of a 46XX fetus can be assessed with ultrasound for

evidence of virilisation. Prenatal treatment has been reported, consisting of the administration of dexamethasone as for the 21-hydroxylase deficiency form of CAH.

3β-Hydroxysteroid dehydrogenase deficiency is the rarest form of CAH. Virilisation is of moderate severity, but salt loss and hyponatraemia are severe. Plasma dehydroepiandrosterone, 17-hydroxypregnenolone and ACTH are elevated. The management is similar to that for 21-hydroxylase deficiency.

Aromatase deficiency

This oestrogen synthetase enzyme is present in particularly high concentrations in the placenta and is involved in the synthesis of oestrogens from androgenic precursors. Deficiency of this enzyme results in an accumulation of androgens and consequent fetal virilisation.

Virilisation by androgens of maternal origin

This is a rare cause of 46XX DSD, with possible causes which include androgen-secreting tumours of the adrenal or ovary and maternal treatment with progestational agents. Examples of virilising anomalies of the female external genitalia which have a teratogenic rather than an endocrine aetiology include isolated clitoral hypertrophy and abnormalities associated with urogenital sinus and cloacal anomalies.

46XY DSD (male pseudohermaphroditism)

In this group of disorders, 46XY male infants exhibit varying degrees of inadequate virilisation which can be ascribed either to defects in androgen production or metabolism or to abnormalities of receptor sensitivity in the target tissues.

Defects of testosterone production

These may be the outcome of rare testicular abnormalities such as testicular dysgenesis or Leydig cell aplasia. Alternatively, the testes may be morphologically normal but the production of testosterone is impaired by an enzymatic block in the biosynthetic pathway.

Defects of testosterone metabolism

The enzyme 5α-reductase is responsible for converting testosterone to the more potent androgen dihydrotestosterone. 5α-Reductase deficiency is responsible for a particular pattern of virilisation defects found in inbred communities in the Dominican Republic, and, rarely, in certain other parts of the world.

Defects of receptor sensitivity

Failure of virilisation can occur despite the presence of normal or elevated levels of testosterone and/or dihydrotestosterone if the target tissues are resistant to androgens.

Androgen insensitivity syndrome (AIS) is inherited as an X-linked recessive disorder associated with a mutation on the long arm of the X chromosome. In the complete form (CAIS; previously termed *testicular feminisation syndrome*), the external genitalia are phenotypically female. In contrast, the internal genitalia have differentiated normally down a male pathway in response to MIS secreted by the fetal testis. Typically the condition is discovered during the investigation of primary amenorrhoea, or following the discovery of a testis during hernia surgery in a girl. Partial androgen insensitivity (PAIS) has a broad phenotypic spectrum characterised by impaired virilisation of varying severity.

Abnormalities of MIS activity

Deficiency of MIS or a target receptor defect which renders the internal genitalia insensitive to MIS is characterised by a combination of normally masculinised external genitalia and varying degrees of persistence of internal müllerian structures (vestigial uterus, tubes, upper vagina) (Figure 20.5). The condition usually comes to light during a surgical procedure for cryptorchidism or inguinal

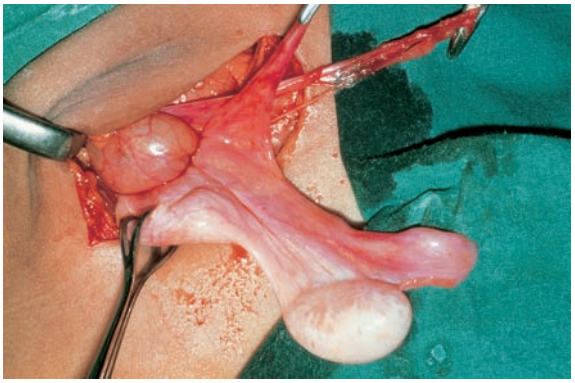

Figure 20.5 Laparotomy findings in a case of MIS deficiency. Intra-abdominal testis, persistence of paramesonephric duct structures – vestigial fallopian tubes and uterus.

hernia. The diagnosis is confirmed by measuring circulating MIS, which is low in cases due to impaired synthesis of MIS and high in those cases due to mutation of the gene encoding for the MIS receptor.

Idiopathic 46XY DSD (male pseudohermaphroditism)

In up to 50% of cases no genetic or hormonal abnormality is identifiable. In such instances the malformation of the genitalia may be attributed to teratogenic factors, to mutations in yet unknown genes or to genes acting downstream of androgen or MIS receptors.

Gonadal dysgenesis

Dysgenesis is a term applied to a fundamental abnormality of gonadal development in which the degenerate testis or ovary persists as a non-functioning 'streak' gonad. In a 46XY fetus the failure of the dysgenetic testes to produce testosterone and müllerian inhibiting substance results in an entirely female phenotype. Partial gonadal dysgenesis may be unilateral or bilateral, and so gives rise to varying degrees of sexual ambiguity.

Mixed gonadal dysgenesis is most commonly the result of 45X/46XY mosaicism. A mixed gonadal phenotype ensues: for example, an inguinal testis (with limited endocrine function) on one

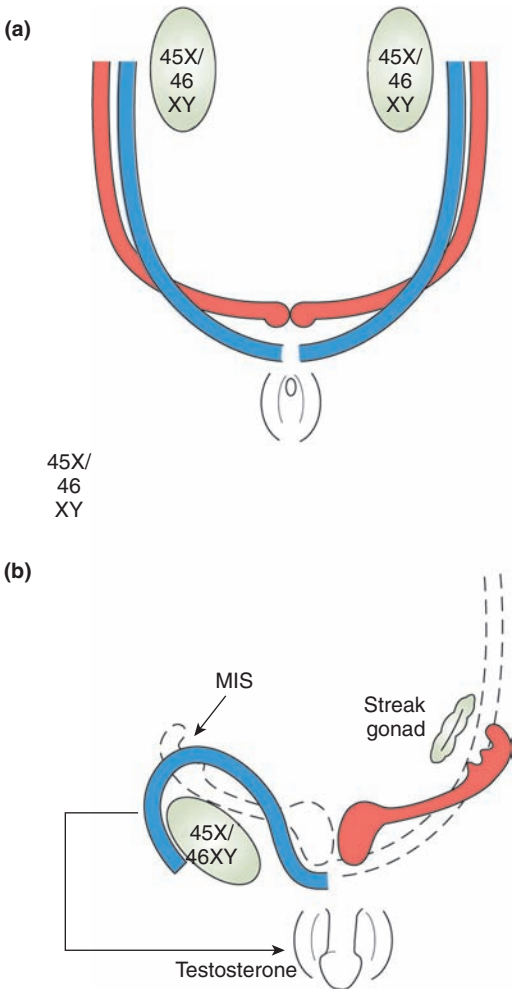

Figure 20.6 Gonadal dysgenesis. (a) Undifferentiated state. (b) Varying embryological patterns and phenotypes. For example, non-functional streak gonad with persistence of paramesonephric structures (left). Mosaicism, right gonad, with male internal genital tract owing to presence of Y chromosome and MIS and testosterone production. Incomplete external virilisation.

side accompanied by a contralateral dysgenetic streak gonad with persistent müllerian derivatives. The external genital phenotype is also variable and, although predominantly female, may, in some instances, be sufficiently virilised to permit rearing as a male (Figure 20.6).

Ovarian dysgenesis (Turner syndrome, 45X or 45X/46XX mosaicism) does not result in sexual

ambiguity, since no tissue containing a Y chromosome is present. Streak or dysgenetic gonads carry a significantly increased risk of malignant change.

Ovotesticular DSD (true hermaphroditism)

This is a variant of gonadal dysgenesis in which the individual possesses both testicular and ovarian tissue, either in separate gonads or coexisting in the same gonad as an ovotestis.

The genitalia are invariably ambiguous. Several karyotypes have been documented, including 46XX/46XY, 46XX and 46XY. The diagnosis is suggested by exclusion of other causes of DSD and is confirmed by macroscopic and microscopic examination of the gonads. The choice of sex of rearing may raise difficulties. In case of female rearing, spontaneous puberty may occur and even pregnancy; in case of male rearing, pubertal development may require sex hormone therapy and there is a significant risk of gonadal malignancy.

Investigation of disorders of sex development

In the newborn period the aims are twofold:

- To recognise any life-threatening underlying metabolic disorder (notably congenital adrenal hyperplasia).
- To establish a precise diagnosis so as to permit an informed decision on gender assignment. Legal registration of the birth should not be performed until such investigation is complete.

Clinical evaluation

Details of the history should include an enquiry about siblings and other family members and details of the pregnancy.

Examination of the newborn should focus on:

- Appearances of the external genitalia, assessment of the degree of virilisation and the presence of pigmentation (favouring a diagnosis of CAH) (Figure 20.7).

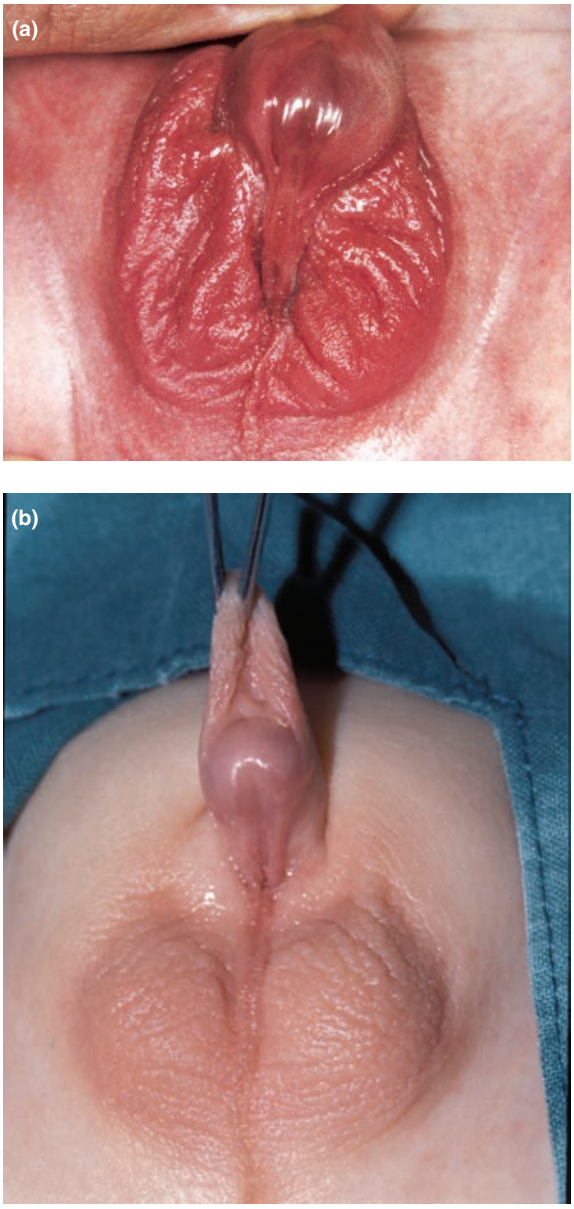

Figure 20.7 Two examples of ambiguous genitalia in 46XX newborn infants with CAH. (a) Ambiguous genitalia in a newborn infant. Severe hypospadias accompanied by an empty scrotum. (b) Appearance which might be mistaken for proximal hypospadias in a male infant. In this situation, however, the absence of palpable gonads should always signal the need for urgent investigation to identify possible CAH.

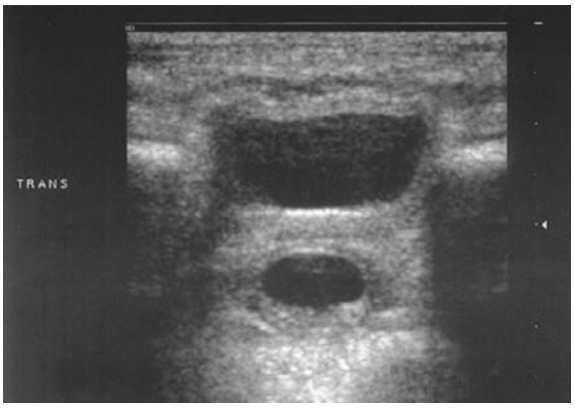

Figure 20.8 Pelvic ultrasound. Transverse view illustrating the bladder (top) and dilated müllerian structure lying posteriorly.

- The presence or absence of palpable gonads.
- The presence of any coexisting abnormalities outside the genital system (which are indicative of a probable teratogenic aetiology).

Laboratory investigations

In addition to routine initial investigations (karyotype, 17-hydroxyprogesterone and plasma electrolytes), more detailed evaluation may include plasma testosterone, basal level and following hCG (human chorionic gonadotrophin) stimulation, steroid assay, e.g. 11-deoxycortisol, MIS levels, DNA analysis to look for specific gene mutations, and studies of binding capacity and androgen receptor activity in genital skin fibroblasts.

Diagnostic imaging

Ultrasound is aimed at identifying gonads and/or a uterus within the pelvis. An enlarged müllerian remnant can often be visualised in the undervirilised male (Figure 20.8).

A genitogram (also termed a 'sinogram') is a contrast study performed via a catheter introduced into the urethra, vagina or the opening of a common urogenital sinus. It demonstrates the anatomy of the urogenital sinus and the junction of the vagina/müllerian structure and lower urinary tract (Figure 20.9). This information is of value when planning the surgical approach to genital reconstruction. In addition, it may be possible to visualise the uterine cervix, uterine canal, fallopian tube(s) or vas deferens.

Magnetic resonance imaging (MRI) is proving to be a very valuable diagnostic tool for elucidating pelvic anatomy in older children but its use in infants is somewhat limited by technical factors and by the need for general anaesthesia to prevent movement during the duration of the study (see Chapter 3).

Surgical investigations

In addition to the information yielded by non-invasive investigations, diagnostic surgical intervention is often required in the form of:

- endoscopy of the lower urinary and genital tracts **(cystourethroscopy and vaginoscopy)**
- **laparoscopy** to identify internal structures (uterus, tubes, gonads)
- in some cases the information needed to establish the diagnosis and guide management will require **pelvic laparotomy and biopsy of the gonads.**

Diagnostic features of disorders of sex development

Where the abnormal physical findings are confined to ambiguous genitalia and impalpable gonads the diagnosis is most likely to be **congenital adrenal hyperplasia**. An elevated plasma level of 17-hydroxyprogesterone associated with positive visualisation of a uterus and ovaries on ultrasound is confirmatory. Although an emergency buccal smear for sex chromatin determination (positive in the case of CAH) can also be performed, modern techniques of karyotyping are preferable and will provide rapid authoritative confirmation of an XX genotype within 48–72 hours. A contrast genitogram will define the level of confluence of the vagina with the urogenital sinus.

The finding of palpable gonads in conjunction with an abnormal sex chromosome karyotype (typically 45X/46XY) points to a diagnosis of **mixed gonadal dysgenesis** or some form of **ovotesticular DSD** (*true hermaphroditism*)

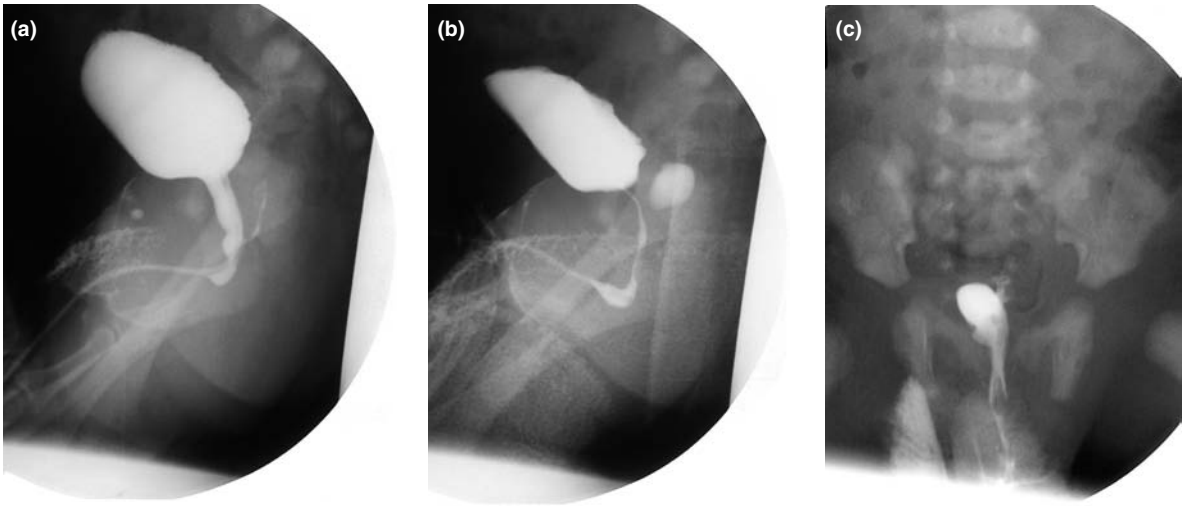

Figure 20.9 Contrast sinogram (genitogram). (a) Injection of contrast through a catheter positioned too low in the urethra/urogenital sinus may fail to fill the müllerian structure. (b,c) Visualisation of müllerian structure in relation to the lower urinary tract.

(e.g. 46XX/46XY). A normal male karyotype (46XY) is suggestive of (PAIS).

The presence of müllerian structures (uterus, fallopian tubes) indicates a lack of MIS consistent with a diagnosis of gonadal dysgenesis or ovotesticular DSD. MIS deficiency or MIS receptor defect in a 46XY patient is not associated with ambiguous genitalia. The absence of müllerian structures in an infant with genital ambiguity provides evidence of MIS activity and points to a diagnosis of **46XY DSD** (*male pseudohermaphroditism*) due to androgen insensitivity or, rarely, a block in testosterone synthesis.

Gender assignment

This is the defining step in management of a child with a disorder of sex development. The decision on the sex of rearing should be delayed until a precise diagnosis has been established and the likely functional potential of the genitalia has been adequately assessed. This may take some time, particularly when it is necessary to await the outcome of hCG tests or assessment of the potential for penile development in response to androgen stimulation.

Advice on gender should be carefully considered before it is communicated sympathetically to the parents by the key members of the multidisciplinary team. At that time, the plan of further management should be set out as precisely as possible. Once a decision on gender has been agreed it is vital that no uncertainty should persist about the sex of rearing of the child (e.g. ambiguous first names should be avoided).

Although management may have to be individualised according to the particular features of each case, the following broad generalisations apply to the more common categories of DSD anomalies:

- **46XX DSD** (***female pseudohermaphroditism***) – these patients are mostly virilised females with CAH who have normal female internal genitalia, normal ovaries and a normal expectation for fertility. Female sex of rearing is invariably advised, and only in the most exceptional circumstances (e.g. late presentation with established male identity) would it be appropriate to consider male gender assignment.
- **46XY DSD** (***male pseudohermaphroditism***) – female gender assignment is generally advised where the external genitalia are predominantly

or entirely female and there is no realistic prospect of constructing a functional phallus. The presence of androgen insensitivity greatly strengthens the case for female sex of rearing. By contrast, where there is a significantly male phenotype and where a positive stimulation test indicates responsiveness to androgens, male gender assignment is preferable. Typically the phenotype in such cases is characterised by severe hypospadias and bilateral cryptorchidism.

- **Mixed gonadal dysgenesis and ovotesticular DSD** (***true hermaphroditism***) – in both conditions the sex of rearing depends on the phenotype (notably the size of the phallus) and upon the potential for androgen production as revealed by stimulation tests. In practice, female assignment is usually judged the better option, but a male sex of rearing may be considered appropriate if the phallus is amenable to reconstruction and functioning gonadal tissue is predominantly testicular.
- **Müllerian inhibitory substance deficiency or receptor insensitivity** – with the exception of bilateral cryptorchidism and the persistence of some internal müllerian remnants, the phenotype is male. Affected individuals are reared as males.

Cultural considerations may impinge upon the decision regarding sex of rearing. For example, in some situations parents and their medical advisers may believe it is better for a highly virilised child with 46XX DSD (*female pseudohermaphroditism*) to be raised as a male. In some societies an affected individual may find it easier to lead an independent adult life as an undervirilised male than as a sterile female.

Surgical management

Once the sex of rearing has been determined with the parents, appropriate surgical correction of the genital abnormalities should be planned, with the timing being dependent on the nature and severity of the genital abnormality and the preference of the surgeon. The indications for feminising genitoplasty and the nature and timing of surgical intervention have generated considerable controversy in recent years. Where there is agreement between parents and clinicians that feminising genitoplasty is in the child's best interests this should, ideally, be undertaken during the first 6 months of life. The optimum timing for masculinising genitoplasty is between the ages of 6 and 18 months.

The steps in **masculinising genitoplasty** comprise:

- **Hormonal treatment** with testosterone preparations to stimulate phallic enlargement.
- **Excision of müllerian structures.**
- **Phalloplasty** – surgical reconstruction of the severe hypospadias combines correction of chordee to achieve a straight penis and urethroplasty to create an orthotopic meatus. In addition, transposition of scrotal skin may be required to overcome the 'buried' phallus and to improve the overall cosmetic appearances of the genitalia. A two-stage phallic reconstruction is favoured by most paediatric urologists (see Chapter 16).
- **Orchidopexy** is frequently required.

The key steps involved in **feminising genitoplasty** include:

- **Clitoroplasty to reduce the size of the glans and shaft,** which is achieved by combining excision of corporeal erectile tissue with preservation of the neurovascular bundles aimed at preserving normal sensation of the glans (Figure 20.10). Long-term follow-up studies have unfortunately demonstrated significant morbidity and sensory denervation following clitoroplasty in childhood. Some patient groups strongly advocate deferring any surgery until the affected individual is competent to provide informed consent. However, this approach represents a largely untested hypothesis and little, if anything, is known about the psychological impact on the child and parents of rearing a girl with a prominently enlarged phallus resembling a penis. The weight of professional opinion therefore still favours undertaking a careful clitoral reduction in girls with prominent phallic enlargement.
- **Vaginoplasty and labioplasty,** which is surgery to separate the vagina and urethra from the

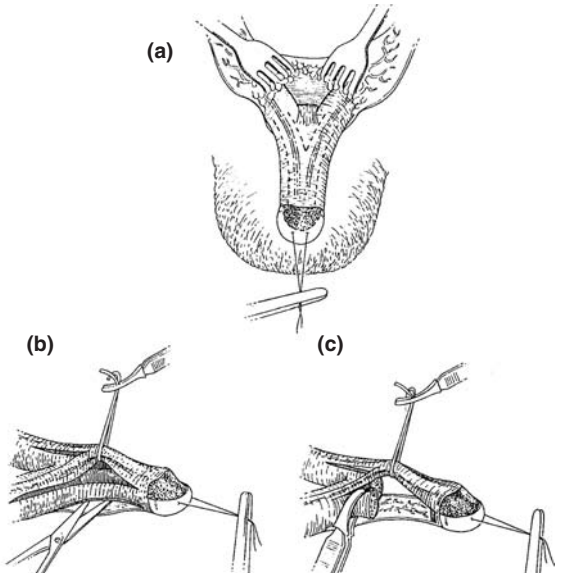

Figure 20.10 Feminising genitoplasty: clitoroplasty. (a) Exposure of the corpora and neurovascular bundles. (b) Mobilisation of the neurovascular bundles. (c) Resection of erectile tissue (the corporeal bodies).

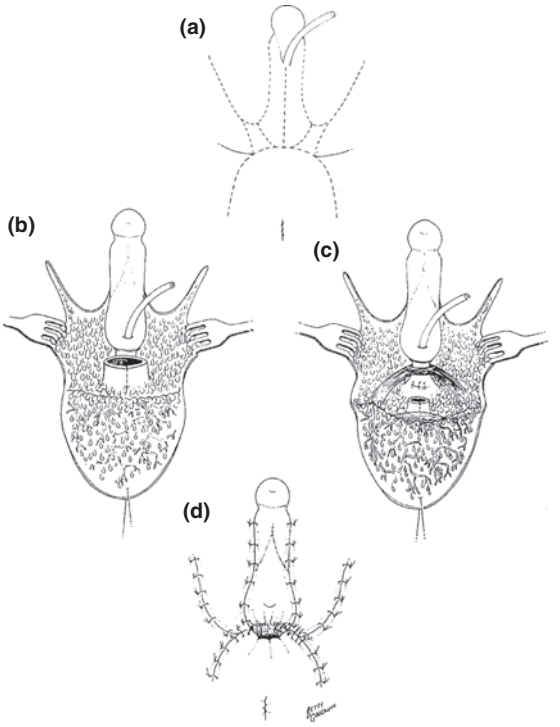

Figure 20.11 Feminising genitoplasty: vaginoplasty. (a) Lines of incision. (b) Exposure of low-lying vagina. (c) Exposure of high vagina. (d) Completed vaginoplasty and labioplasty.

common urogenital sinus and create two separate perineal orifices (Figure 20.11). The introitus and vagina should be adequate to permit normal menstruation and intercourse in adult life. Flaps of 'scrotalised' skin are fashioned so as to create as far as possible normal labial appearances (Figure 20.12). Vaginoplasty may be technically challenging in cases when the vagina opens high in the urogenital sinus. A number of surgical techniques have been advocated to overcome this problem, including perineal, abdominal or anterior sagittal transanorectal approaches (ASTRA).

Whereas it is reasonable to correct low confluence forms of urogenital sinus at the time of clitoroplasty, it may be preferable to defer surgical correction of the 'high' vagina until the menarche and the subsequent onset of sexual activity. This timing permits genuinely informed consent. Moreover, the tissues are more robust and amenable to reconstructive use and there is some evidence that the relative anatomy of the 'high' vagina changes during the course of childhood and early adolescence, making it more accessible to perineal exposure. Finally, if postoperative dilatation is required (which is often the case), this is much better undertaken by a motivated young woman herself than being performed on an apprehensive child. Long-term follow-up studies of feminising genitoplasty performed in childhood have reported a high incidence of vaginal stenosis, necessitating some form of further revision (Figure 20.13).

In the alternative technique of **total urogenital mobilisation (TUM)** the urogenital sinus, urethra and vagina are mobilised as a single unit, which is then brought down towards the perineum. The urethra and vagina are exteriorised and some of the tissue derived from the common urogenital sinus is refashioned to contribute to the reconstructed

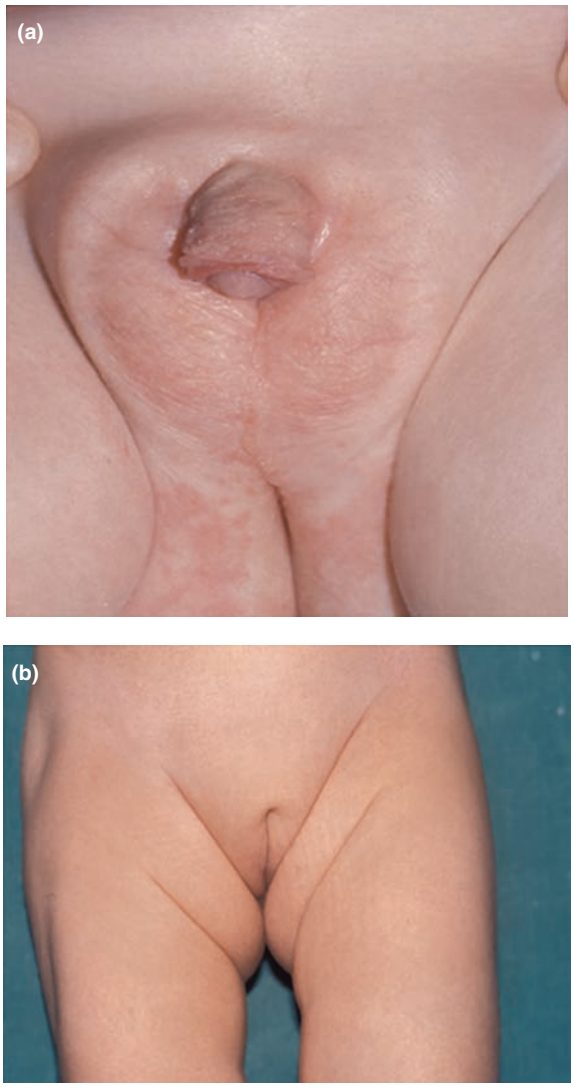

Figure 20.12 (a) CAH. Preoperative appearances of virilised external genitalia prior to feminising genitoplasty. (b) Appearance following labioplasty.

introitus. The long-term results have yet to be fully assessed and concerns have been expressed about the possible risk of sphincteric weakness and stress incontinence.

CAH is the most common indication for feminising genitoplasty. In conditions not associated with external virilisation and where the vagina is absent or grossly atretic, it is generally agreed that vaginoplasty should be deferred until after puberty.

Gonadal management

- **46XX DSD** (*female pseudohermaphroditism*): the ovaries are normal and no specific treatment is required.
- **46XY DSD** (*male pseudohermaphroditism*): where female gender is assigned (as in complete androgen insensitivity), the testes should be removed, although whether this should be performed in infancy, childhood or after puberty remains a subject of debate. Where it is decided to rear an affected individual as a male, orchidopexy is performed to bring the testes to the scrotum.
- **Mixed gonadal dysgenesis and ovotesticular DSD** (*true hermaphroditism*): gonadal biopsy may be required to define the nature and distribution of the different gonadal tissues. Streak (dysgenetic) gonads are excised, whereas gonadal tissue concordant with the sex of rearing is conserved. Sex hormone replacement therapy may be needed at and after puberty.

In view of the high risk of malignancy after puberty any retained testicular tissue should be placed surgically within the scrotum to facilitate careful monitoring. This is particularly important in cases of gonadal dysgenesis or ovotesticular DSD. Lifelong follow-up is required, involving testicular self-palpation, ultrasound and, eventually, postpubertal testicular biopsy for evidence of carcinoma in situ.

Persistent müllerian remnant (prostatic utricle)

This is predominantly a feature of impaired virilisation, with proximal hypospadias or DSD accounting for more than 90% of cases. At one end of the spectrum, the müllerian remnant consists of little more than a slightly enlarged prostatic utricle, whereas more severe cases may comprise a pseudovagina (vagina masculina), accompanied by a rudimentary uterus and fallopian tubes.

In many instances the anomaly is identified during the investigation of ambiguous genitalia or, for

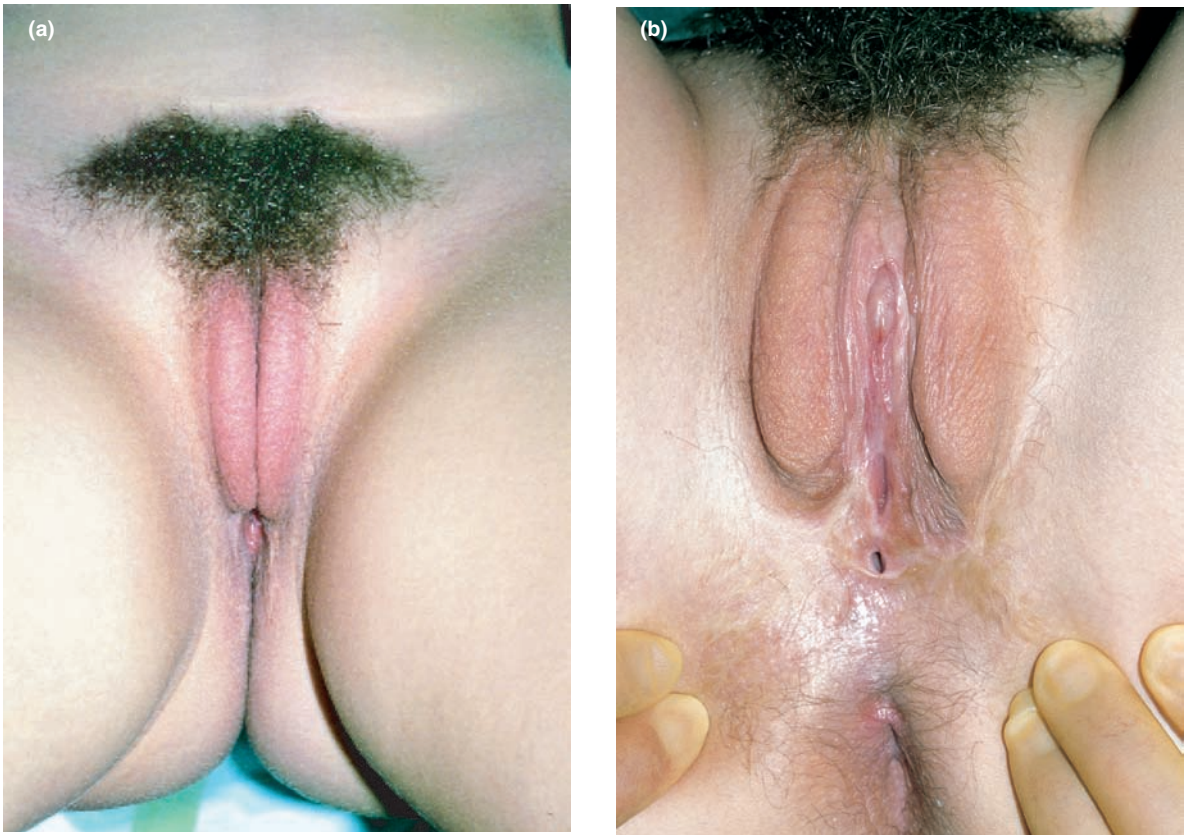

Figure 20.13 Postpubertal outcome of feminising genitoplasty for the correction of virilisation associated with congenital adrenal hyperplasia. Single-stage feminising genitoplasty previously undertaken in the first year of life. (a) External cosmetic outcome satisfactory, with no visible phallic hypertrophy and normal appearance of labia created from 'scrotalised' skin. (b) Retraction of the labia reveals introital scarring, requiring introitoplasty to permit normal, comfortable intercourse.

example, when it interferes with bladder catheterisation during hypospadias repair. Symptomatic presentation includes infection (e.g. epididymo-orchitis due to associated vasal reflux), stone formation within the stagnant urine in the prostatic utricle, postvoid dribbling, obstructed voiding and haemospermia. In such cases, diagnosis is by contrast radiology, ultrasound and MRI. Small asymptomatic müllerian remnants are managed conservatively. Where treatment is indicated the options include endoscopic incision or deroofing or formal excision. In the past, this was performed via a transvesical approach, employing a midline trigonal incision to expose and excise the distended müllerian remnants. More recently, however, laparoscopic excision has been reported.

Gynaecological disorders of childhood

Symptoms relating to the external genitalia of prepubertal girls are common and often generate considerable parental anxiety. A balanced approach is required to avoid causing unnecessary distress by overinvestigating healthy children while recognising those clinical features that may denote more significant pathology.

'Vulvovaginitis'

The term vulvitis is strictly more accurate in most cases, as true vaginitis is rare in childhood, whereas

non-specific inflammation of the non-oestrogenised prepubertal skin of the intoitus and vulva is very common. Irritation and itching are the dominant symptoms, accompanied by localised dysuria and slight discharge.

Parents tend to interpret the symptoms of vulvitis as evidence of 'cystitis' or of urinary infection.

It is therefore important to enquire specifically about those aspects of the history, such as frequency, fever, suprapubic or loin pain, which help to distinguish genuine urinary infection from localised vulvitis (although the two diagnoses may sometimes coexist).

Hyperaemia of the vulval skin may be apparent if there is florid active inflammation, but examination generally reveals normal external genitalia.

Treatment is aimed at correcting any identifiable predisposing causes, such as poor perineal hygiene, tight-fitting clothes and threadworm infestation. Antibiotic treatment is often effective and may be justified on an occasional short-term basis where symptoms are severe (although culture swabs generally reveal a mixed growth of perineal commensal flora).

Longer-term antibiotic usage should be avoided. Similarly, the use of antimicrobial pessaries is inappropriate in children. Unfortunately, some girls continue to experience troublesome episodes of symptomatic non-specific vulvitis despite a range of simple preventative measures. Reassurance and an explanation of the aetiology and self-limiting nature of the condition is often helpful in allaying parental anxiety.

Labial adhesions

Labial adhesions are inflammatory in aetiology and are a consequence of vulvitis. The condition presents most commonly between the ages of 2 and 6 years. Gentle separation of the labia majora reveals flimsy midline fusion of the labia minora occluding part or most of the introitus.

In time, labial adhesions always resolve spontaneously. However, active measures to separate the adhesions may be indicated if anxious parents seek positive reassurance that their daughter's genitalia are normal. Active intervention is also justified if occlusion of the introitus by labial adhesions results in dribbling of urine which has pooled in the vagina (Figure 20.14).

The simplest treatment comprises a 7–10-day course of an oestrogen or topical steroid cream applied to the area of adhesions. Alternatively, where it is thought justifiable to intervene surgically, the adherent labia are separated with a probe or pair of artery forceps under general anaesthesia. Parents should be warned that recurrent adhesions are not uncommon.

Vaginal discharge

A copious or purulent vaginal discharge is uncommon and should be investigated. Possible causes include a vaginal foreign body, specific bacterial infections and perineal ectopic ureter. Although vaginal rhabdomyosarcoma typically presents with a bloody discharge, this is not always the case. Depending upon the clinical picture, initial investigation generally includes ultrasound imaging of the pelvis and urinary tract and examination under anaesthesia. The possibility of sexual abuse and sexually transmitted infection should be considered and the relevant bacteriological examinations performed (i.e. for *Neisseria gonorrhoeae*) at the time of the examination under anaesthesia.

Vaginal bleeding

Although inflammation of the vulval region may occasionally be associated with slight spotting of blood on the underclothes, the passage of frank blood or a bloodstained vaginal discharge is potentially an ominous sign demanding prompt investigation at a specialist centre.

Rhabdomyosarcoma of the vagina (sarcoma botryoides) is a tumour of infancy and early childhood, whereas uterine rhabdomyosarcomas occur from the teens onward. Other causes of vaginal bleeding include trauma, foreign body, vascular malformations and precocious puberty.

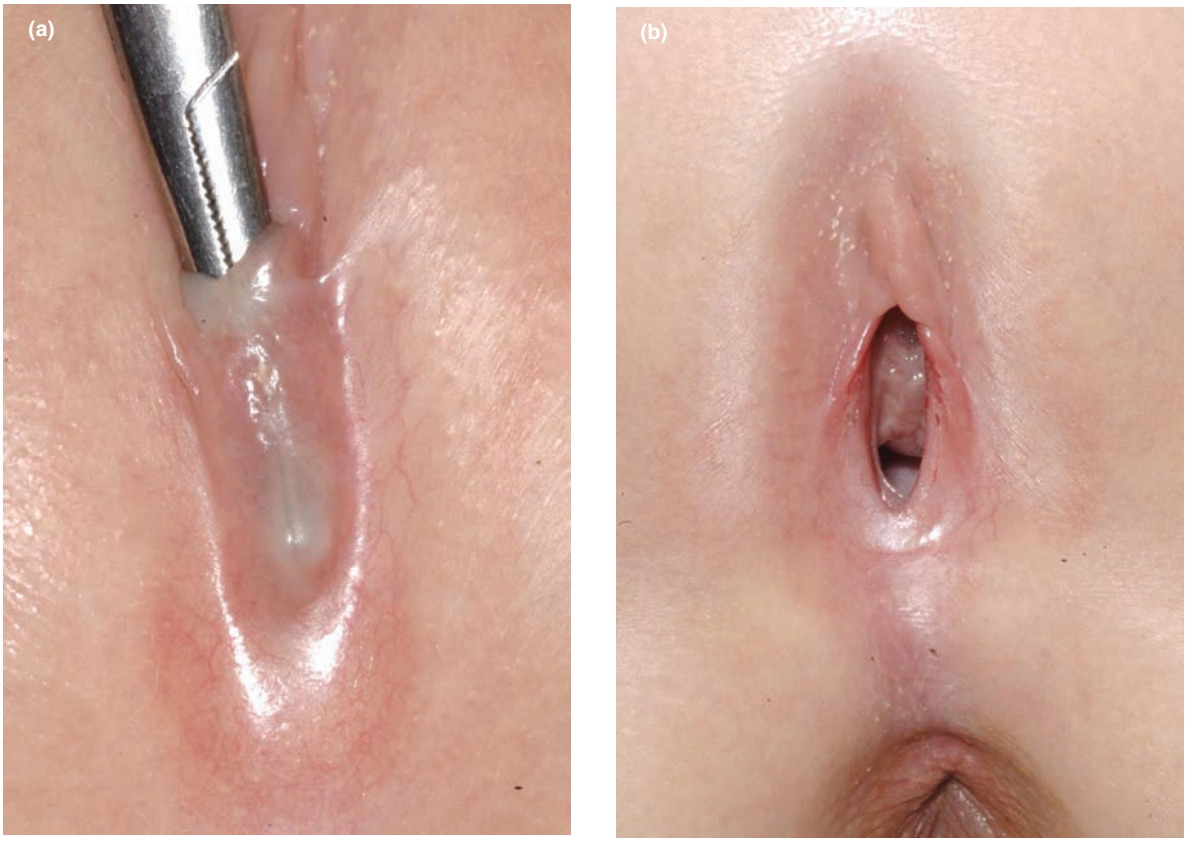

Figure 20.14 (a) Separation under general anaesthesia of extensive labial adhesions causing introital occlusion and postvoid dribbling. (b) Normal appearance of external genitalia confirmed following separation of adhesions.

Congenital anomalies of the vagina

In girls with **imperforate hymen** the vagina is obstructed but otherwise embryologically normal. Accumulation of secretions within the obstructed vagina and/or uterus (hydrocolpos or hydrometrocolpos) characteristically presents clinically as a bulging introital mass in the newborn period, or as primary amenorrhoea (or occasionally urinary retention) in pubertal or postpubertal girls. Nowadays the distended vaginal and/or uterine mass may be detected on prenatal ultrasound. Treatment comprises incision of the hymenal membrane.

Mayer–Rokitansky–Küster–Hauser syndrome is characterised by müllerian aplasia. Associated renal anomalies and abnormalities of the skeletal system occur in 10–40% of patients. A familial recurrence rate of 1–2% has been reported and the disorder is thought to be polygenic in aetiology. The spectrum of müllerian anomalies is broad, encompassing conditions such as transverse vaginal septum, vaginal agenesis (complete or partial), absence of the vagina and uterus with rudimentary uterine horns, bicornuate uterus (sharing a common cervix) and uterus didelphys.

The syndrome characteristically presents in early adolescence with primary amenorrhea. In the absence of normal uterine/endometrial tissue, menstruation does not occur and the primary amenorrhea is otherwise asymptomatic. In cases where uterine tissue is present which responds to

cyclical oestrogenic stimulation, obstructed menstruation gives rise to cyclical abdominal pain and, if undiagnosed, an abdominal mass. Alternatively, primary amenorrhoea may be associated with retrograde menstruation, endometriosis and pelvic pain.

Management should ideally be undertaken by a specialist adolescent gynaecologist. Thin vaginal septae can be excised to create continuity between the vagina on either side of the obstruction. More extensive septae or localised atretic segments are more difficult to treat and complex surgery is required to 'bridge the gap'. Longitudinal septae are manifestations of duplication anomalies, which may also include obstruction in one limb of a bicornuate uterus. Excision of the obstructed hemiuterus is undertaken in conjunction with excision of the septum.

Techniques for vaginal replacement include a split skin graft reconfigured as a vaginal pouch over a mould or substitution with a segment of colon or ileum which is mobilized on its vascular pedicle and brought down to the perineum using a combined abdominoperineal approach. Problems can include mucus discharge and diversion colitis.

Ovarian pathology

Streak gonads and ovarian dysgenesis are considered above. Unilateral ovarian agenesis may be associated with unilateral renal agenesis as an isolated anomaly, or as part of a more complex manifestation of the Mayer–Rokitansky–Küster–Hauser syndrome.

Ovarian cysts in infants and young girls are generally benign follicular cysts. Small to medium-sized cysts (5 cm in diameter) detected incidentally on pre- or postnatal ultrasound can be managed expectantly and monitored with ultrasound. The management of larger, asymptomatic cysts is controversial, with the rationale for surgery hinging on diagnostic uncertainty and the risk of torsion.

The classification of ovarian tumours in children is beyond the scope of this book. Benign teratoma is the most common pathology, although malignancy can arise in any of the cell lines of which the teratoma is composed. Some patients present acutely with torsion of the bulky ovarian mass (Figure 20.15).

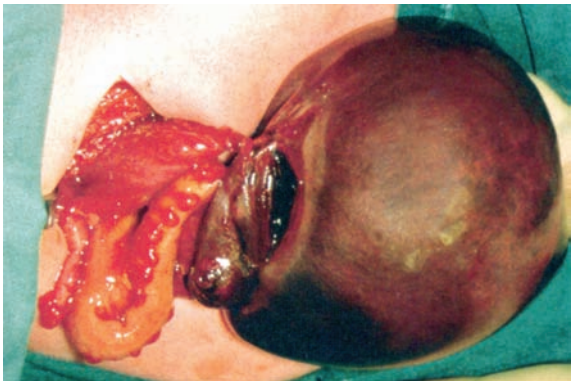

Figure 20.15 Torsion of a large (benign) ovarian cyst.

Key points

- By international consensus, the terminology used to classify these disorders has recently undergone revision, with potentially pejorative terms such as 'intersex' and 'true hermaphroditism' being replaced by 'disorders of sex development (DSD)' and 'ovotesticular DSD', respectively.
- The management of children with DSD should be concentrated in the hands of specialised multidisciplinary teams working in collaboration with local paediatricians and primary care physicians.
- Errors in diagnosis or early management can have disastrous and lifelong consequences for affected individuals and their families. Gender should not be assigned until a firm diagnosis has been established and a clear plan of management defined.
- Congenital adrenal hyperplasia (CAH) is the most common cause of ambiguous genitalia in Western Europe, accounting for approximately 80–85% of cases. Affected individuals are almost invariably reared as

females. Salt-losing forms of the condition are potentially life-threatening unless recognised early.
- Gonadal dysgenesis (associated with differing patterns of sex chromosome abnormalities) represents the second largest group. Sex of rearing and surgical management are individualised according to the phenotype and the potential for sexual function.
- Mild inflammatory vulvitis and labial adhesions are common in young girls. Simple measures are generally helpful but there is no uniformly effective treatment. Other gynaecological symptoms in this age group are uncommon and merit specialist referral for further investigation.

Further reading

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Genitourinary malignancies 21

Patrick G Duffy and Neil J Sebire

Topics covered
Paediatric renal tumours (Wilms' tumour)
Rhabdomyosarcoma
Paediatric testicular tumours

Renal tumours

Introduction

Nephroblastoma (Wilms' tumour) accounts for more than 90% of malignant renal tumours encountered in children and, since the presentation of renal malignancies is broadly similar in this age group, this chapter will focus primarily on nephroblastoma.

With an incidence of 7 per million children per year, nephroblastoma accounts for 6–7% of all childhood cancers, and approximately 100 cases in the UK a year. Although Jessop performed the first nephrectomy in 1877, the tumour is named after Max Wilms, who described a group of children with this malignancy in 1889. Radiation treatment was originally described in 1915, but the prognosis was much improved following the introduction of actinomycin as a chemotherapeutic agent in 1995.

The current 5-year survival rate of greater than 90% has been achieved by the judicious use of surgery, chemotherapy and radiotherapy. Such progress is the result of collaborative national and international clinical trials, including the National Wilms' Tumor Study (NWTS) in the United States, the UK Wilms' Tumour Studies (UKWs) and the International Society of Paediatric Oncology (SIOP) trials. Currently, trials in the United States and Europe differ mainly in the initial management of the patient, and hence the trials are examining slightly different issues. In general, in the United States, children with renal tumours undergo primary nephrectomy followed by chemotherapy, whereas in the UK and Europe, the initial management is biopsy and preoperative chemotherapy followed by interval surgery.

Epidemiology/aetiology

Nephroblastoma is by far the most common renal neoplasm of childhood, although other entities exist (Table 21.1). In the older literature, many of these other lesions, which are now recognised as separate entities, were classified as favourable or unfavourable variants of Wilms' tumour, examples being clear cell sarcoma of the kidney (CCSK) and renal rhabdoid tumour (RRT), both of which were previously categorised as unfavourable histology patterns of Wilms' tumour.

The prevalence of Wilms' tumour is 50% higher among Afro-Caribbean children than children of other races. Although the tumour usually occurs sporadically, a number of syndromes are known to predispose to the development of this malignancy (Table 21.2). Nephroblastoma may also occur in association with aniridia, hemihypertrophy, cryptorchidism and hypospadias.

At least three genes are linked to Wilms' tumour. Located on chromosomes 11p13, 11p15 and 16q, they are found mainly in children with the predisposition syndromes. Specific gene mutations are found only in around 10% of sporadic Wilms' tumours (sporadic tumours account for 90% of cases).

The peak age of presentation of sporadic Wilms' tumour is 3–4 years of age, but children with bilateral disease (5%), or a predisposition syndrome,

Table 21.1 Classification of childhood renal tumours

Benign	Malignant
Mesoblastic nephroma (<1 year of age)	Wilms' tumour
Cystic nephroma	Clear cell sarcoma (bone secondaries)
Angiomyolipoma	Rhabdoid tumour (bone/brain secondaries)
Haemangioma/ lymphangioma	Neuroblastoma (usually retroperitoneal)

Table 21.2 Syndromes predisposing to Wilms' tumour

Denys–Drash	Renal disease (glomerulosclerosis/male pseudohermaphrodite)
WAGR	Wilms', aniridia, genitourinary malformation, mental retardation
Beckwith–Wiedemann	Macroglossia, omphalocoele, visceromegaly

Table 21.3 Differential diagnosis – childhood abdominal mass

Benign	Malignant
Xanthogranulomatous pyelonephritis	Nephroblastoma
Large hydronephrosis	Neuroblastoma
Renal cysts	Hepatic tumour
Splenomegaly	Soft tissue sarcoma
Bowel duplication	

usually present at younger ages. Mesoblastic nephroma is a tumour that is essentially confined to infants under 1 year of age.

Presentation

Nephroblastoma is the most common solid abdominal tumour of childhood and typically presents as a painless abdominal mass in an otherwise well child (Table 21.3). Pain is uncommon and usually results from bleeding into the tumour. Haematuria occurs in 10–15% of cases. Tumour rupture may result from minor trauma and so lead to presentation with an acute abdomen. A left varicocoele sometimes occurs in association with unusually large tumours. Hypertension is more often seen in mesoblastic nephroma.

Symptoms of metastatic spread are rare. The diagnosis of a solid renal tumour can be made solely on ultrasound in most instances, although occasionally the appearances are mimicked by xanthogranulomatous pyelonephritis, a chronic inflammatory reaction within the kidney usually associated with renal calculi (see Chapter 11). This latter condition also presents with a large renal mass, typically with a long-standing history of listlessness and with a finding of anaemia.

Investigations

The routine tests for malignancy are performed (Table 21.4). Specific features to be assessed by ultrasound are extension of the tumour into the renal vein or inferior vena cava, and the blood lakes characteristic of bleeding into the tumour. Computed tomography (CT) scanning clearly demonstrates the renal origin of the tumour, as well as the anatomy of the opposite kidney, and contributes to assessment of tumour within the inferior vena cava, which, if detected, should be treated by chemotherapy prior to surgery. Although useful for planning surgery and assessing tumour size, such imaging techniques are not especially accurate in distinguishing Wilms' tumour from the other less common renal tumours of childhood. Proteinuria may be indicative of Denys–Drash syndrome, with concomitant increased risk of bilateral disease. Wilms' tumour may occasionally manufacture anti-von Willebrand's factor, leading to a bleeding disorder. The presence of elevated VMA

Table 21.4 Investigations for suspected Wilms' tumour

Abdominal ultrasound	–	to include renal vein and inferior vena cava
Chest X-ray	–	anteroposterior (AP) and lateral
CT scan	–	abdomen and lungs
Urinalysis	–	protein, vanillylmandelic acid
Brain/bone scan	–	clear cell sarcoma and rhabdoid tumours only
Blood count	–	to include partial thromboplastin time

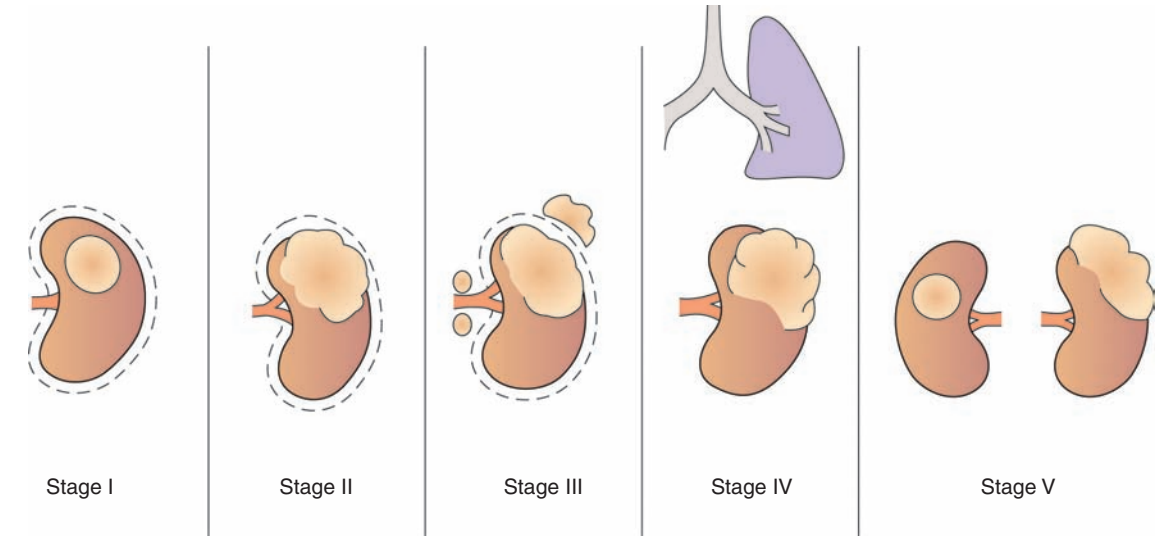


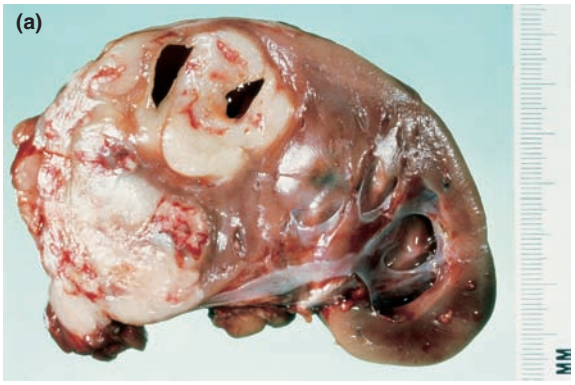
Figure 21.1 Staging of Wilms' tumour. Stage I: tumour confined to the kidney and completely excised macro- and microscopically. Stage II: tumour extending beyond the kidney but completely excised macro- and microscopically. Tumour rupture and spill confined to flank. Stage III: tumour (a) invading adjacent tissues and incompletely excised; (b) incompletely resected because of local invasion; (c) positive lymph nodes; (d) tumour spill not confined to the flank. Stage IV: metastatic disease (usually pulmonary). Stage V: bilateral Wilms' tumours.

(vanillylmandelic acid) in the urine raises the possibility of neuroblastoma, a retroperitoneal tumour usually of non-renal origin.

Treatment

- Biopsy/chemotherapy
- Surgery
- Chemotherapy/radiotherapy.

Management of these lesions in the UK usually consists of initial biopsy and chemotherapy followed by surgery, with further chemotherapy and/or radiotherapy according to the histopathological features of the resected tumour. By contrast, the policy in the United States is to proceed to primary nephrectomy with the aim of removing the malignant tissue as soon as possible following diagnosis. In most of Europe, preoperative chemotherapy is administered in order to reduce the tumour burden and induce chemotherapy-associated shrinkage of the primary tumour to maximise the chance of complete resection.



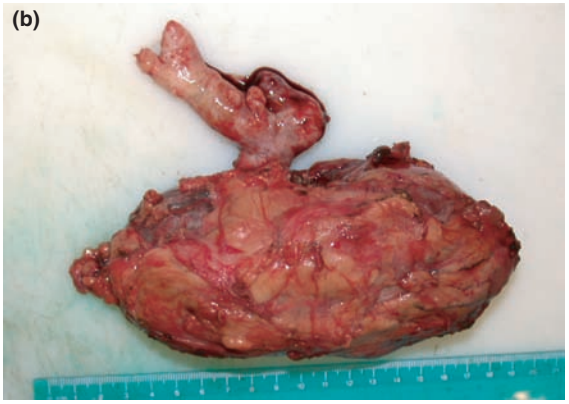


Figure 21.2 (a) Nephrectomy specimen stage II Wilms' tumour. Localised penetration of renal capsule with some tumour extension. Full macroscopic and histological clearance achieved. (b) A nephrectomy specimen from a patient with a Wilms' tumour. The renal capsule is intact and there was obvious tumour extension into the renal vein and inferior vena cava.

In the UK, an initial image-guided needle biopsy is carried out for diagnosis, with the rationale that high-risk tumours, such as clear cell sarcoma of kidney, renal rhabdoid tumour and anaplastic Wilms' tumour, are treated with more intensive chemotherapeutic regimens from the outset. In addition, the other rare entities such as intrarenal neuroblastoma and primitive neuroectodermal tumour can be appropriately treated.

Definitive treatment is determined by tumour staging (Figure 21.1) based on both clinical and imaging assessment, and histopathological findings at surgical excision (Figure 21.2a,b). In unilateral disease, which accounts for 90% of cases, surgery consists of removing the tumour and kidney intact, inspecting the contralateral kidney, and sampling lymph nodes. If tumour shrinkage is sufficient and the site of tumour is favourable, nephron-sparing partial nephrectomy may be an option.

The procedure is performed via a large transverse abdominal incision so as to expose both kidneys and to allow easy access to the inferior vena cava (Figure 21.3a). After ensuring that no tumour is present in the contralateral kidney, the sequence of surgical steps comprises mobilisation of the colon (Figure 21.3b), identification of the major vessels (i.e. the aorta, inferior vena cava, renal artery and vein), ligation of the renal vessels after checking for tumour in the renal vein or inferior vena cava (Figure 21.3c,d) and removal of the kidney and tumour without rupture (Figure 21.3e). All cases receive chemotherapy usually employing vincristine, actinomycin D and doxorubicin (Table 21.5). Radiotherapy is used to treat gross abdominal disease and lung secondaries that have not fully responded to chemotherapy and may also be indicated for local control in stage III tumours.

Complex simultaneous cardiac surgery is occasionally required for cases where inferior vena cava tumour extension has not responded to chemotherapy.

Table 21.5 Example of conventional 'standard' chemotherapy regimens

Stage	Peri-operative Treatment	Period
I	VA	10 weeks
II	VA +/– D	6 months
III	VA +/– D +/– RT	1 year
IV	VCyCD +/– RT	1 year

V = Vincristine; A = ActinomycinD;
D = Doxorubicin; Cy = Cyclophosphamide;
C = Carboplatin; RT = Radiotherapy.

Current chemotherapy regimens are more sophisticated, being tailored to individual staging, histology and other clinical features. A more detailed account is, however, beyond the scope of this chapter

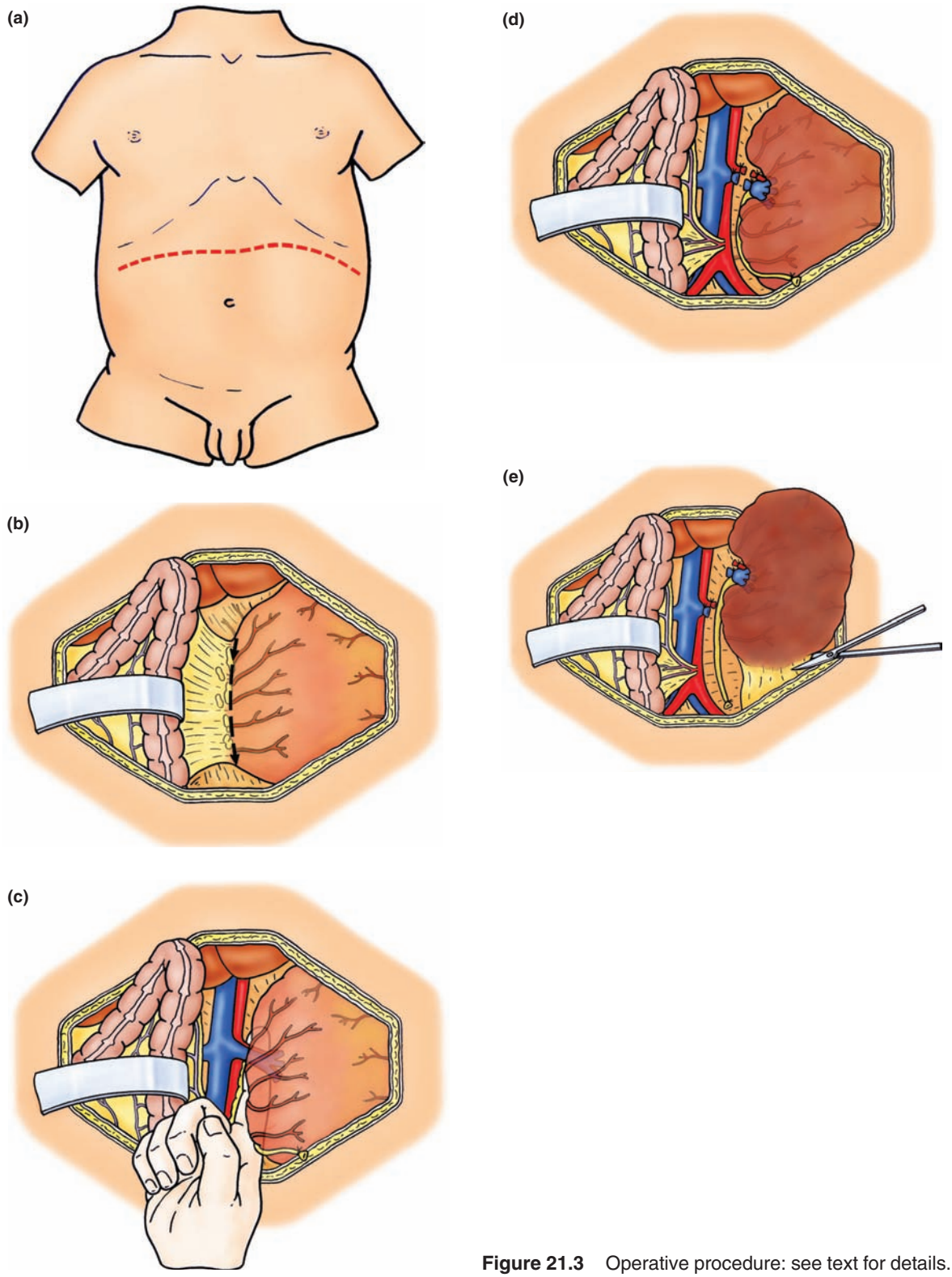


Figure 21.3 Operative procedure: see text for details.

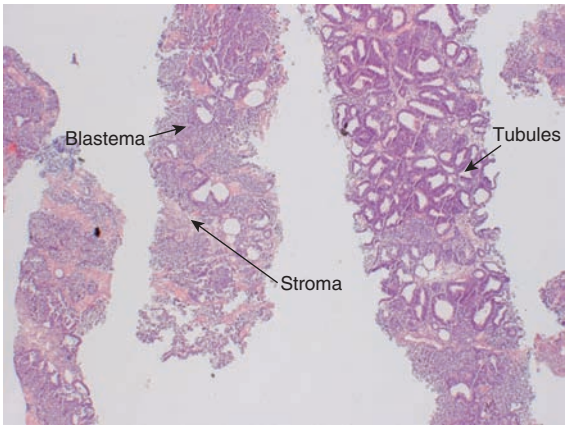


Figure 21.4 Triphasic nephroblastoma. Photomicrograph of a core biopsy from a 3-year-old child with a unilateral renal mass showing the characteristic triphasic histological features of Wilms' tumour.

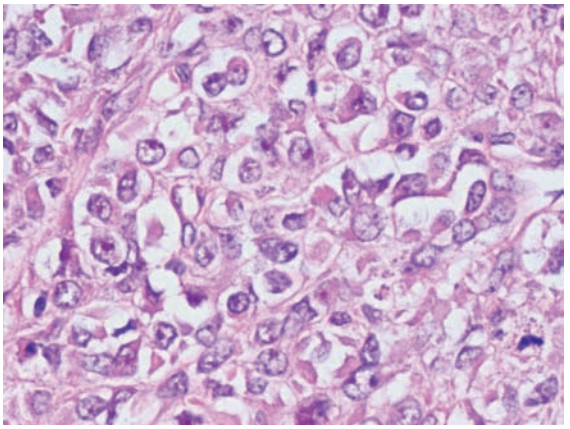


Figure 21.5 Renal rhabdoid tumour. High-power photomicrograph of a 2-year-old child with a unilateral renal mass, which on biopsy was diagnosed as a renal rhabdoid tumour. There is a sheet-like tumour infiltrate, and many cells have characteristic pink intracytoplasmic inclusions, which give rise to the name rhabdoid tumour (although this tumour is completely unrelated to rhabdomyosarcoma).

Histopathology

On histopathology, Wilms' tumour has a characteristic triphasic appearance comprising elements reminiscent of the developing kidney, including immature and poorly differentiated **blastema**, epithelial elements forming **tubules**, and a variable **stromal** component (Figure 21.4). Cases with unfavourable histology represent only around 10% of cases but account for 60% of tumour-related deaths. Categories of unfavourable histology include nephroblastoma with anaplasia, blastemal-type nephroblastoma, and clear cell sarcoma of kidney or renal rhabdoid tumour (Figure 21.5).

Further management of the patient is determined by the histopathological findings of the tumour at nephrectomy following initial chemotherapy. Following histopathological examination, tumours are classified according to the SIOP WT 2001 protocol into low-risk, intermediate-risk and high-risk groups.

Nephroblastomatosis

This uncommon tumour-like condition is characterised by foci of immature elements reminiscent of the developing kidney – with no pseudocapsule. These features are assumed to be precursor lesions for the development of Wilms' tumour and are noted in almost all cases of bilateral Wilms' tumour. They are also present in a minority of tumour specimens removed for unilateral Wilms' tumour, although the significance remains uncertain (Figure 21.6). Rarely, there may be massive bilateral renal enlargement due to extensive involvement with nephroblastomatosis.

Bilateral Wilms' tumour

- Biopsy
- Chemotherapy
- Radiotherapy.

Bilateral disease is managed initially by biopsies (open or trucut) of both kidneys, followed by chemotherapy intended to minimise the extent of subsequent surgery. Fundamental to the latter is preservation of functional renal tissue while at the same time excising all tumour, if necessary employing an extracorporeal technique. In predisposition syndromes (e.g. Denys–Drash syndrome), where both kidneys inevitably become involved, bilateral nephrectomy is followed by haemo- or peritoneal

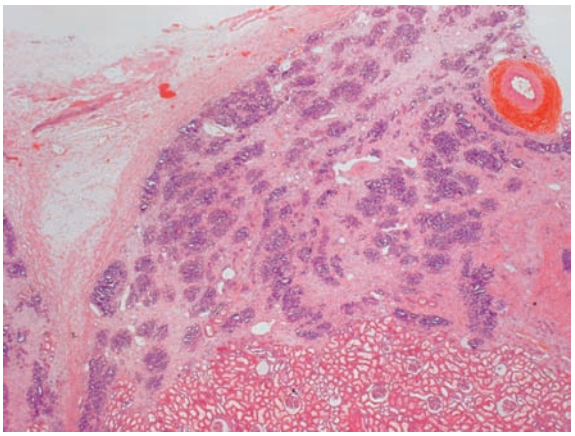


Figure 21.6 Nephrogenic rests. Low-power photomicrograph of a nephrectomy specimen showing the presence of nephroblastomatosis, in which there is an abnormal area of immature epithelial tubular structures in a subcapsular location.

Table 21.6 Wilms' tumour (favourable histology) – 5-year survival rates

Stage	5-year survival (%)
I/II	>90
III	80–85
IV	60–80
V (bilateral)	70–80

Table 21.7 Malignant renal tumours of unfavourable histology – 5-year survival rates

Tumour type	Survival (%)
Anaplastic nephroblastoma	60
Clear cell sarcoma of kidney	70–80
Rhabdoid tumour	20

dialysis. Renal transplantation may then be undertaken in the event of 2-year disease-free survival.

These management strategies for unilateral and bilateral disease are derived from the UK trials. Other regimens employed elsewhere incorporate the same basic principles but have subtly different balances in the burdens of chemotherapy and radiotherapy. The European and UK regimens, for example, achieve similar results using less radiotherapy but more chemotherapy. Vincristine and doxorubicin are administered preoperatively to reduce the risk of tumour rupture and the need for subsequent radiotherapy, and whole lung radiation is not routine for stage IV disease. Renal bed irradiation is omitted in cases where local lymph nodes are disease-free and, although the local relapse rate is higher, this is not at the expense of survival rates, possibly because tumour histology is downgraded by preoperative chemotherapy.

Survival rates are good for patients with favourable histology Wilms' tumour (Table 21.6), but less so in high-risk tumours (Table 21.7). Although improved outcomes have been achieved in patients with high-risk disease, these tumours still carry a poor prognosis, especially clear cell sarcoma of the kidney and renal rhabdoid tumour.

In the event of relapse, approximately 50% of patients are still curable, principally those with subdiaphragmatic relapse and those who, although treated by chemotherapy, have received no previous abdominal radiotherapy.

Although Wilms' tumour currently carries an excellent prognosis, the challenge for the future is to maintain these outcomes while at the same time reducing the morbidity inherent in adjuvant chemotherapy and radiotherapy.

Rhabdomyosarcoma

Introduction

Rhabdomyosarcoma, which occurs principally during childhood, arises from undifferentiated mesenchyme. As this is the origin of skeletal muscle, differentiation towards tissue resembling mature muscle is a common histological characteristic. Rhabdomyosarcoma is rare, accounting for

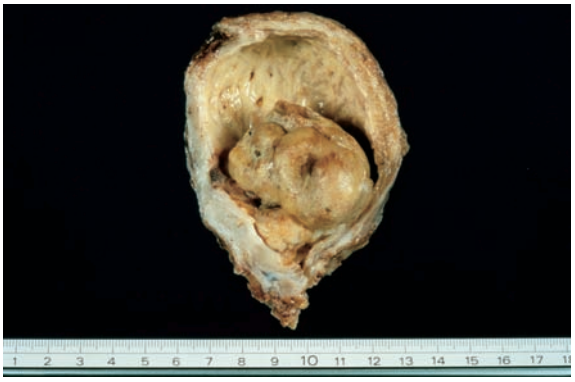


Figure 21.7 Macroscopic appearances of bladder rhabdomyosarcoma in cystectomy specimen.

10–15% of solid malignant tumours of childhood. It affects around 1 in 2 million people annually, with a male preponderance and an increased incidence among Afro-Caribbeans. Although it occurs throughout the body, one-third of tumours arise in the genitourinary tract, in the bladder, particularly the base, or in the prostate, vagina, uterus, or paratesticular region.

Pathology

There are two main categories within the histological classification of rhabdomyosarcoma: embryonal and alveolar. The majority of cases occurring in the genitourinary tract are of the embryonal subtype, typically with a botryoid configuration (Figure 21.7). In girls the tumour classically presents as a grape-like mass protruding from the vagina. Paratesticular rhabdomyosarcomas account for approximately 10% of solid scrotal mass lesions in childhood and usually demonstrate a characteristic spindle cell histology. They are believed to be a subtype of embryonal rhabdomyosarcoma.

The characteristic feature is early differentiation towards skeletal muscle phenotype, which may be manifest as eosinophilic cytoplasm with cross-striations indicative of rhabdomyoblasts. However, the majority of cells may simply appear as immature mesenchymal cells within a loose stromal background. A range of immunohistochemical markers are used to demonstrate the presence of differentiation towards a skeletal muscle phenotype, including desmin and myogenin, and the introduction of these markers has significantly improved the diagnostic accuracy of these entities. Alveolar rhabdosarcoma is now recognised as a sub type with an unfavourable prognosis and increased risk of metastatic disease. Definitive diagnosis, especially on a small biopsy, often requires molecular detection of the characteristic *PAX-FKHR* gene fusion transcript, using fluorescence in-situ hybridisation (FISH) or reverse transcriptase polymerase chain reaction (RT-PCR).

The tumour disseminates principally by local invasion, and less often by lymphatic spread (20%) or by distant metastasis (10%).

Clinical presentation

Clinical presentation includes:

- urinary symptoms, e.g. urgency/frequency
- abdominal pain and/or mass
- protruding botryoid vaginal mass.

Rhabdomyosarcoma may occur at any time during childhood, although the uterine form is confined almost exclusively to adolescence. Paratesticular tumours arise both in pre- and postpubertal boys.

Tumours at the most common sites (the bladder base and prostate) give rise to urinary frequency, urgency or retention, and similarly tumours of genital origin if forming a pelvic mass. Lesions obstructing the urinary tract may lead to hypertension or to symptoms of renal failure (Figure 21.8). Haematuria is rare. Vaginal neoplasms may cause correspondingly sited pain or may present as a protruding botryoid mass. Examination typically reveals a lower abdominal mass or a distended bladder.

Investigation

Routine initial investigations comprise chest X-ray, pelvic and urinary tract ultrasonography, cross-sectional imaging (CT; Figure 21.9) or magnetic resonance imaging (MRI) of the pelvis and chest,

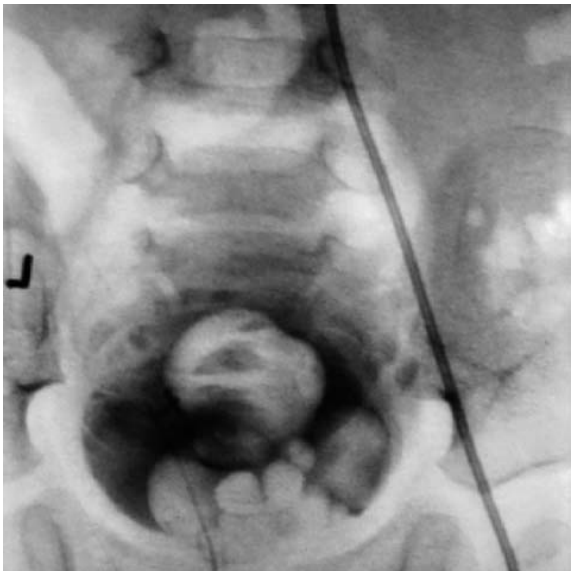


Figure 21.8 Micturating cystourethrogram demonstrating a lobulated filling defect (rhabdomyosarcoma) in the bladder of a 14-month-old child who had presented in renal failure owing to bladder outlet obstruction.

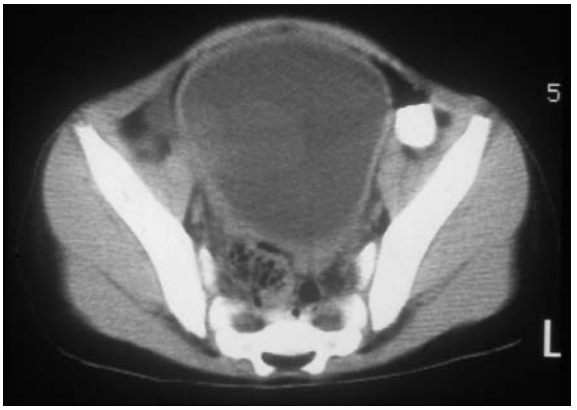


Figure 21.9 CT scan of the pelvis in a child with rhabdomyosarcoma presenting with an abdominal mass (distended bladder).

radioisotope bone scintigraphy and bone marrow aspiration. Renal function should be assessed if there is evidence of upper tract dilatation.

Although the imaging studies are usually diagnostic, specific histological assessment is mandatory prior to treatment. The necessary biopsy tissue may be obtained percutaneously, transurethrally or by open surgery according to circumstances. Endoscopic examination is a further prerequisite in most instances.

Management

- Biopsy
- Chemotherapy and/or radiotherapy
- Organ-sparing surgery.

Management is determined by considerations of histology, anatomy and local or distant spread. Except in rare instances where tumours at a favourable site (e.g. the bladder dome) can be dealt with by excision biopsy, initial treatment is chemotherapy, which is followed by surgery preserving, if at all possible, the organ of origin. Chemotherapy regimens involve vincristine, actinomycin D, cyclophosphamide and ifosfamide in various combinations. Radiotherapy, either as an external beam or as a radioactive iridium wire inserted into the urethra or vagina, is employed to treat microscopic disease following surgery or, rarely, as the principal form of treatment in cases where adequate tumour control cannot be achieved without major ablative surgery.

Surgery may take the form of partial cystectomy, submucosal resection of intravesical lesions, or excision of tumour masses adherent to bladder or prostate. Total cystectomy, with or without urethrectomy, represents a salvage procedure to be used only in cases with intravesical, bladder base or prostatic recurrence following chemotherapy, radiotherapy and previous conservative surgery.

Prognosis

The evolution during the last 20 years of multimodal therapies based on collaborative international trials has achieved 70–80% 5-year survival rates. Nonetheless, although such success is achievable while retaining the bladder in some two-thirds of cases, this is not without cost, particularly in respect of persistent urinary frequency and incontinence.

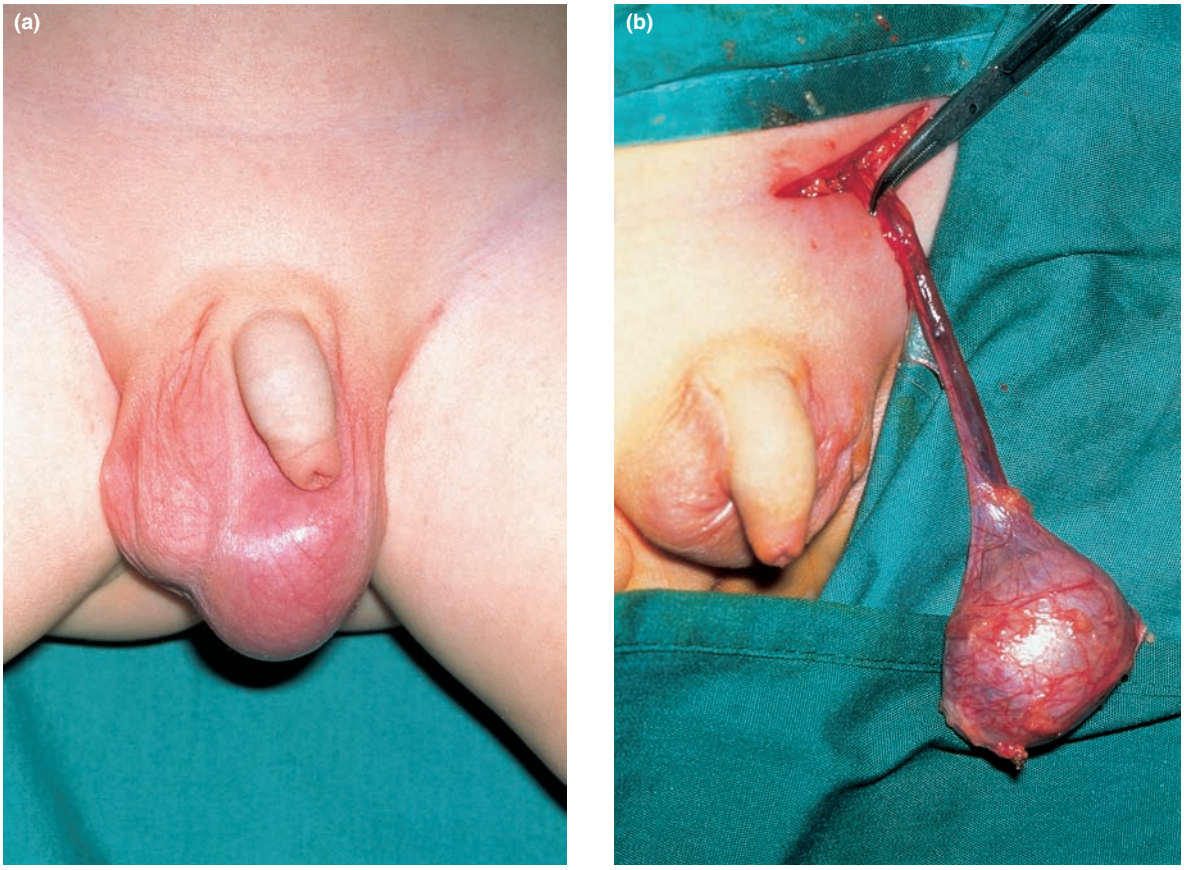


Figure 21.10 (a) Paratesticular rhabdomyosarcoma presenting as a solid testicular swelling. (b) Operative findings in the patient in (a). As in adults, exploration and orchidectomy should be performed via an inguinal approach and not by a scrotal incision.

The major challenge for the future lies in improving survival rates while at the same time reducing morbidity, both generally and in relation to local sequelae.

Testicular tumours

The incidence of testicular malignancies in the paediatric age group is in the range 0.5–2 per 100 000. They are conveniently categorised according to the usual age at the presentation. Testicular tumours in this age group do not tend to metastasise and mostly come to light as a painless scrotal swelling, sometimes in association with a (usually small) secondary hydrocoele.

Germ cell tumours

Yolk sac tumours

With few exceptions presentation is before 2 years of age, and in most cases treatment amounts to no more than excision of the affected testis after clamping the cord via an inguinal approach. α-Fetoprotein is a sensitive marker of this tumour and, if serum levels do not return to normal following orchidectomy, metastatic spread is likely. This may be confirmed by chest X-ray or CT scan.

The occurrence of metastases is seen in only 13% of cases and is generally treatable by chemotherapy.

Teratoma

The second most common testicular neoplasm of childhood, teratoma principally affects the very young, 18 months being the mean age at presentation. Orchidectomy is curative, as metastatic disease does not occur in prepubertal boys.

Other testicular tumours

Sex cord stromal tumours

Leydig and Sertoli cell tumours usually present between 5 and 10 years of age. In contrast, juvenile granulosa cell tumours present at birth. Secondary tumours of the testis in prepubertal boys are almost always associated with lymphoma or leukaemia; 4% of such patients are affected.

Germ cell tumours and testicular maldescent

Approximately 10% of germ cell tumours in adults arise in undescended testes, the higher the location of the gonad the greater being the risk. The evidence remains somewhat contradictory on whether the risk is reduced by orchidopexy, and, if so, by its timing (see Chapter 18). The contralateral gonad is also at enhanced risk of malignancy.

Paratesticular rhabdomyosarcoma

These tumours account for 10% of solid scrotal mass lesions in childhood. Presentation is with a discrete testicular lump, often in association with a small secondary hydrocoele (Figure 21.10a,b). Investigation and treatment are approached in a similar fashion to that already described for rhabdomyosarcoma in other anatomical sites. The reported 3-year survival rate is in the order of 90%.

Key points

- Wilms' tumour now has an excellent prognosis, with treatment based on a combination of surgery, chemotherapy and, in some cases, radiotherapy. The challenge for the future is to maintain excellent survival figures while reducing the morbidity related to intensive treatment regimens.
- Rhabdomyosarcoma is a rare malignancy managed by chemotherapy, radiotherapy and organ-sparing surgery insofar as this is feasible. The difficulty lies in balancing the desirability of localised excision which preserves an intact bladder and urethral sphincter against the risk of local recurrence of an aggressively malignant tumour. Where the tumour is totally excised the long-term prognosis is good.
- Most childhood testicular malignancies can be managed by orchidectomy and close follow-up.

Further reading

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Urogenital trauma

22

David FM Thomas

Topics covered
Renal trauma
Ureteric injuries
Bladder injuries
Urethral injuries
Injuries to the external genitalia

Introduction

Although minor injuries to the genitourinary tract are relatively common in childhood, major trauma is fortunately rare and, with the exception of isolated blunt renal trauma, tends to occur in conjunction with other injuries. Penetrating injuries resulting from gunshot or stab wounds of the type encountered by paediatric urologists in the United States are exceptionally rare in Western Europe, where the overwhelming majority of injuries to the urogenital tract in children result from blunt injury.

Although the general principles of the management of urological injuries in children follow broadly similar lines to those in adults, the overall management of the injured child demands specialist paediatric expertise and the input of a number of relevant disciplines.

The organisation of trauma services for children is beyond the scope of this book, but it is generally accepted that children with multiple trauma involving the urinary tract should be transferred to a specialist regional centre once their initial condition has been stabilised. Trauma of a minor nature, however, can generally be managed locally, with advice being sought from a specialist paediatric urologist where appropriate.

Although isolated genital injuries often have an innocent explanation, the possibility of sexual abuse, particularly in girls, should never be overlooked, and the early involvement of a paediatrician with appropriate expertise should be sought, particularly as forensic samples may be required.

Renal trauma

In childhood, the kidney is more susceptible to blunt trauma because it lacks the degree of protection afforded to the adult kidney by the bulk of surrounding perirenal fascia and overlying muscle. In addition, the ribs are less well ossified in childhood and the kidney is more vulnerable because it occupies a relatively larger space within the retroperitoneum. Although abnormalities such as pelviureteric junction (PUJ) obstruction render the kidney more susceptible to injury (sometimes of a seemingly trivial nature), pre-existing pathology is a contributory factor in fewer than 10% of cases of blunt renal trauma (Figure 22.1).

Data collected by the US National Pediatric Trauma Registry recorded renal injuries in approximately 2% of 49 651 paediatric trauma cases. The average age of children sustaining a renal injury was 10.6 years, with boys outnumbering girls by a ratio of almost 2:1. In this large series of renal injuries, there were no reports of injury to a solitary kidney. The causes of renal injury included road traffic accidents, cycling and a range of sporting activities – notably American football.

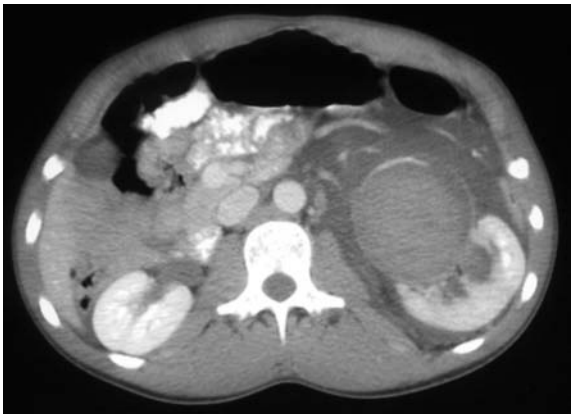

Figure 22.1 A 12-year-old boy was admitted with renal trauma after receiving a seemingly trivial blow to the abomen while at school. The CT scan demonstrates extensive extravasation and blood clot within the dilated left renal pelvis. Exploration confirmed rupture of the renal pelvis associated with pre-existing pelviureteric junction obstruction. There was full recovery and preservation of normal differential function following repair of the renal pelvis and pyeloplasty.

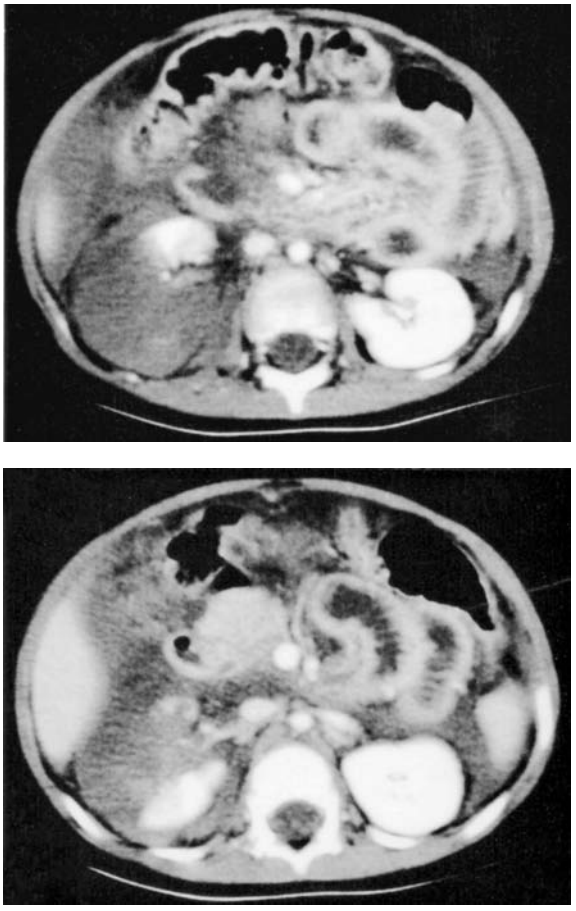

Figure 22.2 CT scan with contrast. Two images demonstrating transection of the upper pole of the right kidney in an 18-month-old child. Seatbelt injury sustained in road traffic accident. An associated duodenal rupture was managed by laparotomy but the renal injury was treated conservatively.

Presentation

Isolated renal trauma most commonly results from a sporting or playground injury. In children the extent of the renal injury may not correlate closely with the apparent severity of the trauma, and seemingly insignificant injuries can be associated with deceptively severe renal damage. Moreover, children have the capacity to sustain significant blood loss before developing hypotension and other manifestations of hypovolaemia. The presenting clinical features of renal trauma typically include haematuria, loin pain and tenderness, an expanding perirenal mass, and external evidence of injury such as bruising or abrasions.

In children with multiple injuries the renal injury may sometimes dominate the clinical picture, but is often overshadowed by coexisting visceral injuries such as liver, splenic or duodenal rupture (Figure 22.2). In these circumstances it is not uncommon for renal contusion or laceration to be identified during the course of abdominal or initial assessment with computed tomography (CT) scanning.

Investigations

All children with suspected renal injury should be admitted for observation and monitoring of vital signs. Laboratory tests include urine microscopy, full blood count and haematocrit. Renal trauma is almost invariably accompanied by haematuria, but it should be noted that the severity of the haematuria does not correlate well with the extent of the renal injury.

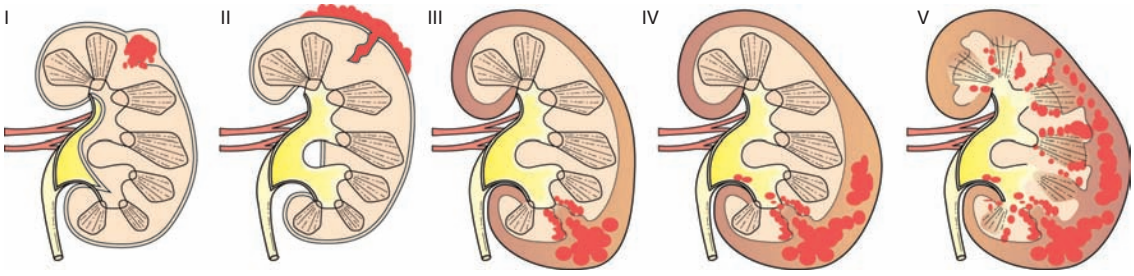

Figure 22.3 Grading of renal trauma. Grade I, renal contusion. Grade II, parenchymal laceration not extending into collecting system. Grade III, parenchymal laceration involving collecting system, perirenal haematoma and extravasation. Grade IV, extensive laceration/parenchymal avulsion injury. Grade V, shattered kidney and/or avulsion of vascular pedicle.

Imaging

In view of the vulnerability of the kidney in children and the potentially deceptive clinical picture in this age group, renal imaging is mandatory in the presence of haematuria or a suspected renal injury. The pattern and extent of imaging, however, may be determined by the overall clinical condition and the availability of imaging modalities. Children with clinical or radiological evidence of a significant renal injury, haemodynamic instability, or evidence of coexisting injuries should be transferred to a specialist centre.

Computed tomography with contrast is the imaging modality of choice, particularly where there is any suspicion of coexisting abdominal visceral trauma. CT is now available in all major paediatric centres and most larger district general hospitals. It permits grading of the renal injury and an assessment of renal perfusion (Figure 22.3). Further CT scans may be required to monitor the course of the injury and to guide any decision on possible surgical intervention.

Ultrasound is a reasonable first-line investigation in a child who is clinically stable and who is thought to have sustained only minor renal trauma. However, appearances in the initial phase following injury can appear misleadingly normal. If ultrasound reveals evidence of renal trauma, a CT scan is always advisable to permit a more detailed functional assessment. Although the intravenous urogram (IVU) has been largely superseded by CT, it remains a useful investigation where CT is not readily available. Unlike CT, however, the IVU provides no additional information on possible injury to other abdominal viscera. Arteriography has likewise been largely replaced by CT scanning, and in any event is of little practical value as the prospects of salvaging renal function by revascularisation in avulsion injuries are remote. The interval between devascularisation and even the most prompt surgical intervention invariably exceeds the warm ischaemic time of devitalised renal parenchyma.

Management

The broader aspects of trauma management in children are beyond the scope of this chapter. However, the guiding principles can be defined as follows:

- All children with a suspected or proven diagnosis of renal trauma (even if seemingly trivial) should be admitted for observation, monitoring of vital signs and imaging.
- Blunt renal trauma should generally be managed conservatively, but in cases of major renal trauma the possible indications for surgical intervention should be actively reviewed at regular intervals. Conservative management of moderate to major renal trauma comprises active monitoring of vital signs, correction of

hypovolaemia (with blood if necessary), and reimaging with ultrasound and further CT or other modalities where indicated. Minor injuries require inpatient observation until frank haematuria has resolved.

Indications for surgical intervention are relative rather than absolute and include:

- **Haemorrhage** resulting in haemodynamic instability, particularly if accompanied by an expanding retroperitoneal haematoma or haemoperitoneum.
- **Urinary extravasation**: a minor or moderate degree of urinary extravasation is not uncommon and does not, in itself, amount to an indication for surgical exploration. Localised collections can be aspirated or drained percutaneously (Figure 22.4a,b). In one series of 374 paediatric renal injuries, even relatively severe (grade IV) injuries were successfully managed non-operatively in 41% of children. Surgical exploration, however, may be warranted if the renal parenchyma is largely intact and there is evidence of a pelvic tear or avulsion of the ureter.
- **'Shattered kidney' (grade V injury)**: even if haemodynamic stability can be achieved, removal of a non-functioning 'shattered' kidney may be justified to hasten recovery and reduce the risk of complications. If there are no other intra-abdominal injuries, exploration can be deferred for a few days rather than undertaken acutely. In the presence of other intra-abdominal injuries requiring laparotomy, a 'shattered' kidney should be removed at the same time.
- **Vascular injuries**: the prospects of successful revascularisation are minimal in view of the relatively short warm ischaemic time of the kidney. Nevertheless, an attempt at revascularisation might be justifiable in the rare event of devascularisation of a solitary kidney or bilateral injury.

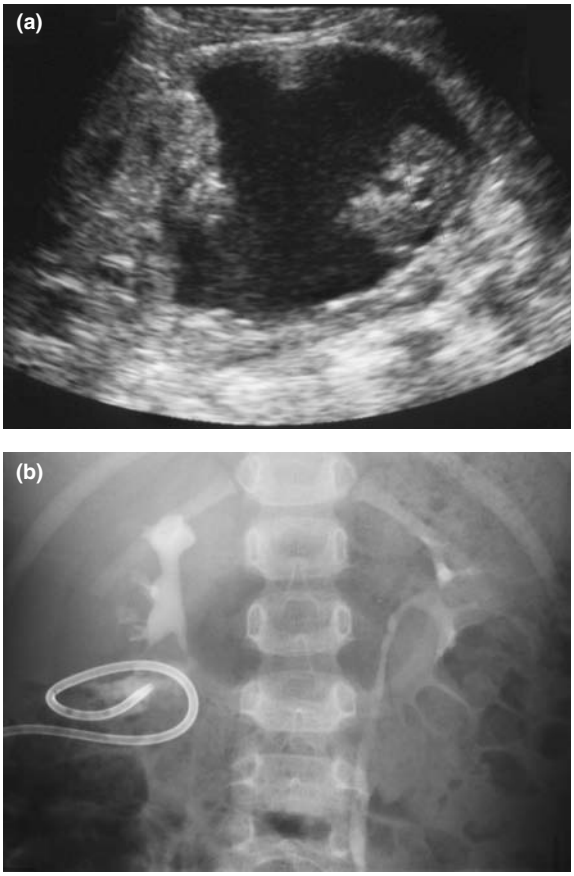

Figure 22.4 (a) Ultrasound scan demonstrating the avulsed lower pole of the right kidney lying free in a large perirenal urinary collection. (b) Pigtail catheter inserted percutaneously to drain an enlarging urinary collection despite 6 days of conservative management. IVU demonstrating leakage of contrast from the severed lower pole calyx. In this case surgical exploration was required some days later to close the leaking calyx and remove the necrotic, avulsed lower pole.

Technical considerations

The kidney should be explored transperitoneally via a midline or upper transverse incision, depending on the age of the child. Laparotomy provides an opportunity to examine the other intra-abdominal viscera for injury and provides better access for vascular control. Prior to exposure of the kidney, the renal artery and vein(s) are identified by their respective points of origin on the aorta and inferior vena cava, and vascular control is achieved by passing vascular slings around the vessels to permit temporary occlusion if required.

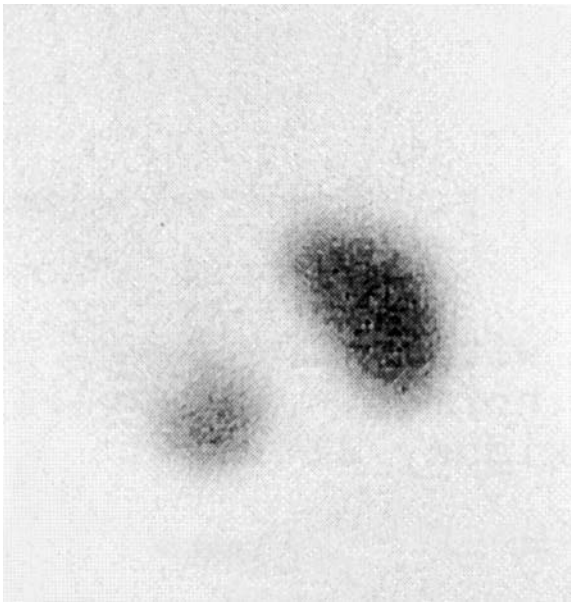

Figure 22.5 DMSA scintigraphy 4 months after renal injury (CT demonstrating right upper pole transection in the patient illustrated in Figure 22.2). DMSA shows complete loss of function in the devascularised lower pole. Differential function right kidney 21%, left kidney 79%.

The nature and extent of the surgical procedure is determined by the operative findings and may include, for example, repair of a parenchymal laceration with closure of any associated collecting system defect, repair of a pelvic tear, or reanastomosis of an avulsed ureter, or debridement and partial nephrectomy. When renal salvage is not feasible or is not justified by the amount of residual functioning renal tissue, nephrectomy is undertaken. However, it is crucially important to have previously obtained positive confirmation that a normal functioning contralateral kidney is present before proceeding with nephrectomy.

Outcome

Early complications include urinoma, infection and abscess formation. Secondary haematuria is not uncommon within the first few weeks of the injury, but is rarely of sufficient severity to require active intervention. Follow-up imaging comprises ultrasound and DMSA (dimercaptosuccinic acid), which is best deferred for 2–3 months after the injury (Figure 22.5). Hypertension is the principal long-term complication, although the true incidence is difficult to assess because of the lack of reliable long-term data. The overall risk of renal-related hypertension following childhood renal trauma is thought to be low – probably around 2–3% – but the relative risk is likely to be greater when a significant bulk of devascularised tissue has been left in situ. There is some evidence that if hypertension is going to occur, the risk is greatest in the first 2 years following injury. Nevertheless an annual lifelong check of blood pressure is advisable for individuals who have sustained significant parenchymal injuries.

What advice should be given to the parents of a child with a solitary kidney? Parents often receive differing advice, with little consistency in the recommendations regarding contact sports. Insofar as it is possible to provide evidence-based advice (e.g. from the findings of the US Trauma Center Study) the statistical risk to a solitary kidney appears to be extremely low. There appears to be little objective justification for limiting the quality of life of children and young people by imposing constraints on normal sporting activities.

Ureteric injuries

Injuries to the ureter are very rare in children and are more likely to be iatrogenic than traumatic in aetiology. Management is individualised according to the nature and level of the injury. Options include spatulation and end-to-end anastomosis over an indwelling JJ stent; mobilisation of the kidney; nephropexy; and pyeloureterostomy for proximal ureteric injuries. Psoas hitch and ureteric reimplantation may be feasible for injuries to the distal ureter.

Bladder injuries

Penetrating injuries of the bladder are exceedingly rare in children and when they do occur are usually

iatrogenic in origin, for example inadvertent damage to the bladder wall during herniotomy. Blunt injuries are similarly rare in this age group and, when they occur, are almost invariably the result of motor vehicle accidents. Spontaneous rupture of the bladder is a recognised and potentially lethal complication of enterocystoplasty, and has also occurred following impaction of a calculus at the bladder neck.

Bladder injuries are traditionally classified according to whether urinary extravasation is confined to the perivesical space (extraperitoneal rupture) or whether there is free leakage of urine into the peritoneum (intraperitoneal bladder rupture).

The presentation of bladder injuries depends on the circumstances in which they have been sustained – for example, iatrogenic bladder perforation during cystoscopy is either recognised during the course of the procedure or becomes apparent as a suprapubic swelling arising out of the pelvis in cases where a catheter has not been left in the bladder postoperatively. Iatrogenic damage to the bladder during herniotomy may be apparent as urinary leakage from the skin incision. Seatbelt injuries present with pain, and major injuries associated with pelvic fractures should be identified during the course of initial evaluation for major trauma. Whenever circumstances permit, the diagnosis should be confirmed by urethral catheterisation and contrast cystography.

Management

Endoscopic extraperitoneal perforation can usually be managed by a period of continuous catheter drainage, but it is advisable to undertake formal repair of any other iatrogenic bladder perforation incurred for example during herniotomy or appendicectomy. Intraperitoneal bladder rupture demands prompt surgical exploration, closure of the bladder defect and, where possible, closure of the overlying peritoneum. Following repair of any bladder injury, continuous postoperative bladder drainage via a urethral or suprapubic catheter should be maintained for a number of days.

The possible diagnosis of bladder perforation or spontaneous rupture should always be actively considered in any patient with a history of bladder augmentation, who subsequently presents with abdominal pain, distension or unexplained systemic ill health and metabolic disturbance.

Urethral injuries

Urethral injuries are generally confined to the male urethra. Three broad mechanisms of injury can be identified:

- Perineal blunt trauma, typically 'stride' or 'straddle' injuries to the bulbar urethra.
- Injuries to the posterior and membranous urethra associated with pelvic fractures (usually road traffic accidents in children).
- Urethral damage resulting from instrumentation or prolonged urethral catheterisation.

Presentation

Blunt trauma – 'straddle injuries'

Children generally present with a history of a traumatic episode and evidence of perineal bruising. Depending on the severity of the injury, the clinical picture may also include urethral bleeding, haematuria or painful urinary retention with bladder distension. Imaging is not usually contributory in the acute phase, although it is advisable to perform an ultrasound scan (and plain X-ray if bony injury is suspected). Ascending contrast urethrography or attempted catheterisation and cystography are not usually tolerated in younger children, but an ascending urethrogram may be feasible in an older boy or adolescent.

Management

Children with suspected or proven urethral injuries should be admitted for observation until the initial discomfort has settled and voiding has been re-established. Where there is evidence of a more severe injury, particularly associated with retention or anuria, the initial management is aimed at

establishing bladder drainage and evaluating the severity of the urethral injury.

If the child does not pass urine despite analgesia, the safest course of action is percutaneous insertion of a suprapubic catheter under general anaesthesia. Urethral catheterisation or urethroscopy may be considered, provided these manoeuvres are undertaken cautiously by an experienced paediatric urologist. However, injudicious attempts at catheterisation or traumatic urethroscopy should be avoided, as this may compound the urethral damage.

After a period of drainage of several days' duration, the urethra is then visualised by contrast descending cystography (and, ideally, an ascending urethrogram). If there is no evidence of extravasation or disruption, the suprapubic catheter can be clamped and normal urethral voiding re-established. More severe injuries of the bulbar urethra are best managed by a sustained period of suprapubic diversion, followed by urethroplasty (see below).

Pelvic fractures

The possibility of injury or disruption of the posterior and/or membranous urethra should be actively considered in any child with a pelvic fracture. As in adults, management of these injuries is controversial, the options comprising:

- prolonged suprapubic drainage followed by elective urethroplasty or
- open exploration, debridement and attempted re-alignment approximation of the urethra over a catheter once the initial effects of the injury have subsided, e.g. after 7–14 days.

Post-traumatic urethral stricture

The treatment options are summarised in Figure 22.6 and consist of the following procedures:

Optical urethrotomy (Figure 22.6a)

This procedure is best suited to short, diaphragm-like strictures. Using a 'cold knife' blade mounted on a paediatric or neonatal resectoscope with a 0° or 5° end-viewing lens, the stricture is visualised, and if necessary a ureteric catheter passed through the central lumen to enable the blade to be positioned accurately. The stricture is then incised under vision with radial cuts. A silicone catheter is left in situ for 48–72 hours postoperatively.

Although optical urethrotomy can be repeated, it is unlikely to prove curative if the stricture recurs despite two or three episodes of treatment.

Urethroplasty

The length and severity of the stricture is delineated preoperatively by a combination of cystography and urethrography, and by instrumentation at the time of surgery. A perineal approach usually gives adequate exposure, but an abdominoperineal or transpubic approach may be required for strictures resulting from pelvic fracture injuries. The techniques of choice in children comprise:

- excision of the strictured urethral segment, mobilisation of the urethra and end-to-end anastomosis (Figure 22.6b)
- incision ('laying open') of the stricture and onlay grafting, ideally with a free graft of buccal 'mucosa', or alternatively with a pedicled or free skin graft (Figure 22.6c).

The surgical management of urethral strictures should only be undertaken by paediatric or reconstructive urologists with extensive experience of urethral reconstructive surgery.

Genital injuries

Genital injuries are uncommon but typically result from playground injuries or animal bites. Scrotal lacerations and severe blunt scrotal trauma should be explored under general anaesthesia to permit debridement and inspection of the testis. When a testicular injury is identified, devitalised tissue is excised, the tunica albuginea repaired, and the scrotum then closed in layers, with attention to haemostasis. Intravenous broad-spectrum antibiotics should be administered for 48 hours postoperatively.

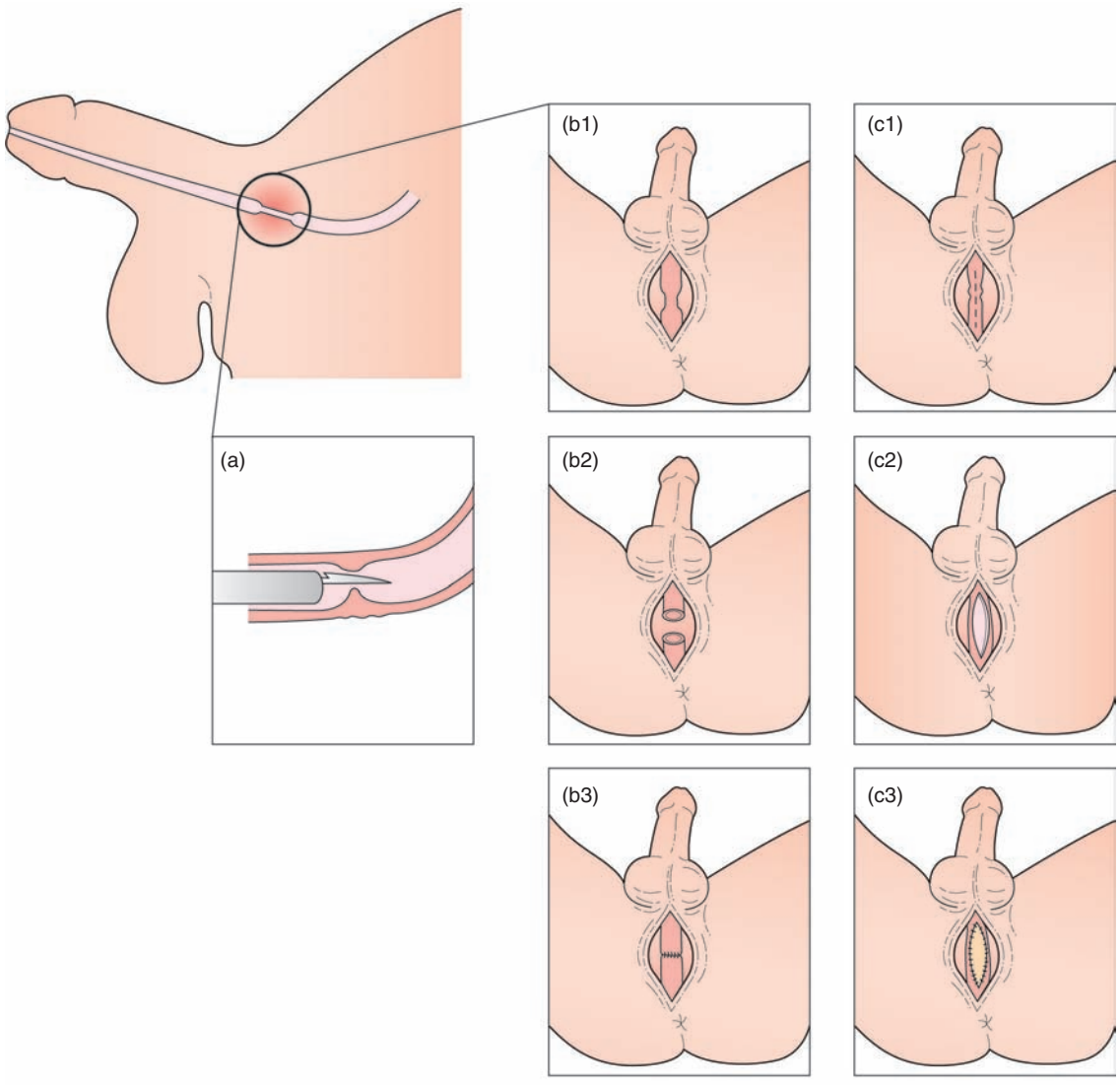

Figure 22.6 Urethral stricture: treatment options. (a) Optical urethrotomy. Best suited to short, well circumscribed strictures. Stricture incised with radial cuts using a cold knife blade mounted on a paediatric resectoscope. (b) 1 Perineal exposure of the bulbar urethra; 2 excision of the strictured segment, mobilisation of healthy urethra; 3 end-to-end primary anastomotic urethroplasty over a silicone catheter. (c) 1 Perineal exposure of the strictured bulbar urethra; 2 incision to lay open strictured segment ('stricturotomy') extended into adjacent healthy urethra; 3 onlay graft of buccal mucosa sutured into the defect.

Penile injuries should be managed according to their site and severity. The possibility of sexual abuse should not be overlooked.

Injuries to the **female external genitalia**, such as stride or straddle injuries, may result in bruising and superficial laceration of the perineum and external genitalia. A short period of suprapubic or urethral catheter drainage may be required in severe cases until the initial early oedema and bruising have resolved. Long-term complications such as strictures are not encountered in girls, as the female urethra is less anatomically vulnerable than in the male. Sexual abuse (rape or attempted rape) is a serious cause of genital injury in girls,

and for this reason the circumstances of the injury should always be actively investigated in any girl presenting with unexplained genital trauma.

Key points

- Potentially serious renal trauma can occur after seemingly insignificant injury. All children with suspected renal trauma should be admitted for observation, imaging and evaluation.
- Most renal injuries can be managed conservatively, but in cases of severe renal trauma the indications for possible surgical intervention should be actively reviewed at regular intervals.
- The (limited) available evidence indicates that the risk of significant injury to a solitary kidney is extremely low and does not justify constraints on normal sporting and leisure activities in childhood.
- The surgical management of post-traumatic urethral strictures should only be undertaken by an experienced paediatric or reconstructive urologist.
- The possibility of sexual abuse should always be considered in any child presenting with an injury to the external genitalia.

Further reading

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Laparoscopic paediatric urology 23

Imran Mushtaq

Topics covered
Benefits and limitations of laparoscopic surgery in children
Patient selection
Fundamentals of technique
Procedures, indications and outcomes
Nephrectomy
Heminephrectomy
Pyeloplasty (including robotic pyeloplasty)
Adrenalectomy
Others

Introduction

Laparoscopic skills are now essential 'tools of the trade' for both paediatric surgeons and paediatric urologists. The benefits of minimally invasive surgery, coupled with parental awareness and demand, have led to its increasing popularity in recent years. Diagnostic laparoscopy for cryptorchidism was first described in 1976 by Cortesi and rapidly became an established technique. By contrast, therapeutic laparoscopy was slow to evolve and it was not until 1990 that Clayman performed the first transperitoneal laparoscopic nephrectomy. Two years later, in 1992, Gaur described the first retroperitoneoscopic nephrectomy.

Benefits and drawbacks

The benefits of laparoscopic surgery to children are well known and include reduced postoperative pain, increased postoperative comfort, reduced hospital stay, quicker return to normal activities, improved cosmesis and reduced wound complications. Although very few randomised controlled studies have been performed to demonstrate these advantages, there is sufficient evidence in the literature to support the philosophy of minimally invasive surgery. The relatively smaller size of the paediatric patient provides the surgeon with the unique advantage of being able to access both the upper (kidney) and lower (ureter) urinary tract through the same port sites. This advantage applies to both the transperitoneal and retroperitoneoscopic approaches, although the purists would prefer the transperitoneal route for access to the very distal ureter. Laparoscopy also provides superior access to the pelvis when dealing with müllerian duct remnants, intra-abdominal testes and cloacal anomalies as examples.

Clearly there are drawbacks to every surgical approach and there are some that are unique to the paediatric population. Paediatric surgeons and urologists have to deal with a very wide spectrum of disease, covering congenital anomalies, benign tumours and malignant conditions, and in addition with the variation in age (neonates to adolescents) and size of the patients. We therefore need to be adaptable to deal with the different situations we may find ourselves having to manage. There are, of course, the technical difficulties of operating in a relatively small space, and this is particularly the case with the retroperitoneoscopic approach. However, recent advances in camera technology and instrumentation have overcome the majority of these limitations. Finally, the financial costs of certain forms of treatment will have a bearing on their acceptance. This can be measured in the adult population as loss of earnings or time to return to

normal activities (particularly their employment in the case of adults). In the paediatric population, the economic advantages of a reduced duration of hospital stay are less obvious.

When laparoscopic surgery was first introduced, it was perceived to carry a greater risk of complications, and it is the case that there are some complications that are unique to laparoscopic surgery. However, retrospective reviews, randomised controlled studies and multicentre trials have reassured the surgical community that laparoscopic surgery can be as safe as open surgery. Complications of laparoscopic surgery in children are similar to those in adults. However, the smaller working space combined with the relatively larger size of the liver, spleen and bladder mean that the insertion of trocars and instrumentation must always be performed under direct vision. The use of a Veres needle to establish pneumoperitoneum is routine in adult practice but is nevertheless associated with some degree of morbidity. In the paediatric population the most common complication associated with its use is extraperitoneal insufflation and surgical emphysema. The close proximity of the intra-abdominal organs, bowel and major vessels places them at risk of iatrogenic injury with the Veres needle. For these reasons the open Hasson technique is the method of choice to establish pneumoperitoneum in children.

Patient selection

The principal urological indications for minimally invasive surgery in children are as follows:

- nephrectomy
- partial nephrectomy
- pyeloplasty
- adrenalectomy
- renal cyst excision/marsupialisation
- pyelolithotomy and ureterolithotomy
- ureteric stumpectomy after partial nephrectomy
- ureteric reimplantation
- impalpable testis
- varicocoele
- disorders of sex development (gonadal biopsy/excision)
- müllerian remnants
- ovarian disorders.

Contraindications

The majority of conditions encountered in paediatric urological practice are either congenital in origin or, if acquired, are of a benign nature; as such, these conditions are all generally suitable for a laparoscopic approach. The role of laparoscopy in the management of malignant tumours in children is yet to be defined, and certainly for Wilms' nephrectomy it is currently not recommended. In the case of malignant adrenal tumours the recommendations from the oncological groups still favour open surgery. However, there are already some reports in the literature describing successful laparoscopic surgery for malignant adrenal tumours.

Absolute contraindications include:

- significant comorbidity (e.g. cardiac, respiratory disease)
- uncorrectable coagulopathies
- sepsis.

Fundamentals of technique

Anaesthesia

Anaesthesia for minimally invasive surgery procedures in children requires endotracheal intubation and the use of volatile and/or intravenous anaesthetic agents. In some cases, such as retroperitoneoscopic surgery for example, the use of a reinforced endotracheal tube may be advisable. Respiration in infants and young children is primarily diaphragmatic in origin. Abdominal insufflation during transperitoneal surgery may compromise diaphragmatic excursion and for this reason insufflation pressures should be kept <10 mmHg in children under 10 kg and <12 mmHg in larger children. When performing retroperitoneoscopic surgery with the patient in the prone position, the chest and pelvis should be kept raised to allow the abdomen to be free of the operating table.

Children are at significant risk of developing hypothermia during laparoscopic surgery, especially with prolonged operating times and a high gas flow. Therefore, the use of warming blankets and padded cotton wool is recommended for all cases.

Most paediatric anaesthetists now routinely recommend pre-emptive analgesia. This can be provided by means of the instillation of analgesic agents into the caudal space, by means of an indwelling epidural catheter or by means of instillation of local anaesthetic drugs into the site of the incision(s). A 'top-up' at the end of a prolonged procedure should be considered, provided the maximal administrable dose is not exceeded.

Instrumentation

Recent advances in digital video technology and instrumentation now allow a wide spectrum of urological conditions to be managed using minimally invasive techniques. Laparoscopic instruments are available in 2, 3 and 5 mm sizes, although the 5 mm instruments remain the most popular for general use. The use of a 5 mm 30° laparoscope provides optimum visualisation for most procedures. The Hasson cannula, which is used for the initial access, is available in 5 mm and 10 mm sizes. For diagnostic and reconstructive procedures (e.g. pyeloplasty), the 5 mm cannula is sufficient. However, a 10 mm cannula is required when use of an Endopouch retrieval device is expected for specimen extraction.

A wide assortment of instrument trocars are now available, both reusable and disposable. Bladeless trocars are generally safer for use in children, where the abdominal wall is more compliant and less muscular.

Access

There are two methods available to access the peritoneum: the blind technique and the open (Hasson) technique. The blind technique involves insertion of a Veres needle adjacent to the umbilicus through all layers of the abdominal wall into the peritoneal cavity. Entry into the peritoneal cavity is confirmed by dropping a small amount of saline into the open end of the Veres needle.

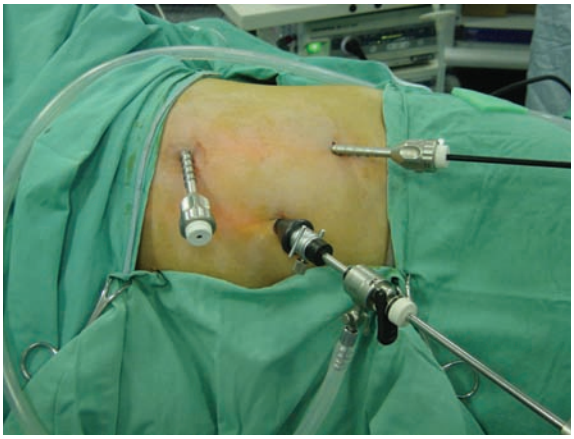

Figure 23.1 Port placement for a transperitoneal laparoscopic nephrectomy. The camera (Hasson) port is placed in a periumbilical position in an open manner, with the cone securely against the incision to prevent loss of pneumoperitoneum.

The open Hasson technique is the preferred approach for access to the peritoneum in children, for reasons already outlined above. A stab incision is made in the supraumbilical skin crease, and is enlarged along Langer's line by inserting and opening the jaws of an artery forceps. The underlying linea alba is grasped and opened transversely with scissors or a scalpel. The peritoneum is grasped and opened in a similar manner. The Hasson cannula is introduced into the peritoneal cavity, keeping the cone of the cannula snug against the skin incision. The cannula is secured in place with a suture through the skin (Figure 23.1). For retroperitoneoscopic procedures a blunt approach is used to access the retroperitoneum and this is described below in the nephrectomy subsection of this chapter.

Current indications for minimally invasive surgery in paediatric urology

Laparoscopic nephrectomy

Over the last decade, the minimally invasive approach for the treatment of benign renal conditions has gained great popularity. Laparoscopic nephrectomy

and nephroureterectomy are now standard procedures in centres where this expertise is available. Laparoscopic heminephrectomy, however, is still not widely practised despite the publication of comparable results to the open technique.

The retroperitoneoscopic approach, initially described by Gaur, is now the approach to the kidney favoured by most paediatric urologists. It avoids colonic mobilisation, the risk of injury to hollow viscera and the potential risk of adhesion formation. However, the reversed orientation of the kidney and hilum with the patient in a semiprone or prone position, combined with the comparatively smaller working space, may make this approach difficult to master. The transperitoneal route has the advantage of a larger working space and may be preferred if the surgeon is relatively inexperienced or when there has been previous renal surgery. Regardless of the approach utilised, the benefits to the child in terms of a faster postoperative recovery and improved cosmesis are without question.

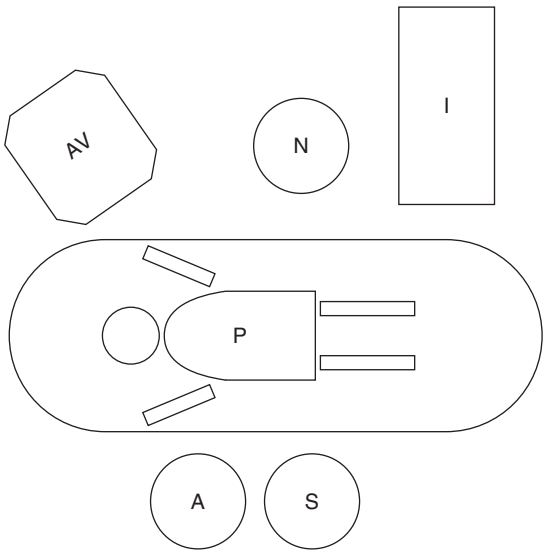

Figure 23.2 Theatre layout for left retroperitoneoscopic nephrectomy, with patient (P) in prone position: monitor and stack system (AV), theatre nurse (N), operating surgeon (S), assistant (A) and instrument table (I).

Indications

Laparoscopic nephrectomy or nephroureterectomy is indicated in the following situations:

- congenital dysplastic kidneys
- multicystic dysplastic kidneys, which, on follow-up, have failed to involute or are associated with systemic hypertension
- pelviureteric junction (PUJ) obstruction with loss of function
- reflux-associated nephropathy
- intractable protein loss associated with congenital nephrotic syndrome
- pretransplant in children with focal segmental glomerulosclerosis.

Operative technique for retroperitoneoscopic nephrectomy

The theatre layout for a retroperitoneoscopic nephrectomy is shown in Figure 23.2. The patient is positioned prone, with the chest and pelvis raised to allow the abdomen to be free. Pressure points are protected in an appropriate manner (Figure 23.3). Topographic landmarks and anticipated port sites are marked as shown in Figure 23.4. A 5 mm transverse incision is made midway between the iliac crest and the tip of the 12th rib, just lateral to the outer border of the sacrospinalis muscle. Through this incision, a small area of the retroperitoneum is dissected bluntly with artery forceps to allow the insertion and inflation of a balloon to create the retroperitoneal working space.

A Hasson cannula is inserted into the port site, followed by insufflation of the retroperitoneum with CO_2 to a pressure of 10–12 mmHg. An instrument port is placed under direct vision below the tip of the 11th/12th ribs and above the iliac crest. A second instrument port can be placed through the paravertebral muscles if required.

Gerota's fascia is incised in a cruciate manner to enter the perinephric space. The kidney is dissected on its posteromedial aspect to expose the hilar vessels: these are individually displayed and divided between haemoclips or with a harmonic scalpel. The ureter should be traced inferiorly as far as necessary and divided. In children with ipsilateral

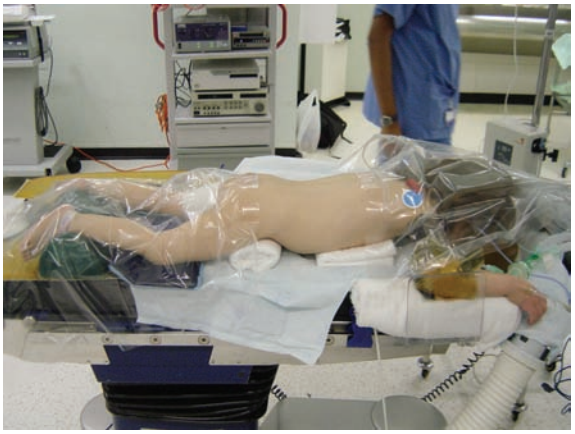

Figure 23.3 Patient positioned for right retroperitoneoscopic nephrectomy. The chest and pelvis are raised to allow the abdomen to lie in a dependent manner. The pressure points (face, arms, knees and toes) are protected with gel pads.

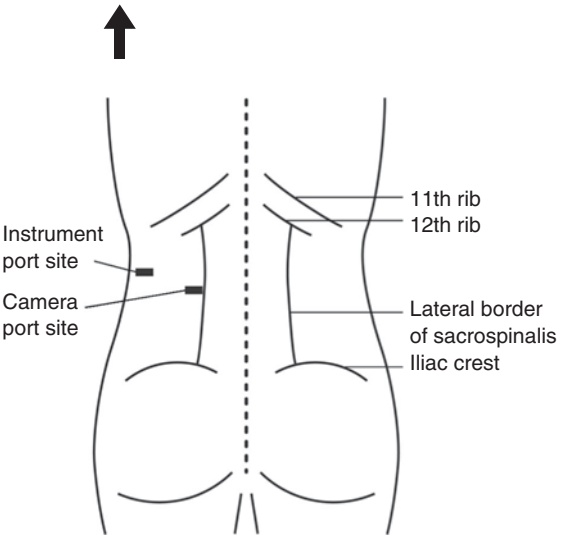

Figure 23.4 Schematic representation of port position. A second instrument port can be placed through the sacrospinalis muscle in a position medial to the camera port site.

vesicoureteric reflux, the ureter should be ligated or the bladder drained with a urethral catheter for 48 hours.

Small kidneys can be removed directly via the camera port, whereas larger specimens may require entrapment in an Endopouch retrieval device and piecemeal removal.

Results

A recent study from Scotland compared the results of laparoscopic and open nephrectomy in children. It was found that a laparoscopic nephrectomy may take longer to perform, but that the children suffer less postoperative pain and have a shorter duration of hospital stay. Furthermore, they found that those children who had a retroperitoneoscopic nephrectomy made an even faster recovery. The technique of retroperitoneoscopic nephrectomy is now well established and has been shown to be applicable to all age groups, with a low conversion (<3%) and complication rate. The technique has been adapted to the management of children who have end-stage renal disease and who require bilateral native kidney nephrectomy. As the peritoneum can be maintained intact, it allows for immediate postoperative peritoneal dialysis. This approach has been utilised in the management of 20 children in the author's institution. One child required conversion to open and 17 children were established on peritoneal dialysis immediately after surgery. The technique continues to evolve and a recent development is the SIMPL (single instrument port laparoscopic) nephrectomy, which is a modification of the posterior prone retroperitoneoscopic nephrectomy. The entire procedure can be performed through a single instrument port without compromising safety and operative time. It has been used in the author's centre in the management of 80 children, ranging from 1 month to 18 years of age. The average operative time is 60 minutes and there have been no complications or conversions.

Laparoscopic heminephrectomy

The first laparoscopic heminephrectomy was performed in 1992 by the transperitoneal route. Two years later, Gill performed the first retroperitoneoscopic heminephrectomy. Despite the unquestionable benefits of the laparoscopic

approach for nephrectomy in children, laparoscopic heminephrectomy has not yet gained widespread popularity. The difficulty of achieving near total ureterectomy, coupled with the suggestion of higher complication rates, is perhaps the reason why. Current results in children are discussed later in this chapter.

Indications

The indications for a laparoscopic heminephrectomy are similar to those for standard open heminephrectomy and include the following conditions:

- Renal duplication anomalies. Upper pole heminephrectomy is performed most commonly, typically in cases characterised by dilatation of a poorly functioning upper pole and dilated upper pole ureter.
- Renal duplication in girls with ectopic insertion of upper moiety ureter with urinary incontinence and poorly functioning upper pole.
- Lower pole heminephrectomy is performed in cases of reflux-associated nephropathy with loss of lower pole function or rarely in cases of lower moiety PUJ obstruction with loss of function.

Caution should be exercised when considering a laparoscopic heminephrectomy in a child with a history of recurrent or recent upper urinary tract infection(s). In this situation it is not uncommon to encounter dense adhesions between the kidney, the ureter and the peritoneum which may make dissection difficult and blood loss excessive. In such cases, an open approach may be more suitable.

Operative technique for retroperitoneoscopic heminephrectomy

The steps for surgical access to the kidney are the same for a retroperitoneoscopic heminephrectomy as they are for a retroperitoneoscopic nephrectomy. In particular, the position of the patient and the port sites are identical. Once the kidney is located, it is mandatory to visualise both the upper and lower moiety ureters to confirm the anatomy and provide a guide to the vascular supply. The vessels supplying the affected moiety are selectively identified and divided and the ureter from the affected moiety is separated from the ureter to be preserved and divided. The proximal stump of the ureter can be used to expose the anteromedial surface and any additional vessels supplying the affected moiety. Blanching of the parenchyma secondary to hypoperfusion will delineate the portion of renal parenchyma that needs to be resected. Transection of the parenchyma between the two moieties can be performed with monopolar diathermy, harmonic scalpel or with the use of an endoloop to constrict the parenchyma (Figure 23.5).

The distal ureteric stump should be removed as far down into the bony pelvis as possible, taking care to visualise and protect the ureter draining the unaffected moiety.

Results

Laparoscopic heminephrectomy has only been introduced recently and is still limited to a relatively small number of centres. For this reason, very little has yet been documented regarding the efficacy, complications and long-term outcomes of this approach. Recently a group from Miami reported a 10% serious complication rate and a group from Toronto a 14% complication rate (consisting mainly of urinary leakage from the remaining kidney tissue at the resection margin). In our own centre we prefer the use on an endoloop to constrict or 'cinch' the parenchyma, which significantly reduces the risk of urine leak. In a retrospective review of 54 successive retroperitoneoscopic heminephrectomies performed between 2001 and 2005 in our centre, no case of postoperative urine leak was encountered.

Laparoscopic pyeloplasty

Laparoscopic pyeloplasty in adults has been shown to be an effective modality for the treatment of PUJ obstruction. Its use in the paediatric population was first described in 1995, and it has now become an established technique in the

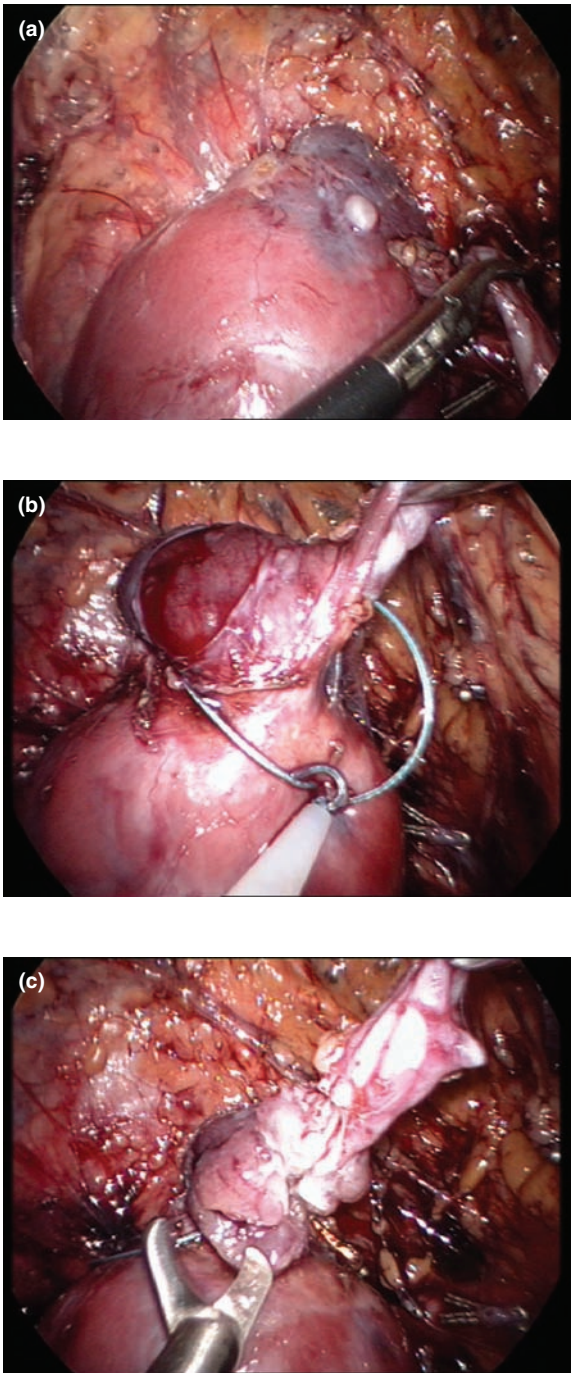

Figure 23.5 Intraoperative images of retroperitoneoscopic left upper pole heminephrectomy. (a) The upper pole vessels are selectively ligated and divided. (b) Blanching of the affected moiety occurs. (c) The affected moiety is removed with the use of an endoloop to constrict the parenchyma.

management of older children with PUJ obstruction. Recent reports suggest that it is also feasible in infants and smaller children, where the clinical benefits of a laparoscopic approach would be marginal.

Indications

Indications for laparoscopic pyeloplasty are similar to those for open pyeloplasty and comprise:

- symptomatic PUJ obstruction
- worsening hydronephrosis on serial imaging
- anteroposterior (AP) diameter >20 mm with calyceal dilatation and renal function <40%
- AP diameter >30 mm with calyceal dilatation.

Contraindications for laparoscopic pyeloplasty may include a small extrarenal pelvis, prior renal surgery and anatomical variants, such as a horseshoe kidney.

In our own institution we offer laparoscopic pyeloplasty to children >6 years old who fulfil the above criteria for surgery. From a clinical viewpoint, it is the older children and adolescents who are most likely to benefit from a minimally invasive approach, both in terms of postoperative pain and improved cosmesis.

Operative technique for laparoscopic pyeloplasty

Laparoscopic pyeloplasty can be performed via the transperitoneal or the retroperitoneal route. Both approaches are well described, with no particular advantages of one over the other, although in our own centre we prefer the transperitoneal route since it provides a relatively large working space for intracorporeal suturing. This technique is described below.

The patient is positioned in a lateral decubitus position with the affected kidney uppermost. The camera port is placed using the open Hasson technique in the region of the umbilicus, and is secured in place with a skin suture. Two working ports are inserted under direct vision: one under the costal margin and the other in the ipsilateral iliac

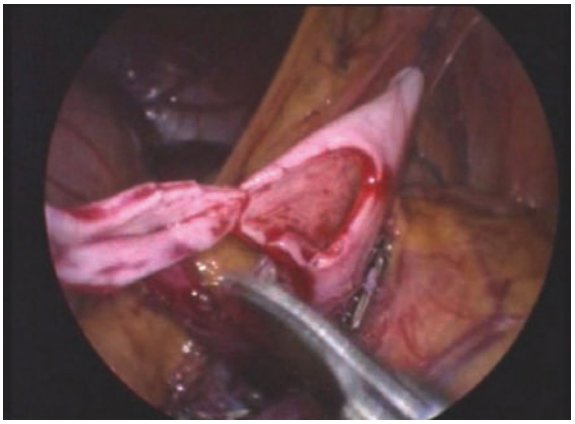

Figure 23.6 Intraoperative view of laparoscopic left pyeloplasty. The renal pelvis is stabilised with a 'hitch stitch' through the lateral abdominal wall (top right corner). An antegrade double J stent is placed across the anastomosis over a guidewire.

fossa. The kidney can be identified either by reflecting the colon medially or through a transmesenteric window. It can often help to identify the ureter first and then trace this cranially towards the hilum of the kidney. Once the PUJ has been identified and displayed, the renal pelvis is stabilised with a 'hitch stitch' through the abdominal wall. The renal pelvis is then dismembered from the ureter and a portion may be excised. The ureter is spatulated and the anastomosis is commenced by securing the tail of the spatulation to the inferior border of the divided edge of the renal pelvis (Figure 23.6). The posterior wall of the anastomosis is performed with a continuous absorbable suture. An antegrade silicone double J stent is placed across the anastomosis over a guidewire and the remainder of the anastomosis is completed with a further continuous absorbable suture. A urethral catheter should be left in situ for a minimum period of 48 hours or until the patient is fully mobile. The stent is removed cystoscopically after a period of 4 weeks.

Results

In experienced hands the technique of laparoscopic pyeloplasty provides comparable results to those obtained with the open technique. In a consecutive series of 170 procedures in adults, one UK group reported a success rate of 96% at a median follow-up of 12 months. A similar success rate of 96% was reported in a cohort of 46 paediatric patients from Hanover, Germany. Recent reports have documented the feasibility of laparoscopic pyeloplasty in children <2 years of age, in children with horseshoe kidneys as well as in children with duplex kidneys with associated PUJ obstruction. It is becoming increasingly reasonable to assert that laparoscopic pyeloplasty is the gold standard in the management of PUJ obstruction in older children and adolescents.

Recent innovations in pelviureteric junction obstruction

Recently there have been two developments relating to the minimally invasive management of children with PUJ obstruction: first, the introduction of robotic-assisted laparoscopic pyeloplasty; second, the development of the laparoscopic 'vascular hitch' operation for children with symptomatic PUJ obstruction secondary to lower pole accessory vessels.

Robotic pyeloplasty

The introduction of the da Vinci system enabling precise laparoscopic manipulations has opened the door for a whole range of intracorporeal reconstructive procedures. Robotically assisted pyeloplasty in children has been one of the first applications, with encouraging early results. The advantages of the da Vinci system include a magnified three-dimensional view of the operative field, wrist-like movements of the instrument tips with 6° of freedom of movement and the elimination of hand tremor (Figure 23.7). A major disadvantage of the da Vinci system is the lack of tactile feedback, which requires the operator to rely to a far greater extent on visual cues. Another disadvantage of the system is the large capital outlay and the ongoing costs of consumables. Despite these drawbacks, the da Vinci system has already secured a place in modern paediatric surgery and urology.

The group from Boston Children's Hospital compared an age-matched cohort of 33 children

Figure 23.7 The da Vinci system. (a) The da Vinci has three main components: the surgeon's console; the AV stack system; and the surgical cart. (b) The robotic instruments are attached to the arms of the surgical cart and inserted into the patient. (c) The articulation at the tip of the instruments provides 6° of freedom of movement.

undergoing open or robotic-assisted laparoscopic pyeloplasty. The average age in each group was around 7 years old. The robotic-assisted surgery had advantages in terms of reduced hospital stay and narcotic analgesic requirements, with operative times approaching those for open surgery. A more recent report from a group in California showed similar findings, whereas a group from Philadelphia successfully performed robotic-assisted laparoscopic pyeloplasty in 9 infants with ages ranging between 3 and 8 months. Clearly, robotic-assisted surgery has a place in the paediatric population and the challenge is to identify the correct balance between cost, ethics and clinical benefit.

Laparoscopic 'vascular hitch'

In children with antenatally detected PUJ obstruction, lower pole crossing vessels are a rare finding, being present in only 6–11% of cases. By contrast, lower pole crossing vessels are a feature of 50–60% of cases of PUJ obstruction in older children – particularly in those who present with pain.

When crossing vessels are identified during pyeloplasty, the usual approach is to transpose them posterior to the ureteropelvic anastomosis.

The aetiological relationship between crossing renal vessels and PUJ obstruction remains controversial, with opinion divided over whether crossing vessels are incidental, aggravating or causative factors. A causative role for crossing vessels may be suggested by the direct intraoperative examination of the PUJ: if dissection of crossing vessels away from the PUJ appears to relieve obstruction, and there is no evidence of intrinsic obstruction, then it is probable that the vessels are the sole cause of the obstruction and symptoms. In such cases, transposing the vessels superiorly without performing a dismembered pyeloplasty may be curative. Pesce et al reported a successful outcome in 60/61 children treated with vessel transposition alone, and Meng and Stoller reported success in 9/9 adults treated with laparoscopic vessel transposition. At our institution, laparoscopic vessel transposition is offered to children with a clinical presentation suggestive of intermittent obstruction

and crossing vessels at laparoscopy, provided intraoperative inspection of the PUJ reveals no evidence of intrinsic obstruction. We routinely perform preoperative magnetic resonance angiography (MRA) to demonstrate the presence of crossing vessels (Figure 23.8). The procedure itself is performed in a transperitoneal manner, similar to a laparoscopic pyeloplasty. The crossing vessels are dissected away from the PUJ, which is carefully examined for evidence of intrinsic obstruction following an intravenous fluid bolus. Provided there is no evidence of intrinsic obstruction, the vessels are sutured superiorly away from the PUJ, typically by fixation into a tunnel created from the anterior wall of the dilated renal pelvis. This procedure offers the advantage of not incising the upper urinary tract, and is a considerably shorter procedure than laparoscopic pyeloplasty. To date we have performed the laparoscopic vascular 'hitch' in 20 children between 5 and 17 years of age. With one exception, all patients experienced immediate resolution of symptoms, with a reduction in the degree of hydronephrosis and improved drainage parameters on follow-up imaging. One child developed recurrent symptoms within a short interval and required a laparoscopic dismembered pyeloplasty. Laparoscopic vascular 'hitch' is an alternative procedure in a select group of children who have symptomatic PUJ obstruction due to crossing renal vessels.

Laparoscopic adrenalectomy

Laparoscopic adrenalectomy is now considered by many to be the standard of care for surgical excision of the adrenal gland. Since the initial report of laparoscopic adrenalectomy in 1992, it has evolved into a feasible and reproducible minimally invasive procedure for both benign and malignant adrenal tumours. Both the transperitoneal and retroperitoneoscopic approaches are well described. Although the transperitoneal approach is used more widely, the retroperitoneoscopic approach offers distinct advantages that make it a valuable alternative route to the adrenal gland.

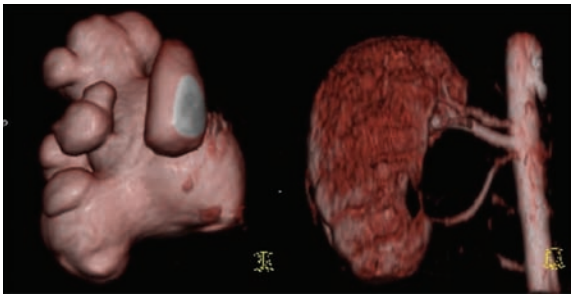

Figure 23.8 Magnetic resonance angiogram. Three-dimensional image reconstruction demonstrates anatomy of the collecting system and the renal vasculature. The lower pole crossing artery overlies the region of PUJ, indicating a possible aetiological relationship in intermittent PUJ obstruction.

Indications

Laparoscopic adrenalectomy is indicated for the following conditions:

- phaeochromocytoma
- adrenal adenoma
- ACTH (adrenocorticotrophic hormone)-dependent Cushing's syndrome
- neuroblastoma.

Contraindications to a laparoscopic approach include previous renal surgery, large tumours >8 cm in diameter, coagulation disorders and in children with known adrenal carcinoma.

Preoperative work-up

A detailed ultrasound of the adrenal glands provides information relating to the location and size of the mass, and whether it is cystic or solid. CT is also a very valuable modality (Figure 23.9). In some cases, typically 'central' Cushing's syndrome, there is bilateral diffuse enlargement of the adrenal glands without a focal lesion. In addition to visualising the adrenal lesion itself, it is also essential to determine if there is intravascular extension into the adrenal vein and inferior vena cava. This

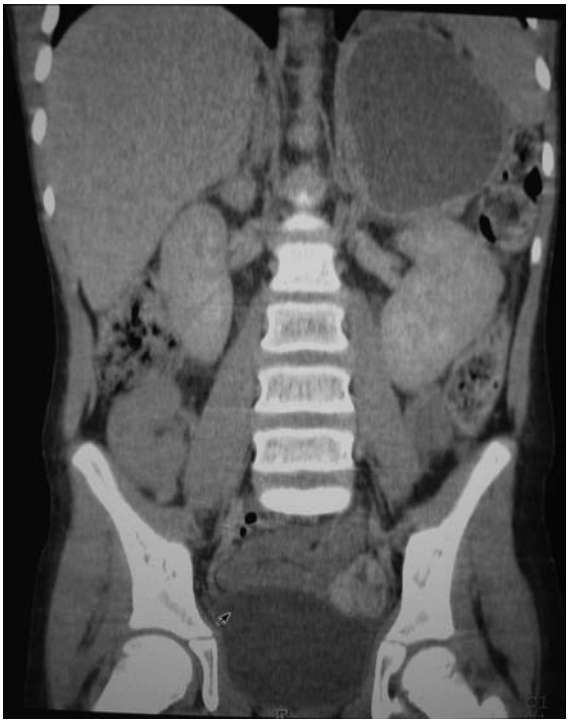

Figure 23.9 CT scan showing left cystic phaeochromocytoma in an 8-year-old male child.

information serves as a guide to the suitability of a laparoscopic approach and also for planning the safest approach for specimen retrieval, e.g. Endopouch, cyst aspiration, etc.

All hypertensive patients with a phaeochromocytoma require preoperative preparation with the administration of phenoxybenzamine for 7 days prior to surgery. In addition, the administration of β-blockers (propranolol) can decrease the risk of tachyarrhythmias, but should not be given without prior α-blockade.

Operative technique for retroperitoneoscopic adrenalectomy

The operative strategy is based on complete dissection of the adrenal gland outside the surrounding adipose tissue. This minimises bleeding, which can occur with dissection on the surface of the gland. Left adrenalectomy is more difficult than a right adrenalectomy due to the absence of clear landmarks such as the vena cava, coupled with the smaller size of the gland and adrenal vein. The key to success is starting the dissection on the medial aspect in order to identify and ligate the vessels at an early stage in the operation.

The patient is positioned fully prone in a similar manner to a retroperitoneoscopic nephrectomy. The same landmarks and access technique are used to enter the retroperitoneum.

The kidney is dissected first, commencing at the apex and along the medial aspect to expose the posterolateral aspect of the kidney. The lateral and inferior attachments are not divided as they help to anchor the kidney in position and aid in exposure of the upper pole. The inferior margin of the adrenal gland can be visualised at the superomedial border of the kidney. The arterial blood supply is identified first and divided. The adrenal vein on the left side is less prominent than on the right and thus is less easily identified. On the right side, the adrenal vein is short and enters directly into the vena cava. Once identified, the adrenal vein should be divided between clips, to avoid thermal injury to the vena cava. The gland is fully mobilised and freed of all attachments, placed within an endobag and removed through the camera port incision.

There is little doubt that laparoscopic adrenalectomy is a safe and effective procedure in both adults and children. Controversy exists, however, on whether the transperitoneal or retroperitoneoscopic approach is preferable. A recent publication from Germany describes more than 560 laparoscopic adrenalectomies, of which 520 were performed retroperitoneoscopically. They reported low conversion (<2%) and major complication (<2%) rates with this approach. Similar studies are lacking in the paediatric age group, with most centres reporting their individual experiences and preferences based upon relatively small numbers of patients. In the author's institution, eight retroperitoneoscopic adrenalectomies have been performed in seven patients, including one bilateral synchronous adrenalectomy. Diagnoses included adrenal cyst, cystic phaeochromocytoma, adrenal cortical tumour and ACTH-dependent

Cushing's syndrome. The technique provided excellent intraoperative haemodynamic stability and all lesions were completely excised. In experienced hands, laparoscopic adrenalectomy is a safe procedure in children, utilising either the transperitoneal or the retroperitoneoscopic route.

Other techniques

Laparoscopic ureteric reimplantation

The gold standard for antireflux surgery remains the Cohen cross-trigonal reimplantation, with success rates of 96%. The Lich–Gregoir extravesical reimplantation does not require cystotomy and has success rates approaching 90%, although there are concerns surrounding postoperative voiding dysfunction.

Various surgical techniques have been described for the endoscopic correction of reflux using subureteric injection of a variety of substances (see Chapter 5). Unfortunately, many patients require more than one injection, particularly for high-grade reflux.

Recently, a new approach has been described for the surgical management of reflux which consists of endoscopic intravesical reimplantation using the Cohen technique. Since the bladder is a naturally occurring cavity, it can be insufflated with CO_2 to create a pneumovesicum. The refluxing ureter is mobilised in a similar manner to the open technique and is then positioned in a cross-trigonal submucosal tunnel. Preliminary results in 16 children have shown that this is a safe and effective technique, with results comparable to the open operation. Apart from the cosmetic advantages, it is claimed that patients experience less postoperative bladder spasms and can be discharged on the day after surgery.

Laparoscopy in disorders of sex development

Laparoscopy can play a valuable role in the investigation and management of children with disorders of sex development (DSD). It allows direct visualisation of the internal genital anatomy including the uterus, müllerian duct remnants, gonads and vasa deferentia. Laparoscopy also provides an opportunity to perform gonadal biopsies where indicated and to remove dysgenetic gonads or gonads which are discordant with the sex of rearing (see Chapter 20). Symptomatic müllerian duct remnants can be evaluated and removed with relative ease. Access to the depths of the male pelvis can be challenging with open techniques, with restricted visualisation of the seminal vesicles, ureters and vasa. The laparoscopic approach provides a magnified view of these structures, which can therefore be meticulously separated and preserved.

Laparoscopic cystolithotomy

Stone formation is a well-documented and relatively common complication of bladder augmentation. When stones occur, the key to preventing their recurrence is to minimise stone fragmentation during removal. This usually mandates the use of open cystolithotomy rather than in situ lithotripsy. An alternative approach is to remove the stones without intravesical fragmentation using an Endopouch retrieval device. A laparoscope is inserted via a small 10 mm suprapubic cystotomy. Under direct laparoscopic vision, a second 5 mm trocar is placed into the augmented bladder. The laparoscope is moved to this trocar and a 10 mm Endopouch is inserted into the bladder via the 10 mm cystotomy. The stones are captured within the Endopouch and removed either intact or by fragmentation within the pouch. The suprapubic cystotomy should be closed with an absorbable suture and the bladder drained for 1 week before recommencing intermittent catheterisation.

Key points

- Minimally invasive alternatives to conventional open urological procedures are increasingly available in most paediatric urology centres. Examples of procedures are nephrectomy, heminephrectomy, pyeloplasty and adrenalectomy.
- The relatively small size of paediatric patients permits access to both the

upper and lower urinary tract through the same ports. Both the transperitoneal and retroperitoneoscopic approaches are utilised in children, although the retroperitoneoscopic technique is increasingly favoured for renal procedures.

- Laparoscopic pyeloplasty remains a technically challenging procedure, which at present is generally better suited to older children and adolescents. The advent of robotic technology has made some aspects of the operation simpler.
- The advent of minimally invasive techniques has provided a new insight into disease processes, allowing the emergence of novel operations such as laparoscopic vascular hitch for intermittent PUJ obstruction due to crossing vessels. The technical boundaries of what can be achieved are being constantly extended, e.g. with the recent development of pneumovesicoscopic ureteric reimplantation.

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Adolescent urology

24

Christopher RJ Woodhouse

Topics covered
Vesicoureteric reflux
Bladder exstrophy
Female genital reconstruction
Hypospadias
Posterior urethral valves
Prune-belly syndrome
Enterocystoplasty
Spina bifida
Fertility

Introduction

The major anomalies of the genitourinary tract are now reconstructed in infancy and from the paediatric point of view the results are good. However, they leave a legacy of potential morbidity in adolescence and adult life. Many problems are predominantly medical or psychosocial rather than surgical in nature and it is essential to adopt a holistic approach to long-term care. Close collaboration between paediatric and adolescent or adult urologists is also important to ensure continuity of follow-up and specialist care.

Renal function

The renal damage associated with many of the congenital urological anomalies dates from foetal life and despite correction of the structural anomaly, such as a posterior urethral valve, shortly after birth (or even in utero) hypertension and renal failure may supervene in later life. Monitoring of renal function is therefore an integral part of adolescent care – with blood pressure measurement, plasma creatinine and testing for proteinuria forming an essential part of the annual review.

Patients who reach adolescence with a glomerular filtration rate (GFR) of less than 40 ml/min/1.73 m^2 are at a substantial risk of progressing to end-stage renal failure within 16 years (Figure 24.1). The downward progress can, however, be delayed with rigorous control of proteinuria and blood pressure through the use of angiotensin-conversion enzyme inhibitors (ACEIs).

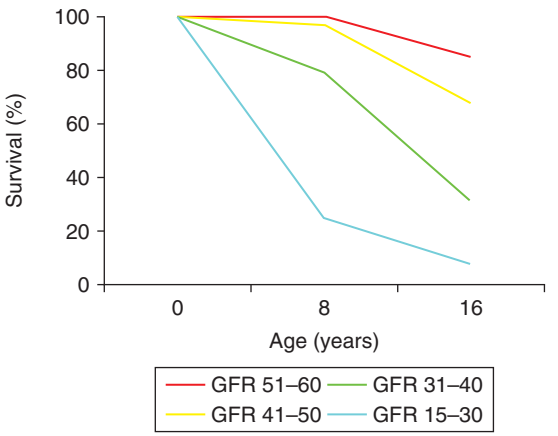

Figure 24.1 Percentage of patients surviving *without* dialysis/transplantation by initial GFR (ml/min) corrected to 1.73 m^2. Time zero was at entry into adolescent follow-up around puberty.

Hyperperfusion injury of the surviving nephrons is the mechanism which is generally responsible for this late decline in renal function, but it is important not to overlook the additional contribution of high-pressure bladder dysfunction, particularly in boys with a history of posterior urethral valves (PUV).

Vesicoureteric reflux

Four groups of adults must be considered:

1. **Adults whose vesicoureteric reflux (VUR) has either ceased or been corrected in childhood**. If there is no renal damage no follow-up is necessary.
2. **Adults whose VUR has ceased or been corrected in childhood but in whom reflux nephropathy is present**. These patients need lifelong follow-up. By the age of 18 years 11% of those with unilateral scarring and 18% of those with bilateral scars have developed hypertension, a figure rising to 23% at 27 years. If the renal damage is sufficiently severe to reduce the GFR below 40 ml/min/1.73 m^2, late renal failure may be inevitable.
3. **Reflux persisting from childhood beyond puberty.** There is no consensus on management, but it is has been the author's practice to recommend surgical reimplantation in females since reflux nephropathy may be acquired in pregnancy. However, it has been reported that women who have previously undergone reimplantation are at greater risk of urinary infection in pregnancy than any other group. Whether this is because their urinary tracts were the most damaged originally, or because of some consequence of reimplantation is unknown. In asymptomatic males there seems to be no indication for surgery in the absence of bladder outflow obstruction.
4. **Adults presenting for the first time with vesicoureteric reflux**. Because most are symptomatic, surgical treatment (either endoscopic or open) is indicated.

Bladder exstrophy

Most children with exstrophy have an isolated anomaly and generally grow up very well, being both intelligent and well motivated. Despite the excellent results of bladder reconstruction reported from major centres, there remains a lingering suspicion that early diversion is also an acceptable form of management and one with a lower complication rate. Certainly, reconstruction should only be undertaken by surgeons with very wide experience. For this reason, and because of the declining number of new cases, the surgical management of bladder exstrophy is now concentrated in two supraregional centres in England and Wales.

The reconstructed bladder may not be durable into adulthood. Historically, only 23% of exstrophy patients who underwent bladder reconstruction in childhood progressed into adult life without the need for urinary diversion. Of those whose bladder reconstruction did survive beyond childhood, 60% required further reconstruction in adolescence or early adult life.

The risk of developing bladder cancer at a young age is greatly increased in exstrophy patients, with an incidence which is 645 times greater than that of the normal population by the age of 40 years. Most reported cases have occurred in bladders which were defunctioned by urinary diversion in childhood and it is possible that the risk of malignancy will be lower in patients with a functioning reconstructed bladder.

Genital reconstruction in exstrophy

Males

The penis in exstrophy is short but of normal calibre. An intrinsic component of the deformity is tight dorsal chordee which, if uncorrected during infancy, will prevent penetrative sexual intercourse (Figure 24.2). In adults the deformity is investigated by artificial erection, infusing both corpora with saline. Minor defects may be corrected by a ventral Nesbit's procedure, whereas severe penile deformity requires more extensive correction by a Cantwell–Ransley operation.

Females

The vagina is short and lies in a more horizontal plane than normal. The labia are located on the

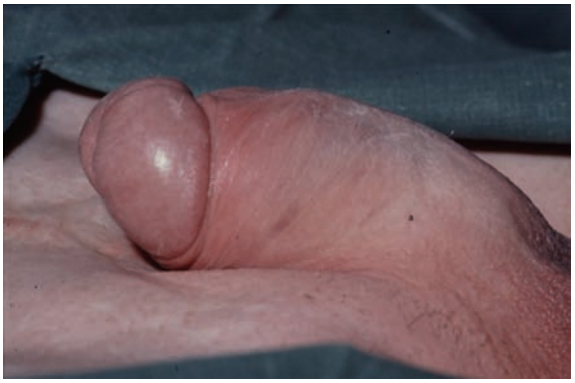

Figure 24.2 Clinical photograph of an epispadiac penis showing dorsal chordee and retraction into the recessed mons area.

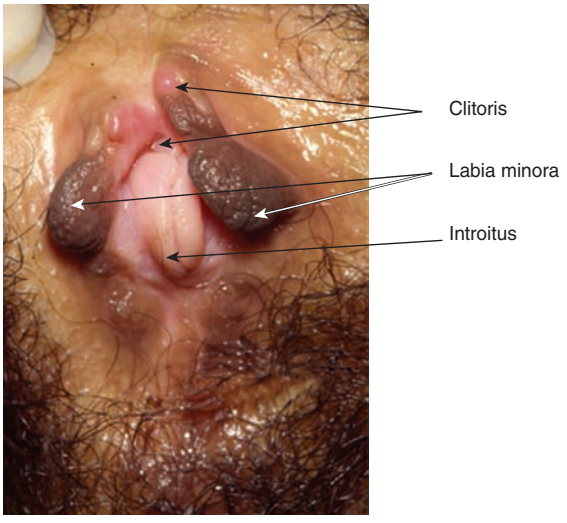

Figure 24.3 Female perineum in exstrophy.

anterior abdominal wall, the introitus is narrowed and the clitoris bifid (Figure 24.3). Although the labia cannot be repositioned, the overall abnormality can be disguised and patients can have normal sexual function. Fertility is unaffected, but uterine prolapse (procidentia) can be particularly troublesome for up to 50% of women. When one parent has bladder exstrophy the risk of exstrophy or epispadias in their offspring is approximately 1:70.

Female genital reconstruction of ambiguous genitalia

The timing and nature of female genital reconstruction for conditions such as congenital adrenal hyperplasia is a source of growing controversy. Historically, very few studies have attempted to document the long-term functional and psychological outcome of feminising genitoplasty and vaginoplasty performed in childhood. However, evidence is accumulating from recent follow-up studies which challenges some of the assumptions underpinning the current approach to female genital reconstruction, particularly the belief that one-stage surgery in childhood will suffice. It is increasingly clear that the majority of young women will require further vaginal surgery, ranging from simple introital revision to complex vaginoplasty, to permit normal comfortable intercourse (Figure 24.4). Furthermore, impaired clitoral sensation is not uncommon. Continuity of follow-up from childhood into early adulthood is essential, with further care being undertaken in a centre specialising in adolescent gynaecology to ensure access to relevant specialist expertise and appropriate psychological support.

Hypospadias

There are so many operations for the repair of hypospadias that the non-specialist may despair of ever understanding even the basic techniques. By adult life, however, most patients have experienced a satisfactory repair, at least by the standards of the surgeon. Surgeons tend to view their own results in an overoptimistic light, sometimes with glowing reports of straight erections and normal urine stream in 100% of cases. When viewed more objectively, the late results are less impressive and up to 50% of men experience a poor functional or cosmetic outcome.

Patients themselves are less easily satisfied than their surgeons, with dissatisfaction centering on some of those aspects of hypospadias that are least easy to correct such as penile and glans size and the absence of a normal prepuce.

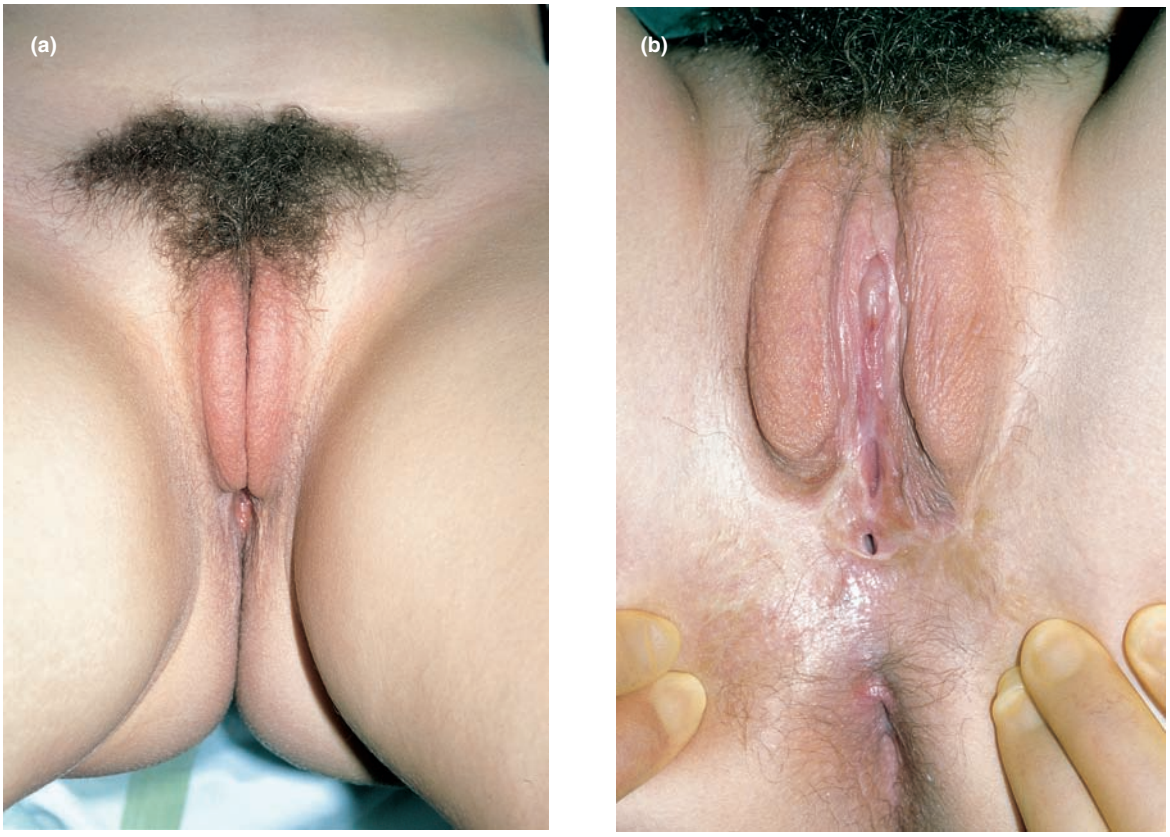

Figure 24.4 Postpubertal outcome of feminising genitoplasty for the correction of virilisation associated with congenital adrenal hyperplasia. Single-stage feminising genitoplasty previously undertaken in the first year of life. (a) External cosmetic outcome satisfactory, with no visible phallic hypertrophy and normal appearance of labia created from 'scrotalised' skin. (b) Retraction of the labia reveals introital scarring, requiring introitoplasty to permit normal, comfortable intercourse.

There is little consensus on the effect of hypospadias on sexual development, one problem being that today's adults underwent correction of their hypospadias using techniques that are now outdated.

If there are gross persistent anomalies, especially chordee, intercourse may be impossible (Figure 24.5). With lesser anomalies, particularly of a cosmetic variety, sexual debut and intercourse may be nearly normal. When compared to boys operated for hernia or for phimosis, there are no differences in the development of standard sexual milestones. Reduced semen quality has been reported in up to 50% of men, although this does not appear to be accompanied by a corresponding increase in the incidence of infertility.

Following repair of penoscrotal or perineal hypospadias (which has often presented initially as ambiguous genitalia) intercourse is possible but ejaculation is poor and infertility is common.

Posterior urethral valves

Bladder function

It is essential to understand that the main long-term consequences of PUV occur because of damage to the bladder caused by the period of obstructed voiding in utero and in the neonatal period before the obstruction is relieved by valve

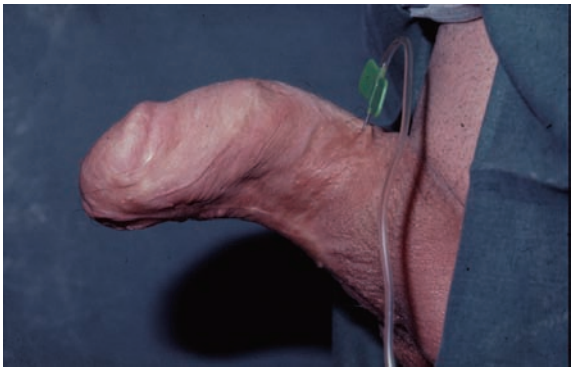

Figure 24.5 Clinical photograph of a patient with persistent chordee following repair of hypospadias in childhood.

resection. The pattern of bladder dysfunction is characterised by poor compliance, detrusor instability and reduced functional capacity (the 'valve bladder'). In adulthood, the pattern may change to one of chronic retention, often with high pressure.

Although bladder dysfunction does not occur in all boys with a history of posterior urethral valves, the potential is always present and may not be manifest until adolescence or early adult life. The symptoms will be familiar to all urologists as frequency, urgency and incontinence. What may not be recognised is the relentless effect of bladder dysfunction on the kidneys.

Renal function

The progressive nature of renal failure in PUV boys has been recognised for many years. A study published in 1988 reported the incidence of renal failure as 23% at 10 years, 30% at 16 years and 43% at 30 years. In spite of improvements in management and a greater understanding of the pathophysiology of the valve bladder, the figures have not greatly improved, with an incidence of 18%, 32% and 36% at comparable ages, reported in 2005. It is important to note that normal levels of serum creatinine at the beginning of puberty do not guarantee that the plasma creatinine will still be normal at the end of puberty.

Apart from the renal damage dating from the period of unrelieved obstruction before the valve resection, further ongoing damage is caused by the poorly compliant bladder. Upper tract obstruction causes damage to the medulla, resulting in renal tubular concentration defects and consequent polyuria. There are, therefore, more bladder filling cycles in a day so that longer periods are spent with dangerously high bladder storage pressures, thus creating a vicious cycle of worsening renal damage.

Significant prognostic factors indicating poor long-term outcome include:

- diagnosis before the age of 1 year (including prenatal diagnosis)
- diurnal incontinence persisting after 5 years of age
- persistent bilateral reflux
- polyuria.

Recent work has suggested that the risk of renal failure can be averted or reduced by aggressive bladder management with anticholinergics, self-catheterisation and clam cystoplasty.

Ejaculation

Like the bladder, the prostate is damaged by back pressure before the valve is resected. This may lead to abnormal semen and poor ejaculation in up to 50% of patients. The seminal abnormality is characterised by lack of liquefaction, low sperm count, poor motility and high pH (up to 9.5). The effect on fertility is unknown but up to a third of patients appear to have some difficulty in achieving paternity. The dilated posterior urethra means that inadequate pressure is established at the beginning of orgasm, resulting in less forceful (or absent) ejaculation.

Transplantation

A bladder which has contributed to the destruction of the two native kidneys and caused end-stage renal failure is likely to do the same to a transplanted kidney. In the past, the published 5-year graft survival in PUV patients was approximately 50% lower than in all other recipients. However, current 5-year graft survivals figures are comparable, although PUV

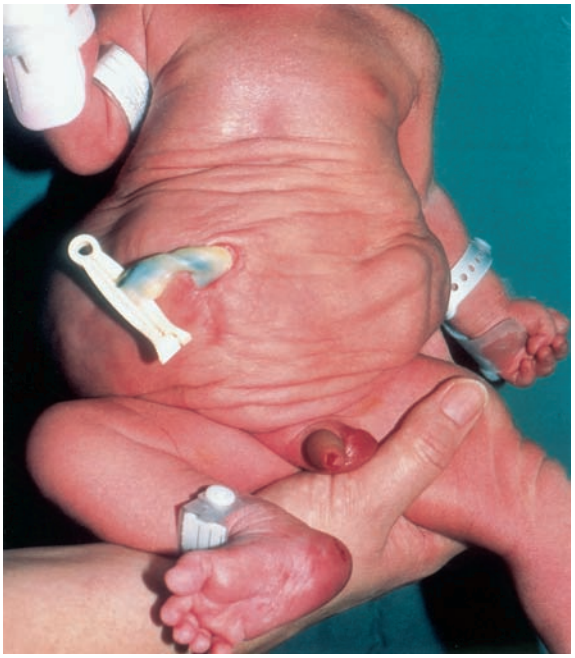

Figure 24.6 Characteristic appearance of the abdominal wall in a newborn infant with prune-belly syndrome.

transplant patients have more infections and higher levels of plasma creatinine than other transplant patients, especially from 7 years onwards. It is essential to correct any bladder abnormalities, by augmentation if necessary, before renal transplantation.

Prune-belly syndrome

Prune-belly syndrome is now very rare, at least in the UK. The most likely explanation is that affected pregnancies are being terminated. However, the improved survival that was seen from the 1960s onwards has left a group of adults who have grown up very well.

There are three components to the syndrome (Figure 24.6):

- bilateral undescended testes
- absence of the muscle of the anterior abdominal wall
- variable functional and anatomical anomalies of the urinary tract.

Although each of these components has the potential to affect long-term development, prune-belly patients generally grow well and tend to be tall. Other, associated anomalies, notably skeletal, have been described, but with the exception of kyphoscoliosis are seldom of great consequence.

Undescended testes

In the 1950s and 1960s it was believed that the testes were so intrinsically abnormal that there was little prospect of fertility. Likewise it was incorrectly thought that the testes were too dysplastic to carry any appreciable risk of malignancy. Men with prune-belly syndrome were thought to be sterile and testicular biopsies showed Sertoli cells only. Orchdiopexy was, therefore, delayed either until a major reconstruction was performed or until late childhood. It has now become apparent that some germ cells are present and so the outlook is not so bleak. There have been reports of sperm in the semen. At least one pregnancy has been achieved using intracytoplasmic sperm injection (ICSI), which resulted in twins, one of whom was normal but the other had multiple anomalies. There have also been three reported cases of germ cell neoplasia.

Endocrine function is usually adequate to produce virilisation and maintain masculinity but only at the price of high pituitary drive. Serum testosterone levels in adulthood are usually in the normal range but serum luteinising hormone (LH) levels are two or three times normal.

The abdominal wall

The literature on the value of abdominal wall reconstruction during childhood is contradictory (Figure 24.7). Although it is certainly possible to improve the wrinkled appearance of the skin, it is doubtful whether there is any long-term benefit. Tightening of the skin is very unlikely to result in sustained improvement without the necessary underlying muscular or fascial support.

In adult life the abdomen is protuberant, resembling a premature 'pot belly'. However, there is no functional problem other than an inability to sit up

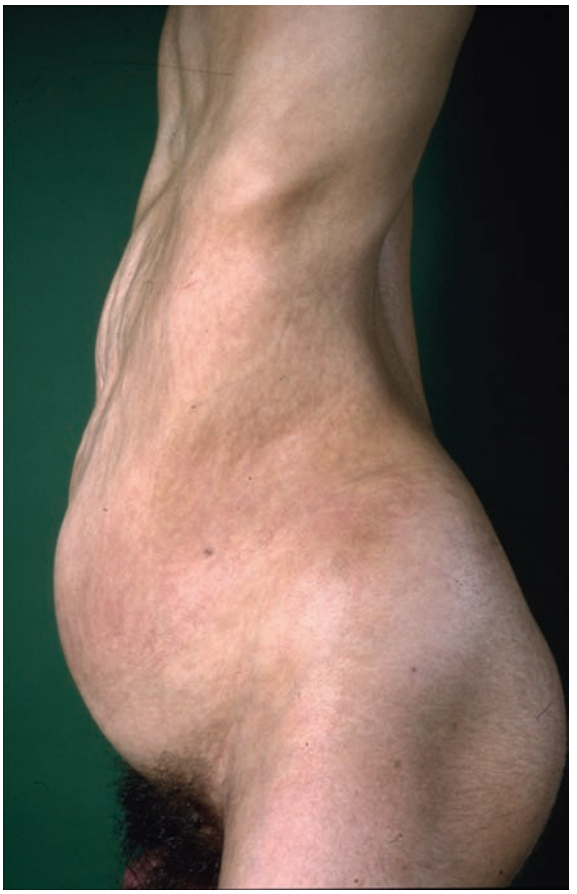

Figure 24.7 Clinical photograph of an adult with prune-belly syndrome. Note the 'pot-belly'. Pectus cavus, a common anomaly in prune-belly syndrome, is also present.

directly from the lying position. Patients in the author's practice are physically fully active and include a long distance cyclist and a mountaineer.

The kidneys

The long-term function of the kidneys is dependent on the degree of development in utero (severity of any renal dysplasia) and the management of urinary tract abnormalities in childhood. By the time adult life is reached, however, renal function has usually stabilised. In a cohort of adult patients in the author's practice who underwent minimal surgery in childhood, 17 out of 21 patients have normal renal function, with a mean GFR of 85 ml/min/1.73 m^2 at a mean age of 24 years. Four are in end-stage renal failure and another four are hypertensive. Early, major reconstruction was only performed in boys with significant renal impairment at birth. In this group, the prognosis has been worse and amongst the eight patients who have reached adulthood five are in end-stage renal failure.

Satisfactory bladder function is generally maintained, although cystitis may occur and should always be investigated, particularly to look for residual urine after voiding. If this problem is identified, it is most important to look for possible outflow obstruction, either at the level of the urethra or the bladder neck. Bladder outflow obstruction is a more likely cause of progressive upper tract dilatation than upper tract obstruction.

Enterocystoplasty

All urinary reservoirs made of intestine have the same basic long-term problems. Hyperchloraemic acidosis occurs in up to 14% of patients though many more may have a metabolic acidosis with respiratory compensation. Anaemia occurs in 8%. Vitamin B_{12} deficiency is a risk after 5 years especially if terminal ileum is used. Reservoir stones occur in 12–15% of patients. Risk factors include infection, need for self-catheterisation and retained mucus. Recent work has suggested that there may be metabolic abnormalities in some patients with enterocystoplasty that predispose to stone formation.

The incidence of **malignancy** in patients with ureterosigmoidostomies is 22% after a mean interval of 20 years. The interaction of urine and faecal bacteria in the sigmoid has been shown to result in the presence of nitrosamine and other known carcinogens. Although low concentrations of such urinary carcinogens have also been identified in bladders following enterocystoplasty, the overall risk of malignancy is likely to be lower. One recent study found a 3.8% incidence of bladder malignancy in a large cohort of enterocystoplasty patients followed for 20–25 years. Patients who undergo

enterocystoplasty in childhood require careful long-term follow-up into adult life, with protocols which should include periodic cystoscopy.

Spina bifida – social and sexual development

In spite of great advances in management of babies born with spina bifida, the long-term problems are legion. Approximately 20% of babies die in the first year of life. There is then a period of stability before a second wave of deaths occurs from about puberty. By the age of 35 years only about 45% of patients are still alive (Figure 24.8). Cardiovascular and pulmonary diseases are the commonest causes of adult death. About 10% of adolescents are unfit for major surgery, which makes it essential that reconstructive surgery is completed in childhood. Few if any of the problems experienced by spina bifida patients improve with the passage of time.

Patients with spina bifida have a spectrum of disabilities, ranging from virtual normality to wheelchair dependence and poor intelligence. During childhood a heavy burden falls upon the parents, but independent self-care should always be the long-term objective. Achieving this goal depends on:

- adaptation of daily living to permit self-sufficiency in tasks such as dressing, washing and performing routine household chores
- bowel and bladder management
- sexual education
- general education.

The urologist has a role in all these aspects of development.

Daily living

Parents tend to be overprotective. Only 15% of spina bifida patients undertake the same household chores as their normal siblings and 16% do not even acquire a basic level of self-sufficiency. Twenty-eight per cent of females are not taught hygenic management of menstruation. Up to 46% of

Figure 24.8 Survival curve for all patients born with spina bifida.

individuals with spina bifida develop pressure sores at some time.

Bowel management

Even the mildest neurological deficit leads to incompetence of the anal sphincter. Faecal continence is usually dependent on acquiring a pattern of 'controlled constipation'. The concept of the Malone antegrade continence enema (MACE) has been an important advance in the management of the neuropathic bowel.

Bladder control

Only a small percentage of individuals are continent without the use of clean intermittent catheterisation, which in many cases is in addition to reconstructive procedures. It is most important that surgery required to establish continence is completed before puberty, as the natural tendency is for continence to deteriorate rather than to improve. Very few adults with spina bifida, especially females, can learn urethral self-catheterisation if not taught in childhood. Moreover, about 10% of wheelchair-bound patients become unfit for radical surgery in adulthood because of inadequate respiratory reserve.

Sexual development – females

The impact of spina bifida on sexual function is closely related to the level of the spinal cord lesion and the severity of the associated neuropathic bladder. Most females whose neurological

impairment is below L2 are normal, as are most of those who are continent of urine. In contrast, only about 20% of women with higher levels of cord damage or with urinary incontinence experience normal sexual function. Nevertheless, two-thirds form steady sexual relationships, regardless of the degree of handicap or continence. Pregnancies are difficult, with high rates of urinary infection and deterioration in bladder function. The overall risk of neural tube defect among offspring is 1:23 (1:50 for sons and 1:13 for daughters) though it can be significantly reduced by folic acid supplements for 3 months prior to conception. Few spina bifida patients will accept antenatal screening and termination of affected pregnancies.

Sexual development – males

Males with intact sacral reflexes and urinary continence are potent. Of those with absent sacral reflexes, 64% of those whose primary neurological level is below D10 are potent, but the figure falls to 14% in men with higher neurological levels. There is doubt about the true sexual nature of such erections. Sildenafil (Viagra) may be helpful in treating erectile dysfunction in some cases. Semen can be obtained from impotent men by electroejaculation, but analysis reveals azoospermia. Despite these drawbacks 60% of adult males with spina bifida have a regular sexual partner regardless of their degree of mobility or continence.

General education and social adaptation

Risk factors for poor social outcome are:

- mental handicap
- poor manual dexterity
- inappropriate schooling
- overprotective parents.

The latter two factors can be overcome if they are recognised and if appropriate support is provided. The presence of neuropathic bladder and bowel and the overall level of neurological deficit (excluding intellectual impairment) have little direct bearing on educational potential and social integration.

Fertility and pregnancy: general considerations

Most genitourinary anomalies have the potential to cause sexual and reproductive problems in adolescence, with spina bifida, bladder exstrophy and posterior urethral valve patients being at particular risk. Many others require reconstruction to allow sexual normality.

Many anomalies also affect fertility and pregnancy and while advances in reproductive technology have improved matters very considerably they are nevertheless accompanied by stress and expense.

Poor male fertility is a feature of adults with bladder exstrophy, prune-belly syndrome, renal failure, disorders of sexual differentiation (DSD) and spina bifida. Boys born with a unilateral undescended testis (UDT) probably have normal prospects of fertility. Those with bilateral UDT successfully operated in childhood have about a 50% chance of fathering a child.

Reduced fertility is seen in women with chronic renal failure, DSD (including congenital adrenal hyperplasia) and anomalies of uterine development. There is a specific problem in confirming pregnancy in women whose urine is stored within an intestinal reservoir; the standard human chorionic gonadotrophin (hCG) antibody (blue line) urine test is commonly positive in the absence of pregnancy.

Pregnancy itself is associated with particular problems in women with spina bifida, enterocystoplasty, reimplanted ureters and bladder exstrophy. Almost all of the problems encountered in pregnancy resolve after delivery. Women should always be advised of such problems but few will be deterred from having a baby. However, women with a GFR below 50 ml/min/1.73 m^2 and a diastolic blood pressure (untreated) above 90 mmHg are notable exceptions and pregnancy carries very significant risks of irreversible deterioration. Between one-third and two-thirds of women with

this degree of renal impairment will be precipitated into end-stage renal failure during pregnancy. About 20% will be left with worse hypertension and 20% with worse proteinuria after delivery.

Key points

- Individuals with evidence of renal scarring (reflux nephropathy) should undergo lifetime measurement of blood pressure. Closer monitoring is required for those with severe scarring who are at risk of renal impairment.
- Approximately one-third of boys with posterior urethral valves are destined for renal failure by the time of adolescence or adult life.
- The incidence of new cases of prune-belly syndrome has fallen dramatically following the introduction of antenatal screening.
- Enterocystoplasty may be associated with stones and metabolic disturbances. The full extent of the risk of malignancy in reconstructed bladders may not be apparent for some decades.
- Measures needed to restore urinary continence in patients with spina bifida should be commenced during childhood and completed before adulthood.
- Congenital urinary tract malformations can have a major long-term impact on fertility. Advances in in vitro fertilisation and improved obstetric care may, however, offer the prospect of fertility to some of those who would previously have been denied parenthood.

Further reading

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Children and young people as urological patients

25

David FM Thomas

Topics covered
Psychological aspects of surgical treatment in children
Timing of surgery
'Child friendly' facilities
Adolescents
Consent for surgery

Introduction

Surgeons who care for children and young people must demonstrate professional skills and attitudes which differ considerably from those employed in adult urological practice. One of the most obvious differences between paediatric and adult practice is the extent to which the surgeon's responsibilities extend beyond the individual patient to their parents and family. Communicating effectively with parents and children who range in age from toddlers through to young adults calls for empathy, patience and a varied range of communication skills. A report by the Healthcare Commission noted, however, that only 7–9% of surgeons and anaesthetists caring for children had received any relevant communication skills training.

Faced with the additional complexities inherent in treating children (and their anxious parents) it is perhaps understandable that many surgeons choose to confine their consultant practice to adults. But those who do opt for a mixed adult and paediatric practice and those who specialize in paediatric urology or paediatric surgery know that no other age group of patients is more rewarding to treat.

The aims of this brief chapter are to highlight the most important differences between adults and children as urological patients, to review the evidence on the impact of surgery and hospitalisation in the paediatric age group and to consider the implications for the provision of urological services. The chapter concludes by looking at the important issues surrounding decision-making, competence and informed consent.

History taking and examination: practical considerations

Whether in the ward or outpatient clinic it is important to establish the relationship of the adults to the child at the time of the first meeting. In some circumstances this may be particularly important in order to clarify who has responsibility ('competence' in legal terminology) to provide consent on behalf of the child. Confidence and trust are not conferred automatically, particularly when parents are anxious and acutely concerned for the welfare of their child. For this reason it is essential that the surgeons introduce themselves, explaining their role in the team and outlining the purpose of the consultation in relation to the possible sequence of events in the child's treatment. The initial priority is to establish a professional working relationship with the parents and to share information honestly with them in order to arrive at a course of action which all parties believe is in the best interests of the child. This process may involve other health professionals and, possibly, other family members.

When taking the history from the parents, it is helpful to try and uncover any unspoken concerns. For example, the completely innocent swelling which results from a collection of smegma trapped between the prepuce and glans may nevertheless raise the spectre of cancer in the minds of some parents. Obtaining a careful history from the parents can sometimes be the only means of establishing the diagnosis of an inguinal hernia since this may not be clinically apparent, even as a cough impulse, when the child is examined in the outpatient clinic. In toddlers and younger children the history will inevitably be obtained primarily from the parents, but, beyond this age, the information provided by the child can also make a very important contribution to the correct diagnosis. For example, in the assessment of daytime wetting, tactful questioning of the child herself may uncover the fact that the child spends the entire day at school without visiting the toilet, a pattern which strongly predisposes to dysfunctional voiding. Information volunteered by the child regarding voiding habits at school often comes as a considerable surprise to the child's parents.

The physical examination should always be undertaken with respect for the privacy of the child and in the presence of a parent or chaperon. Time spent putting the child at ease is usually well rewarded – as are a gentle approach and respect for the adage 'warm smile and warm hands!'

Hospitalisation

The psychological impact of hospitalisation on young children has been well documented by a number of important studies. Typically this is characterised by an acute reaction of stress, anxiety and behavioural disturbance. The stress created by the strange and potentially threatening environment of a hospital ward is compounded if infants are separated from their parents. Behavioural disturbance after discharge from hospital is also relatively common, particularly in children under 5 years of age. Long-term studies have demonstrated that psychological morbidity is increased by hospitalisation that exceeds 1 week in duration and by repeated admissions. Moreover, prolonged or repeated hospitalisation in the early years has been shown to lead to reduced educational attainment in later childhood.

The following measures can help to minimise the harmful effects of hospitalisation on behaviour and emotional development:

- Wherever possible, routine urological procedures of a minor or intermediate nature should be performed as day cases.
- There should be no restrictions to parental access. For day-case procedures, parents should accompany their child to the anaesthetic room and be available in the recovery area after the initial stages of recovery.
- Children should always be admitted to designated childrens wards. Under no circumstances should children be admitted to adult wards. Facilities for play should be provided.
- Facilities for schooling should also be available for children requiring longer periods of hospitalisation.

Timing of surgery

In the first few months of life, separation from the parent does not appear to have the same impact on subsequent emotional development as separation at a later stage in development. By 6 months, however, babies form stronger attachments to certain adults, particularly their mother. Separation distress becomes apparent at around 6 months and is maximal in the second year of life. By 2 years of age, self-awareness is well established and children become conscious of gender differences; it is also around this age that children develop the capacity to acquire memories of painful or distressing events. By 4–5 years of age, however, children are more receptive to simple explanations of what they may encounter in hospital and can be persuaded to accept periods of separation from their parents.

Current paediatric urological thinking therefore favours the complete surgical correction of most congenital genitourinary anomalies in the first year or two of life, when the experience of hospitalisation is less likely to result in distressing memories and subsequent behavioural and emotional disturbance. In this context the timing of corrective surgery for hypospadias has been the subject of a number of studies. Some earlier studies identified a degree of late psychological morbidity in men who had undergone correction of hypospadias in childhood. (However it should be noted that the techniques in question are now outdated.) By contrast, the findings of more recent studies have been broadly reassuring: for example, one recent study found no significant differences in psychosocial outcomes between individuals who had undergone hypospadias repair and a cohort of age-matched controls. Another study found that the incidence of emotional and behavioural disturbance was not significantly different from normal, unless the hypospadias surgery had resulted in repeated hospitalisation. A further study comparing adults who had been treated for hypospadias with adults who had undergone inguinal hernia operations at a comparable age in childhood found no differences in psychological parameters between the two groups.

By contrast to the low risk of late psychological sequelae arising from a single procedure in childhood, chronic conditions, repeated hospitalisation and numerous surgical interventions are associated with a far more significant burden of late psychological morbidity and mental health problems. For this reason the provision of specialised psychological support should be available from an early age for young patients with chronic renal failure, disorders of sex development and other serious urological disorders requiring ongoing or long-term treatment.

The practical implications include the following:

- Children requiring surgery that is likely to be an isolated event such as orchidopexy or single-stage hypospadias repair should, ideally, be operated upon between 6 and 18 months of age. Every effort should be made to limit the period of hospitalisation, ideally by day-case surgery whenever possible.
- Complex reconstruction requiring repeated or staged procedures should be completed by 18–24 months of age whenever this can be achieved without compromising the long-term outcome. If further surgery is required, this should be planned for later childhood and surgery should be avoided between the ages of 2 years and 6 years.
- The timing of procedures which are dependent upon cooperation and self-management by the patient (e.g. intermittent self-catheterisation of a catheterisable stoma) should be determined by a number of factors, including the emotional maturity and motivation of the young patient and the level of support available within the family and school.
- Certain procedures such as complex vaginoplasty or vaginal substitution should be deferred until the patient reaches adolescence or early adulthood when she can give genuinely informed consent herself and can cooperate with postoperative management such as vaginal dilatation.

Importance of the 'child friendly' environment

The needs of children and their families are best met within the environment of a dedicated children's hospital. Nevertheless, considerable progress has been made in recent years in creating 'child friendly' facilities within non-specialist district general hospitals. The recommendations of a number of different professional bodies have been instrumental in setting standards:

- **Outpatient activity should be organised in such a way that children are seen in designated surgical clinics held in a paediatric outpatient environment rather than in mixed clinics devoted primarily to adults**. If this cannot be achieved, a segregated area suitably furnished for children should be provided.

- The majority of routine urological procedures in children can be performed on a day-case basis. **Wherever possible, elective paediatric cases should be concentrated in separate designated paediatric operating lists**. Where this cannot be achieved, childrens' operations should be grouped together at the beginning of the theatre list to avoid the need for an overnight hospital stay. A survey published by the Healthcare Commission in 2007 found that 79% of elective general surgery in children was performed on child-only theatre lists, although the figure was considerably lower for ear, nose, and throat surgery.

Multidisciplinary team

Paediatric urology nurse specialists, who are based predominantly in specialist centres, make an invaluable contribution to the overall provision of a high-quality service for children, young people and their parents. Examples of their roles include teaching self-catheterisation and providing ongoing support in the home and community setting for young people with severe bladder dysfunction, liaising with schools and practice nurses and performing urodynamics. Their varied roles also encompass preoperative counselling and postoperative outreach care following more routine procedures such as hypospadias surgery. Skilled inpatient nursing care is also important to ensure optimal management of tubes and catheters. The sympathetic approach and experience of the inpatient nursing team is also very important in alleviating the apprehension which commonly surrounds procedures such as catheter and drain removal. Effective teamwork is one of the hallmarks of a successful paediatric urological unit.

Young people and adolescents

The needs of this emotionally vulnerable age group have been inadequately recognised in the past and there is little doubt that many young people have been disadvantaged by the arbitrary division into paediatric and adult services. The importance of improving services for young people as they grow into adulthood was identified as one of the priorities of the UK Government's National Service Framework for children and young people. Designated adolescent units are already provided in some hospitals – predominantly specialist units, but currently these are very much the exception rather than the rule. Although most young people at the upper age limit of childhood (typically defined in most non-specialist hospitals as the 16th birthday) can be safely treated in either an adult or children's environment, they should ideally be offered the choice. The delivery of safe clinical care is not the sole priority, and far more effort is needed to create hospital environments tailored to the psychological and emotional needs of this age group.

Children and young people with serious urological abnormalities are now surviving into adult life, with a requirement for ongoing long-term specialist care. The transition from paediatric- to adult-oriented health services has been poorly managed in the past, with the risk of loss of follow-up and consequent morbidity and mortality. Where possible, the transition from the care of a paediatric specialist to an adolescent or adult urologist should be managed as a process of transition rather than a 'one-off' transfer of care. For young patients with complex disorders and disabilities, the transition will also encompass other important aspects of multidisciplinary care: e.g. transfer from paediatric to adult nephrologists, psychologists and endocrinologists.

Consent

The legal issues surrounding consent in children and young people are complex and largely beyond the scope of this short chapter. The following summary is intended as a guide rather than a detailed account of current position in English Law.

For children between the ages 0 and 16 years old legal 'competence' to provide consent ultimately rests with the adult(s) with 'parental responsibility'.

In practice the legally competent adults are usually the child's parents. Although the legal requirement placed on the doctor is limited to obtaining consent from one person with parental responsibility, it is clearly preferable to involve both parents in the decision-making process. It should be noted, however, that in some circumstances the law recognises that young people under the age of 16 do have the capacity to provide consent without the involvement of their parents (based on the Gillick court ruling).

The legal position regarding those with 'parental responsibility', as defined by the Children Act 1989, is as follows:

- **The child's parents automatically have responsibility if they were married to each other at the time of birth.**
- **The child's mother (but not the father) automatically has legal responsibility if the parents were not married at the time of birth. However, this consideration does not apply if the father subsequently acquired parental responsibility through the courts or a parental responsibility agreement – or if the couple subsequently marry.**

In some circumstances parental responsibility may be assigned to:

- **A legally appointed guardian who has been appointed either by a court or by a parent with parental responsibility subject to their own death.**
- **A representative of a local authority designated in a Care Order.**

Children who have reached the age of 16 years old are presumed, in law, to be competent to give consent for their own surgical treatment and, as such, can be regarded, in most respects, as adults. Nevertheless, it is clearly good practice to involve parents in the decision-making process and to encourage young people with legal competence (ages 16 and 17) to provide their consent after discussion with their parents. The position is more complicated if someone of this age refuses treatment, but in general this request should be respected. Life-threatening illnesses are a possible exception.

Although the ultimate responsibility for providing consent for **children under the age of 16 years old** rests with the person with parental responsibility, the surgeon is also obliged to obtain the consent of the young patient insofar as this is feasible. Clearly, the extent of the child's involvement is dependent upon their level of understanding and emotional maturity. The information provided and the degree of detail, particularly relating to possible complications and adverse events, should be modified accordingly.

On the one hand, it is important to maintain reassurance and to avoid frightening the child by volunteering potentially distressing information; on the other hand, the child is owed a simple and honest account of what to anticipate postoperatively. A misleadingly bland or inaccurate assurance that it 'will not hurt' will undermine the child's confidence and trust in the doctors and nursing team if it proves to be untrue.

Young people who have reached the age of 18 years old are adults and, as such, have sole responsibility for their own decisions provided they have the capacity. Incapacitated adults and younger patients aged 16 or 17 years old may be treated in a variety of circumstances on the basis of other people's assessment.

Obtaining informed consent is a process rather than a 'one-off' event documented by a signature on a surgical consent form. Before arriving at the point at which the consent form is signed, the information provided to parents (and young patient, if appropriate) during outpatient consultations or ward rounds should include the indications for surgery and an outline of possible risks and complications. **The person giving consent** must be competent to do so (see above), should have been provided with sufficient information and should not be subjected to pressure or duress.

The person obtaining consent should, ideally, be the surgeon who will be responsible for

performing the operation. When this is not possible, the consent should be obtained by someone who is capable of performing the procedure in question. It is not acceptable for a surgeon to delegate responsibility for obtaining consent for a major or risky operation to a junior trainee.

Although there is some variation in wording and layout, most National Health Service (NHS) hospitals employ a standardised consent form. 'Procedure specific' consent forms which were devised for some specialties have not been widely adopted within the NHS because of legal concerns, whereas, patient (or parent) information sheets are being used increasingly and are seen as a valuable contribution to the consent process.

The introduction of **new interventional procedures** into surgical practice is now more formally regulated than in the past and mechanisms for assessment and peer review are now in place within the NHS. An individual surgeon planning to adopt a new operation which has been developed elsewhere must be able to demonstrate that he or she has received the appropriate training. Surgeons are also under an ethical and legal obligation to provide parents with an honest and balanced assessment of the perceived benefits and risks of any innovative procedure, together with information on their experience and results.

Occasionally, during the course of an operation, it may become apparent that an additional procedure is required for which consent has not been obtained. In this situation, the surgeon is under a legal obligation to obtain further consent for the additional procedure. Indeed, the surgeon is only permitted to proceed to perform the additional procedure if the failure to do so would result in death or irreversible harm. NHS consent forms generally include **consent for photography and the use of diagnostic images** when this forms part of the child's management and for the purposes of teaching and research, providing the child cannot be recognised. However, specific consent must be sought if the child can be recognised or identified in any material intended for teaching or research. Likewise, additional consent must be sought if clinical photographs are intended for publication, even if the child cannot be recognised.

Key points

- The professional relationship between surgeons and children and parents requires a different set of communication skills and professional attitudes to those employed in adult surgical practice.
- The psychological impact of hospitalisation in early childhood is well documented. Wherever possible, elective urological procedures should be performed as day cases.
- Isolated procedures such as hypospadias repair or orchidopexy should ideally be undertaken between 6 and 18 months of age and staged reconstructive surgery completed before 18–24 months.
- The needs of adolescents in hospital have been inadequately recognized and greater effort is needed to create hospital environments better suited to this age group.
- Although legal responsibility for consent in children under 16 years old ultimately rests with those who have parental responsibility, surgeons have a responsibility to involve young patients in the consent process and obtain their consent, insofar as this is feasible according to age and capacity.

Further reading

Department of Health. www.doh.gov.uk/consent

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Appendix I

Self-assessment section: Questions

Introduction

This section is intended to provide readers with an opportunity to test their understanding of the content of individual chapters by answering a series of multiple choice questions (MCQs).

- All questions have been set using the 'single best answer' or 'single correct answer' format. This type of question is now widely used for testing factual knowledge in postgraduate examinations, including the Intercollegiate examinations in Urology and Paediatric Surgery (FRCS (Urol) and FRCS (Paed)), the in-service examination of the European Academy of Paediatric Urology and the Fellowship of the European Board of Urology. This MCQ format is also widely used for postgraduate assessment in North America.
- Five answers are provided after each question – of which only one answer is correct. There is no negative marking for incorrect answers.
- All the information needed for the reader to answer the MCQs correctly is provided within the relevant chapter.
- Where percentages are quoted (for example, to incidence, complication rates etc), the "correct" answer is the figure quoted in the chapter. It is recognised that there is sometimes considerable variation in quoted incidences of different conditions in the published literature. However, the authors have, as far as possible, cited figures for incidence, complication rates, etc, which are evidence-based and derived from a range of sources.

Chapter 1: Embryology

1 Which of the following mechanisms is primarily responsible for initiating early development of the kidney?

a) Differentiation of the pronephros
b) Interaction between the mesonephric ducts and metanephros
c) Intraction between the ureteric bud and the mesonephros
d) Interaction between the paramesonephric ducts and metanephros
e) Interaction between the ureteric bud and metanephros

2 Which of the following is a recognised function of Mullerian Inhibitory Substance (MIS)?

a) Causes regression of the mesonephric ducts
b) Causes regression of the paramesonephric ducts
c) Converts testosterone to dihydrotestosterone
d) Stimulates the second phase of testicular descent
e) None of the above

3 Which of the following statements does *not* apply to the paramesonephric ducts?

a) They are present from the 6th week of gestation
b) They give rise to the fallopian tubes, uterus and upper vagina
c) They regress in response to exposure to foetal MIS
d) Their development is dependent upon exposure to foetal oestrogens
e) They may persist in some individuals with a 46XY karyotype

4 Which of the following common conditions have been shown to be linked to single gene mutations?

a) Polycystic kidney disease
b) Vesico ureteric reflux
c) Hypospadias
d) Ureteric duplication
e) All of the above

5 Klinefelter's syndrome is most commonly associated with which of the following karyotypes?

a) 46XY
b) 47XYY
c) 45Y
d) 47XXY
e) 45X

Chapter 2: Renal Physiology and Renal Failure

1 Which of the following patterns of physiological disturbance is most commonly encountered in neonates?

a) Metabolic alkalosis
b) Respiratory alkalosis
c) Compensatory hypernatraemia
d) Dilutional hyponatraemia
e) Compensatory hypokalaemia

2 Which of the following statements is most applicable to renal osteodystrophy in children with chronic renal disease?

a) It presents at an early stage with severe spinal pain
b) The presentation is often non-specific and may go unnoticed
c) Soft tissue calcification is more common in children than adults
d) Secondary hypoparathyroidism is found in 70-90% of patients
e) Skeletal deformity does not occur in children

3 Which of the following statements best describes the use of Erythropoietin in children with chronic renal failure or end stage renal disease?

a) It is usually administered orally
b) It is usually administered subcutaneously
c) Dosage is increased until a target haemoglobin of 14.5g/dl is achieved
d) Cardiac failure due to polycythemia has been reported in 5–10% of cases
e) Erythropoietin treatment avoids the need for iron supplements

4 Which of the following is the commonest cause of graft loss following renal transplantation in children?

a) Acute rejection
b) Renal vascular thrombosis.
c) Complications of immunosuppressant medication
d) Chronic rejection
e) Recurrence of primary disease

5 A 6 month old child has a plasma creatinine of 180 μm mol/L. At what age is the development of end stage renal failure most likely?

a) 12–18 months
b) 2–5 years
c) 5–10 years
d) Older than 10 years
e) Never – good long term prognosis for renal function

Chapter 3: Diagnostic Imaging

1 Which of the following statements best describes indirect isotope cystography in children?

a) Uses intravenous I^{131}mercapto-acetyltriglycine
b) Uses intravenous Tc^{99m} dimercapto-succinic acid
c) Uses intravenous Tc^{99m} mercapto-acetyl-triglycine
d) Is more sensitive than MCUG for the detection of Grades I and II VUR
e) Is equally suitable for children of all ages.

2 On initial postnatal ultrasound, which of the following measurements of renal pelvic Antero Posterior diameter denotes the presence of clinically significant pathology?

a) Any degree of renal pelvic dilatation
b) Renal pelvic AP diameter 5mm
c) Renal pelvic AP diameter 7 mm
d) Renal pelvic AP diameter 10 mm
e) None of the above

3 Which of the following statements best describes the use of ultrasonography in the evaluation of the urinary tract in children?

a) The bladder should be empty to facilitate visualisation of ureteroceles
b) Ultrasound is a sensitive modality for detecting minor renal scarring in infants
c) Ultrasound is a sensitive modality for visualising non-dilated ureters in children
d) Ultrasound is a sensitive modality for visualising calculi in children
e) Ultrasound is a sensitive modality for detecting grades I to III VUR in children

4 Which of the following statements most accurately describes the role of MRI in children?

a) MRI is inferior to plain X-ray for the investigation of spinal dysraphism
b) T2-weighted images provide better anatomical detail than T1-weighted images
c) Modern MRI scanners no longer require sedation or anaesthesia in infants or young children
d) MRI is the cross-sectional imaging technique of choice in acute abdominal trauma
e) MRI can be used to visualise 'crossing vessels' associated with PUJ obstruction

5 By what approximate factor does the radiation dose from a combined abdominal and pelvic CT examination exceed the radiation dose of a chest ray?

a) 5 to 10 times higher radiation dose
b) 50 to 70 times higher radiation dose
c) 200 to 300 times higher radiation dose
d) 500 to 600 times higher radiation dose
e) None of the above

Chapter 4: Urinary Tract Infection

1 A 7 year old girl is admitted acutely with a temperature of 39.5 C and left loin pain. What is the most appropriate method of collecting urine to confirm the presumed diagnosis of pyelonephritis?

a) Suprapubic puncture
b) Clean catch mid-stream specimen
c) Catheter urine specimen
d) Adhesive collection bag applied to the genitalia
e) Percutaneous renal aspiration

2 According to the 2007 NICE guidelines which of the following is not regarded as a feature of 'atypical' urinary infection meriting further investigation?

a) Family history of vesico ureteric reflux
b) Palpable bladder
c) Infection with an organism other than E.Coli
d) Failure to respond to appropriate antibiotics within 24 hours
e) Elevated plasma creatinine

3 A 4 year old girl presents with symptoms of dysuria, urgency and 'smelly' urine but is otherwise well. A urine dipstick test is negative for leucocyte esterase negative but positive for nitrite. According to the 2007 NICE guidelines what action should be taken next?

a) Send urine sample for microscopy and culture but await result before commencing antibiotics
b) Commence antibiotic treatment. It is not necessary to send urine for microscopy and culture
c) Do not commence antibiotics and do not send urine for microscopy and culture
d) Advise increased oral fluid intake and repeat dipstick test in 48 hours
e) Commence antibiotic treatment and send urine for culture

4 Which of the following is regarded as diagnostic of infection in a clean catch mid-stream specimen of urine?

a) Pure growth of $>10^7$ bacterial colony forming units (CFU) per ml
b) Mixed growth of $>10^7$ bacterial colony forming units (CFU) per ml
c) Pure growth of $>10^2$ bacterial colony forming units (CFU) per ml if pyuria is also present
d) Pure growth of $>10^4$ bacterial colony forming units (CFU) per ml if nitrites positive on dipstick
e) Pure growth of $>10^5$ bacterial colony forming units (CFU) per ml

5 A 6 month old male infant has made a full recovery following a non-specific febrile illness which proved to be a urinary infection. Ultrasound demonstrates bilateral upper tract dilatation (collecting systems and ureters). Which of the following is the most appropriate next investigation?

a) Intravenous urogram (IVU)
b) Micturating cystourethrogram (MCUG)
c) Indirect MAG3 isotope cystogram
d) Direct MAG3 isotope cystogram
e) MRI

Chapter 5: Vesicoureteric Reflux

1 The injectable implant material Deflux consists of which of the following materials?

a) Dextranomer/hyaluronic acid copolymer
b) Polytetrafluoroethylene (PTFE)
c) Polydimethylsiloxan (PDMS)
d) Deactivated bovine collagen
e) Deactivated bovine collagen/hyaluronic acid copolymer

2 Which of the following statements best describes the familial basis of vesico-ureteric reflux?

a) VUR can be demonstrated in 70-80% of siblings of children with known VUR
b) VUR can be demonstrated in 30-40% of siblings of children with known VUR
c) VUR can be demonstrated in 10-20% of the offspring of parents with known VUR
d) 40–45% of children with non-syndromic VUR have an associated mutation of the PAX2 gene
e) None of the above

3 In the United Kingdom approximately what percentage of cases of end stage renal failure in children and young people are due to reflux nephropathy?

a) 5–10%
b) 10–15%
c) 20–25%
d) 40–50%
e) 50–60%

4 Which of the following statements best describes the Cohen technique of ureteric reimplantation?

a) It is an extravesical procedure
b) The overall success rate for the complete correction of VUR is 80-85%
c) It is the operation of choice when reimplanting grossly dilated mega ureters
d) The submucosal tunnel length should be 4 or 5 times greater than the ureteric diameter
e) All of the above

5 Which of the following statements most accurately describes the aetiology of reflux nephropathy?

a) Focal scarring seen on DMSA is more likely to be due to infective damage than congenital dysplasia
b) Ongoing reflux of sterile urine results in progressive renal scarring
c) Asymptomatic bacteruria can result in renal scarring
d) The maximum risk of scarring occurs with the second and subsequent urinary tract infections
e) None of the above

Chapter 6: Upper Tract Obstruction

1 Unilateral upper tract dilatation has been detected antenatally in a male infant. Postnatal imaging is as follows: Ultrasound ureteric dilatation (diameter 1.1cm) and pelvicaliceal dilatation with a renal pelvic AP diameter of 1.3cm. MAG3 at 6 weeks – ipsilateral differential function 49%, minimal washout with diuretic (type 3 B curve). MCUG - no reflux, normal bladder and urethra. Which of the following would be the most appropriate management in this case?

a) Cutaneous ureterostomy
b) Leadbetter Politano ureteric reimplantation
c) Cohen ureteric reimplantation
d) Percutaneous nephrostomy
e) Antibiotic prophylaxis, follow up ultrasound at 6 months

2 Which of the following statements best describes pyeloplasty in children?

a) The Anderson-Hines pyeloplasty is no longer the operation of choice
b) The overall long-term success rate of open pyeloplasty is greater than 95%
c) Randomised controlled studies have shown that the use of JJ stents significantly reduces the risk of post-operative complications
d) The lumbotomy incision offers greater flexibility to deal with unexpected operative findings
e) None of the above

3 A 6 year old girl is referred following an episode of left abdominal/loin pain which has now resolved. Ultrasound demonstrates moderate dilatation of the pelvis (AP Diameter 30mm) and calyces. Which of the following would be the most appropriate next investigation?

a) Intravenous urogram
b) 99mTc MAG3 isotope renogram
c) Micturating cystourethrogram
d) CT scan
e) Antegrade pyelogram

4 Which of the following statements best describes the aetiology of pelviureteric junction obstruction?

a) It has a familial basis in 30-35% of cases
b) It is inherited as an autosomal recessive condition in 10-15% of cases
c) Aberrant 'crossing vessels' are present in 30-35% of infants with prenatally detected PUJ obstruction
d) It occurs more commonly in boys than girls by a ratio of 3:1
e) It affects the left kidney more commonly than the right by a ratio of 2:1

5 Which of the following statements best describes the use of MAG3 (Mercaptoacetyltriglycine) for the investigation of upper tract obstruction?

a) Imaging is commenced approximately 3 hours after injection
b) The radio pharmaceutical agent is I^{131} MAG3
c) MAG3 is more sensitive than MR urography for quantifying differential renal function
d) Obstruction can be reliably diagnosed from drainage curve data in the first month of life
e) Measurement of Glomerular Filtration rate can be combined with imaging

Chapter 7: Duplication anomalies, ureteroceles and ectopic ureters

1 According to the Meyer-Weigart Law,

a) the ureter draining the upper renal pole always enters the urinary tract below the bladder neck in females
b) the ureter draining the upper renal pole always joins the ejaculatory ducts in males
c) the upper and lower pole ureters may both drain into the bladder
d) the ureter draining the lower pole enters the urinary tract in a more cephalid position than the ureter draining the upper renal pole
e) the ureter draining the lower renal pole drains ectopically into the vagina in 10-15% of cases

2 During investigation of urinary tract infection a 4 year old boy is found to have a unilateral right-sided single system (orthotopic) ureterocele. A MAG3 study demonstrates obstruction with 32% differential function in the affected kidney. Which of the following would be the most appropriate management in this case?

a) Endoscopic incision
b) Heminephroureterectomy
c) Vesicostomy
d) Trans-uretero ureterostomy
e) Pyelopyelostomy

3 What is the autopsy incidence of upper tract duplication in the general population?

a) 0.0–0.1%
b) 0.5–1%
c) 1.5–2.5%
d) 2.5–5%
e) 5–10%

4 A 7 year old girl is referred with wetting. Although the history is suggestive of a possible diagnosis of duplex kidney with ectopic ureter the ultrasound findings are normal. Which of the following investigations should be undertaken next to pursue the presumptive diagnosis further?

a) IVU
b) MRI
c) 99m Tc MAG3 scan.
d) Laparoscopy
e) Careful examination of the perineum under anaesthesia

5 Which of the following statements best describes the occurrence and management of vesico-ureteric reflux (VUR) in duplex systems

a) VUR typically affects the lower pole ureter in cases of complete duplication
b) VUR typically affects the upper pole ureter in cases of complete duplication
c) VUR in duplex systems is more likely to resolve spontaneously than VUR in single systems
d) VUR should never be managed by ureteric reimplantation
e) Endoscopic correction of VUR is more successful in duplex ureters than single ureters.

Chapter 8: Posterior urethral valves and other urethral abnormalities

1 Which of the following is *not* a recognised predictor of long term renal impairment?

a) Maternal oligohydramnios
b) Proteinuria
c) Clinical presentation after 7 years of age
d) Bilateral vesico ureteric reflux
e) Impaired daytime urinary continence after the age of 5 years

2 A 3.5kg term infant is born with an antenatal diagnosis of posterior urethral valves which is confirmed postnatally on MCUG. His plasma creatinine on the second day of life is 46mmol/L. Which of the following would be the most appropriate form of intervention at this stage?

a) Vesicostomy
b) Endoscopic valve ablation
c) Bilateral nephrostomies
d) Bilateral loop ureterostomies
e) Bilateral end ureterostomies

3 In the United Kingdom approximately what percentage of boys with posterior urethral valves are currently diagnosed antenatally?

a) 10-20%
b) 20-30%
c) 40-50%
d) 60-70%
e) >80%

4 Which of the following statements best describes the current status of vesico amniotic shunting for foetuses with prenatally detected posterior urethral valves?

a) The long term benefits of shunting have been confirmed by the United Kingdom's PLUTO trial
b) Shunting has been shown to reverse renal dysplasia providing it is performed before 16 weeks gestation
c) Shunting may increase the severity of pulmonary hypoplasia
d) Shunting may reduce the severity of pulmonary hypoplasia
e) The long term results of intra uterine valve ablation are superior to vesico amniotic shunting

5 An 11 year old boy is referred with a 4 month history of dysuria and occasional spotting of blood from the urethral meatus. The most likely diagnosis is

a) Cobbs collar
b) posterior urethral polyp
c) urethral calculus
d) urethritis
e) rhabdomyosarcoma involving the posterior urethra

Chapter 9: Cystic renal disease

1 Which of the following statements best describes the features of autosomal recessive polycystic kidney disease?

a) The kidneys typically appear small and cystic on antenatal ultrasound
b) This form of polycystic disease may be associated with maternal oligohydramnios
c) The disorder typically presents with hypertension, abdominal pain, abdominal mass, etc, in late childhood or adult life
d) Mutations of the PK2 gene are present in 85-90% of cases
e) Percutaneous cyst drainage reduces the incidence of pain and infection

2 Which of the following statements most accurately describes the inheritance of multicystic dysplastic kidney (MCDK)?

a) MCDK is most commonly inherited as an autosomal recessive disorder
b) MCDK is most commonly inherited as an X-linked recessive disorder
c) MCDK is most commonly inherited as an autosomal dominant disorder
d) MCDK is associated with mutation of the PK1 gene on chromosome 16 in 65-70% of cases
e) MCDK is most commonly a sporadic anomaly

3 What percentage of adults on end stage renal replacement programmes have autosomal dominant polycystic kidney disease?
   a) 1–5%
   b) 5–10%
   c) 15–20%
   d) 20–25%
   e) 25–30%

4 A female infant has an antenatally detected unilateral MCDK. Her contralateral kidney is normal and she is otherwise healthy. What is her approximate life time risk of developing a Wilms tumour in the MCDK?
   a) Less than 0.1%
   b) 0.5–1%
   c) 1–1.5%
   d) 1.5–2%
   e) Greater than 2%

5 Postnatal ultrasound in a newborn infant reveals findings consistent with a diagnosis of unilateral multicystic dysplastic kidney. Which of the following would be the most appropriate next investigation?
   a) 99mTC DMSA scan
   b) IVU
   c) Measurement of glomerular filtration rate (GFR)
   d) CT scan
   e) MRI

Chapter 10: Prenatal Diagnosis

1 At what stage in gestation is routine antenatal ultrasound screening for foetal anomalies (including the genitourinary tract) most commonly performed in the United Kingdom?
   a) 10 to 12 weeks
   b) 12 to 14 weeks
   c) 15 to 20 weeks
   d) 20 to 25 weeks
   e) 25 to 30 weeks

2 Which of the following antenatal ultrasound findings would *not* routinely merit a routine a postnatal MCUG?
   a) Duplex kidney
   b) Thick walled bladder
   c) Unilateral pelvicaliceal dilatation (AP diameter renal pelvis 25 mm) without ureteric dilatation
   d) Unilateral pelvicaliceal dilatation AP diameter renal pelvis 25mm with ureteric dilatation
   e) Bilateral upper tract dilatation in a male infant

3 At 20 weeks gestation dilatation of the left renal pelvis and calyces (AP diameter renal pelvis of 16mm) is identified in a male foetus. The right kidney is normal. What would be the most appropriate advice to the parents regarding management at this stage in the pregnancy?
   a) Termination of pregnancy
   b) Ultrasound guided nephrostomy to decompress the left kidney
   c) Fetoscopic pyeloplasty
   d) No intervention, re scan in the third trimester
   e) Elective pre term delivery at 34 to 36 weeks followed by urgent neonatal pyeloplasty

4 Which of the following is *not* regarded as a predictor of poor outcome for renal function in a foetus with outflow obstruction?
   a) Foetal plasma creatinine greater than 150μmol/L
   b) Oligyhydramnios
   c) Foetal urinary sodium greater than 100mEq/L after 20m weeks gestation
   d) Increased levels of urinary beta 2 microglobulin
   e) Elevated urinary calcium (greater than 1.2mmol/L)

5 Approximately what percentage of newborn infants with a prenatally diagnosed urinary tract abnormality are also found to have relevant clinical signs on neonatal examination?

a) <5%
b) 5–10%
c) 10–15%
d) 15–20%
e) > 20%

Chapter 11: Stone disease in children

1 A 9 year old boy presents with a 1.1cm stone in the distal left ureter. There is moderate dilatation of the ureter and collecting systems on ultrasound. He is pain free but the appearances on further imaging after two weeks are unchanged. Which of the following is now the optimal management of this young patient?

a) External shockwave lithotripsy (ESWL)
b) Conservative – re-assess with further imaging after two months
c) Open ureterolithotomy
d) Basket extraction
e) Ureteroscopy and laser lithotripsy

2 Which of the following statements best describes the role of percutaneous nephro lithotomy (PCNL) in children?

a) PCNL can be employed safely and effectively in all age groups of children
b) PCNL can be performed without anaesthesia in older children
c) Stones are most commonly disintegrated with an ultrasound probe
d) Stones are most commonly extracted intact from the kidney using a modified stone basket
e) Renal cooling is undertaken to minimise the risk of parenchymal damage

3 A 10 year old girl is referred with a provisional diagnosis of xanthopyelonephritis? Which of the following features of her presentation and investigation is *not* consistent with this diagnosis?

a) Differential function 28% on DMSA scan
b) Elevated ESR
c) Weight loss
d) Haemoglobin 8.5g/dl
e) Palpable mass

4 Which of the following is the most common cause of metabolic stones in children?

a) Hyperoxaluria
b) Cystinosis
c) Hypercalcuria
d) Uric acidaemia
e) Xanthine oxidase deficiency

5 A 2 year old boy presents with haematuria. An ultrasound scan on admission demonstrates a 'staghorn' calculus in the left kidney. Urine culture is positive. What is the most likely infecting organism in this case?

a) E.Coli
b) Strep faecalis
c) Enterococcus
d) Staph aureus
e) Proteus

Chapter 12: Urinary incontinence

1 During the process of normal voiding, detrusor contraction is initiated in response to stimulation via which of the following pathways?

a) Voluntary somatic S2 -4 pathways
b) Parasympathetic S 2 to 4 pathways
c) T 10 to 12 lumbar sympathetic pathways
d) T 10 to 12 lumbar parasympathetic pathways
e) None of the above

2 A 6 year old girl is referred with a history of diurnal and nocturnal incontinence. She came out of nappies at 2 ½ years of age and was dry during the daytime (but not at night), until around 3 years of age. Since then, she has been wetting on an almost daily basis. Which of the following is the most likely diagnosis based upon this history?

a) Occult spinal dysraphism
b) Sacral agenesis
c) Dysfunctional voiding
d) Pelvic floor weakness (stress incontinence)
e) Ectopic ureter

3 A 7 year old boy is referred with a lifelong history of nocturnal enuresis. He wets the bed virtually every night but has been consistently dry during the daytime since the age of three. Physical examination is normal. Which of the following would be the most appropriate?

a) Ultrasound scan with pre and post void bladder views
b) Early morning urine osmolality
c) Urodynamics
d) Spinal x-ray
e) Reassurance, no investigation

4 A 12 year old girl is referred with a history of incontinence which is confined to occasions when she is laughing and joking with friends. She is dry at other times. Which of the following forms of treatment would have the highest chance of providing symptomatic relief in this patient?

a) Pelvic floor exercises
b) Methylphedinate
c) Oxybutinin
d) Tolterodine
e) Desmopressin

5 Which of the following anatomical causes of urinary incontinence in girls is least likely to be detected on visual examination of the perineum?

a) Congenital cloacal anomaly
b) Urogenital sinus anomaly
c) Primary epispadias
d) Ectopic ureter
e) Labial adhesions

Chapter 13: Neuropathic bladder

1 'Intermediate' neuropathic bladder dysfunction is characterised by detrusor hyperreflexia combined with partial sphincteric incontinence. What percentage of children with myelomeningocele exhibit intermediate neuropathic dysfunction?

a) 15–25%
b) 25–35%
c) 35–45%
d) 55–65%
e) 65–75%

2 Which of the following structures is usually used to create the Monti continent catheterisable conduit?

a) Ileum
b) Caecum
c) Colon
d) Appendix
e) Rectus sheath

3 Using the formula provided in the chapter, what is the calculated functional bladder capacity of a normal 6 year old child?

a) 110 to 130ml
b) 160 to 180ml
c) 200 to 220ml
d) 260 to 280ml
e) 310 to 370ml

4 Which of the following is *not* a recognised form of treatment for reduced bladder capacity associated with detrusor over activity?

a) Ileocystoplasty
b) Botulinum toxin A
c) Sigmoid colocystoplasty
d) Alpha agonist medication
e) Anti cholinergic medication

5 What is now the most common cause of neuropathic bladder in children?

a) Spinal injury
b) Occult spinal dysraphism
c) Transverse myelitis
d) Sacral agenesis
e) Myelomeningocele

Chapter 14: The urinary tract in anorectal malformations, multisystem disorders and syndromes

1 What percentage of children with anorectal malformations have co-existing anomalies of the urinary tract?

a) 15–25%
b) 25–35%
c) 35–45%
d) 45–55%
e) 55–65%

2 A newborn male infant has a low anorectal anomaly. What imaging modality is currently recommended for initial imaging of his spine?

a) MRI
b) CT
c) Spinal x-ray and ultrasound
d) Bone scan
e) Contrast myelography

3 Which of the following is *not* a recognised feature of the VACTERL association?

a) Vertebral anomalies
b) Anorectal anomalies
c) Eye anomalies (coloboma)
d) Renal anomalies
e) Limb anomalies

4 A healthy newborn female infant is born with a presumed diagnosis of unilateral renal agenesis – based on antenatal ultrasound. Only one (normal) kidney is seen on the postnatal ultrasound scan. What investigation (if any) is indicated next?

a) None. The diagnosis of renal agenesis had been confirmed on two ultrasound scans
b) MRI
c) CT
d) Laparoscopy
e) DMSA scan

5 Which of the following statements does *not* apply to horseshoe kidneys?

a) Horseshoe kidney is well visualised on DMSA renography
b) Horseshoe kidney occurs more commonly in children with Turners Syndrome
c) The autopsy incidence of horseshoe kidney is reported to lie between 1:400 and 1:1800
d) 35–45% of horseshoe kidneys are associated with fusion of the upper pole renal parenchyma
e) Horseshoe kidney is associated with an increased incidence of PUJ obstruction

Chapter 15: Bladder exstrophy and epispadias

1 The incidence of bladder exstrophy is approximately:

a) One in 5000 live births
b) One in 25 000 live births
c) One in 50 000 live births
d) One in 150 000 live births
e) One in 300 000 live births

2 Which of the following is *not* a common feature of primary epispadias?

a) Sphincteric weakness
b) Pubic diastasis
c) Normal calibre ureteric orifices
d) Urethra sited on the dorsal aspect of the penis
e) Anterior ectopic anus.

3 A 3.5kg male infant with classic bladder exstrophy is transferred to a specialist centre at 6 hours of age. He is otherwise well with no evidence of cardiac or other anomalies. What is now the optimal management of this infant?

a) Primary closure with pelvic osteotomy in the first 48 hours of life
b) Primary closure without pelvic osteotomy in the first 48 hours of life
c) Parental nutrition for one month followed by closure with pelvic osteotomies.
d) Temporary urinary diversion with ureterostomies following by primary closure and undiversion at 6 months
e) Delayed closure with augmentation cystoplasty at 12 months.

4 Which of the following anomalies are associated with cloacal exstrophy?

a) Sacral agenesis in 30- 40% of cases
b) Renal anomalies in 15-25% of cases
c) Skeletal abnormalities affecting the pelvis and lower limbs in 10-20% of cases.
d) Small bowel defects in 60-70% of cases
e) All of the above

5 Which of the following statements best describes the features of primary epispadias in girls?

a) Normal continence occurs spontaneously in 85% of cases by 7 years of age
b) Sphincter weakness incontinence is invariably present
c) The external genitalia are usually normal
d) The clitoris is usually absent
e) The overall chances of achieving pregnancy are less that 10%

Chapter 16: Hypospadias

1 Which of the following statements is most applicable to the Mega Meatus Intact Prepuce (MIP) variant of hypospadias?

a) The MIP variant is usually detected on routine neonatal examination
b) Circumcision is sufficient to create a satisfactory cosmetic appearance
c) The MAGPI procedure is the operation of choice for correcting the MIP variant
d) The MAGPI procedure is unsuited to the correction of the MIP variant
e) None of the above

2 What is the overall incidence of co-existing upper urinary tract anomalies in boys with hypospadias?

a) 1–5%
b) 5–10%
c) 10–15%
d) 15–20%
e) 20–25%

3 Which of the following graft materials is most widely used in the first stage of a two stage repair of proximal hypospadias?

a) Post auricular skin
b) Buccal skin
c) Bladder mucosa
d) Porcine dermis
e) Inner preputial skin

4 Which of the following statements best describes the aetiology and epidemiology of hypospadias?

a) The incidence is increased in low birth-weight infants
b) The incidence is increased in the offspring of older mothers
c) The overall incidence of male first degree relatives is 5-20%
d) Hypospadias is more common in monozygotic twins
e) All of the above

5 A healthy infant is referred with hypospadias. The urethral meatus is located at the junction of the proximal two thirds and distal one third of the penile shaft and there is no evidence of chordee. What type of operative repair is currently favoured by most paediatric urologists for this type of hypospadias?

a) Two stage repair
b) Buccal mucosa graft
c) Onlay island flap
d) Meatal advancement and glanluloplasty (MAGPI)
e) Tubularised incised plate repair (Snodgrass)

Chapter 17: The prepuce

1 Which of the following statements best describes the aetiology and management of balanitis xerotica obliterans (BXO) in children?

a) BXO carries a 1-3% risk of penile carcinoma before the age of 20 years
b) Treatment with topical steroids avoids the need for surgery in 80-85% of cases
c) Preputioplasty is preferable to circumcision for the treatment of BXO in boys over 10 years of age
d) Glans involvement is present in 5-7% of cases
e) BXO is rare in children under 5 years of age

2 The parents of a 4 year old boy are concerned because they have observed obvious ballooning of his prepuce during micturition. Which of the following is most applicable in this case?

a) The ballooning probably denotes the presence of BXO
b) Measurement of his urine flow rate is likely to show a significant reduction
c) The most likely diagnosis is congenital mega prepuce
d) The parents can be reassured that ballooning is a self-limiting phenomenon of no pathological significance
e) The presence of ballooning is a strong indication for circumcision

3 Which of the following statements best describes the features of congenital mega prepuce?

a) The condition is characterised by an excessively long, redundant prepuce
b) The overall appearances may resemble a 'buried' penis
c) Circumcision usually gives satisfactory cosmetic results
d) Any male siblings will also have a 1:4 chance of being born with this condition
e) Any male siblings will also have a 10-15% chance of being born with this condition

4 Which of the following statements is most applicable to preputioplasty?

a) Preputioplasy can be used as an effective alternative to circumcision in 70-80% of boys with BXO
b) Retraction of the prepuce should be avoided for three to six months after the procedure
c) Regular retraction of the prepuce should be advised in the early post-operative period
d) Preputioplasty is equally successful in all age groups
e) None of the above

5 A 5 year old boy is referred with a non-retractile prepuce. The prepuce is healthy but cannot be retracted beyond the tip of the glans because of preputial adhesions. What management should be advised?

a) Reassurance, see again only if symptoms arise
b) Circumcision
c) Preputioplasty
d) Surgical release of adhesions under general anaesthesia
e) Surgical release of adhesions under general anaesthesia if the prepuce is still partially adherent to the glans at 6-7 years of age

Chapter 18: Testis, hydrocele and varicocele

1 A 17 year old patient presents for the first time with a small palpable testis in the inguinal region. Orchidectomy is performed. The histological appearances of these testis are most likely to show:

a) Germ cell hyperplasia
b) 'Sertoli cell only' appearances
c) Normal appearances
d) Well-differentiated seminoma
e) Leydig cell hyperplasia

2 A three year old boy is referred with a unilateral impalpable testis. The most reliable means of confirming the presence or absence of the testis is:

a) Abdominal ultrasonography
b) MRI
c) CT scan
d) Retrograde venography
e) Laparoscopy

3 A 2 ½ year old boy presents with a lax left sided scrotal swelling which can be transilluminated. The clinical findings are those of a hydrocele. Which of the following statements best describes the clinical features and management in this patient?

a) The hydrocele is most likely to be of the non-communicating variety
b) There is a 90% probability of spontaneous resolution in the next 12 months
c) The hydrocele should be aspirated and re-assessed after 6 months
d) Inguinal ligation of the processus vaginalis would be the most appropriate operative procedure
e) A Jaboulay operation would be the most appropriate operative procedure

4 An 11 year old boy presents with a painless grade III left sided varicocele. What advice should be given to his parents?

a) Infertility is inevitable unless some form of intervention is undertaken
b) Treatment of the varicocele is likely to carry a 50% failure rate regardless of the mode of treatment
c) A CT renal scan should be performed in view of the 2% risk of Wilms tumour
d) An ultrasound scan of the testes and kidneys is all that is required at this stage
e) A semen sample should be analysed before determining further management

5 Testicular ultrasound in a 14 year old boy demonstrates bilateral microcalcification. This is essentially an incidental finding following a sporting injury. What action should be advised in the light of these findings?

a) Reassurance, no further follow up unless symptomatic
b) Urgent testicular biopsy
c) Testicular biopsy around the age of 19 or 20 years
d) Bilateral prophylactic testicular fixation in view of the high risk of testicular torsion
e) Six monthly ultrasound review for 5 years with annual ultrasound examination thereafter

Chapter 19: The acute scrotum

1 Scrotal exploration is being performed in a 14 year old boy for a presumed diagnosis of right testicular torsion. He has a 10 hour history of symptoms. The diagnosis is confirmed but despite detorsion, the testis remains dark blue in colour with no evidence of perfusion. What action should the surgeon take?

a) Right orchidectomy. Defer fixation of the left testis until a second operation in view of the risk of infection
b) Right orchidectomy combined with simultaneous fixation of the left testis within a dartos pouch
c) Right orchidectomy combined with simultaneous fixation of the left testis with prolene sutures
d) Leave the right testis in situ (in the hope it may contribute to endocrine function). Simultaneous suture fixation of the left testis
e) Right orchidectomy and implantation of silicone gel prosthesis, simultaneous suture fixation of the left testis

2 A 5 year old boy presents with diffuse swelling involving both sides of the scrotum He is afebrile and has only minimal discomfort. What action should be taken next?

a) Urgent surgical exploration to exclude an atypical presentation of bilateral synchronous testicular torsion
b) Commence intravenous antibiotics
c) Full blood count, platelet count and plasma viscosity
d) Oral Prednisilone
e) No specific treatment

3 A 13 year old boy presents with severe right iliac fossa pain of sudden onset. No abnormality if detected on abdominal palpation. His right testis is moderately tender but there is no erythema of the overlying scrotal skin. How should he be investigated and managed?

a) Scrotal ultrasound
b) Admit for observation, re-assess clinical findings after 4 hours
c) Doppler ultrasound
d) Radionuclide scan
e) No investigation, proceed directly to surgical exploration

4 A 17 year old patient with testicular torsion has undergone unilateral orchidectomy for a non-viable testis. What advice should be given in response to questions regarding the prognosis for endocrine function and fertility?

a) Reassurance that semen quality will be unaffected
b) Testosterone levels should be checked annually since endocrine replacement treatment may be required
c) Semen quality is likely to be impaired but it is not possible to predict the extent to which this might affect paternity
d) Semen quality is likely to be impaired and available evidence indicates that infertility is inevitable
e) None of the above

5 Which of the following statements does *not* apply to torsion of the Hydatid of Morgagni?

a) The 'blue dot' sign is present in 50-60% of cases
b) The peak incidence is between 10 and 12 years of age
c) It can usually be diagnosed on clinical grounds
d) The pain is usually more gradual in onset than testicular torsion.
e) Conservative management can be safely considered if symptoms are mild or resolving

Chapter 20: Disorders of Sex Development

1 Which is the commonest disorder of sex development encountered in Europe and North America?

a) Ovotesticular DSD
b) 5 Alpha reductase deficiency
c) 46XX DSD due to congenital adrenal hyperplasia
d) Mixed gonadal dysgenesis
e) 46XY DSD (male pseudo hermaphroditism)

2 Which of the following statements best describes the features of children with Turner's Syndrome?

a) Clitoral hypertrophy is present in 80-90% of patients
b) Normal ovarian tissue is present in 55-75% of patients
c) The lifetime risk of gonadal malignancy is significantly increased
d) The lifetime risk of gonadal malignancy is not significantly increased
e) The diagnosis is most commonly made during investigation of ambiguous genitalia in infancy

3 Which of the following statements best describes the aetiology and epidemiology of congenital adrenal hyperplasia (CAH)?

a) CAH accounts for 20-25% of all infants with ambiguous genitalia
b) The most common underlying endocrine defect is 11 Beta hydroxylase deficiency
c) CAH is an autosomal dominant disorder with variable expression
d) CAH is an X linked recessive disorder
e) CAH is an autosomal recessive disorder

4 As a consequence of the findings during a hernia operation, Sarah, aged 5, is diagnosed with complete androgen insensitivity syndrome. Which of the following statements best describes the other features of her phenotype and genotype?

a) The most likely karyotype is 47XXY
b) The most likely karyotype is 46XY
c) The most likely karyotype is 47XYY
d) The gonads identified in the hernial sacs are most like to be dysgenetic streak gonads
e) The internal genitalia are most likely to comprise a vestigial uterus and fallopian tubes.

5 Which disorder of sex development is characterised by an elevated plasma level of 17 OH progesterone?

a) Mixed gonadal dysgenesis
b) Ovotesticular DSD (true hermaphroditism)
c) 46XY DSD (male pseudohermaphroditism)
d) Mullarian inhibitory substance receptor insensitivity
e) 46XX DSD (female pseudohermaphroditism) due to congenital adrenal hyperplasia

Chapter 21: Genitourinary Malignancies

1 Which of the following statements most accurately refers to the epidemiology and aetiology of rhabdomyosarcoma?
   a) This tumour accounts for 40-50% of all solid tumours in childhood
   b) This tumour accounts for approximately 30% of all tumours of the genito urinary tract in childhood
   c) Approximately one third of all rhabdomyosarcomas in children arise within the genito urinary tract
   d) This tumour is less common in children of Afro Caribbean origin.
   e) Girls are affected more commonly than boys

2 A 2 year old boy presents with urinary retention and haematuria. Initial ultrasound demonstrates a polypoid mass in the region of the trigone and bladder neck. Both upper tracts are normal. Which of the following would not be routinely included in the diagnostic protocol for this child?

   a) Cystoscopy
   b) Biopsy
   c) CT scan
   d) Bone scan
   e) Glomerular Filtration Rate (GFR)

3 What is the approximate current overall 5 year survival rate for children with nephroblastoma (Wilms tumour)?

   a) 20–30%
   b) 40–50%
   c) 50–60%
   d) 80–90%
   e) >90%

4 In the United Kingdom and Europe, which of the following is currently the most commonly used sequence of treatment modalities for Wilms tumour?

   a) Nephrectomy followed by post operative radiotherapy
   b) Nephrectomy followed by post operative chemotherapy and radiotherapy
   c) Nephrectomy followed by post operative chemotherapy
   d) Biopsy, pre-operative radiotherapy followed by nephrectomy
   e) Biopsy, pre-operative chemotherapy followed by nephrectomy

5 Which of the following is *not* a feature of Beckwith-Weidemann Syndrome?

   a) Macroglossia
   b) Anidiridia
   c) Wilms tumour
   d) Omphalocoele
   e) Visceromegaly

Chapter 22: Urogenital trauma

1 A 6 year old boy has been brought to the accident and emergency department following a fall from a playground swing. He is haemodynamically stable but is tender in the left upper quadrant. His urine contains +++ blood on dipstick testing. Ultrasound in the A&E department demonstrates haematoma in the region of the upper pole of the left kidney. Which of the following (if any) would be most appropriate following admission to the paediatric ward?

   a) Urgent DMSA scan
   b) Repeat ultrasound scan after 48 hours
   c) Intravenous urogram
   d) CT scan
   e) No further imaging required if clinical condition remains stable.

2 What is the estimated risk of hypertension associated with a renal injury in childhood?
   a) Less than 5%
   b) 5–10%
   c) 10–15%
   d) 15–20%
   e) 20–25%

3 Which of the following procedures would be the most appropriate surgical management of a 0.5 cm length post-traumatic urethral stricture in the bulbar urethra of a 10 year old boy?
   a) Laying open the stricture and two stage urethroplasty with buccal skin
   b) Laying open the stricture and two stage urethroplasty with post auricular skin
   c) Excision of stricture and substitution urethroplasty with vascularised preputial skin
   d) Excision of stricture and end to end urethral anastomosis
   e) Transpubic sphincterotomy

4 A 7 year old girl with a blunt renal injury to the right kidney is assessed with ultrasound and CT. Imaging reveals a laceration of the renal parenchyma extending across most of the lower pole of the right kidney accompanied by peri-renal haematoma and urinary extravasation. What grade of renal injury do these findings represent?
   a) Grade I
   b) Grade II
   c) Grade III
   d) Grade IV
   e) Grade V

5 A 2 ½ year old girl is brought by her mother to the accident and emergency department following an accident which occurred whilst being looked after overnight by a neighbour. No one saw the accident occur. Examination reveals bruising of the perineum and labia, contusion of the introitis and a superficial laceration of the vaginal mucosa. What measures should be taken next?
   a) Admit to hospital, proceed to urgent cystoscopy
   b) Admit to hospital. Contact the duty paediatrician to investigate the circumstances of the injury
   c) Prescribe antibiotic cream and regular baths. Arrange further review in the outpatient clinic in 2 days
   d) Prescribe oral antibiotics and regular baths. Arrange further review in the outpatient clinic in 2 days
   e) Reassure, no antibiotics prescribed but advise regular baths. No arrangement for follow up

Chapter 23: Laparoscopic paediatric urology

1. Which of the following statements best describes the use of laparoscopic pyeloplasty for PUJ obstruction in children?
   a) The first series of laparoscopic pyeloplasties in children was reported in 1990
   b) Non-dismembered pyeloplasty is usually performed for cases of PUJ obstruction without crossing vessels
   c) Laparoscopic pyeloplasty can be performed by a retro peritoneal approach in children
   d) Laparoscopic pyeloplasty cannot be performed by a retro peritoneal approach in children
   e) Robotic laparoscopic pyeloplasty cannot be performed safely in children

2 Which of the following is *not* regarded as an absolute contra indication to laparoscopic adrenalectomy in children?

a) Phaeochromocytoma
b) Cardiac failure due to severe congenital heart disease
c) Respiratory insufficiency due to cystic fibrosis
d) Uncorrectable coagulopathy
e) Systemic sepsis

3 What is the optimal insufflation pressure for laparoscopic procedures in children whose weight is the range 10–20kg?

a) <12 mmHg
b) 15–17 mmHg
c) 17–19 mmHg
d) 21–23 mmHg
e) 23–25 mmHg

4 Which of the following is *not* a well recognised indication for laparoscopic nephrectomy?

a) Dysplastic kidney associated with hypertension
b) Non-functioning hydronephrotic kidney
c) Severe reflux nephropathy with hypertension
d) Stage I or Stage II Wilms Tumour
e) Intractable protein loss associated with nephrotic syndrome

5. What was the first laparoscopic procedure to gain widespread acceptance in paediatric Urology?

a) Laparoscopic nephrectomy
b) Diagnostic laparoscopy for impalpable testes
c) Laparoscopic pyeloplasty
d) Laparoscopic excision of mullarian remnants
e) Laparoscopic hemi nephrectomy

Chapter 24: Adolescent urology

1 What is the most common cause of death in adult spina bifida patients?

a) Renal failure
b) Uncontrolled hydrocephalus
c) Bladder cancer
d) Cardiovascular and respiratory disease
e) Suicide

2 What is the approximate risk of malignancy associated with enterocystoplasty after a latency period of 20–25 years?

a) 2–5%
b) 5–7%
c) 7–10%
d) 10–12%
e) 12–15%

3 Which of the following is *not* a well recognised feature of Prune Belly Syndrome?

a) Renovascular malformations
b) Bilateral undescended testes
c) Absent abdominal wall musculature
d) Kyphoscoliosis
e) Urinary tract dilatation

4 Which of the following statements best describes the prognosis for sexual and reproductive function in female bladder exstrophy patients?

a) Substitution vaginoplasty is usually required to permit normal intercourse
b) Uterine prolapse occurs in up to 50% of women
c) Fewer than 15% of women with a history of bladder exstrophy can achieve pregnancy
d) Sensory function is usually impaired as a result of clitoral agenesis
e) Infertility is inevitable because of the association between bladder exstrophy and uterine agenesis

5 Which of the following is a well documented prognostic indicator of long term renal impairment in patients with posterior urethral valves?

a) GFR 65 mls/min/1.73m2 at 8 years of age
b) Daytime incontinence after 5 years of age
c) Diagnosis after 5 years of age
d) Non refluxing upper tracts
e) High urine osmolality

Chapter 25: Children and young people as urological patients

1 In the United Kingdom, which of the following adults do not have parental responsibility (defined by the 1989 Children Act) to provide consent for a child to undergo surgery?

a) The child's mother regardless of marriage status
b) The child's father regardless of marriage status
c) The child's father if the parents were married at the time of birth or married subsequently.
d) A legally appointed guardian
e) A local Authority representative designated in a Care Order

2 At what age do young patients have sole legal responsibility to consent to treatment or to refuse it?

a) 15 years
b) 16 years
c) 17 years
d) 18 years
e) 21 years

3 If the operating surgeon is unable to obtain consent for a major procedure in person, which of the following should obtain consent on his/her behalf?

a) Any qualified doctor
b) Any surgical trainee of the specialist registrar grade
c) A surgeon who has observed the procedure in question
d) A surgeon who is capable of performing the procedure in question
e) A nurse specialist

4 At what age do children typically develop self-awareness and become conscious of gender differences?

a) 6 months
b) 12 months
c) 2 years
d) 4 years
e) 7 years

Appendix II

Self-assessment section: Answers

Chapter 1 Embryology

Question 1 e
Question 2 b
Question 3 d
Question 4 a
Question 5 d

Question 4 Comment: Although conditions such as vesico ureteric reflux, hypospadias and ureteric duplication have a well documented familial basis, attempts to implicate individual gene mutations have been unfruitful and it is generally believed that they result from the interaction of multiple genes. By contrast, specific mutations have been identified in autosomal dominant polycystic kidney disease – see Chapter 9: Cystic renal disease.

Chapter 2 Renal physiology and renal failure

Question 1 d
Question 2 b
Question 3 b
Question 4 d
Question 5 d

Question 1 Comment: Hyponatremia (plasma sodium less than 130mmol/L), due to water retention and sodium depletion is a common feature of sick and premature newborn infants. Monitoring of sodium and fluid balance in such infants is particularly important in the early weeks of life.

Chapter 3 Diagnostic imaging

Question 1 c
Question 2 e
Question 3 d
Question 4 e
Question 5 c

Question 2 Comment: A renal pelvic AP diameter of greater than 10mm is regarded as abnormal but is not necessarily indicative of clinically significant pathology.

Chapter 4 Urinary Tract Infection

Question 1 b
Question 2 d
Question 3 e
Question 4 e
Question 5 b

Question 1 Comment: A child of this age should be able to cooperate in the correction of a 'clean catch' midstream sample – the least invasive, reliable method of collecting an uncontaminated specimen.

Question 3 Comment: Leucocyte esterase negative, nitrite positive. This finding represents presumptive evidence of UTI. The NICE guidelines recommend that antibiotic treatment should be commenced and a urine sample sent for culture.

Chapter 5 Vesico ureteric reflux

Question 1 a
Question 2 b
Question 3 c
Question 4 d
Question 5 a

Chapter 6 Upper tract obstruction

Question 1 e
Question 2 b
Question 3 b
Question 4 e
Question 5 c

Question 1 Comment: The imaging points to a diagnosis of obstructed megaureter with good preservation of function. In the majority of cases the natural history is one of gradual spontaneous resolution. In this case, conservative management would be more appropriate than any form of surgical intervention at this stage.

Chapter 7 Duplication anomalies, ureteroceles and ectopic ureters

Question 1 c
Question 2 a
Question 3 b
Question 4 b
Question 5 a

Chapter 8 Posterior urethral valves and other urethral abnormalities

Question 1 c
Question 2 b
Question 3 e
Question 4 d
Question 5 d

Chapter 9 Cystic renal disease

Question 1 b
Question 2 e
Question 3 b
Question 4 a
Question 5 a

Chapter 10 Prenatal diagnosis

Question 1 c
Question 2 c
Question 3 d
Question 4 a
Question 5 a

Question 4 Comment: Plasma creatinine is not a meaningful measure of renal function in the foetus, since creatinine crosses the placental barrier. Even if foetal plasma creatinine could be measured, a value of greater than 150mmol/L would raise concern about renal impairment in the mother but tell us nothing useful about renal function in the foetus.

Chapter 11 Stone disease in children

Question 1 e
Question 2 c
Question 3 a
Question 4 c
Question 5 e

Chapter 12 Urinary incontinence

Question 1 b
Question 2 c
Question 3 e
Question 4 b
Question 5 d

Question 3 Comment: This boy has monosympomatic nocturnal enuresis. In the absence of daytime wetting or any other unusual features the yield from investigation is minimal and the parents can be reassured that he will become dry.

Question 4 Comment: Giggle incontinence is a rare but distinctive disorder. Treatment with anticholinergics is usually unhelpful, but Methylphedinate (Ritalin) can sometimes be dramatically effective.

Chapter 13 Neuropathic bladder

Question 1 d
Question 2 a
Question 3 c
Question 4 d
Question 5 e

Chapter 14 The Urinary tract in anorectal malformations, multisystem disorders and syndromes

Question 1 e
Question 2 c
Question 3 c
Question 4 e
Question 5 d

Question 4 Comment: A pelvic kidney can be missed on ultrasound. A DMSA scan is indicated to identify any ectopic function in renal tissue principally to look for a pelvic kidney.

Chapter 15 Bladder exstrophy and epispadias

Question 1 c
Question 2 e
Question 3 b
Question 4 d
Question 5 b

Chapter 16 Hypospadias

Question 1 d
Question 2 a
Question 3 e
Question 4 e
Question 5 e

Chapter 17 The prepuce

Question 1 e
Question 2 d
Question 3 b
Question 4 c
Question 5 a

Chapter 18 Testis, hydrocele and varicocele

Question 1 b
Question 2 e
Question 3 d
Question 4 d
Question 5 a

Question 3 Comment: Surgery is not necessarily indicated at this stage but if it is decided to operate the correct procedure for a presumed communicating hydrocele is ligation of the processus vaginalis.

Chapter 19 The acute scrotum

Question 1 c
Question 2 e
Question 3 e
Question 4 c
Question 5 a

Question 2 Comment: The diagnosis is idiopathic scrotal oedema for which no specific treatment is required.

Chapter 20 Disorders of sex development

Question 1 c
Question 2 c
Question 3 e
Question 4 b
Question 5 e

Chapter 21 Genitourinary malignancies

Question 1 c
Question 2 e
Question 3 e
Question 4 e
Question 5 b

Chapter 22 Urogenital trauma

Question 1 d
Question 2 a
Question 3 d
Question 4 c
Question 5 b

Chapter 23 Laparoscopic paediatric urology

Question 1 c
Question 2 a
Question 3 a
Question 4 d
Question 5 b

Chapter 24 Adolescent urology

Question 1 d
Question 2 a
Question 3 a
Question 4 b
Question 5 b

Chapter 25 Children and young people as urological patients

Question 1 b
Question 2 d
Question 3 d
Question 4 c

Question 1 Comment: The child's father is not automatically deemed to be competent to provide consent unless he was married to the mother at the time of the child's birth or they married subsequently.

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