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HAROLD E. HENKES

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PHOTOGRAPHY, ELECTRO-OPHTHALMOLOGY AND ECHO-OPHTHALMOLOGY IN OPHTHALMIC PRACTICE

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CONTENTS

PREFACE

The 1973 - postgraduate courses in ophthalmology held under the auspices of the Netherlands Ophthalmological Society, mark the 25th anniversary of the rebuilt Rotterdam Eye Clinic.

The themes set for these courses: 'Ophthalmic Photography', 'Electro-ophthalmology' and 'Echo-ophthalmology', have been chosen from a multitude of rapid developments in ophthalmology during this period.

The aim was to provide the clinician with a lead in a bewildering field of apparatus and techniques and to help him in selecting methods that provide useful results without too much specialised knowledge.

However, sophisticated techniques and discussion of results have been added now and then, so that the more advanced reader still finds sufficiently interesting material in this report.

This holds e.g. for the section on fluorescence-angiography which section has been extended on the base of the probability that the clinician in general practice too, has been or will be confronted with this rapidly expanding and fascinating field.

The reason to bring together two methods of objective examination of visual functions i.e. electro-ophthalmology and echo-ophthalmology, is clearly due to the intimate connection between the two.

In many ways these methods complement each other in providing the final diagnosis.

This report does not intend to replace text books, nor to outdate treatises on superspecialised ophthalmic subjects; it simply tends to provide the clinician with a basic information on selected techniques, stimulating the reader to start using them in daily practice.

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OPHTHALMIC PHOTOGRAPHY

PHOTOGRAPHIC AIDS IN OPHTHALMIC PRACTICE

A. L. AAN DE KERK

(*Rotterdam*)

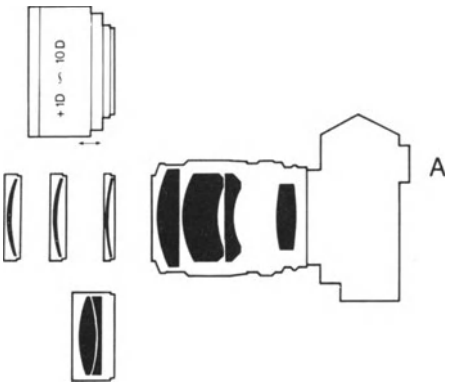
This article gives a review of both expensive and inexpensive photographic aids for eye photography. The inexpensive photographic aids are described in more detail because most of these cameras are simple to handle for ophthalmologists and technicians.

The following subjects will be dealt with:

I. Photographic aids for external eye photography (single reflex cameras with accessories for close-up photography, special 'all ready' close-up cameras, which simplify eye photography for untrained operators and – for the more professional workers – photo slitlamps).
II. External eye photography and retinal photography with hand-held cameras.
III. Retinal cameras (hand-held and table top).
IV. Sensitive materials.
V. Flashlight illumination for close-up photography (conventional external flash units and special macro-flashlight).
VI. Filing and storing of: negatives, transparancies and photographs.

I. PHOTOGRAPHIC AIDS FOR EXTERNAL EYE PHOTOGRAPHY

To size up the image we can use a magnifying glass in front of the subject or extend the space between the camera-body and the lens unit (myopia). These basic principles for close-up photography are shown in Fig. 1.



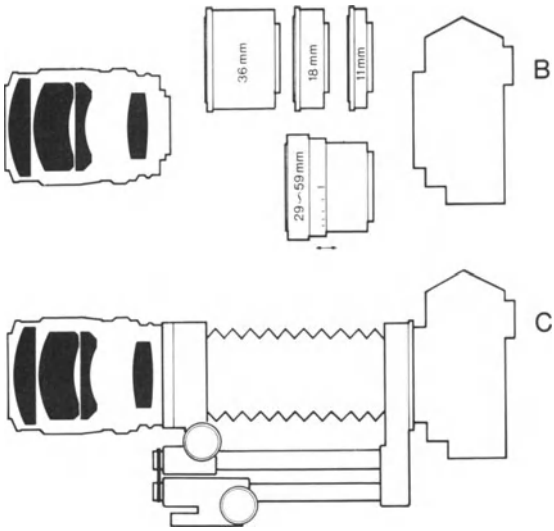


Fig 1. Principles for image enlarging in close-up photography
A. camerabody, 135 mm lens and supplementary lenses,
B. camerabody, extension tubes, 135 mm lens,
C. camerabody, extension bellows, 135 mm lens.

1. Camera-body and 135 mm lens in conjunction with positive supplementary lenses (magnifying glass) (A).
2. Camera-body, extension tubes, and 135 mm lens (B).
3. Camera-body, extension bellows, and 135 mm lens (C).

Close-up photography of the external eye can be done with almost any single reflex camera (Fig. 2), special 'all ready' close-up cameras (Fig. 6), and photo slitlamps (Fig. 3). (See review in Table I and Table II).
The characteristics of close-up cameras are given in Table I. Single reflex cameras are preferable because they can be used for private and for numerous other purposes. Most of these cameras can be extended with a complete system of accessories, for example: motor transport for fluorescence photography (Fig. 5). Single reflex cameras are adaptable to close-up photography with special accessories. Single reflex cameras with bayonet mount guarantee rapid interchanging of the lens and components. This saves time when shooting medical photographs. Special 'all ready' close-up cameras simplify rapid eye photography and are especially designed for close-up photography. These snapshooting cameras are relatively simple and present no problems. In addition, no preparations are required for lighting, focus, exposures, field size and depth of field. Close-up photographs with the 'all ready' close-up cameras are made within a few seconds which results in minimum disruption.

Most cameras are hand-held, which is very important for bed-ridden patients and for surgical photography. Portable cameras too, have a great mobility.

Fig. 2. The ideal set-up for close-up eye photography: 35 mm reflex camera back, automatic extension bellows, 135 mm lens, flash bracket and electronic flash.

Photographic experience

With most cameras no photographic experience is required to get professional results. Especially the Kodak Instatech II, simple box camera with fixed focus lens, is very simple and efficient to operate. This camera is very popular in the field of dental close-up photography (GIBSON, 1971). For operation of the more expensive cameras, such as the Donaldson Stereo camera, a little more experience is needed (DONALDSON, 1954, 1955).

The most ideal lens for general eye photography is one with a longer focal length (e.g. 135 mm telephoto lens) than the normal focal length of 50 mm. It is not necessary to buy specially designed macro-lenses; the resolution and

Table I. Close-up cameras for anterior ocular photography

Table I.	Set up as in fig. 1a (Supplementary lenses)	Set up as in fig. 1b (Extension tubes)	Set up as in fig. 1c (Extension bellows)	J-D Clinicamera VI	Kodak Instatech. II	Nikon Medical Nikkor	Photoeaze single unit reflex camera	Polaroid CU-5 close up camera	Surgicam	Donaldson Stereocamera	Realist Stereocamera
Price	Dfl. 1.778	Dfl. 1.779	Dfl. 1.983	$ 175	Dfl. 334	Dfl. 2605	$ 395	Dfl. 3500–5500	$ 1800	$ 3500	$ 539
Handheld	●	●	●	●	●	●	●	●	●		●
No photographic experience required	●	●	●	●	●		●	●	●		●
Focal length of the lens:											
normal	●	●	●	●	●	●	●	●●	●	●	●
long	●	●	●			●					
Natural perspective proportions (in full face photographs)	●	●	●			●		●	●●	●●	
Image enlarging:					●		●				●
supplementary lens(es)	●	●	●	●		●		●	●●●	●	
tubes or bellow extension	●	●	●	●	●	●	●	●●		●●●●	●
Focus and composing											
view finder	●	●	●		●				●	●	
image/spots projection					●	●●●●●	●	●●●●		●	●
frame/rods	●	●	●	●	●	●	●	●	●	●	●
Image sizes:											
1:15	●	●	●	●		○					
1/8	○	○	○		●	●	●	●	●	●	●
1/3	●	●	●	●							
1:1	●	●	●	●●	●	●	●	●	●	●	●
2:1	●	●	●								
Sensitive materials:											
35 mm	●	●	●	●	●	●	●	●	●	●	●
126 Cartridge	○	○	○			○					
Polaroid						○		●			
Data recording						●					
Flashlight:											
external flash	●	●	●	●	●	●	●	●●	●	●	●
flashcube											
ringflash											
built-in											
Field of applications	1+2+3 4+6+7	1+2+3 4+6+7	1+2+3 4+6+7	1+2.	1+2+3 4+6	1+2+3 4+6	1+2	1+2+3 4+5+7	2+6	1+2+5	3+5
Miscellaneous									8		
Distributors	14	15	16	9	10	11	12	13	17	18	19
Private use	●	●	●		●	●					

sharpness of a conventional long focal length is equal to that of the special macro-lenses. The focal length of a lens is usually engraved on the mount. Long focal lenses have the following advantages: larger working distance, more room for manipulation with electronic flash etc. and non-interference with the surgeon in surgical photography.

Working very close to the subject with a normal lens tends to distort the proportions of the subject. If you are frequently taking binocular photographs or anterior and lateral views of the full face, a system which corrects perspective proportions should be chosen. Especially binocular photographs of eye motility studies must be made with a very long focal length. Fixation of the

Table I: close-up cameras for anterior ocular photography.

O	these cameras can be fitted with Speed Magny for instant photography
●	characteristics
....	no response received
Dfl	prices in Dutch florins as on 1 July 1973
$	prices in dollars as on 1 January 1973, valid for the U.S.A.; These cameras have no distributor in Europe
1.	ophthalmic photography
2.	medical photography
3.	dental photography
4.	scientific photography
5.	scientific 3 Dimensional photography
6.	surgical photography
7.	also outdoor pictures
8.	sterilisable in an autoclave
9.	Jenkel-Davidson, Optical Company, 366 Post Street, San Francisco, U.S.A.
10.	Kodak distributor
11, 14, 15 and 16.	photodealer distribution
12.	Photoeaze Mfg. Inc., 241 East 10 St., New York, N.Y. 10003, U.S.A.
13.	Polaroid distributor
17.	Meddev Corporation, PO Box 1352, Los Altos, California 94022, U.S.A.
18.	Mentor Division, Codmann & Shurtleff, Inc., Randolph, Massachusetts, U.S.A.
19.	Realist Inc., N93 W16288 Megal Drive, Menomonee Falls, Wisconsin 53051, U.S.A.

eye must be at infinity because while we work too close to the subject, the eyes are converging.

There are three types of positive supplementary lenses. Simple supplementary lenses, variable focus supplementary lens and high quality supplementary lenses. Positive supplementary lenses are mostly used in cameras with a fixed focus and not-interchangeable lenses, such as the Kodak Instatech II (Fig. 6). Usually they are screwed on, or clipped to the front of the camera lens.

Simple supplementary lenses usually consist of a set of three lenses. When used individually, only a narrow range of subject distances is covered, but

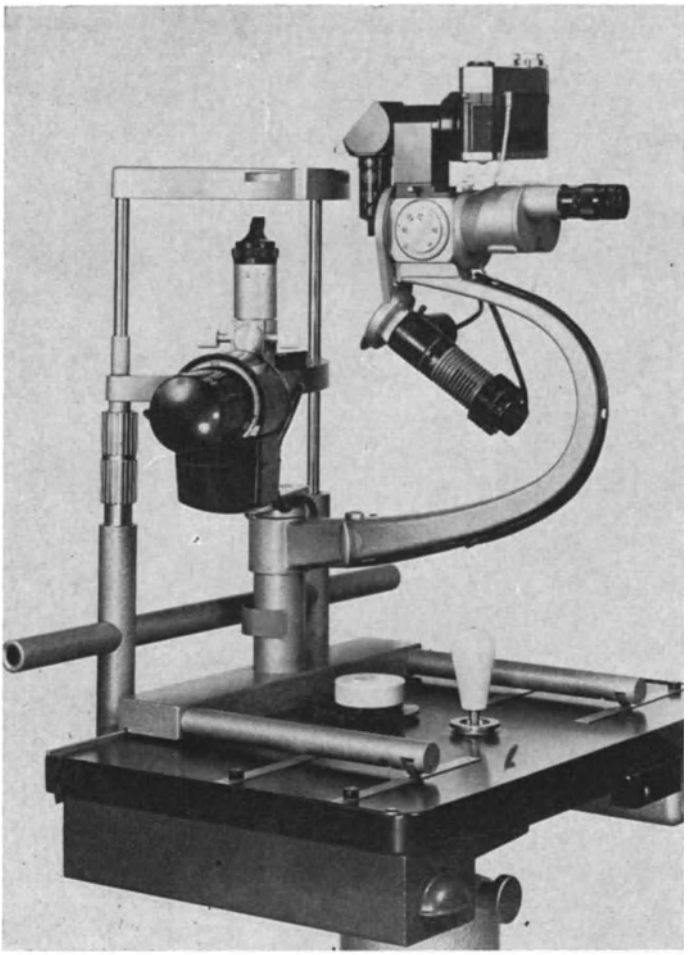


Fig. 3. Zeiss photoslitlamp.

they can also be used in combination. These are simple, uncorrected elements and the lens aperture – diaphragm in the path of the light rays – must always be well stopped down if critical definition is required (f/32).

The variable focus supplementary lens is built up of several converging and diverging units, such as the Maximar Vario-prox which is a zoom-type continuous close-up lens with a variable diopter range from plus 1 diopter to plus 10 diopters.

Diopters are changed by the rotation of its calibrated focusing mount. This has an obvious advantage over the use of a number of simple supplementary lenses which have to be interchanged. Such additions as simple supplementary lenses and a variable focus supplementary lens upset the correction of the camera lens and introduce most of the aberrations. Even with

a stopped-down lens aperture the definition is not as good as it would be with a camera lens in conjunction with extension tubes or extention bellows. However, there is an advantage in that the supplementary lens does not affect the f. number of the camera lens when focused at infinity. High quality supplementary lenses are supplied by some manufacturers such as the Leitz Elpro for Leicaflex lenses. These achromat high quality supplementary lenses give marked improvement in image quality (KEELING, 1972).

Automatic extension tubes and automatic extension bellows can only be used if the lens can be removed from the camera body. The extension tubes

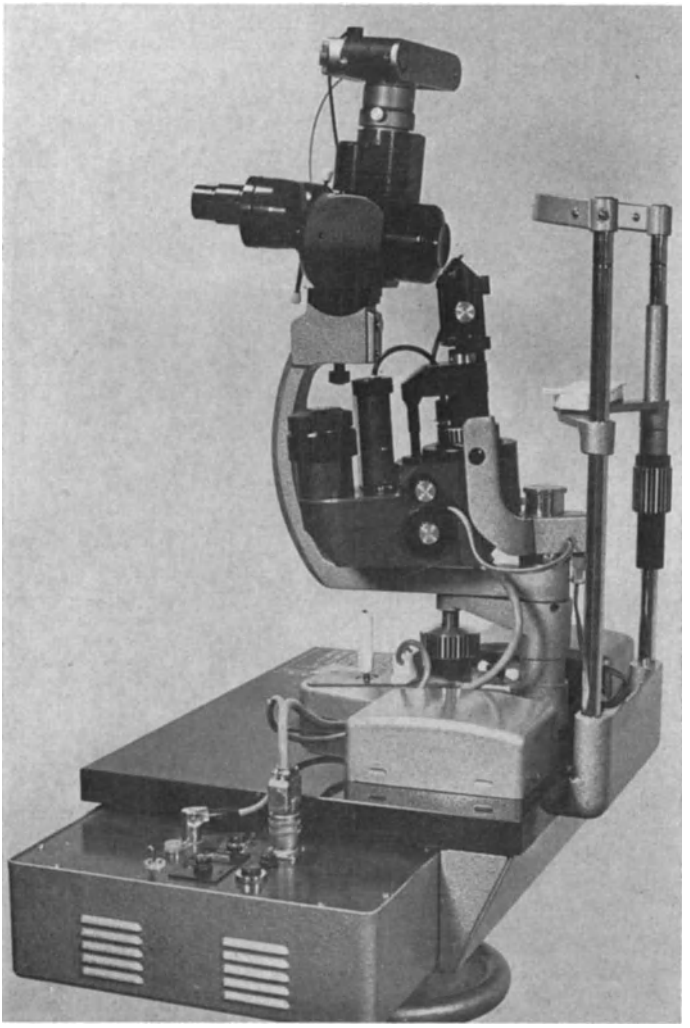


Fig. 4. Gambs photoslitlamp.

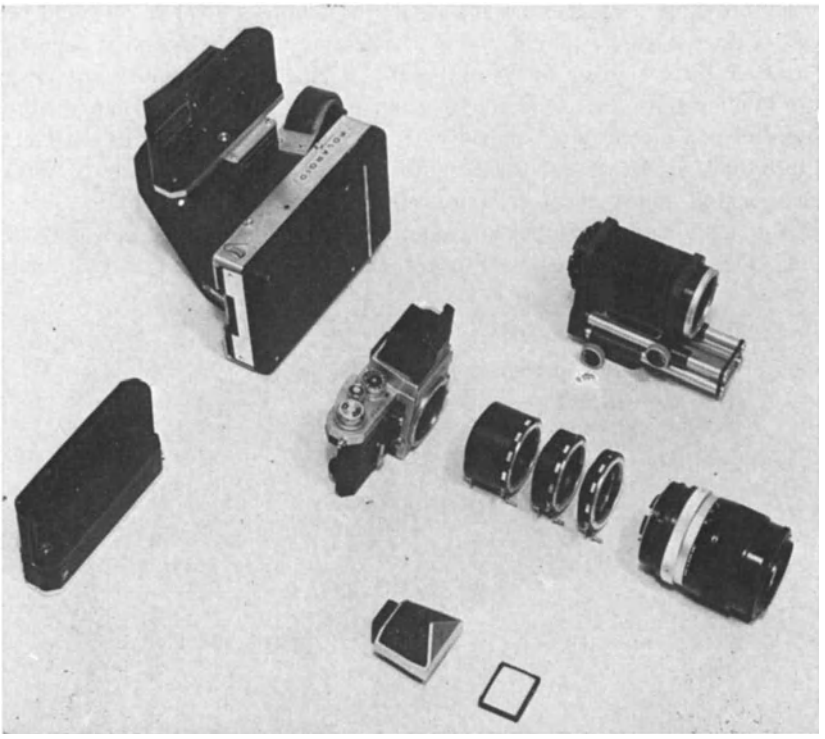


Fig. 5. A single reflex camera with a complete system of accessories.

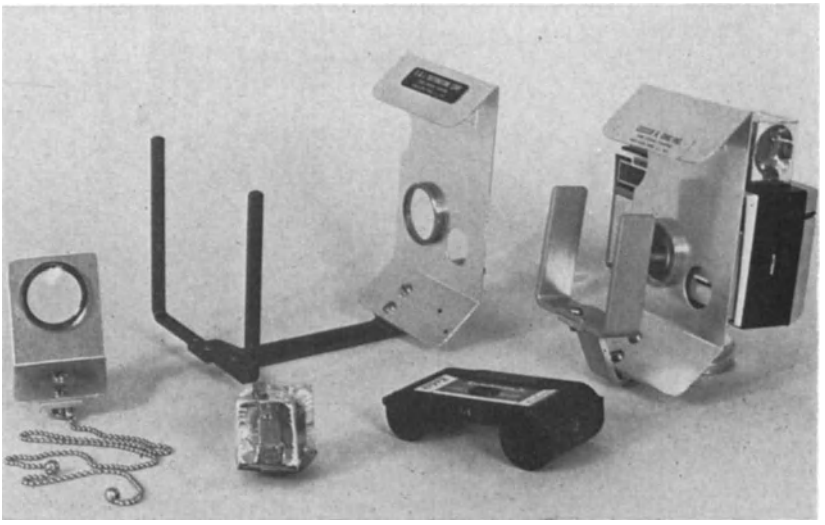


Fig. 6. Kodak Instatech II close-up camera.

and extension bellows are inserted between the camera body and the lens unit. This decreases the working distance and gives a magnified image. The obvious advantage over the use of supplementary lenses is that they do not upset the good correction of the camera lens. However, this method presents a disadvantage in as far as it affects the f. number when a double or triple extension is used (see Table IV).

The extension tubes and extension bellows must be of the automatic type for fully automatic diaphragm operation. This avoids time parallax between focusing and pressing the shutter release button.

Automatic extension tubes are usually a set of three standard lengths, such as the Soligor 11 mm, 18 mm and 36 mm. The tubes can be used individually, which covers only a narrow range, or they can be used in combination. Variable extension rings are also available for specific cameras such as Leica and Topcon.

Automatic extension bellows such as the Novoflex Balnik-A provide a variable extension for close-up work over a continuous range of distances. The set-up of: lens, bellows and single reflex camera is the most ideal combination for close-up photography (Fig. 1c).

Focusing and composing

The best system for positioning and focusing is to make use of the viewfinder which has no parallax. Visual focusing has the advantage of focusing at full aperture and previewing the final effect of the depth of field with pre-set working lens aperture, usually to f/22. Pre-viewing of the final effect is not possible with the image/spots projection.

Viewing and focusing the subject are done through the viewfinder by moving towards the subject. Accurate focusing on a special ground glass screen is essential, because the depth of field is only a few mm in close-up photography. The larger the magnification the smaller the depth of field.

Viewfinder and image/spots projection are both good systems for accurate positioning and focusing. The advantage of image projection are that we can suffice with low intensity light for focusing photophobic patients, and the precise field of view is clearly indicated on the subject (CORY, 1962).

Spots projection is done with two angled, converging light beams which are focused to a point in front of the housing. When the light beams coincide the image is in focus.

Focusing with viewfinder or image/spots projection is done by moving towards the subject.

The frame-rods focusing and composing works faster than the other three systems mentioned above. The frame/rods positioning always needs contact with the subject. For surgical photography the frame/rods must be sterilised.

The frame/rods method is not parallax-corrected. The attached distance gauge or field frame is fit to the camera and placed over the object area (Fig. 7). The frame does not show on the film. Usually there are different sizes of subject frames, which should be changed for each object area. The new Kodak

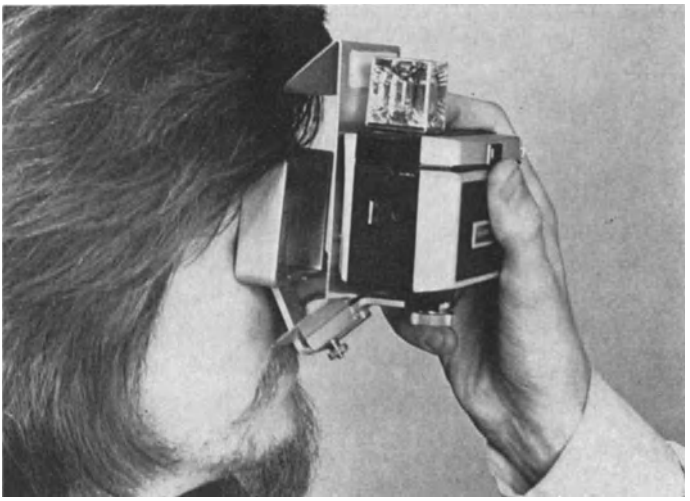


Fig. 7. The Kodak Instatech II close-up camera in use for 1:1 image size (life size).

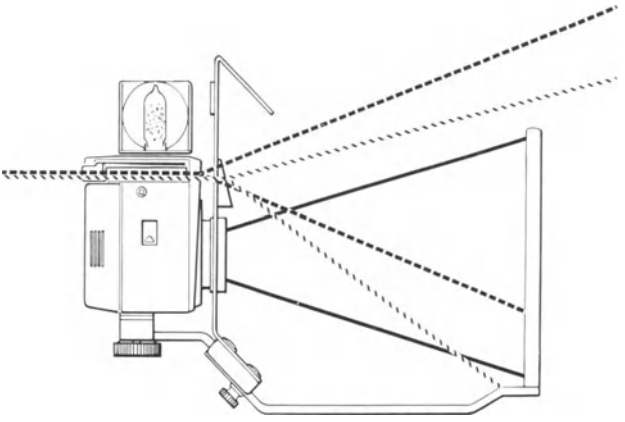


Fig. 8. Diagram Instatech II illustrates the way in which the prism changes the effective angle of the viewfinder, and hence the field of view, to match the camera field, (after Gibson).

Instatech II (GIBSON, 1971) can also be used, without a frame, with a prism viewfinding. We can see the entire area covered by the camera (Fig. 8).

Although optical, the frame/rods positioning is not ideal because the positioning and focusing are not accurate. For critical definition the lens aperture must be stopped down.

Most cameras cover a complete range which permits focusing from infinity up to a part of a single eye. In practice, however, it is recommended to standardize the range of image sizes to five standard areas for eye photography (Fig. 9) (HANSELL, 1961).
This is very usefull in the case of a succession of photographs taken before, during and after treatment. All image sizes have different depths of field. The depth of field is greater with an image size of 1:15 (area nr. 5, Fig. 9) and is smaller with an image size of 1:1 (area nr. 2, Fig. 9). It increases also when a smaller lens aperture is used.

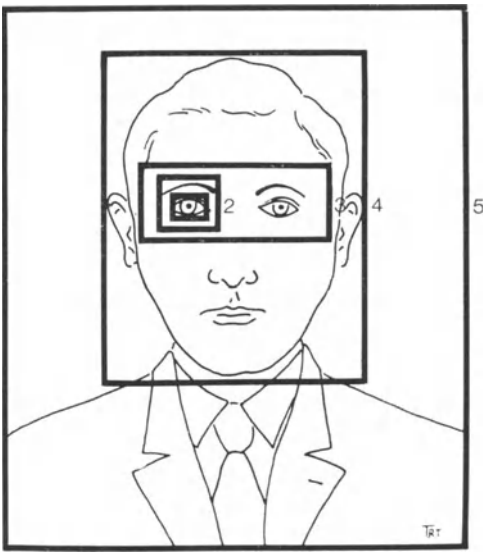


Fig. 9. The standard areas for eye photography after Hansell. Image sizes 1:15 (area 5); 1:8 (area 4); 1:3 (area 3); 1:1 (area 2); 2:1 (area 1).

The image areas 2 to 5 (Fig. 9) can be done with portable cameras for close-up photography. For the more enlarged areas nrs. 1 and 2 it is recommended to place the entire set-up on a geometric stand (Fig. 21) or a standard tripod, and to use a headrest consisting of a chinrest and forehead brace, to immobilize the head.

With these aids the camera can be accurately positioned in relation to the patient's head. Table IV shows the lens setting and bellows extension for different image sizes with set-ups as in Fig. 1.

The lens apertures are found experimentally by making test exposures or with exposure calculators, which are supplied with most of the close-up electronic flash systems. The photoslitlamps are fitted with optics and flash illumination which is more adaptable for extreme close-up photography as in area nr. 1 (Fig. 9).

The only close-up camera with built-in data recording is the Nikon Medical Nikkor. Frame-number or image sizes are projected at the right-hand bottom corner. If a Leica MD or Contarex camera body is used for a set-up as in Fig. 1, strip indication can be used. These are small plastic strips on which various data can be written. The strip is slipped into the bottom of a special camera back. The data on the plastic strip is projected over a small part of the subject on the negative.

With all other cameras we can photograph a ruler or mm paper or other data with the subject (OGG, 1962).

Field of applications

BOCKELMAN (1970, 1973) strongly recommends the Nikon medical Nikkor, and for instant photography the Polaroid CU5 close-up camera for the oph-

Fig. 10. The Polaroid CU-5 close-up camera with special focussing spotting lights for image size 1:1.

thalmic practice (Fig. 10). The medical Nikkor is an excellent optical system for medical photography, but the ringflash is not ideal for eye photography. This illumination gives flat 'shadowless' pictures (Kodak, 1972).

Better results are obtained if the ringflash illumination unit is removed from the lens camera and is put to one side. The Polaroid CU5 close-up camera is a very popular instant close-up camera for scientific workers. BOCKELMAN (1971) simplified working with this camera for ophthalmic use with the addition of spots projection (BOCKELMAN, 1970).

It is quite convenient, of course, if the same camera or part of it is suitable for general photography. The three set-ups (Fig. 1) for single reflex cameras and the medical Nikkor must be extended with a normal lens. The Kodak Instatech II gives parallax at infinity, the camera viewfinder is corrected with a prism for short-working distance.

Photoslitlamps (Table II)

Photoslitlamps are commonly used to obtain extreme close-ups of the eye from 1:1 up to 5:1, as well as optical sections of the eye. The photoslitlamps are better fitted for extreme close-up photography due to the headrest, stand, lightsource, optics for photography and fixing-light. At present, the Zeiss photoslitlamp is considered the best (Fig. 3) whereas the Gambs photoslitlamp is the simplest to operate for an inexperienced operator (Fig. 4).

The characteristics of photoslitlamps are given in Table II. The Jena photoslitlamp as well as the Zeiss photoslitlamp in combination with microscope optics are not frame-filling. The Jena photoslitlamp is designed for an image field of 24 mm diameter. Photographs made with the Zeiss photoslitlamp with microscope optics are designed for an image field of 22 mm diameter. They are not frame-filling.

The image field will be frame-filling with a x2 auxiliary objective which must be mounted between photographic adapter and camera body (LITTMANN & WITTEKINDT, 1970). Zeiss also has a photographic attachment which is placed on the corneal microscope. With this attachment a x2 auxiliary objective for frame filled image is not needed (LITTMANN, 1965).

The advantage of 3-dimensional photography is recording depth in the external eye photography. The separation of the optical axes of the lenses at high magnification is smaller than that with low magnification. With the Jena photoslitlamp the 24 × 36 mm film format is split-up into two half-frame stereophotographs of 15 mm diameter each. The definition of this half-frame stereo-pair cannot be as good as two 24 × 36 mm stereo-photographs. Especially in the case of stereo-photography it is very important to use a fine grain film with a high resolving power. For stereo-photography with the Zeiss photoslitlamp the manufacturer recommends the microscope optics in conjunction with two cameras mounted to a small beamsplitter and two photographic adapters, with an image field of 22 mm diameter. The image field will be frame-filling with a x2 auxiliary objective, which must be mounted between the photographic adapter and camera body. Better definitions are

Table II. Photo-slitlamps and their characteristics.

Table II.

	Gambs (1)	Jena photoslitlamp SLF (2,3)	Nikon (zoom)	Zeiss (4,5)
Price range	II	II	....	II+III
Slitlamp photography with: own optics				●
microscope optics	●	●	●	●
Number of magnifications	2	3	zoom x 0,7 - x 3,5	3 or 5
Stereo		●		●
Film	24x36 mm	24x36 mm	24x36 mm and 12x16,5 mm	24x36 mm
Polaroid camera	●		●	
Maximum output (W/sec)	700	480	200	840
Supplementary fill-in illumination with:				
own electronic flash				●
main electronic flash	●	●		
Fluorescein angiography				●
Excitor filter				Schott BG12
Barrier filter				Schott GG14

● characteristics
.... no response received
II price range Dfl. 10.000 — Dfl. 20.000
III price range Dfl. 20.000 — Dfl. 30.000
1. photographs mirrored
2. not frame-filling
3. split up 24 × 36 mm format into two half-frame stereo pair
4. photographs with the microscope optics are only formatfilled with magnification attachment ×2
5. price range III for fluorescein angiography

obtained with the system of OOSTERHUIS (1968). He modified the Zeiss photoslitlamp with two photographic attachments (VON WINNING, 1973).

Just as is advocated in external photography (using less magnified pictures) we must also standardize the image sizes for slitlampphotography to 2 or 3 magnifications e.g., 1:1, 2:1 and 3:1. Increasing magnifications presents two disadvantages: loss of light (see exposure factor table IV) and reduction in

the depth of field. For this reason we must focus more carefully than is normally done.

The best slitlamp photographs are made with specific photographic optics, because these optics are better corrected for aberrations.

The best optical sections for slitlampphotography are obtained with a very narrow slit and small lens aperture. For this reason we need a photoslitlamp with a power pack, delivering a flash of high energy, such as the Zeiss photoslitlamp.

Fluorescence photography is only possible with a special photoslitlamp, such as the Zeiss photoslitlamp. This photoslitlamp has some special provisions as forced cooling of the flash tube and a high power, rapid-charge flash generator.

The latitude of the reversal colour film is not wide enough to reproduce light (slit) and dark (surrounding) of the subject in one transparancy. For this reason we need sometimes supplementary fill-in illumination in slitlampphotography, to lighten up the surrounding of the slit for orientation and to eliminate high contrast in the subject.

The best and most economic system for supplementary fill-in illumination is to use the main flash. Secondary light source and power unit for fill-in illumination is an expensive solution. With the Jena photoslitlamp, the supplementary fill-in illumination is obtained with a special slit-diaphragm in the illumination pathway of the slitlamp. The Gambs takes with a small light-guide scattered light from the primary flash tube for fill-in illumination. We have modified the Zeiss photoslitlamp, after the same principle of the Gambs

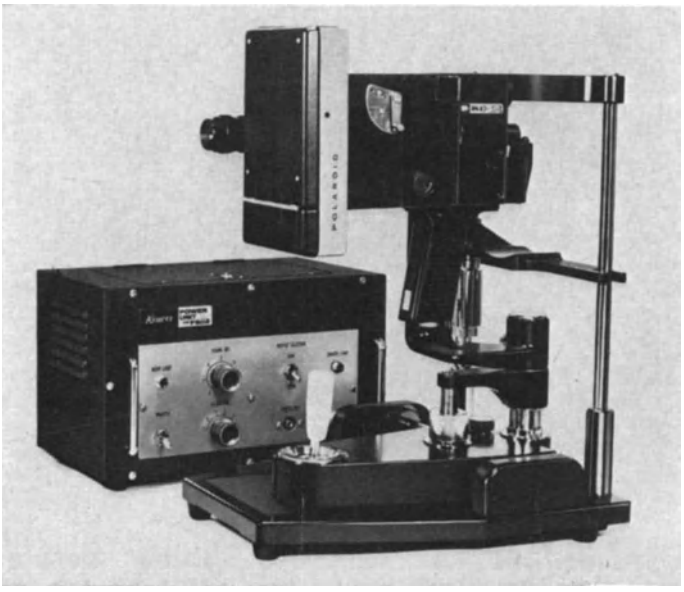


Fig. 11. Kowa RC-2 retinal camera with Polaroid back, joy-stick stand and special power supply unit for Polaroid and fluorescence photography.

fill-in illumination. In working with the Zeiss photoslitlamp, this modification has the advantage that rapid and easy manipulation is possible with the microscope and slitlamp and no special supplementary flash and power units are needed for fill-in illumination.

II. EXTERNAL EYE- AND RETINAL PHOTOGRAPHY WITH HAND-HELD CAMERAS

With hand-held cameras not only retinal photographs can be made, but they have also been sucessfully used in recording of the anterior segment (AAN DE KERK & CRAANDIJK, 1968). In my opinion these cameras are versatile for consulting room practice.

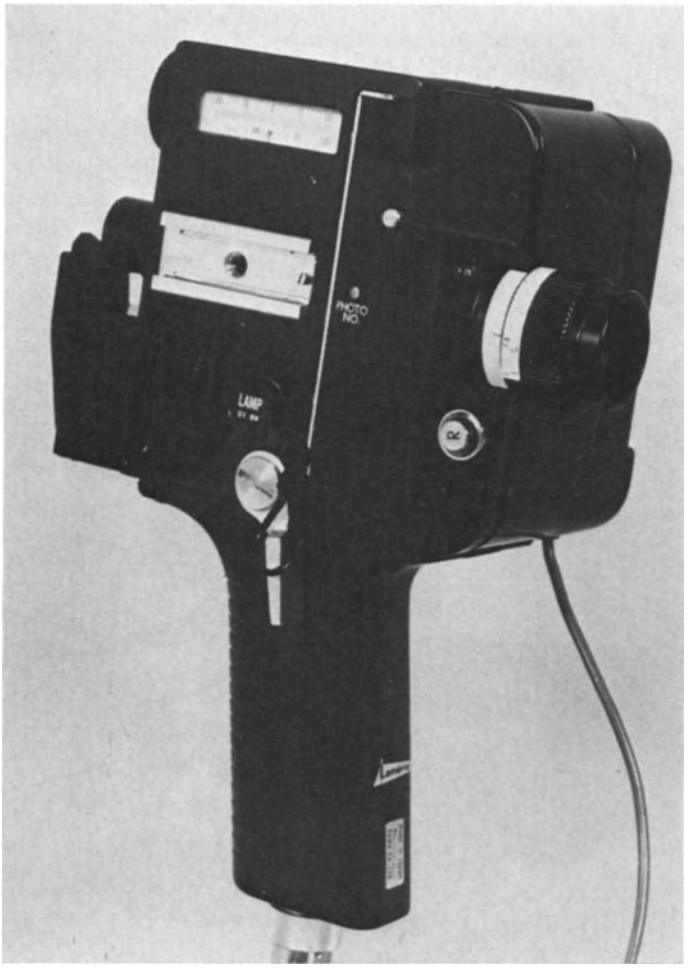


Fig. 12. A Kowa RC-2 with built-in motor-drive film winding device for fluorescence photography.

At present, two Japanese hand-held retinal cameras are available, the Olympus PRC (Fig. 16) and the Kowa RC-2 (Fig. 11). I prefer using the Kowa RC-2 hand-held retinal camera for two reasons. The angle of view is the same as that of most table-top retinal cameras and, in addition, the Kowa system can be extended with a complete system of accessories. The Kowa RC-2 camera permits easy interchange of camera body and lenses to adapt the camera for instant photography and fluorescence photography (Fig. 11 and Fig. 12).

Many authors such as LICHTER (1972), MIKUNI (1969, 1969), NAGATA & TSURUOKA (1972), OOSTERHUIS (1972), SLOAN & LICHTER (1967) have successfully used this camera for more specialized ophthalmic techniques. Some of these special photographic techniques are retinal photographs with an angle of view of 30°, retinal photographs with an angle of view of 15°, photographs of anterior segment and full face, goniophotography with mirror contact lens, fluorescence photography of the fundus and anterior segment (iris, cornea and conjunctiva), stereophotography of the fundus and anterior segment, instant photography of the fundus, anterior segment and full face.

However, this camera also presents disadvantages. For instance, an extremely close working distance of 8 mm from the cornea is required, and heat is produced if the electronic flash is used for a long time at maximum energy, e.g. for fluorescence photography.

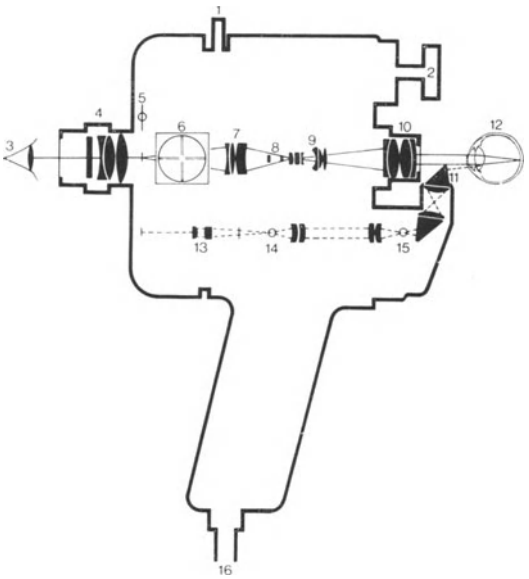


Fig. 13. Optical diagram of the Kowa RC-2 camera.
1. Connecting for eye-fixation lamp. 2. Forehead rest. 3. Observer's eye. 4. Finder. 5. Film plane. 6. Focusing glass. 7. Relay-lenses no. 2. 8. ×2 lenses. 9. Relay-lenses no. 1. 10. Objective lens. 11. Illuminating prism. 12. Patient's eye. 13. Light path for photo numbers recording. 14. Focusing light. 15. Electronic flash tube. 16. Power source connecting cord.

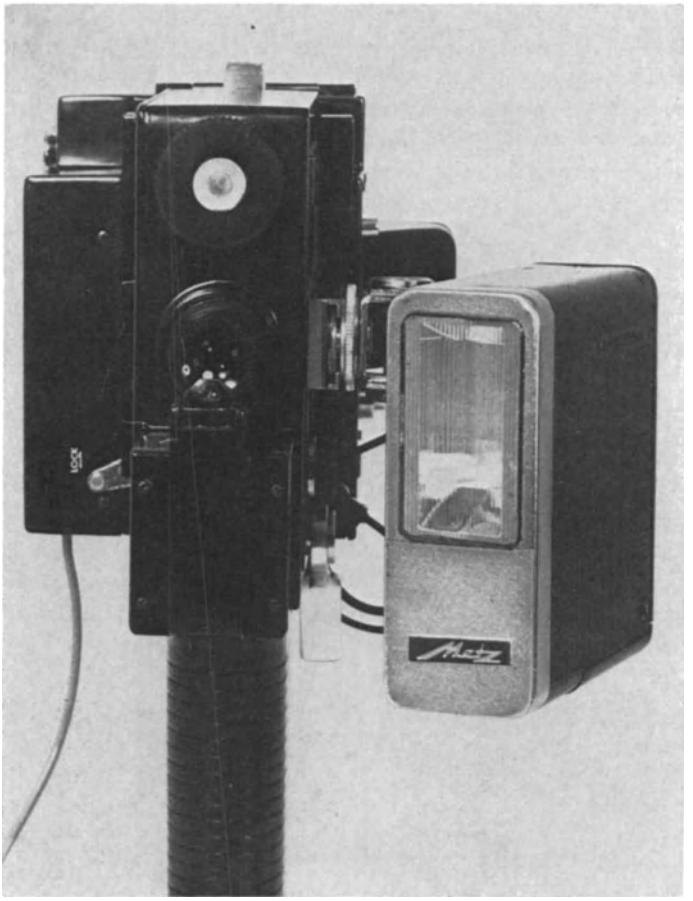


Fig. 14. Flash tilter bracket and external flash connected to the synchronizing socket of the Kowa RC-2 retinal camera used for large working distances.

We have tested the Kowa RC-2 hand-held retinal camera and all the accessories during a period of four months. The colour, fluorescence- and instant photographs are excellent and the image quality is the same as that of other table top models.

Remarkable is the great depth of field for anterior segment photographs. For instance, this result is not possible with the Zeiss retinal camera which gives distortion. The fundus fluorescence photographs are more plastic (three-dimensional) illuminated than fluorescence photographs made with other retinal cameras and brings out relief into the image. This happens because the fundus is illuminated through the lower edge of the pupil and not from the same direction as the optical system for photography or observation. Both systems are strictly separated from each other (Fig. 13). With most of the

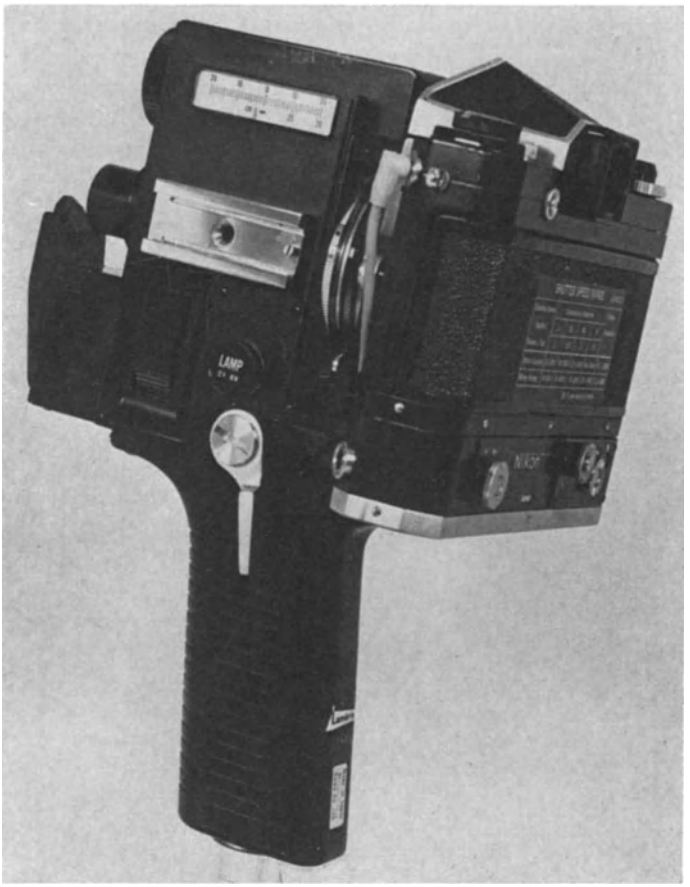


Fig. 15. A single reflex camera especially adapted to the Kowa RC-2 retinal camera.

retinal cameras the illuminating- and optical systems come from the same direction (Fig. 18).

The Kowa Excitor filter Fuji no. 18 and Barrier filter Kodak 15 G for fluorescence photography cause pseudo-fluorescence. We replaced the Fuji no. 18 filter with a Baird Atomic BA 4 filter. This combination gives excellent fluorescence photographs without pseudo-fluorescence at maximum flash intensity with a recycling time of under 1 sec.

For full-face photographs and other subjects at large working distance, the built-in electronic flash is not strong enough. For these image sizes we disconnected the flash cord of the built-in electronic flash and plugged the flash cord of an external flash into the synchronizing socket of the camera (Fig. 14). The full face photographs are not frame-filling, but are 24 mm diameter on the negative.

At last some useful tips: The Kowa RC-2 retinal camera has no built-in correction for astigmatism. To get sharp retinal photographs notwithstanding corneal astigmatism we use the Henkes ERG-low vacuum diagnostic contact lens of 0 power (ALLEN, 1964; WORST, 1961). The contact lens is attached to the eye by means of a slight negative surface pressure. Thus the contact lens surface corrects the astigmatic corneal surface. This technique also has other advantages. It protects the cornea surface from damage because the working distance is small. Moreover, the cornea does not dry out. A dried-out corneal surface reduces the sharpness of the viewing- and photographing image which results in poor photographs.

In principle, any single reflex camera with special cross-hairs focusing screen is usable to be adapted to the Kowa RC-2 (Fig. 15). The body of the single reflex camera can also be used for outdoor pictures. With this system we obtain a larger angle of view than with the standard camera back, because there is no mask built-in in the camera. This body with motor drive, provides faster film advance than does the built-in motor drive of Kowa.

Fig. 16. Olympus PRC hand-held retinal camera.

III. RETINAL CAMERAS (HAND-HELD AND TABLE TOP) (see Table III).

There is a range of table top retinal cameras and two lightweight hand-held models (See also chapter II and HANSELL (1967); MATSUI (1971)). The Fisba table top and Nikon hand-held retinal cameras reviewed by HANSELL are no longer produced. The optical design of the Olympus and Topcon table top retinal cameras is based on the Zeiss retinal camera (Fig. 18).

In principle, all retinal cameras are suited to the ophthalmologist's practice. The Nikon Retinapan 45 (AAN DE KERK, 1972) and the Zeiss retinal camera (LITTMANN, 1956) possess several features which are more valuable to the professional photographic worker.

The characteristics of the various retinal cameras are given in Table III. The Kowa RC-2 hand-held retinal camera with the fullrange of accessories is worth its price. This camera can be mounted on a special chinrest stand

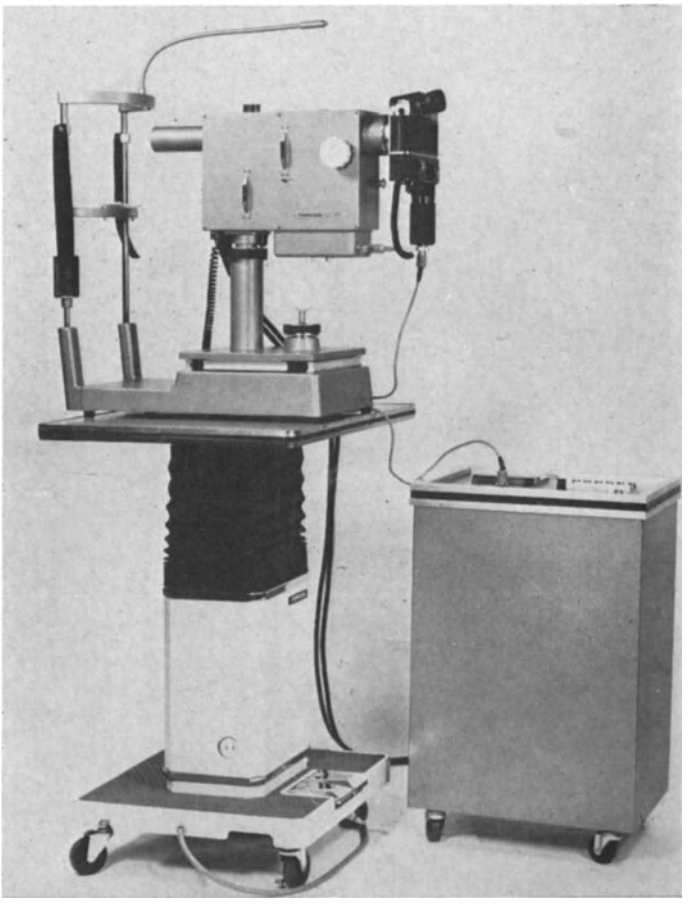


Fig. 17. Topcon retinal camera model TRC-F3 on motorized table.

Table III. Retinal cameras and their characteristics.

Table III	Jena Retinophot	Kowa RC-2 (1)	Mamiya FR-200 (2)	Nikon Retinapan-45 (3)	Olympus GRC-FF-II	Olympus PRC	Topcon-J (4)	Topcon TRC-F2 (4)	Topcon TRC-F3 (4)	Zeiss
Type: table top	●	●	●	●	●	●	●	●	●	●
hand held										
Price range	I-II	I	....	IV	....	I	I	II	III	III-IV
Angle of view	28°	30°	....	45°	28°	24°×28°	30°	30°	30°	30°
Working distance (mm)	80	8	30	40	70	6,7	45	45	45	50
Swing: horizontal		●		●●			●	●	●	●●
vertical				●			●	●		●
Lateral motion	●	●	●	●	●		●	●	●	●
Astigmatism correction				●						●
Data recording: frame number	●	●	●●	●●	●●		●	●●●	●●●	●●●
time										●
name				●	●		●	●	●	●
Fluorescein angiography	●	●	●	●	●					●
Excitor filter	....	Fuji no.18	....	KW 47A	....			Fuji no.18 or Baird Atomic	Fuji no.18 or Baird Atomic	KW 47A
Barrier filter	....	KW 15G	....	Green X1	....			KW 15G	KW 15G	Schott GG14
Electronic flash maximum output (W/sec)	100	50	200	200	250	60	50	300	350	480
recyling time (sec)	3	1	3	1	2	1	5	2	0.3	840
Film	35 mm	35 mm	35 mm	35 mm	35 mm	Half-frame 18×24 mm	35 mm	35 mm	35 mm	1.5 35 mm
x2 magnification attachment		●			●		●	●	●	○
Sighting mirror	●		●				●	●	●	○
Eye phantom							●	○	●	○
Polaroid camera		○	○	○			○	○	○	○
Motor drive		●		●			○	○	●	●
Stereo separator							○	○	○	○

● characteristics
○ accessories against special order
.... no response received
I price range Dfl. 3.000 — Dfl. 10.000
II price range Dfl. 10.000 — Dfl. 20.000
III price range Dfl. 20.000 — Dfl. 30.000
IV price range Dfl. 30.000 — Dfl. 40.000
1. built in ×2 lenses
2. also larger format cameras up to 5″ × 4″
3. still in experimental stage
4. two types of stereo attachments

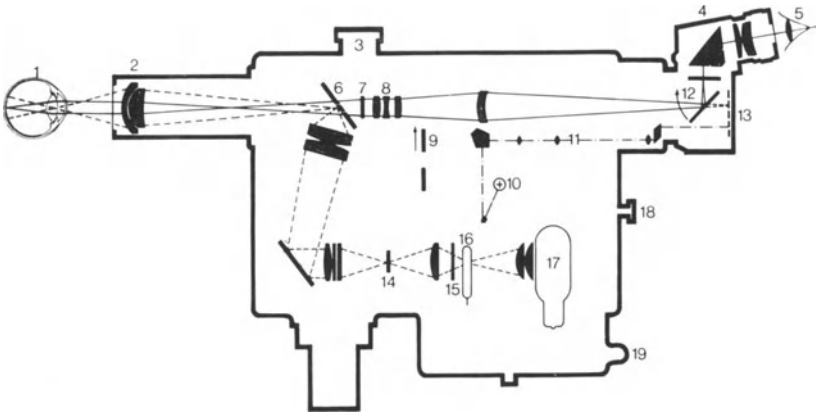


Fig. 18. Optical diagram of the Topcon TRC-F3 camera.
1. Patient's eye. 2. Non-spherical objective. 3. Filter switching knob. 4. Motor-drive camera with eyepiece. 5. Observer's eye. 6. Perforated reflecting mirror. 7. Filter plane (yellow KW 15 G). 8. Objective. 9. Correction lens. 10. Counter number illumination lamp. 11. Light path for data recording. 12. Swinging mirror. 13. Film plane. 14. Illumination filter plane (B.A. interference filter). 15. Iris diaphragm. 16. Electronic flash tube. 17. Focusing light. 18. Counter illumination switch. 19. Ready-light lamp for electronic flash.

for table use (Fig. 11). The price of the Topcon retinal cameras is also very moderate. The Jena Retinophot, Nikon Retinapan-45 and Zeiss retinal cameras need a special instrument table. The other types do not need a separate instrument table.

Most retinal cameras have an angle of view of 30°. Only the Nikon Retinapan-45 has a wide angle of 45°, which is 50% greater than that of most of the conventional retinal cameras. The angle of view of the other cameras can also be enlarged by attaching a wide angle contact lens to the eye. The angle of view with these wide angle lenses is 45° and 90° (GOVIGNON & POMERANTZEFF, 1972; POMERANTZEFF & GOVIGNON 1971; SCHIRMER, 1970).

The short-working distance of the hand-held cameras however, can cause damage to the eye and therefore, the long-working distance of most of the other cameras is preferable. The horizontal swing and lateral motions are essential for table top retinal cameras. The vertical tilting, which can be done with the Nikon Retinapan-45 and Zeiss retinal cameras to photograph the perifery of the retina, is not essential. This can also be done by tilting the patient's head backwards or forwards.

There are two cameras with astigmatism correction. The Zeiss has built-in compensating lenses for astigmatism correction and the Nikon Retinapan-45 has a push-in accessory with compensating lenses for astigmatism correction. The cylindrical lenses can be placed in the optical pathway.

There exist various systems of data recordings designed for retinal photography, such as exposure number, name, date of birth, diagnosis, data and

circulation time. The circulation time is especially important for fluorescence photography.

With most systems, the data are recorded aside of the image on the sensitive layer. The Zeiss, in conjunction with the Robot motor drive, has the disadvantage of recording the data partly over the image. Apart from this, data recording can also be seen by the operator in the eye-piece in all Topcon retinal cameras.

With most retinal cameras we can do fluorescence photography. However, a good pair of fluorescence filters is essential as most of the standard filters give pseudo-fluorescence. The excitor Baird Atomic B4 filter and most barrier filters give no pseudo-fluorescence. The characteristics of the light transmission of the interference filter are given by VAN BEEK (1973). The excitor filter is inserted in the illumination pathway and the barrier filter in the photographic pathway.

Most of the light is absorbed by the combination of the excitor filter and barrier filter. Therefore, for fluorescence photography a high power, rapid-charge flash generator is required.

When taking a complete series of fluorescence photographs, the camera must be able to take photographs at the rate of 1 frame every 0,5–1 sec at maximum output of the flash.

x2 magnification attachments are available as an accessory to most retinal cameras. In combination with this lens we can take a detail of the retina (angle of view 15°). With the Carl Zeiss retinal camera we must remove the 30° cone in the camera body, in order to utilize the entire 24 × 36 mm film format. Only the Kowa has this lens built-in. It is however, not necessary to use a x2 magnification attachment to get more enlarged details of the fundus. We can also select and magnify a detail from a slide which must be made on fine grain film. This slide is copied with a duplicating attachment 1:1 or more enlarged (AAN DE KERK, 1973).

Also, neither sighting mirror nor eye phantom are absolutely necessary accessories. However, a sighting mirror is advisable when working with big retinal cameras, such as the Mamiya in which it has been built in. In operating this camera it is difficult to see the patient's eye without a sighting mirror.

The Polaroid camera attachments are only suitable for retinal instant photography. We use a Polaroid back, which can be used for retinal photography and external eye photography (AAN DE KERK & CRAANDIJK, 1970).

A motor-drive camera is essential for fluorescence photography and stereo-photography. because the film must be advanced rapidly after exposures. The Kowa motor camera also has an electrical rewind transport.

For stereo-photography of the retina, we need: quick flash recycling, motor drive camera, a stereo separator and last but not least an intelligent and cooperative patient.

Stereo-retinal photography with a stereo separator is very popular in America and Japan (ALLEN, 1964, 1966), to record depth in fluorescence photographs. To prevent missing fluorescence filling phases of the retinal veins and arteries, Topcon and Zeiss developed an automatically controlled stereo separator.

This separator flips automatically in the other position after exposure. The stereo separator consists of a glass plate and can be attached in front of the prime objective of the retinal camera.

IV. SENSITIVE MATERIALS

A review is given of the most often used 35 mm films in ophthalmic photography. Especially 35 mm films are discussed because most apparatus for eye photography utilize small camera bodies with 35 mm film loading. Only the Kodak Instatech II needs other filmloading, namely 126 cartridge.

The use of monochrome and colour reversal films is recommended for the practicing ophthalmologist, because he will not need a darkroom and photographer.

Black and white films. We need a fast negative or reversal black and white film with high sensitivity for fluorescence photography. The film which is used most is the Kodak TRI-X Pan ASA 400 – the higher the ASA number, the faster the film speed (FERRER, 1969). The film is available in lengths of 36 exposures [TX 135–36] and 20 exposures [TX 135–20]. For fluorescence photography we need a filmlength of 36 exposures to photograph the various vascular filling phases.

35 mm Colour reversal films (AAN DE KERK, 1971). Kodak Kodachrome II daylight ASA 25. The price of this film includes the processing of the film. For a list of processing laboratories see the instruction sheet. This film is used for regular retinal photography and external eye photography. It is the only film with a very high definition and is still the best one for ophthalmic photography.

Kodak High Speed Ektachrome EH daylight ASA 160. This film does not include processing costs. The High Speed Ektachrome is used in those cases of eye photography where a more sensitive film is necessary, such as: slitlamp photography, colour fluorescence photography and colour retinal photography with monochromatic light (redfree light). Both colour reversal films are available in a length of 36 exposures [K 135–36 P, EH 135–36] and a length of 20 exposures [K 135–20 P and EH 135–20].

For eye photography with electronic flash we need only daylight type colour films, because the electronic flash has a colour temperature of daylight (6500°K).

In the ophthalmologist's practice, in general a filmlength of 20 exposures is preferable.

126 Cartridge. As is the case with the Kodak Instamatic amateur camera, the Kodak Instatech II also needs 126 cartridge loading with square negatives – $1'' \times 1''$ –, and slides. All conventional 126 cartridge black and white negative and colour reversal films can be used. This cartridge loading has the advantage of rapid and simple loading.

Polaroid is the most ideal sensitive material for an immediate visual document during a patient's visit in the consulting room. The ophthalmologist does not need a photographer and the photograph is developed in a few seconds. Instant photographs are valuable for the patient's file, a detailed record to sent to colleagues, and a ready reference for photo-coagulation.

All Polaroid attachments for retinal photography and slitlamp photography are designed for use with Polaroid pack films. There are two types of pack films, for black and white, type 107 ASA 3000 with a developing time of 15 sec at 20°C, and for colour (daylight) type 108 ASA 75 with a developing time of 60 sec at 20°C. One pack contains 8 films. The Polaroid picture is developed outside the camera and gives no negatives.

With the exception of Kodak Tri-X 35 mm black and white film, only colour diapositive films have been reviewed. This was done intentionally to simplify the choice of the film. I prefer, and strongly recommend, to use colour reversal films only as this simplifies eye photography for the ophthalmologist. The original transparancy can be used for all kinds of purposes. It can be printed in black and white, and in colour, and duplicated 1:1 or more enlarged with a slide copying attachment (AAN DE KERK, 1973).

V. FLASHLIGHT ILLUMINATION FOR CLOSE-UP PHOTOGRAPHY (CONVENTIONAL EXTERNAL ELECTRONIC FLASH AND SPECIAL MACRO-FLASHLIGHTS)

There is no doubt about the superiority of the electronic flash as the main illuminating source over incandescent light and, therefore, it is an absolutely essential illumination for eye photography. The advantages of making use of the electronic flash are: constant colour temperature of daylight 6500°K, light output never decreases with age of the apparatus, absence of heat, extremely short flash duration, and high intensity. The pictures are taken at a flash duration of 1/800 to 1/2,000 sec. With this short flash exposure all movements of the subject and/or camera, even the slightest, are 'frozen'. This guarantees sharp exposures even if a portable flashlight is used. Cameras with a faster synchronization shutter speed are more preferable. The short synchronization shutter speed also reduces the effect of any prevailing light, so exposure takes place almost exclusively by the light of the flash tube.

Close-up flash photography can also be done with conventional electronic flash and conventional flash cubes. We can attach any pocket size electronic flash with a flash mounting bracket to the lens, such as the Novoflex flash bracket, code name X-shoe (Fig. 2).

The bracket can be attached to the lens with step-up adapters, which are screwed to the filter thread. The flash reflector can be angled precisely at the subject. The guide number of these flash units must be between 20 and 30. The light output is higher in electronic flashes with high guide numbers.

A guide number of 20 to 30 permits the use of a small lens aperture at around f/22, to improve sharpness and to increase depth of field – a zone extending in front of and behind the focused distance – with 1:1 image size.

Table IV. Data for close-up photography of the eye.

Table IV. Data for close-up photography (see set-ups fig. 1)

	Image sizes	Supplementary lenses 0,1,2	Extension tubes nr. 1 11 mm, nr 2 18 mm, nr. 3 36 mm	Bellow extension	Focus setting	Subject-lens distance	Exposure factor
Supplementary lenses set up as in fig. 1[a]	1/15				2 m	1,8 m	
	1/8				1,5 m	1,3 m	
	1/3	nr. 1			∞	0,4 m	
	1:1	nr.0+1+2			1,5 m	0,15 m	
Extension tubes set up as in fig. 1[b]	1/15				2 m	1,8 m	
	1/8				1,5 m	1,3 m	1,3
	1/3		nr. 3		∞	0,62 m	1,8
	1:1		nr.1+2+3		1,5 m	0,32 m	4
Bellow set up as in fig. 1[c]	1/15				2 m	1,8 m	
	1/8				1,5 m	1,3 m	1,3
	1/3			5 cm	∞	0,5 m	1,8
	1:1			13 cm	∞	0,26 m	4

Normally we involve an exposure-increase factor (see Table IV), to compensate for the extra-extention. This factor is compensated by the closer flash-subject distance, so that in this range the exposure remains reasonably constant.

The flash unit must be attached to the lens as near as possible and must always illuminate the eye from the temporal side, in image sizes, such as area nr. 2 in Fig. 9, to avoid shadow projection from nose and eyelids. The flash unit should never be attached to any other place as in that case the flash unit will illuminate other objects in addition to the eye, e.g. camera body and white coats. The images are reflected on the cornea and cause extraneous reflections. For photographs of areas nr. 3 to 5, the flash reflector may be attached to the top-side position.

The Kodak Instatech II is the only close-up camera which uses flash cubes. Normally, I advise against the use of flash bulbs in view of the risk of possible injury to the patient and the disadvantage of interruption when changing the bulbs. However, the cubes involve no risk of explosion. One flash cube has four built-in normal flash bulbs. After each exposure the flash cube automatically turns one quarter and locks into its new position ready for use.

For close-up photography, special electronic flash units are also made, including power units. These are characterized by the fact that the focusing light and flash light are coming from the same direction. The built-in viewing light(s) is practical for effective positioning of the light. The flash is situated behind or nearby the viewing light. These close-up flash units are mostly used at a short working distance and have a great flexibility.

Close-up electronic flash units are manufactured by Leitz, Multiblitz and Bowens.

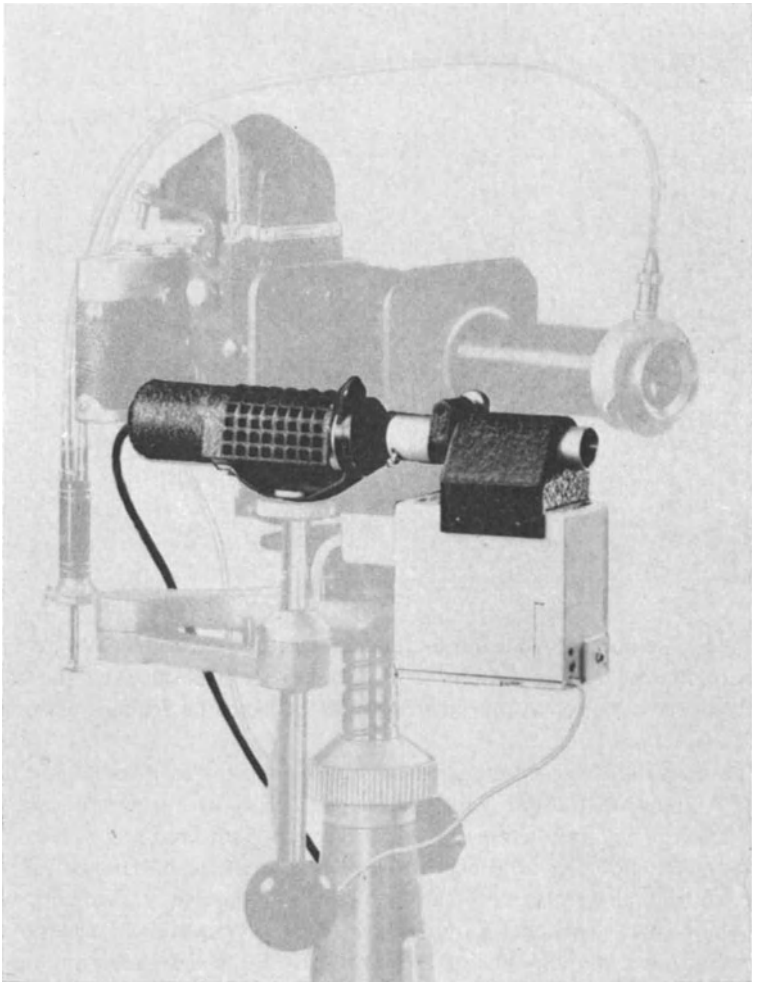


Fig. 19. Leitz focusing light with normal external flash unit.

The Leitz macroscope spot-light lamp can be adapted to all small conventional external electronic flash light (Fig. 19). The flash light of the conventional flash unit is mirrored on the subject by a semi-transparant mirror, which is located in the illumination pathway of the viewing light. About half the flash light energy is absorbed by the mirror and therefore we need a flash unit with a guide number around 30.

The Multiblitz Macrotron ringflash (Fig. 20) (ISERT, 1972). The built-in ring flash tube fits around the lens. The output is adjustable by a selector switch. I do not favour the ring flash because the illumination gives a flat 'shadowless' lighting and low contrast to the subject, and we need more plastic (three-dimensional) illumination of the external eye (Kodak, 1972).

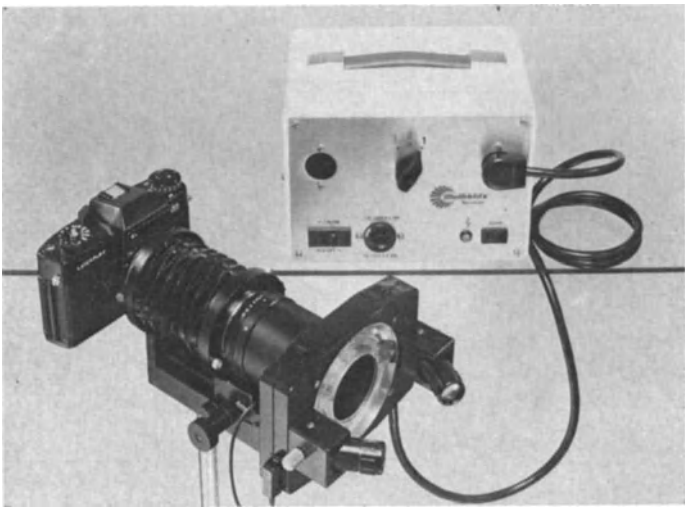


Fig. 20. Multiblitz Macrotron ringflash for close-up photography.

The Multiblitz Macrotron can also be supplied with a set for polarized light to keep down the cornea reflex of the ring flash. This results in lifeless and unreal photographs. The Macrotron has for focusing projecting light spots. (See also characteristics Table I: focusing and composing).

Bowens has two special electronic flashes for close-up photography: the Texture lite, four flash tubes around the lens, and Macrolite with two compact flash heads mounted on flexible arms, each with a switch and modelling light (MAUDE, 1973). With these systems we can take photographs with more than one flash tube for plastic lighting of the subject. In ophthalmology, we must watch for undesirable reflections on the cornea. No more than one flash tube should be used.

The corneal reflex may not obscure a point of interest in the eye. Each tube has an independent switching and its own pilot light. The output of the Bowens electronic flashes are also adjustable by a selector switch.

For more extreme close-up photographs from 1 : 1 on, it is better to use photoslitlamps, because they are more adapted for close-up lighting and control of corneal reflex (See also characteristics of the photoslitlamps, Table II).

VI. FILING AND STORING OF: NEGATIVES, TRANSPARANCIES AND PHOTOGRAPHS

We can cut the whole negative film into strips of six exposures. The strips can be stored in negative storing sheets and these sheets can be put in ringbinders. A filmstrip viewer is used for viewing the negatives (Fig. 24).

We can ask the processing laboratory to return the colour transparancies either in (1) stripform or (2) framed in readymounts.

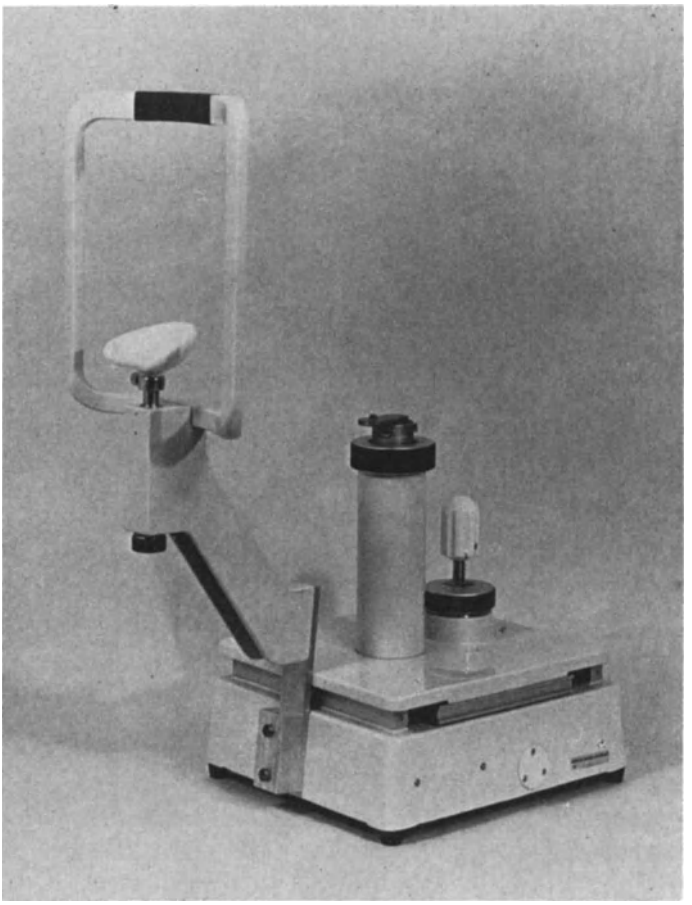


Fig. 21. A special stand is of great help in making external close-up photographs of the external eye.

1. *What to do with strips:*

a. We keep the strip uncut on full length 35 mm film and store in special cupboards for film strips. For viewing we can use a filmstrip-viewer or a filmstrip projector.

b. We can cut the whole film into strips of six exposures. These strips can be stored in special Jepe transparancy files (Fig. 22b) and we can store the files in ringbinders. Viewing and projection being the same as mentioned above.

c. We can cut the total film with a scissor or filmcutter into 36 separate transparancies.
We can store the transparancies in files (Fig. 22a) (WORST, 1965), to be filed in ringbinders or on sheets in the patient's record (Fig. 26). For viewing we must insert the slide carefully in a glassless plastic frame.

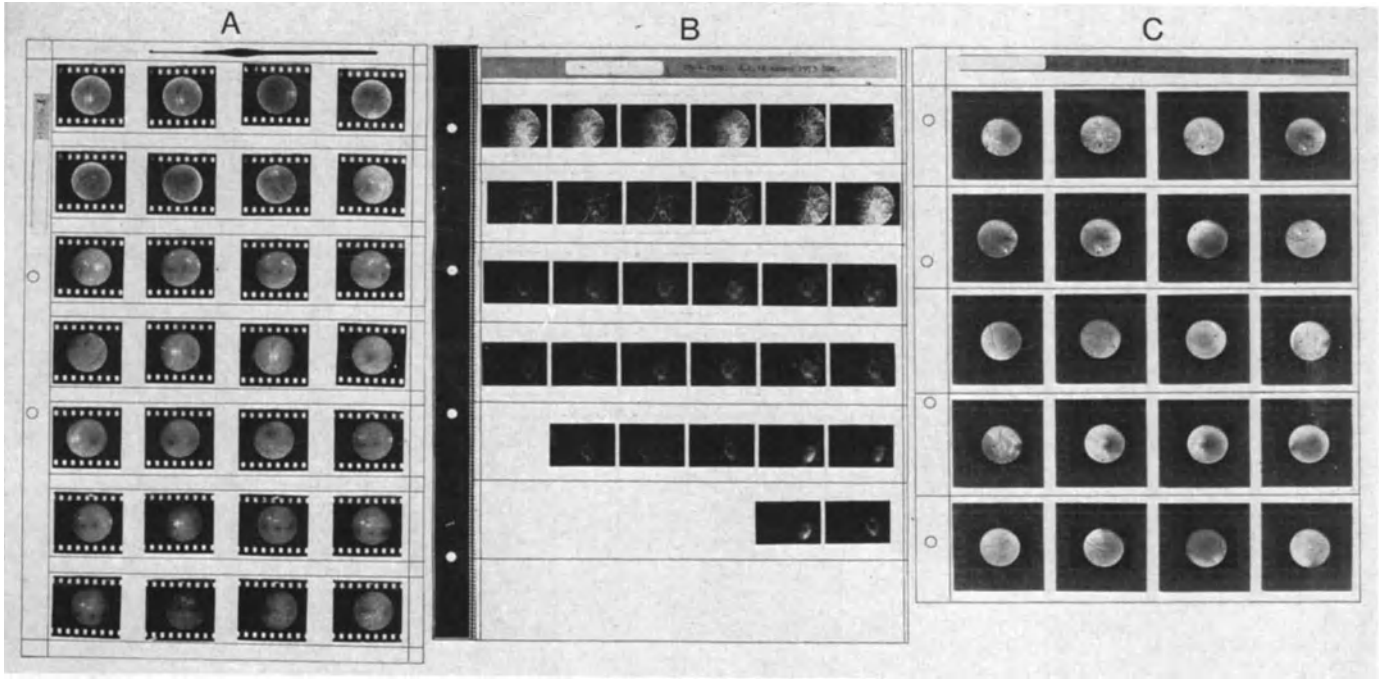


Fig. 22. Files systems for ringbinders:
From left to right, A: Bronkhorst file for 28 separate transparancies, B: Jepe file for 7 strips 35 mm film, 35 frames and C: Kindermann files for 20 readymounts, order nr. 1131.

The slide can be viewed with a viewer or daylight projector. After viewing we remove the slide from the glassless plastic frame and return the slide for refiling in the system.

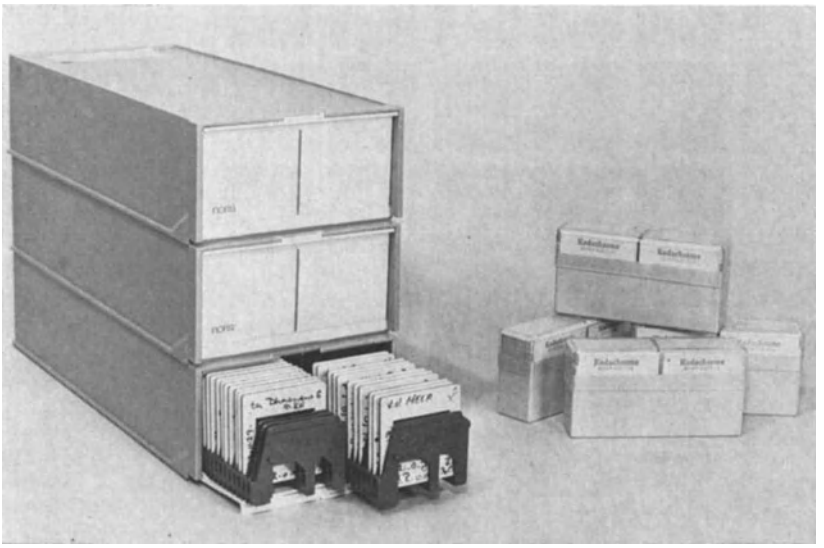


Fig. 23. Standard slides store boxes and laboratory store boxes.

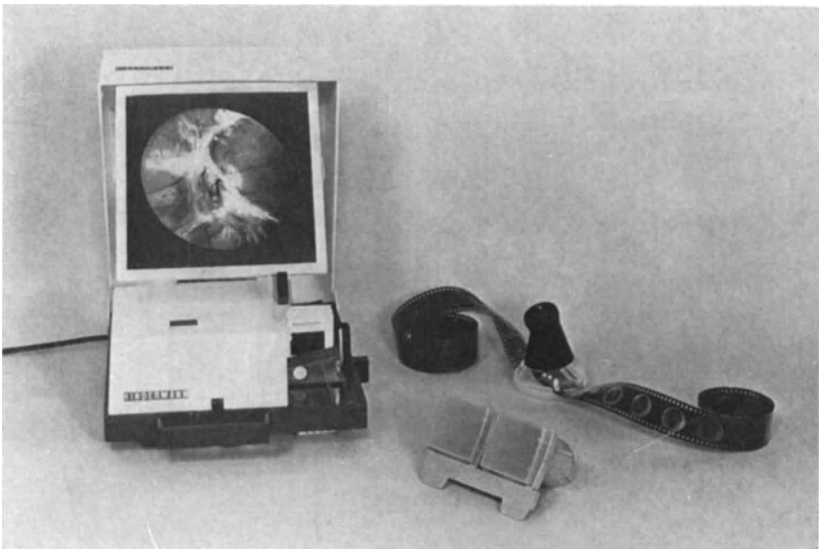


Fig. 24. Kindermann table daylight projector, Gitzo stereoviewer and film strip viewer.

2. *Readymounts:*
We can keep readymounts in boxes in which the slides come back from the laboratory (Fig. 23) or store them in Kindermann files, the files can put in ringbinders (Fig. 22c). Standard slide store boxes contain two cartridges, which can also be used for projection. The readymounts can also be stored in a hanging portfolio which will fit in a drawer or a filing cabinet (Fig. 25).

We can also protect the film strips and readymounts for dust, moisture and fingerprints, with the aid of Secol sleeves for film strips and Secol 'Tecs' or special Perrocolor mounting glasses for individual 35 mm 2″ × 2″ readymounts (Fig. 27).

Photographs

The instant photographs can be stored in special maps (Fig. 28) or in patient's record or be stuck on special cards for drawer or filing cabinet storage. This can also be done with conventional photographs. An easy manner to keep fluorescence photographs in order, is shown in Fig. 28 by using a clip.

All hardware shown in pictures can be ordered from any photodealer or in The Netherlands from the distributor of Jepe transparancy files: Jepe photo, Jonker Fransstraat 121, Rotterdam. The Jepe files are also ideal for positive fluorescence transparancies.

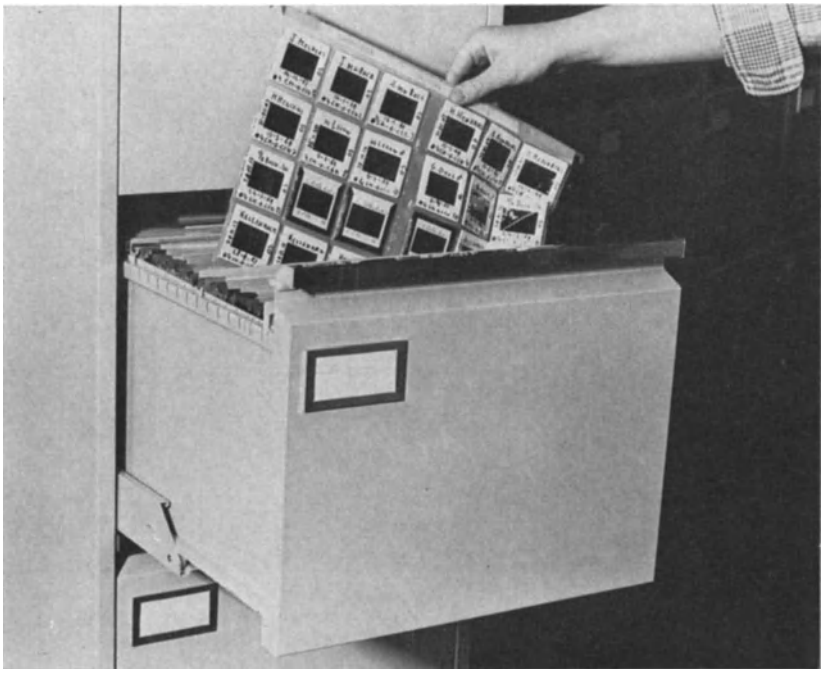


Fig. 25. Hanging portfolios for filing cabinet.

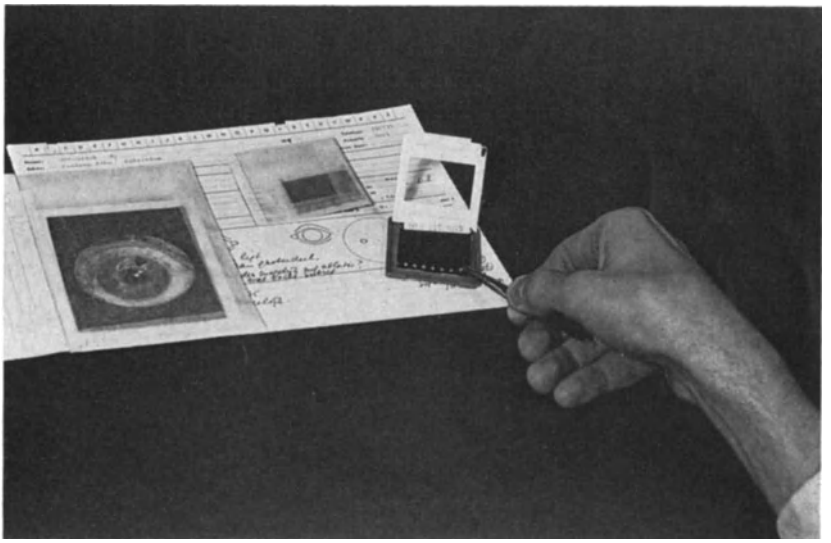


Fig. 26. Patient's record with photograph and separate transparancy. A slide is being inserted into the glassless plastic frame for viewing.

Fig. 27. Secol sleeves for film strips and Secol 'Tecs' for individual 35 mm 2″ × 2″ readymounts.

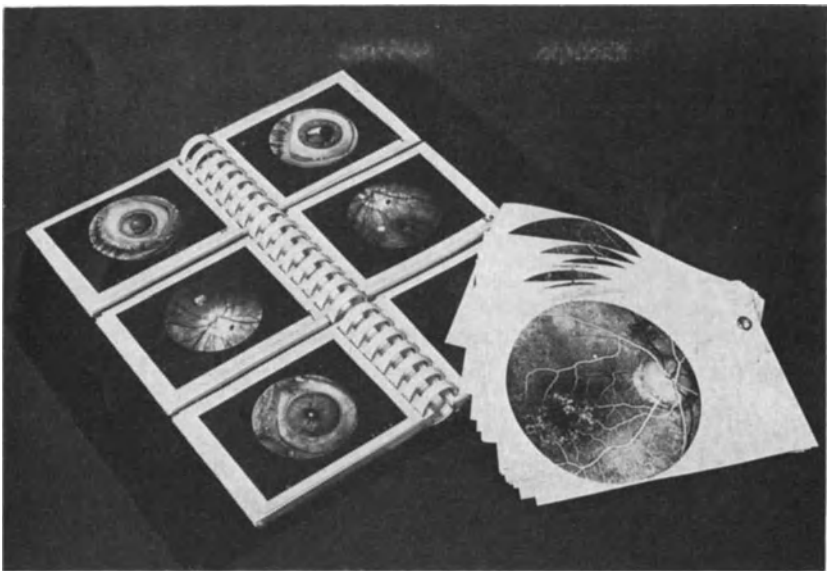


Fig. 28. Polaroid album for instant prints and a complete series of clipped fluorescence photographs.

The whole file with the fluorescence transparancies can be put on an overhead projector for a total view of the fluorescein photography on a screen (GASS, 1967).

The special daylight projector is from Kindermann, this projector can also be used for wall projection in small rooms. We can view single slides and a pair of stereo transparancies with the Gitzo stereoviewer Stereart II.

The system which needs less room for transparancy filing is the system shown in Fig. 22a and Fig. 26, but this system has the disadvantage of damaging the transparancies by handling the slide for viewing.

The three filing systems all have an identification area and can be kept in ringbinders. One of the most ideal fitting systems is to keep the slides in readymounts and stored in Kindermann files, which can be put in ringbinders.

CONCLUSION

The Japanese retinal cameras of Kowa and Topcon are considerably less expensive, and the image quality is the same as that of other table top models.

After testing the cameras for external and retina photography we have come to the following conclusions:

The most ideal camera in the consulting room practice for photography of the external eye and the retina is the Kowa RC-2 hand-held retinal camera with accessories. A disadvantage is that the Kowa RC-2 retinal camera has a short working distance of 8 mm, as this could present problems for an untrained photographer.

The rather inexpensive table top retinal cameras of Topcon present little problems for untrained people.

The Topcon TRC-F2 and Topcon TRC-F3 are excellent retinal cameras, with an ideal data recording for fluorescence photography. For the ophthalmologist who can afford more, the very expensive Nikon Retinapan-45 or Zeiss retinal camera are recommended.

For external eye photography cameras in all price ranges are available from the simple Kodak Instatech II box camera to the sophisticated Donaldson stereo camera.

The author's preference goes to a simple and effective set up as shown in Fig. 2, which consist of a 35 mm reflex camera back (Nikkormat), Novoflex automatic extension bellows, 135 mm lens, Novoflex flash bracket and electronic flash.

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STEREOPHOTOGRAPHY IN OPHTHALMOLOGY

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Historical and technical details of stereophotography of the eye are presented, together with a survey and examples of specific applications. This may help the ophthalmologist to decide whether to use stereoscopic photography, viewing or projecting, in his practice.

Stereophotography has never flourished as luxuriantly as other photographic specialisations, and is largely looked upon as a harmless passtime only fit for fervent hobbyists who are willing to sacrifice a great deal of time and money to their ideal, which is, too often, leading to results that are convincing only for fans, but much less for outsiders. This sorry state of matters is reflected in the many apparates being no longer available, books on stereophotography since long out of print and the lack of standardisation. On the other hand, the challenge to make use of stereoscopic devices has never quite faded in our ophthalmic speciality and in the last few years there is a definite re-development: most ophthalmic clinics possess a collection of stereo-pictures and viewers for teaching and demonstration purposes. Moreover, several atlasses have been published, fitted with stereoscopic pictures related to the text (BECKER, 1972; BRALEY et al., 1970; GASS, 1970; HOYT et al., 1966; OKUN et al., 1970). Stereoscopy and -photography is widely used in roentgenology.

For a practical discussion as the present one, we must try to offer a contribution to the problem: should the ophthalmologist do something with stereophotography and, if so, what? As to most questions, the answer cannot be of general validity, but must be given individually. The present contribution towards a motivated answer will be:

- a historical review;
- discussion of some basic principles;
- demonstration of projected and viewed stereopictures (at the meeting);
- an estimation of the requirements.

Stereography can be applied to the following fields in ophthalmology:

- photography of the anterior segment of the eye;
- slit lamp photography;
- photography of the optical media in retro-illumination;
- fundus photography;
- X-ray photography;
- schematic drawings.

Stereoscopic suggestion of depth is brought about by the slight difference between the two parts of the double picture (called disparity), caused by the distance between the camera-axes during the exposures; this, of course, imitates the situation in binocular vision.

There are available several books with a full discussion on the principles of stereoscopy (VAN ALBADA, 1931; FERWERDA, 1961, 1962; MORGAN & LESTER, 1954; PIETSCH, 1955, 1962; VIERLING, 1965) and references (SELLE, 1971) while Stereo-clubs like the 3.D Club (Secretary J. WILLINK, van Lumeystraat 53, The Hague, The Netherlands) are indispensable for know-how; similar clubs exist in other countries. A specialized shop for stereo is: Der Stereo-Derpsch, 6451 Bruchköbel, Rossdorferstrasse 1, West-Germany.

The goal we aim at in ophthalmic stereophotography may be:
- a natural depth suggestion;
- an emphasized depth suggestion;
- the maximally attainable stereo-effect.

Already at the very start of this discussion, psychologic factors make their appearance among the more clear-cut quantitative data, for how do we define the expression 'natural'? Provided that one camera is used for stereophotography of distant objects an approximation of the natural situation is reached when the sidelong displacement of the objective in between the two exposures is about 65 mm, being the average interpupillary distance.

For ophthalmologists, the routine- and therefore the natural way of viewing the anterior segment of the eye is through the binocular microscope of the slitlamp. Thus, any optical set-up imitating that of the slitlamp may be claimed to be natural. In making pictures of the fundus it is difficult to define what we will call natural: routine ophthalmoscopy being a monocular performance. The most convenient criterion seems to be that the fundus appears slightly, but not excessively concave. A slightly exaggerated stereoscopic effect may be desirable in conditions where depth is an essential feature of the condition such as a glaucomatous excavation of the optic disc, or the representation of an optical section in the slitlamp image.

Finally, a maximal stereoscopic effect – that is a maximum disparity of the two pictures, just falling short of causing diplopia in the observer – is aimed at when the question arises whether two structures in the picture are situated at the same depth, or whether one is deep to the other. Such a question may arise in retinal, pigment epithelial and choroidal changes.

STEREOPHOTOGRAPHY OF THE ANTERIOR SEGMENT

This is a special field of macrophotography, where magnifications of $\times 1$ and more are used. In view of the impossibility for the patient to keep his eyes and eyelids steady which makes two successive exposures impracticable, we are thrown upon the remaining possibility of simultaneous exposures, which requires two cameras working synchronously with the flashlight.

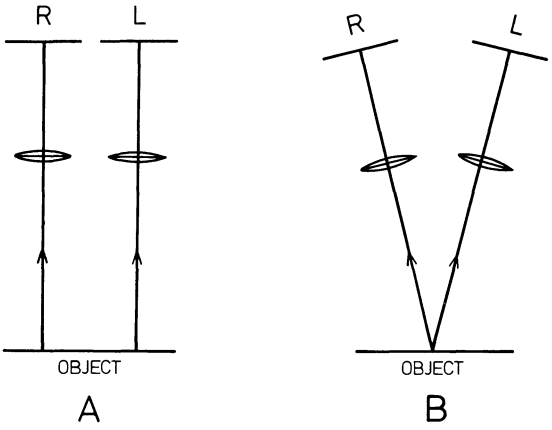


Fig. 1. Parallel and convergent stereomacrophotography. A: Parallel displacement of camera. Because of the lateral shift of the images they are projected partly outside the film window; these parts are lost. B: Convergence of cameras.

Position of the cameras (Fig. 1)

Three possibilities are used in stereomacrophotography:
- parallel displacement of the axes of the camera or cameras;
- convergence of the axes of the cameras towards the object;
- a combination of these two.

For critical stereomacrophotography the first method is used. The base (that is, the lateral displacement) depends on the lens-object distance and the depth of the object. The interrelations are laid down in formulas and graphs (PIETSCH, 1955). The aim is that both the photographic and the stereoscopic field of depth comprise the depth of the object. For the depth of our object of 3,5 mm (the depth of the anterior chamber) this would lead to a base of only a few millimeters. Constructions which could theoretically be practicable are the double diaphragm built in an existing camera and the two-way prism (FERWERDA, 1961). None of these instruments are commercially available (Fig. 2). The figures show that there is a sidelong displacement of the images on the film, to such an extent that the images are partly projected outside the film window. This causes a considerable loss of useful width of the picture. Correction of this would need extensive rebuilding of the camera.

When the axes of the two cameras converge towards the object, this last inconvenience is avoided; but on the other hand, some perspective distortion of the object is introduced, which might interfere with stereoscopic fusion. However, convergence may be tolerated up to a base which does not exceed $\frac{1}{4}$ of the object distance (PIETSCH, 1955). This corresponds to a convergence with a base of 2 cm and an object distance of 8 cm, which are normal values in slitlamp photography.

Systems of stereophotography of the anterior segment using mainly convergence of the optical axes, are incorporated in:

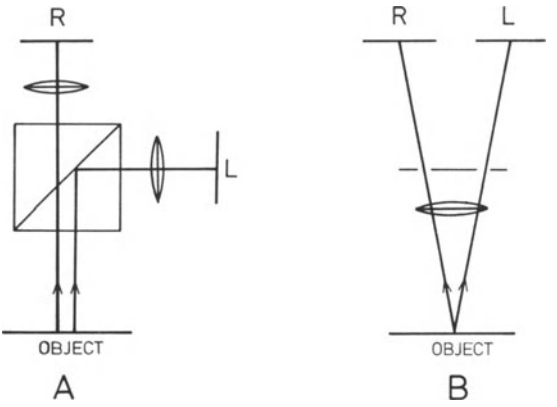


Fig. 2. Simultaneous stereomacrophotography using parallel displacement of the optical axes. A: Two-way prism; B: camera with double diaphragm. In both methods the necessary small base can be realized.

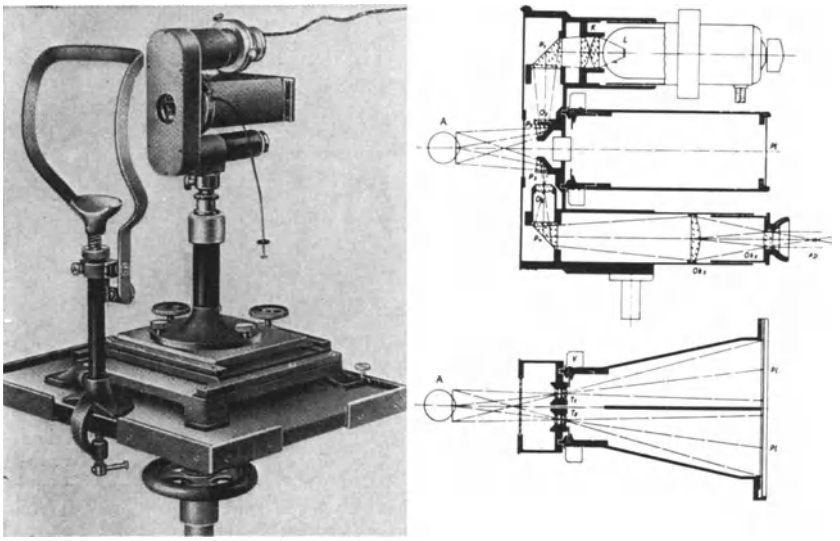


Fig. 3. The iris-stereocamera of HARTINGER (Zeiss). There are two separate front lenses, a continuous illumination and a separate viewer.

- the iris-stereocamera of Zeiss (HARTINGER, 1927) (Fig. 3);
- the stereocamera of DEKKING (DEKKING, 1930) Fig. 4);
- the two models of the stereocamera of DONALDSON. Apart from the magnification, the rate of convergence and the base are variable by prisms placed in front of the objectives (DONALDSON, 1950, 1954) (Fig. 5);
- several systems using stereo-adapters, stereoscopic cameras in combination with the microscope, and other constructions which are of little importance nowadays (MATHÄUS, 1966);

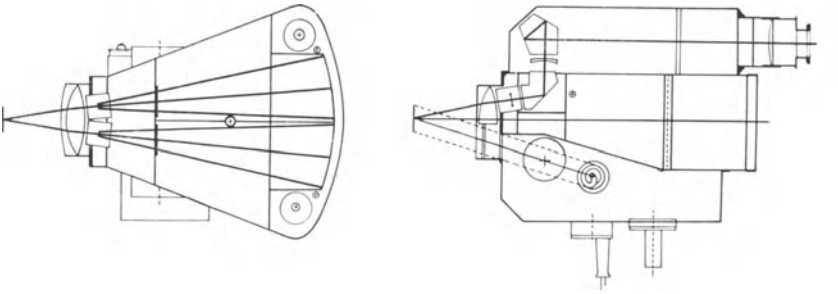


Fig. 4. Stereocamera of DEKKING. Flash-light illumination, separate viewer, film size: 6 × 6 cm.

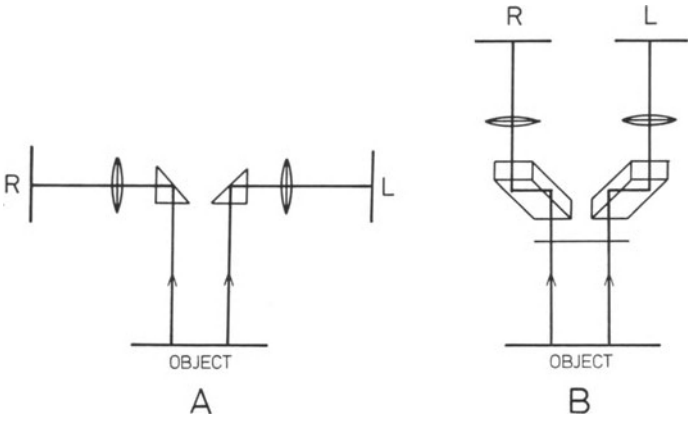


Fig. 5. Simplified plan of the DONALDSON stereocamera. A: 1950 model; B: 1954 model. Both base and angle of convergence can be adjusted.

- the new photo-slitlamp of Zeiss, Oberkochen. The front lens of the microscope is used for stereophotography. The optical path is directed both to the right and the left. A third camera, fitted with a much better objective takes single photographs (Fig. 6). A drawback of this model is the moderate quality of the front lens – however by inserting a pinpoint diaphragm (in the tubes) this disadvantage is mitigated. A definite advantage is that the system works like a double one-eyed reflex camera: the cameras cover exactly the same field as the viewing microscope. This is needed in critical work like fundus-stereophotography, and when light reflexes should be recorded or avoided.
- the photoslitlamp of Zeiss, Oberkochen, modified according to OOSTERHUIS. This modification has several points in favour: the apparatus and the optical parts added for stereoscopic photography are regular factory products. One only need to do some constructional work in order to modify the frame and

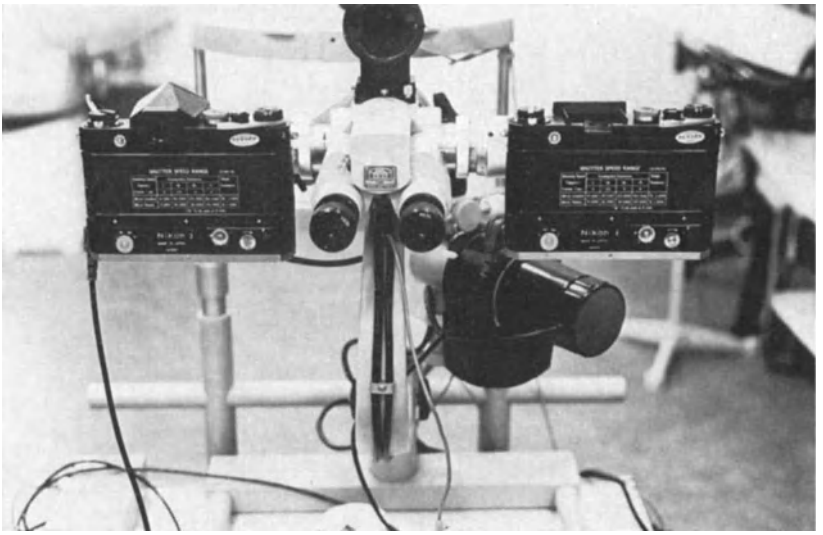


Fig. 6. Stereo-photoslitlamp of Zeiss. The two cameras are at each side of the microscope; the front lens of the microscope serves as the photographic objective. The image seen through the microscope coincides exactly with that of the cameras. The auxiliary third camera on top of the microscope is fitted with a macrolens and is used for taking mono-pictures.

to synchronize the cameras and the light source. The drawback is however, that the microscope does not see exactly what the cameras see unlike in the foregoing instrument.

Figure 7 shows how a second camera fitted with a macroscopic objective, an angled tube and prisms, is placed to one side, in such a way that the distance between the two lenses is only 18 mm. The two optical axes are slightly convergent. A simplified drawing of the two last-mentioned models is presented in Figure 8.

Focussing is still more critical in stereophotography than in monophotography, as the stereoscopic field of depth is even less than the photographic field of depth. However, sharpness of the image in itself aids greatly in attaining a satisfactory stereoscopic impression.

Several possibilities of focussing are depicted in Figure 9. The microscope or any other type of viewer needs little light, has a small field of depth and, therefore, allows exact focussing. Binocular viewing is not essential. If no viewer is available, focussing can be done by projecting the filament of a continuous light source on the object. Finally, the viewer of a reflex camera, with open diaphragm, is a possibility; however, a lens with a large aperture will not produce images nearly as sharp as regular macro-objectives, which have very small apertures.

The stereograms (Figs. 10-13) show some results of anterior segment stereophotography. One may get a satisfactory view by placing an additional lens of

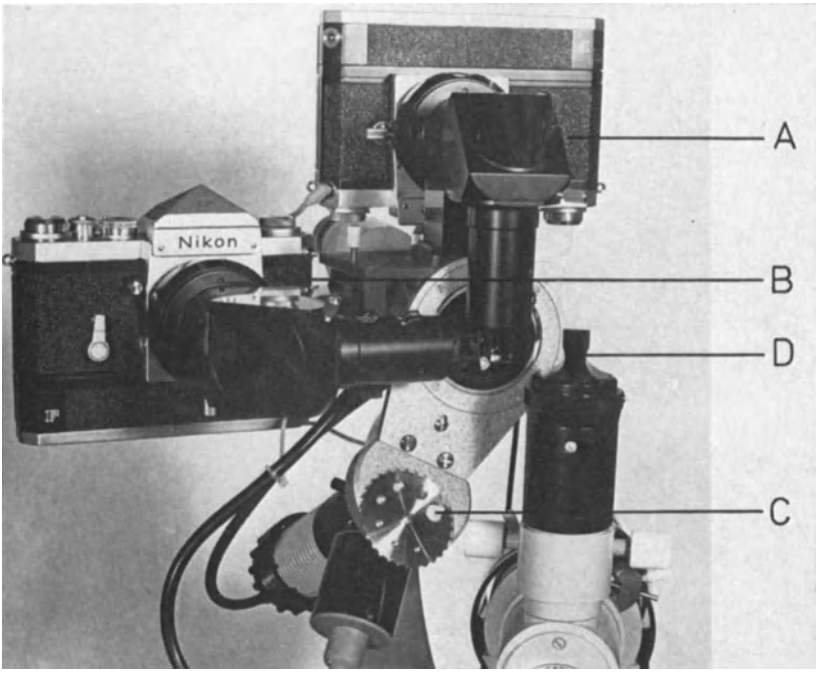


Fig. 7. Stereoscopic modification according to OOSTERHUIS, of the Zeiss photoslitlamp. A: left camera. B: right camera. C: Fill-in light. D: main light.

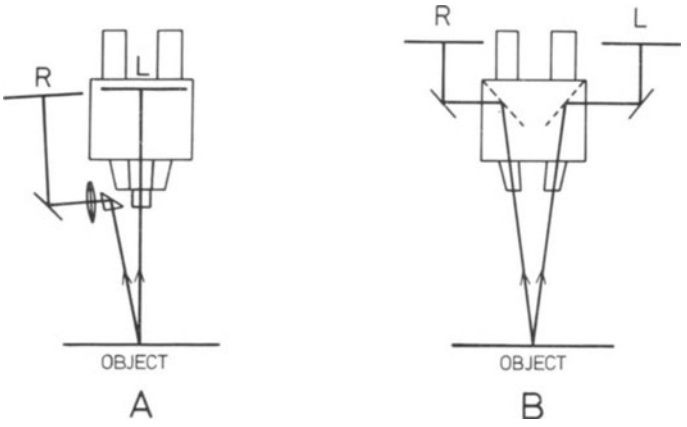


Fig. 8. Simplified drawing of two modifications for stereophotography of the Zeiss photoslitlamp. A: according to OOSTERHUIS. B: the Zeiss stereoscopic photoslitlamp.

+5 Sph. in combination with about 8 prism diopters, base out, in front of one's distance correction.

Illumination may consist of a simple flash light, close to the objectives, so that frontal illumination is obtained. However, illumination by projecting a slit-

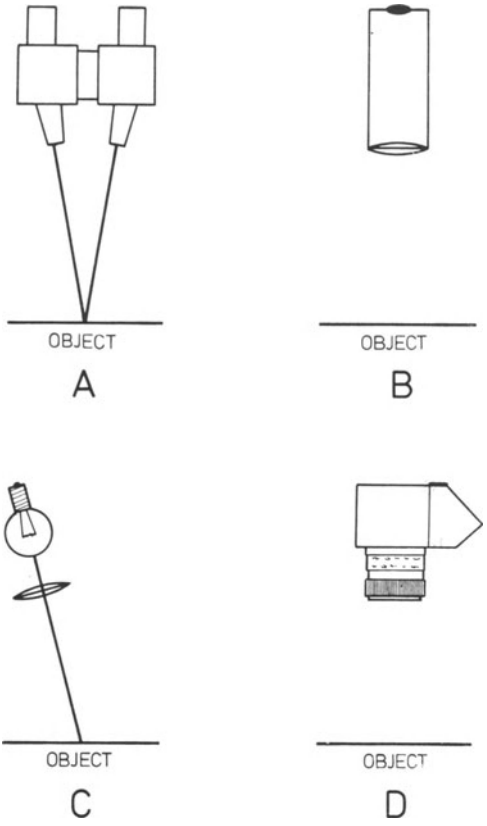


Fig. 9. Methods of focussing. In a simple apparatus, one of these methods of focussing may be employed. A: microscope. B: telescopic viewer. C: focussed lamp filament; D. viewer of reflex camera with open diaphragm.

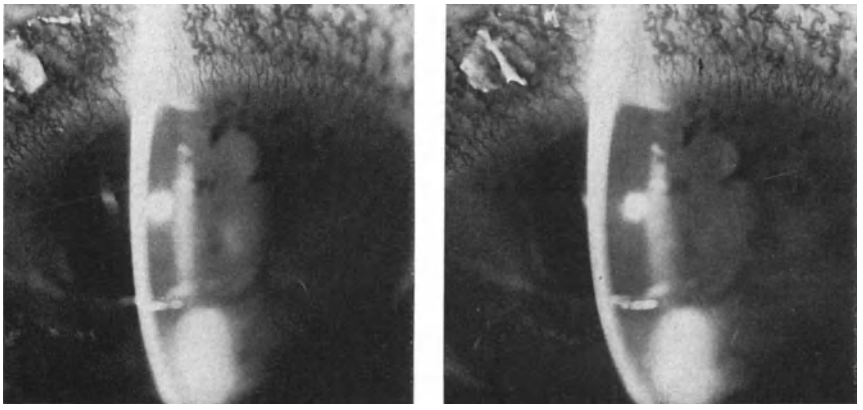


Fig. 10. Stereogram showing optical section in a case of iridocyclitis.

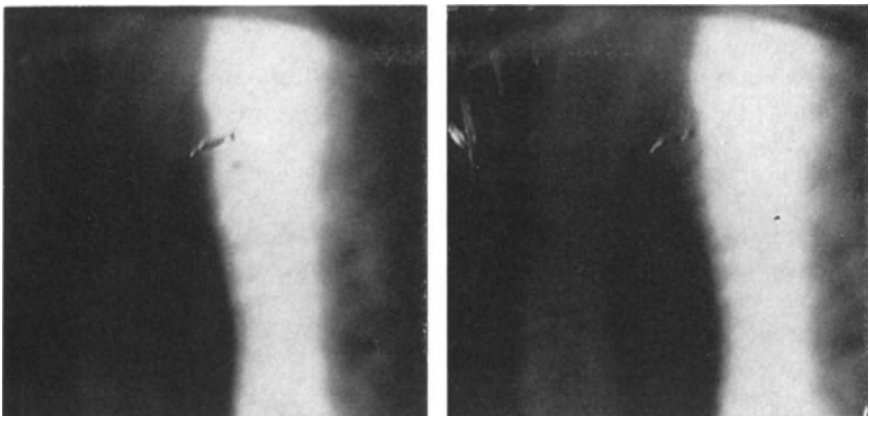


Fig. 11. Stereogram showing a small piece of glass deep in the cornea. The dept suggestion is realistic despite most of the background being out of focus.

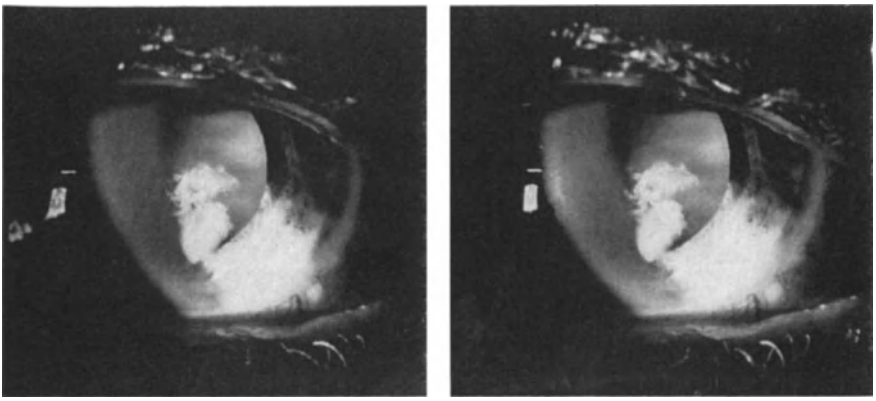


Fig. 12. Stereogram of a perforating injury. The opaque areas of the cornea and that of the lens are separated when viewed stereoscopically.

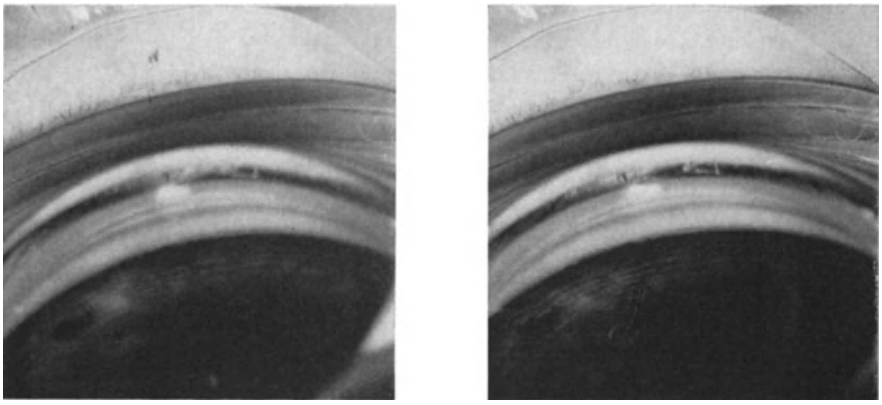


Fig. 13. Stereogram of chamber angle, in a case of pigment glaucoma.

shaped diaphragm, as is usual in slitlamp microscopy, is the method of choice for the following reasons:

- it helps in the formation of a kind of image familiar to the ophthalmologist;
- it helps to grasp the idea of the optical section for those not initiated in this field;
- both optical section and stereoscopy contribute, although in different ways in building up a three-dimensional image resulting in a very strong depth perception;
- the presence of a second clue (the optical section) to depth perception allows some deviation from the strict rules for stereomacrophotography. This means in our case a non-real extension of object depth, but in fact sufficient for depicting the whole anterior chamber;
- the strong illumination with which these instruments are generally equipped, allows the use of very small diaphragms, resulting in an extreme photographic depth of field.

STEREOPHOTOGRAPHY OF THE CHAMBER ANGLE (Fig. 13)

In view of the versatility of the illumination, the magnification, the stability of the instrument, and the short working distance, the photoslitlamp is the instrument of choice in combination with Goldmann's gonioscopic contactlens. The patient must watch the fixation light with the other eye, and the contact lens must be positioned so as to yield an optimum view without reflexes. Yet as the optical pathways of the light to the cameras differ in most instruments from the ones seen by the observer, the photographs may show annoying reflexes. This is the reason, that a series of simultaneous exposures should be taken, and the best stereo-pair should be selected.

STEREOPHOTOGRAPHY OF THE POSTERIOR OCULAR MEDIA

For practical reasons we define the posterior ocular media as comprising the posterior half of the lens, and the vitreous. Stereophotography may be accomplished enploying:

a. the fundus camera with retro-illumination;
b. the slitlamp with retro-illumination; and
c. the slitlamp with focal illumination.

a. Two successive exposures must be made for one stereophoto. We must be aware that the posterior lens capsule, and still more the vitreous are situated quite a distance behind the iris, so that the parallactic displacement of these structures is considerable. This is the case even in small movements, either ductions of the eye or sideways movements of the camera. Here again the best method seems to be taking a series of exposures, letting the patient fix steadily the fixation light, and making very small parallel lateral movements with the camera in between the exposures. Afterwards, the best stereo-pair is selected.
b. The slitlamp offers the huge advantage of enabling the taking of stereo-pictures simultaneously. Retro-illumination requires a slit not larger than

the pupillary diameter and a slit width which enables us to get a fundus reflex into the two oculars of the microscope at the same time. The light bundle has to pass along the opacity which makes the latter appear in silhouette. The corneal reflex should leave the opacity free. In depicting opacities lying deeper in the vitreous, it is difficult to fulfill all requirements. In some instances, only mono-pictures can be obtained.

c. For opacities situated in the posterior vitreous or in the plane of the retina, diffuse illumination as stated above, does not work. Now the opacity lights up and stands out against the red fundus.

Focal illumination with the slit-bundle may demonstrate i.a., very subtile changes such as posterior vitreous detachments. To photograph these changes stereoscopically requires a great skill and some luck. As the angle between the two camera-axes is about 15°, there is little room left for the optical section to be viewed from the same side by both cameras.

STEREOPHOTOGRAPHY OF THE FUNDUS OF THE EYE

Thorner's camera

A salute is due to THORNER who, as long ago as 1909, obtained good stereo-pictures using an apparatus that, after taking the first picture, had to be turned over in order to take the second exposure. THORNER used a kerosene lamp for viewing and the combustion of magnesia powder as a flash light (Fig. 14).

Donaldson's camera

Only a few designers have attempted to construct a fundus camera for simultaneous stereoscopic photography. DONALDSON (1965) has been the most successful one. A good deal of the optics were made by Zeiss on special order. The camera is equipped with two 'end-on' electronic flash tubes, and has apart from one single aspheric ophthalmoscope lens, two separate optical pathways to the two film windows and the two reflex viewfinders (Fig. 15). The pupil leaves space for two vertically situated areas for illumination and two horizontally placed areas are reserved for the two image-forming optical pathways (Fig. 16). Of this apparently ideal apparatus only a few specimens have been build. The camera is not commercially available.

Modern cameras

It is a pity that fundus cameras for simultaneous stereophotography are not commercially available. Consequently, we have to resort to successive exposures. As the pictures obtained are circular and relatively small, we cannot afford to have a considerable horizontal shift and consequently, a loss of stereo-image field. Hence, we prefer to converge the two optical pathways toward the object. This is accomplished, not by swinging the camera through the angle of convergence, but by parallel displacement of the camera. Parallel rays traversing

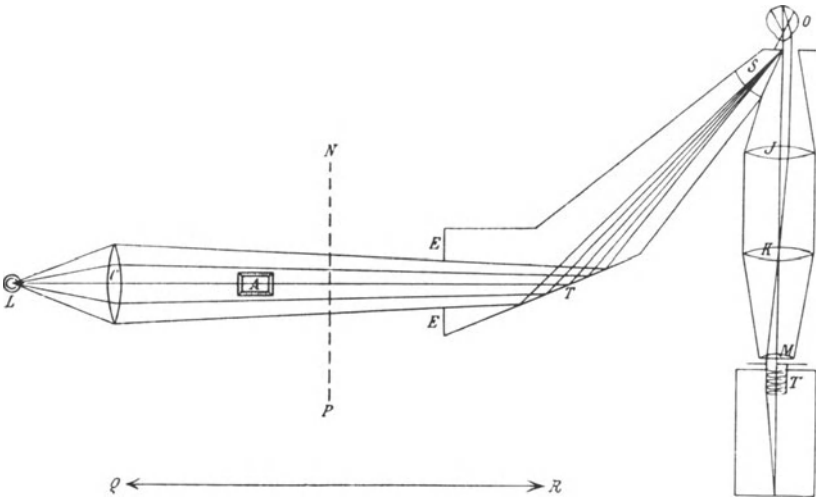


Fig. 14. THORNER's stereoscopic fundus camera. L: Kerosene lamp; A: magnesia-powder; T: mirror; S: prism and excentrically-placed diaphragm; O: subject. (From Thorner 1909).

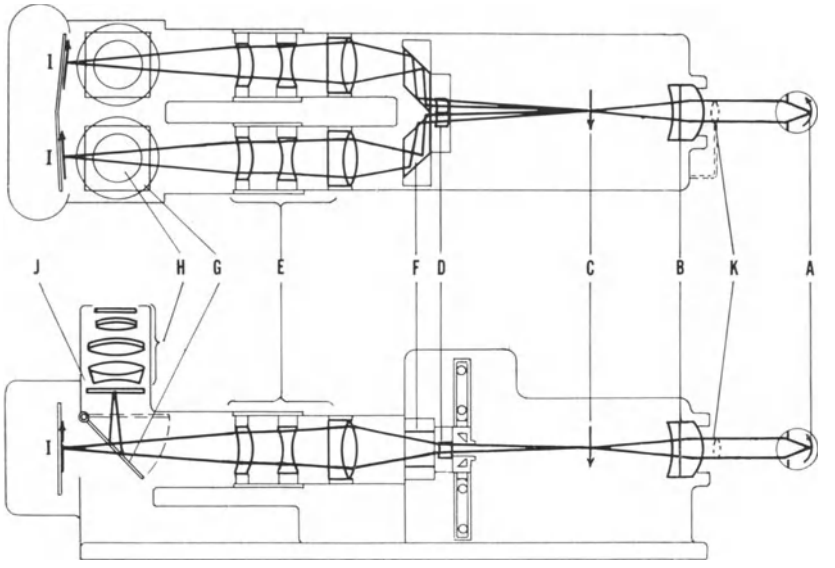


Fig. 15. DONALDSON's stereoscopic fundus camera. Top view (above) and side view (below). A: indicates fundus of patient's eye; B: aspheric ophthalmoscope lens; E: paired camera lenses; F: modified rhomboid prisms; G: reflex mirror; H: ocular (focussing eyepieces); I: film plane; J: reticle; K: small plus spherical lens. (From: DONALDSON, 1965).

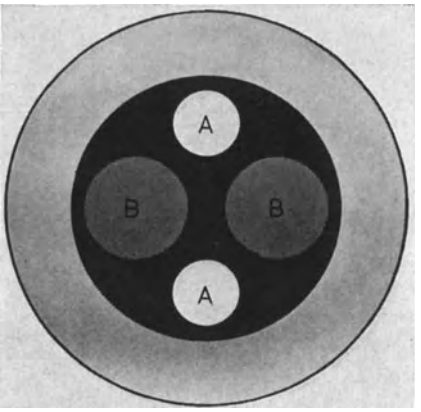


Fig. 16. Separation of A: illuminating beam and B: optical pathway at the level of the pupil, in DONALDSON's stereoscopic fundus camera.

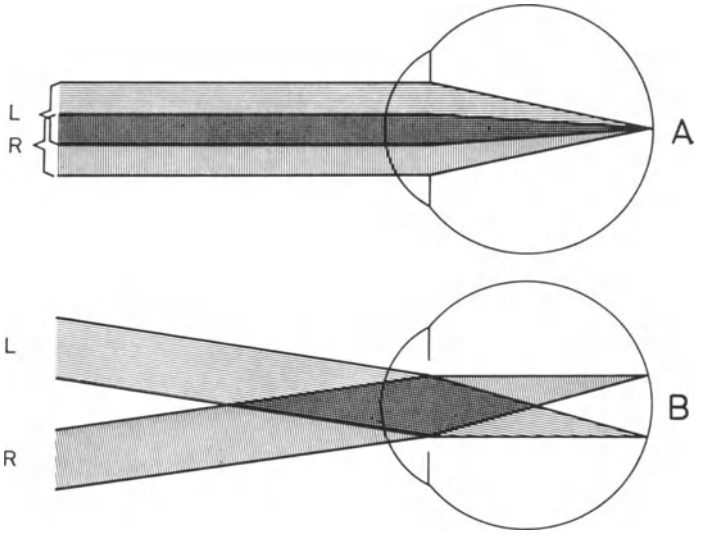


Fig. 17. Parallel and converging stereophotography. A: parallel displacement of the camera, resulting in optical pathways that converge towards the same retinal area. B: converging optical axes of the camera, resulting in displacement of the beam towards different retinal areas with the same angle of incidence, and therefore with the effect of parallel displacement.

the pupillary area at any plane, converge to one retinal point in the emmetropic eye (Fig. 17). The maximal sideway shift that can be effected depends of the leeway of the optical pathway in the pupil. For a pupillary diameter of 8 mm, a displacement of 3,5 mm is possible (Fig. 18). This displacement produces an angle of convergence on the retina of 15°, which is rather sufficient to create a stereoscopic impression. Moreover, this corresponds to the angle of convergence in reading at 25 cm distance and an inter-pupillary distance of 65 mm. In a way,

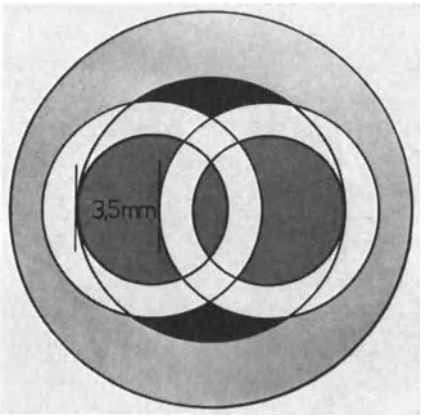


Fig. 18. Shift of illuminating beam (white) and optical beam (gray) inside the pupil in stereo-fundus photography.

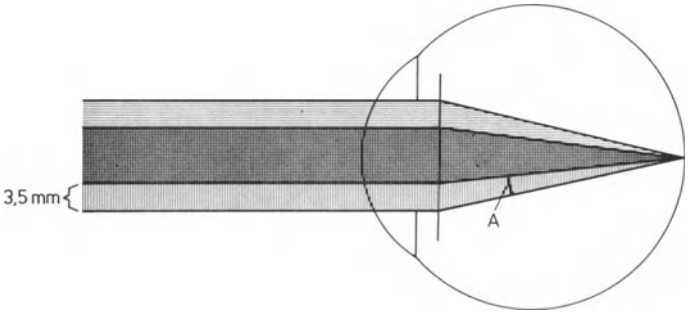


Fig. 19. Horizontal section of the shift of the two light beams (vertical and horizontal hatching respectively) with an angle of convergence (A) of 15° maximally.

we may coin the resulting stereoscopic impression as natural (Fig. 19).

The different steps in securing an optimal stereoscopic fundus image were aptly described by ALLEN (1964). Quick and measurable parallel displacement of the optical axes between the exposures for the two pictures of a stereo-pair is greatly aided by a clever construction, likewise designed by the same author and called the Allen separator. It consists of a plan-parallel glass plate mounted in front of the objective. The plate can pivot upon a vertical axis through a predetermined angle. This produces a parallel displacement of the optical pathway (see VAN BEEK, 1973). When activated by impulses from the motorised camera, successive exposures within $\frac{1}{2}$ second may be taken.

FLUORESCEIN STEREO-ANGIOGRAPHY OF THE FUNDUS

The rapid sequence stereo-exposures just described have contributed to the possibility of making stereograms of the early phases of the fluorescein inflow. Still, the inflow pattern has changed somewhat during this short interval, but the 'lustre' in viewing the stereogram is, in most cases, not a serious impediment,

for the strong black and white contrast compensates for this defect. The arterio-venous and late phases are relatively free from differences in vessel contents, but the diffusing fluorescein may obscure the picture and impair the stereoscopic effect (ALLEN, 1971).

Instead of making negatives and prints, it is also possible to use instant photography with a Polaroid setup (ALLEN et al., 1966).

Depth discrimination

In describing certain fundus changes, it is often important to define their depth localisation, whether retinal, pigment epithelial or other. This accounts for a difference in depth of about 0,2 mm. Considering the angle of convergence of 15°, this amounts to a parallax of 4′ or ten times the stereoscopic power of discrimination under optimal conditions (Fig. 20). Problems like these require not a natural stereoscopic effect, but a maximal effect. In order to obtain this, all possible contributing factors should be employed: maximal sharpness, maximal contrast, maximal separation of the pair of stereo-pictures, a viewer with a long focal distance, and last but not least an examinator with a strong

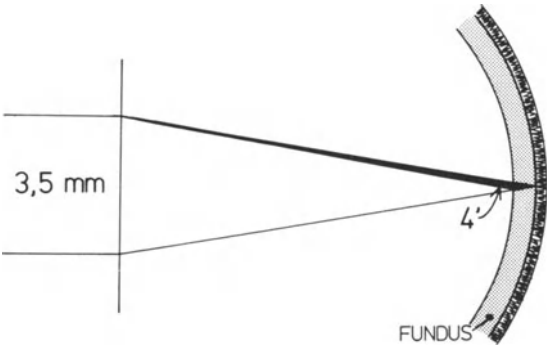


Fig. 20. Object depth (fundus) beam displacement (3,5 mm) and parallactic angle (4′) in fundus stereophotography.

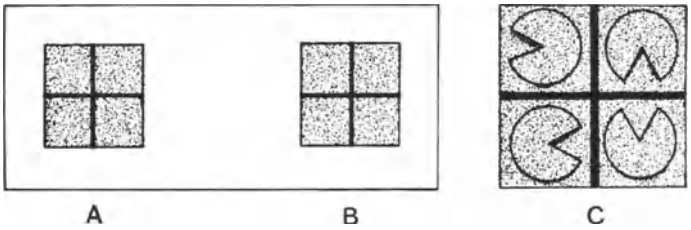


Fig. 21. Stereograms for measuring stereoscopic acuity (WALRAVEN & BOGAARD, 1970). The transparencies A and B are identical save for certain fields in which the fine pattern is displaced symmetrically, so as to create disparity. This is invisible in monocular viewing, but the figures are detached from their surroundings by the stereoscopic effect of the displacement (C). The degree of displacement which is necessary to see the figures is related to the stereo-acuity.

stereoscopic discriminating power. This faculty can be tested very efficiently with a simple quantitative device (WALRAVEN et al., 1970, Fig. 21). The subject has to wear his full correction.

Photogrammetry

The above mentioned technique has lead to the development of quantitative evaluation of differences in depth in the fundus, resembling the photogrammetric techniques employed in cartography. In order to yield results, corrections must be made for projecting the concave fundus on a flat surface, and for the oblique position of the camera; this involves the use of a very expensive stereoplotter, a staff of experts and much time. It is, thus, still in an experimental stage (CROCK et al., 1969).

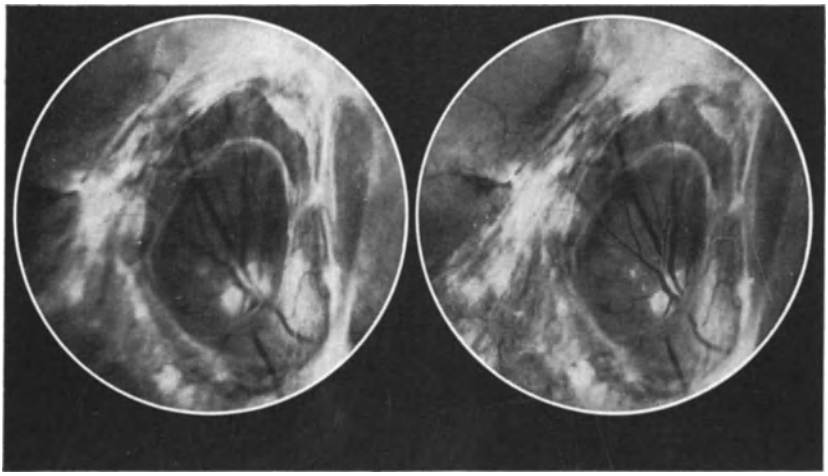


Fig. 22. Newly-formed vessels in the vitreous in diabetic retinopathy.

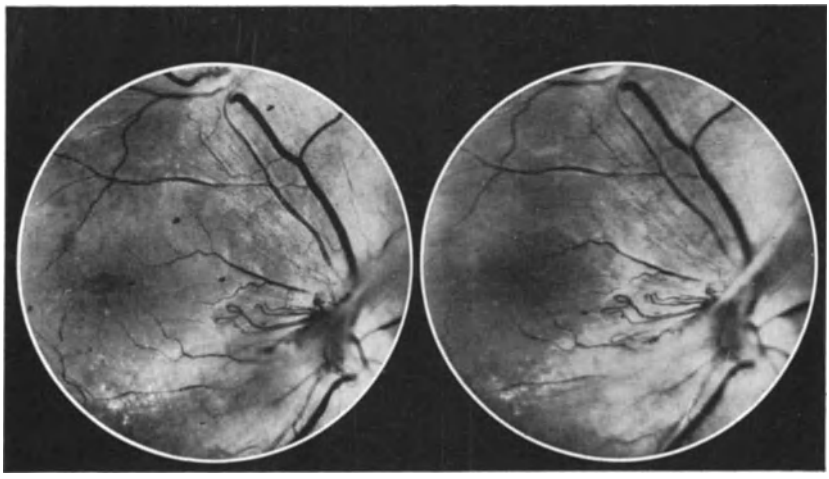


Fig. 23. Advanced retinopathia proliferans.

In the Figures 22 and 23 stereograms of the fundus with depth suggestion are presented.

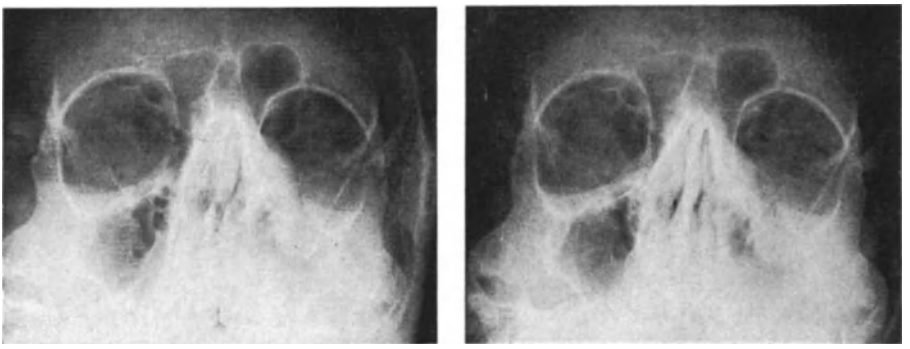
X-RAY STEREOPHOTOGRAPHY OF OPHTHALMOLOGICAL INTEREST

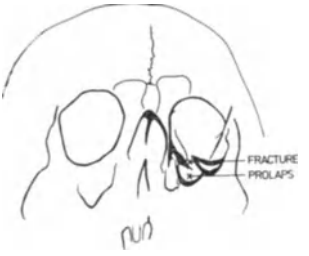
The main indications are:
- fractures and other skeletal changes of the orbit;
- arterial and venous angiograms of orbital processes.

X-ray photography is part of the routine examination in orbitateams (e.g. the Amsterdam Orbital Centre; HÖTTE, 1970). It gives invaluable information of the three-dimensional structure and of the changes visible on the X-ray picture (Fig. 24). The stereoscopic pictures are taken successively, shifting the tube 5°, measured from the object. Care must be taken to stabilize the head. The photographs are placed in front of an illuminated screen using a binocular viewer.

X-ray angiograms are equally helpful for the localisation of orbital processes which go with occlusion, displacement, changes in calibre or formation of new blood vessels.

Contrast, and consequently stereoscopy, is greatly enhanced by using the subtraction method of ZIEDSES DES PLANTES (1961, 1963). In this technique, a positive printing of the negative without vascular filling is covered with the transparent negative with vascular filling; all details are now eliminated, except the vessels filled with contrast dye. The angiogram appears isolated in very high contrast (Fig. 25). By using two tubes, placed under a 5° angle and a quick transportation system of the plates, it is possible to take the two pictures of the





Stereo-roentgenogram of a case presenting a leftsided fracture of the orbit at the frontozygomatic suture and an orbital floor fracture through which the orbital contents prolapse into the maxillary sinus.

Fig. 24

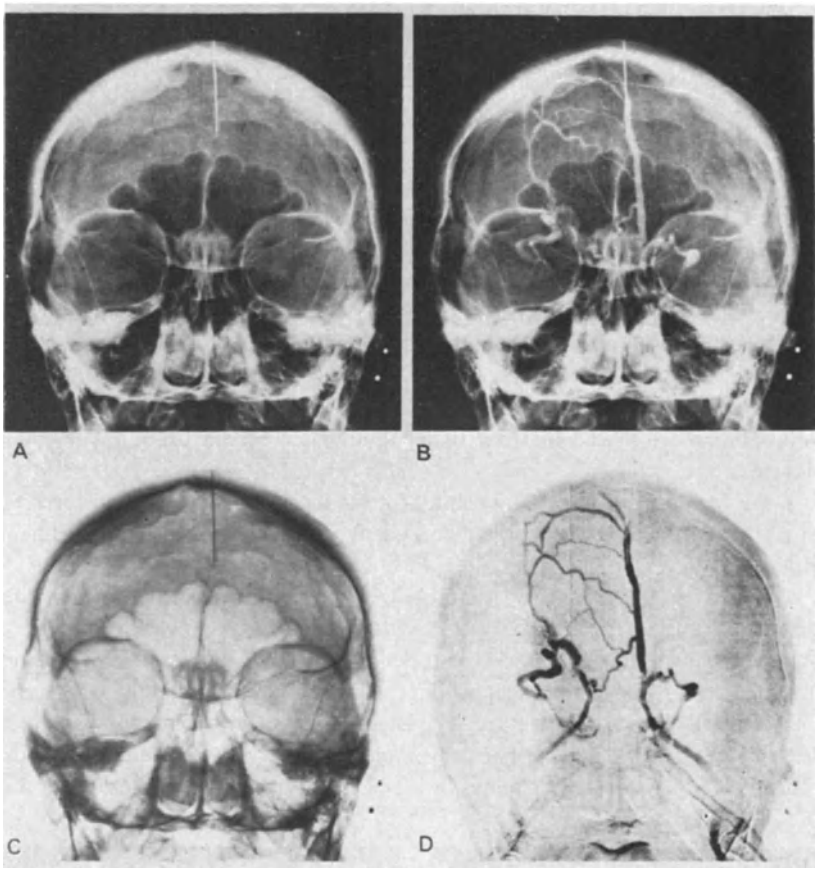


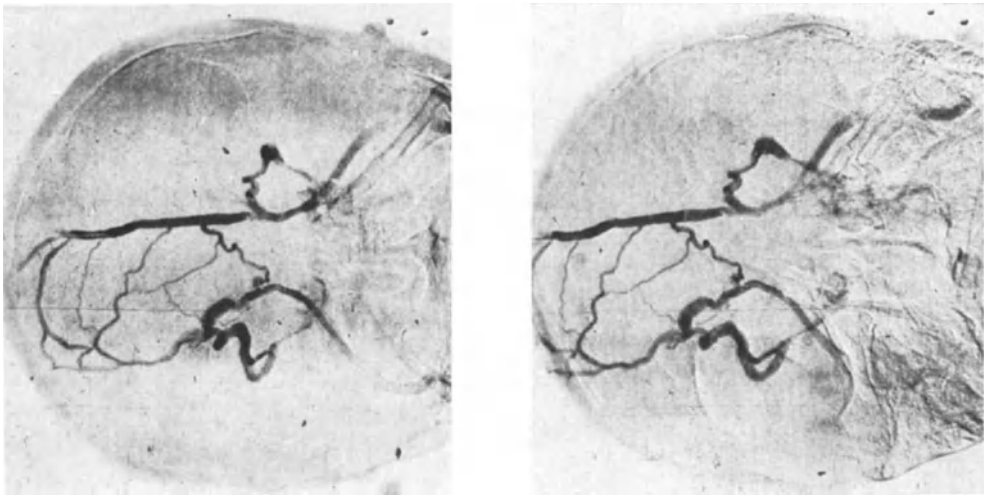
Fig. 25. Subtraction angiography. A: plain radiograph; B: phlebogram; C: transparent positive print of A (mask.). D: print made from the phlebogram B after covering this with the mask C. (Photo Prof. B. G. Ziedses des Plantes).

stereogram within $\frac{1}{3}$ of a second; vascular filling differences between the two pictures are neglectible (Fig. 26).

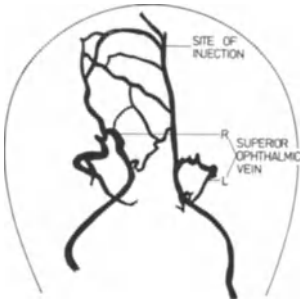
STEREOGRAPHIC DRAWINGS IN OPHTHALMOLOGY

Only the simple forms of drawing a stereoscopic image will be considered. Several methods may be employed:

- drawing two planes of depth and displacing these. An example is to draw the fundus (plane 1), cutting out a hole at the place of the disc, and drawing the bottom of a glaucomatous excavation (plane 2). Then make two pictures, plane 2 having been displaced horizontally in the second exposure (Fig. 27).
- a simple three-dimensional model may be photographed stereoscopically and be traced graphically (Figures 28 and 29).
- a combination of photographic stereogram with stereoscopic drawing. The



Stereoscopic subtraction phlebogram of the same patient, showing a displacement of the left superior orbital vein, caused, as subsequent pathologic examination disclosed, by an orbital pseudotumor. Due to the stereoscopic shift being longitudinally, the stereogram had to be tilted 90°. (Photo Prof. B.G.Ziedses des Plantes).



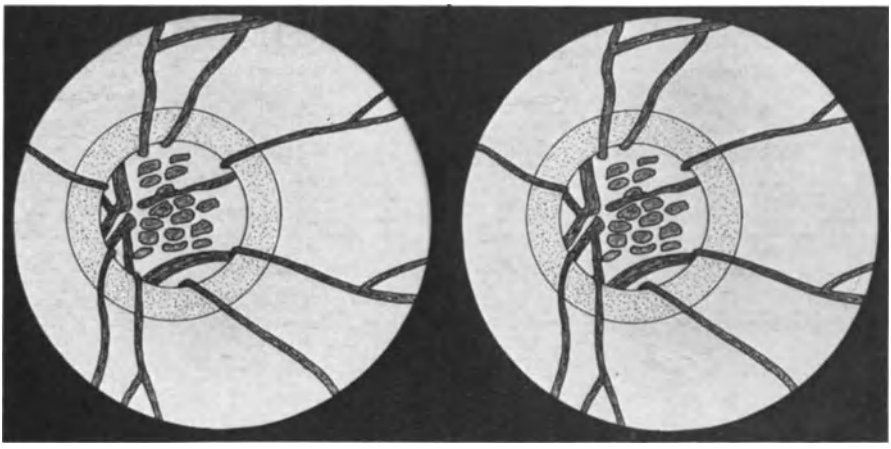


Fig. 27. Schematic stereoscopic drawing of a glaucomatous disc excavation. The disc was cut out, and the bottom separately drawn; photographs were taken with a horizontal shift of the bottom.

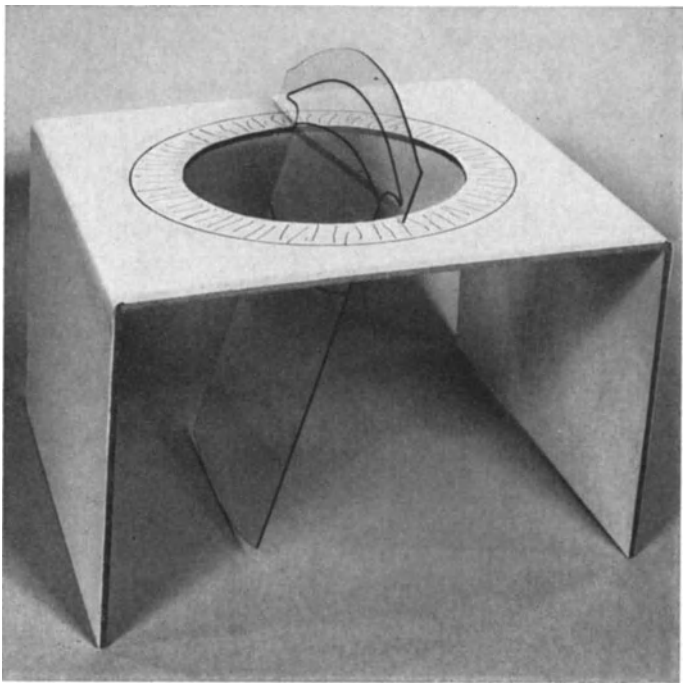


Fig. 28. Simple model made of paper and transparent plastic of pupil and optical section.

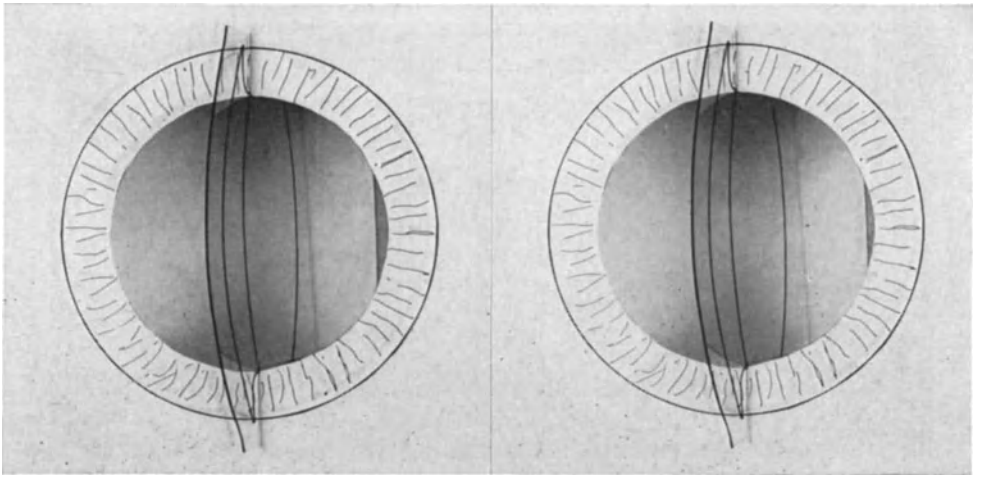


Fig. 29. Schematic stereoscopic drawing of optical section made by photographing the model of Fig. 28 stereoscopically.

mono-version may be completed to stereo by drawing the second picture directly, using a large mirror-stereo-viewer.

Requirements for ophthalmic stereophotography

Stereophotography of the fundus requires only a regular fundus-camera and a little more skill in centering than is needed for mono-photography.

Stereophotography of the anterior segment, including slitlamp photography, requires a rather expensive instrumentation.

All stereo-work requires much more material, apart from viewing and projecting facilities.

Instead of performing all of these tasks oneselves, one can also have transparancies or prints copied from current publications. This requires in one's own department only viewers or projectors. But even for this restricted stereo-activity, some general knowledge of stereoscopic mounting, viewing and projection is indispensable.

CONCLUSION

Stereophotography needs considerable basic knowledge and much care, money and energy to result in good pictures. Stereophotography therefore, is to be confined to a few well-equipped photographic departments.

Stereophotographs are an invaluable aid in teaching and demonstrations. Adequate viewing and projecting material should be present and in good working order in any large teaching-centre.

This holds especially for ophthalmology due to its visually-orientated character.

Key words

Stereophotography.
Stereo-photoslitlamp.
Stereo-fundus camera.
Stereoscopic roentgenograms.

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SOME THOUGHTS ON SLITLAMP PHOTOGRAPHY AND REFLECTOGRAPHY

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A sound experience in slitlamp observation and a modest one in photography are essential for making good macrophotographs with the kind of illumination a slitlamp affords.

Observation through the ordinary slitlamp is rather a complex event because it amounts to the mental integration of a whole series of subsequent static pictures, which differ in the area observed, the illumination being used, the plane of focus and in contrast. These can never be confined in one diapositive, but a single photograph can often be taken in such a way that it is suggestive, which is even more than descriptive.

Most of all one should know what can be seen through a slitlamp, what can be expected, because one tends to see only what one knows. It may be unnecessary to remark that one's personal memory is small as compared to the large external memories stored in the atlasses of VOGT, BERLINER, BUSSACCA and DONALDSON, and in many individual papers. In several respects the oldfashioned drawings and paintings surpass our photographic techniques in suggestiveness and even in the representation of details. The artist is able to enhance the features of the pattern he wants to stress and he is independent of many technical limitations. He can draw things a photograph is unable to reveal; he also can summarize in one drawing what would require many photographs to reveal. But the time required to make one good drawing is prohibitive so that for nearly all of us drawings, which are both artistic and accurate, are out of the question. For the medical record however, a single sketch will often be of tremendous value in the follow-up of the patient.

In this time where costs are rising and the costs of health-care especially so, the purpose of our picture-taking should be a point of consideration. One can imagine several purposes for making such pictures:

a. for teaching. Here a limited number suffices, provided that each picture is representative and of excellent quality. We found that about two hundred diapositives easily cover the entire range of normal and abnormal situations which our students need to have seen.
b. photographic documentation for the patients record is rarely needed, unless one is dealing with a rare and progressive disorder one wants to follow. The follow-up of a questionable tumor of the iris is a typical example.
c. research. Here a standard procedure has to be developed and more often

than not a special instrumentation and procedure is required.

d. most pictures are probably being made in order to fill a collection or to fulfil a collectors needs; though this is a quite legitimate purpose I am convinced that a large number of slitlamp pictures are being made with no specific purpose at all in the mind of the photographer.

Whatever the need for pictures, they should be of good quality. For most purposes colorpictures will do best. I found that Kodak Ektachrome is an excellent medium.

The lightsource: the normal tungsten source of the slitlamp is not adequate to make good pictures within the short exposure time necessitated by the ever present eye movements. An electronic flash is therefore required.

It must be a small source so that the plane in which the slitdiaphragm is situated can be illuminated evenly. If pictures are to be made within short intervals, the problem of cooling arises. In my opinion by far the best solution to the many optical problems that arise in slitlampphotography has been proposed by NIESEL (1966). Such an apparatus however is not commercially available.

Instead of a simple camerabody a reflexcamera is preferable, and it may even replace the usual microscope. The lack of brightness and sharpness of the groundglass can be overcome by substituting a clear glass window, requiring of course that the observer does not accommodate. This seems the only way to ascertain that one exactly photographs what one sees.

Another point to consider is the lens. A Zeiss Luminar of 40 mm focal length is probably at this moment the best that money can buy.

A magnification of 1 : 1 is most of the time sufficient. This means that the film plane is at twice the focal distance of the lens.

Even with this excellent apparatus which has been in use in the Royal Netherlands Ophthalmic Hospital at Utrecht since 1965 there remains the need for a preset diaphragm in the Luminar lens, so that one can study the object with open diaphragm and expose the film at the desired stop.

Let us now consider the various illuminating techniques.

DIRECT SURFACE ILLUMINATION

One problem here is that a good exposure setting for the iris, automatically entails an overexposure of the sclera. Another difficulty is that the corneal scatter easily puts a veil over the underlying structures. This is caused by the high blue content of the source and bluish light provides a far greater amount of scatter than does for example the yellowish tungsten light, according to Tyndalls law.

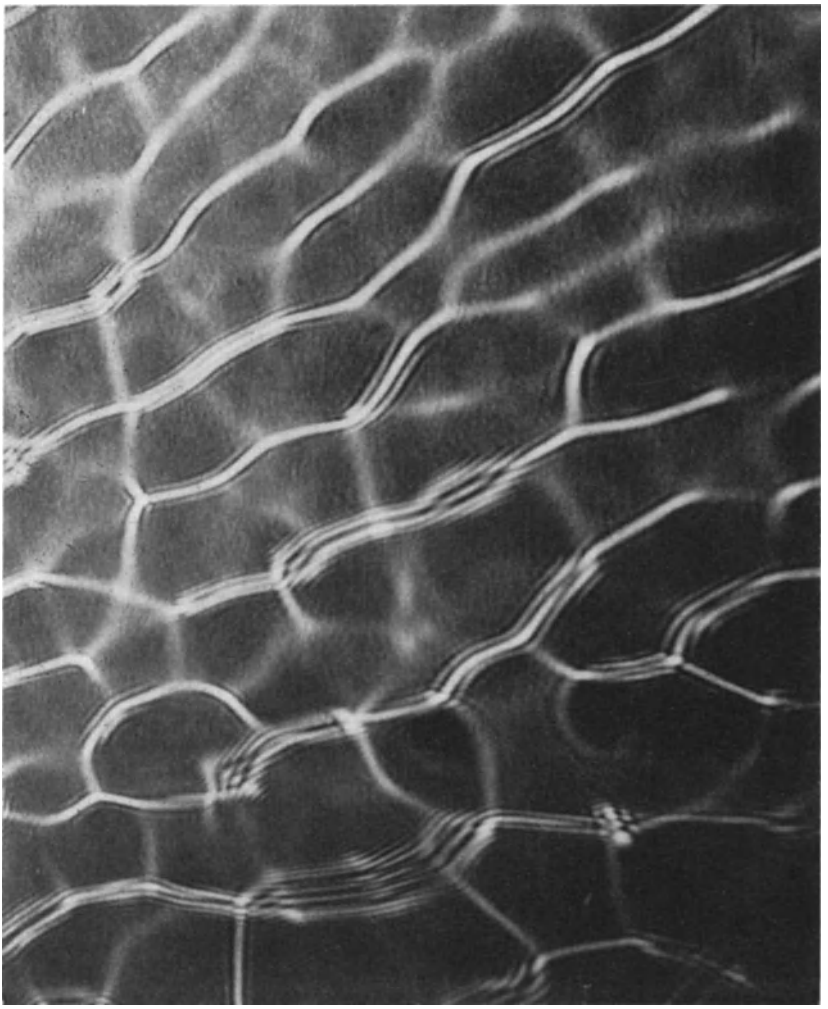
Therefore a tangential illumination is by far the best and the border of the slitprojection should not encompass the center of the cornea which then may act as a picture window. A very tangential illumination has a further advantage in that it creates an impression of depth and increases the texture shown by the iris and pupillary border. Doubtless this method creates the most suggestive pictures of synechiae and of irregularities on the surface of the iris.

RETROGRADE ILLUMINATION

The light reflected from either the iris or the fundus is used as a secondary source. The first possibility requires a tangential illumination of the iris and a focussing of the camera slightly in front of that plane. The latter possibility, photography of irregularities in the lens or in the cornea against the red glow of the fundus is more difficult, unless one uses the camera itself as the viewing system. With all systems in which the viewing and the recording system are separated the narrowness of the beam reflected from the fundus leads to trouble.

BY REFLECTION

The reflections of the anterior and the posterior surfaces of the lens can be easily photographed and minute changes will clearly show.



This is not true for the reflecting surfaces of the cornea. The reflex of its anterior surface, as obtained with the slitlamp, is far too bright to give a well exposed picture. The border of the reflected image of the lightsource however contains some information about the regularity of the corneal surface in that particular area. The posterior surface reflex of the cornea cannot be photographed because it is so near the anterior reflex which is over one hundred times brighter.

However the particular structure, if present, of the anterior corneal surface can be brought into view with the aid of *reflectography*.

Reflectography is a method whereby a lightbeam, after reflection by a mirror-like surface is intercepted by a screen or a film. All the irregularities of the surface will be apparent on that screen. For the cornea this method has been developed by FISCHER (1928) in the late twenties. He directed a more or less parallel beam of light perpendicularly onto the corneal surface and intercepted the strongly divergent reflected beam on a sensitive film. This method can be improved by using a laser beam (SCHWEITZER, 1967).

If the corneal surface is regular, the screen shows a bright center, the brightness falling sharply off towards the periphery.

Any irregularities in the epithelial texture will be apparent in the reflections on the screen, where very complicated patterns arise (Fig. 1). These patterns certainly hold a clue as to the three dimensional characteristics of the reflecting surface. However, interpretation of this clue is very complicated and it is improbable that the patterns thus obtained contain diagnostic evidence which cannot be obtained by less sophisticated methods of observation.

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DIAPHANOSCOPY AND DIAPHANOPHOTOGRAPHY

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A new technique of diaphanophotography, based on indirect transorbital diaphanoscopy, a method developed by the authors, is described. Use is made of a sophisticated electronic camera which allows a reduction in exposure time. Background and planning for further research are discussed.

Basic information regarding diaphanoscopy or transillumination may be found in the textbooks of DUKE-ELDER (1962) and VELHAGEN (1969).

There exists an indirect and a direct approach to diaphanoscopy. According to DUKE-ELDER, *indirect* diaphanoscopy was first described by STEVENSON (1893), who placed a powerful light source in the mouth. He gave a vivid description of his observation: 'The eyes shot out from their uncontracted pupils a blood red glare, as from two miniature danger signal lamps'. Soon this method became a routine procedure for a diagnosis of postaequatorial fundus tumors. The investigator adapted in the dark room, the patient wore a black mask with holes for the eye to eliminate glare from the illuminated sinusses and then the watercooled lamp of HERTZELL (1908) was placed in the mouth.

We tried this method out using direct and indirect ophthalmoscopy but on account of the faint red illumination and the very low contrast, not much information could be obtained.

The common technique of diaphanoscopy, first published by VON GRAEFE (1868) and HIRSCHBERG (1868) is the well known and generally applied *direct method.*

This method enables us to detect tumors in the anterior part of the fundus. Only recently it has been perfectioned by NEUBAUER (1965), but even now the method does not give sufficient information regarding a process in the posterior part of the fundus.

Direct diaphanoscopy was extended to the postaequatorial area by GOLOWIN (1926). However, it was necessary to dissect the conjunctiva and Tenon's capsule. This technique was recently perfected by BÖKE & AZARBAYDJANI (1964).

Interest in posterior direct diaphanoscopy was considerably promoted by the development of detachment surgery. New instruments, based upon this principle and intended for the localization of retinal tears, were devised and published by WEVE (1934), GOLDMANN (1936) and in 1946 by HAGEDOORN.

Ophthalmoscopy and simultaneously direct posterior diaphanoscopy as already proposed by LINDAHL in 1920, became a routine procedure, which could

be combined with coagulation of the retina. This resulted in development of various new instruments e.g., the instruments of OOSTERHUIS (1968) and VELZEBOER (1971). The latter instrument makes use of fibre optics and a powerful light source (150 Watt projection lamp with dichroitic mirror).

With the masked patient in the dark room with Hertzell's lamp in mind, it seemed worthwhile to investigate whether it would be advantageous to illuminate the retrobulbar orbital tissue directly instead by way of the mouth. On paper we devised various conductors, some resembling lid retractors, to assure an even distribution of the light along the posterior pole. A first crude model was so easy to apply, preserving a clear cornea and the possibility for normal blinking, that we put a new model on our research program but continued research with this simple instrument.

In experiments with this light conductor connected by fibre optics to the 150 Watt light source the retrobulbar orbital tissue became well illuminated. We found that thus a rather bright image of the posterior fundus was reached, even enabling diaphanophotography (HAGEDOORN et al., 1972). However, discrimination of detail remained poor on account of the long exposure time (1 second and over). This induced us to plan a stronger light source with a more efficient light conductor. However, as recent papers point at the possibility of damage to the rods and cones by excessive and prolonged exposure to light (FRIEDMAN & KUWABARA, 1968), we looked for another possibility to achieve our aim: image amplification, allowing photography with a short exposure time.* This resulted in a new type of camera. In order to keep the instrument as handy as possible the film was placed close to the anode without the interposition of an optical system: a new procedure. This led initially to difficulties, but these could be overcome. One of the problems was an artefact caused by

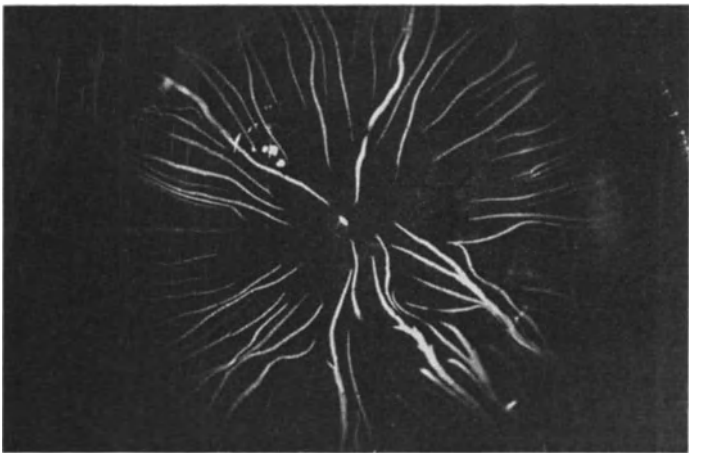

Fig. 1. From the preliminary experiments: static discharge.

* We are very grateful to the electro-optical factory 'De Oude Delft' which made it possible for us to develop an electronic camera.

static discharges (Fig. 1). We tested the quality of the pictures obtained using a television test image (Figures 2 A and 2 B).

The picture (photoamplification $\times 100$) turned out to be amazingly sharp showing only slight differences with the original image – within the necessary tolerance for our work. In 1973 we published our first results, giving i.a. a picture of a very unusual inflammatory (?) tumor, containing no pigment, which had not been diagnosed with the ultrasound technique (HAGEDOORN et al., 1973).

It was evident from the comparison of the pictures made with the original

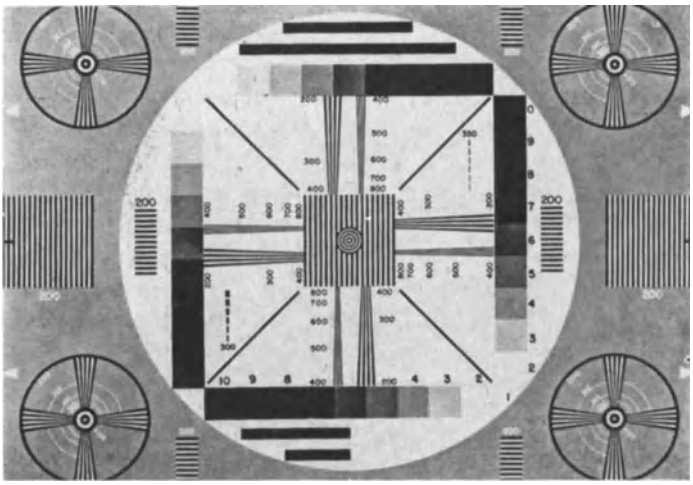

Fig. 2A. Normal photograph of TV-test image.

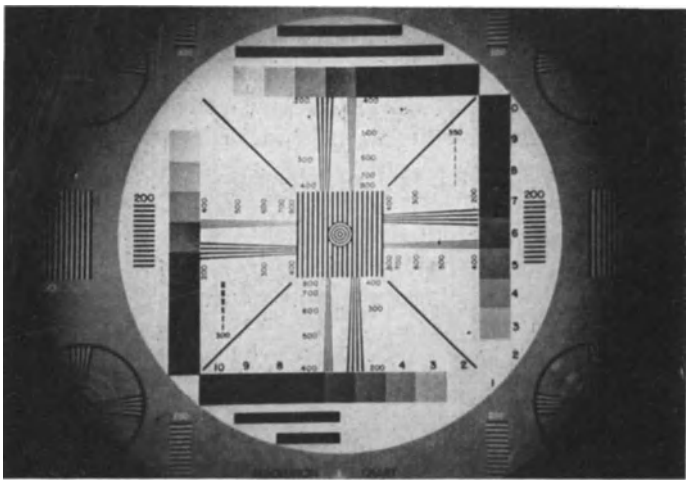

Fig. 2B. Photography of the same test image using the photo-amplifier: a slight 'cushion' effect, slightly diminished overall size, contours and contrast maintained, slight drop in brightness towards the perifery.

technique in 1972 and with the new electronic technique in 1973 that far more detail became visible on account of the short exposure time (HAGEDOORN et al., 1973. This confirms the thesis, mentioned in VELHAGEN's textbook that normal pigment is translucent for red rays but pathological pigment is not.

In the last 10 years, diaphanoscopy has been practised less in the differential diagnosis of a suspect process in the posterior fundus on account of the advance of fluorescein angiography. In that technique exposure times are short, the resulting photographs are mostly of quite good quality, allowing a comparison of pictures in order to detect growth.

DIAPHANOPHOTOGRAPHY

Diaphanophotography was practised by OGG (1960), BILLEP (1968) and NEUBAUER (1965). REMKY et al. (1965) used diaphanophotography to bring out the vascular system of the choroid and the retina and especially the long ciliary arteries. A strong light stimulus deriving from a ring-shaped photoflash was used in combination with direct diaphanoscopy.

We believe however, that only a diffuse overall illumination by indirect diaphany combined with electronic camera may furnish information for accurate and detailed documentation.

There exists one major set-back. The electronic amplifier translates the picture into different shades of green, eliminating the advantage of color.

However, this is less important since the light in indirect orbito-diaphanoscopy has a strong red hue so that in practice only pathological pigment is clearly visible on a red background lacking much detail.

The red color of the fundus is not a spectral red, but has a spectral composition close to hemoglobin. A large literature has accumulated over the years on the use of colored light, partly centred around VOGT's method of demonstrating the yellow color of the macula. SCHIRMER (1964) furnishes valuable information in this respect. By using appropriate filters it is possible to improve the definition of bloodvessels markedly.

BEHRENDT & WILSON (1965) emphasize the possibilities of black and white photography through interference filters. They introduced the concept of retinal spectral reflectance, discussing reflectance, absorption and transmission. In diaphany only transmission has to be considered.

VELHAGEN mentions the work of VODOVOSOV (1960), who examined the eye using light of different spectral composition. For this purpose VODOVOSOV constructed an ophthalmoscope armed with various color filters.

Subjects for further research are:

1. *The illumination*

In the experimental stage we employed a powerful flash light (800 Watt/sec.) as is incorporated in the apparatus of RICHARD WOLF. It came out that the results in indirect diaphanoscopy were inferior to the ones obtained with a 150 Watt lamp. For this reason we started to build a much more powerful light source.

A second point of consideration is how to get a more even distribution of light to the orbita. This may be achieved by an improved input in the conjunctival sac.

A third point is how to enhance electronically the contrast of the pale area's of the diaphanoscopic pictures.

Intensifying the local contrasts as done in space photography (MURRAY et al., 1970) may be the answer. The signal-to-noise ratio is presumably high in our case.

2. *The use of colored filters*

Using indirect orbital diaphanoscopy, it seems wise to obtain first a spectral analysis of the light leaving the eye through the pupil. This was endeavoured by NIEDERMEYER (1958) in an attempt to measure the thickness of the choroid. CRISTINI & FIORENZI (1961) abandoned this method on account of its complexity, using a more simplified photometric method. Intentionally we restricted our efforts to the experimental use of different filters and films along the trial and error method.

A powerful light generator has been built fitted with a 400 Watt 36 V halogen lamp and two fibre optic light conductors. The light stream from both sides has to pass through sets of filters which enables us to make any combination desired.

IRIS DIAPHANY

As soon as we started to use this apparatus with the electronic camera, it became clear that our light intensity was such that in normal blondes the iris seemed very translucent (Fig. 3 A and 3 B). This brings the differentiation between normal and pathological diaphany of the iris on quite another plane: the quantitative factor became important. We now measure by photometry of the

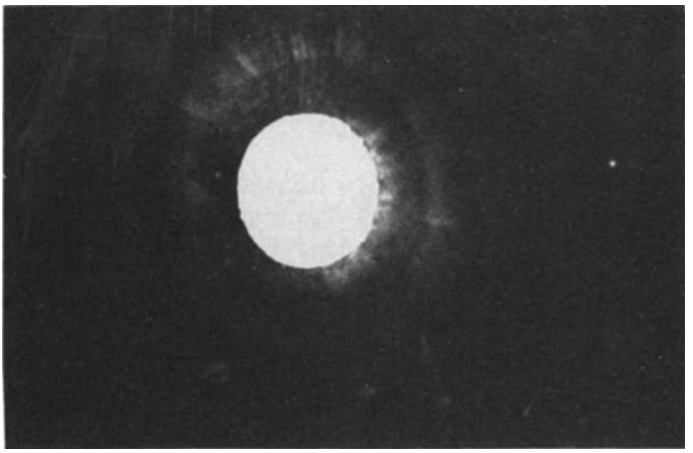

Fig. 3A. From the preliminary experiments: a probably normal moderately pigmented iris.

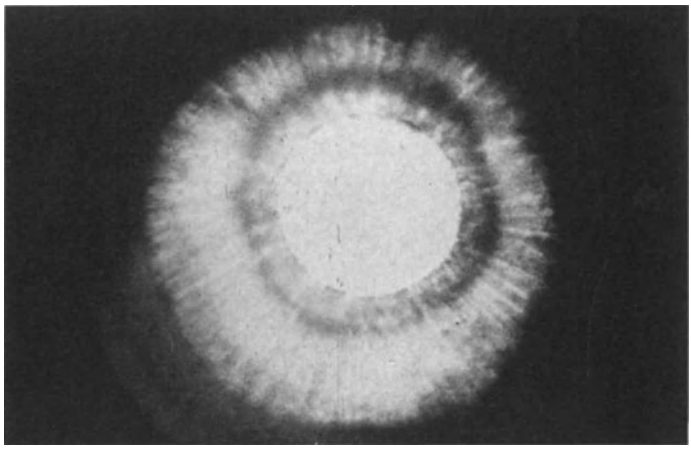

Fig. 3B. From the preliminary experiments: a highly translucent but probably normal blue iris.

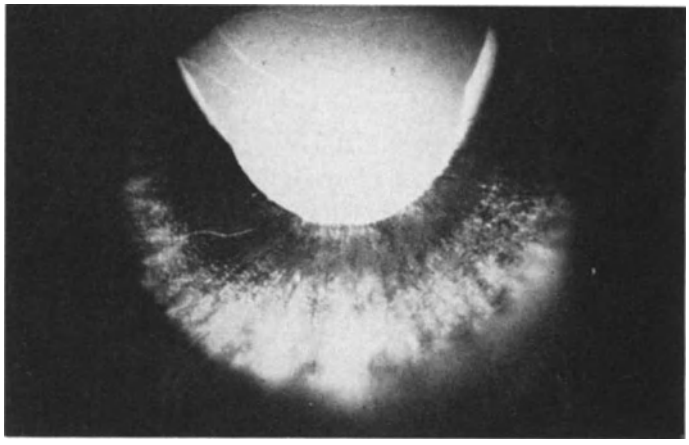

Fig. 4. From the preliminary experiments: iridectomy and pathological diaphany. Static discharge simulating a translucent line.

negative the intensity of the light leaving the pupil. The light passing through the choroidal and retinal pigment of slightly pigmented eyes will be more intense than the light leaving the pupil of heavily pigmented eyes, consequently, the iris appears more translucent – resulting in an impression of pathological diaphany. An example of pathological diaphany is given in Figure 4.

We are convinced that the simplicity of the method allowing photography of the entire iris will certainly contribute to routine iris diaphanophotography.

An advantage of the method is that there is no illuminating light pencil within the pupil occupying space and dispersing light. In consequence there will be less 'noise' and stereoscopy may be easier to perform.

We hope that this outlook in the future soon will be substantiated with facts. SCHIRMER stated in a letter (personal communication 17-10-1972):

'My interest in this method is basically that transpupillary illumination is rapidly reaching its limits as a useful method. When we look into a room through a key hole one shouldn't have to illuminate the room into which one looks first. This is actually the idea of transillumination and by cutting down the red content with green filters it is attempted to get a more balanced illumination of the inside which, of course, is diffuse and not focal. Both, however, can be easily combined, that is, transscleral illumination through the pupil as well'.

This fits in very well with the statement of REMKY, AMALRIC, BESSOU & FARENC (1965):

'En effet, si nous avons intitulé cette communication note préliminaire, c'est que nous avons conscience que ces technique diaphanophotographique sont promises à un très brillant avenir'.

This new apparatus with its electronic camera may also allow accurate documentation in various other fields of medicine, e.g. in sinus opacities, in competition with infrared photography and in hydrocephalus in young infants.

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ILLUMINATION IN EYE PHOTOGRAPHY

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ABSTRACT

Understanding of the essentials of illumination is compulsory for obtaining high quality eye photographs. The characteristics of illumination, both spatial (direct and indirect illumination, retro-illumination and reflecting illumination) and spectral (infrared, red-free, blue and ultraviolet, and the selection of filters for angiography) are discussed. It is hoped that this contribution may help the ophthalmologist to translate his visual impression more accurately into photographical terms.

The various techniques of illumination which we use in visual ophthalmic examination often result, by a combination of impressions, in a satisfactory composite picture. However, analysis and selection of these techniques allow a much more precise presentation of details. (BERLINER 1943, DUKE-ELDER 1962). Especially in slit lamp examination the experienced diagnostician is recognisable by his correct lighting technique. The requirement of optimal illumination applies particularly to eye photography, for one single picture has to yield the same information as in visual examination is gained by scanning. At the present time it is possible to a great extent to translate impressions into photographic pictures. The main reason is that in modern equipment like the photoslitlamp and the fundus camera the light rays from the continuous light source coincide with those the of flash light. Thus we can predict from what we see in the viewer what kind of effect one particular type of illumination will have on the final picture. In this review we will analyse the merits of several modes of illumination used in eye photography. Moreover, some principles of illumination using specific wavelengths will be discussed, while other properties like coherence (LASER) and polarisation, because of their restricted practical value, are only mentioned here.

1. DIRECT ILLUMINATION

The object is illuminated directly.

a. Frontal illumination (Fig. 1 A)

The angle between the direction of illumination and examination (photography) is small, usually 30° or less. It is a useful lighting for:

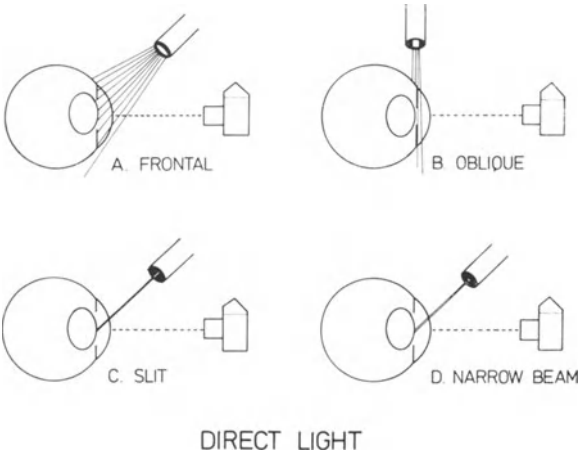


Fig. 1. Different techniques of direct illumination. Figures show the light source with diaphragm, illuminating beam (continuous line) and the light beam to the camera (interrupted line).

– General purposes, e.g. photography of body and face;
– Photography of the anterior segment of the eye using a conventional flash light placed beside the objective. The corneal reflex is near central and there are no problems of shaded parts. On the other hand, the scattering of light in the foremost parts of the eyes makes it virtually impossible to depict objects lying deep to the pupillary plane. Softness of the picture can be achieved by placing a diffusing screen before the light.

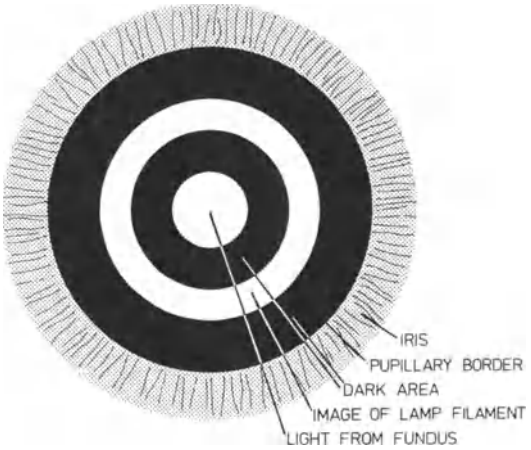


Fig. 2. The pupil in photography of the fundus. Separation of incident and returning light prevents the appearance of corneal and lens light reflexes in the picture.

– Fundus photographs. As a consequence of the restricted size of the pupil the light beam enters the eye at a very acute angle to the camera axis, resulting in a frontal type of illumination. The problem of avoiding corneal and lens reflexes is solved by separating the lighting beam from the light returning to the film, in such a way that, in the pupil, each occupies its own territory (Fig. 2).

b. Oblique illumination (Fig. 1 B)

The object is illuminated from aside, at an angle larger than 30°. Extremely oblique lighting is specifically useful for emphasising surface relief. While this is incidentally used for reproducing minute uneven areas of the adnexa and skin, the main indication is photography of the anterior segment of the eye, especially alterations in the shape of the iris-lens diaphragm. For instance, the convex shape if the iris in eyes with a very narrow anterior chamber is rendered much more impressive by oblique than by frontal illumination. Shadows may become too black in this technique, and this strong contrast may be mitigated by using the fill-in light of the slit lamp, or otherwise a small reflecting screen placed opposite the light.

c. Slit-shaped illumination (Fig. 1 C)

The light aimed directly at the object is bounded by the focussed image of a slit-shaped diaphragm the width of which may be varied at will. This simple device, invented in the early twenties, has resulted, as we know, in a dramatic improvement of our diagnostic possibilities. The image of the slit-shaped diaphragm produces an optical section, although optimal definition is present only in the focal plane. A broader beam is useful when the object should be illuminated both directly and indirectly. The value of the broad beam lies in its manoeuvrability, which allows quick scanning. When the slit is very narrow, a real optical section is produced, which enables us to visualise the internal structure of tissues that are transparant but still dispersing some light, such as the cornea and the lens. In viewing an optical section, we have the advantage over examining microscopic sections, that we may move our slit lamp sideways over the object, so that adjoining sections blend into each other. This advantage is lost in photography so that we are obliged to accumulate maximum information into one representative picture. An essential feature of slit light is the avoidance of surface scatter, so that visualisation of deeper-lying structures, even of the fundus, is possible. These two features of slit light, viz. producing optical sections, and penetrating deeply into the eye, characterize the modern photoslitlamp as the preferred tool for anterior segment photography.

In handling it, we must be aware that there are three optical systems all of which must be focussed on the object, namely:
- the microscope (both oculars must be checked separately);
- the camera with its objective;
- the slit light.

Each of these three systems has its own depth of focus. A series of test photographs is required to show to the individual photographer, the positioning of both oculars separately in order to obtain a sharp image of a test object, and to prove that in that same place of the test object the extremely narrowed slit is optimally sharp. A further quality in which photography differs from visual examination is the more restricted range of contrast. When using the narrow slit, very little light is scattered from the optical section, so that all other parts of the picture are rendered dark. To overcome this undesired effect a fill-in light is mounted on modern slit lamps, which flashes simultaneously with the main light. Its position and intensity can be varied. This gives a much better orientation of the slit into the whole picture (Fig. 6 A). Direct slit illumination is useful in photographing almost every visible part of the eye: conjunctiva, cornea, iris, lens and vitreous. By utilising diagnostic contact lenses, also the chamber angle, and the fundus, from its posterior pole up to beyond the ora serrata can be photographed. Photography of these deeper parts with the slit lamp requires considerable skill. Moreover, the problem of fill-in light is not yet adequately solved for fundus photography.

d. Narrow bundle illumination (Fig. 1 D)

The illuminating light bundle is of restricted height and width. Width is adjusted by the slit-diaphragm, and height is adjusted by a second diaphragm. Thus the bundle may be varied in size as well as in direction. It is used specifically to demonstrate turbidity and cells in the anterior chamber fluid. The sharp delineation of the bundle emphasises the minute contrast between the lighted, gray, opaque fluid and the unlighted, dark surroundings. If the turbidity is little, focussing may be difficult and is best done by first focussing on the cornea, then on the lens and finally somewhere between. The pupil serves as a dark background. The optimal direction and size of the bundle may differ for photography and visual observation, so that for difficult cases it is recommended to take several exposures under varying conditions.

2. INDIRECT ILLUMINATION

The area to be photographed receives its light from a directly illuminated adjoining area.

a. Indirect illumination in strict sense (Fig. 3 A)

Here, too, the effect of varying slit width, the direction and decentration of the incident light in regard to the object can be chequed visually, up to a certain degree. This critical preparative viewing discloses that tissue condensations situated in more or less opaque surroundings, such as corneal maculae or processes deep in the iris mesoderm, become visible only by carefully adjusted lighting. A convincing result of this technique is the visualisation of the normal pupillary sphincter muscle or the border of a colobomatous lens (Fig. 6 B).

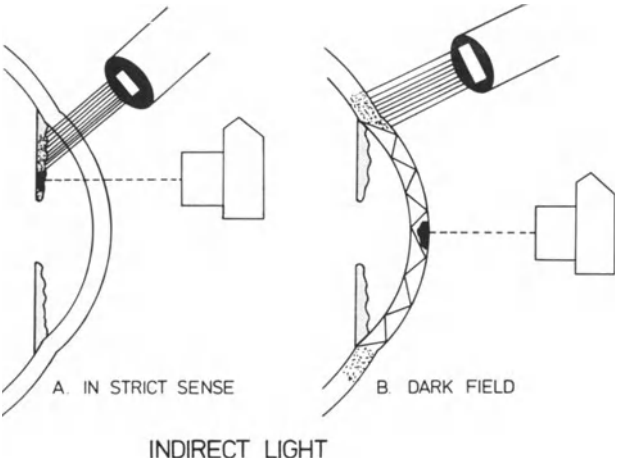


Fig. 3. Two different ways of indirect illumination. The illuminated area acts as secondary light source.

b. Dark field illumination (Fig. 3 B)

This method consists of indirect illumination of corneal nebulae from scleral scattered light. The sclera near the limbus is illuminated with a large patch of light. As the camera is focused on the corneal nebula it is in most cases necessary to decentre the direction of the light from that of the observation. The scattered light from the illuminated sclera travels, due to total reflection, along the outer parts of the corneal stroma, which is recognisable by the secondary illumination of the opposite scleral part. The corneal nebula is illuminated by this intra-corneal light and the whole surface pattern appears with surprising clearness and contrast against the non-illuminated, dark background.

3. RETRO-ILLUMINATION

The aim is silhouette-like imaging of an opacity in the optical media against an illuminated part of the eye. With this technique, decentration of the illuminating light may be necessary, as this light should pass along the opacity at which the camera is focussed. The directly illuminated surface may be:

a. The lens (Fig. 4 A)

Especially when opaque, the lens provides a brightly illuminated background.

b. The iris (Fig. 4 B)

A typical example is the inspection of the site of the cornea where a foreign body has been removed; if this has been effectively done, only some transparent

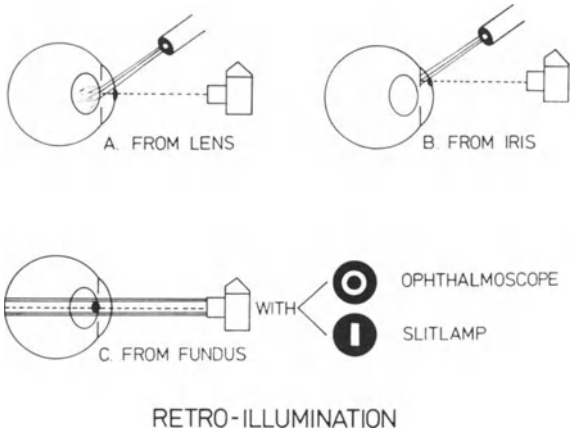


Fig. 4. Three different techniques of retro-illumination. The shape of the illuminating beam is shown separately in C.

coloured patch of impregnated iron salts remain, which may be left alone. If, on the other hand, a dark silhouette is seen, further removal is mandatory. Also, with this technique, ingrowth of fine vessels into the cornea is more clearly appreciated.

c. The fundus (Fig. 4 C)

The incident light from the photoslitlamp or the fundus camera should nearly coincide with the optical axis of the objective of the camera. The pupil should be maximally dilated and the incident light should avoid, as much as possible, the iris, in order to avoid scattering of light. In this technique, decentration is

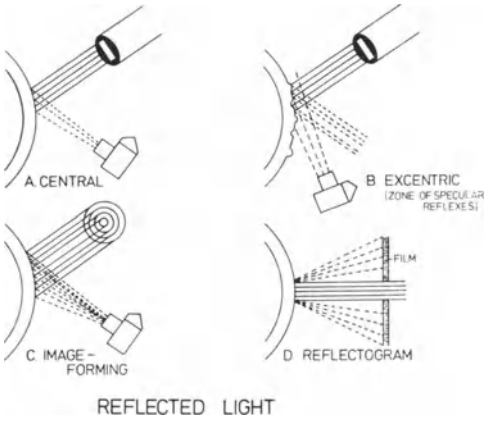


Fig. 5. Four ways of photography in reflected light. Of these, method B is most frequently used.

restricted due to the pupillary diameter. Consequently the opacity is illuminated both frontally and from the rear. As the intensity of the reflected light from the fundus is greater than that of the frontal light, a silhouette effect is created.

Not only opacities of the media, but also an abnormal diaphany of the pigment layer of the iris is a very suitable situation for this type of photography (Fig. 7). In this case, the slit lamp has the advantage over the fundus camera that the beam of incident light, directed axially, can be restricted in size so as to fill the pupil without illuminating the iris, avoiding as much as possible light scatter (Fig. 8).

Finally, the method is very appropriate for depicting optical effects caused by such conditions as keratoconus, lenticonus, and subluxation of the lens.

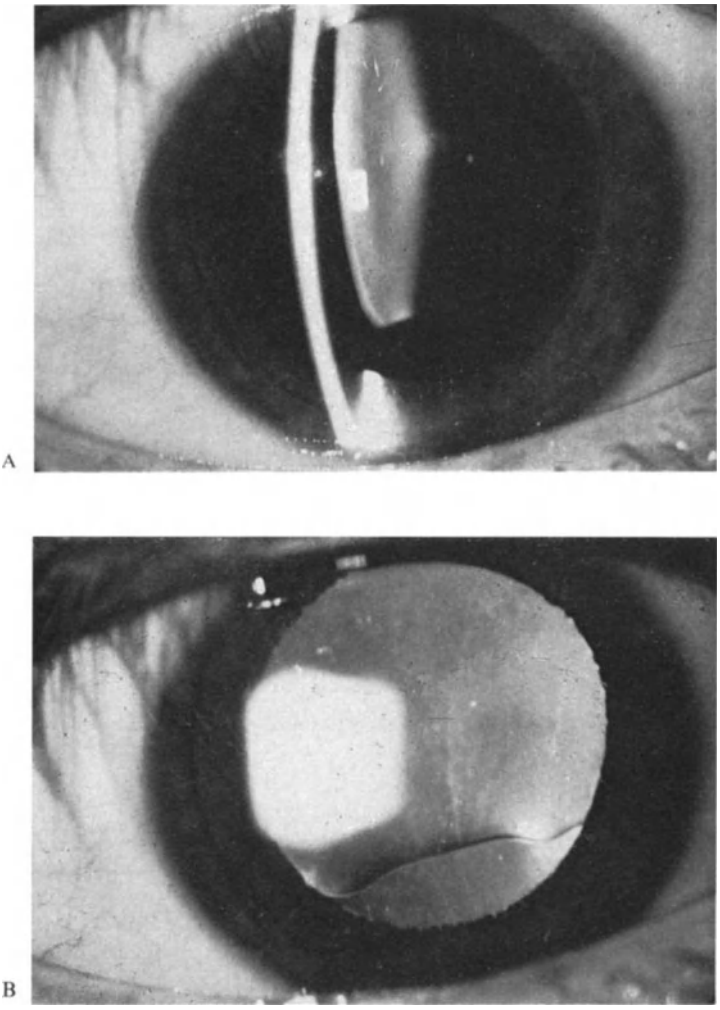


Fig. 6. A: Lens coloboma in optical section. B: The same eye in retro-illumination.

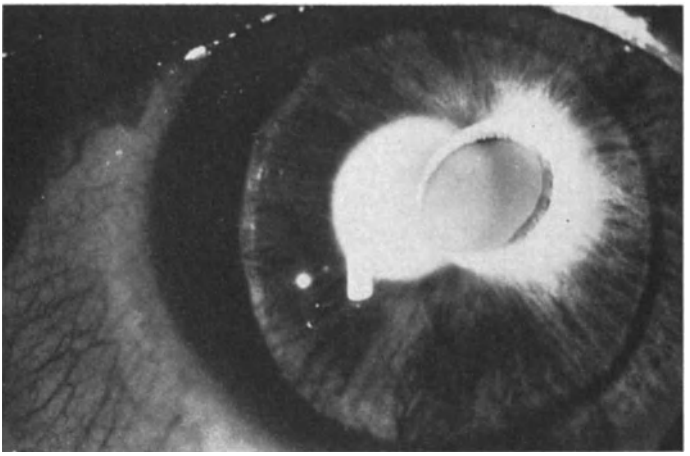


Fig. 7. A case of diaphany of the iris, shown in retro-illumination. As the incident light beam was wider than the pupil, some direct iris illumination occured, causing troublesome light scatter. The sharply defined dark ring is caused by total reflection at the lens equator.

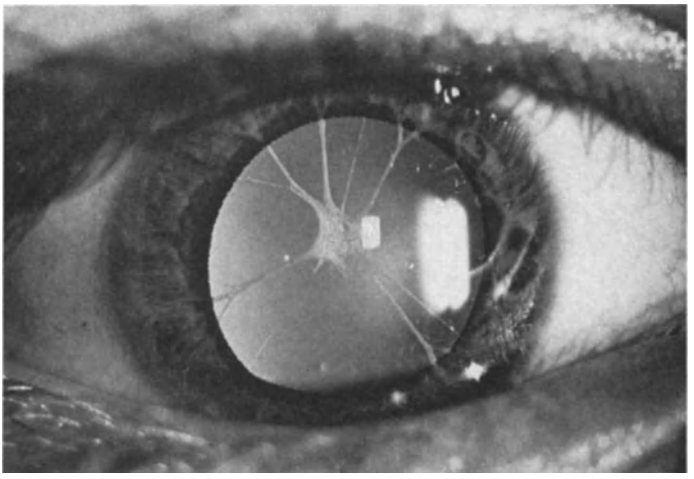


Fig. 8. Membrana pupillaris. The anomaly is visible in a combination of frontal and retro-illumination.

Of the results obtained with the various lighting methods, the results of retroillumination correlate best with the visual impairment of the patient, as both depend on the qualities of transmitted, rather than those of incident light.

4. REFLECTED ILLUMINATION

Any image formation using the reflective properties of cornea, lens and retina.

a. Central (Fig. 5 A)

If the illumination and the observer's eye are placed according to the law that the angle of incidence and of reflection are equal, a dazzling bright light patch appears on the reflecting surface and very slight irregularities in this surface are clearly visible. The camera should be focussed on the reflecting surface.

A special case is that of fundus reflexes. The angle of incidence and of reflexes are both nearly zero. The reflection from the internal limiting membrane appears as a more or less continuous pattern, which, however, can be greatly modified by slight changes in the incidence of the light, indicating that there are no appreciable variations in prominence. In the case of a really prominent lesion such as a papilloedema, the retinal and vascular light reflexes are not only interrupted, but, moreover, they do not change their location on shifting the incident light.

b. Eccentric (Fig. 5 B)

When the angles of incidence and observation/photography are slightly different, the reflecting surface as such does not create the image. Slight irregularities in this surface, however, act as little convex or concave mirrors, thereby creating a very lively picture of the surface relief outside of the central field of reflection. This (extended) field is called the area of specular reflection. As no reflection surface is perfectly smooth, the area of specular reflection is formed whereever two media of unequal optical density are separated by a continuous surface. By changing the place and direction of the light and the camera, the whole of such a surface may be scanned, or representative areas for photography may be chosen.

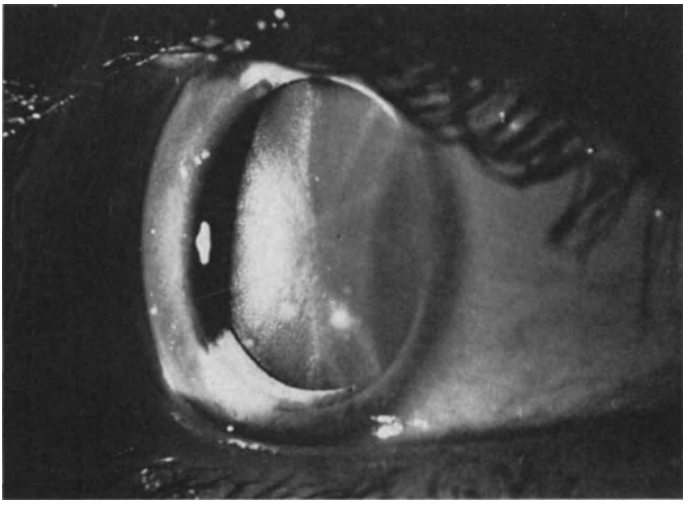


Fig. 9. Specular reflections on a normal anterior lens capsule. The underlying lens sutures are clearly visible.

Impressive pictures can thus be obtained from the anterior capsule of the lens with its intricate structure and of the zones of discontinuity of the lens (Fig. 9).

c. Reflected pattern illumination (Fig. 5 C)

Image-formation of the pattern of the light source by way of a reflecting surface. Just as, in shaving, we may focus on either the mirror or on our face (the light source), we may focus our camera on the corneal surface (the mirror) or on the light source. The daylight-illuminated window may act as such a light

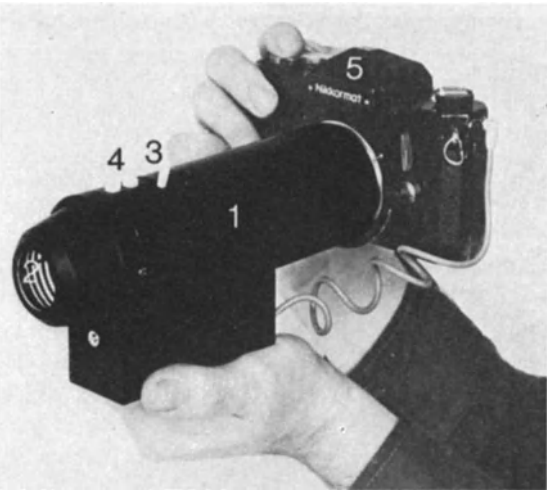


Fig. 10. The E.H.R. photokeratoscope. 1: Extension tube; 2: Target; 3: Diaphragm lever; 4: Flash control; 5: Camera.

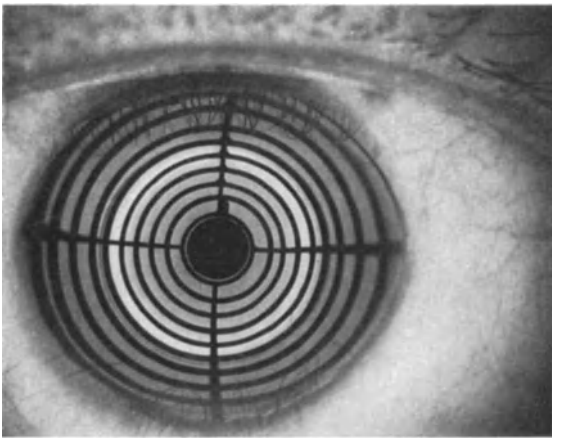


Fig. 11. Photokeratogram of normal cornea. The ring pattern is evenly distributed over the whole cornea.

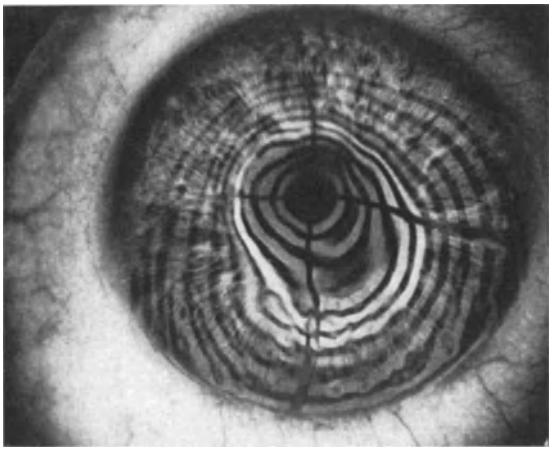


Fig. 12. Photokeratogram in irregular astigmatism.

source, but much more information is to be gained from a purposedly designed pattern such as the Placido disc, placed in front of the light source. By sophisticated modifications of the Placido pattern the reflected picture covers the whole of the corneal surface. The distance between the rings are chosen in such a way that in normal cases these distances are recorded as about equal. This creates the possibility of a very exact evaluation and follow-up of changes in the corneal surface (Fig. 11 and 12).

Recently, an apparatus satisfying these requirements has become available as a compact unit (AAN DE KERK et al.; Fig. 10).

d. Reflectography (Fig. 5 D)

A beam of light reflected by the cornea can form without interference of any refracting unit an image on a photographic film. This image is to represent the grouping of reflected rays caused by minimal corneal irregularities. This effect is comparable to the patterns of light resulting from the reflection of sun rays on an undulating water surface. Image definition has been improved by the use of coherent light of a Laser. (SCHWEIZER, 1967).

Up to now the method possesses only experimental value.

5. ILLUMINATION OF SPECIFIC WAVELENGTHS

Spectral influences on the image formation are mainly:
- the spectral composition of the light source;
- the filter transmission characteristics;
- the reflecting, absorbing and transmitting qualities of the object;
- the spectral sensitivity of the film;
- fluorescing properties of the object or of artificially added substances.

Apart from these, other factors are also operative, e.g. the developing, printing, viewing and projecting of the pictures. In view of this multitude of factors, many

of which are hard to standardize, it is not surprising that, besides scientifically founded methods, there exist many experimental recipes that are difficult to reproduce and consequently, are hard to evaluate. Trials of ophthalmic photography using monochromatic lights over a wide range (BEHRENDT et al. 1965 and 1966) are helpful to build up a body of experience. Rather than trying to give all data published thus far we will indicate the working principles underlying those methods which have proven to be of value.

a. Infrared illumination

Its specific use is correlated with the properties of these long wavelengths. These rays penetrate opaque media easier, and therefore give better recordings of iris atrophies, colobomas, posterior synechiae and the like photographed through an opaque cornea. (DEKKING 1933 and 1934). Other examples are: recording of fundus detail in the presence of opaque vitreous (Kodak 1969) and of normal and diseased choroid through the pigment epithelium of the retina, even in the macular region (ALMARIC 1971).

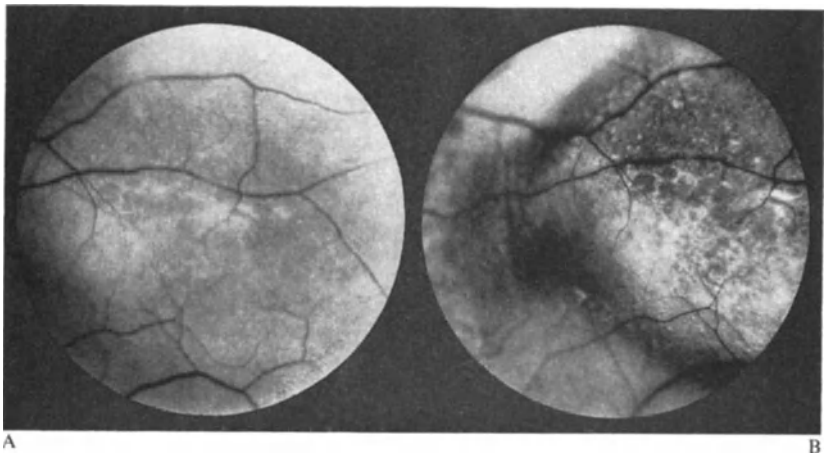
Due to the spectral composition of the light, infrared typical effects can be produced as a result of specific absorption and reflection in the ocular tissues. Whereas on infrared colour film superficial pigmented lesions such as conjunctival and retinal naevi appear dark red, these same lesions appear dark blue when shielded by an opaque substance. Due to the easy transmission in blood, retinal vessels and haemorrhages are nearly invisible. For that reason, they are easily differentiated from dark-appearing pigmentations. As the choroidal network contrasts sufficiently against the sclera, the choroidal vasculature can be recorded in the presence of an intact pigment epithelium. Some indications for infrared photography emanating from the foregoing are the recording of choroidal processes of obliterative, neoplasmatic or reparative nature, and macular degenerations, especially when the alterations are difficult to interpret, like in senile disciform degeneration. The advantage of infrared photography in recording a malignant melanoma of the choroid is illustrated in Figure 13.

For infrared recording, infrared black and white film may be used instead of infrared colour film. This has the definite advantages of being more economical, faster and of greater latitude, and easier in storage and processing. With this film pigment appears dark, and blood is concealed for the greater part.

Technically, the light from the electronic flash unit should be filtered in such a way that all visible light for which the film is sensitive too, is excluded. This filter should therefore be fastened in front of the camera in an absolute light-tight way. Because of the less convergent action of the objective on these rays than on visible light, focussing should be aimed at a point slightly in front of the object (a slight increase of the lens-film distance).

b. Red light illumination

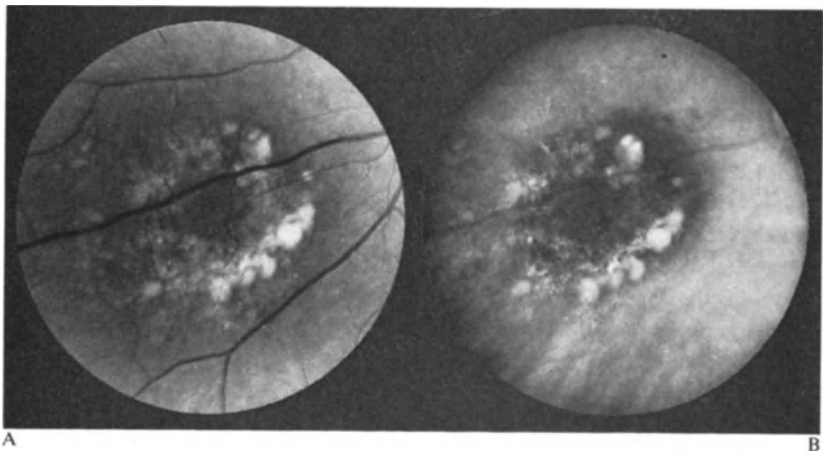
Many a feature of infrared illumination is displayed, though less characteristically but with considerably more ease in operation by using visible red light.



A B

Fig. 13. The advantage of infrared photography in recording deep fundus lesions. A: Choroidal malignant melanoma: black and white print from an unfiltered colour transparancy. B: The same fundus, printed from a transparancy taken with a Schott GG 14 filter and Kodak Ektachrome Infrared film IE 135-20.

A Kodak-Wratten filter No. 29 or a similar filter mainly transmitting red light, placed in front of the film, in combination with a conventional colour or panchromatic black and white film, will give satisfactory results (Fig. 14). Both for infrared and red light photography the results are somewhat more predictable and therefore the indications more clearly defined when the observer first examines the object in the red light transmitted by the same red-filter or in the light of an unfiltered neon-discharge tube (BALLANTYNE et al. 1970). To do this, the observer should be adapted to darkness or to green light.



A B

Fig. 14. The advantage or red light illumination in recording deep fundus lesions. A: Drusen of the choroid, arranged in a ring-shaped pattern. From a colour-transparancy. B: The underlaying choroidal naevus is much better visible with red light (Filter: Kodak Wratten No. 29; film: Kodachrome II).

c. Red-free illumination

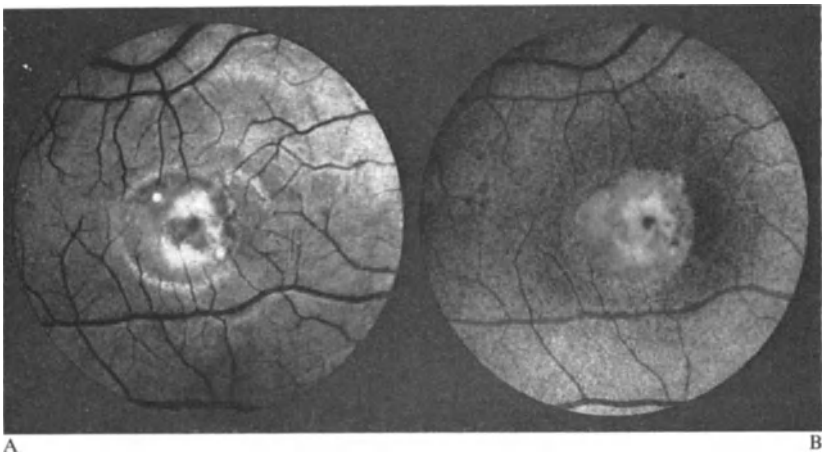
This is an illumination used especially for fundus photography, and is produced by a conventional electronic flashlight in combination with a green filter, excluding long wavelengths and most of the shorter ones. It may be used in combination with colour film or with black and white film (panchromatic or orthochromatic emulsion). With colour film, the whole fundus is green-coloured, and the macula stands out as a yellow spot. Both with colour or black and white film the reflexes from the internal limiting membrane of the retina, and the structure of the nerve fibres, are vividly displayed. Red-free light is, for the greater part, reflected by pigment, so that the choroid is invisible, and deep pigmentations are only weakly displayed. The red light is absorbed by haemoglobin so that blood vessels of the retina and retinal haemorrhages are nearly black. This results in optimum contrast and hence very sharp definition of the smallest vessels. Typical indications for this method of illumination are:

- superficially-situated lesions in the retina, like minute exudates and degenerative spots, more specifically early vessel changes in arteriosclerosis, hypertension and diabetes; micro-aneurysma, pin-point haemorrhages, new vessel formation, cysts and holes in the retina.
- changes in the nerve fibres, such as coarseness of the fibres in optic neuritis, and patch-like disappearance in cases of optic atrophy.
- Alterations of the macular yellow in macular degeneration, and its absence in albinism.
- Disappearance of the normal macular reflexes in macular degeneration; formation of superficial retinal wrinkles in papilloedema, macular and retinal oedema resulting from scleral deformation or hypotony.

Whereas the designation red-free is rather vague, illumination with monochromatic light in these short-wave regions yields a still more detailed information of the optimal wavelength for recording various structures. Thus, green light is best for recording the macular area and macular reflexes and retinal vessels, while shorter wavelengths (more blue) are needed for recording papillary and fine macular vessels, and also nerve fibres. (BEHRENDT et al. 1965 and 1966). Experiments with broader band transmission filters gave similar results (MINUZO et al. 1971, BALLANTYNE et al. 1970). The main differences in photography using light with and without red rays can also be demonstrated by using black and white panchromatic and orthochromatic film respectively, together with unfiltered light from the electronic flash. On panchromatic film the deep structures are better displayed, whereas the more superficially located structures appear in much more detail on orthochromatic film (CRAANDIJK et al. 1969, Fig. 15).

d. Blue light photography

With an ordinary cobalt blue filter placed in front of the electronic flash, fluorescein-coloured areas of the conjunctiva, the cornea and the tear lake appear bright yellow, in striking contrast to the blue surroundings which serve only as a general orientation of the whole image. For still more contrast the



A B

Fig. 15. Orthochromatic and panchromatic film. In this case of vitelliruptive maculopathy. A, taken with orthochromatic black and white film (Agfa Copex Ortho) accentuates the fundus reflexes and retinal vessels, while B, taken with panchromatic black and white film (Agfa Copex Pan) clearly demonstrates the widespread granular lesions of the pigment epithelium.

blue-coloured surroundings may be suppressed with a yellow filter placed over the front lens of the camera. It provides additional information to a regular colour slide.

e. Ultraviolet photography

Only the long wave part of the ultraviolet radiation will be considered. The wavelengths are:
- emitted by ordinary electronic flash units;
- transmitted by most camera lens objectives;
- innocuous to the eyes in the usual photographic dosage.

Because of the light scattering in the ocular media, the long wave ultraviolet can only be used for photography of superficial structures. This part of the spectrum is strongly absorbed by pigment. Pigmentations of the skin, such as melanomas and phenothiazine deposits, are accentuated and appear black, while light areas, such as vitiligo, appear still lighter. Pigmentations of the conjunctiva and cornea and specific corneal alterations such as the Kayser-Fleischer ring also appear black (Fig. 16 B). Due to the fluorescence of the lens, the pupil appears light. Any electronic flash may be used, but the Balcar unit has a practical tube-shaped ultraviolet transmission filter fitting over the flash lamp. Alternately, one may place the filter (e.g. a Schott U 95) in front of the film. Any slow-acting black and white film may be used, but the Agfa Isopan FF has proven satisfactory (VAN DER KAMP, 1972). A colour film like Ektachrome yields also good results (STEIN, 1957).

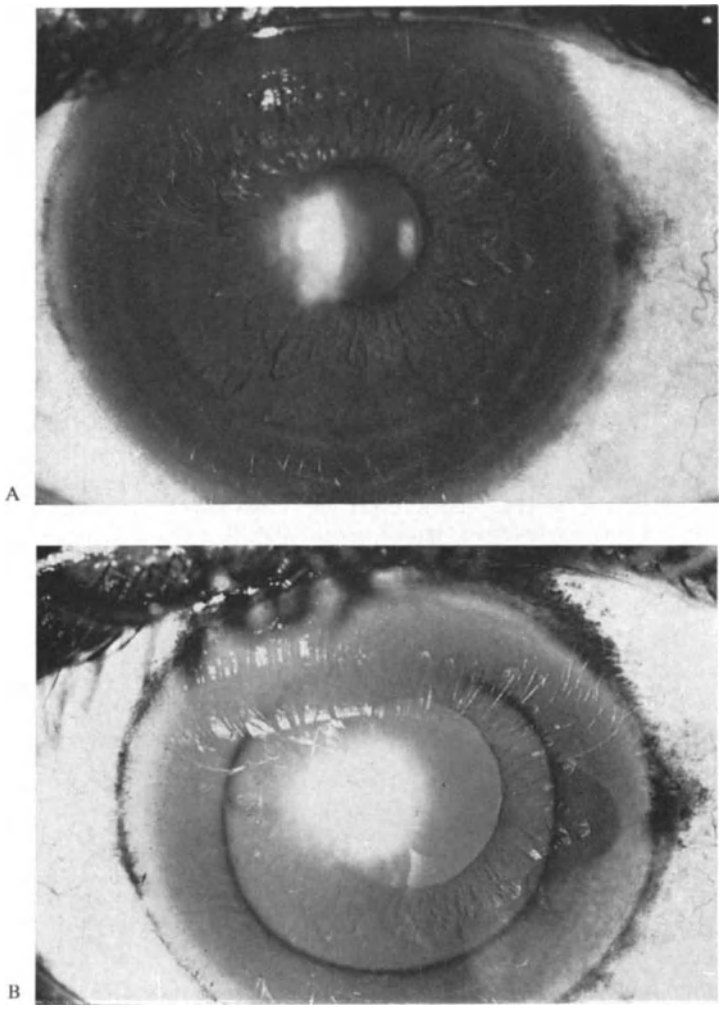


Fig. 16. Kayser-Fleischer ring in the cornea. A: Print from a colour transparancy. The ring is hardly visible; B: Ultraviolet photograph (see table 1). The Kayser-Fleischer ring stands out clearly.

f. Fluorescein angiography

In order to emphasize the contrast between tissues containing fluorescein and those which do not, use is made of the property of fluorescein viz. that this substance, if illuminated with blue light, emits yellow light (fluorescence). Hence, when an exciter filter transmitting only blue light is placed in front of the light source, and a yellow barrier filter is placed in front of the film, only light emitted by fluorescein is recorded. The exciting possibilities of this enormous field are discussed elsewhere in this volume.

g. Infrared absorption angiography

Although the choroidal network can be recorded in infrared and red light photography, these rays are easily transmitted by the choroidal vessels, resulting in a rather weak contrast. In order to accentuate this contrast, and, moreover, to demonstrate dynamic changes in the choroidal circulation, Indocyanin

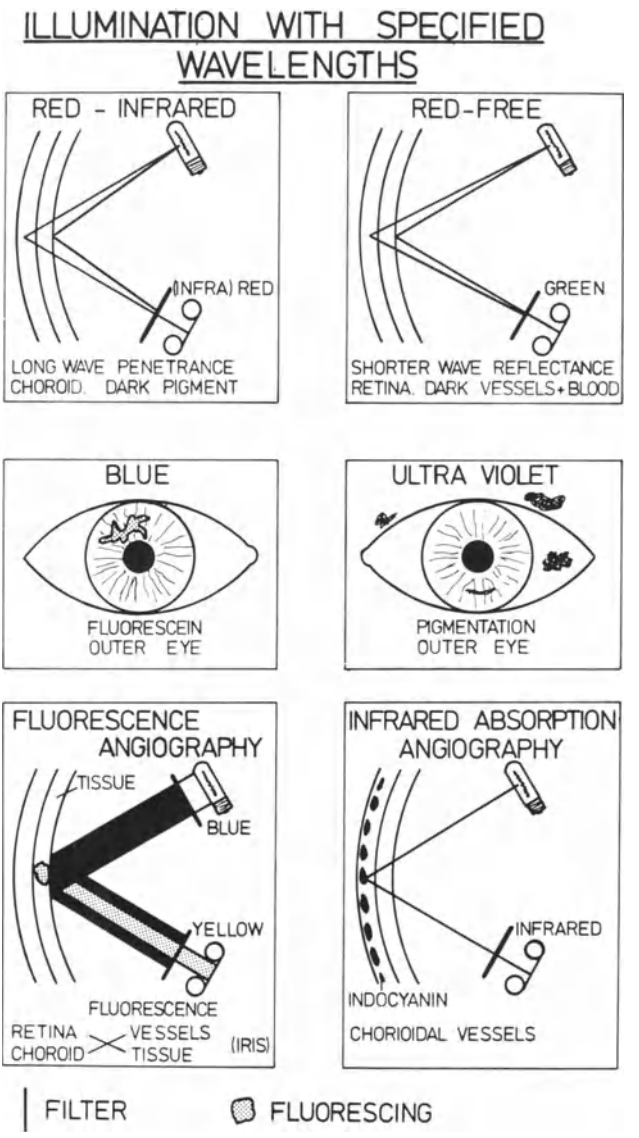


Fig. 17. Memotechnical drawings of the characteristics of various techniques of spectral illumination in eye photography.

(Cardiogreen) can be injected into the blood stream. This substance absorbs red and infrared radiations. Areas where this absorption occurs are recorded on infrared colour film as dark blue, and on infrared black and white film as black. In this way, the choroidal vasculature is recorded with good contrast, also in the macular area. The method is still in the experimental stage, as it suffers from the following inconvenients:

- Cardiogreen is very expensive;
- In order to obtain sufficient contrast, intracarotidean injection is needed (KOGURE et al., 1970). However, experimental work with infrared black and white film suggests the future possibility to use the intravenous route (HOCHHEIMER, 1971).

A survey of a number of techniques using restricted wavelengths is presented in Table 1. Some basic features are depicted in Figure 17.

TABLE I

Method	Filters	Film	Diagnostic features
Infrared (colour) photography	K.12 (deep yellow) or Schott GG 14	Kodak Ektachrome infrared	Penetration into opaque tissues. Deep pigment: blue. Choroidal vessels: deep red.
Infrared (black/white) photography	K.88A or K.87 or K.89B (infrared)	Kodak High speed infrared (x)	Penetration into opaque tissue. Deep pigment: dark. Choroidal vessels: dark.
Red light (colour) photography	K.29 (deep red)	Kodachrome II	Penetration into opaque tissue. Deep pigment: dark red. Choroidal vessels: deep red.
Red light (black/white) photography	K.29 (deep red)	Agfa Copex Pan	Penetration into opaque tissue. Deep pigmentation: dark. Choroidal vessels.
Red-free (colour) photography	K.58 (green) K.65A (deep green)	Kodachrome II	Green-coloured fundus Emphasis on superficial retinal changes. Retinal vessels: dark. Enhanced retinal reflexes. Sharp definition of detail.
Red-free (black/white) photography	K.58 (green) K.65A (blue green)	Agfa Copex Ortho	Same features, except green colour.
Blue light (colour) photography	K.47A Sch BG 12 1 mm (blue)	Ektachrome	Fluorescein colouring of exterior of the eye.
Blue light (black/white) photography	K.47A Sch BG 12 Leitz KP.490	Agfa Copex Ortho	Papillary vessels. Nerve fibres. Smallest retinal vessels.

Method	Filters	Film	Diagnostic features
Ultraviolet (black/white) photography	Schott U 95 2 mm Balcar U.V. Shell (ultraviolet)	Agfa Isopan FF	Pigmentations of skin, conjunctiva and cornea. Hypopigmentation of skin. Lens changes.
Ultraviolet (colour) photography	Schott U 95 1 mm Balcar U.V. Shell (ultraviolet)	Ektachrome	The same.
Infrared (colour) absorption photography	K.12 or Schott CG 14 (deep yellow) + K.20 (neutral density)	Kodak Ektachrome infrared (x)	Dynamics of choroidal circulation in blue following intra-arterial injection of indocyanin (Cardiogreen)
Infrared (black/white) absorption photography	K.88A (infrared)	Kodak High Speed Infrared film	The same, in black instead of blue.
(Black/white) fluorescence angiography	Baird Atomic 4 (blue) in front of flash. Baird Atomic 5 (yellow) in front of film.	Kodak Tri-X	Dynamics of retinal and choroidal circulation: Pigment epithelial changes; Tissue damage (binding of dye).

K = Kodak Wratten.

(x) Recently this film has been replaced by Kodak Ektachrome infrared films SO 117, with slightly different characteristics.

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Key words

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Illumination
Filters

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FAULTS IN NEGATIVES AND PRINTS

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Ophthalmic photography plays a very important role in ophthalmological diagnosis, and as such is a photographic technique where at all times a true to life photograph must be the end result. An artistic approach must at all cost be avoided. Retouch is to be considered a major crime, since by this method a series of new diseases can be manufactured in the dark room: the dark room syndrome (Fig. 1).

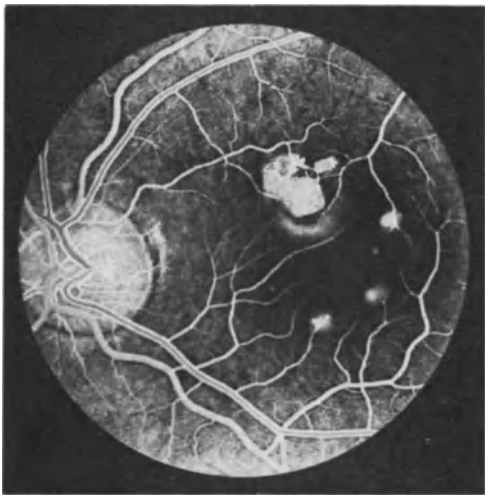


Fig. 1. Darkroom syndrome.

This macula degeneration was made by dropping bleaching agent on a print and photographing this effect through a yellow filter.

From the following series of photographs it will become clear that carefull processing of the film and prints is essential for the correct interpretation of the photographs.

The first series of pitfalls is the faulty alignment of the camera and incorrect focussing of the fundus resulting in various reflexes (Fig. 2 A and 2 B).

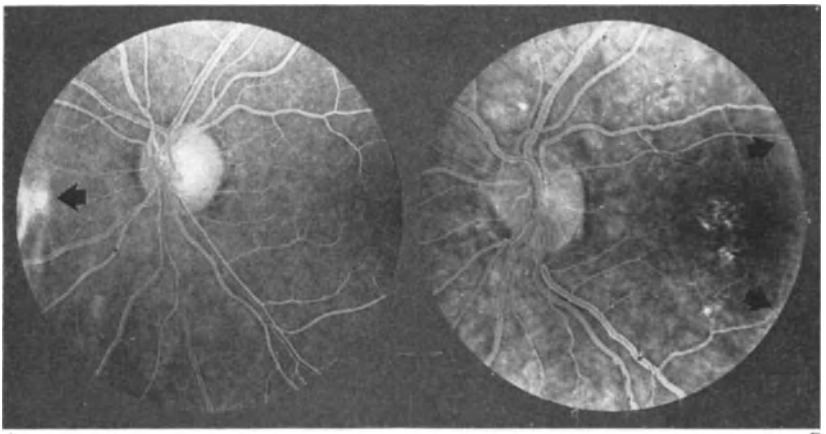


Fig. 2 A and 2 B. Reflexes due to faulty focussing.

A fairly common error is an incorrect flash synchronisation resulting in a partly exposed film (Fig. 3), a similar effect can be obtained by photographing on the first inches of the film.

Dust on the aspheric objective of the fundus camera can certainly with high myopes cause a variety of white spots on the film, they sometimes resemble microaneurysms or small drusen (Fig. 4).

Another fundus camera error occurs when the mirror does not return to its resting position and stays halfway between the camera and the eyepiece. Exposures obtained in this manner will show elliptical reflexes (Fig. 5).

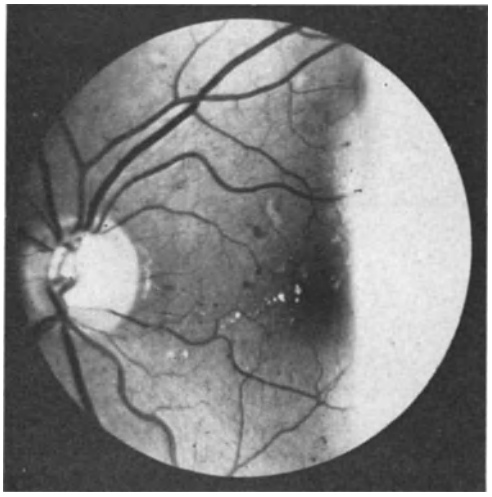


Fig. 3. Incorrect flash synchronisation.

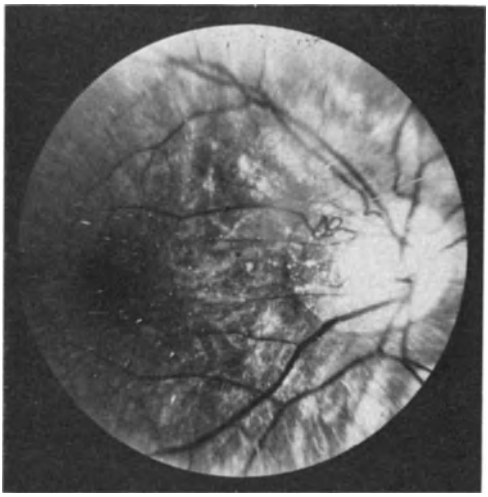


Fig. 4. Dust on the aspheric objective of the fundus camera.

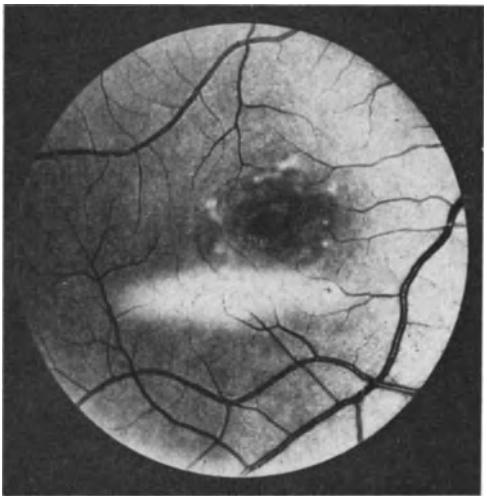


Fig. 5. Mirror of the camera in the halfway position.

Light sensitive patients who fail to keep their eyes open, sometimes need a helping hand, however this help can be too vigorous as is shown in Fig. 6, the foggy finger is the helping finger and not a melanoma of the choroid, which it resembles.

When foreign objects occur between the shutter and the film than black marks may result on printing, in this case a hair is shown (Fig. 7).

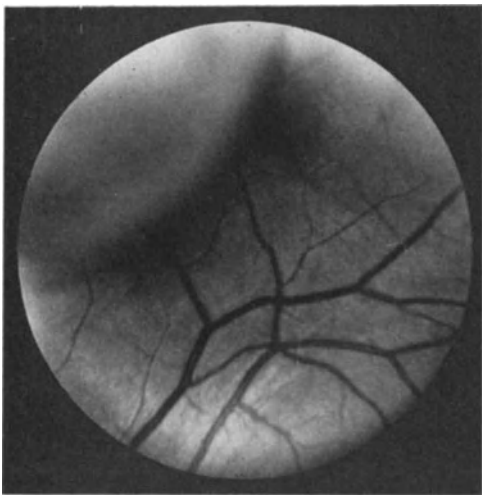


Fig. 6. Helping finger.

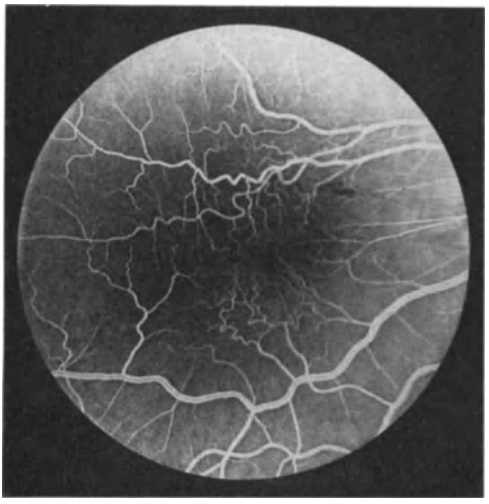


Fig. 7. Hair between shutter and film.

If the film is not locked into the negative holder of the enlarger Newton rings may result in the prints as is shown in Fig. 8.

The following series of errors concern the incorrect handling of the negatives. Firstly abrasion marks caused in this case by grit on the velvet light trap of a casette. These marks may be light or dark (Fig. 9).

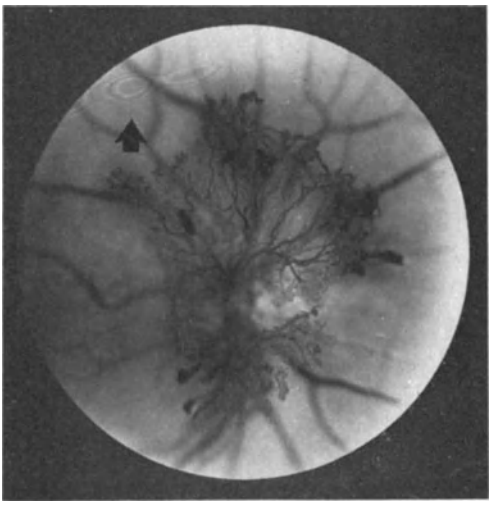


Fig. 8. Newton rings.

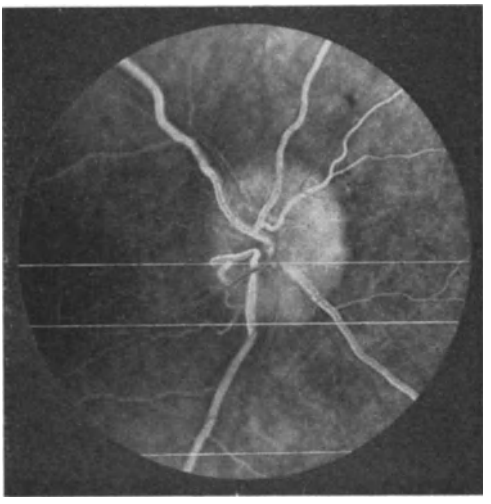


Fig. 9. Abrasion marks caused by grit in the casette.

Rough handling of the film, during washing, may cause abrasion, when an area of the gelatin emulsion is scraped of leaving a white mark (Fig. 10).

The next series of errors are the result of careless handling in the printing process.

Amongst the angioid streaks you see a large white area resembling a finger

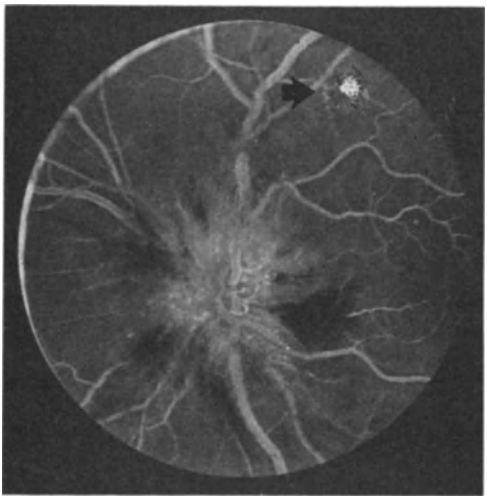


Fig. 10. Abrasion marks caused by rough handling of the film.

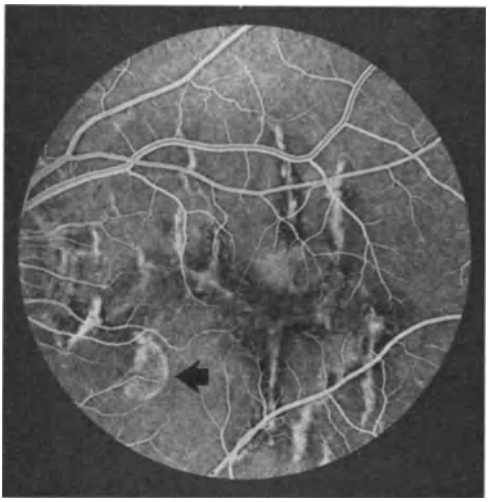


Fig. 11. Finger prints caused by handling the paper with chemically contaminated fingers.

print, this finger mark was caused by handling the printing paper with chemically contaminated fingers (Fig. 11).

Water marks caused by water splashes on the paper emulsion resemble drusen as is shown in Fig. 12.

When splashes of fixer have fallen on the paper emulsion before development

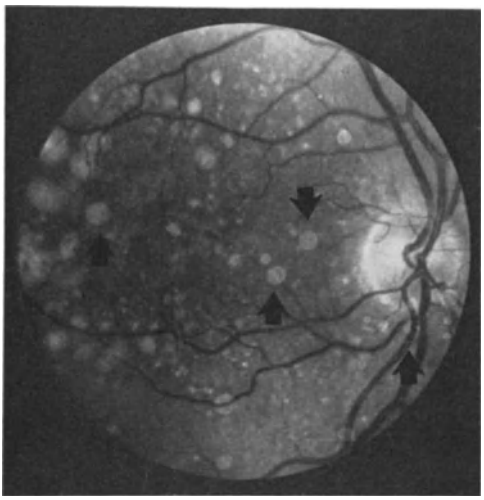
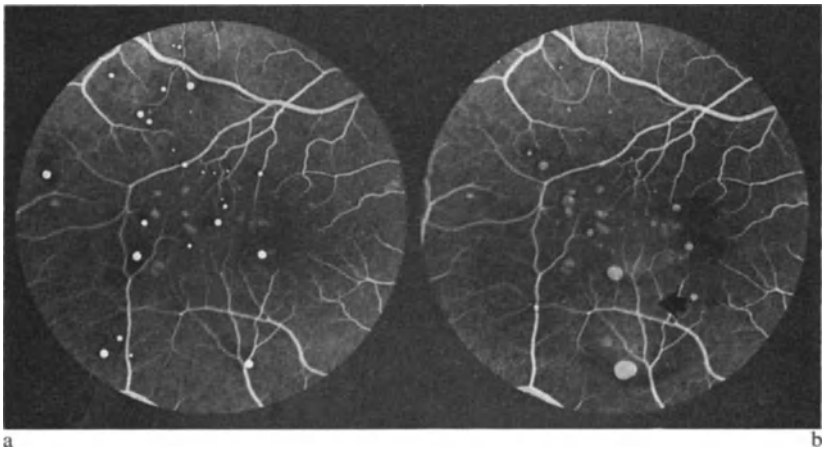


Fig. 12. Water marks caused by water splashed on the paper emulsion.



a b

Fig. 13A. Splashes of fixer on the paper emulsion.
Fig. 13B. Splashes of fixer on the paper emulsion when moved.

than bright white blotches will result, if we repeat this when moving the paper during development than the blotches will become hazier (Fig. 13 A and 13 B).

Overexposure will increase the graininess and shows a gross loss of detail (Fig. 14).

Faults caused by an extended washing time of the prints.

Normally the prints are washed for some 15 minutes, if this time is extended

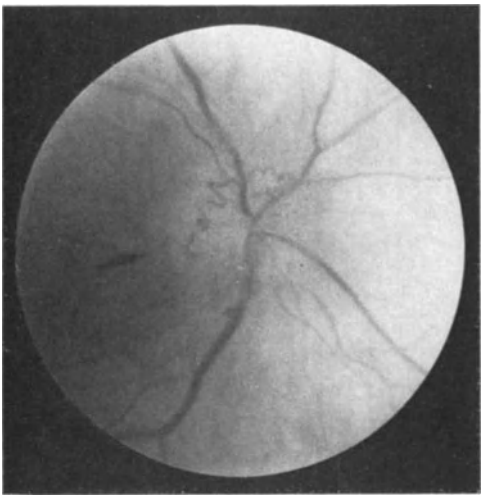


Fig. 14. Overexposure

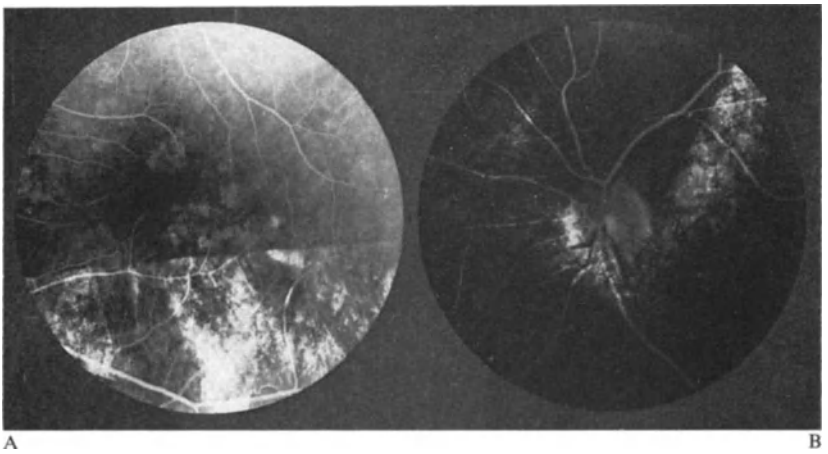


Fig. 15A. Bleaching of the emulsion with extended washing.
Fig. 15B. Bleaching of the paper emulsion due to extended washing.

to some 10 hours a bleaching effect of the emulsion results in the most bizarre fluorescence angiograms (Fig. 15 A and B).

Many are the faults due to careless handling of the film and prints during processing and these may interfere with the subsequent interpretation of the resulting prints.

It is stressed that artistic photographers with a love for retouch should not enter the field of ophthalmic photography (Fig. 16).

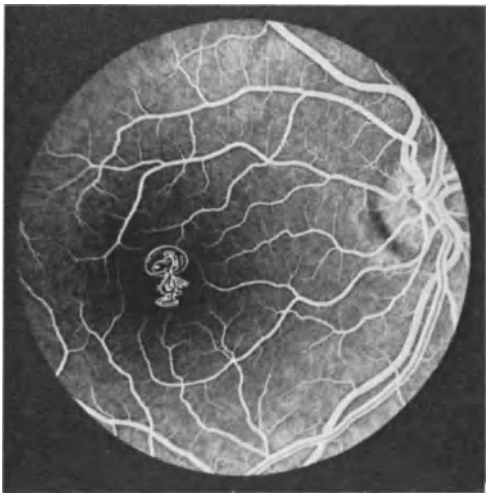


Fig. 16. He speaketh not; and yet there lies
A conversation in his eyes.
LONGFELLOW.

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I am indebted to Mr. C. A. VAN BEEK and Mr. A. L. AAN DE KERK who made the photographs and to Mr. J. S. A. STONE for his artistic work, with apologies to Mr. C. SCHULZ and Snoopy.

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TECHNICAL TIPS FOR OPHTHALMIC PHOTOGRAPHY

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(*Rotterdam*)

EXTERNAL EYE PHOTOGRAPHY

Reducing corneal reflexes and a reflector attachment to the headrest.

In external eye photography the size and positioning of the corneal reflexes are very important, because the reflex may obscure the area to be photographed and thus may mask details. That's why we must keep the reflex of the lightsource as small as possible. We can do this effectively by putting the electronic flash further away from the subject, or remove, or black the lamp reflector, or tape off it partly (Fig. 1). Last method is the simplest (KODAK, 1972).

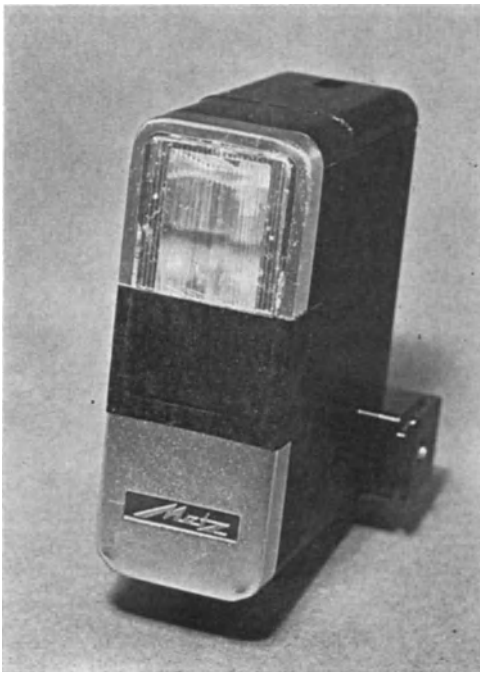


Fig. 1. Electronic flash with a partly taped off reflector.

Some electronic flashes show an uneven distribution of light output, falling off rapidly from centre to periphery which may be disturbing when we take binoculair photographs using one electronic flash light only. We can correct this afterwards by dodging the prints but it is more preferable to lighten up these parts already during the exposure. This can be done using two reflectors mounted on a conventional headrest (Fig. 2) (LUNNON 1952).

RETINAL PHOTOGRAPHY

Fixation target; reduction of corneal astigmatism; central mask mounted in diaphragm wheel and copying techniques from retinal colour slides.

One of the most important things in retinal photography is to have a good fixation light. Most fixation lights are badly seen and appear out of focus. Focussing on a fixation light has in addition the disadvantage of converging the patient's eyes.

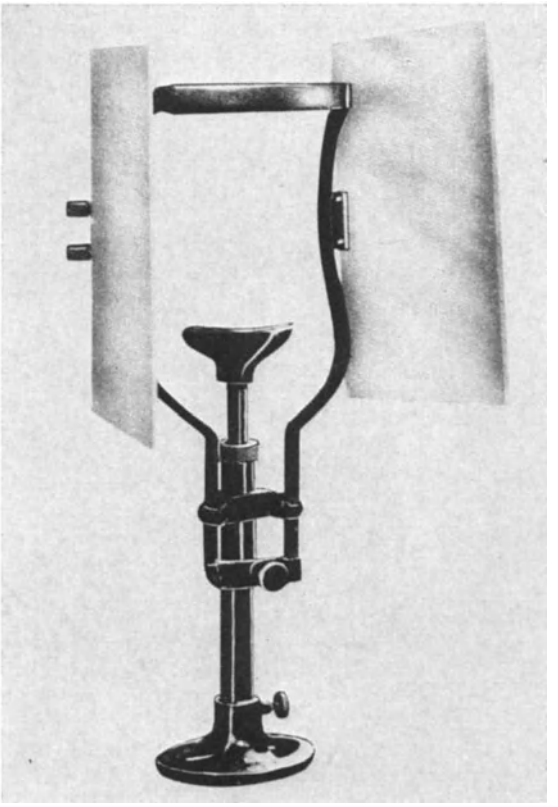


Fig. 2. Reflectors mounted to a headrest (after Lunnon).

ALLEN introduced the Haag-Streit 900 fixation target for retinal photography with the Zeiss retinal camera (Fig. 3). This light can be adjusted to the patient's refraction and it is thus perfectly visible for the unaccommodated eye, even for patients with a rather low vision. This results in a more relaxed patient.

Not all retinal cameras have the possibility to compensate for astigmatism. With the aid of a contact lens we can correct the corneal astigmatism.

We use the Henkes ERG-low vacuum diagnostic contact lens of 0 power (WORST & OTTER, 1961). The contact lens is attached to the eye by means of a slight negative surface pressure (Fig. 6). This technique has an additional advantage, as the cornea does not dry out during retinal photography.

A most common problem is how to take retinal photographs without disturbing artefacts as reflexes and fogging haze (Fig. 4 a). These problems are due to

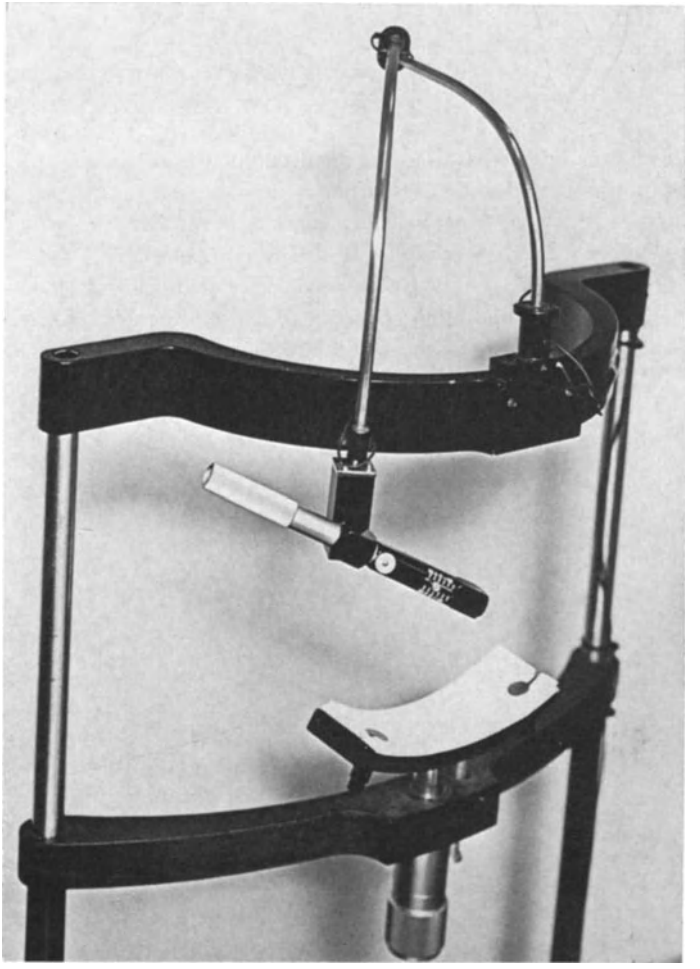
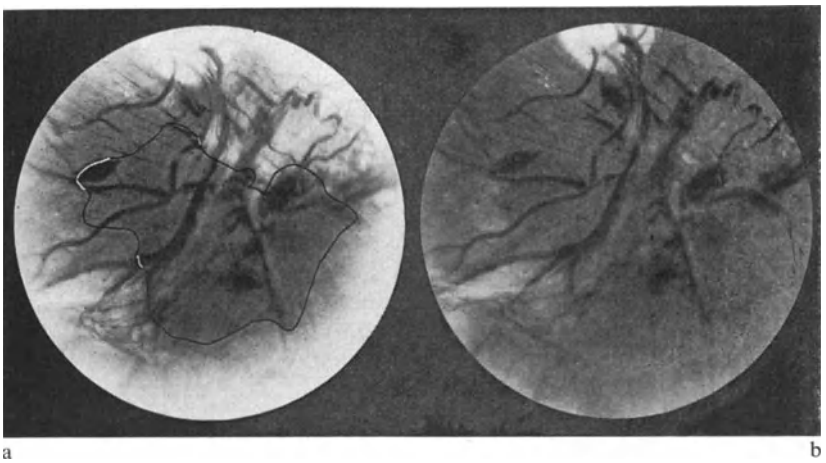


Fig. 3. The Haag-Streit fixation target mounted on a Zeiss headrest.



a b

Fig. 4a. Fogging haze in the straight print.
Fig. 4b. Same negative and paper-grade, but corrected with shading technique.

light, which falls on the lens and the anterior vitreous. Especially in patients with slight cataract and vitreous opacities we may expect to get more of these artefacts. Allen designed a special central mask to be mounted in the diaphragm aperture wheel of the Zeiss retinal camera (Fig. 5) (ALLEN, 1964).

This accessory mask is now available on special order from Zeiss, order number 30.09.90. Disappointing results in retinal photographs taken without the mask can be improved by the shading technique (Fig. 4 b).

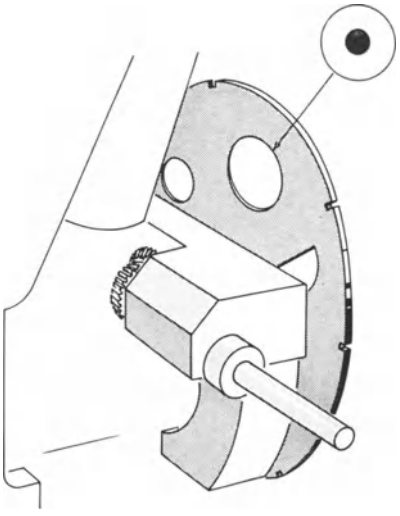


Fig. 5. Diaphragm aperture wheel of the Zeiss retinal camera and central mask accessory.

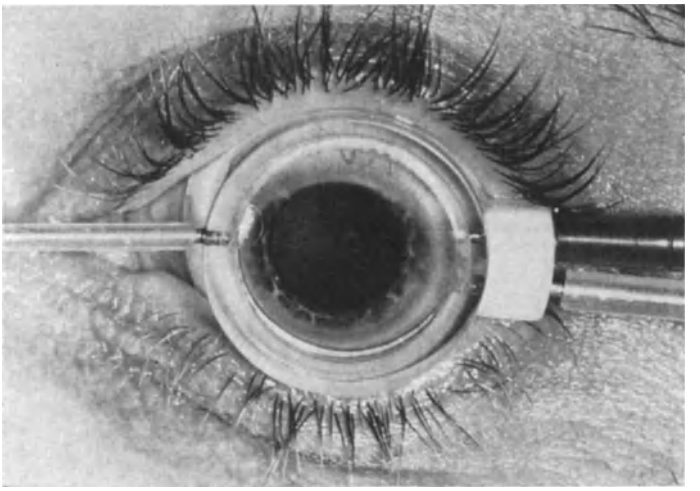


Fig. 6. The Henkes ERG-low vacuum diagnostic contact lens in situ, to reduce corneal astigmatism.

Retinal photography is mostly done on colour film with an angle of view of 30° as provided by most retinal cameras. With a special copying technique from fundus colour slides to be described, black and white retinal photographs, retinal photographs using monochromatic light, and retinal magnifications with ×2 magnification attachment, can be made easily afterwards. This saves time when making the actual photograph. However, it is of vital importance that the colour slide is made on a fine grain colour film such as the Kodak Kodachrome II colour film. This film is still the best colour film available for retinal photography.

Different kinds of copying techniques are possible, such as: copying with graphic orthochromatic or panchromatic black and white films; copying with magnifications from 1 : 1 upward to high section of the original slide; and copying using monochromatic light or Kodak Wratten gelatine filters.

This technique of copying colour slides has thus the following advantages:

- during the actual photographic procedure, a wide angle of 30° subtending visual angle is always maintained;
- a lower flash intensity can be used during actual photography;
- higher contrast for better visualization of the retinal vessels can be obtained;
- colour correction of the original slide, if desired, is possible;
- one can choose any retinal detail of the slide to be copied. The enlargement obtained may thus comprise details which are – in respect to each other – vertically orientated.

MATERIALS AND METHODS

1 : 1 copy, or copying details from colour slides.

Requirements are: a slide copying attachment, or set-up for macro-photog-

raphy; an electronic flash and a Kodak Ektachrome High Speed reversal colour film.

The camera body is loaded with Kodak Ektachrome High Speed daylight colour film, and the magnification is chosen by varying the bellow extension between camera body and lens. The colour slide is illuminated with an electronic flash which is placed at the back of the slide.

Copying with monochromatic light or Kodak gelatine Wratten filters

The same materials, apparatus and method are used as mentioned above. The only difference is that an interference filter or a Kodak gelatine Wratten filter is placed between the electronic flash and the original slide. Duplicates thus made using a Kodak gelatine filter KW 58 give exactly the same results as are obtained while photographing with red free light.

Copying on graphic orthochromatic and panchromatic black and white films

The materials and method are the same as above, but now the camera body is loaded either with a graphic orthochromatic (Agfa ortho, 25 ASA) or panchromatic (Agfa pan, 25 ASA) black and white film. As can be seen in Fig. 7 a and b, these films give prints with a colour translation in black and white, which is quite different from the original colour slide.

The results are nearly the same as obtained in black and white photography using monochromatic light of different wavelengths (BEHRENDT & WILSON, 1965; BEHRENDT & DUANE, 1966), and in retinal photography when using orthochromatic and panchromatic film (CRAANDIJK & AAN DE KERK, 1969).

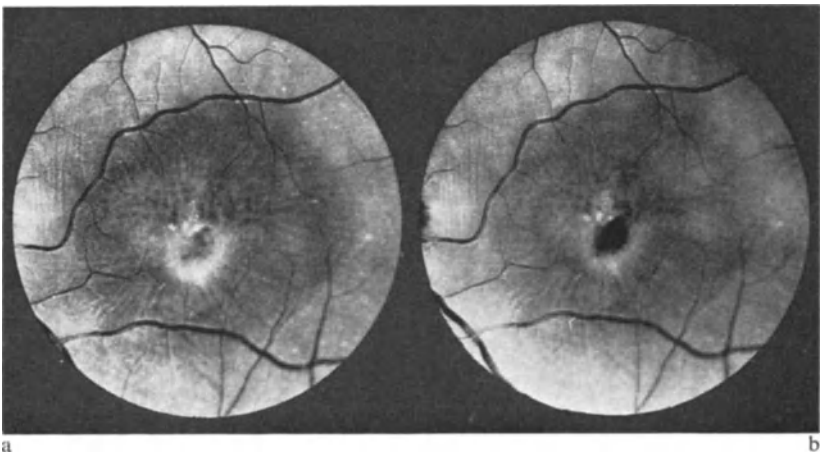
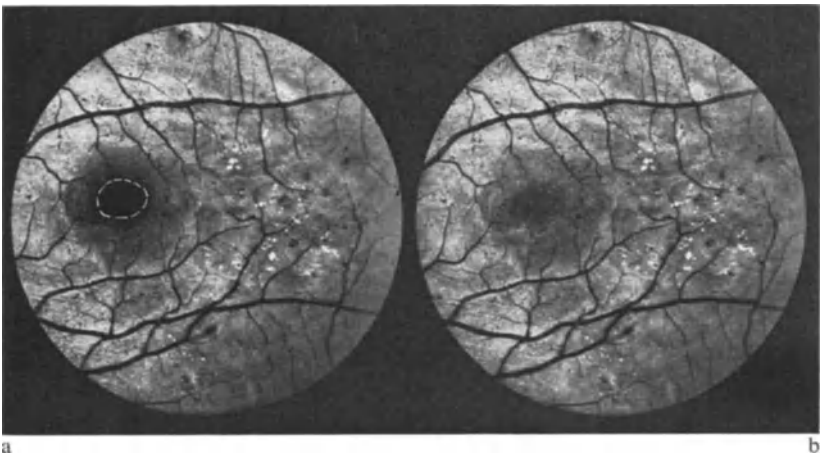


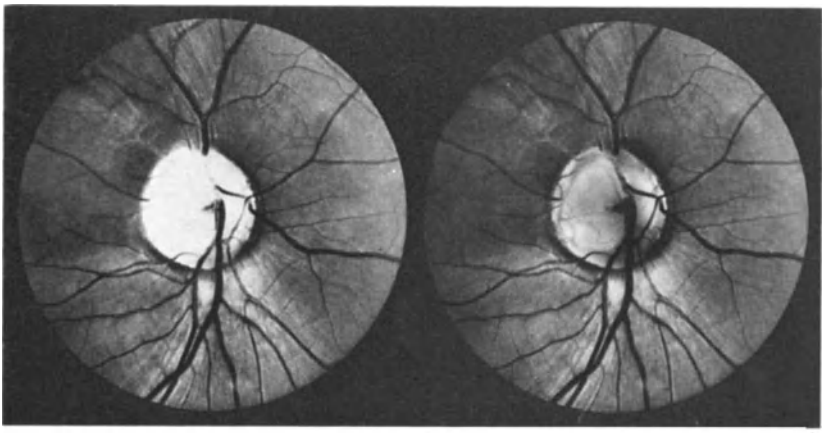
Fig. 7a. Copy of a colour slide made on orthochromatic film.
Fig. 7b. Same slide but now copied on panchromatic film.

Sometimes we are unable to get well-illuminated retinal photographs. This can be caused by: lens alterations, vitreous opacities, photophobic patients and too much contrast in the subjects to be photographed. This results mostly in negatives with a very large range of densities. We can reduce the contrast and improve the quality of the enlarging with: soft paper, unsharp masking and dodging and shading techniques.



a b

Fig. 8a. A straight print; macula is too dark with as a result loss of detail.
Fig. 8b. Same negative and paper-grade, but macular region corrected using dodging technique.



a b

Fig. 9a. A straight print, with an invisible crater-like hole in the optic disc.
Fig. 9b. Same negative and paper-grade, but corrected with shading technique.

Soft paper may improve the range of tones, but cannot give the full range of tones in the negative. The prints are not brilliant and look weak. Unsharp masking, dodging and shading permits enlarging on higher contrast paper with as a result a better contrast. Unsharp masking however, is a time-consuming job and is only advisable when a series of prints has to be made from one negative (FRISÉN & HOYT, 1973).

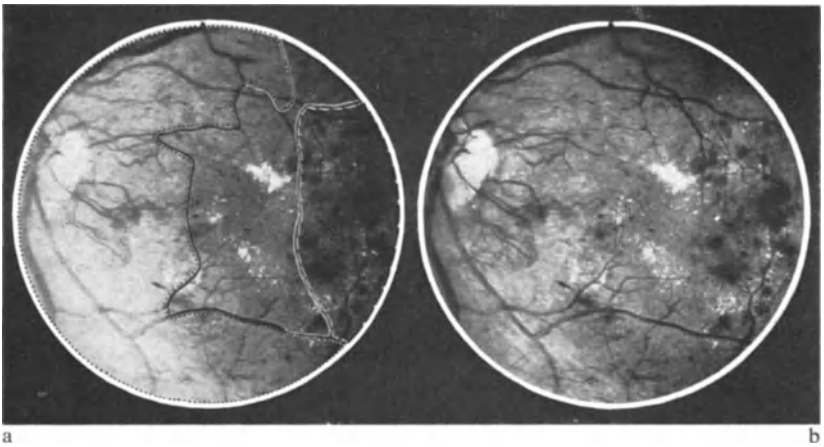


Fig. 10a An uncorrected straight print.
Fig. 10b Same negative and paper-grade, but corrected using the dodging and shading technique.

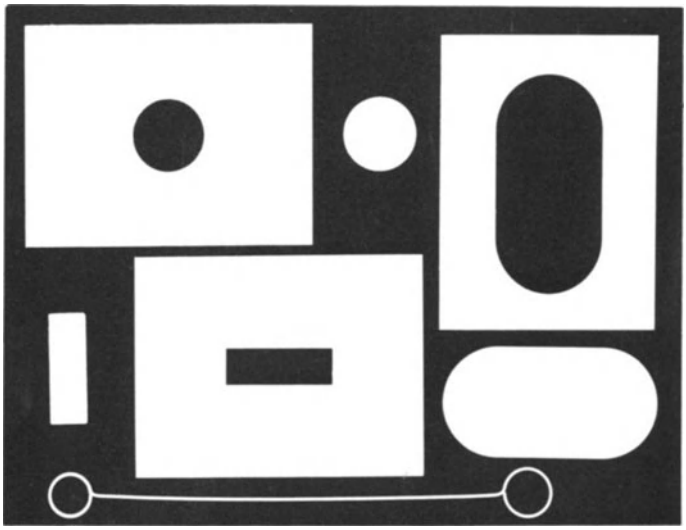


Fig. 11. A photogram of dodging and shading tools.

More advisable is the application of dodging and shading. Dodging gives intentionally less exposure to a selected area during the printing exposure time and is mostly applied to light areas of the negative, such as the macula (Fig. 8 b). Shading is just the reverse of dodging. After the basic overall exposure, an additional exposure is given to a selected area of the enlarging in order to darken these areas like the optic disc, while holding back light from the surroundings (Fig. 9 b and 10 b).

Dodging and shading can be done with special tools (Fig. 11), made from a piece of wire, cardboard and tape, or can be done by hand. I prefer using my hands, because this method gives greater freedom and flexibility. During the exposure the tools or hands must be constantly moved between the enlarger lens and the projected image of the enlarger, to avoid a print with sharply contrasting parts.

Before enlarging we first make a test print on a small sheet of enlarging paper to judge the final effect.

COMPOSITE PHOTOGRAPHS

The normal retinal photographs have an angle of view of 30° and in a number of cases this angle is not wide enough for a total view of the diseased area. There

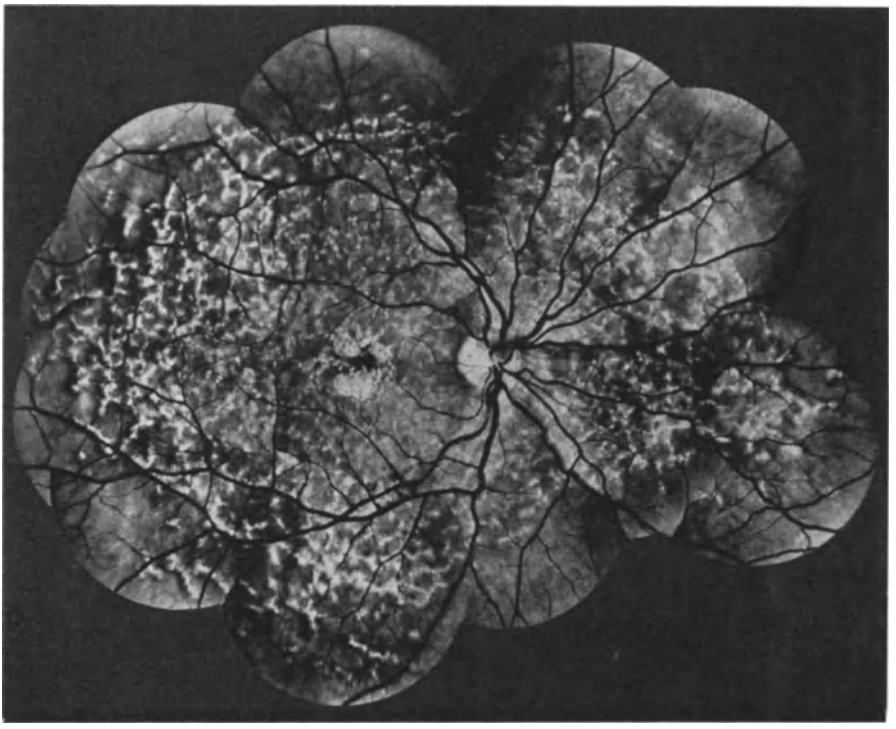


Fig. 12. Composite photograph of a fundus flavimaculatus (after DEUTMAN, 1971).

are three methods to enlarge the angle of view. We can use: a wide angle retinal camera, a normal retinal camera with wide angle contact lens or a composite photograph from the prints obtained with the normal retinal camera (Aan de Kerk, 1973; Govignon & Pomerantzeff, 1972; Pomerantzeff & Govignon, 1971; Schirmer & Shea, 1970).

The definition, illumination and depth of field of the retinal photographs with the first and second method, are at this moment not as good as with the conventional 30° retinal photographs. That's why composite photographs are still preferable.

The technique of composite photographs is ideal for a very extensive view of the retina (Fig. 12), but also for processes located in front of the retina. The depth of field is not large enough in one retinal photograph, having the whole area in focus. With the composite technique we can mount together photographs which are focused on different planes of interest (Fig. 13).

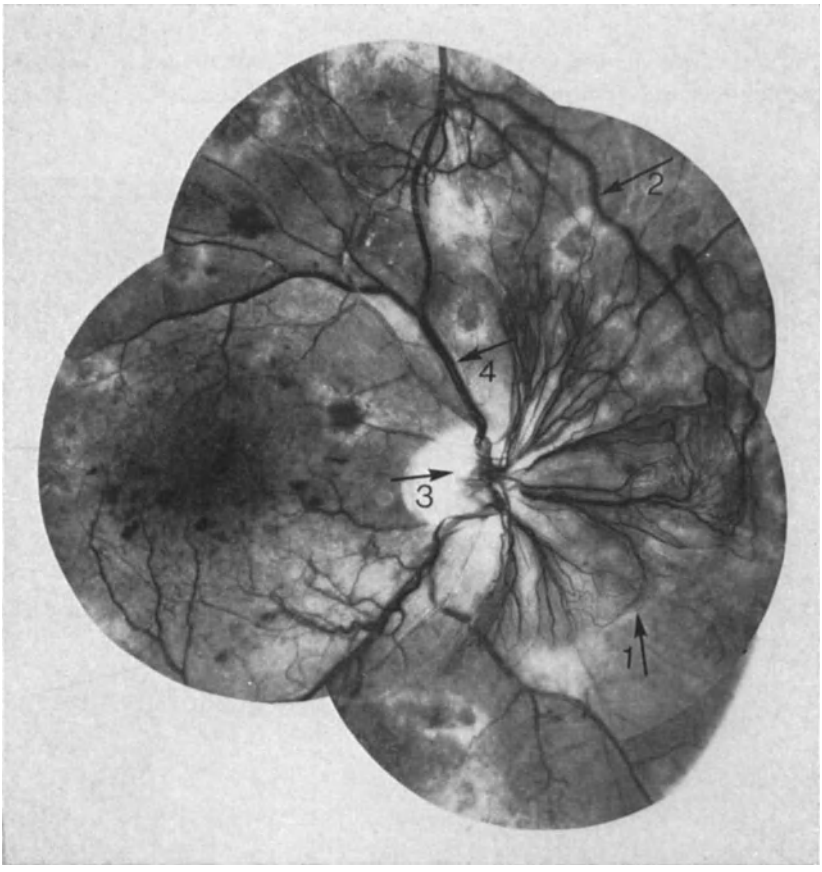


Fig. 13. Composite photograph of a diabetic retinopathy with newly formed vessels in front of the optic disc (after Riaskoff, 1972).

Successful results in composite photographs are obtained if we have patients without astigmatism, qualitatively good prints, and if we trim and mount the photographs along the vessels.

RETOUCHING

The purpose of retouching is to remove or to add grey tones in order to make a better picture.

We must deliver a clean and if needed, retouched enlarging. On strong enlargements in particular, we may find on the negative white spots and lines caused by dust and scratches (Fig. 14 a).

For retouching we need retouching tools, brushes and knives etc. The white areas are best removed by spotting with a fine sable brush and diluted grey retouching dye or water colour pigment, which correspond to the surrounding tone (Fig. 14 b). Still better is it to prevent retouching, by handling and cleaning the negative carefully.

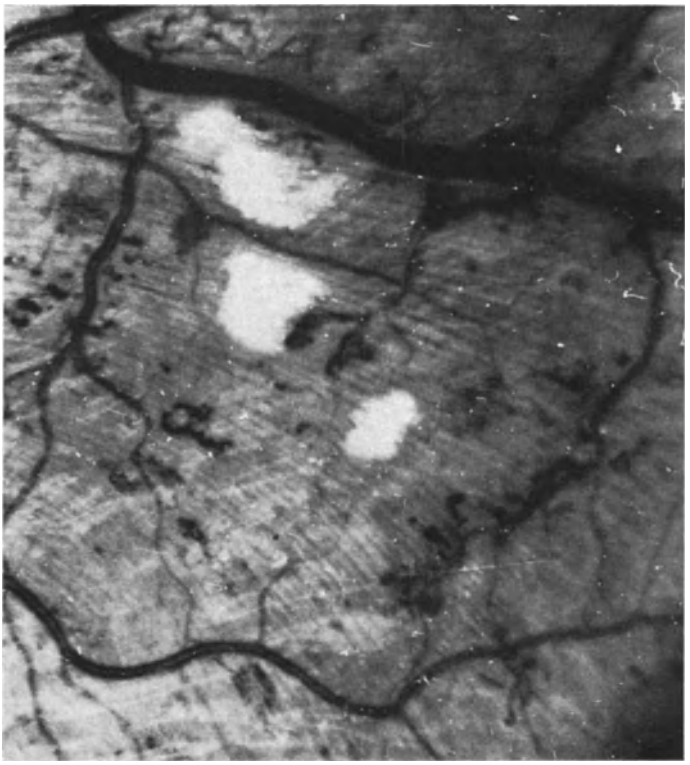


Fig. 14a. Unretouched photograph of a highly enlarged negative, with numerous white spots and lines caused by dust and scratches on the negative (after RIASKOFF, 1972).

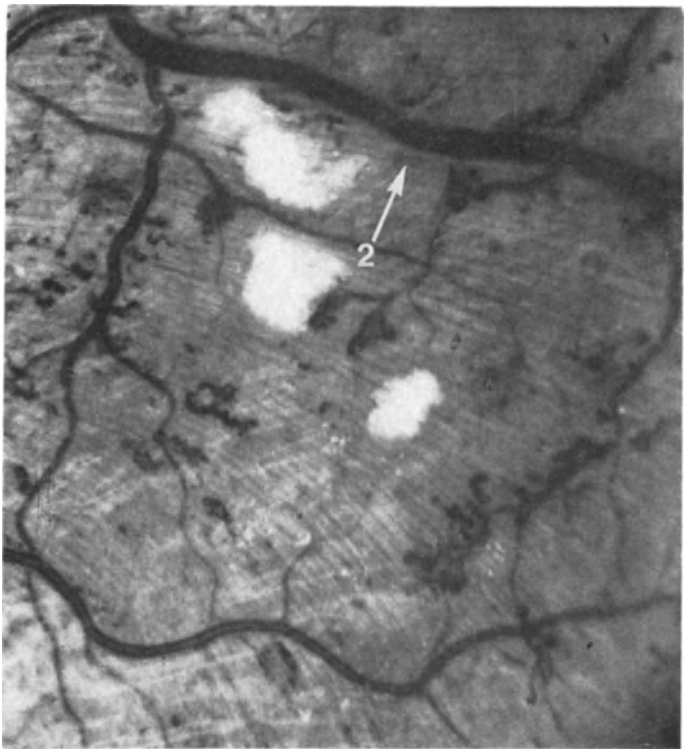


Fig. 14b. Same photograph retouched with retouching dye (after RIASKOFF, 1972).

CLEANING

Cleaning tools are very important for retinal photography and enlarging. Dust on the non-spherical objective of the retinal camera gives artefacts on the print in patients with high myopia (CRAANDIJK, 1973), dust too gives loss in light energy, contrast and definition.

Cleaned negatives prevent retouching of the print. For cleaning the negatives and negative carrier of the enlarger, all cleaning tools available can be used. The non-spherical objective of the retinal camera must be handled and cleaned most carefully. Small dust particles can be removed with a part of a blower brush or a small vacuum cleaner (Fig. 15). If they stick, they must be removed carefully with special lens tissues.

PROJECTION

Projection of retinal colour slides showing vascular diseases can be improved using a Kodak Wratten gelatine filter KW 58 over the projector lens. This results in a better contrast and visibility of the vessels. The results are similar to those obtained with red free light ophthalmoscopy (AAN DE KERK & DE BRUYN).

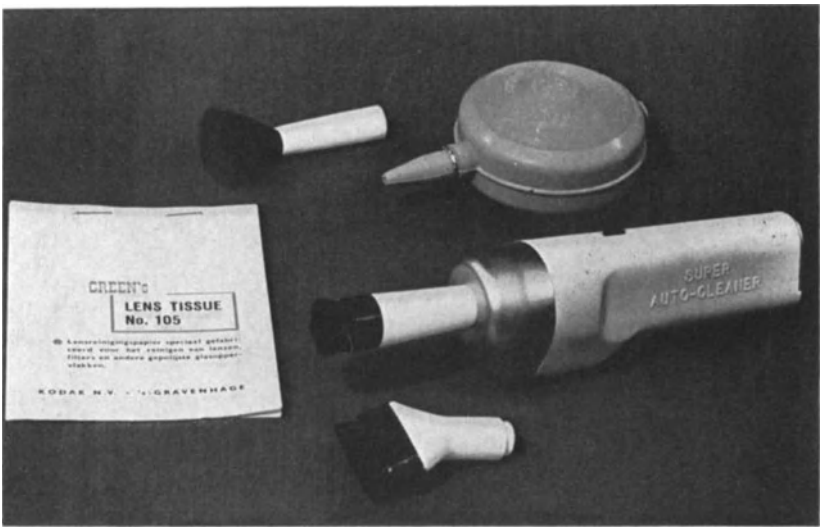


Fig. 15. Cleaning tools: blower brush, brush vacuum cleaner and lens tissues.

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BASIC PATHOPHYSIOLOGIC PRINCIPLES OF FLUORESCEIN ANGIOGRAPHY

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ABSTRACT

Basic pathophysiologic principles in fluorescein angiography are related to circulation, affinity of tissues to fluorescein, extravasation, filtering and atrophy. The importance of these factors and their fluorographic consequences are discussed for the normal and the pathologic ocular fundus.

Thirteen years ago fluorescein angiography added a new dimension to the clinical examination of the ocular fundus. Since then a rapidly increasing amount of data has become available on the dynamics of blood flow in retina, choroid and optic disc. The fluorographic pattern of almost all pathologic conditions of the ocular fundus has been described, except when technical problems interfered with the visualization of the fluorescence pattern. Our knowledge as to the interpretation of the great variety of pathologic patterns of fluorescence has expanded rapidly; it has been considerably enhanced by the histologic studies after fluorescein injection in the normal eye (BAURMANN, 1971) and by correlating the angiographic aspect with the histologic findings in many eye diseases.

In the description and interpretation of the fluorograms of fundus lesions structural alterations and functional changes, e.g. of circulatory origin, were the primary basis for interpretation.

Despite the fact that the numerous fascinating and sometimes intriguing fluorograms may show innumerable variations, fundus lesions of quite different origin may show a striking similarity in fluorescence pattern (OOSTERHUIS & VAN WAVEREN, 1968). We therefore know that evaluation of the fluorogram without any further knowledge of the fundus lesion will inevitably lead to major mistakes in the interpretation, which can only be avoided when the fluorographic findings are correlated with the results of all other ophthalmic examinations.

The fact that fluorograms may be similar in different fundus lesions points to the fact that also the characteristics of fluorescein behaviour in the ocular fundus greatly determine the fluorescence pattern. In fact, there are only a few basic principles which can explain almost all aspects of the normal and pathologic fluorographic patterns. These are: *circulation*, *affinity*, *extravasation*, *filtering* and, only in the pathologic eye, *atrophy*; they will be discussed below, first in the normal fundus and subsequently in pathologic conditions.

1. *Circulation*

a. *flow*

I will not discuss the various *retinal* filling phases extensively as this has frequently been done in recent years.

The arterial phase is only short, peak fluorescence of the retinal arteries being reached with one or two seconds. The capillary phase is characterized by an increased visibility of the vascular structures, which will be discussed later. The most striking feature of the early venous phase is the laminar flow consisting of an axial stream derived from the retinal periphery, not yet containing fluorescein, which does not mix with the fluorescent blood stream close to the vessel wall derived from tributaries in the peripapillary area. In the late venous filling phase the retinal veins become uniformly fluorescent.

Choroidal fluorescence develops about ½-1 second before retinal fluorescence. As the filling phase of the short ciliary arteries is rapidly followed by filling of the choriocapillaris, ciliary arteries are only incidentally visible in the fluorogram. The intense, diffuse fluorescence of the choriocapillaris, sometimes starting in an irregular 'geographic' pattern, makes any further visualization of the underlying large choroidal vessels impossible. In the late phase choroidal fluorescence gradually fades away.

There are four phases of fluorescence of the *optic disc*, the first three of which develop so rapidly that they are only incidentally observed separately. The first phase is a slight, diffuse fluorescence of the optic disc, originating from the deep capillary plexus behind the lamina cribrosa. It is followed by filling of the prelaminar capillary plexus, without a special pattern, not surpassing the margin of the optic disc, originating from the choroidal vessels in the peripapillary area. The structure is rapidly masked by the filling of the radial epipapillary capillaries which, in contrast to the afore mentioned capillaries, show a very distinct radial structure (SHIMIZU, 1973).

b. *increased visibility of the vasculature*

Fluorography not only enables us to study the flow pattern but also facilitates the evaluation of the small vessels in the fundus by their increased visibility. This especially applies to the capillaries in the perifoveal area and the radial peripapillary capillaries (HENKIND, 1967; SHIMIZU, 1973).

2. *Affinity*

In the normal *retina* the affinity of the vessel walls to fluorescein is only slight. Fluorescence of the major retinal vessels fades away in several minutes. After that a slight staining of the vessel walls may persist, especially of the large retinal veins, visible as slightly fluorescent lines along the margins of the vessels.

Affinity of the *choroidal* vasculature to fluorescein can generally not be assessed owing to the diffuse fluorescence by extravasation, but we may assume that it does not exist in any appreciable amount since in the late phase fluorogram of the scarcely pigmented fundus one may see the vorticose veins and their collector vessels as dark silhouettes against the diffuse fluorescence of the choroidal tissue (OOSTERHUIS & BOEN-TAN, 1971).

The vessels on the *optic disc* behave in a similar way.

3. *Extravasation*

'Leakage' and 'extravasation' are generally used at random to indicate permeability of the vessel walls to fluorescein, which, however, may lead to confusion as extravasation is part of the normal physiologic condition, whereas leakage indicates an increased, abnormal permeability. As only the retinal and cerebral vessels are impermeable to fluorescein under normal conditions, one may only speak of 'leakage' in case of penetration of fluorescein through the *retinal* vessel wall, including those on the optic disc (Fig. 1). Penetration of fluorescein through the retinal pigment epithelium, in normal condition not permeable to fluorescein, may equally be called leakage. The walls of all other vessels, especially the choroidal capillaries, are already easily permeable to fluorescein under normal conditions so that penetration of fluorescein through these vessel walls should only be called extravasation. Newly formed vessels in the retina and vessels growing into the vitrous do not behave as normal retinal vessels and therefore leakage from these vessels is in fact extravasation.

Thus in the normal eye there are two barriers to fluorescein. The first one is the retinal vessel wall; the second one is the retinal pigment epithelium. Both

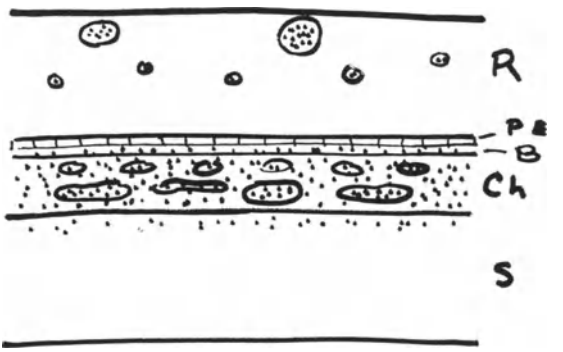


Fig. 1. Extravasation of fluorescein in the normal fundus. The retinal vessel walls are impermeable to fluorescein but in the choroid fluorescein diffuses freely into the tissue and penetrates into Bruch's membrane and the superficial scleral layers. The retinal vessel wall and the retinal pigment epithelium act as barriers preventing fluorescein from penetrating into the retinal tissue. The black dots represent the presence of fluorescein.
(R = retina; PE = pigment epithelium; B = Bruch's membrane; Ch = choroid; S = sclera)

prohibit diffusion of fluorescein into the retinal tissue, which is a very fortunate circumstance as this would greatly interfere with visualization of the retinal vasculature, as happens in the choroid, where rapid extravasation of fluorescein in the capillary filling phase, i.e. when the 'geographic pattern' has disappeared, causes the diffuse background fluorescence in which the individual choroidal vessels and their circulation pattern can not be studied any more. Therefore, fluorescein angiography gives more information on retinal than on choroidal circulation but for the latter other techniques or dyes, such as Cardio-Green absorption photography, may eventually give useful information not obtainable by fluorography (FLOWER & HOCHHEIMER, 1973).

In the optic disc extravasation may become visible in the late phase fluorogram as diffuse marginal fluorescence due to fluorescein from the peripapillary choroidal vessels diffusing into the optic disc periphery.

4. *Filtering*

The fluorescent light emitted from the normal choroid is easily absorbed by the overlying pigment of the pigmentepithelial layer. This explains the difference in intensity of the background fluorescence in heavily pigmented versus albinotic fundi in which the background fluorescence may become so intense that it can interfere with a good visualization of the fluorescence pattern of the retinal vessels. It also explains that the more pigmented macular area is darker than the less pigmented surrounding region.

PATHOLOGIC CONDITIONS

1. *Circulation*

a. *flow*

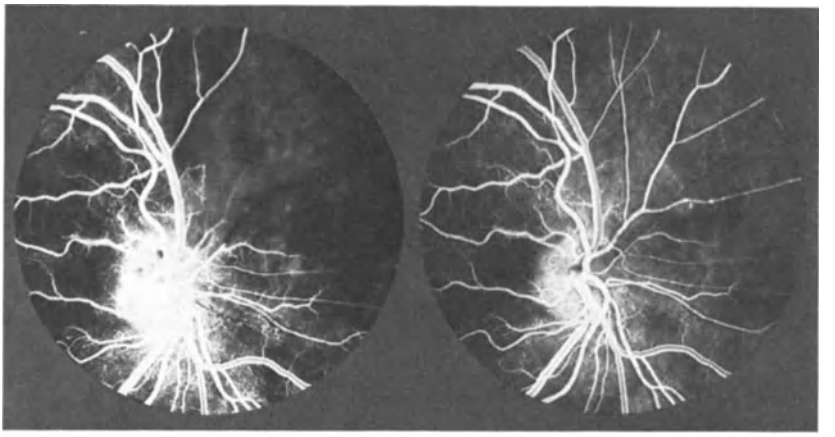
In arterial or venous obstruction, whatever its cause, delayed filling in occluded vessels and their capillary territory can be assessed more or less quantitatively by fluorescein angiography. On comparison with later fluorograms the degree of restoration of the circulation, either by reopening of the occluded vessel or by the development of anastomoses, can be studied (Figs. 2 A, B).

Disturbance of the laminar flow pattern may occur at pathologic retinal vessel crossings, but in our experience is only observed in very severely sclerotic crossings.

Filling defects in the choriocapillaris have been observed in experimentally elevated intraocular pressure; its importance in primary glaucoma in man is still to be assessed. Occlusion of the ciliary arteries and their branches has been described extensively by AMALRIC & BONNIN (1969) in the 'triangular syndrome'.

b. *increased visibility*

As more of the capillary system is visible on fluorescein photography than on



A B

Fig. 2 A. Embolic branch occlusion of the central retinal artery. The fluorogram shows the defect of filling in the vasculature served by the occluded artery.
Fig. 2 B. Same fundus 2 months later after reopening of the occluded vessel. Circulation is only slightly delayed. Note increased affinity to fluorescein of the vessel wall at the site of the embolus.

ordinary photography or ophthalmoscopy, the presence and development of abnormalities in their pattern can be studied in more detail. Small areas of closure can be detected, e.g. in incipient diabetic retinopathy and retinal vein occlusion, as well as their increase in size to larger avascular areas. Also microaneurysms and newly formed vessels become better visible.

2. *Affinity*

Abnormal affinity of fluorescein to tissues without leakage implicates those tissues to be in a pathologic condition, not associated, however, with exudation or transudation. Abnormal affinity to the retinal vessels can be seen in almost all conditions which cause a metabolic disturbance of the retinal vessel wall (Fig. 3). Localized plaques of vascular sclerosis or sites of arterial emboli (Fig. 2 B) may show an intense, persistent staining. The hypoxic state of the retina, either caused by vascular occlusive disease, diabetic retinopathy or other diseases, inevitably leads to increased staining of the retinal vessel walls. On the other hand, one can conclude from decrease or disappearance of abnormally intense staining of the vessel wall that its condition has improved (Fig. 4 A, B). Affinity of fluorescein may also show when abnormal material has been deposited into the tissue outside the vessels, such as in drusen of Bruch's membrane or of the optic disc.

Abnormal affinity in the choroidal vessels can not be evaluated due to the rapid extravasation.

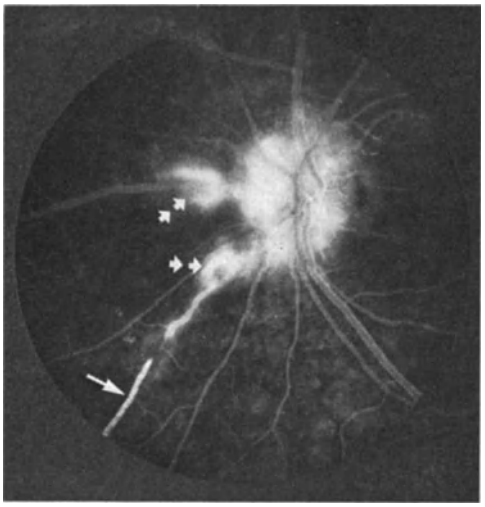


Fig. 3. Abnormal fluorescence in retinal periphlebitis. Metabolic disturbance due to delayed flow causes increased affinity but no leakage in the late phase fluorogram (arrow). Sites of inflammation (double arrow) show not only increased affinity but also leakage: diffusely spreading fluorescence.

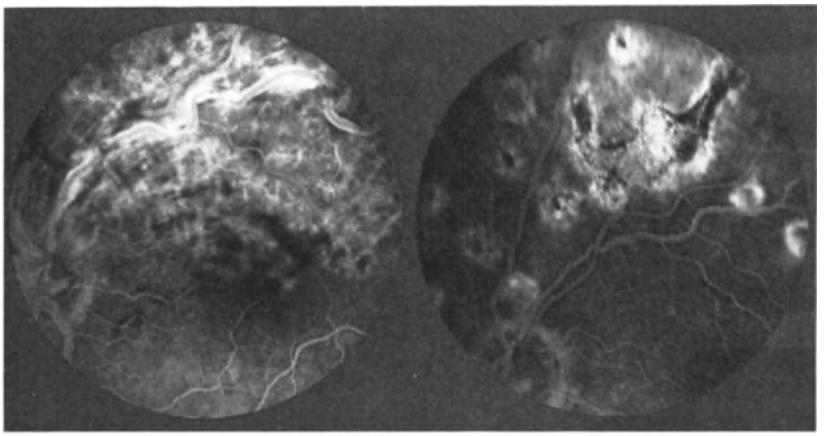
3. *Leakage*

In many abnormal conditions of the ocular fundus leakage can be considered to be the next phase following increased affinity to fluorescein, indicating the lesion to be more serious. In both increased affinity and leakage there exists an increased, long lasting fluorescence. The main difference is that in increased affinity the fluorescence is restricted to the area of the lesion only; it does not spread beyond this territory in the late phase fluorogram and the margins of the abnormally intense fluorescence remain more or less sharply defined. Characteristic of the leakage is that fluorescence is gradually spreading from the site of leakage, the area of fluorescence thus gradually increasing in size and not being sharply defined in the late phase fluorogram (Figs. 4 A, B and 5). In both increased affinity and leakage fluorescence may become very intense.

Leakage of fluorescein in the choroid can not be demonstrated but probably does not exist as fluorescein already permeates freely into the intercapillary tissue in the normal eye.

Leakage implicates a lesion of a physiologic barrier to fluorescein, the main ones in the ocular fundus being the retinal vessel wall and the retinal pigment epithelium. Leakage from retinal vessels can be observed in very many circulatory and inflammatory disorders. The extravasation of intra- and preretinal newly formed vessels has already been discussed. The vessels in neoplasms, mainly choroidal melanomata and metastatic tumours, may show a variable intensity of long lasting, diffuse fluorescence.

Also in the retinal pigment epithelium an increased affinity indicates a lesser degree, leakage a more severe stage of the lesion. For instance, we regularly



A B

Fig. 4 A. Occlusion of the superior temporal retinal vein. Marginal fluorescence of the vessel wall indicates increased affinity of the vessel wall to fluorescein. Diffuse late phase fluorescence indicates metabolic disturbance of the vasculature.
Fig. 4 B. Same fundus 14 months after xenon arc photocoagulation. Fluorography reveals improvement of the metabolic condition of the vessel wall since both abnormal affinity and leakage have disappeared.

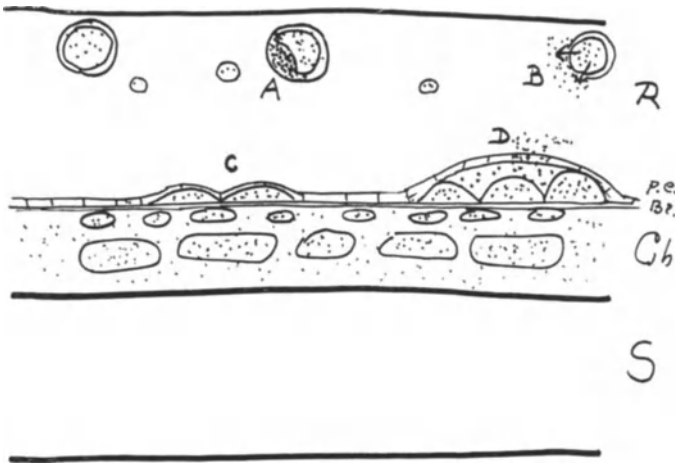


Fig. 5. Schematic drawing showing abnormal affinity and leakage. The black dots are indicative of fluorescence.
A: increased affinity to retinal vessel wall at the site of a sclerotic plaque; *B:* leakage through the retinal vessel wall as can be observed in all conditions associated with hypoxia; *C* Drusen of Bruch's membrane; increased fluorescence partly due to abnormal affinity, partly due to the decreased filtering of thinned pigment epithelium; *D:* when the former lesion is more intense, leakage may occur leading to detachment of the pigment epithelium and even penetration of fluorescein through the diseased pigment epithelium into the retina can be observed.

observed that drusen of Bruch's membrane in the macular area, packed densely together, at first only showed long lasting fluorescence but gradually developed leakage, leading to the picture of serous detachment of the pigment epithelium (Fig. 6). The most striking example of leakage is observed in the fluorogram of the central serous retinopathy.

Long lasting intense fluorescence of the optic disc is due to leakage from the optic disc vessels, which is a valuable help in the differentiation between papilloedema and pseudopapilloedema.

Also inflammatory lesions may lead to profuse leakage, which in its most excessive way is observed in Harada's disease (SHIMIZU, 1973).

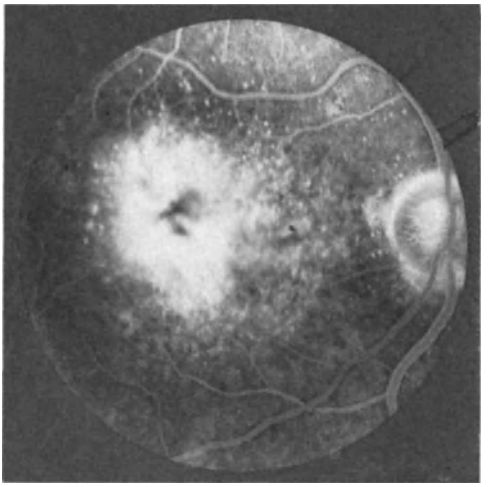


Fig. 6. Drusen densely packed together in the macular area showing increased affinity to fluorescein and, around the posterior pole, incipient leakage in the late phase (6 min) fluorogram consistent with incipient detachment of the retinal pigment epithelium.

4. *Filtering*

Pigment, but also other substances such as blood, absorb fluorescence. Therefore, deep pigmentations can be visualized as silhouettes against the fluorescent glow of the ocular background, the pattern of the silhouette sometimes even being the main guide to the diagnosis; for instance, the reticular pattern of pigmentation which can be found in non-typical macular degeneration may point to the existence of an ocular manifestation of elastosis (VON WINNING & OOSTERHUIS, 1973/74) (Fig. 7).

Localized depigmentation is the end stage of many processes in the ocular fundus. These spots or areas show an increased fluorescence, which is very sharply defined and restricted to the area of depigmentation only. The fluorescence in these areas gradually fades away but, being more intense, remains visible somewhat longer than in the surrounding normal areas.

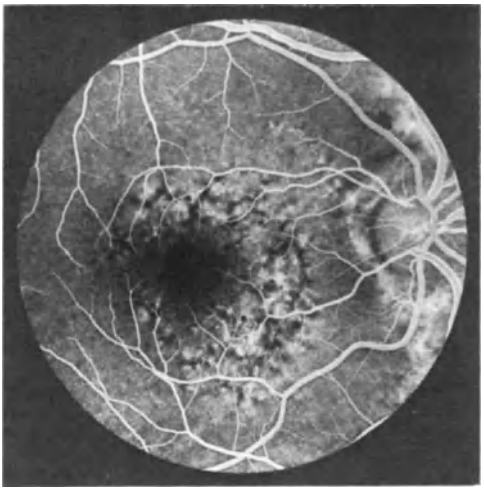


Fig. 7. Non-typical macular degeneration showing a reticular pattern of pigmentation on fluorescein angiography only, which was a guide to the diagnosis of the Grönblad-Strandberg syndrome.

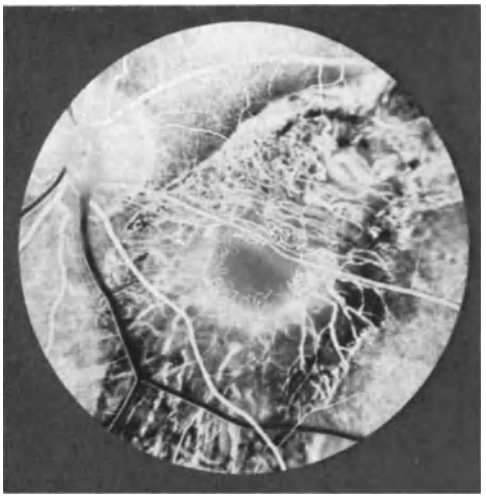


Fig. 8. Chorioretinitis scar; atrophy of the choriocapillaris uncovers the pattern of the large choroidal vessels; the dark areas between these vessels are caused by non-fluorescence of the sclera.

Leakage does not occur in dystrophy unless it is part of the primary process leading to dystrophy which has not yet completely regressed, such as chorioretinitis and detachment of pigment epithelium or neuro-epithelium. Therefore, fluorography is a useful tool to follow the healing process in the course of time.

5. *Atrophy*

Atrophy can greatly influence the fluorographic pattern as it may uncover structures normally not visible (Fig. 8). This especially applies to the choroid, in which the large vessels may become visible when they are not hidden any more by the diffuse fluorescence of the choriocapillaris. Even the slight, diffuse late phase fluorescence of the sclera may become visible when all other layers in the ocular fundus have atrophied completely, as can for instance be seen in atrophic chorioretinal scars.

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FLUORESCEIN ANGIOGRAPHY OF DIABETIC RETINOPATHY IN RELATION TO PROGNOSIS AND PHOTOCOAGULATION TREATMENT

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ABSTRACT

Fluorescence angiography allows the study of vascular changes in diabetic retinopathy in great detail.
It is indispensable in the prognosis and treatment with photocoagulation.
Diminished oxygen need of the remaining retina tissue together with an improvement in the circulation in the retinal tree may explain the favourable effects of this treatment.

Diabetic retinopathy – which is a local manifestation of a general vascular disease – has many similarities with other retinal vascular disorders.

The symptoms in advanced stages of various angiopathies are sometimes so similar that one hesitates to decide whether the underlying cause is a diabetic or a hypertensive angiopathy. However, in the beginning stages the differential diagnosis is not difficult, due to the very specific localization of the first pathological changes: at the level of the capillary network in diabetic retino-

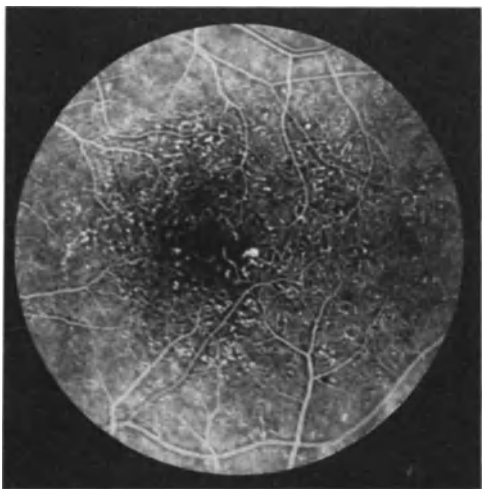


Fig. 1. Beginning proliferative diabetic retinopathy (male, 30 years old). Arteriovenous phase; dilated capillaries, small areas of non-perfused capillaries; macro- and microaneurysms.

pathy, and at the level of the arterial and venous branches in hypertensive retinopathy. As capillaries are vessels of very small size and as these are not affected to the same degree at the same moment, pathophysiological consequences of capillary changes are never as dramatic as in case larger vessels of the retina are involved.

Small and rather numerous pathologic areas may exist in the capillary network for many years before these manifest themselves clinically.

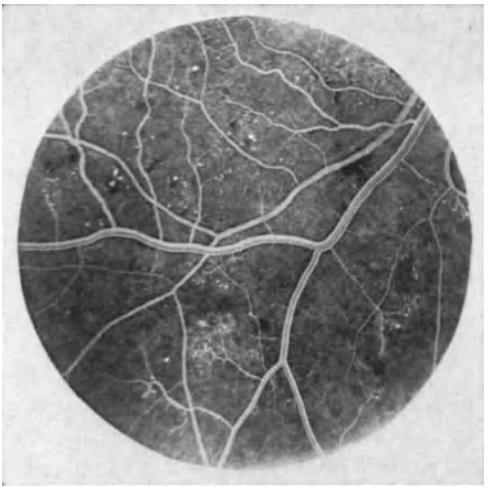


Fig. 2. Beginning proliferative diabetic retinopathy (male, 34 years old). Early arteriovenous phase: small area of capillary non-perfusion, adjacent capillary dilatation and beginning neovascularisation. (Black dots: hemorrhages.)

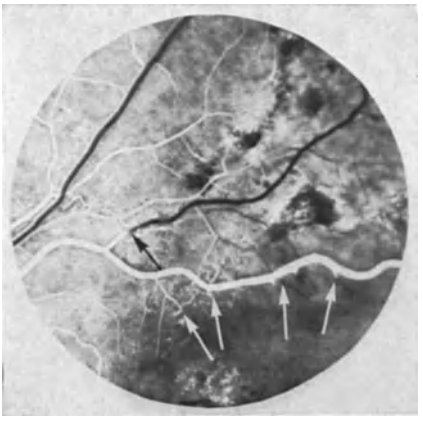


Fig. 3. Advanced proliferative diabetic retinopathy (female, 45 years old). Arterial phase: arrows indicate numerous occluded arterial branches, with corresponding large area of nonperfusion in the lower part of the picture.

Fluorescein angiography provides us with the earliest information about abnormalities of the capillary network in diabetic retinopathy. It shows a dilation of capillary vessels and small areas of capillary closure (Fig. 1, Fig. 2). Moreover it demonstrates the evolution of this occlusive process and its spreading to the small arteriolar branches (Fig. 3).

The most important consequence of capillary closure is the transformation of the capillary network which is slowly setting in in the neighbourhood of the occluded areas.

This transformation is realised by two forces: the bloodstream and the

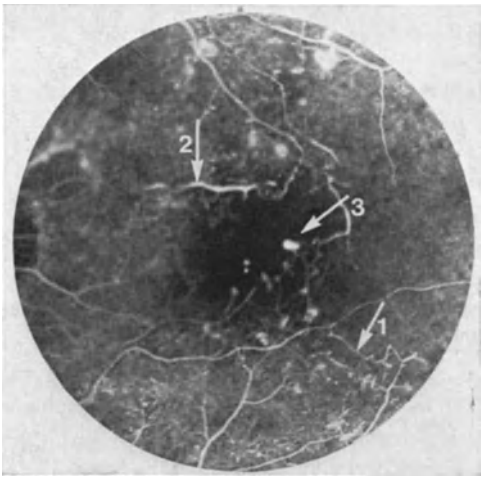


Fig. 4. Advanced proliferative diabetic retinopathy (male, 27 years old). Arterio-venous phase: arterio-venous shunt vessels indicated by arrows 1 and 2. Large areas of non-perfusion. Neovascularization. Macro(3)- and microaneurysms.

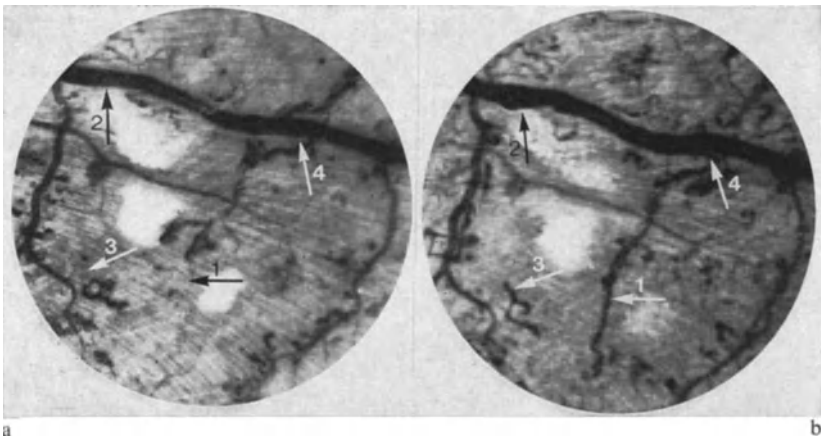


Fig. 5a, b. Beginning proliferative diabetic retinopathy (female, 23 years old). Arrows indicate differences in both pictures. The interval is 3 months.

capacity of the vascular system to proliferate when the tissues become hypoxic.

This results in the formation of two different patterns of vessels: those which bypass the closed areas of the capillary network, the so-called 'shunt vessels', and those which develop gradually from small capillary loops to large vessel fans (Fig. 4; Fig. 5 a, b; Fig. 6 a). It has been shown that blood flow in the arterio-venous communications is slow. Therefore it can not be assumed that they fulfill a real shunting function. However, 'shunt vessels' have still some circulatory functions because they establish connections between arteries and veins in a region where the normal intermediary capillaries become occluded.

The same is not true for the newly-formed vessels which rise sideways of the normal blood stream. They develop outside the normal network of the retinal vascular tree and grow finally outside the retinal tissue. They are therefore functionally useless.

If there exists an arterial supply of this newly formed network, one may distinguish one or more feeder vessels in the arterial phase of fluorescein angiography (Fig. 6 b, c). In many instances however, the filling of the newly formed vessels does not appear before the venous phase, which thus demonstrates their purely venous origin.

These findings may be important when treating neovascularizations with light coagulation.

Another important feature of the disturbed circulation in diabetic retinopathy is the increased permeability of the vessel walls. This is clearly shown in fluorescein angiography by the staining of, and leakage through the vessel wall (Fig. 7; Fig. 8). The leakage is mostly confined to pathologic areas, which in general can easily be identified by ophthalmoscopy (Fig. 6), but it may also appear in areas where ophthalmoscopically no pathologic signs are seen (Fig. 9 a, b).

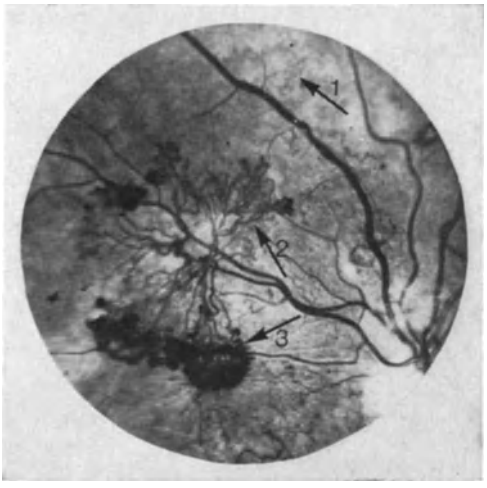


Fig. 6 Advanced proliferative diabetic retinopathy (male, 27 years old).
a. Conventional photograph: small (1) and large fanlike neovascularizations (2 and 3).

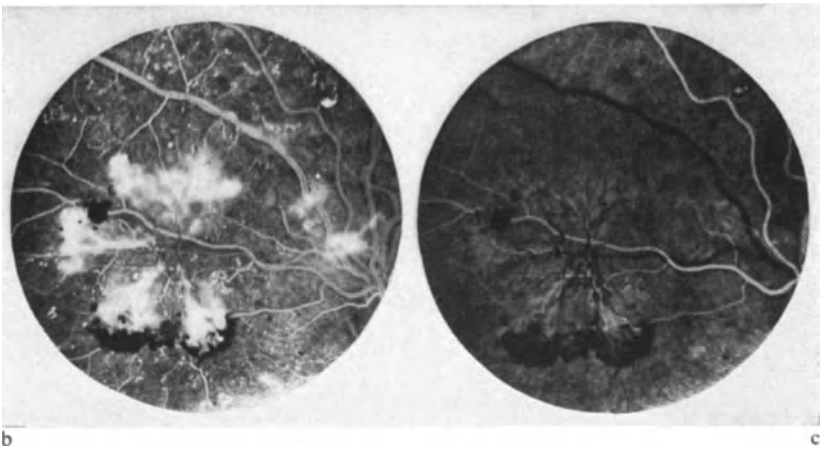


Fig. 6. b. arterio-venous phase: beginning of massive leakage; the distal parts of vascular loops are covered with hemorrhages (black).
c. early arterial phase: well distinguishable feeding vessels.

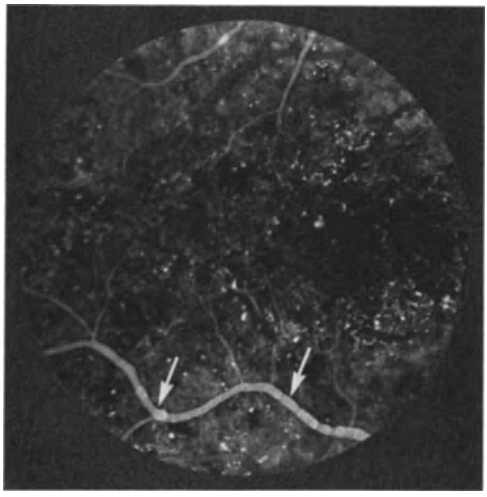
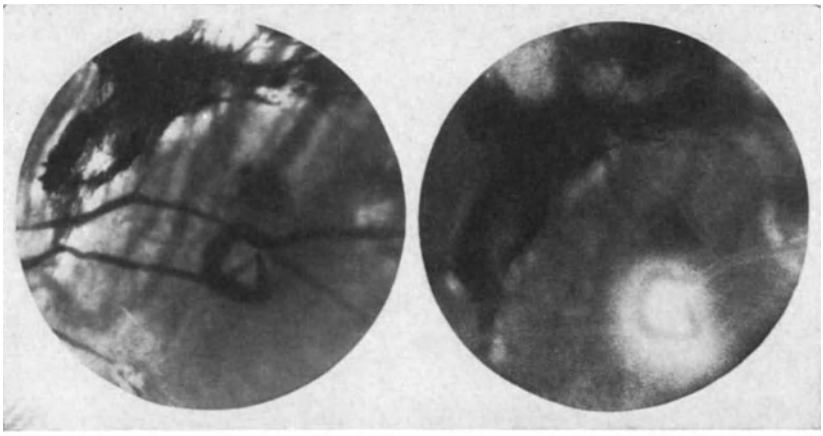


Fig. 7. Beginning proliferative diabetic retinopathy (male, 30 years old). Late venous phase: staining of the wall of one of the main retinal veins, with sausage-like dilatations (arrows).

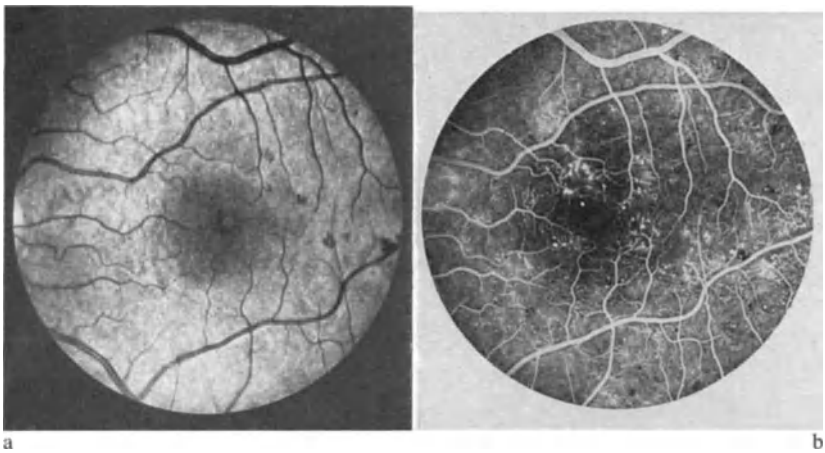
Fluorescein angiography is able to outline retinal vessels and the capillary network even in areas of massive exudation (Fig. 12 c) where in ordinary photographs the retinal vessels hardly can be found (Fig. 12 a).

This supplementary information provided by fluorescein angiography reveals to be of special value when treating diabetic retinopathy with light coagulation. It helps us to evaluate the case prognostically and to make up our mind whether light coagulation can be useful or not.



a b

Fig. 8. Advanced proliferative diabetic retinopathy (male, 50 years old).
a. venous 'omega' loop formation (conventional photograph).
b. late venous phase: intensive leaking through the wall of the venous loop.



a b

Fig. 9. a. conventional photograph: except some small retinal hemorrhages, microaneurysms and a somewhat engorged retinal vein, no pathology is visible.
b. arterio-venous phase: note the numerous foci of capillary leakage, dilated capillaries and the great number of microaneurysms.

Fluorescein angiography too helps us to interprete the effectiveness of our treatment. The prognosis is very poor when on fluorescein angiography extensive areas of the capillary network are closed and numerous arterial branches are obliterated (Fig. 3). Prognosis however is relatively good when the capillary network is only congested (Fig. 10 a, b), even if there are multiple foci of leakage (Fig. 11 a, b) or widespread exudation (Fig. 12 a, b, c, d).

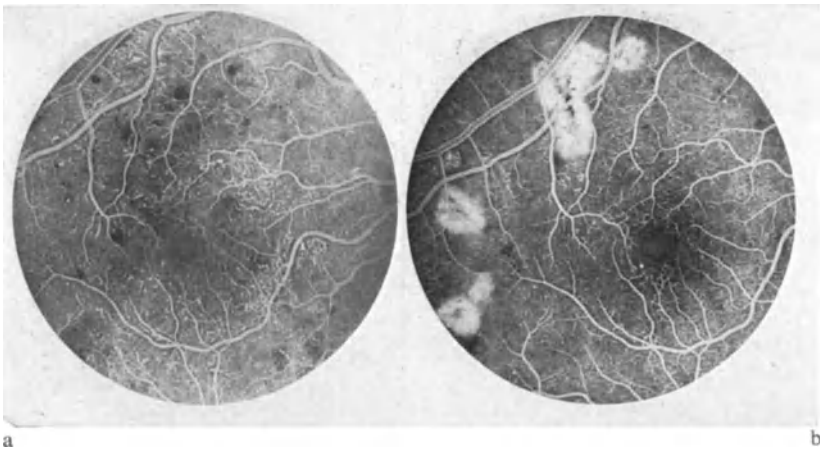


Fig. 10. Beginning proliferative diabetic retinopathy (female, 27 years old).
a. early arterio-venous phase, before treatment with light coagulation. Note engorged capillary network, great number of microaneurysms and small intraretinal hemorrhages (black spots).
b. half year after light coagulation: capillaries are less engorged, the number of microaneurysms and hemorrhages is reduced.

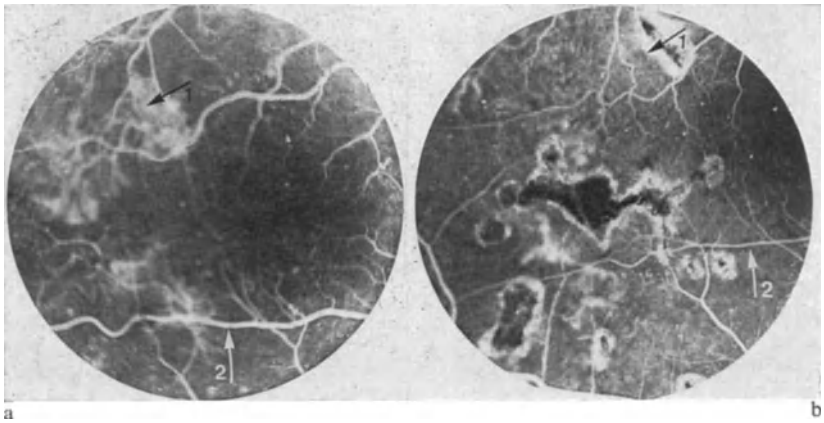


Fig. 11 Advanced proliferative diabetic retinopathy (female, 33 years old).
a. note extensive leakage from newly formed vessels (arrow 1) and engorged retinal vein (arrow 2).
b. one year after light coagulation. Leakage has almost disappeared, caliber of retinal vein is reduced.

After photocoagulation a marked improvement can be seen in these cases, contrary to the first prognostically poor case (Fig. 3) in which, in spite of the overall improvement, visual acuity deteriorated progressively.

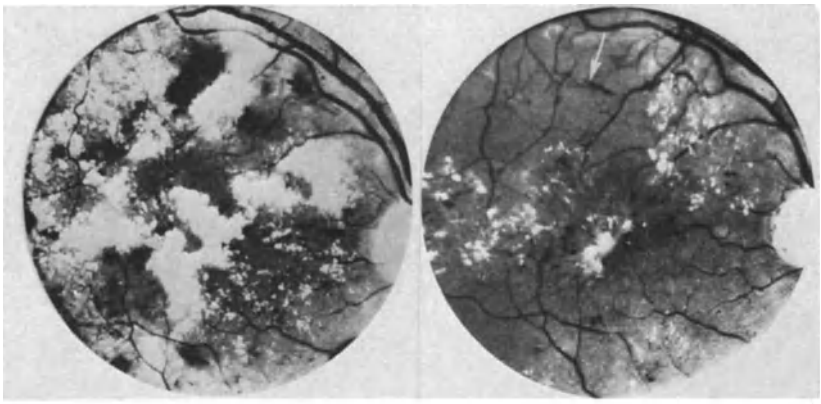
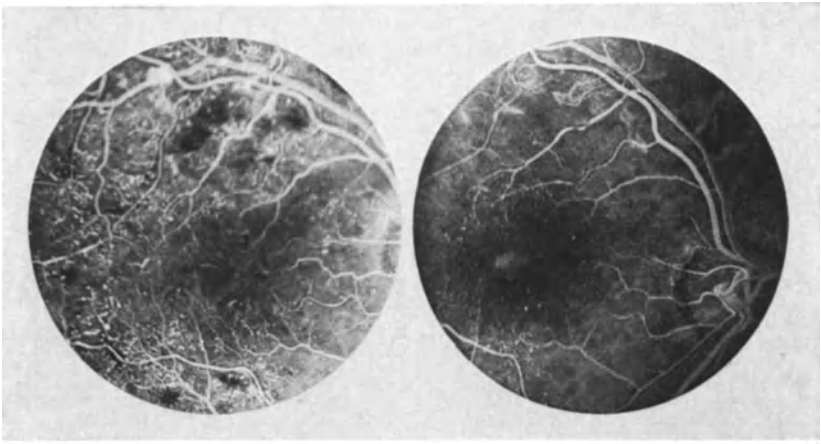


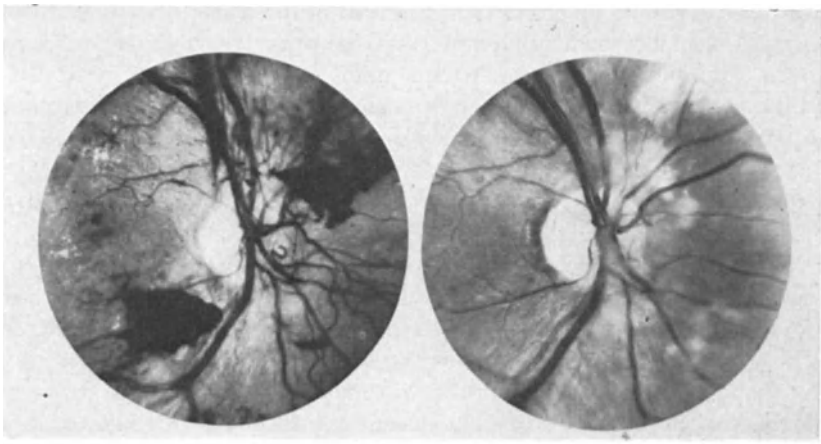
Fig. 12. a, b. Advanced exudative diabetic retinopathy (female, 52 years old). Conventional photographs. Before and 2 years after light coagulation.



c, d. Arterio-venous phase of fluorescence angiography shows the underlying capillary alterations: dilatation, microaneurysms, small areas of capillary closure. Following light coagulation the vessels are less engorged and the number of microaneurysms is drastically reduced.

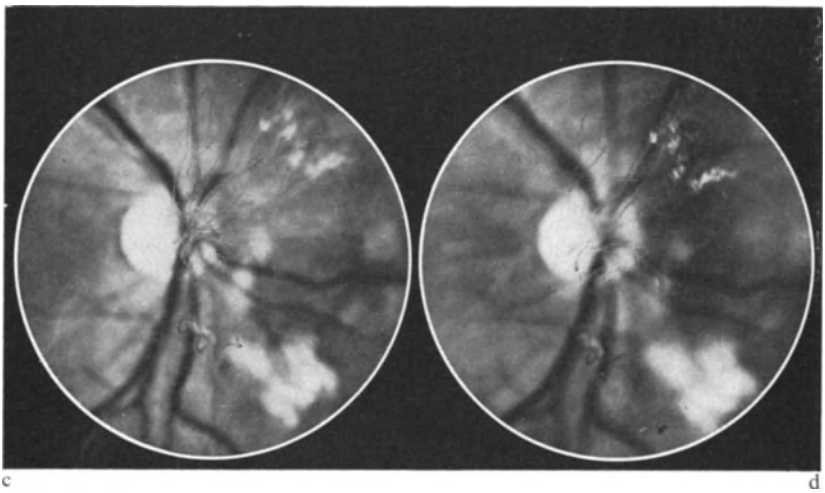
The essential effects of light coagulation are:

1. the narrowing of previously dilated retinal veins in and around the coagulated areas;
2. the resorption of retinal haemorrhages and retinal exudates, sometimes not only in the coagulated area but also at some distance of it, and
3. the fading of neovascularization on the optic disc even if coagulation has been performed in the peripheral parts of the retina (Fig. 11 a, b; Fig. 13 a, b).



a b

Fig. 13. Advanced proliferative diabetic retinopathy (female, 31 years old).
a. very active neovascularization at the disc; large preretinal hemorrhages. At this stage extensive light coagulation was performed.
b. marked improvement one year later.



c d

c, d. Conventional stereophotograph at stage b. The newly formed vessels at the disc have been pulled forward by the retracting vitreous body. They are almost obliterated. No more hemorrhages.

DISCUSSION

The explanation of the favourable effect of light coagulation is commonly searched in a possibility favourable effect on the balance between oxygen need and oxygen supply, which balance is undoubtedly disturbed in all acute and chronic vascular disorders. Cicatrization of the retina is supposed to restore the

balance by diminishing the total oxygen need of the retina. Another possible explanation of a favourable effect of light coagulation on the circulation in the vascular tree of the retina may be found in the multilayered capillary network of the retina which seems to possess especially high hemodynamic requirements. A disregulation is easily established if in some areas of the vascular tree the blood supply, or the blood outflow, is already impaired by anatomic and/or hemodynamic obstacles. A stagnation of the blood circulation in such an area may occur easily with all its consequences.

Light coagulation makes it possible to reduce the whole volume of the capillary network. By using the remaining rarefied and simplified vascular network, the bloodstream finds a shorter and easier connection between arteries and veins. By this way stagnation may be abolished and a fair circulation may be restored. If this speculation is true, we should be able to demonstrate, using fluorescein angiographic follow-up studies, a reduction of the mean transit time, i.e. the time lapse between filling of the feeding artery and draining of the vein in the treated area of the retina, implying a reduction of the total blood volume in the vessels of this sector as well.

Until now, however we have not succeeded in demonstrating such a reduction. We can only conclude indirectly from the narrowing of the retinal veins in the coagulated area that a reduction of the blood volume has most probably occurred in this part of the vascular tree. If we may further assume that light coagulation does not influence the arterial blood supply, i.e. that the quantity of blood passing per time unit has remained unchanged, we may be allowed on the ground of the reduced blood volume to draw the next conclusion: that not only a reduction of the blood volume, but too, that a real acceleration of the blood flow in the coagulated area has occurred.

This concept of an improved circulation makes it easier to understand why hyperpermeability, hemorrhages, exudates and even newly-formed vessels may disappear after treatment with light coagulation. It establishes also a link with the known improvement of diabetic retinopathy following hypophyseal suppression, and it may explain the remissions observed in case no treatment is given. The common basic factor which promotes those – sometimes spectacular – improvements in the course of diabetic retinopathy is most likely of hemodynamic nature.

It has been shown that plasma-noradrenalin is considerably increased in hypophysectomised patients. This may lead to sympathetic vasoconstriction and increased capillary resistance. It is more likely that episodes of regression in the natural course of diabetic retinopathy are caused by circulatory changes, rather than by organic changes in the vessel wall of the retinal vascular tree.

In the more advanced stages of diabetic retinopathy when vessels of greater caliber become involved, the retinal circulation is affected to such a degree that it hardly can be restored by photocoagulation or hypophyseal suppression.

Frequently, emphasis is put on the far-advanced proliferative process as an argument against further therapeutic attempts. The real reason of the non-effectiveness of therapy in these cases is lying, in our opinion, in the widespread obliteration of the vascular tree, especially of the arterial part of it.

There is no method which can demonstrate this deplorable condition of the retinal vasculature better than fluorescein angiography (Fig. 3). This is a reason to emphasize the value of fluorescein angiography not only as an indicator of the necessity to start treatment, but also as an indication to renounce in case treatment must be considered useless.

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FLUORESCENCE ANGIOGRAPHY OF RETINAL VEIN OCCLUSION IN RELATION TO PHOTOCOAGULATION AND LASER TREATMENT

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ABSTRACT

A survey is given of features observed in fluorescein angiography of patients suffering from retinal vein occlusion.
Light- and LASER coagulation is recommended only after a prolonged period of careful observation during weeks or months.
Early active treatment is recommended in case of imminent damage to the macula and in case of early neovascularisation surrounding the area of obstruction.

Fluorescence angiography in retinal vein occlusion presents many features identical with or similar to those seen in diabetic retinopathy, though in a different sequence and accentuations (OOSTERHUIS, 1968; OOSTERHUIS & VINK, 1968).

Pathological changes of the veins, such as dilatation and tortuosity, staining of the venous wall and leakage of fluoresceine through the wall of even the main

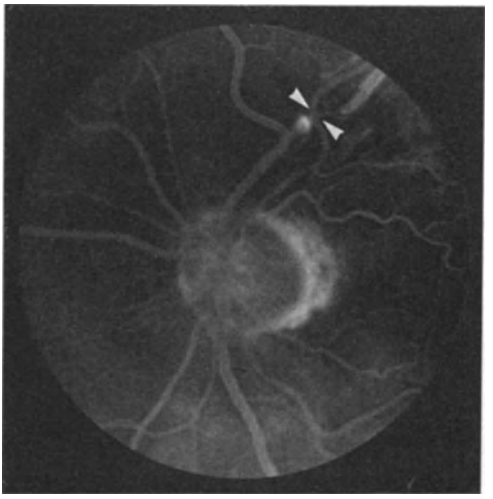


Fig. 1. Recent venous branch occlusion. Late venous phase. Excessive narrowing of the vein at the arterio-venous crossing (→ ←). Intensive staining of the vein distally and proximally from the crossing.

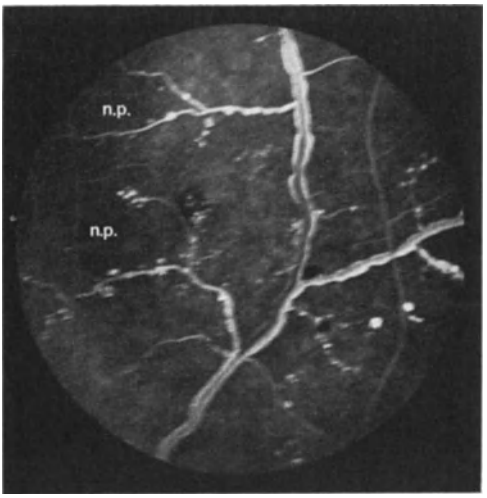


Fig. 2. Long standing venous branch occlusion. Venous phase. Sausage-like dilatations and staining of the venous wall. Irregular dilatations of the preterminal veins. Micro- and macroaneurysms. Areas of non-perfusion (n.p.).

venous branches, a late phenomenon in diabetic retinopathy, appear soon in venous occlusion. The site of the blockage or stenosis at the disc in stem occlusion (Fig. 5 b), or at the arterio-venous crossing in branch occlusion (Fig. 1) can be seen in many cases.

Long standing cases of venous occlusions may show the same beaded, sausage-like dilatations of the veins as seen in advanced cases of diabetic retinopathy (Fig. 2).

The arterial component in the development of venous occlusion is apparent in patients with long arm-retina time, in conspicuous changes in the calibre of the retinal arteries and even staining of the arterial walls (Fig. 3). In most of the cases the intraretinal circulation time in the involved area is also prolonged, either through slowing down of the venous outflow, or due to a reduced arterial inflow as well.

Very soon, changes of the retinal capillaries appear in the pathologic areas adjacent to haemorrhages.

There is an irregular dilatation of the arteriolar as well as venous capillary bed (Fig. 4), with formation of microaneurysms and, eventually, even macroaneurysms. The dilated capillaries and aneurysms leak in the venous and late venous phase. Side by side with these changes are areas of non-perfusion with obliterated capillaries (Fig. 3 and 7), especially at the site of previous haemorrhages.

Further course of vein occlusion varies from case to case. A great percentage of cases improves either spontaneously or due to adequate treatment of the underlying systemic disease. In a survey of several years ago (Zahn et al., 1960) patients with vein occlusion suffered from one or more of the following diseases: hypertension (68%), arteriosclerosis and/or cardiovascular disease (43%),

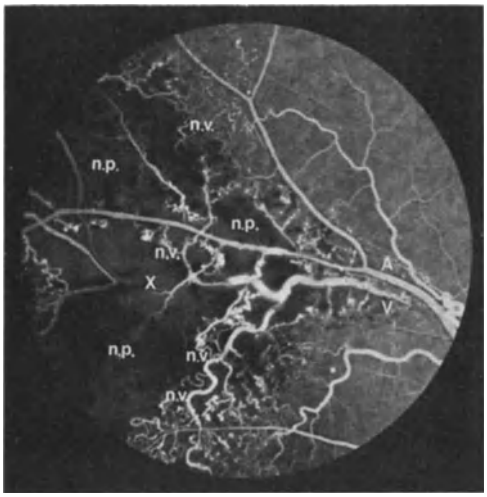


Fig. 3. Branch vein (V) occlusion. Arterio-venous phase. Marked irregularity of the caliber and staining of the arterial wall (A). Non-filling of several arterial branches. Large areas of non-perfusion (n.p.). Staining of the distal part of the occluded vein Peripheral branches of the superior macular vein do not show any connections (X) with the central part and drain into the neighbouring venous branches. Dilated capillaries with microaneurysms at the borders of the non-perfused areas. Formation of newly formed vessel loops (n.v.) at the borders of the non-perfused area.

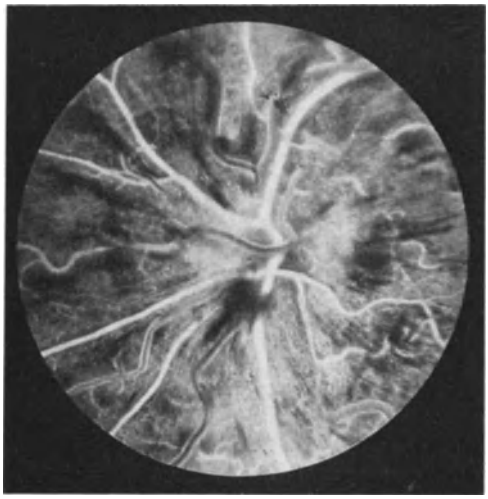


Fig. 4. Recent venous stem occlusion. Early arterio-venous phase. Venous engorgement, haemorrhages at the disc and in all retinal quadrants (black spots). Oedema of the disc. Dilated capillaries on and around the disc.

diabetes (without manifest retinopathy; 3%), blood dyscrasias (6%). In our recent material of 65 cases there is a very conspicuous shift in the direction of diabetes or prediabetes (40% and 80% respectively) and hyperlipaemia (70%), due only partially to improved biochemical diagnostic methods. The percentage of hypertension was about the same (72%).

Recovery, with resorption of the haemorrhages, is seen in fluorescence angiography as disappearance of staining at the site of the eventual blockage (Fig. 5 c, d), disappearance or diminished staining of and leakage from the

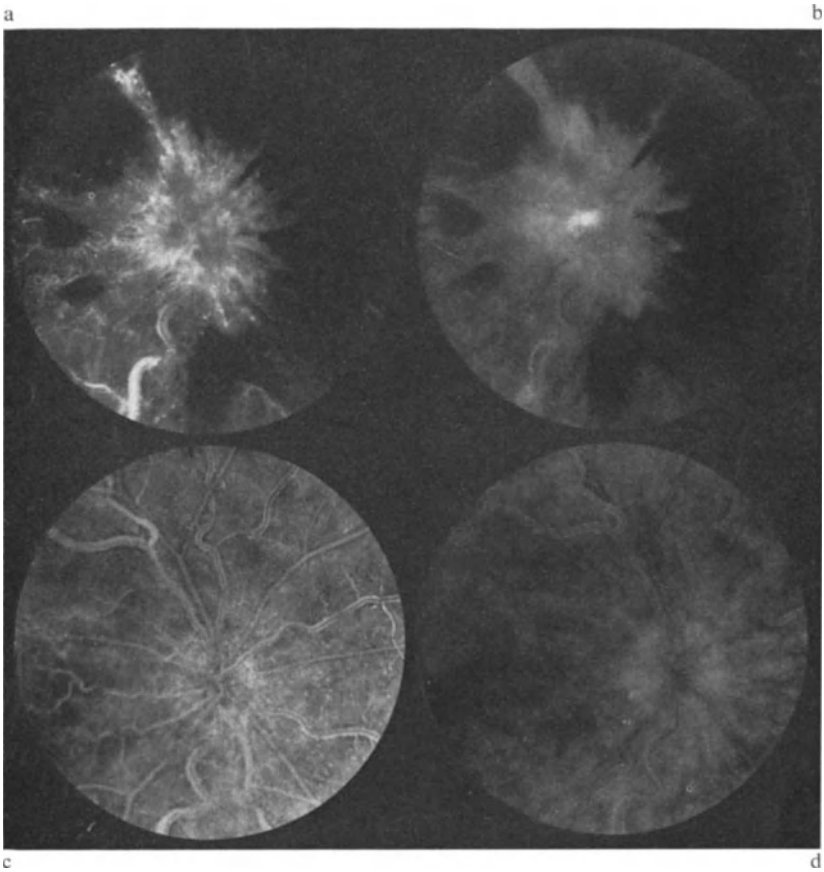
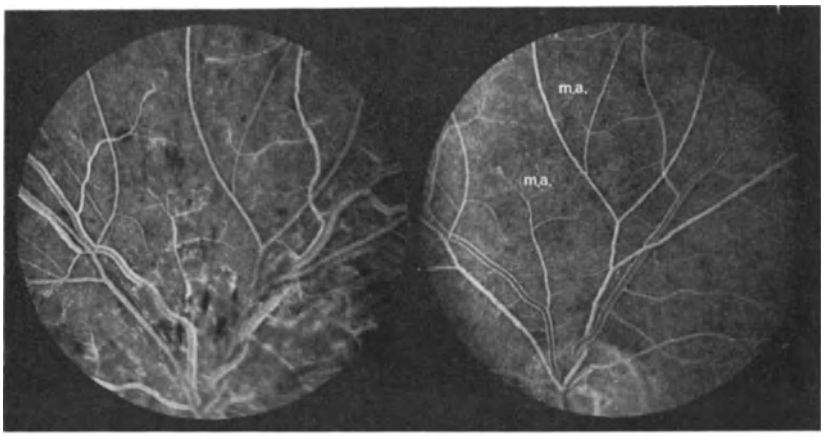


Fig. 5a. Recent venous stem occlusion. Venous phase. Marked oedema of the disc. Extensive haemorrhages. Dilated capillaries with microaneurysms at the disc. Engorgement of the veins.

Fig. 5b. Intensive staining of the venous stem in the late venous phase representing the presumed stenosis.

Fig. 5c. The same patient 5 months later. Venous phase. Reduced oedema of the optic disc. Dilatation of the capillaries with microaneurysms. Less venous engorgement. Haemorrhages subsided.

Fig. 5d. Late venous phase. Some staining of the disc. No more staining of the venous stem. Engorgement and some staining of the peripheral venous walls.



a b

Fig. 6a. Recent occlusion of the superior venous branches at the margin of the disc. Arterio-venous phase. Very narrow arterioles. Venous engorgement. Haemorrhages (black spots). Irregular dilatation of and leakage from the preterminal venules.
Fig. 6b. The same patient 3 months later. Except narrowing of the arterioles and areas with dilated capillaries with microaneurysms (m.a.), no vascular pathology is visible. The haemorrhages disappeared.

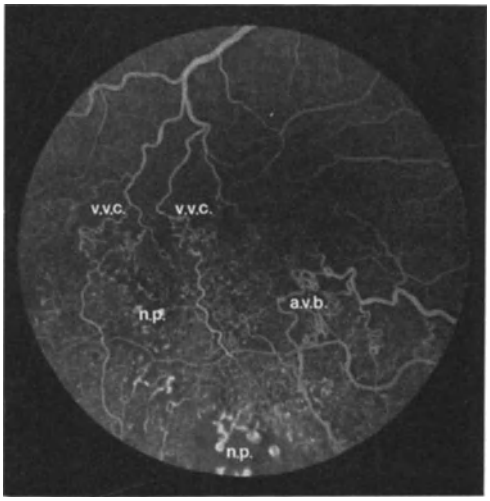
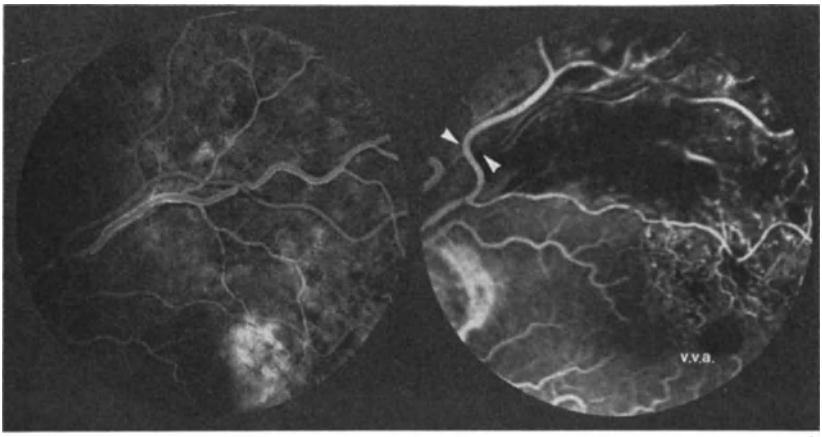


Fig. 7. Longstanding venous branch occlusion. Arterio-venous phase. Arterio-venous bypasses (a.v.b.) and veno-venous collaterals (v.v.c.). Tufts of neovascularisations and macroaneurysms at the borders of the non-perfused areas (n.p.).

venous wall, improvement of the tortuosity and calibre of the involved veins (Fig. 6 a, b). Shortening of the intraretinal circulation time was observed and resorption of haemorrhages was found. All these changes would suggest a reopening of the previous stop or stenosis.



a b

Fig. 8a. Recent venous branch occlusion. Late venous phase. Leakage from neovascularisations above the macula.

Fig. 8b. The same patient 4 months later. Arterio-venous phase. Repeated massive haemorrhages. Persisting stenosis (→ ←) of the venous branch at the arterio-venous crossing. Dilated capillaries with microaneurysms, neovascularisations, veno-venous anastomoses (v.v.a.) vertically through the macular area. Macular oedema.

However, if the blood flow through the obstacle is not restored, other reparatory mechanisms are to be seen. At this stage, or earlier still, first capillary and later on communications of greater calibre are to be found by fluorescence angiography between the veins of the involved area and the adjacent veins, as veno-venous collaterals or, eventually, as arterio-venous bypasses (Fig. 7).

Disappearance of the stop as well as formation of the collaterals may result in disappearance of capillary dilatation, leakage and disappearance of the microaneurysms.

If this compensatory mechanism does not take place or is much delayed, first capillary dilatation and, later on, venous and arteriovenous neovascularisations develop which leak intensively and may be the source of repeated haemorrhages (Fig. 8 a, b).

Other cases of vein occlusion show no symptoms of improvement for several months and remain more or less stationary, and still other suffer from repeated haemorrhages, retinal as well as intravitreal, months and even years after the onset of the occlusion. These cases are prone to haemorrhagic glaucoma if we are dealing with a stem occlusion.

PHOTOCOAGULATION AND/OR LASER TREATMENT OF VEIN OCCLUSION

Owing to improvement which occurs spontaneously or due to treatment of the underlying systemic disease in a great percentage of patients, expectant attitude

is mostly recommended for several weeks or months before decision is taken for photocoagulation or laser treatment (PATZ, 1972; OOSTERHUIS & SEDNEY, 1972).

Age of the patient, his systemic condition and response to medical treatment are important prognostic factors. Absence of visible stops or stenosis in the fluorescence angiogram, only slightly delayed circulation time, no gross pathology of the venous wall, and only slight reaction of the capillaries around the macula, all indicate a favourable prognosis. Also the existence of a vein draining the macular area without being involved in the disturbed circulation is an indication of good prognosis.

Even in the presence of severe pathology expectant attitude is recommended until at least partial disappearence of large haemorrhages because even then repair may occur due to recanalisation of the stop, bypass or collaterals.

In our opinion this general rule has, however, two important exceptions.

The first one is imminent damage to the macular area. If dilated, leaking capillaries with microaneurysms are seen on fluorescence angiograms (Fig. 8 b and 9) and cause macular oedema. If veno-venous collaterals, or arterio-venous bypasses begin to form in the immediate vicinity, or even in the macular area itself (Fig. 10), preventive laser-coagulation seems indicated to us.

The second exception seems to be an early beginning of neovascularisation surrounding the area with obliterated capillaries (Fig. 3 and 7).

These two are in our opinion preventive indications for photocoagulation or laser treatment.

If these two conditions do not apply and an expectant attitude is chosen, active treatment becomes indicated:

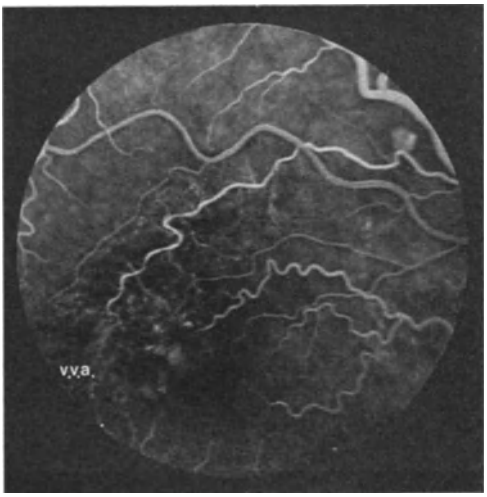


Fig. 9. Secondary vascular changes following occlusion of superior macular vein. Venous phase. Dilated capillaries with microaneurysms, neovascularisations; veno-venous anastomosis (v.v.a.) at the temporal margin of the macular area. Leakage in the macular area, giving rise to cystic alterations in the fovea.

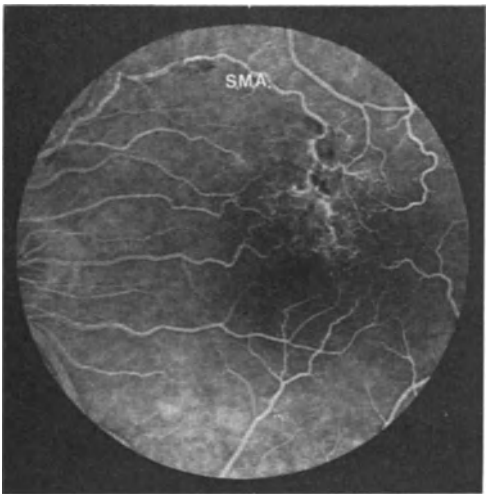
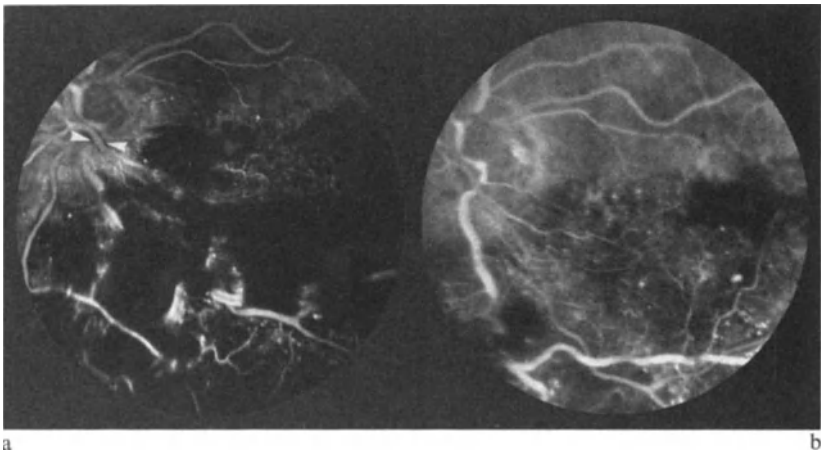


Fig. 10. Long standing venous branch occlusion. Arterio-venous phase. Gross pathology of the superior macular artery (S.M.A.). Arterio-venous bypass through the macular region. Dilated capillaries and neovascularisations in the macular region.

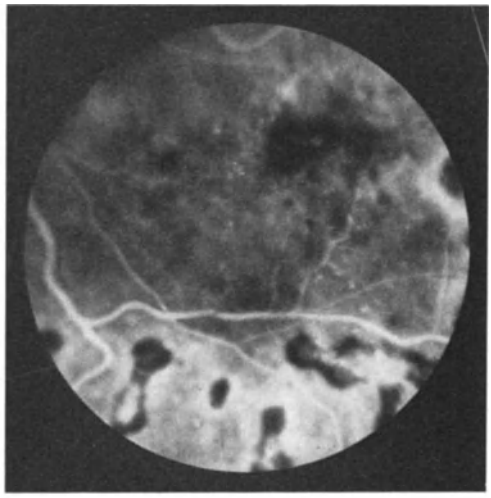
1) If there is no sufficient improvement within 3-4 months, the fluorescein angiography shows gross pathology of the capillaries with leakage, neovascularisations, very slow disappearence of haemorrhages, slight or no improvement of the pathology of the venous wall and eventual persistence of the blockage or stenosis (Fig. 11);
2) If there is no improvement at all and, besides the changes described above, repeated haemorrhages occur already in the first months after the onset of the disease (Fig. 8 and 12);
3) Finally, active treatment is indicated in long standing cases of venous occlusion with repeated retinal and especially intravitreal haemorrhages from extensive neovascularisations.

In all indicated cases photocoagulation is used mostly, laser coagulation being reserved for the treatment of the macular area. Coagulation is aimed in the first place at the neovascularisations, and pathological and leaking capillaries. Collaterals and bypasses are not treated unless they are developing through the macular area. It is mostly recommended (PATZ) not to coagulate large haemorrhages especially in the neighbourhood of the disc, because damage to the nerve fibre layer may occur with large defects of the visual field. This does not apply to haemorrhages persisting without any change for several months. In our experience (Fig. 12) haemorrhages disappear very quickly if coagulated, or even when coagulation is applied simply in a 'stradling way' along the tributary veins in the involved part of the retina. A different problem are extensive exsudates which may arise around microaneurysms or neovascularisation tufts. The coagulation of aneurysms and vascular tufts leads mostly to the disappearance of those exudates.



a b

Fig. 11a. Recent branch occlusion of the temporal inferior vein. Arterio-venous phase. Stenosis located at the arterio-venous crossing at the disc margin (→ ←). Severe haemorrhages. Dilated capillaries with microaneurysms. Gross engorgement. of the temporal inferior vein, with haemorrhages extending into the macular area. Fig. 11b. The same patient 3 months later. Arterio-venous phase. Less haemorrhages, but the macula is still covered with haemorrhages. Dilated capillaries or/and neovascularisations with micro- and macroaneurysms. Photocoagulation was then carried out in the area of the previously occluded vein.



c

Fig. 11c. The same patient one month after photocoagulation. There are no more haemorrhages, neovascularisations or pathologically leaking capillaries in the coagulated area visible. Persisting haemorrhages in the macular area.

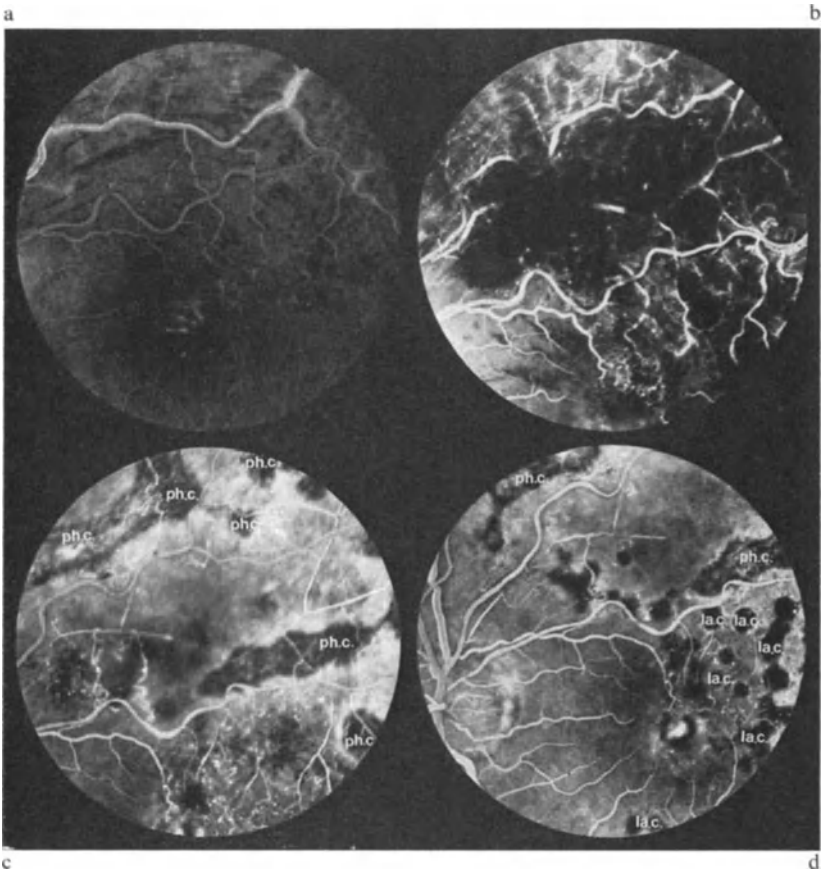


Fig. 12a. Recent temporal superior vein occlusion. Venous phase. Moderate haemorrhages, venous engorgement, staining of the venous wall and leakage from it. Dilated capillaries in the macular area, discrete changes in the macula.

Fig. 12b. The same patient 3 months later. Arterio-venous phase. Severe repeated haemorrhages. Intensive leakage from the preterminal venules above the macula. Dilated capillaries and neovascularisations in the macular region showing fluorescein leakage. Photocoagulation in the whole involved area was carried out.

Fig. 12c. Two weeks after photocoagulation. Arterio-venous phase. Scars from photocoagulation (ph.c.). Haemorrhages subsided. No more venous engorgement. Very little vascular pathology in the vicinity of the coagulated area. Dilated capillaries, neovascularisations, micro- and macroaneurysms above the macula with leakage into the macula. Lasercoagulation above and close to the macular area was now carried out.

Fig. 12d. The same patient one month after lasercoagulation (la.c.). Arterio-venous phase. Vascular status in and around the macular area has improved. Persisting haemorrhage and degeneration of the foveal area. No improvement of visual acuity.

The effect of photocoagulation is very striking. The leaking dilated capillaries with microaneurysms disappear as well as neovascularisations and haemorrhages. The calibre of the arteries and veins becomes normal, fluorescence of the

venous wall disappears. It is even claimed that haemorrhagic glaucoma can be prevented by effective photocoagulation (PATZ, 1972).

COMMENT

The macular area can already be covered with haemorrhages from the onset of venous occlusion. In some cases these resolve leaving a functioning and apparently undamaged macula. In other cases degenerative changes with pigmentations and oedema remain after disappearance of haemorrhages. Oedema and secondary cystoid and other degenerative changes can develop as a sequel of leakage from pathologic capillaries, from leaking and/or bleeding neovascularisations in the vicinity, and the macula can even be destroyed by collaterals or bypasses which course through it. The macular damage may be due to the circulatory insufficiency in this area as well. If drainage of the capillary network around the macula is impaired, the blood flow in those capillaries and the oxygen supply will become chronically insufficient.

In spite of some encouraging reports (CAMPBELL et al., 1973; KRILL et al., 1971) it is still dubious in what percentage of cases involvement of the macula and impairment or loss of central vision can be prevented or improved by photo and/or laser coagulation. Those doubts arise from the uncertainty about the true mechanism of macular damage, and the uncertainty of the mode of action of the photocoagulation in general. Certainly, destruction of a hypoxic area and elimination of its pathological blood vessels (leaking capillaries and neovascularisations) may improve the circulation in the remaining areas, removing at the same time the stimulus for neovascularisation (RIASKOFF, 1972). In this way, elimination of pathologic and neovascular parasitic circulation may bring the existing, eventually reduced, blood volume into restricted but functionally normal channels. It is still not quite clear to what extent also the choroidal circulation participates at the restitution of the retina. Arterio-venous bypasses and venovenous collaterals can develop between the retinal and cilioretinal vessels at or on the disc (AMALRIC & BONNIN, 1969). Capillary anastomoses between the retinal and choriocapillary circulation at the edges of the photocoagulates seem not totally out of the question. They could probably explain the very fast resorption of coagulated haemorrhages.

CONCLUSION

Fluorescence angiography gives detailed information about the haemodynamics, pathology of the retinal vessels and development of reparatory or complicating changes in retinal venous occlusion. It is at present the most important means for the decision whether and when treatment with photo- or lasercoagulation is necessary and allows a reliable assessment of the effect of treatment.

This study indicates that in several cases treatment may be carried out too late. Sometimes insufficient attention had been given to imminent macular damage, either because fluorescence angiography was performed too late after the onset of the disease, or the fluorescence follow-up had been carried out in

too long intervals, or because the danger to the macula had been underestimated. We ourselves learned from this study to become more aware of these imminent dangers, which may lead in future to a better management of these cases.

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FLUORESCENCE ANGIOGRAPHY OF CHOROIDAL TUMORS

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(*Utrecht*)

ABSTRACT

A description is given of the fluorescein-angiographic patterns of the following lesions of the choroid: naevus, malignant melanoma, hemangioma and metastatic tumors.
The value of fluorescein-angiography for the differential diagnosis is discussed.

The problem of accurate clinical diagnosis of choroidal tumors is despite the effort of many investigators not yet solved (ZIMMERMANN, 1973).

The introduction of fluorescence angiography by MACLEAN & MAUMENEE in 1960 offered an important addition to the investigation methods such as: ultrasonography, slitlamp biomicroscopy, fundusphotography and P 32-test, already in use for improving the diagnosis of intraocular tumors.

Since then fluorescence angiography of choroidal tumors and especially its use in the differential diagnosis of malignant melanoma has been described by many authors (AMALRIC, 1967; BONNIN, 1971; EDWARDS et al., 1969; FLINDALL & GASS, 1971; GITTER et al., 1968; HAYREH, 1970; HILL, 1971; KAREL & PELESKA, 1972; OFFRET et al., 1970; OOSTERHUIS & VAN WAVEREN, 1968; PETTIT et al., 1970; RUBINSTEIN, 1967; SNIJDER et al., 1967; WESSING, 1968).

The subject of this paper is to describe the fluorescence angiographic findings in choroidal tumors with special reference to the aspect of malignant melanoma and its differential diagnostic features.

The findings in the following lesions of the choroid will be described:
- naevus
- malignant melanoma
- hemangioma
- metastatic tumors.

NAEVUS OF THE CHOROID

The naevus ophthalmoscopically appears as a homogeneous, small, round or oval shaped, greyish-brown patch with ill-defined borders.

A variable amount of whitish spots can be seen, which represent drusen of Bruch's membrane.

Rarely small alterations in the retinal pigmentepithelium can be seen (NAUMANN et al., 1971).

If the naevus is large (naevi with a diameter of 6 PD have been described) and slightly prominent and if in addition it contains many drusen, fluorescence angiography is very important for the correct diagnosis.

Fluorescence angiography of the naevus

The pattern is characterized by some degree of obscuring of choroidal fluorescence with a rather ill defined border (Fig. 1). The masking of background fluorescence is dependent on the amount of pigment in the naevus and the surrounding tissues and on the position of the naevus in the choroid.

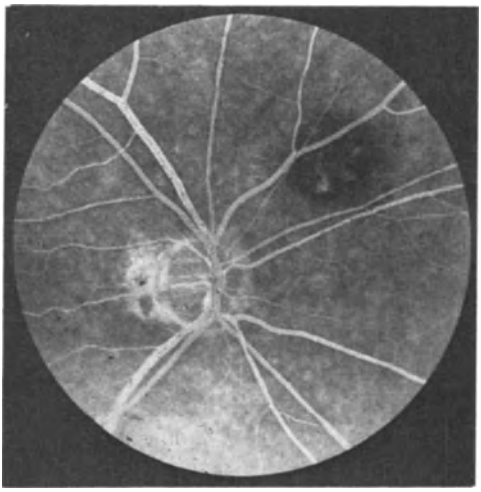
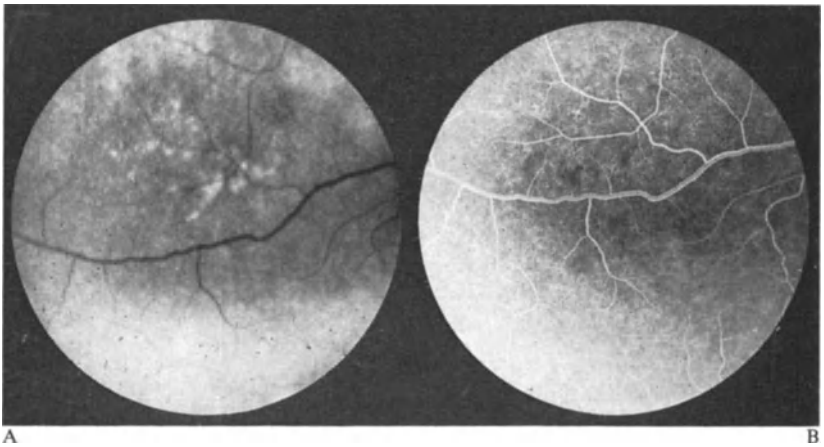
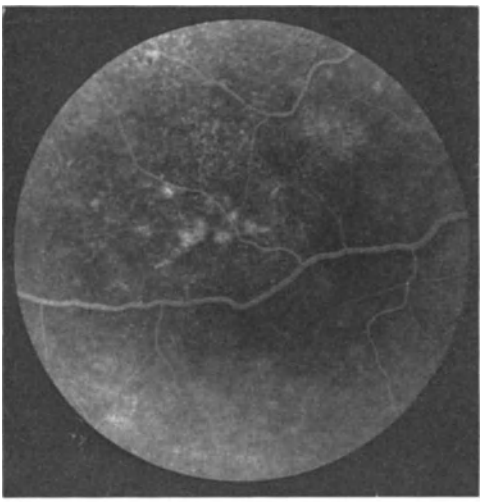


Fig. 1. Small naevus of the choroid with drusen. (venous phase)



A B

Fig. 2. Large naevus with drusen.
A. before fluorescein injection. B. arterio-venous phase.



C

C. late phase. Drusen clearly visible.

Drusen appear as sharply defined bright spots of variable size with a gradually increasing fluorescence up to the late phase (Fig. 2). Alterations of retinal pigmentepithelium can be seen as lighter spots whose intensity vary with choroidal fluorescence (NAUMANN et al., 1971).

A hypertrophic lesion of pigment epithelium has a sharply demarcated jet-black appearance throughout all fluorescence angiographic phases (Fig. 3) (HAYREH, 1970).

It must be stressed that naevi never show diffuse leakage of fluorescein in the lesion, contrary to malignant melanomas who are leaking the dye in the tumor; this is the most important differential diagnostic point.

MALIGNANT MELANOMA OF THE CHOROID

The clinical appearance of malignant melanoma shows a marked degree of variation depending on the pigmentation, vascularity, age and secondary changes in the tumor and the surrounding tissues.

THE EARLY MALIGNANT MELANOMA

This form appears as a roundish, slightly elevated, ill-defined lesion. The colour varies from whitish-grey to dark-brown. The pigment is irregularly distributed, sometimes showing yellow-orange patches. Some degree of retinal detachment over the lesion may be present. The tumor as a rule perforates Bruch's membrane and protrudes into the vitreous cavity. Occasionally, however, the tumor has the tendency to spread in the plane of the choroid (REESE & HOWARD, 1967).

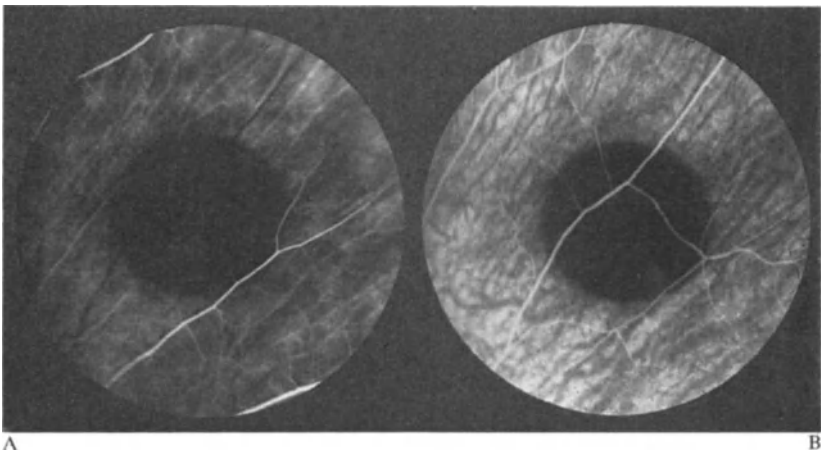


Fig. 3. Hypertrophic lesion of pigmentepithelium.
A. arterio-venous phase
B. late venous phase. Pattern remains the same.

THE PROTRUDING FORMS OF MALIGNANT MELANOMA

These melanomas exhibit an extremely variable degree of pigmentation ranging from the pinkish-white amelanotic melanoma to the densely pigmented dark-brown tumors.

Tumor vessels are often seen on the surface, and haemorrhages readily occur from these pathologic vessels.

Some degree of retinal detachment and cystic degeneration is usually also found. Often a flat grey-brown borderzone is seen around the tumor.

The fluorescence angiographic pattern of the early, flat malignant melanomas

This pattern is shown in Fig. 4. Staining appears in the arterial or arterio-venous phase and has an irregularly mottled aspect (Oosterhuis & Van Waveren, 1968) rapidly reaching a maximum intensity in the early venous phase. The pattern gradually becomes more confluent leading to a diffuse cloudy fluorescence in the late phase lasting for hours (Flindall & Gass, 1971; Oosterhuis & Van Waveren, 1968). Hayreh and Flindall & Gass stressed the fact that in contrast to the behaviour in naevi of the choroid, the ophthalmoscopically pigmented areas show fluorescence while the yellowish non-pigmented areas show little or no staining.

The tumor shows usually sharply demarcated brightly staining spots beginning in the arterio-venous or venous phase. They are situated mostly on the border of the tumor, but can be seen anywhere on the lesion.

The nature of these drusen-like spots has yet to be elucidated (Pettit et al., 1970). The degree of fluorescence in the centre of the lesion may vary considerably in the early phase (compare Fig. 4 and Fig. 5). The retinal capillaries over-

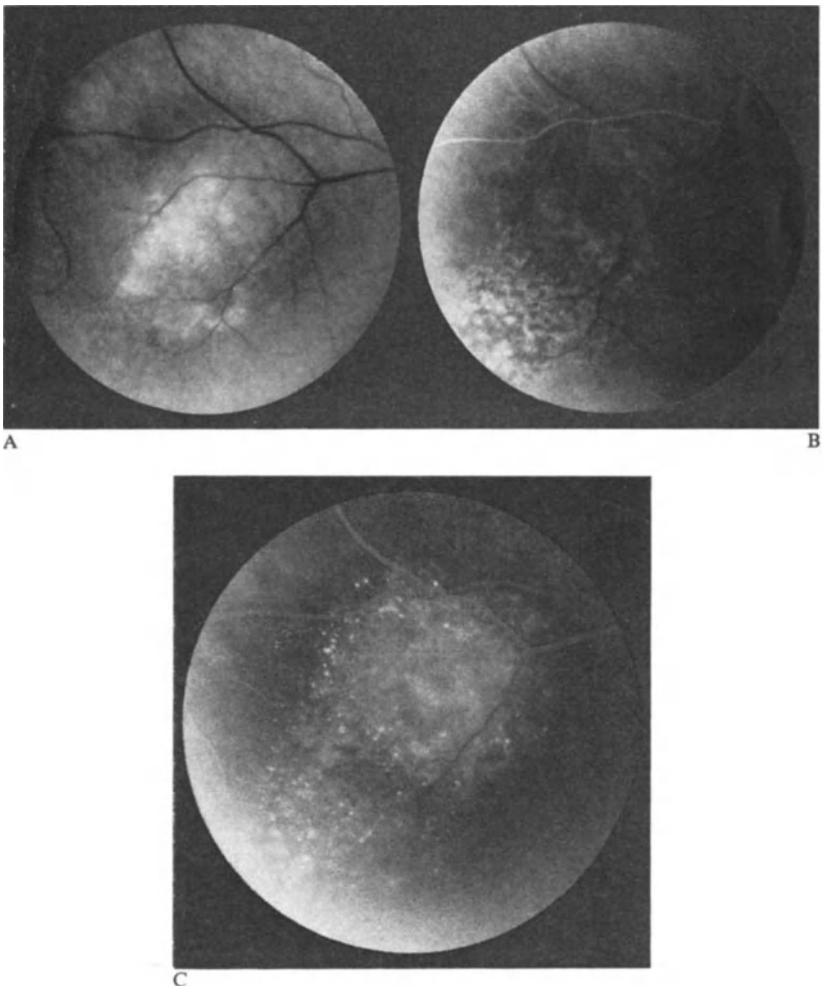


Fig. 4. Malignant melanoma.
A. Before fluorescein injection. B. Arterial phase. Early staining. C. Late phase. Diffuse fluorescence with spotted borderzone.

lying the tumor are generally dilated and may show microaneurysms (OOSTERHUIS & VAN WAVEREN, 1968) and in the late phase dye may pass into subretinal fluid giving rise to a diffuse glow.

The fluorescence angiographic pattern of the protruding melanomas

These tumors show varying patterns of fluorescence. In the least pigmented tumors, the amelanotic melanomas, rapid transition of the dye starts in the arterial or pre-arterial phase. Large coarse tumor-vessels are staining ('double circulation') (OFFRET et al., 1970; THEODOSSIADIS, 1971).

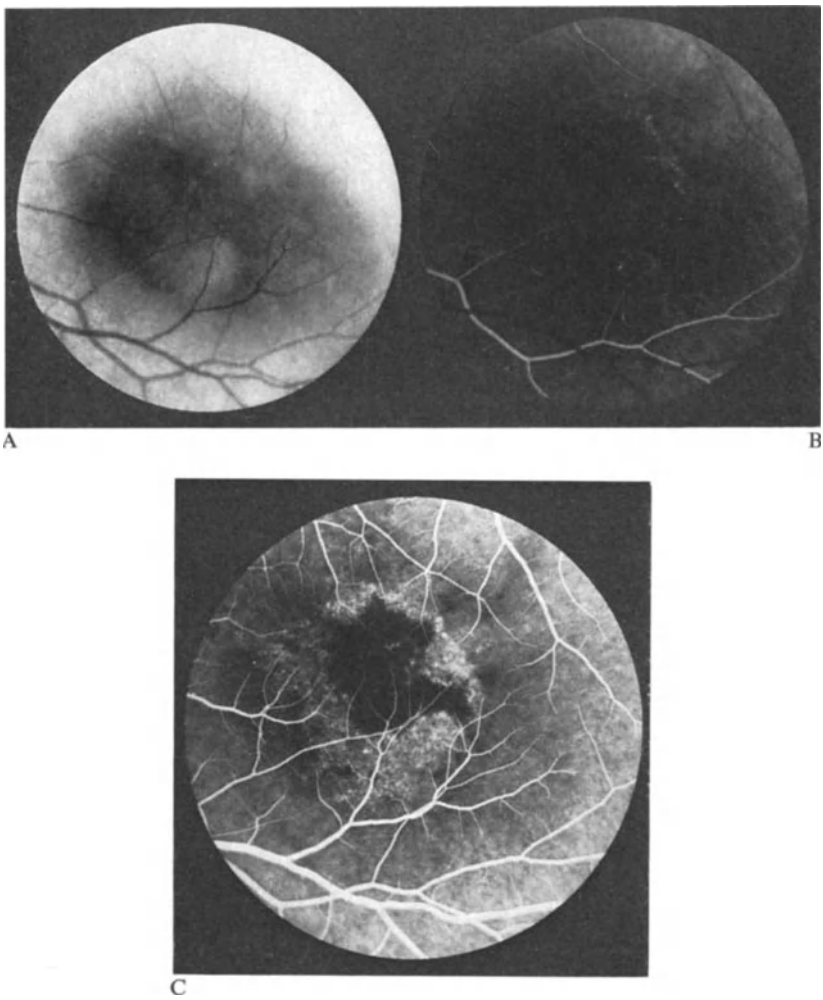


Fig. 5. Malignant melanoma.
A. Before fluorescein injection. B. arterial phase. Early staining. C. Arterio-venous phase. Centre of the lesion remains dark.

Massive leakage of fluorescein occurs giving rise to a nearly diffuse fluorescence as early as in the venous phase. The intensity shows little or no decrease.

In the late phase the larger tumor-vessels devoid of the dye stand out as dark strands against the background of the diffusely fluorescing tumor (Fig. 6 C).

In more heavily pigmented malignant melanomas pathological fluorescence starts in the arterial, arterio-venous or early venous phase.

Tumor vessels may be seen but the network may be partially obscured by areas of surface pigment or patches of haemorrhage. Diffusion of the dye in the tumor gives rise to a long lasting irregular and diffuse fluorescence (Fig. 7).

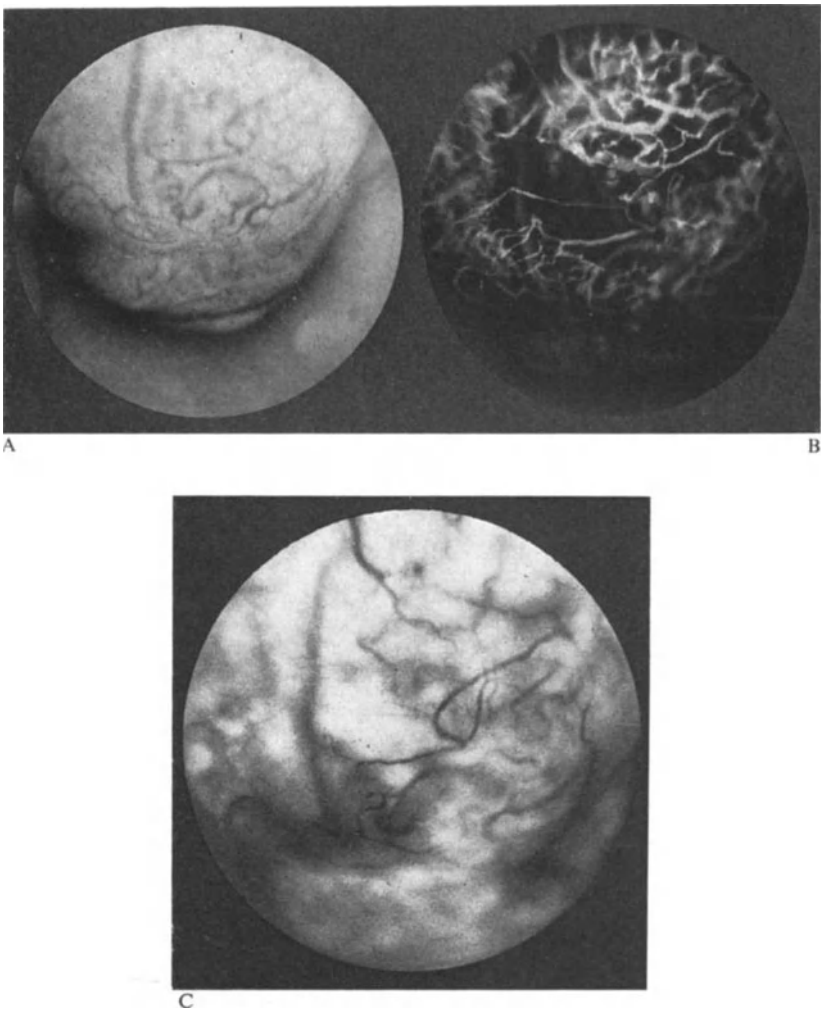


Fig. 6. Amelanotic malignant melanoma.
A. Before fluorescein injection. B. Pre-arterial phase. A network of large tumor-vessels is visible. C. Late phase. Diffuse fluorescein leakage. Dark strands of superficial tumorvessels.

The detached retina usually shows dilatation of capillaries, microaneurysms and cystoid degeneration (Oosterhuis & Van Waveren, 1968).

Fig. 8 shows a heavily pigmented almost non-fluorescent malignant melanoma.

In the early stages only one tumor-vessel is visible.

Retinal vessels are not seen because the tumor perforated the retina, protruding into the vitreous cavity.

In the late phase a faint diffuse fluorescence is seen surrounding the tumor, but the tumor itself remains dark (Flindall & Gass, 1971).

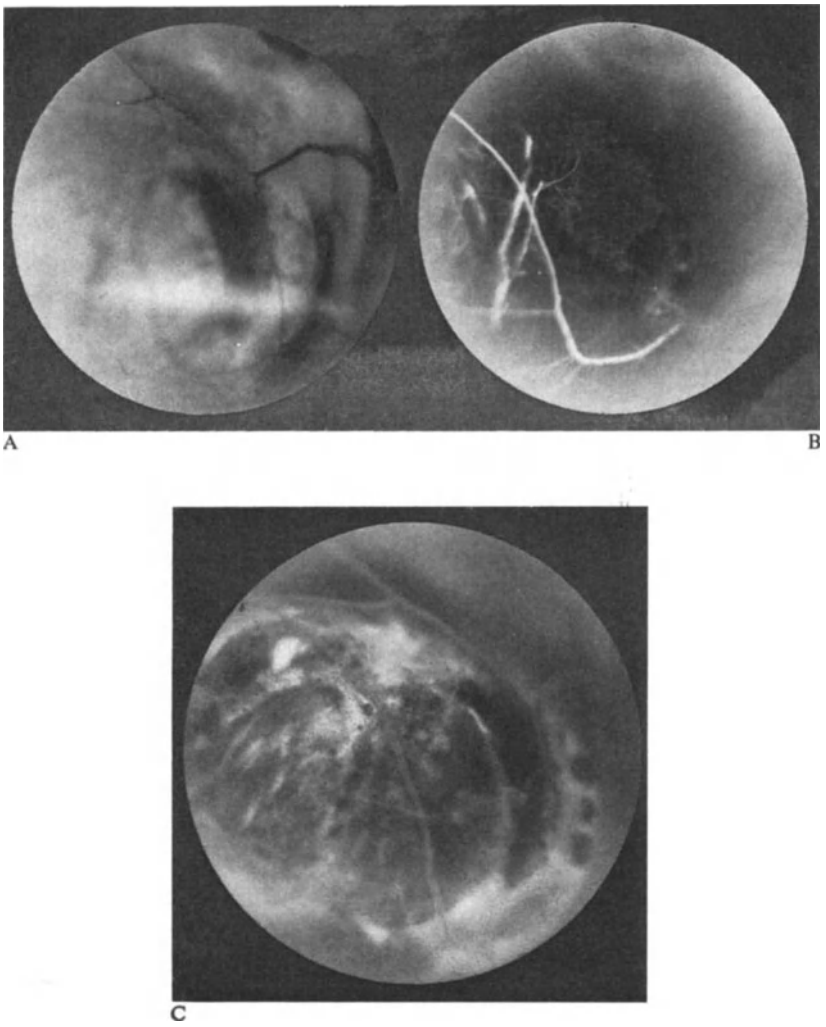
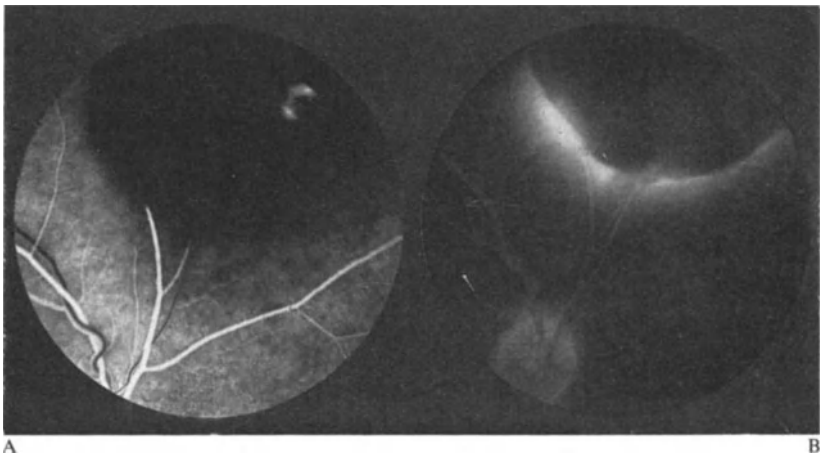


Fig. 7. Pigmented malignant melanoma.
A. Before fluorescein injection. B. Arterial phase. Some tumorvessels are visible. C Late phase. Diffuse leakage of fluorescein partly obscured by pigment.

HEMANGIOMA OF THE CHOROID

The hemangioma manifests itself as a flat tumor of a pinkish-white colour, usually situated in the posterior pole of the fundus in the neighbourhood of the optic disc. A regular pattern of tumor-vessels may be visible. In some instances fine grey foci of pigment are noticed on the border of the tumor (KAREL & PELESKA, 1972).

Some degree of secondary retinal detachment usually accompanies the lesion.



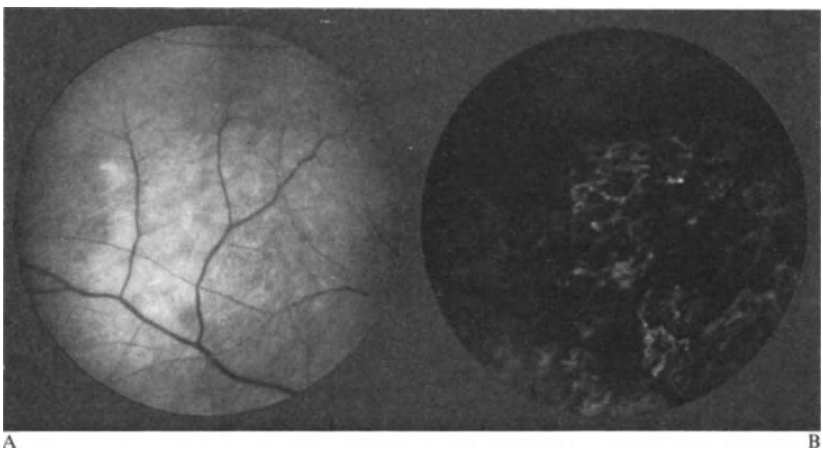
A B

Fig. 8. Heavely pigmented malignant melanoma that has penetrated the retina. A. Arterio-venous phase. Tumor remains dark except one small fluorescent spot. No retinal vessels are visible over the tumor. B. Late phase. Diffuse fluorescein leakage around the tumor. No leakage visible within the tumor.

The fluorescence angiographic pattern

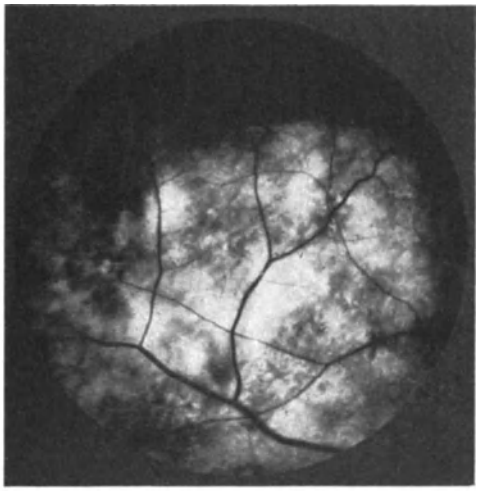
This pattern reveals early fluorescence of the tumor in the pre-arterial or arterial phase.

In the beginning the pattern is sponge-like or regularly and coarsely mottled, but rapidly becomes confluent until in the late phase the aspect is homogeneous or cloudy (Fig. 9). The intensity reaches its peak during the venous phase and remains constant or diminishes slightly in the late phase. Fine fluorescent spots



A B

Fig. 9. Hemangioma.
A. Before fluorescein injection. B. Pre-arterial phase. Early staining with regular pattern.



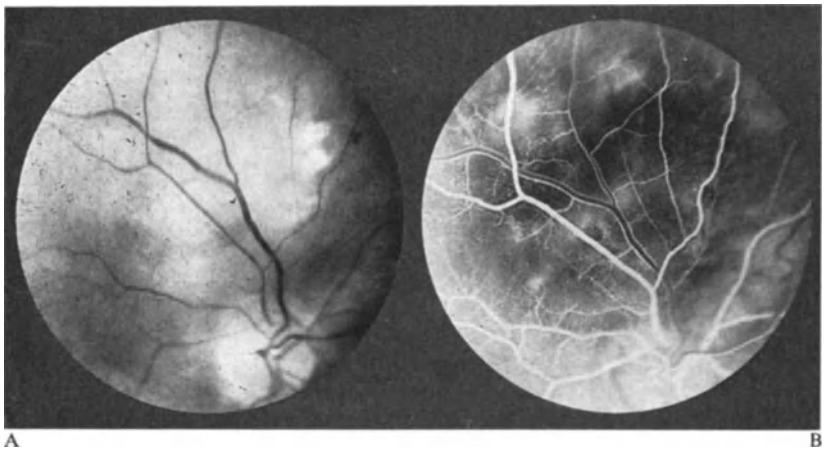
C

Fig. 9 C. Late phase. Diffuse cloudy aspect. No bright spots on the border of the tumor.

as seen on the border of flat malignant melanomas have not been described (KAREL & PELESKA, 1972; NORTON & GUTMAN, 1967; OOSTERHUIS & VAN WAVEREN, 1968; WESSING, 1968).

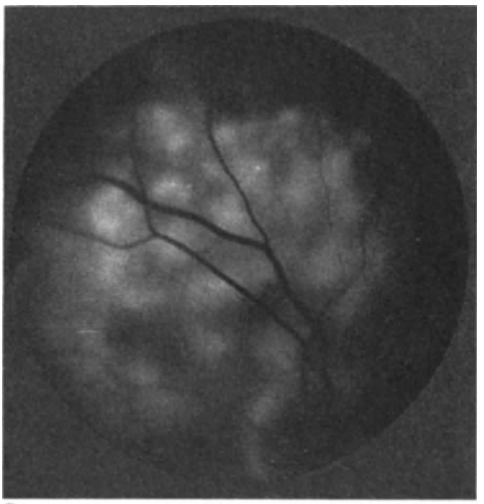
The overlying retina usually shows alterations such as described with malignant melanoma.

The cystic multi-lake-like pattern in the late phase is also seen in malignant melanoma (NORTON & GUTMAN, 1967; OOSTERHUIS & VAN WAVEREN, 1968; PETTIT et al., 1970).



A B

Fig. 10. Hemangioma.
A. Before fluorescein injection. B. Early arterio-venous phase. Early faint staining.



C

Fig. 10 C. Late phase. Staining remains faint.

Rarely a hemangioma may exhibit only faint cloudy fluorescence in the arterio-venous phase which remains less intense than generally encountered in other hemangiomas (Fig. 10).

METASTATIC TUMORS OF THE CHOROID

These lesions are usually flat tumors with a pale grey appearance, located in the posterior pole of the fundus. Their ophthalmoscopic picture may be indistinguishable from malignant melanoma or hemangioma.

The fluorescence angiographic pattern

According to several authors (KAREL & PELESKA, 1972; WESSING, 1968) the patterns may vary considerably.

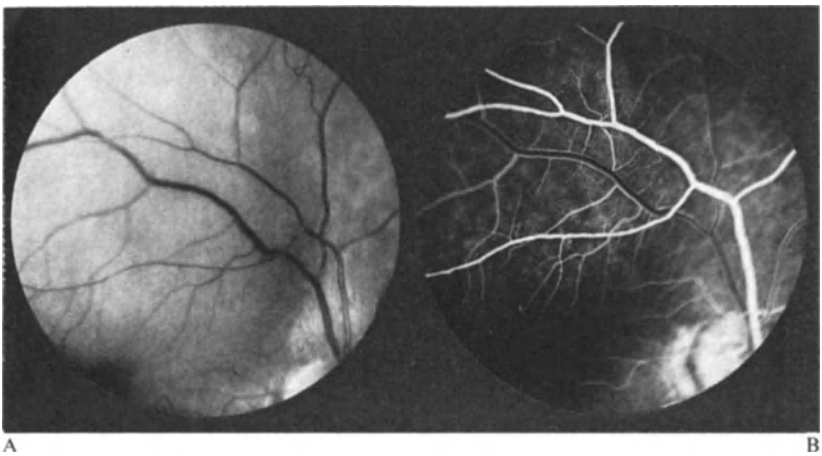
Fluorescence may start as early as the arterial phase or as late as the venous phase, or may even be virtually absent.

The appearance is generally mottled; diffusion of the dye in the tumor may be faint and late (ROSEN, 1969; WESSING, 1968) or rapid and rather intense, resembling malignant melanoma (OOSTERHUIS & VAN WAVEREN, 1968).

A borderzone of bright spots is visible in many cases. The retina shows degenerative changes as described with malignant melanomas (Fig. 11).

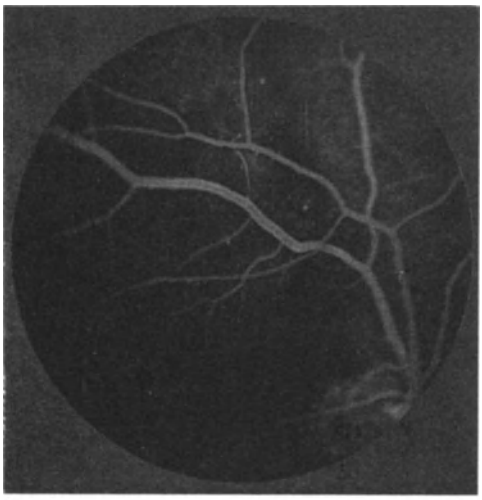
COMMENT

The simple naevus of the choroid is usually not a diagnostic problem. However, since some authors are of the opinion that there is a possibility of malignant



A B

Fig. 11. Metastatic tumor.
Secondary to carcinoma of the breast.
A. Before fluorescein injection. B. Early arterio-venous phase. Very faint diffuse staining. Dilated retinal capillaries.



C

C. Late phase. Tumor remaining almost dark. Spotted borderzone visible.

degeneration (PETTIT et al., 1970; REESE, 1963; ROSEN & GARDNER, 1969) the large naevi with drusen in particular, should be carefully followed by fluorescein angiography.

Fluorescein photography of patients with malignant melanoma of the choroid generally reveals characteristic features of abnormal fluorescence.

However, the general picture can show great variations depending on factors

as vascularity of the tumor, permeability of vessel walls, necrosis, pigment content or haemorrhages in the superficial layers, and disturbances of the pigmentepithelium (FLINDALL & GASS, 1971; OFFRET et al., 1970; SHIELDS & FONT, 1972). Also overlying retinal detachment may obscure the general aspect. A correlation between the fluorescence angiographic patterns and cell-type of the tumor has not been established (EDWARDS et al., 1969).

Because of the variability in fluorescence angiographic patterns in malignant melanoma a differential diagnosis of this tumor with hemangioma and also with metastatic tumors is not always possible.

It must be admitted that fluorescein angiography does not solve all differential diagnostic problems, but it is a valuable aid in the diagnosis of diseases of the retina and choroid, thus reducing the unnecessary enucleation of many eyes (ZIMMERMANN, 1973).

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FLUORESCEIN ANGIOGRAPHY OF THE OPTIC DISC

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(*Amsterdam*)

ABSTRACT

A description is given of the fluorescein angiographic findings of the normal and abnormal optic disc. The data of the normal optic disc are followed by an analysis of the effects of experimentally increased intraocular pressure and of glaucoma. Important facts of differential diagnostic characteristics in various types of optic disc oedema are discussed, and some miscellaneous conditions are delineated. Fluorescein angiography has made a significant contribution to the elucidation of the blood supply of the optic nerve head.

SOME ANATOMICAL DETAILS

The *arterial supply of the optic disc* can be divided into three parts:

1. *Region of the lamina cribrosa*

This region is supplied either by branches of the arterial circle of Zinn-Haller or by branches of the posterior ciliary arteries.

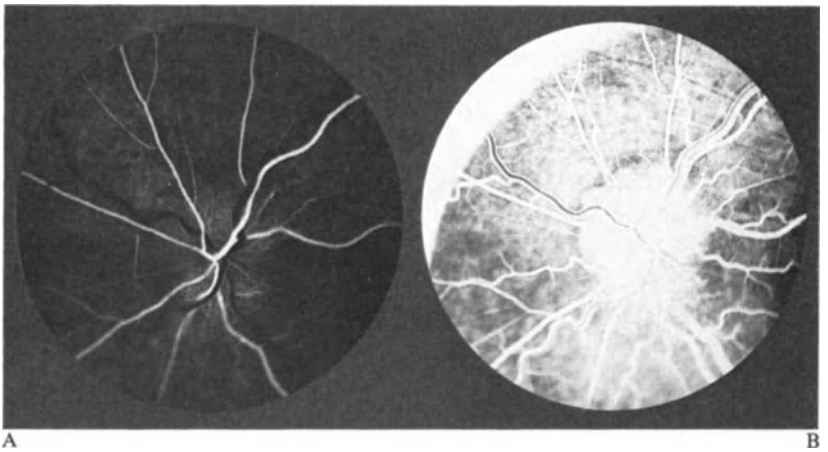

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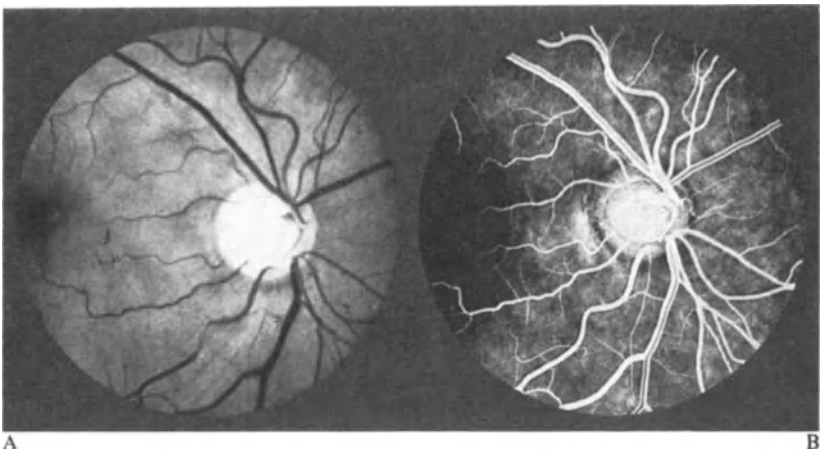
Fig. 1 Temporal variation in the filling of the radial peripapillary capillaries. A: early arterial phase. B: arterio-venous phase.



A B

Fig. 2 Normal vasculature in pseudo-excavation of the optic disc.
A: conventional photograph. B: arterio-venous phase.

2. *The prelaminar region*

This region is supplied mainly by centripetal branches deriving from the peripapillary choroidal vessels; these show a sectorial distribution in this region. The temporal part of this region is much more vascular than the other parts and receives the major part of its blood supply from the choroid. It is presumed that the blood supply of the nasal part derives mainly from the vessels in the underlying region of the lamina cribrosa.

3. *The surface layer of the optic disc*

This region contains the main retinal vessels and a large number of capillaries deriving from branches of the retinal arterioles in the peripapillary region. Sometimes vessels from the choroid are seen on the optic disc. One of these may grow out forming a cilioretinal artery. The capillaries on the surface of the disc are continuous with the capillaries of the peripapillary retina as well as with the radially orientated peripapillary network. The retrolaminar part of the optic nerve is supplied by the intraneural branches of the central artery of the retina with centripetal contribution from the pial branches deriving from the choroidal arteries, the circle of Zinn-Haller, the central artery of the retina, and directly from the ophthalmic artery.

The venous drainage of the optic disc is carried out by the central retinal vein. The prelaminary region drains also into the choroidal veins. A venous channel corresponding to the circle of Zinn has never been demonstrated. The central retinal vein communicates with the choroidal circulation in the prelaminary region. This may be of importance as a possible drain in patients suffering from a complete blocking of the central retinal vein, situated behind the lamina cribrosa.

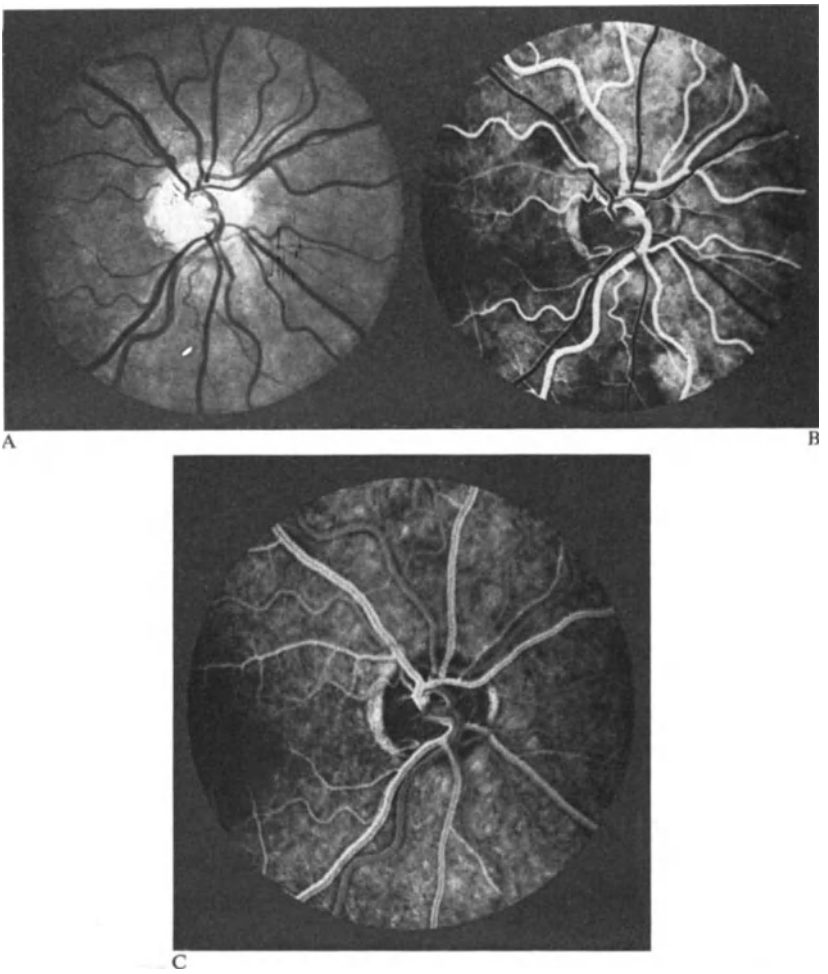


Fig. 3 Marked avascularity in a case of optic atrophy.
A: conventional photograph. B: fluorescence-angiogram; arterial phase. C: arterio-venous phase.

Histological studies by FRANÇOIS & NEETENS (1972) on the angio-architecture of the optic nerve head have demonstrated a network of polygonally arranged small vessels lying within the papilla. These are most prominent in trans-sections but they also connect with the deeper lying vessels of the lamina cribrosa and possibly with occasional lateral capillaries. The major afferent supply to this network arises from the choroid. Efferent connections with the central vein or its branches have been described. Efferent connections with the choroid may also exist. It should be stressed that the number and size of the blood vessels seen in fixed and stained sections does not necessarily reflect the axial dynamics of the blood circulation in vivo. The laminar capillaries show a three dimensional arrangement with most of the meshwork lying transversely.

Capillary intercommunications between the various levels exist. The vessels of the choroidal portion are coated with glia while those of the scleral portion are surrounded by dense connective tissue. The major afferent channels are branches of the circle of Zinn-Haller, and choroidal arterioles. The efferent vessels drain into the central retinal vein but draining into the vessels around the optic disc may be a possibility.

FLUORESCEIN ANGIOGRAPHY OF THE NORMAL OPTIC DISC

The normal angiographic pattern of the optic disc can be divided into different phases. SHIMIZU (1972) describes four phases of optic disc-fluorescence. This author ascribes the first one, the so-called deep glow, to the fluorescence of the capillary plexus situated in the lamina cribrosa. In the second phase, the more superficial reticular capillaries from the choroid or the so-called prelaminary capillaries show up. Fluorescence appears synchronous with the choroidal fluorescence. In the third phase the fluorescence of the optic disc reaches its intensity peak. Added to the optic disc fluorescence is now the inflow of the so-called radial papillary capillaries. These are considered to form the drainage system of the peripapillary retinal bloodvessel system. The vessels are arranged in sectors. Some of these sectors show a delay in filling. In the fourth phase, the so-called peripapillary halo is seen. This halo is surrounded by a peripapillary pigmentring. This phase indicates the staining of the nerve head by fluorescein deriving from the surrounding tissues at the posterior scleral foramen (GRAYSON & LATIES, 1971; ASHWORTH & ROSEN, 1970).

ERNEST & ARCHER (1973) consider the so-called deep glow encountered in the first phase to be the fluorescence of the retrobulbar vessels. This glow is seen in the centre, the thinnest part, of the optic disc. This fact was demonstrated in a blind eye by increasing the intra-ocular pressure above the systolic blood

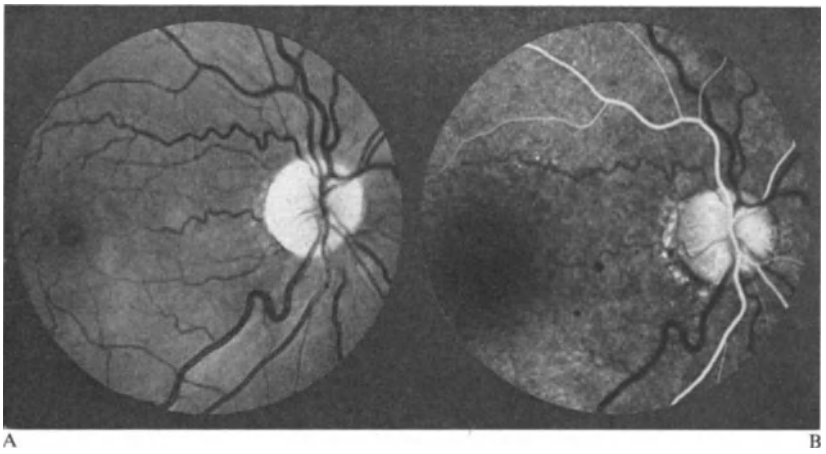
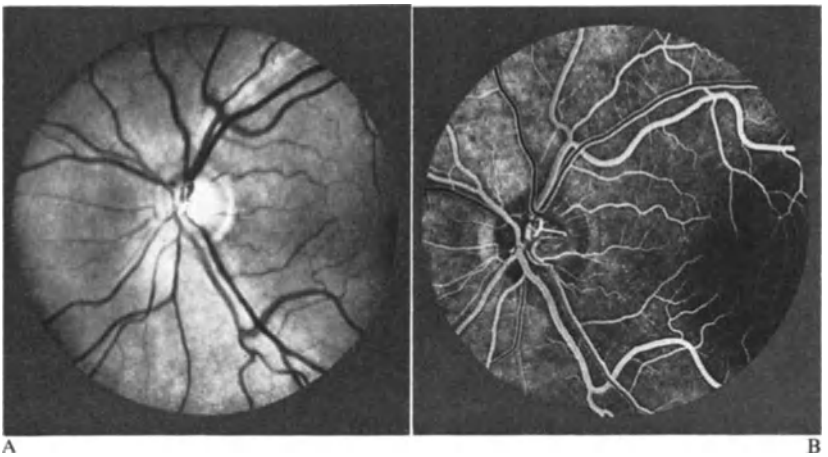
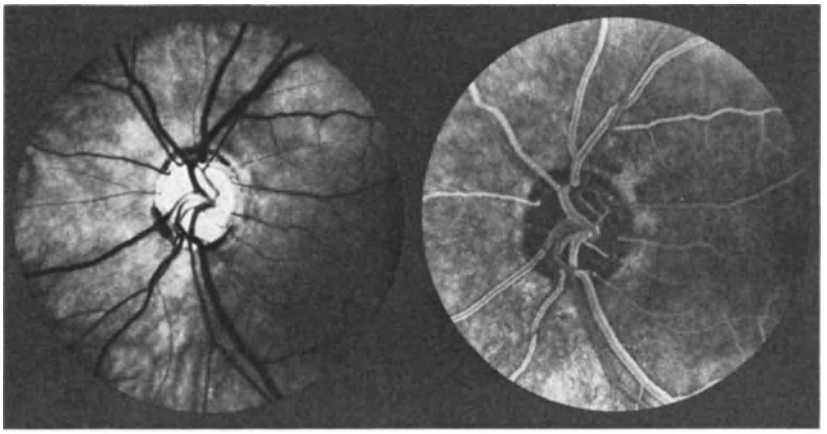


Fig. 4 Optic atrophy. Normal disc vascularity.
A: conventional photograph. B: fluorescein angiogram. Early arterial phase, before filling of radial peripapillary capillaries.



A B

Fig. 5 Glaucomatous cupping of optic disc.
A: conventional photograph. B: fluorescence-angiogram. Arterio-venous phase. Note slightly reduced optic disc vascularity.



A B

Fig. 6 Complete glaucomatous cupping.
A: conventional photograph. B: arterio-venous phase. Note absence of optic disc fluorescence.

pressure using the suction cup method. In this way ERNEST & ARCHER were able to cut off completely the intra-ocular bloodflow. Nevertheless, in the centre of the optic disc fluorescence was still seen.

HAYREH concludes that fluorescein angiography has contributed a lot to an understanding of the ciliary circulation and the blood supply of the optic disc:

1. the capillaries of the optic disc are filled before the dye has reached the central artery of the retina;
2. in occlusion of the central retinal artery the capillaries of the optic disc usually fill while the central artery is empty of dye;

3. the cilio-retinal arteries usually contribute to the blood supply of the optic disc and the retina. Occlusion of these vessels sometimes shows a sector shape filling defect in the optic disc and in a corresponding area of the retina, and
4. in peripapillary degeneration of the pigmentepithelium and choriocapillaries, the prearterial phase discloses the choroidal contribution to the blood supply of the optic disc.

Experimental studies in monkeys confirm the findings in man, thus providing evidence for the preponderant role played by the ciliary vascular system in supplying the optic nerve head with blood.

The blood supply to the optic disc in monkeys appears to be similar to that in man (HAYREH 1969). HAYREH demonstrated spatial and temporal variations

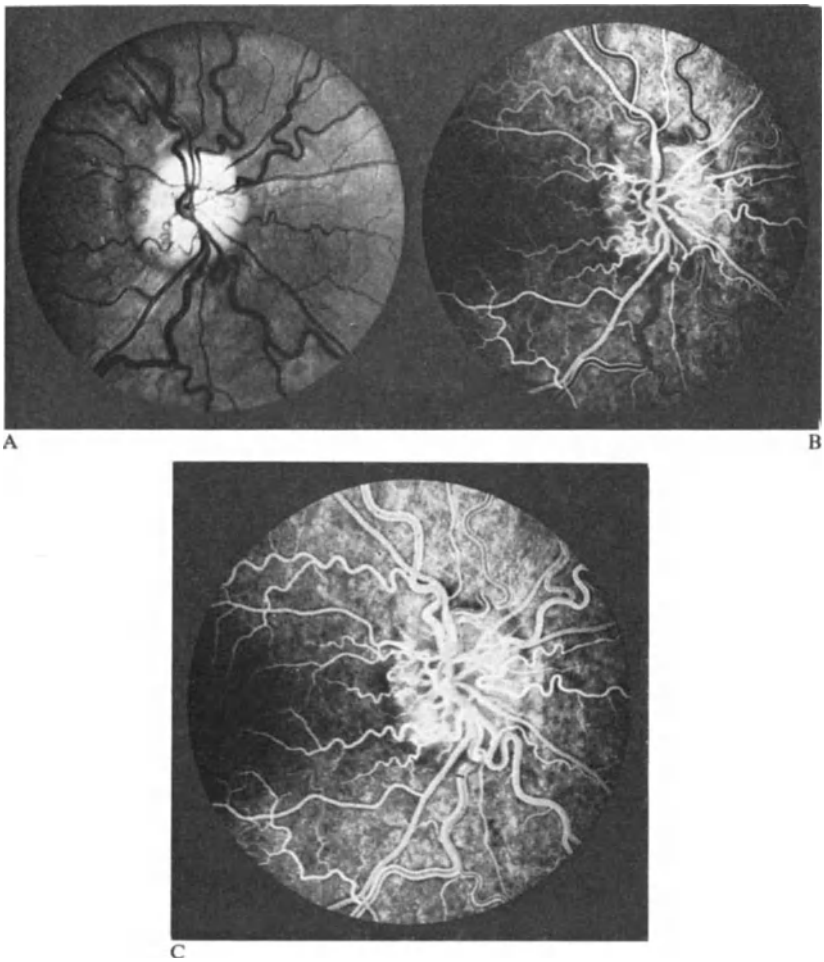


Fig. 7 Opticociliary anastomosis in a case of deeply situated drusen of the optic disc. A: conventional photograph. B, C: fluorescence angiograms; late arterial and arterio-venous phases.

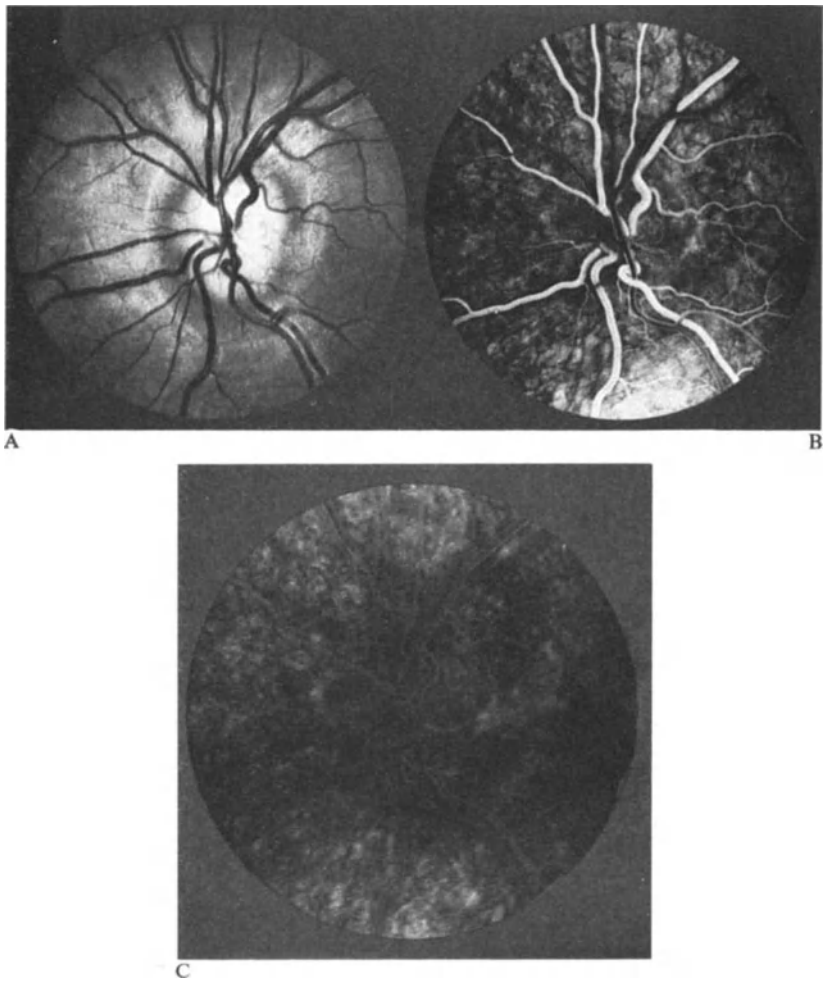


Fig. 8 Suspected papilloedema. Normal vascular pattern. Fluorescence angiography, however, changed the diagnosis in pseudo-papilloedema.
A: conventional photograph. B: fluorescence angiogram; arterial phase. C: after-fluorescence.

in the filling of the retinal capillaries in the peripapillary region. These variations may lead to erroneous conclusions if not recognized as normal. HENKIND too, draws attention to this layer of capillaries. These radial peripapillar vessels derive from the arterioles in the retina, rising to the nerve fiber layer and forming a network of capillaries extending along the path of the nerve fibers.

Since the pattern of these vessels is similar to that of the Bjerrum scotoma, HENKIND suggests a relationship with field defects in glaucoma.

Spontaneous increase in intra-ocular pressure in the cat's eye showed after infusion of indian ink absence of filling of the peripapillary vessels (HENKIND 1967).

HAYREH & PERKINS (1969) were able to show that the effect of increased intra-ocular pressure on the retinal and optic disc capillaries was not due to obliteration of capillaries in the retina or in the surface layer of the disc. When the intra-ocular pressure was raised to such a height that pulsations were observed in the retinal artery, a reduction in the fluorescence of the retinal vessels in the optic disc occurred simultaneous with a reduction in the choroidal and prelaminary bloodflow. HAYREH & PERKINS postulated that the primary factor responsible for field defects and optic atrophy in glaucoma is most probably due to the interference with the choroidal blood supply of the optic disc.

Appreciation of the contribution of the choroidal circulation to the blood supply of the optic disc is difficult, due to the presence of superimposed retinal fluorescence. Blocking the central retinal artery however, reveals the filling of the vessels in the whole of the temporal half of the optic disc. During the later stages the disc as a whole becomes fluorescent and the capillaries in the retina adjoining the temporal side of the disc are filled. At the end of such an experiment the fluorescence pattern is more or less similar to that of the disc with intact retinal circulation.

From the above one can conclude that the main source of blood supply to the optic nerve head is the ciliary circulation. However, the view that the peripapillary choroidal circulation contributes significantly to the blood supply of the optic disc was not confirmed by ERNEST & ARCHER (1973).

These authors concluded from an analysis of fluorescein angiographic studies in patients with peripapillary atrophy that, though no fluorescein was visible in this region, still a normal disc fluorescence appeared.

HAYREH pointed out that the ophthalmic artery usually gives off a lateral and a medial posterior ciliary artery. These arteries penetrate with a number of branches into the sclera and thus supply the choroid and the optic nerve in man by way of the circle of Zinn-Haller.

ERNEST & ARCHER dissected in Rhesus monkeys the lateral posterior ciliary artery. Fluorescein angiography revealed a normal filling of the medial choroid and optic disc. After sectioning the lateral posterior ciliary artery and the central retinal artery, a normal filling of the medial choroid, the peripapillary choroid and the choriocapillaries was observed up to the edge of the disc.

No branches were seen deriving from the peripapillary choroid or the choriocapillaries and penetrating into the optic disc. ERNEST & ARCHER conclude that the branches deriving from the short posterior ciliary artery supplying the optic disc on the one hand, and those supplying the peripapillary choroid on the other, have no connections.

The effect of induced ocular hypertension on the retinal and the choroidal circulation has been studied intensively during the last few years.

DOLLERY et al. (1968) studied in pigs the effect of increased intra-ocular pressure using the suction cup method. These authors found a slow filling in both retinal and choroidal vessels. However, the results published regarding the

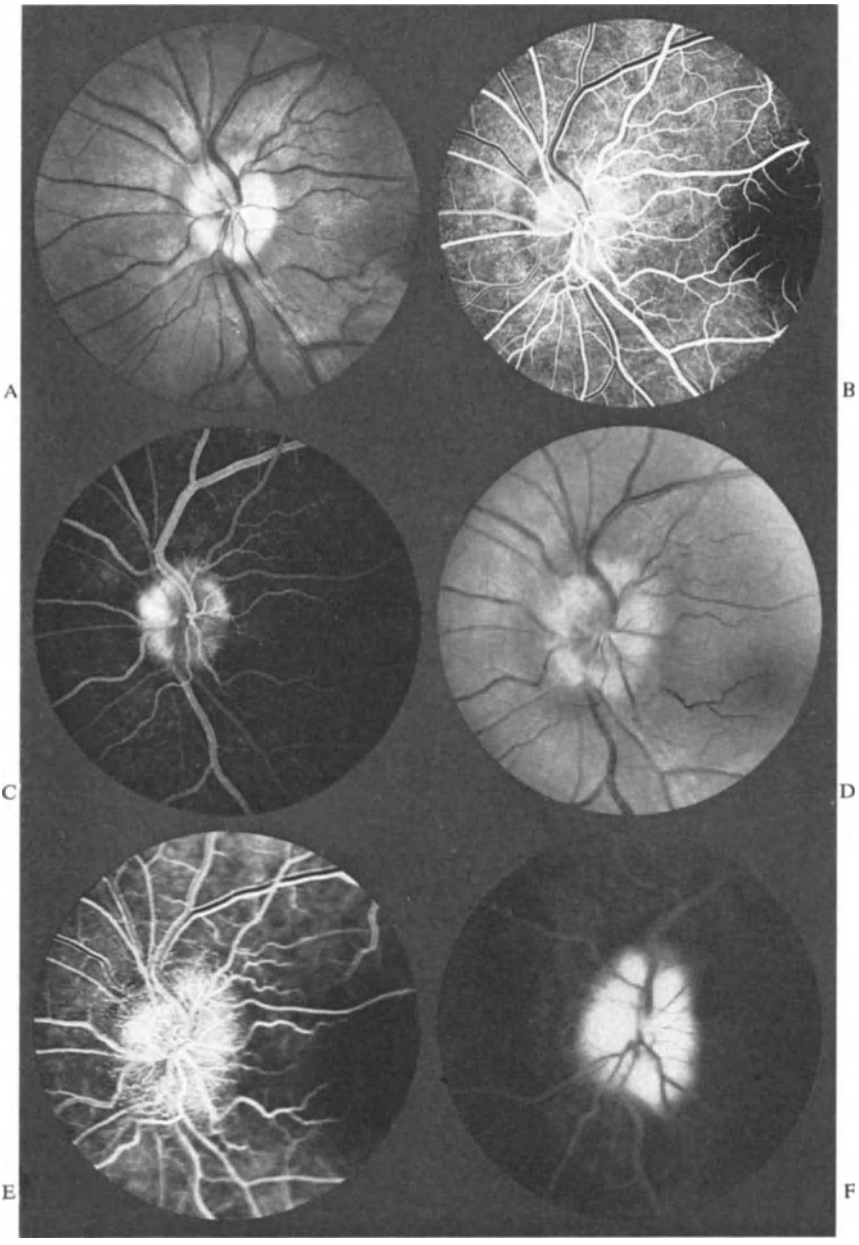
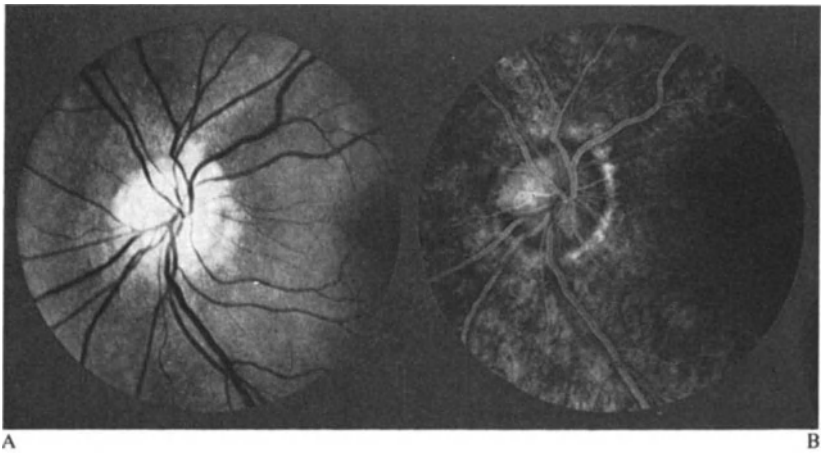


Fig. 9 Fluoro-angiographic findings in a case of suspected papilloedema. A, B, C suggest deep drusen of the optic disc as well. Continuous observation, however, revealed later a full-blown papilloedema (D, E, F).
A and D: conventional photographs. B, C and E, F: fluorescence angiograms. B and E: arterio-venous phase. C: late venous phase. F: after-fluorescence.

effect of elevated intra-ocular pressure on the radial peripapillary capillaries are inconclusive. Some of the radial peripapillary capillaries emptied more slowly than others, but as long as retinal flow was present, obliteration of the radial peripapillary capillary pattern did not occur. It is of interest to note that even high levels of intra-ocular pressure approaching the no-flow point, did not seem to affect the general capillary pattern, or to lead to preferential flow in certain capillaries.

BLUMENTHAL et al. (1971) applied the combined technique of suction cup ophthalmodynamometry and fluorescein angiography to human subjects. They recorded the filling of the retinal and choroidal vascular system at varying



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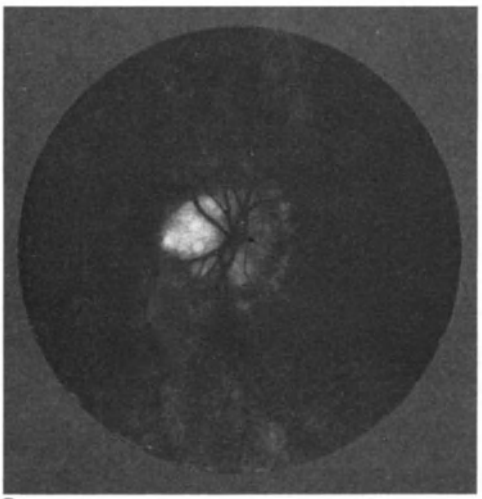


C

Fig. 10 Clearly visible drusen of the optic disc, located on the nasal side. A: conventional photograph. B, C: fluorescence angiograms. B: arterial phase C: after-fluorescence.

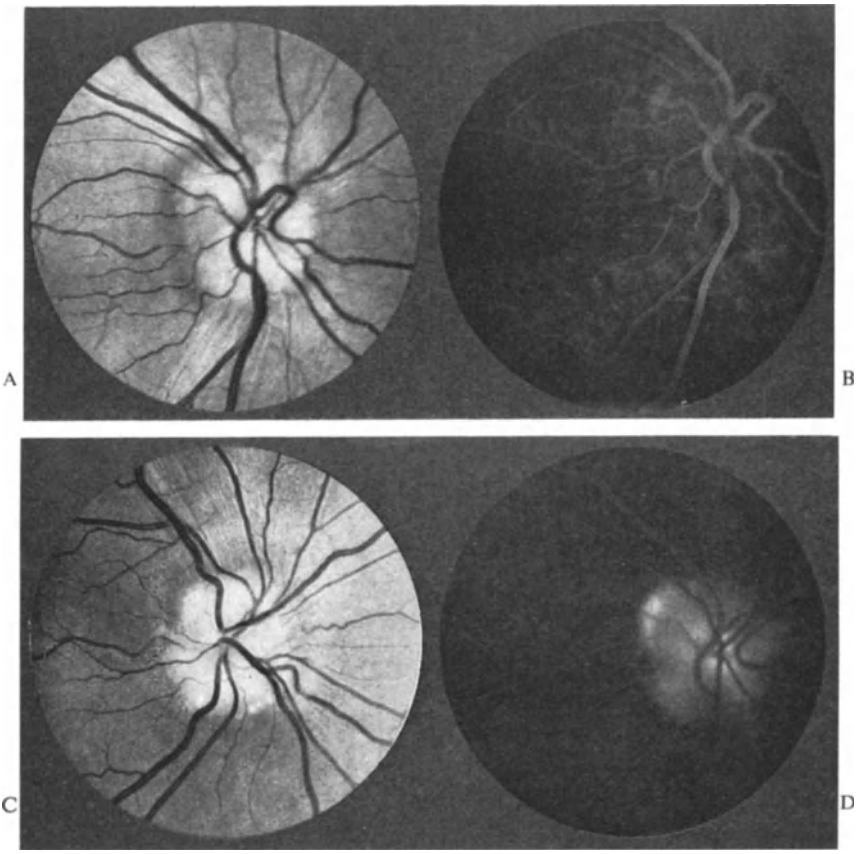


Fig. 11 Typical example of deep drusen of the optic disc.
Note the absence of pathological fluorescence in the late venous phase. (B).
On the later picture (D) the typical after-fluorescence becomes visible.
In the fellow eye (C) more superficially located drusen are visible.

levels of intra-ocular pressure. They found that in normal subjects the large choroidal vessels reopen when the level of the pressure is reduced to values lying about seven millimeters Hg under the level required to permit the return of retinal flow. The peripapillary choroidal vessels and the optic disc vessels reopen at approximately 60 mm Hg.

ARCHER et al. (1972) investigated patients using the same method. Because of the difficulties encountered in observing adequately the perfusion of the choroidal vasculature, the pressures at which simular components of the retinal and choroidal circulation fill could not been accurately established.

Subjects with slightly pigmented fundi as well as albinos have been studied, as these individuals allow good visualization of the choroidal vasculature during angiography. Even nystagmus does not seem to effect the quality of the pictures obtained. At intra-ocular pressures exceeding the systolic pressure in the central

retina artery, neither retinal nor choroidal vessels are filled. Fluorescence is thus confined to the region of the optic disc. This fluorescence is quite faint in the early phase (8-15 sec.), but reaches a maximum 4-7 seconds later.

The fluorescence is most pronounced in the area of the physiologic cup. The precise localization of the dye is not known when papillary fluorescence at systolic pressure of the central retinal artery occurs. It is likely that this fluorescence emanates from dye withing the small vessels of the distal optic nerve, transilluminating the optic disc. It is improbable that the transmitted fluorescence originates from dye within the laminar capillaries, as it has been demonstrated that these vessels are occluded at intra-ocular pressures exceeding the systolic pressure in the central retinal artery.

HAYREH (1969) stressed the fact that the retrolaminar part of the optic disc is supplied by choroidal recurrent vessels and some pial vessels. This situation may explain the damage to this region occurring in glaucomatous patients: the so-called cavernous degeneration of the retrobulbar part of the optic nerve.

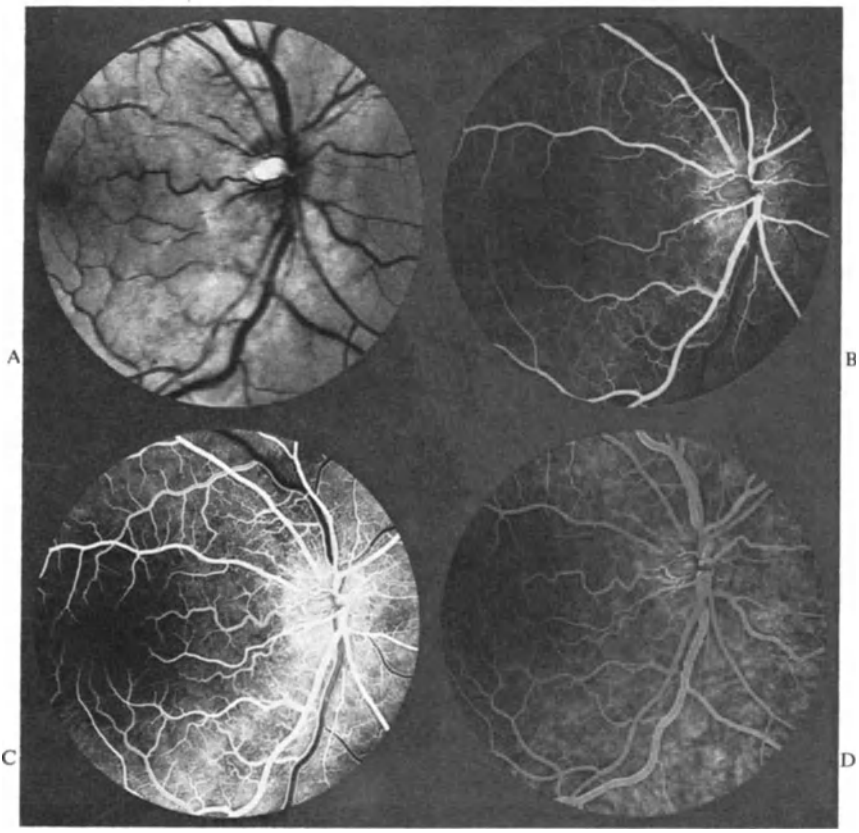
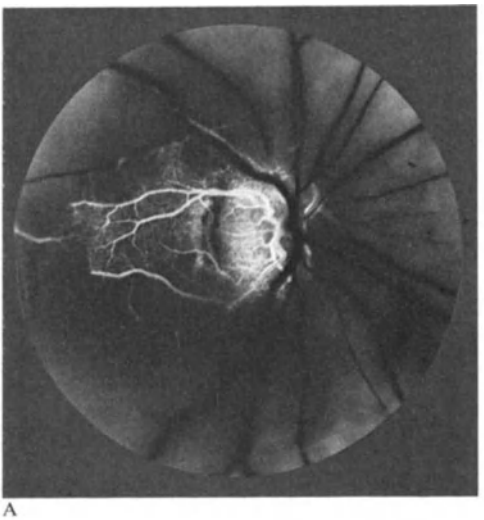
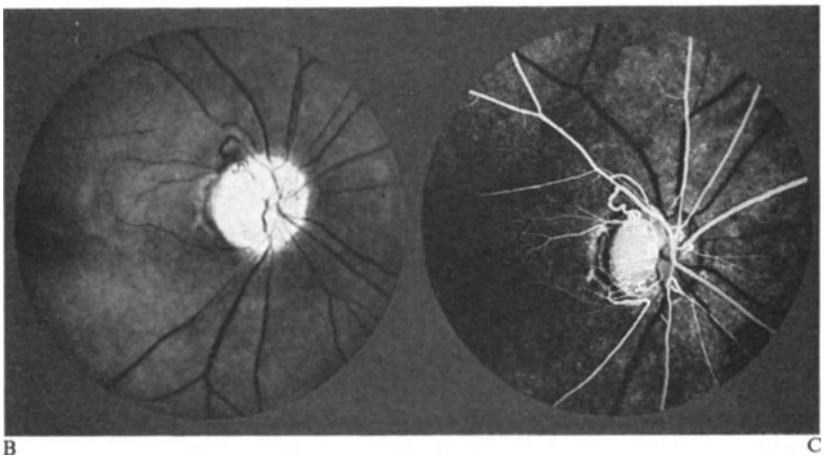


Fig. 12 Papilloedema in a sibling of a family suffering from optic atrophy of Leber. Dilatation of optic disc vessels and peripapillary capillaries. No leakage visible. A; conventional photograph. B,C,D: fluorescence angiograms. B: arterial phase. C: arterio-venous phase. D: venous phase.



A



B C

Fig. 13 Occlusion of central rotinal artery.
A: fluorescence angiogram; arterial phase. Ciliorotinal arteries branching off proximally to the occlusion. The filling of the prelaminar bed is normal. On the nasal side, no radial peripapillary capillaries are visible. B,C: Situation one year later. B: conventional photograph. Markcd pallor of optic disc. C: normal filling of optic disc vessels. Blood supply of the retina has been restored by the formation of cilioretinal anastomoses.

In most cases in which the increased intra-ocular pressure is reduced to a level below the systolic pressure of the central retinal artery, the dye appears simultaneously in the major retinal and choroidal vessels.

However, the major retinal and choroidal vessels exhibit irregularities in filling, when the intra-ocular pressure is slowly reduced from levels above central

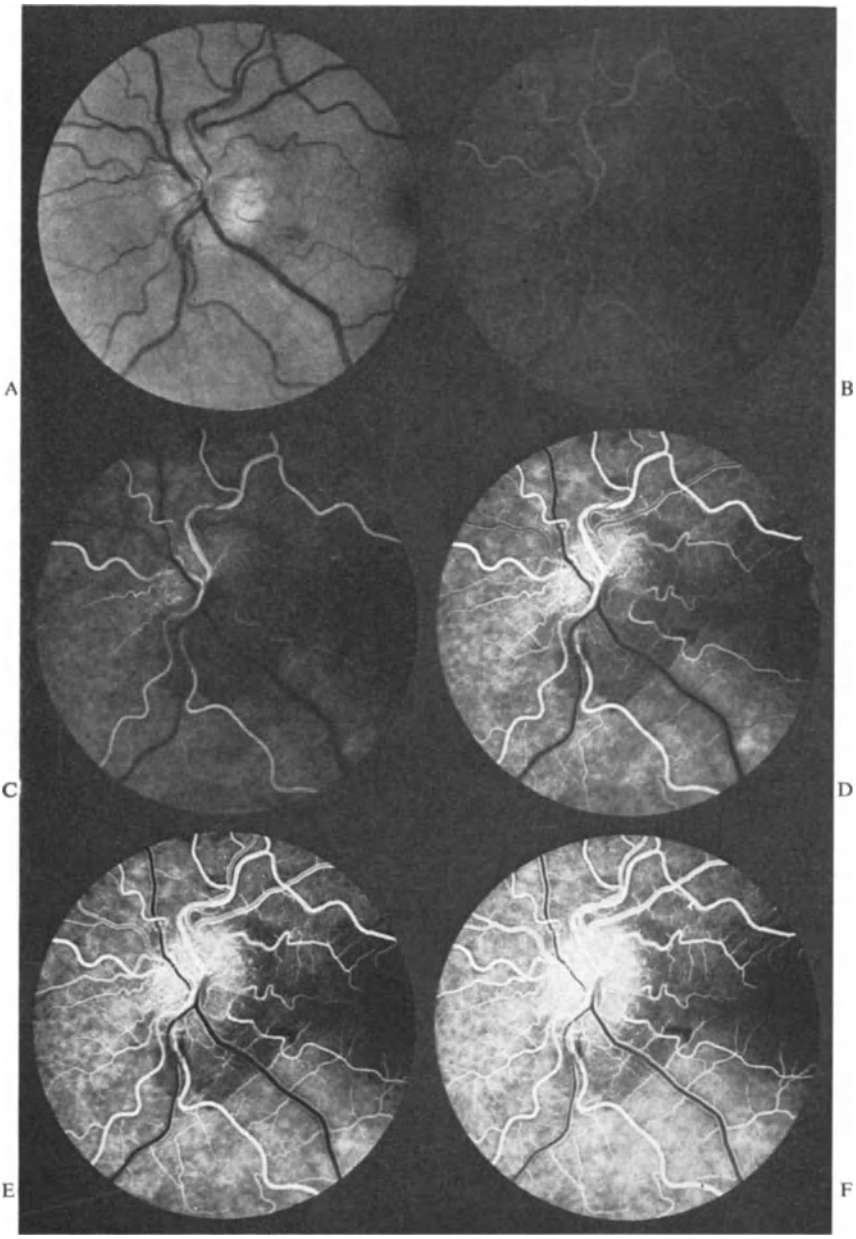


Fig. 14 Ischaemic optic neuropathy. The close relationship between optic disc and choroidal blood flow is demonstrated.
Note extremely delayed filling of the temporo-inferior side of optic disc and adjacent choroid as well as the delayed filling of three small cilio-retinal arterioles.
The filling defect corresponds with a nasal-superior visual field defect.
A: conventional photograph. B-F: fluorescence angiograms.

retinal artery systolic pressure. The major choroidal vessels, situated at different locations throughout the posterior fundus, show marked differences in the level of intra-ocular pressure at which they fill: not two cases exhibit the same pattern of filling. This spatial variation in filling is also seen in the retinal vessels. At an intra-ocular pressure coinciding with the appearance of dye in the second

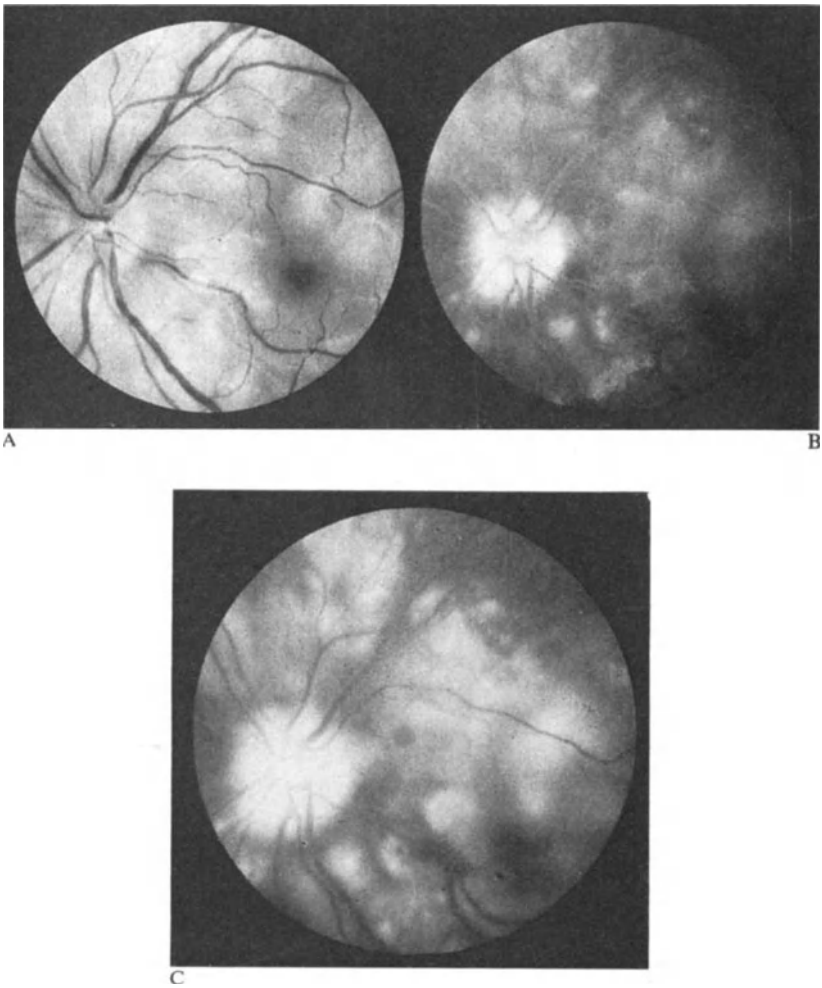


Fig. 15 A: conventional photograph of a patient admitted to the neurological department complaining of headache and vertigo.
The referring physician noted blurring of the optic discs.
The clinical picture was held to be suspicious of a brain tumour.
Having a red eye the patient was seen in the ophthalmological department
In the anterior chamber many cells were seen; the vitreous was cloudy. The optic disc showed papilloedema; the posterior fundus had a greyish aspect.
Diagnosis of Vogt-Koyanagi-Harada disease was made.
Fluoresceinangiography (B,C) confirmed the diagnosis.

and third order retinal arteries, a parallel filling of the smaller vessels in the choroidal system is observed, though a small difference in pressure is noticed at which dye appears in the choriocapillaris and in the retinal capillaries. In most cases the pressure levels at which the choriocapillaris fills is just somewhat higher. This is not in accordance with the findings of BLUMENTHAL et al. (1971). The superficially located papillary capillaries filled with fluorescein at lower levels of intra-ocular pressure than did the retinal capillaries at the posterior pole. The levels for filling the temporal and nasal superior or inferior parts of the fundus showed different values. The filling of the prelaminary capillaries

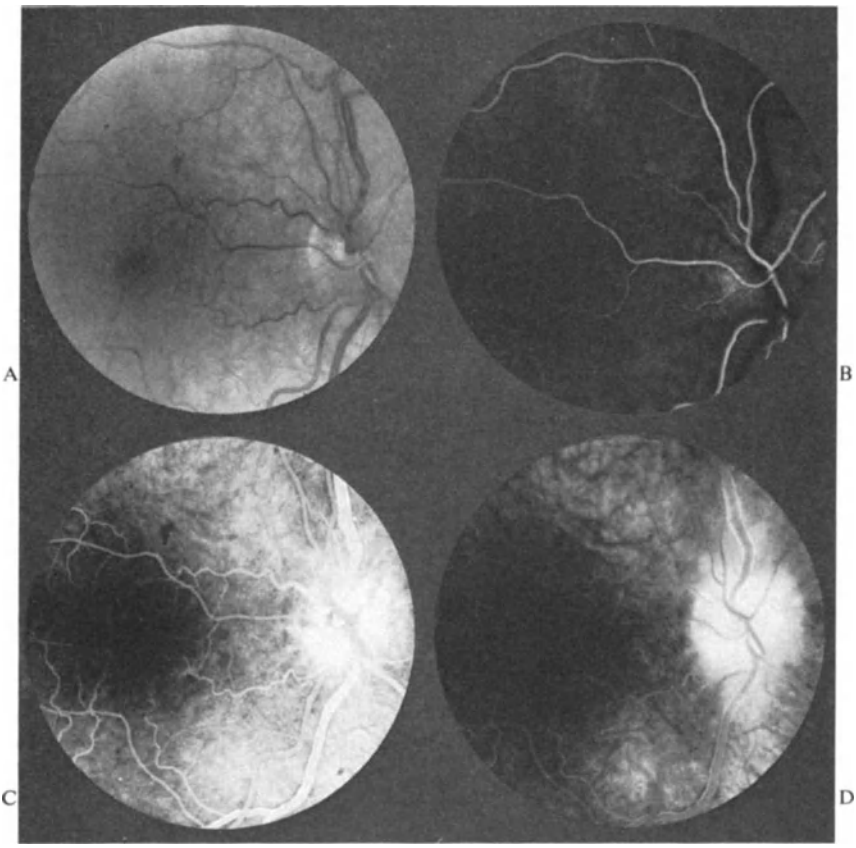


Fig. 16 A: conventional photograph of the fundus of a patient with unilateral optic disc oedema.
A complete neurological check-up (pneumoencephalography and arteriography included) was performed.
Visual acuity: 0,5.
Reinvestigation by the ophthalmologist revealed optic disc oedema, narrow arterial branches, marked dilatation of the veins, and small haemorrhages scattered all over the fundus.
Angiographically the diagnosis central retinal vein thrombosis was assessed.
Between B and C is an interval of 20 seconds.

could not be identified with any degree of certainty. The peripapillary choriocapillaris filled at the same level of intraocular pressure as the choriocapillaris elsewhere in the eye. But the filling showed the same irregular segmental filling pattern as was observed elsewhere in the fundus.

FLOWER (1972) studied the choroidal circulation using the newly developed method of infrared absorption angiography. He found elevation of the intraocular pressure results in obliteration of the retinal circulation while the choroidal circulation persisted up to a critical net ocular perfusion pressure.

These results are contradictory to the reports of BLUMENTHAL et al. The critical closing pressure can be expressed as Pc = Tc.RO (Pc : representing the critical closing pressure in mm Hg. Tc: the active tension in the vesselwall in dynes per centimeter length, and RO : the unstretched radius of the vessel lumen.)

This equation describes the fact that critical closure will occur in smaller arterioles and capillaries earlier, and at lower levels of intra-ocular pressure than in vessels of a large diameter.

The choriocapillaris and choroid show significant anatomical and physiological differences compared with the retinal vessels. The choroidal vessels possess a much larger lumen diameter. Secondly, the choriocapillaries branch off directly from first and second order choroidal arterioles without gradual progression from large to small sized vessels, as is the case in the retinal vasculature. From these characteristics one can expect that the microcirculation of the choroid is more resistant to closure than their retinal counterpart. These theoretical expectations are correlated with the sequence of retinal and choroidal angiographic findings. The different findings laid down in the study of ARCHER & FLOWER and in that of BLUMENTHAL et al. can be ascribed to a difference in interpretation of the initial choroidal filling.

FINDINGS IN PATIENTS SUFFERING FROM CHRONIC GLAUCOMA

HAYREH & PERKINS (1969) found that in the majority of glaucoma patients the disc and choroid show more or less equally intense fluorescence. The more marked the cupping and field defects are, the less the difference between the two.

However, the general pattern of fluorescence is similar to that of the normal disc. OOSTERHUIS & GORTZAK (1970) noticed a complete absence of optic disc fluorescence in the totally glaucomatous excavation.

Normal fluorescence of the optic disc is seen in pseudoglaucoma patients. A decreased vasculature is observed in subtotally and in partially excavated optic discs, some showing visual field loss, while others do not. The reduction in fluorescence is not strictly proportional to changes in optic disc or visual field, but all patients with a visual field defect show a diminished fluorescence of the optic disc.

BEGG et al. (1972) showed in their angiographic studies a complete or relative avascularity of the lamina cribrosa and the neuroretinal rim, accompanying notching and local dissolution of the optic disc substance.

These findings of local changes in vascularity show a relationship with the damaged sector of the disc corresponding to the classical arcuate scotoma.

BLUMENTAL et al. (1971) studied the choroidal blood flow in the optic disc region using the suction cup method. There main objective was the study of the delayed choroidal filling in glaucoma patients. These authors demonstrated that an increased intra-ocular pressure causes a delayed filling of the peripapillary region in glaucoma suspects. In glaucoma patients with cupping and visual field defects, even normal intra-ocular pressure may produce a delay in choroid filling, whereas increased intra-ocular pressure produces a peripapillary defect contiguous with the optic disc.

In patients with total cupping, sometimes extensive filling defects adjacent to the disc are seen. Increase in intra-ocular pressure may result in a larger defect. These findings suggest an involvement of the peripapillary choroidal region in the pathogenesis of optic disc damage in glaucoma patients.

However, EVANS et al. (1973) demonstrated, using cine-angiography, that choroidal filling defects are found in 100% of healthy subjects. These authors also showed that a different film development may result sometimes in the appearance of otherwise invisible choroidal vessels. The paucity of correlation of initial disc filling with peripapillary choroidal fluorescence strongly suggest the possibility that the dark areas in normal eyes are neither defects nor complete temporary perfusion delays, but rather manifestations of delayed choriocapillary filling. Close relationship between the choroidal flush and the dye inflow into the disc capillaries support the assumption that the disc is supplied by the peripapillary choroid. In some cases EVANS and coworkers could demonstrate filling of the prelaminar capillaries through a distinct ciliopapillary arteriole.

Against the hypothesis of an impaired choroidal circulation being responsible for the glaucomatous optic disc defects, the following arguments can be raised:

1. histopathologically, no damage of the outer retinal layers is found;
2. the pigmentepithelium is intact;
3. the ERG is normal in glaucomatous patients;
4. peripapillary atrophy is not seen in all glaucoma patients;

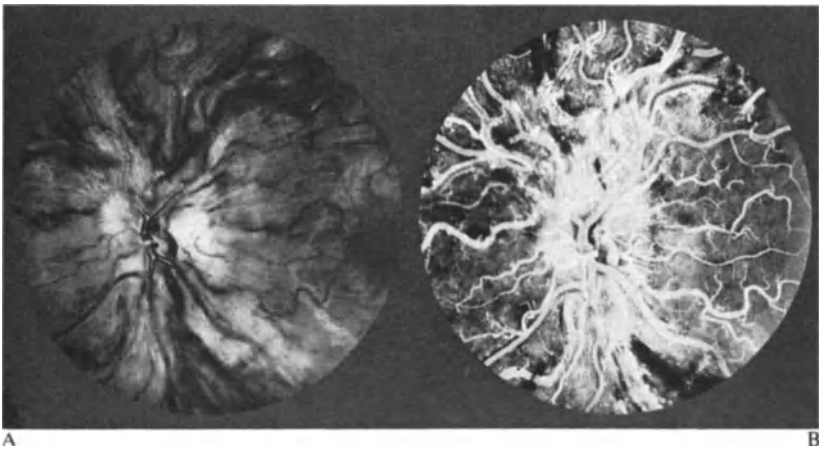
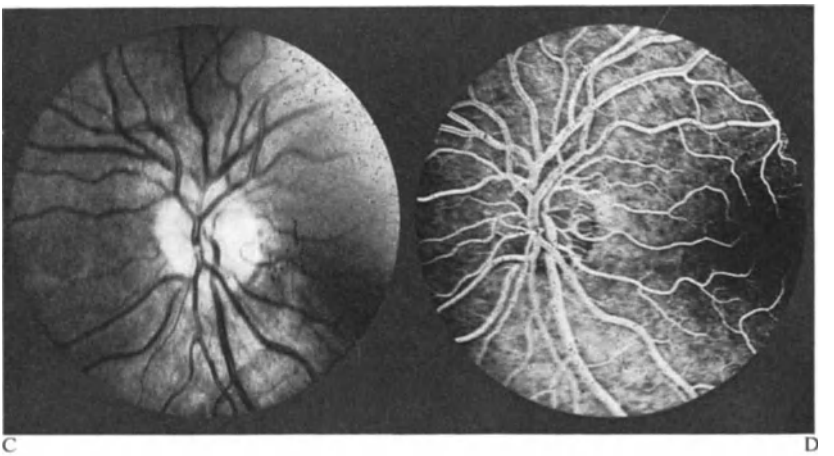


Fig. 17



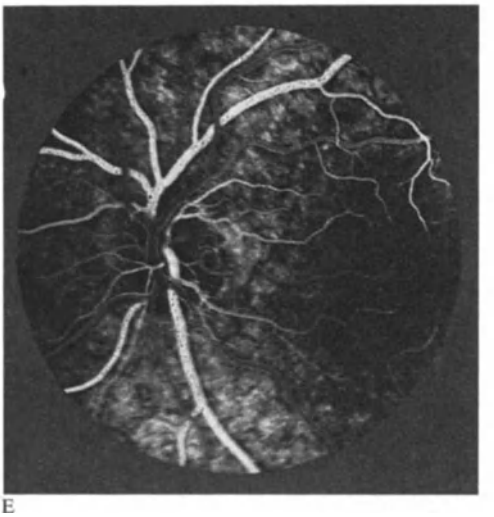
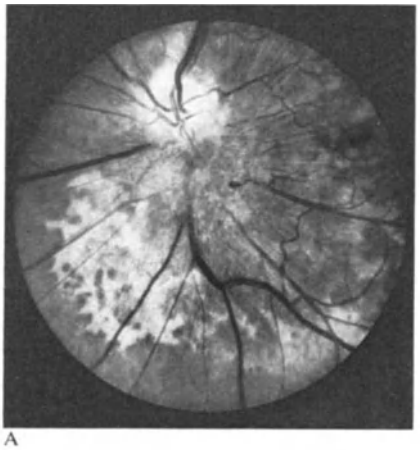


Fig. 17 Presumed optic disc vasculitis in a 14 year old girl.
Good general health.
Complaining of blurred vision of her left eye.
Normal right eye.
The visual acuity of the affected eye was 5/5.
Funduscopy (A) showed marked oedema of the optic disc, dilatation of the vein branches and widespread haemorrhages.
Fluorescein angiography suggested a thrombosis of the central retinal vein (B).
Spontaneous recovery followed after 6 months. (C, D, E).

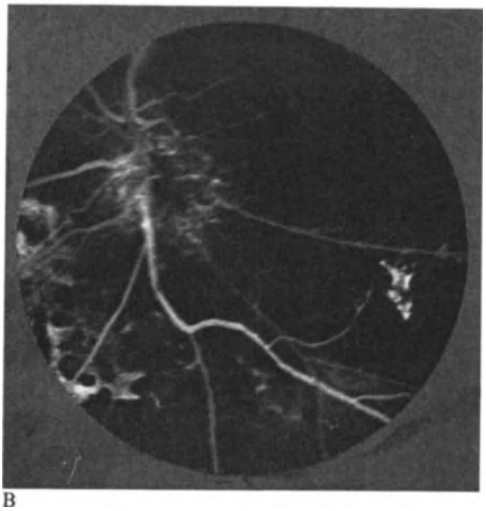
5. the so-called susceptibility of the peripapillary choroid to increased intraocular pressure has not been confirmed by later publications (ARCHER et al., 1972; FLOWER, 1972).
6. the hypothesis that the radial peripapillary capillaries are involved in the pathogenesis of the glaucomatous nerve fiber defect (HENKIND et al. 1972)

is not acceptable. The filling defect seen under experimently raised intra-ocular pressure seems to be an example of the normal spatial variation in the filling of the retinal vasculature (HAYREH 1969).

KORNZWEIG et al. (1968) have shown a selective atrophy of the radial peripapillary capillaries of the retina in patients who had a high intra-ocular pressure. Most of them had no optic disc changes but visual fields were not available. Capillary atrophy, instead of being the cause of nerve fiber degeneration, can be an consequence of nerve fiber atrophy. An example of the latter is the pallor of the disc in optic atrophy due to lesions occurring far away from the optic disc. This implies that the model of reduction of peripapillary choroidal



A



B

Fig. 18 Angiomatosis retinae (von Hippel) with grayish swelling at the tempero-inferior edge of the optic disc, surrounded by a zone of reticular degeneration of the pigment epithelium (A).
Note the dilated vascular system of the tumour (B).

bloodflow causing atrophy of optic disc tissue is not generally valid. Effect of a direct pressure on the optic nerve capillaries is assumed but has not been proven.

The essential difficulties in the elucidation by fluorescein angiography of the pathogenesis of glaucoma showing optic disc damage lay in the first place in the masking effect of the choroidal circulation by the pigment epithelium.

Maybe that infrared angiography and cine angiography will give more specific details in glaucomatous patients.

A second drawback is that the optic disc fluorescence is composed of several phases which partly overlap. This interfers with the interpretation of the separate phases.

OEDEMA OF THE OPTIC NERVE HEAD

In the assessment and the differentiation of oedema of the optic nerve head fluorescein angiography has made a major contribution. Earlier studies showed vascular changes in patients suffering from optic nerve oedema. These studies stated too, that capillary dilatation and leakage with microaneurysms formation at the optic nerve head appear to be similar in all cases, irrespective of the aetiology.

The value of fluorescein angiography in assessing and differentiating papill-oedema has also been studied. The last condition is usually caused by hyper-metropia, anomalous congenital patterns of the disc, or hyaline bodies in the optic nerve head. It was concluded that angiography is of value as a screening test in the absence of positive neurological findings before subjecting a patient with blurred disc margins to extensive neurological investigations.

In neurological literature, the term papilloedema is generally used for those forms of disc swelling that result from increased intracranial pressure.

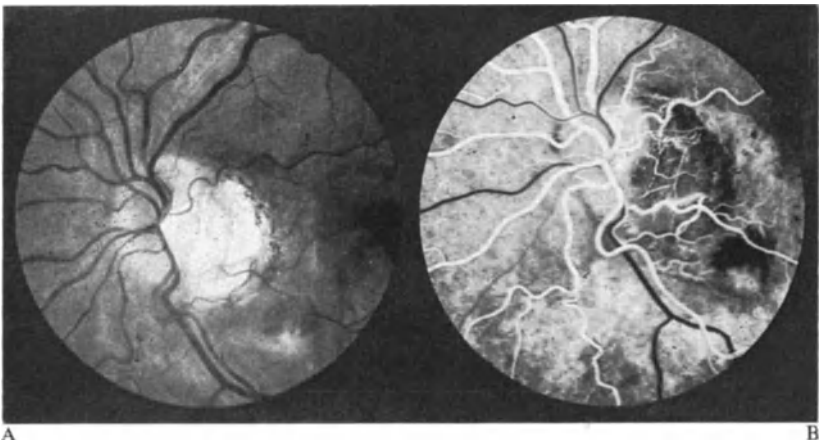
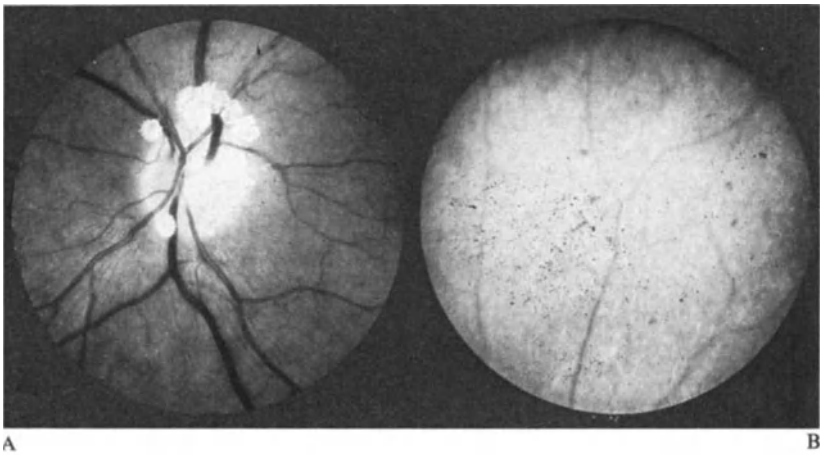


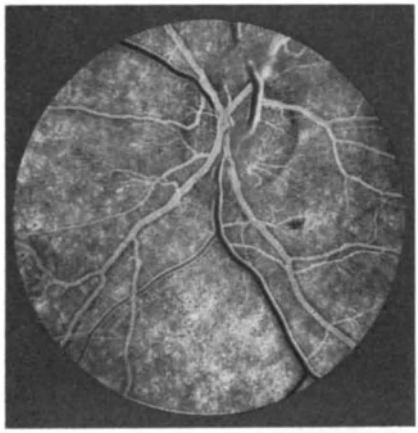
Fig. 19 Pit of the optic disc.
A : conventional photograph. B: fluorescence angiogram; arterial phase.
Hypovascularity and dystrophy of the pigment epithelium in the adjacent region.

The term: oedema of the optic disc, is applied to all other forms of disc swelling of local or systemic aetiology, not affecting vision. In case of significantly affected vision the term optic neuritis is prefered. Angiographically however, there is not much difference between the conditions mentioned above. This is the reason that the term papilloedema is used for all three conditions in fluorescein angiographic studies.

Central venous obstruction, hypertension, perivasculitis and deep drusen may all lead to optic disc oedema. In most cases a differential diagnosis between true papilloedema and the above mentioned conditions can be made, but this is not always the case (ROPER-HALL 1972). Central venous obstruction usually gives retinal oedema, haemorrhages and marked venous engorgement. In some



A B



C

Fig. 20 Optic disc hamartoma in a girl suffering from retinitis pigmentosa.
A, B: conventional photographs. C: fluorescence-angiogram; arterial phase.
Small vessels in the mulberry-like concretions are discernable.
Reduced filtering effect of affected pigment epithelium.

cases the degree of venous obstruction and the interference with the arterial blood supply gives the same reduced perfusion pressure which goes with the development of true papilloedema. For the same reason the fundus pictures observed in malignant hypertension, in renal retinopathy and in brain tumor are almost identical.

Drusen of the optic disc frequently produce a misleading appearance of oedema, but usually haemorrhages are absent. It is important to investigate the relatives of the patient, as they usually show obvious drusen. A detailed examination may reveal the typical glittering deposits. However, diagnosis is not always easy, especially when the drusen are deeply concealed.

THE EVOLUTION OF PAPILLOEDEMA

PIOVANETTI & ECKELHOFF (1972) were able to study the changes occurring during the evolution of papilloedema in a patient suffering from an inoperable intracranial tumor. Other reports describing the fluorescein angiographic changes in papilloedema (capillary congestion, venous distention and leakage in the late phase) are based on findings in single studies of a great many patients.

As papilloedema develops, progressive stasis in the capillary bed leads to distortion of the radial pattern by dilatation and tortuosity. Empty pre-existing capillaries are seen as dark streaks crossing over major blood vessels. These capillaries become visible in a later stage as they fill with blood. Micro-aneurysmatic dilatations in the capillaries appear, which increase in number up to the fully developed stage. Exudates appear on the disc, which are seen angiographically as dask areas that do not show leakage of dye; an appearance consistent with multiple micro-infarctations. Capillary A-V shunts can also be identified.

In the full-blown stage of optic disc oedema there is loss of the glow and ophthalmoscopically this corresponds to a loss of transparancy of the tissue of the disc caused by oedema. The major retinal vessels show a slight venous congestion during the early stages. At the fully established stage further impairment of the venous outflow produces an increase in the tortuosity of the veins. The arterioles remain unaltered. Venous stasis causes alterations in permeability of the walls of the capillaries and the veins, permitting the dye to leak out and produce the late glow of the disc, the fluorescence of the peripapillary retina and the perivenous staining. The extent of leakage of dye is proportional to the stage of papilloedema but is unpredictable from the ophthalmoscopic appearance.

The fluoro-angiograms of *hyaline bodies of the optic disc* (*deep drusen*) are characterized by (see also Figures 7, 9, 10 and 11):

1. a non-dilated capillary network – if present – on the optic disc,
2. an increased fluorescence persisting for some minutes and subsiding slowly, simultaneously with a moderate, shortlasting fluorescence of the hyperplastic glia of the disc.

OOSTERHUIS & BOEN-TAN (1969) observed in some cases drusen of the optic disc showing peripapillary haemorrhages.

KAREL et al. (1972), BRODRICK (1973) and HENKIND et al. (1972) drew

attention to two types of circulatory disturbances in drusen of the optic disc:

1. A short lasting ischaemic oedema of the optic disc with a sudden visual decrease, due to a nerve fiber bundle defect. Fluoroangiography shows dilatation of the papillary and peripapillary capillaries, dye leakage and a long persisting fluorescence of the optic disc;
2. Disturbance of the venous circulation, characterized by venous stasis, ectatic retino-ciliary venous communications and superficial haemorrhages.

As mentioned above, *central venous obstruction* is usually associated with oedema of the optic disc. Haemorrhages in the peripheral parts of the retina are frequently found. Fluorescein angiography may differentiate between papill-oedema due to central venous obstruction and true papilloedema (see Fig. 16). In central venous obstruction considerable dilatation of the venous branches and pronounced slowing of the venous return may be observed.

Sometimes the association of optic disc oedema with headache and tinnitus, as in *Harada's disease*, can be the cause of a faulty diagnosis and may lead to unneccessary neurological investigations (Fig. 15).

Another possibility, though often misdiagnosed, is the *optic disc vasculitis* (LYLE & WYBAR (1961); LONN & HOYT (1966); HAYREH (1969, 1972)). The main features of this condition can be summarized as follows (compare Fig. 17):

Young healthy individuals, showing as a single symptom a vague fogginess of vision of one eye only, though the visual acuity is normal. A marked dilatation and tortuosity of the retinal veins with an appreciable amount of haemorrhages on and around the optic disc. Sheathing of the large retinal veins and dilated capillaries of the optic disc occurring as a late phenomenon.

There is usually a favourable response to high doses of systemic steroids. HAYREH divided the group in two subtypes: one group of patients showing optic disc oedema as a prevailing feature and a second group in which retinal venous obstruction dominates the picture. According to HAYREH this last group shows a less favourable response to corticosteroids.

In some cases of *optic atrophy of Leber* we notice a slight optic disc oedema (Fig. 12). In this respect it is interesting to try to correlate the colour of the optic disc with its vasculature. Ophthalmoscopy reveals that the nasal side of the optic disc usually shows some more redness. On the other hand, on the fluorescein angiogram the temporal part of the optic disc shows more vascularity than the nasal part. As to the pallor of the optic disc: what is its significance in relation to a reduced vascularity? HAYREH (1972) concludes that there is no true significant correlation between the optic disc colour and its vascularity. In the majority of cases HAYREH considers glial tissue being responsible for the colour.

The condition in which acute decrease in vision and papiloedema occurs is usually called *papillitis* or optic neuritis.

Angiographically there are no significant differences between this type of optic disc oedema and optic disc oedema caused by increased intercranial pressure.

Oedema of the optic disc in elderly patients accompanied by an acute decrease in vision and associated with a sectorial field defect is called *ischaemic oedema of the optic nerve*. This condition is often associated with the presence

of temporal arteriitis. Usually a segmentary defect is found according to the segmentary distribution of the posterior ciliary arteries which in this disease are occluded (Fig. 14).

Occlusion of the central retinal artery is not present. Otherwise, oedema of the retina should have been observed. Histopathological studies confirm the above mentioned theoretical conception. A case was found of ischaemic optic neuropathy associated with arteriitis, infarction of the lamina cribrosa with cavernous degeneration of the retrolaminar part of the optic nerve. Vascular lesions were confined to the posterior ciliary arteries. The pial vessels, always thought to be feeders of this area, were normal and so was the central retinal artery.

Fluorescein angiographic findings in *dominant infantile optic atrophy* revealed a much too late and irregular choroid filling, associated with paucity of vessels of the optic disc. Abnormal and even very late fluorescence of the optic disc head, and diminished peripapillary fluorescence was also observed (KOK-VAN ALPHEN et al., 1972). The authors assume that choroidal circulatory disorders may contribute to the pathogenesis of the optic disc lesions.

The so-called *juxtapapillary haemangioma of Von Hippel* has also to be differentiated from optic disc oedema (OOSTERHUIS & RUBENSTEIN 1971). This type of haemangioma forms a more or less round tumor, situated partly on the edge of the optic disc. It shows a rose or grey colour. The tumor is usually located at the temporal inferior side of the optic disc. There is a preference for the left eye. Angiographically a network of small vessels is seen. In the later phases, an intense but diffuse fluorescence is noticed. Secondary degeneration of the pigmentepithelium is found as a complication. As not all haemangiomas are progressive and show pigment epithelial degeneration, the others should not be named Von Hippel tumours (see Fig. 18).

Disc changes due to drusen, are a frequent finding in ophthalmoscopy. The drusen have to be distinguished from the so-called *hamartoma of the optic disc.*

Histologically, drusen show laminated acellular basophilic concretions, situated anterior to the lamina cribrosa. They reach seldom the surface of the optic nerve head. In contrast to drusen, disc hamartomas show evidence of proliferation of astrocytic cells in addition to calcification. The peripapillary retina may be involved. In later stages these tumors look like mulberries, due to the fine nodular surface. Figure 20 illustrates a case of a young girl in which the typical disc condition is combined with a retinitis pigmentosa. Apart from my own case up to the present, six cases of retinitis pigmentosa associated with hamartoma at the disc have been analysed and reported (ROBERTSON 1972).

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FLUORESCEIN ANGIOGRAPHY IN MACULAR DISEASES

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ABSTRACT

A selection of various interesting macular disorders is presented and the great value of fluorescein angiography in outlining the underlying structural abnormalities is demonstrated. An important feature of angiography is that the integrity of the blood-retina barrier and the choroido-retinal diffusion barrier (the tight junctions of the cells of the retinal pigment epithelium) can easily be assessed in vivo. Macular diseases showing leakage of fluorescein, either from the retinal vessels or from the choriocapillaries, are candidates for (laser) photocoagulation and angiography has proven to be indispensable in deciding upon the advisability of photocoagulation and assessing its effectiveness when employed.

Fluorescein angiography may be very helpful in evaluating macular disorders. For a complete diagnostic work-up retinal function studies such as visual acuity, colour vision, visual fields, dark adaptation, ERG and EOG, are indispensable, but it is undeniable that fluorescein angiography is a most helpful and often necessary method of examination in addition to ophthalmoscopy.

Particularly changes in the retinal pigment epithelium and in the retinal vessels are rendered visible much better than with normal ophthalmoscopy and conventional photography, while choroidal affections may also show specific changes.

Since it is impossible to discuss all macular disorders in this chapter I made a selection of various interesting diseases.

A. HEREDITARY MACULAR DEGENERATIONS

The most common juvenile macular dystrophies are X-linked juvenile retinoschisis, Stargardt's disease, cone dystrophy and vitelliform dystrophy. All these distinct entities have a specific ophthalmoscopic and fluorescein angiographic pattern while they also have specific retinal function profiles, which are partly based on differences in anatomical localization (DEUTMAN, 1971).

1. *X-linked juvenile retinoschisis*, where the main abnormality is a splitting of the nerve fiber layer, shows mostly a normal macular fluorescein picture, but occasionally hyperfluorescence due to defective pigment epithelium may be seen (Fig. 1).

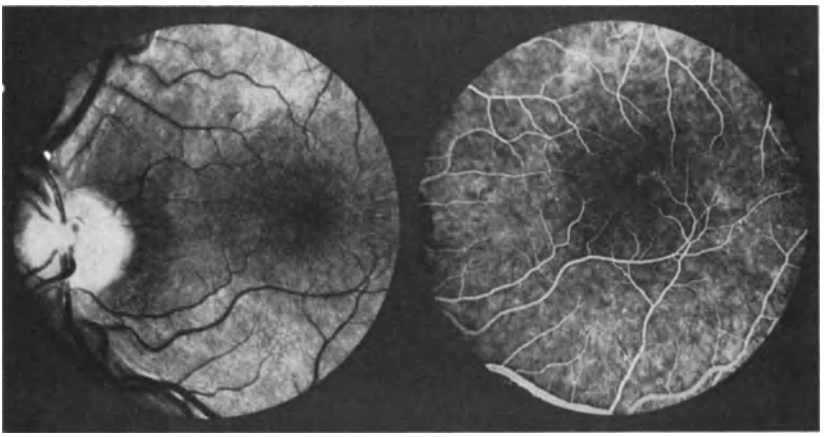


Fig. 1. X-linked juvenile retinoschisis. There is often a normal macular fluorescence pattern in this condition. In this patient, though, there is mild hyperfluorescence centrally due to defective pigment epithelium. The fundus as a whole seems to be slightly more fluorescent than in most normal individuals.

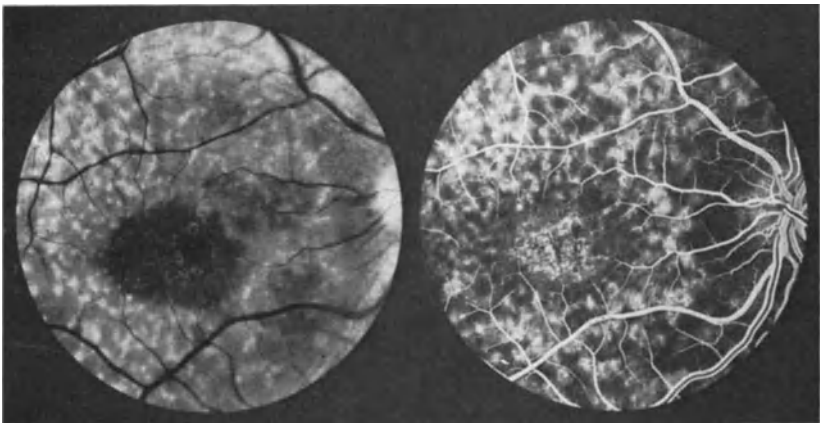


Fig. 2. Typical case of Stargardt disease (atrophic macular dystrophy with fundus flavimaculatus). A central horizontal ovoid zone of pigment epithelial atrophy is surrounded by many fuzzy yellowish flecks which are often arranged in a reticular pattern. The area just temporal to the disc shows intact pigment epithelium. There is widespread pigment epithelial involvement in this disease as manifested by the many areas of hyperfluorescence. Discs, vessels and far retinal periphery are normal in this condition.

2. *Stargardt's disease*, which is the same condition as atrophic macular dystrophy with fundus flavimaculatus (STARGARDT, 1909), reveals nearly always after some time a horizontally ovoid zone of hyperfluorescence surrounded by many fuzzy hyperfluorescent flecks (Fig. 2).

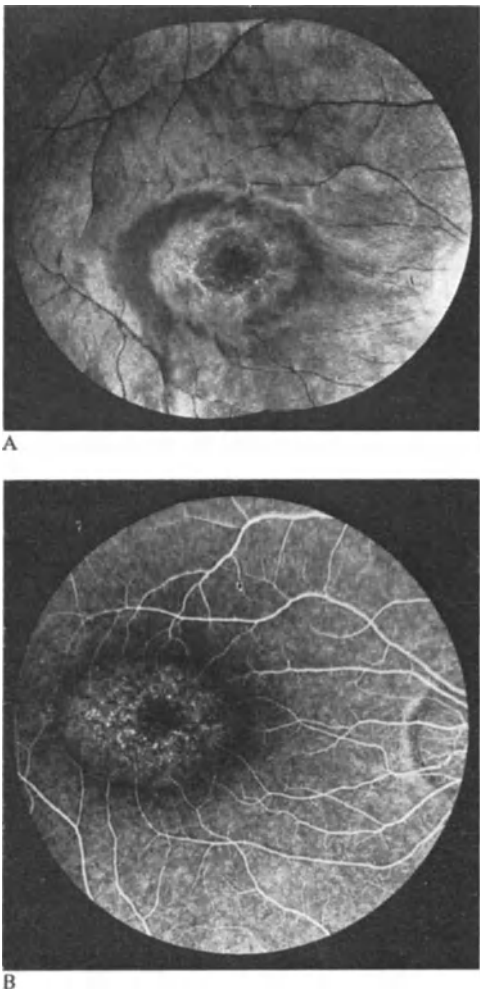


Fig. 3. An 8-year-old boy with cone dystrophy. Note the typical bull's eye macular lesion. Retinal function studies showed predominant impairment of cone function although rod function was also slightly affected. The vessels are already somewhat attenuated. A: conventional photograph. B: fluorescence angiogram; arterio-venous phase.

3. *Cone dystrophy* is often manifested by a bull's eye macular picture (Fig. 3), indistinguishable from the macular pattern in chloroquine retinopathy (Fig. 4). This clinical entity is usually characterized by a predominant affection on the photopic ERG and very poor colour vision (KRILL & DEUTMAN, 1972a ; KRILL, DEUTMAN & FISHMAN, 1973). Occasionally the central retina may show in this disease the ophthalmoscopic picture of central pigmentary retinopathy.

4. *Vitelliform dystrophy* has a hypofluorescent macula in the intact egg-yolk stage, due to blocking of the fluorescence by the egg-yolk substance (Fig. 5).

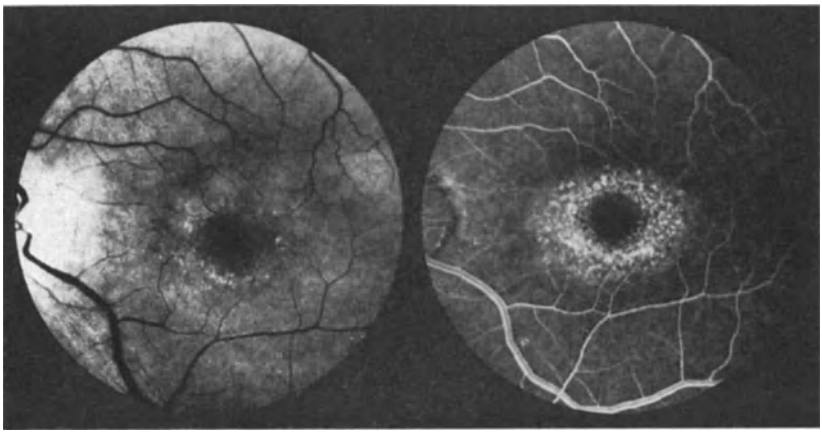


Fig. 4. A woman in her sixties with cloroquine retinopathy, demonstrating the classic pattern of a bull's eye macula, indistinguishable from the one in cone dystrophy.

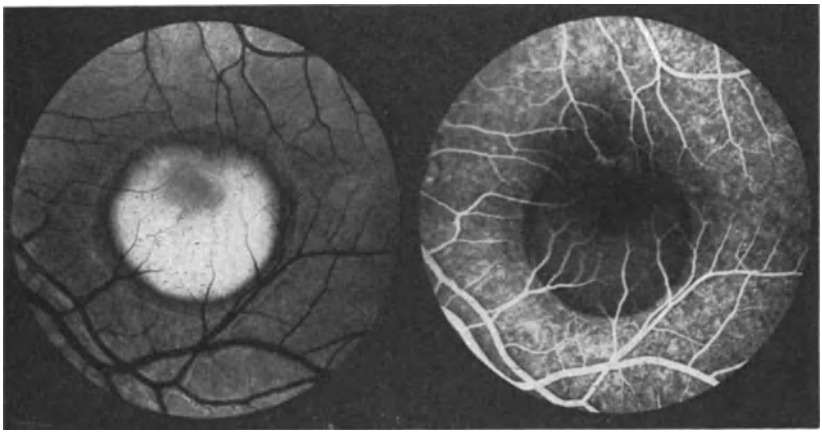


Fig. 5. Classic vitelliform disc (intact egg-yolk) blocking the choroidal fluorescence. This disc is probably located in or very close to the cells of the retinal pigment epithelium.

Later when the disc disintegrates and the scrambled egg stage appears, hyperfluorescence due to defective pigment epithelium is seen (Fig. 6).

Fluorescein angiography is a very important diagnostic tool, precisely in these juvenile macular dystrophies, since the macula may show initially only minimal changes together with severely decreased visual acuity. In these cases macular dystrophies have to be differentiated from optic nerve affections and from hysterical conversion reactions. Minimal macular changes may become clearly visible after fluorescein angiography, particularly in Stargardt's disease and cone dystrophy.

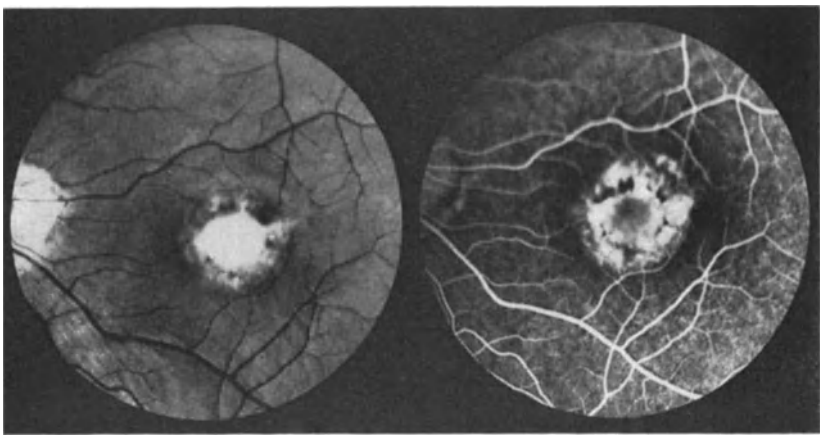


Fig. 6. Disintegrated vitelliform disc (scrambled egg) showing hyperfluorescence due to defective pigment epithelium centrally.

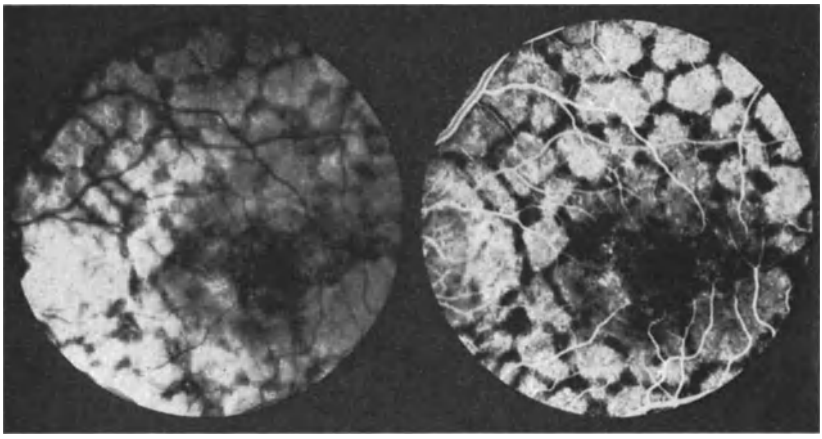


Fig. 7. Sjögren's reticular dystrophy of the retinal pigment epithelium with the pathognomonic fishing net appearance, beautifully outlined on fluorescein angiography.

ERG, EOG, foveal ERG and the visually evoked potentials (VEP's) are also very helpful diagnostic methods. when we have to differentiate these altogether different disorders initially.

5. *Sjögren's reticular pigment dystrophy* and *butterfly-shaped pigment dystrophy* demonstrate dark configurations in front of a brightly fluorescent choriocapillaris due to migration of pigment in the pigment epithelium (Fig. 7, 8).

6. *Drusen of the pigment epithelium*, which may be autosomal dominantly inherited, mostly have sharply defined round areas of hyperfluorescence (Fig. 9). Drusen material ultimately accumulates between the retinal pigment epi-

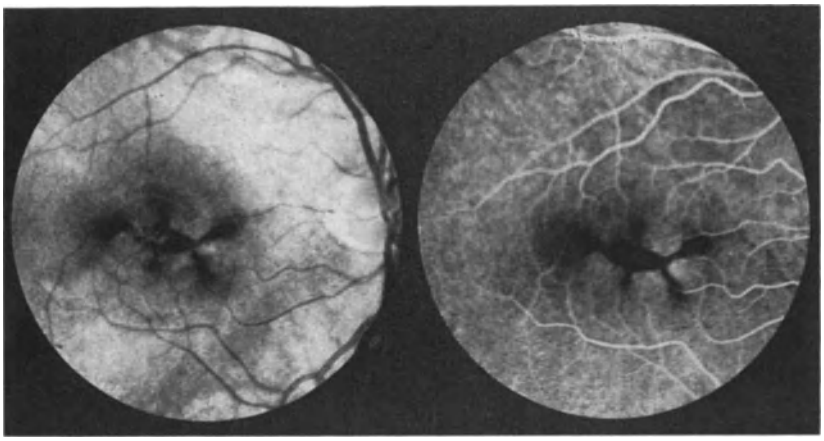


Fig. 8. Butterfly-shaped macular pigment dystrophy with hypofluorescent butterfly in front of a brightly fluorescing choroid.

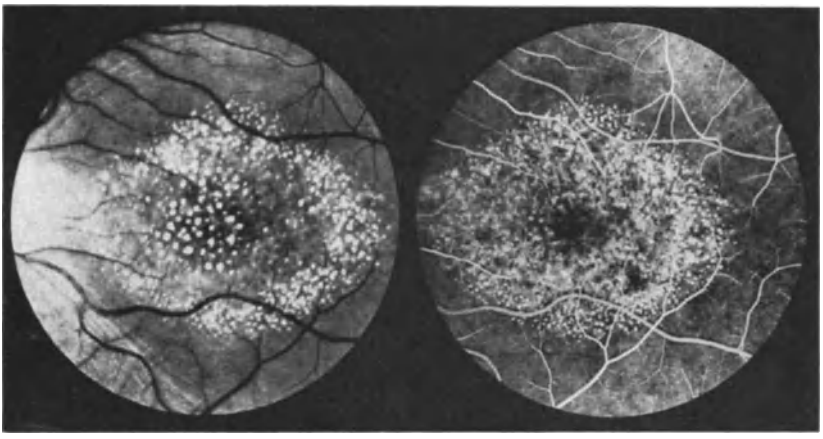


Fig. 9. Dominant drusen of the retinal pigment epithelium. Note the well defined roundish areas of hyperfluorescence at the site of the drusen and also the diffuse hyperfluorescence in the paramacular area.

thelium and Bruch's membrane, giving rise to pigment epithelial atrophy and choroidal atrophy in later stages. Often the areas between the drusen show also hyperfluorescence indicating defective pigment epithelium (Fig. 9 right). Some larger hyalinized drusen may block fluorescence.

7. *Choroidal dystrophies* are manifested ophthalmoscopically by pigment-epithelial- and choriocapillaris-atrophy. In late stages the intermediate and large choroidal vessels may also disappear (Fig. 10). True central choroidal dystrophy usually has an autosomal dominant inheritance pattern.

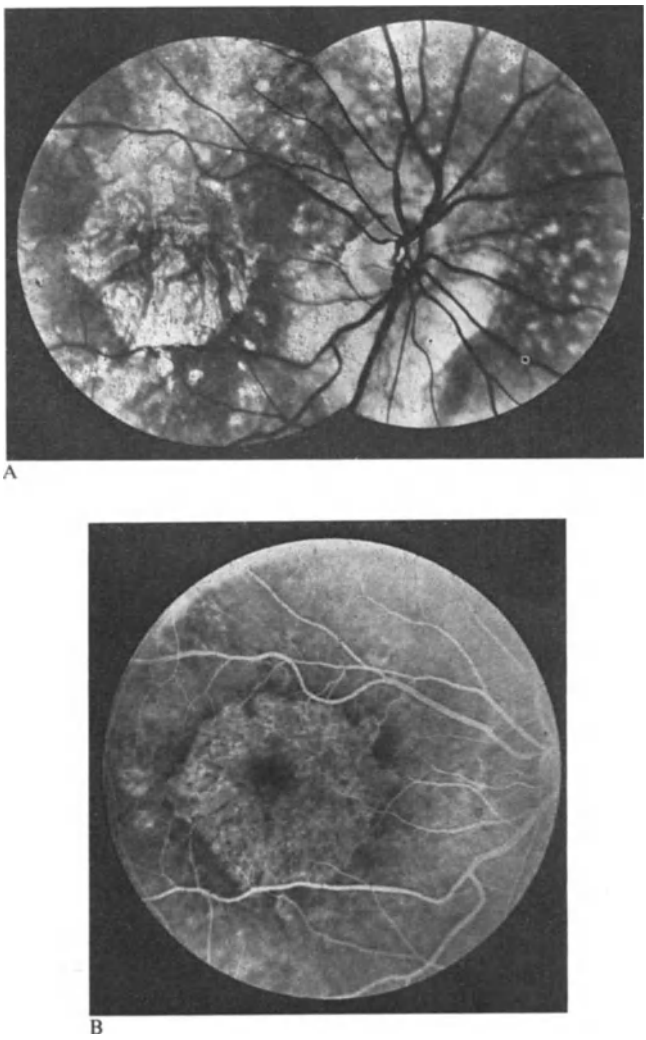
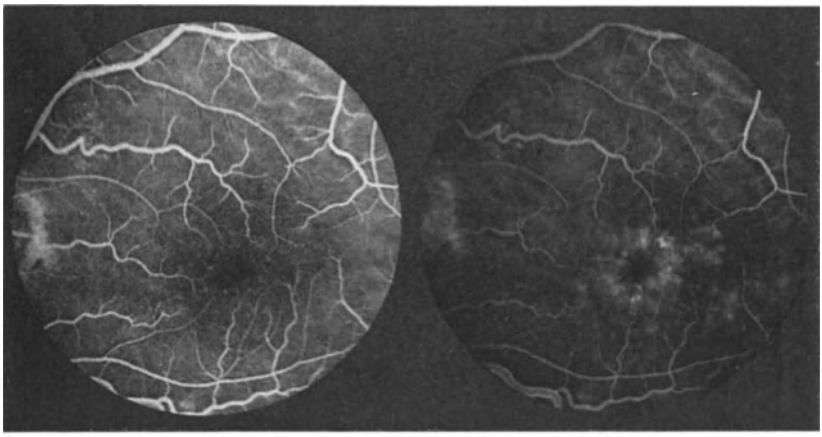


Fig. 10. Right macula in a 76-year-old woman belonging to a pedigree with autosomal dominant central choroidal dystrophy. Most choroidal vessels have disappeared and many drusen surround the central atrophic zone. A: conventional photograph; B: fluorescein angiogram; arterio-venous phase.

In general there is no fluorescein leakage in the hereditary dystrophies. However, occasionally one may see leaking perimacular capillaries in genetically determined pigmentary retinopathy. The cause of this is unknown. This leads to the picture of cystoid macular oedema exactly like the one that is often seen after cataract extractions (Irvine-Gass syndrome) (Fig. 11). Generally spoken, though, the macular area in pigmentary retinopathy is normal, while also the areas of tapetal reflex in carriers of X-linked pigmentary retinopathy, usually temporal to the macula, have normal fluorescence patterns.



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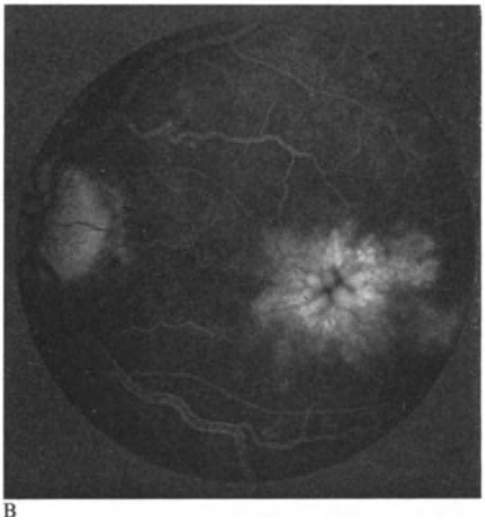


B

Fig. 11. Typical Irvine-Gass syndrome in a patient with acrylic lens implantation. The dilated perimacular capillaries leak dye and this results in the late phases of angiography in the well known flowerlike pattern of cystoid macular oedema. (B) This condition may also be found in pigmentary retinopathy, diabetic retinopathy, venous obstruction, Coats' disease, and 'pars planitis'.

In general, hereditary macular dystrophies tend to show depigmentation and atrophy of the pigment epithelium, manifested by hyperfluorescence as the choriocapillaris becomes perfused with dye. The fluorescence increases in intensity up to the midretinal venous phase in which choroidal fluorescence is maximal. No expansion of the hyperfluorescent area is seen in these pigment epithelial defects. In advanced stages choroidal atrophy may also develop.
Congenital hereditary diseases located in the superficial retinal layers, such as congenital nightblindness and achromatopsia have normal fluorescence pictures.

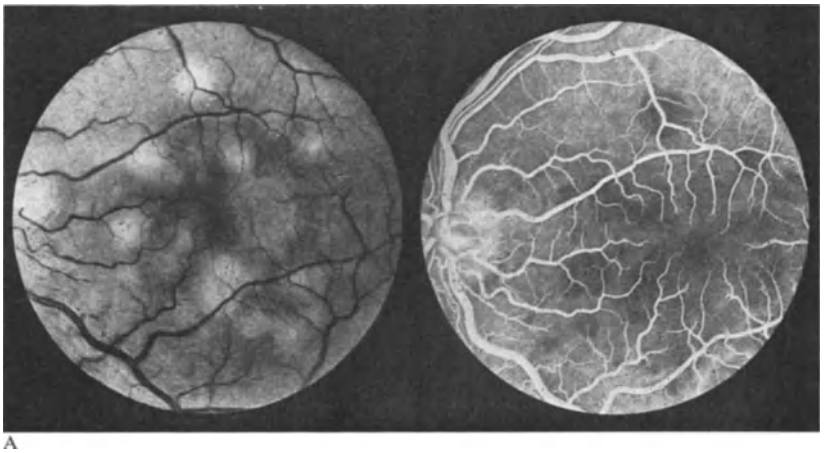
B. TOXIC RETINOPATHIES

Toxic retinopathies may reveal disturbances in the macular pigment epithelium. Chloroquine shows a bull's eye macular lesion (Fig. 4), while the phenothiazines and indomethacin may give rise to mottled defects in the pigment epithelium. One patient we saw with diminished acuity due to digitalis intoxication had a normal fluorescence pattern (to be published).

C. INFLAMMATORY LESIONS

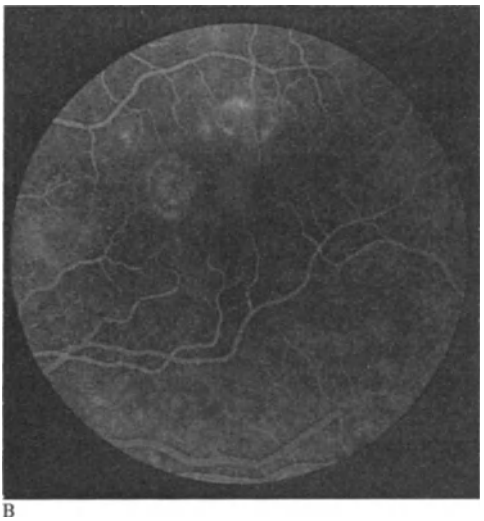
Inflammatory lesions in the macular area form an interesting and important part of the macular lesions. Fluorescein angiography facilitates the exact diagnosis and in this way enables us to make a reliable prognosis for the patient's vision. Recently a few clearly distinguishable entities have been described.

1. *Acute posterior multifocal placoid pigment epitheliopathy* (GASS, 1968) is characterized by rapid loss of central vision secondary to multifocal yellow-white placoid lesions at the level of the pigment epithelium and choroid (Fig. 12). These lesions resemble soft photocoagulates strikingly and they show rapid resolution with permanent alterations in the pigment epithelium with little damage to the adjacent choroid and retina. Significant visual improvement occurs after apparent ophthalmoscopic resolution of the acute lesions, which are located at the posterior pole (Fig. 13). Fluorescein angiography shows hypofluorescence at the site of the lesions in the early arterial phase and hyperfluorescence due to staining of the lesions in the late venous phase. There are indications that this condition may be due to a more or less general vasculitis based on hypersensitivity. It is possible that the primary cause is a chorio-capillaritis rather than a pigment epitheliopathy (DEUTMAN et al, 1972).



A

Fig. 12A. 'Acute posterior multifocal placoid pigment epitheliopathy' in a 22-year-old man. The patches, not unlike soft photocoagulates, show hypofluorescence initially.



B

Fig. 12B. Lesions stain with fluorescein in the late phases of angiography.

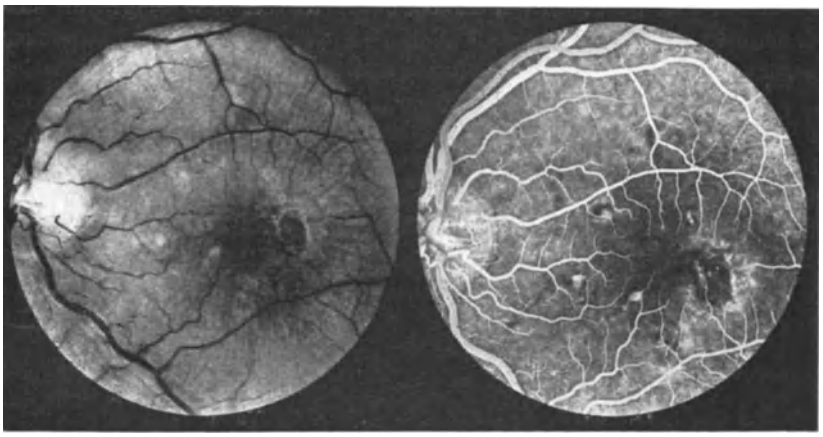


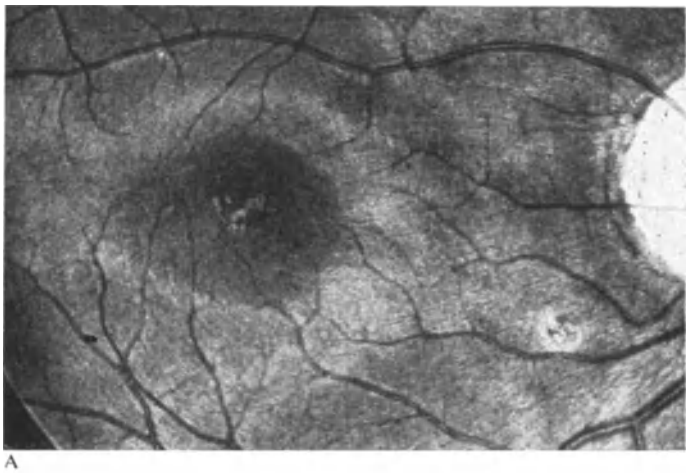
Fig. 13. The same case as depicted in Fig. 12, now two weeks later. Visual acuity had recovered from 0.3 to 1.0. The whitish patches have now nearly completely resolved. All that remains are areas of hyperfluorescence indicating defective pigment epithelium.

2. *Acute retinal pigment epitheliitis* (KRILL & DEUTMAN, 1972) is characterized by an acute onset of visual loss with fairly rapid resolution in usually six to twelve weeks and ultimate recovery to normal vision.

The typical lesion is a deep, fine, dark-grayish, sometimes black spot which is surrounded by a pale yellow halo-like zone.

These lesions typically occur in two to four clusters in the macular area and may be unilateral or bilateral (Fig. 14).

Fluorescein findings are minimal, but hyperfluorescence corresponding particularly to the halo-like zone may be seen (Fig. 14B).



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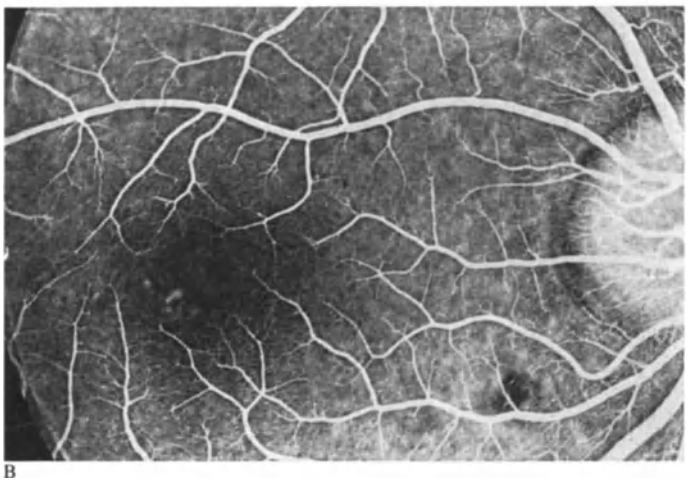


B

Fig. 14. Acute pigment epitheliitis of the macula in a Dutch woman in her early twenties. There was unilateral visual impairment of acute onset. Ophthalmoscopy demonstrated one or two clusters of tiny, dark grayish spots, surrounded by whitish halolike zones localized in the macular area. (A). There was some hyperfluorescence, but no leakage of fluorescein on angiography. (B,C). Visual acuity recovered completely in approximately eight weeks. A viral origin of this process was suspected.

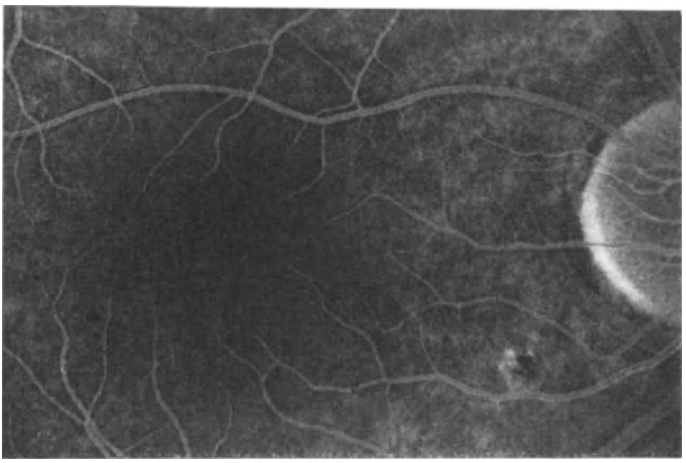


Fig. 14C. Fluorescein angiogram; late venous phase.

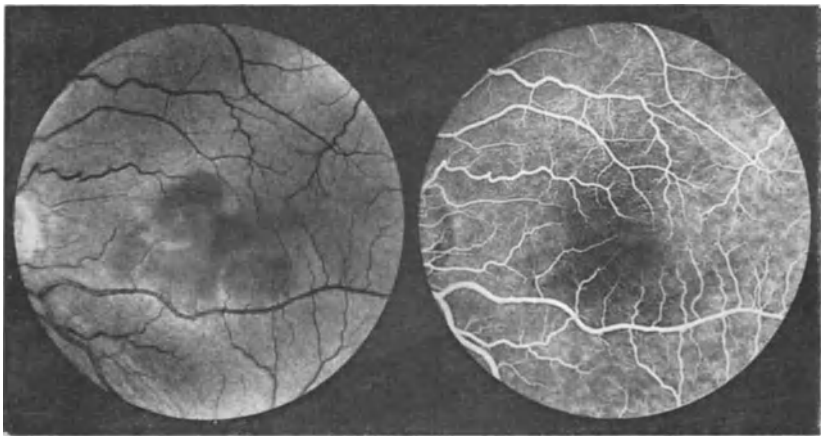
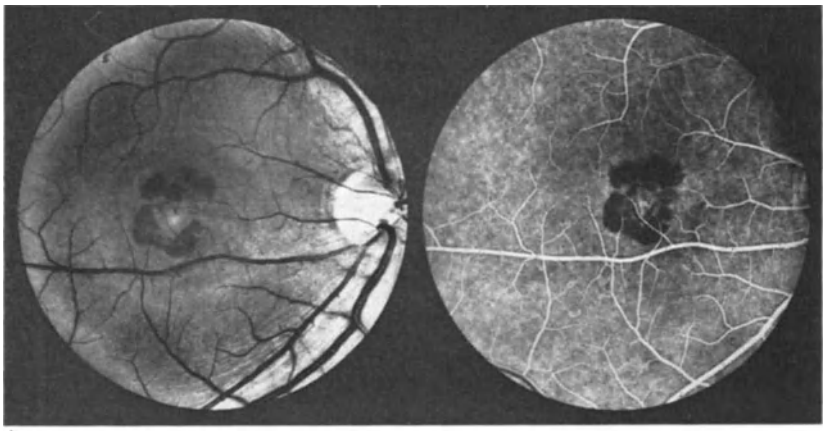


Fig. 15. Acute macular neuro-epitheliitis in a 33-year-old woman, who developed visual complaints suddenly in both eyes during an attack of influenza. There are dark reddish, wedge-shaped lesions not unlike cloverleaves that surround the centre of the fovea. The nerve fibre layer looks swollen with clearly visible horizontal lines supero-nasally to the fovea. Fluorescein angiography shows questionably dilated capillaries superior to the fovea, but there is no leakage of fluorescein, even as far as 15 minutes after fluorescein injection. Paracentral scotomata persisted for many months and there is now, after 6 months, still little improvement observable.

3. *Acute macular neuro-epitheliitis* is a condition which dr. P. Bos of Amsterdam University and I saw so far in 4 women in their twenties (to be published). It is characterized by oedema of the superficial retinal layer in the paramacular area and one or more wedge-shaped, glistening oedematous areas may be seen (Fig. 15).

Central vision is normal or somewhat disturbed, but invariably paracentral scotomas are present. The lesions may be unilateral or bilateral. Resolution is very slow and the lesions may last for months. Fluorescein angiography shows no abnormality or sometimes questionably dilated perimacular retinal capillaries, but no leakage of fluorescein (Fig. 15 right hand figure).

General physical and laboratory examination is normal.



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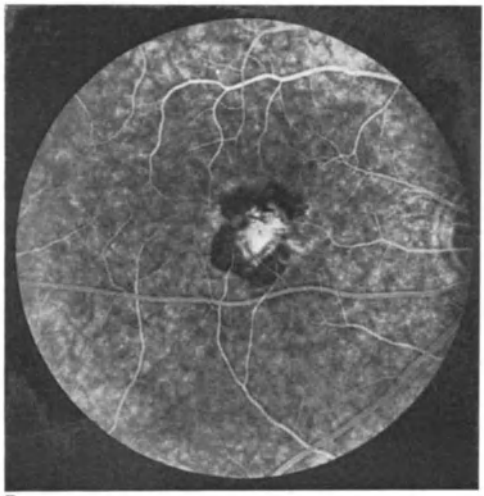


B

Fig. 16. 'Presumed histoplasmin choroiditis' showing a haemorrhage (haemorrhagic detachment of the retinal pigment epithelium) in a 30-year-old Dutch man with a negative histoplasmin skin test. There was no peripapillary atrophy and there were no histo-spots in the mid periphery or far periphery of the retina. Fluorescein angiography outlines new formed vessels (Fig. 16A; right hand figure) sprouting from the choriocapillaris under the retina and giving rise to fluid leakage (Fig. 16B).

4. *Presumed histoplasmin choroiditis:* New vessels originating from the choriocapillaris are present in this condition. They penetrate defects in Bruch's membrane or lie beneath the retinal pigment epithelium or within the subretinal space. Usually a brownish dark ringlike lesion is then visible with ophthalmoscopy. These vessels are rarely obvious on routine ophthalmoscopic examination but can be vividly demonstrated in the early stages of angiography. They are a frequent cause of subretinal and intraretinal haemorrhage. These new vessels lead to haemorrhagic detachment of the retinal pigment epithelium and may be found in variety of conditions such as presumed histoplasmin choroiditis, high myopia (Fuchs' spot), angioid streaks and senile disciform macular degeneration (KUHNT-JUNIUS).

Fluorescein angiography identifies the exact sites and delineates the area of the vascular abnormality and monitors the effectiveness of photocoagulation in obliterating these vessels. If the lesion is not within $\frac{1}{4}$ disc diameter of the central fovea light coagulation with high intensity may be successful.

In the Netherlands we find rather frequently patients with macular lesions such as in presumed histoplasmin choroiditis. However, in these patients the histoplasmin skin-test is always negative. Compared with the American patients from the Ohio- and Mississippi Valley we find less often peripheral histospots and peripapillary atrophy. Often there is a solitary macular lesion (Fig. 16).

5. *Serpiginous choroiditis* is a chronic condition probably of inflammatory origin, although some authors think this to be of hereditary origin. Fingerlike lesions expand over the posterior pole of the eye, with obvious atrophy of pigment epithelium, choriocapillaris and choroid, while at the edge of the expanding lesions a gray opacification is located, which obscures all view of the underlying choroid. There is a slow, relentless progression in this disease and occasionally inflammatory signs may be seen in the vitreous body or in the anterior segment. Radial extensions usually emanate from the optic disc.

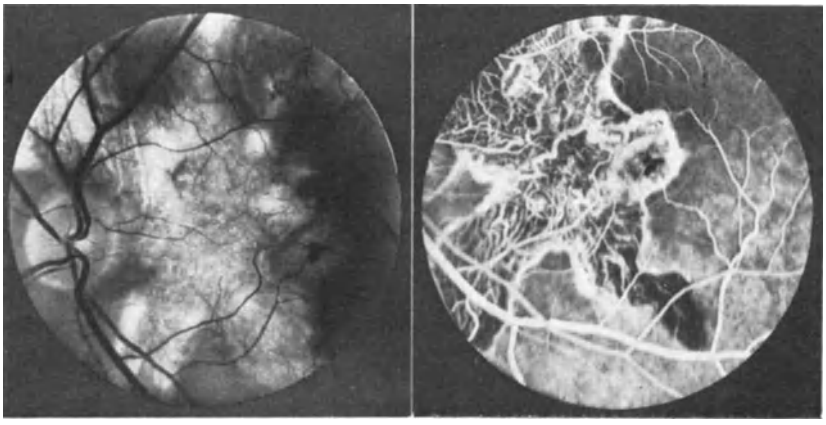
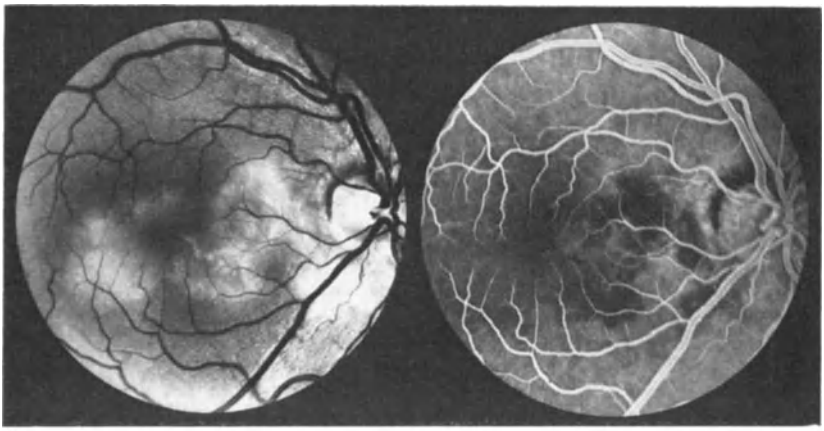


Fig. 17A



B

Fig. 17A. Serpiginous choroiditis with fingerlike lesions in a 48-year-old man. Note the obvious atrophy of pigment epithelium, choriocapillaris, and some of the intermediate choroidal vessels. There are many more vessels patent as seen on fluorescein angiography than normal ophthalmoscopy suggests. Fig. 17B. Another patient with the typical picture of serpiginous choroiditis.

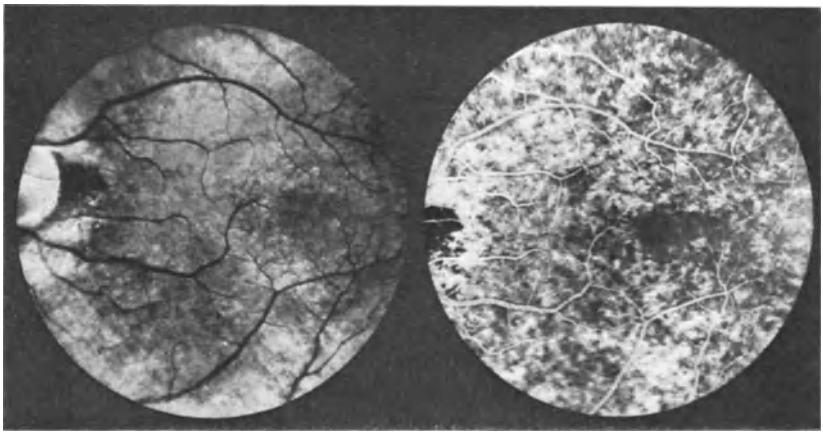


Fig. 18. Typical lesions of congenital rubeola retinopathy showing diffuse blotchy hyperfluorescence and many roundish dark dots. Visual acuity was not affected in this case.

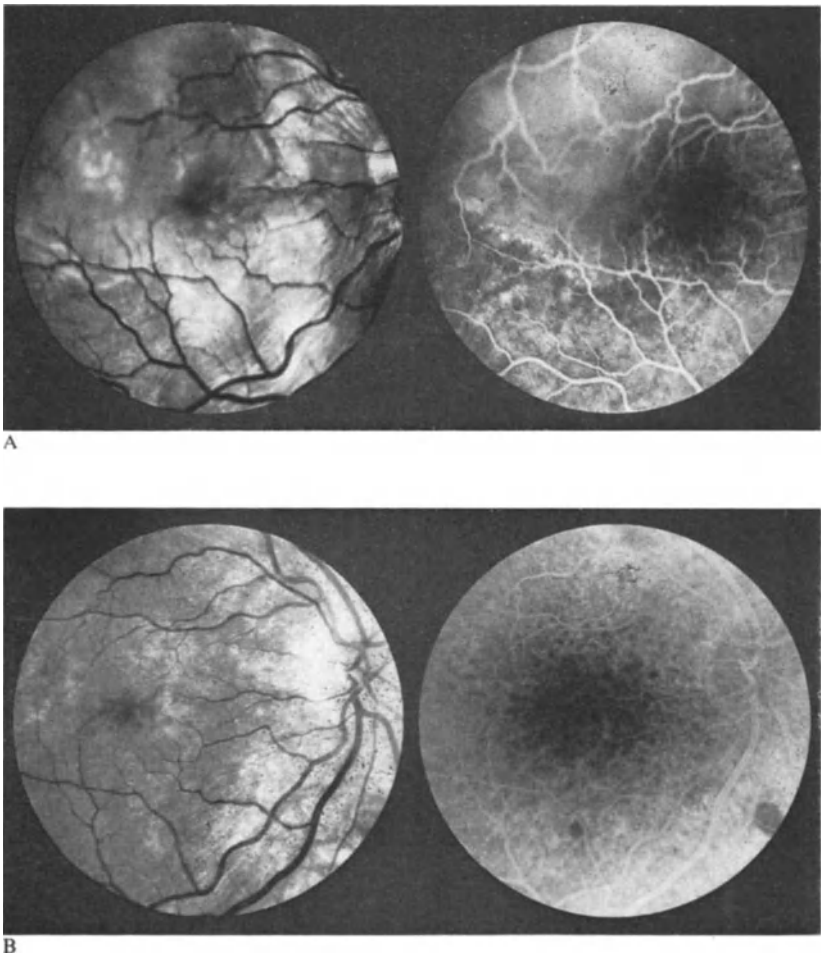
Fluorescein angiography indicates that the grayish opacifications at the edge of the lesions are hypofluorescent, while at the site of the lesions pigment epithelium, choriocapillaris and some of the intermediate choroidal vessels are gone (Fig. 17).

6. *Rubeola retinopathy* is characterized by roundish dark spots surrounded by lighter halos in the posterior pole of the eye (Fig. 18). Visual acuity is

mostly normal or only slightly affected. Fluorescein angiography shows a characteristic spotty pattern of tiny hyperfluorescent zones surrounding hypofluorescent roundish dots. This pattern may also be seen in carriers of choroideremia and in the retinal periphery of carriers of the X-linked ocular albinism.

7. *Harada's disease* is characterized by bullous serous detachment of the retina and uveitis. Initially it may look like central serous choroidopathy, but later large areas of the retina develop a serous detachment (Fig. 19).

Fluorescein angiography shows diffuse leakage of fluorescein at the side of



A

B

Fig. 19. Harada disease (meningo-uveitis) showing large areas of bullous detachment (Fig. 19A). There is fluorescein leakage at the site of the serous detachment. There was complete recovery with return to normal visual acuity (Fig. 19B). A mottled pattern of diffuse pigment epithelial involvement, not unlike congenital rubeola retinopathy, resulted.

the bullous detachment due to increased permeability of the choroidal vessels Harada's disease (meningo-uveitis) is in all probability a specific posterior manifestation of the Vogt-Koyanagi syndrome, of which anterior uveitis forms a part.

8. *Toxoplasmosis retinochoroiditis* shows fluorescein staining of the inflamed area due to increased permeability of the choroido-retinal diffusion barrier. Often vasculitis accompanies this type of retinitis. In scar-stages choroido-retinal vascular communications may develop just like in senile disciform macular degeneration (Fig. 20D).

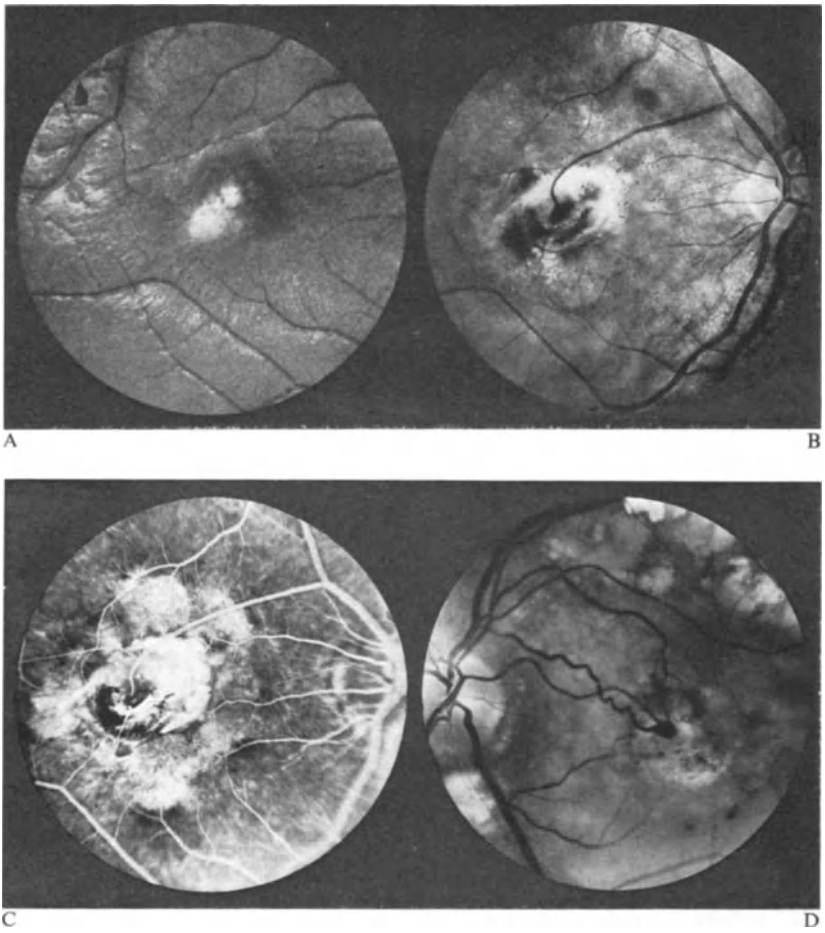


Fig. 20. Toxoplasmosis retino-choroiditis in a 15-year-old boy (Fig. 20A). Seven years later, there is in the centre of the fovea a large retino-choroidal vascular communication, arising from the superior temporal retinal artery (Fig. 20B) and this is outlined beautifully on fluorescein angiography (Fig. 20C). These shunts are also frequently encountered in long standing senile disciform macular degeneration (Kuhnt-Junius disease) (Fig. 20D).

D. INCREASED VASCULAR PERMEABILITY

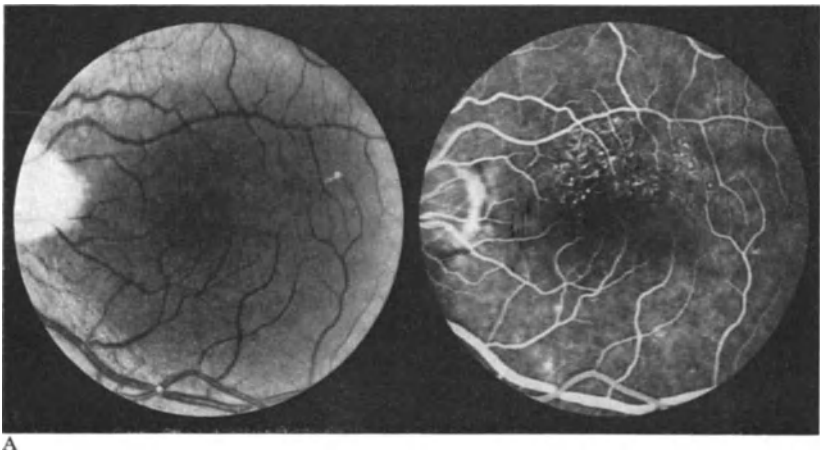
Increased vascular permeability occurs either in the retinal capillaries (1) or in the choriocapillaris (2).

1. *Cystoid macular oedema:* Increased permeability of the perimacular retinal capillaries is nearly always the origin of cystoid macular oedema. Fluid extravasates from these vessels and accumulates in the perivascular microcystoid spaces. With time the fluid diffuses into the large cystoid spaces in Henle's layer.

Fluorescein angiography shows pinpoint areas of dye leakage from the perimacular capillaries in the arterio-venous phase (Fig. 11A). In the late phases a characteristic flowerlike pattern of intraretinal pooling of fluorescein is observed (Fig. 11B). This type of cystoid macular oedema is seen in a variety of conditions. It is found after conventional cataract extractions (Irvine-Gass syndrome) (GASS & NORTON, 1966) while we also saw it as the cause of macular oedema in patients with acrylic lensimplantations.

Furthermore we have seen it in chronic uveitis, such as pars planitis, in diabetic retinopathy, after venous obstruction, in Coats' disease and in genetically determined pigmentary retinopathy (rod-cone dystrophy).

In one patient who had leaking perimacular capillaries, probably as a result of partial obstruction of a small venous branch (Fig. 21). we applied argon laser coagulates between the leaking capillaries. Clinically the patient's vision and macular appearance improved.



A

Fig. 21A. Macular oedema, due to leaking perimacular capillaries above the fovea. These dilated capillaries are in all probability the result of obstruction of a small venous branch from the superior temporal vein. There is leakage of fluid above the macula (Fig. 21B). Laser coagulation between the capillaries gave improvement and there was less fluid in the macula after treatment.

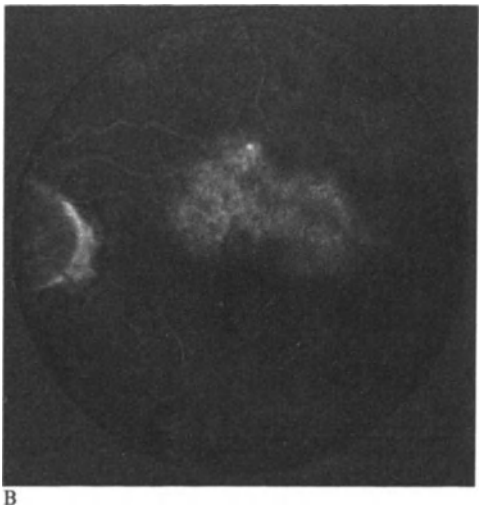


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Fig. 21B. Same case as discussed in Fig. 21A. Fluorescence angiogram; after-fluorescence.

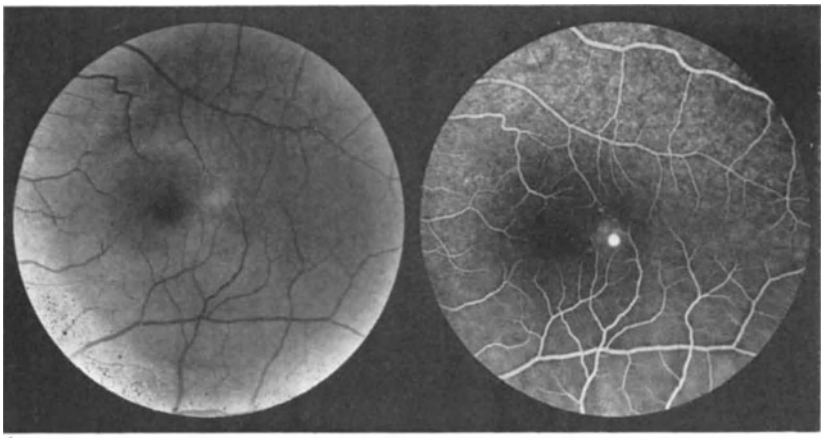
2. *Fluid originating from the choriocapillaris.*

a. Central serous choroidopathy is caused by breakdown of the Bruch membrane and retinal pigment epithelial diffusion barrier. Serous fluid from the choriocapillaris traverses Bruch's membrane and the pigment epithelial cells or the tight junctions between them and accumulates in the potential space between the pigment epithelium and the retinal receptors. Fluorescein angiography is indispensable in eliciting the site or sites of breakdown. One or more bright fluorescence spots become apparent during the arterial phase and they expand gradually and during angiography (Fig. 22). With the help of fluorescein angiography it is possible to decide upon the advisability of photocoagulation.

In my experience it is wise to apply a low energy argon laser treatment early in the disease process. The success rate is nearly 100 percent.

b. *Serous detachment of the pigment epithelium* occurs when the pigment epithelium becomes dislodged from Bruch's membrane by accumulation of serous fluid beneath the retinal pigment epithelium. This fluid originates from the choriocapillaris.

A uniform roundish area of hyperfluorescence develops in the arterial phase of angiography and this area shows no expansion during the phases of angiography (Fig. 23). This condition may occasionally be the forerunner of neovascularization from the choroid. Some cases though have a very favourable prognosis. The firm adherence of the basement membrane of the pigment epithelial cells to the inner portion of Bruch's membrane limits lateral diffusion while the junctional cells prevent the anterior movement of the serous fluid.



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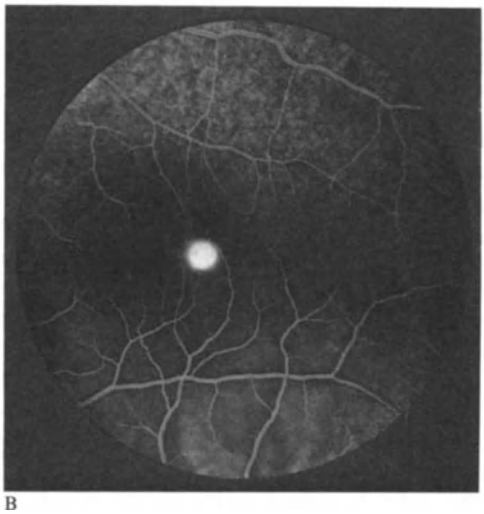


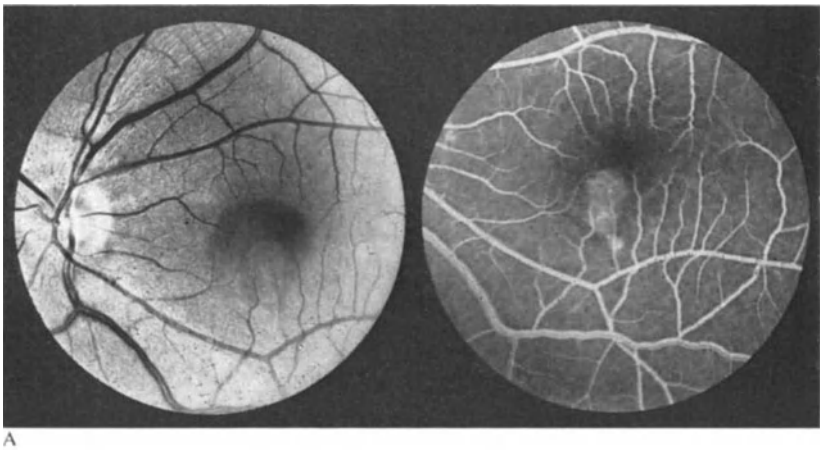
B

Fig. 22. Classic central serous choroidopathy with treatable leakage point temporal to the macula. Note the striking expansion of the dye through the stages of angiography. Favourable case for argon laser treatment.

Argon-laser treatment on the edge and on the surface of the area of serous detachment leads in many cases to disappearance of the localized detachment.

c. *Haemorrhagic detachment of the retinal pigment epithelium* is due to choroidal neovascularization and haemorrhage. The stimulus of this might be a hypoxia.

Defects in Bruch's membrane also appear to stimulate choroidal neovascularization (Fig. 16). We have seen these new vessels under the retinal pigment epithelium in high myopia, angioid streaks, presumed histoplasmin choroiditis and senile disciform macular degeneration (Kuhnt-Junius).



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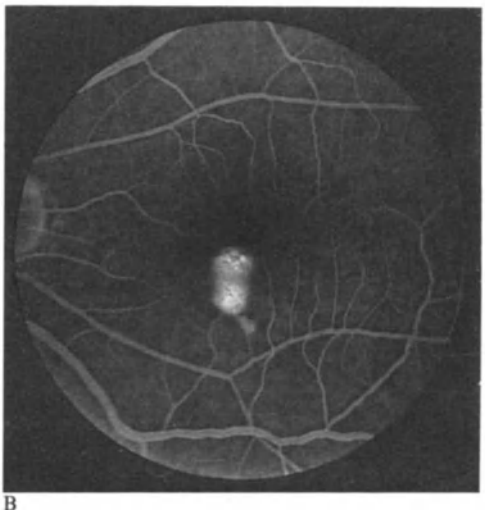

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Fig. 23. Serous detachment of the retinal pigment epithelium. There is no expansion of the dye in the hyperfluorescent area during angiography.

Photocoagulation may be beneficial if the new vessels are not closer than ¼ disc diameter to the macula and only if high energy levels are applied. In general, though, it is very dangerous to apply photocoagulation to these lesions because of the risk of bleeding and ensuing destruction of the macula.

E. OPHTHALMOSCOPIC CHANGES WITH NORMAL FLUORESCENCE ANGIOGRAMS

Certain macular diseases show *clearly changes at ophthalmoscopy* but have sometimes *normal fluorescein pictures*. These lesions are located in the more superficial retinal layers.

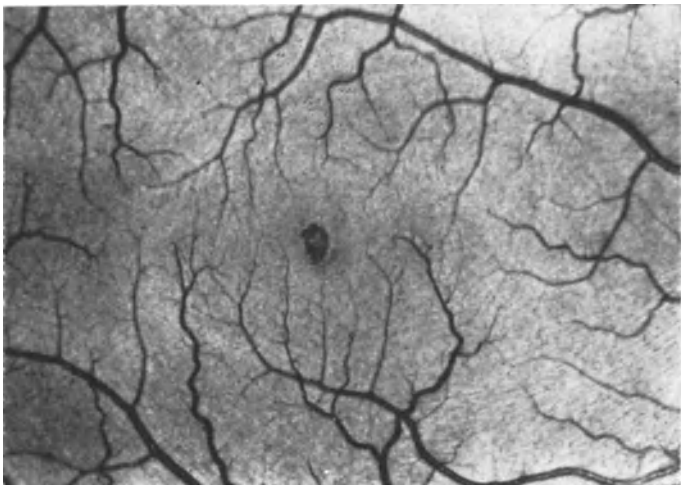


Fig. 24. Typical case of solar retinopathy with tiny lamellar 'hole' in the deeper retinal layers. The pigment epithelium is damaged only slightly or not at all. Fluorescein angiography gave a completely normal angiogram just like in almost all cases of solar retinopathy.

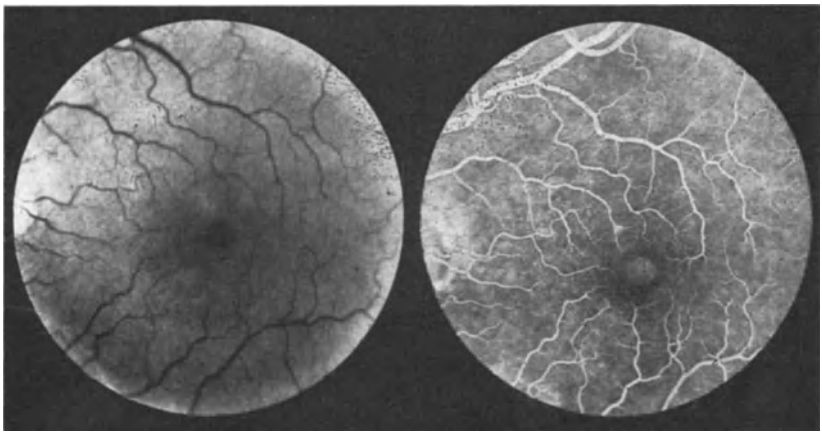


Fig. 25. Macular hole showing mild hyperfluorescence due to defective pigment epithelium at the site of the hole. There was indication of vitreo-macular pulling in this patient.

In *solar retinopathy* (Fig. 24) the fluorescein picture is nearly always normal.

In *X-linked juvenile retinoschisis* and in the multilocular cystic macular changes of *Goldmann-Favre disease* the macular fluorescein pictures is also frequently normal.

Pseudo-holes of the macula due to vitreoretinal traction are sometimes normal on fluorescein angiography, although there may be some hyperfluorescence.

Full-thickness macular holes show distinct hyperfluorescence due to defective pigment epithelium at the site of the hole (Fig. 25).

Macular puckering due to preretinal membrane formation ('fibrosis of the internal limiting membrane' according to some authors) has apart from tortuosity of the retinal vessels mostly a normal fluorescein angiography (Fig. 26). Sometimes there is some slight intraretinal pooling of fluorescein. It is probably caused by proliferation of fibrocytes in the vitreous body and no treatment is helpful.

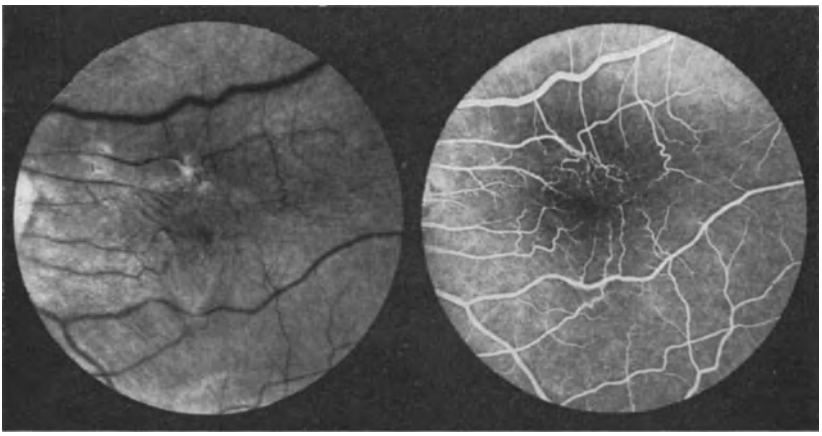


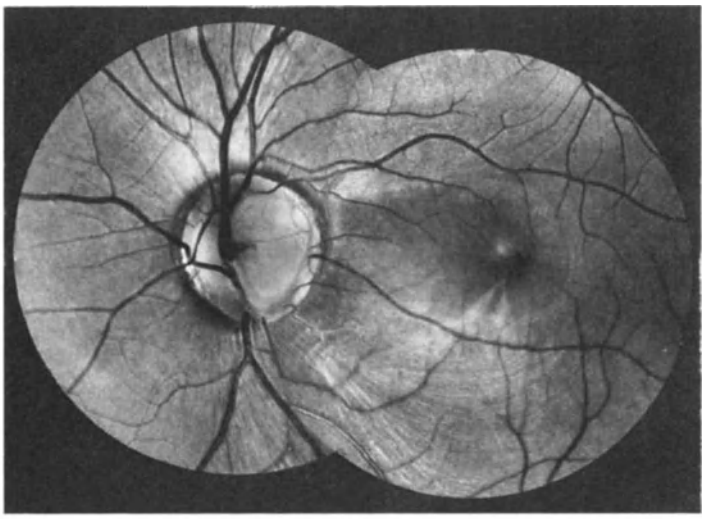
Fig. 26. Macular puckering due to pre-retinal membrane formation. Note the obvious wrinkling of the superficial retinal layers and the tortuosity of the perimacular vessels. There was no leakage or pooling of fluorescein in the late phases of angiography.

Central serous choroido-retinopathy in association with *optic pits* (Fig. 27) does not show treatable leakage points. It is probable, though, that serous fluid leaks from the optic pit in the subretinal space.

In *arterio-venous communications of the retina* (ARCHER et al, 1973) one has to use fluorescence angiography to elucidate the exact structural abnormalities. Particularly in these cases one needs rapid sequence angiography in order to distinguish the direct communication(s) between the arteries and veins (Fig. 28A) or between the arterioles or venules (Fig. 28B).

Finally in *choroidal folds* one may see on fluorescein angiography dark, hypofluorescent lines due to folding of the retinal pigment epithelium (Fig. 29).

In more superficially localized retinal folds there are no dark lines visible on fluorescein angiography.



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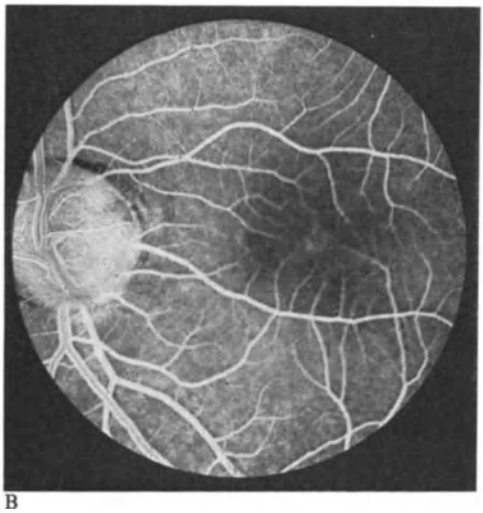
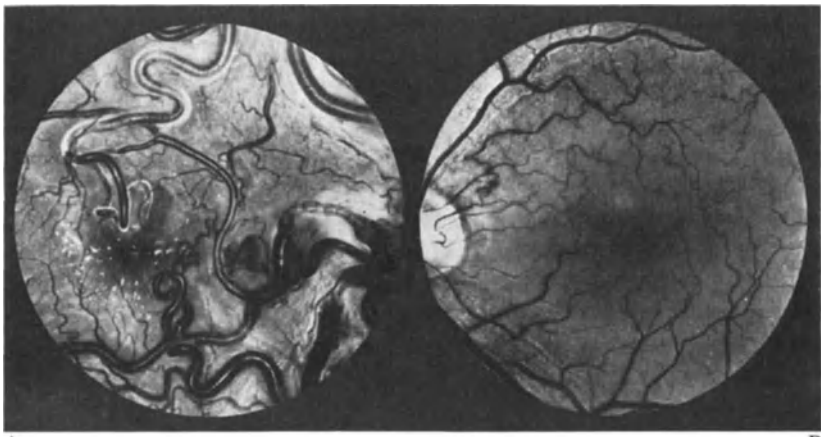


B

Fig. 27. Optic pit and central serous retinopathy. Fluorescein angiography reveals a dark, non-fluorescent pit and some hyperfluorescence due to defective pigment epithelium centrally. No leakage of fluorescein was detectable.

It will be clear from this paper, that fluorescein angiography cannot be missed anymore in diagnosis and particularly in treatment of macular diseases. Dye leakage from impaired vessels or breakdown of the choroido-retinal diffusion barrier is easily detected by this method and this opens the way to treatment with laser photocoagulation.



A B

Fig. 28. Arteriovenous communications of the retina with large anastomosing channels (Fig. 28A) and with interposition of an abnormally dilated capillary plexus between the major communicating vessels (Fig. 28B). The latter case could be a sequel of venous obstruction. The former case is surely congenital and is the ocular manifestation of the Wyburn-Mason syndrome.

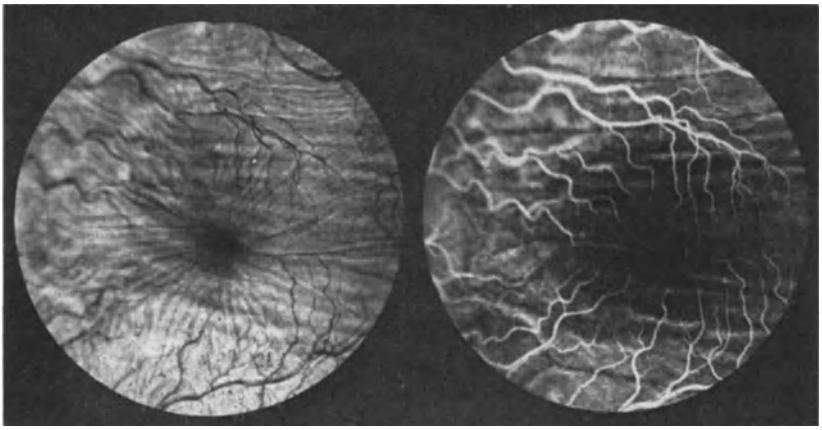


Fig. 29. Choroido-retinal folds showing characteristic horizontal dark lines on fluorescein angiography.

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TECHNICAL ASPECTS OF FLUORESCENCE ANGIOGRAPHY

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ABSTRACT

To scrutinize all technical aspects one may encounter during fluorescence angiography goes beyond the scope of this article. Fluorescence angiography is essentially a photographic technique and it are the photographic aspects which will be reviewed highlighting some of the pitfalls which may occur. In some detail will be discussed the apparatus available for this type of work, the fluorescence techniques, the accessories available for data-recording and time printing, advice regarding the films to be selected, what to do with the exposed films and lastly how to file the results.

The advices given will certainly not fit every situation. In a centre, e.g., in which many fluorescence angiograms are made, the main problem is how to gain time even at the risk of loosing quality. In centres in which only a limited number of angiograms are made, time is less important, and quality plays the prime role.

Before starting fluorescence angiography, one must know how one is going to make fluorescence-angiograms. There are several possibilities: on negative or positive black-and-white film, on colour slide film, or even on 8 mm miniature film or video-tape.

Apart from these possibilities, a visual approach, viz. fluorescence-ophthalmoscopy may be considered. For instance, in central serous retinopathy, in which we are interested only in the localisation of the leakage, one may fluorize visually. After injecting the fluorescein, one looks at the fundus with an ophthalmoscope mounted with a blue filter. A better alternative is a fluoroscope. Two fluoroscopes are on the market, one designed by Almaric with which one can view the fundus at different light intensities and through one of four different filters.

The second possibility is the fluoroscope made by the Medical Workshop (Fig. 1). Here the fundus is viewed through a Heine ophthalmoscope via a light guide attached to a projector.

Both fluoroscopes are easily used. The big disadvantage is that after the fluorescence there are no records left.

1. THE PHOTOGRAPHIC APPROACH

This is the commonly used method. Very good results are obtained using

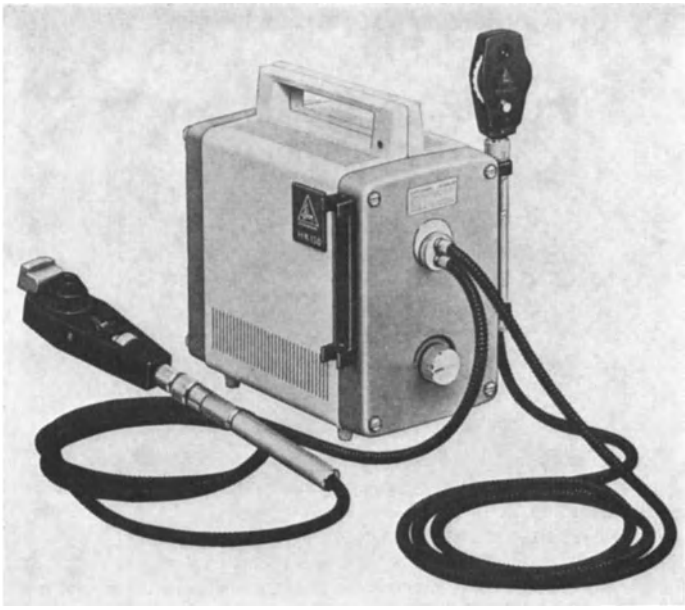

Fig. 1. Heine bifocal ophthalmoscope with fiber optics illumination modified for fluoroscopy.

black-and-white negative film, e.g. Kodak Tri-X 27 din. This is a film with a high resolving power. When developed in Microdol developer dilution 1:1 during 15 minutes, one gets excellent negatives. The high speed of the emulsion of Tri-X film is advantageous since this allows us to use a lower flash intensity, which implies a shorter flash interval. But one may also use slower films, e.g. Kodak plus X 22 din which film has a finer grain than Tri-X.

We can also use a *direct black-and-white positive material*. This material gives after one treatment not a negative, but a positive image as transparancies. This film is supplied by Kodak with a developing set. One can develop the film in one's own dark room.

The third method is to make fluorescence angiograms directly on *Polaroid black-and-white material*. In Holland this technique is not very popular, but in America LEE ALLEN (1966) has used it a great deal. The great advantage is that one gets immediate results; the disadvantages however are three-fold. Firstly, relative poor quality of the photographs, secondly the time taken between two exposures is quite long, and thirdly one cannot duplicate Polaroid photographs.

The fourth method is to use colour fluorescence. A high speed *colour positive material* is used. Again there are several possibilities: Firstly we can do our colour fluorescence without using any special filters. This method is not very practical as the resolving power and the contrast are very poor.

The second colour fluorescence method uses a blue filter in front of the

light source. The fluorescence is seen as a bright yellow-green against a non-fluorescing blue background. This is far from ideal, since many details are lost within the blue background.

A better method seems to be the use of a blue filter in front of the light source, and a yellow filter in front of the film. The quality of the photographs is much better. We see more detail and one can detect the difference between real and pseudo-fluorescence. However, this colour fluorescence method has little advantage over the normal monochrome fluorescence.

SHIKANO & SHIMIZU (1968) using this method, place a Fuji-gelatine filter type TV-B in front of the light source. This filter transmits blue light of less than 500 nm and red light of more than 600 nm. In front of the film they use the Fuji yellow filter type number 12. With this filter combination we get a normal reddish fundus with yellow-green fluorescence. These authors use the Fuji colour positive (slide) film of a speed of 100 ASA.

HENDRICKSON, SHINOBU & ELLIOT (1970) replaced the Fiju TV-B with a Kodak wratten 32. Instead of the Fuji 12 they used a Kodak wratten 36. These authors filmed on Kodak Ektachrome high speed of 160 ASA. Transmission and absorption of these filters is such that we are in between the region of pseudo-, and real fluorescence.

2. FUNDUS CAMERA

A normal fundus camera can be used for fluorescence angiography provided that the flash intensity is high enough. Without special provisions it is impossible to photograph faster than 1 frame per 3 seconds, since the recharging time of the usual powerunit is quite long. As the retinal circulation time is approx. 40 seconds, one can make only 8 or 9 photographs, which is about half the amount one really needs during this periode. This means that certain modifications have to be carried out. These comprises the

filters,
a motor drive camera and
an extra fast working power supply.

FILTERS

In fluorescence angiography we need a blue filter in front of the light source and a yellow filter in front of the film (Fig. 2). When buying a fundus camera it is essential to know what filters come with it. Usually, the camera is fitted with Kodak wratten filters. These, however, do not achieve real fluorescence. They should be changed for Baird Atomic filters B4 and B5 (Fig. 3), which cut out all pseudo-fluorescence. The more expensive fundus cameras are already fitted with this Baird Atomic filter combination.

Motor drive camera

Since we have to take photographs at a frequency of 1, or even more than

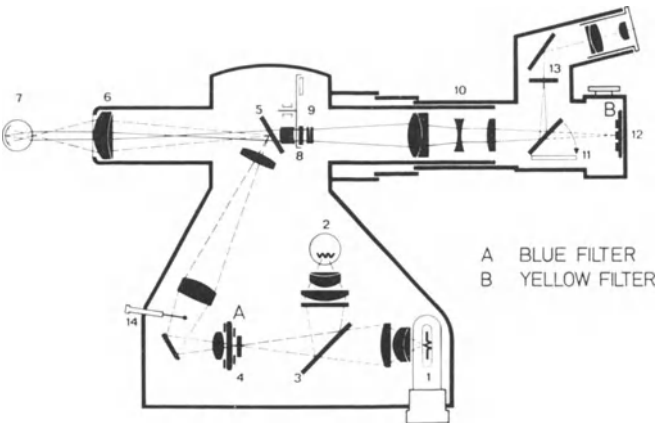

Fig. 2. Diagrammatic drawing of the optical system of the Zeiss fundus camera with filters for fluorescence photography.

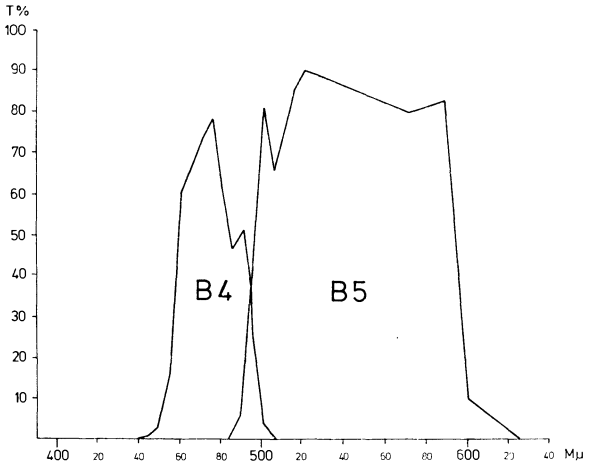

Fig. 3. Transmission curve of the Baird Atomic B4 and B5 filters.

1 per second, a motor drive camera is essential. This camera makes not only the exposure, but also transports the film and resets the shutter.

The Nikon motor drive camera (Fig. 4) can be fitted to most fundus cameras by an adapter. Nikon supplies a battery-powered unit for the motor drive camera but it is possible to modify the flash-unit to power the motor drive camera as wel.

Power supply

It is essential to have an extra fast working power supply that recharges in less than half a second, in order to be able to make exposures at least one

Fig. 4. Nikon motor drive camera.

per second, at a constant flash intensity. Such flash units go at no extra cost with the more expensive fundus cameras.

3. ACCESSORIES

Accessories are needed for handling the camera, for time-recording and data-recording. Furthermore, special accessories for stereo-fluorescence, for bilateral fluorescence and for fluorescence of the anterior segment of the eye are available.

Handling of the camera and time-recording

It is of great importance to make exposures at a fixed frequency. Although this seems a rather simple problem, it is not that simple as the photographer has to align the camera, focus on the fundus continuously and attract at the same time the patient's attention. ALMARIC uses a metronome set at a frequency of one per second to remind the photographer when to expose. Others have used a tape recorder with an acoustic signal at the same frequency.

The Topcon TRC-F2 has a selector button for the rate of firing and a switch for manual or continuous firing (Fig. 5). If the selector button is set on one frame per second, and the switch is set on continuous firing, automatically every second an exposure is made. The expensive Topcon (type TRC-F3) has in addition a foot-switch, attached to the motor drive. The maximum frequency of firing is three frames per second. The obvious advantage of the footswitch is that both hands are free to correct the focussing.

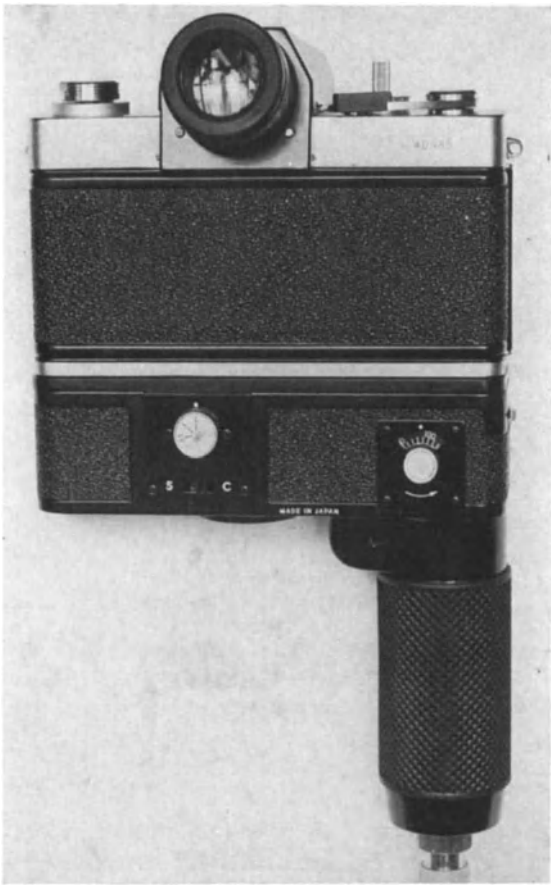

Fig. 5. Topcon motor drive camera.

The Zeiss system is different. A pulse generator is used which can be set at .6, .8, 1, 1.2, 1.5, and 2 seconds (Fig. 6). The Zeiss camera too, uses a foot-switch connected to the camera. A more expensive solution was developed by Zeiss Jena, for the Retinophot camera (Fig. 7). The Retinophot programme unit can be used for single shots black-and-white or colour, as well as for serial photography if the automatic programme position is selected. The programme comprises three stages: initial delay, rapid series and final series.

The initial delay is the time between the start of the programme and the first exposure of the rapid series. This time corresponds with the arm-retina time. The rapid series is controlled by two knobs: one selects the time interval between the flashes, the other determines the number of flashes required within the selected time. The control knob for the final series selects the time interval between flashes for the remaining exposures on the film. It can be set at four seconds or at two seconds. The Retinophot unit offers several programmes: if one is interested in the initial phase of the fluorescence one

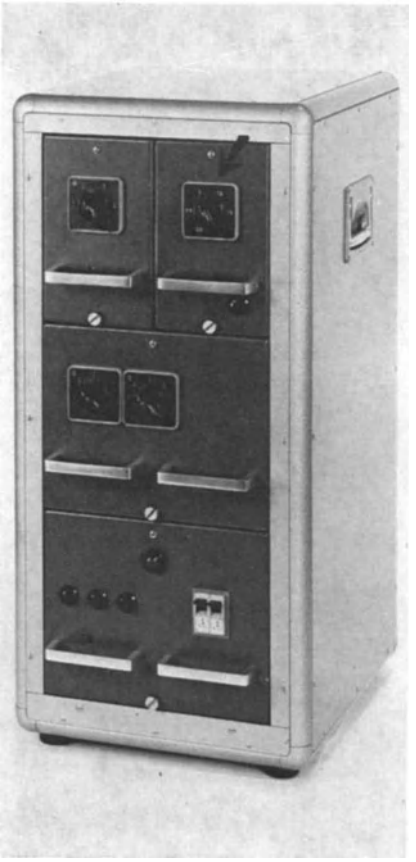

Fig. 6. Power unit of the Zeiss Fundus camera. Arrow: pulse generator.

selects the initial programme; if one wants a later phase, a later programme is selected.

In the Eye Hospital in Rotterdam a sophisticated electronic system is in use, adjustable to whatever programme one selects (Fig. 8). The Eye Hospital in The Hague uses a simple system. A button on the joy-stick of the Zeiss fundus camera controls a relay which depresses the mirror: At the same time a micro-switch operates the transport of the film, as well as the resetting of the shutter. The time is recorded on a digital timer.

Data recording

There are several possibilities for time registration, for instance a digital timer, which prints the time on paper (Fig. 9). The timer can be started with a foot-switch at the moment the fluorescein has been injected. The timer runs continuously. Whenever an exposure is made, the time is printed on paper.

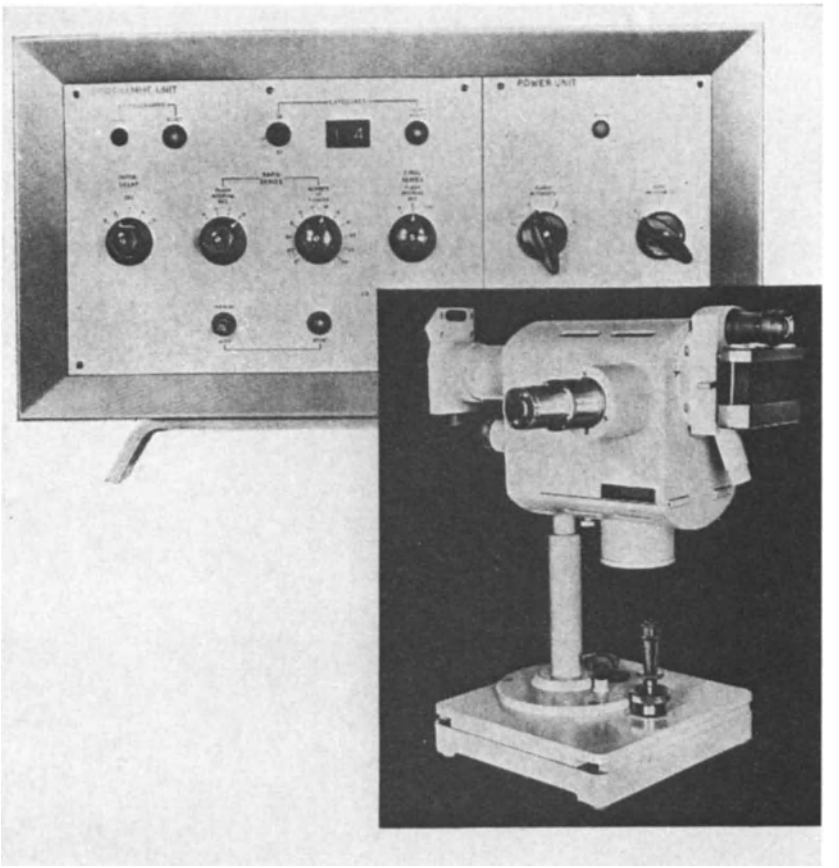

Fig. 7. Zeiss Jena Retinophot, with programme unit.

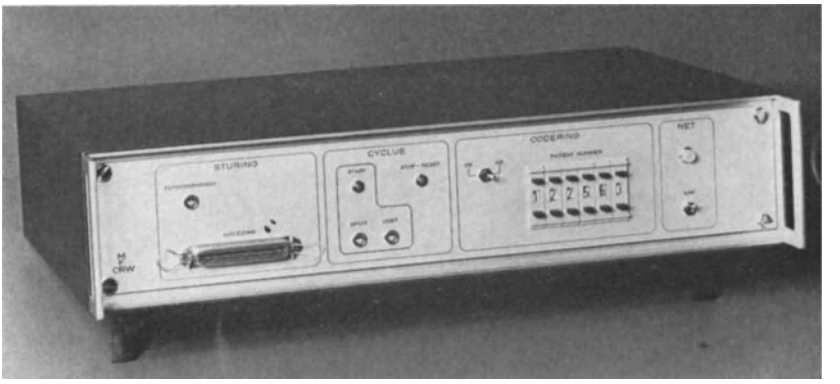

Fig. 8. Data recording unit as developed in the Rotterdam Eye Hospital.

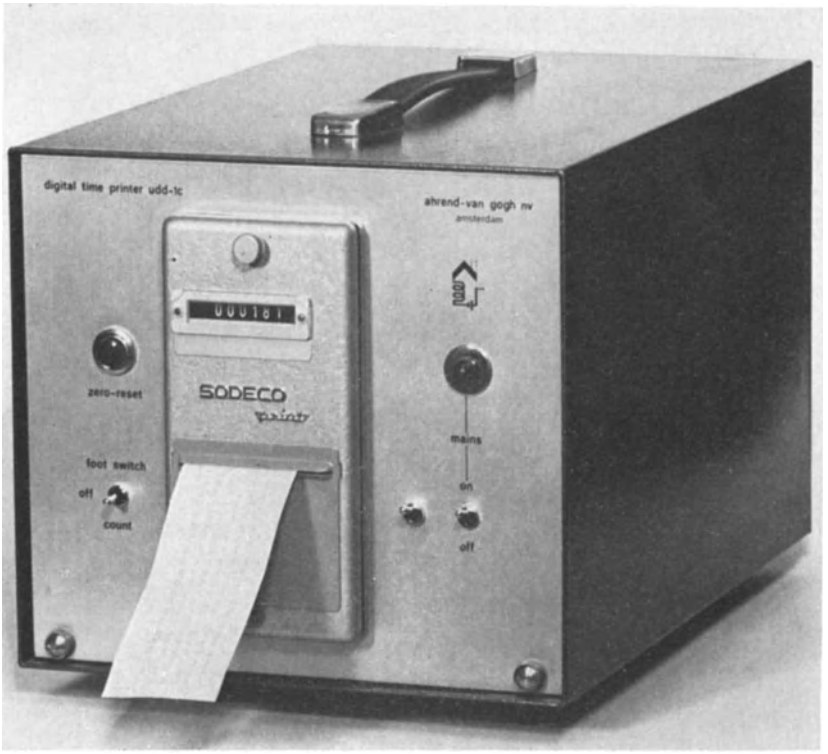

Fig. 9. Digital time printer.

A more satisfying system is to photograph the time of the exposure on the relevant negative. Zeiss achieves this by photographing a stopwatch fixed under the camera (Fig. 10 A + B). The disadvantage is that the photographed stopwatch takes up a lot of space in the fluorescence negative.

An elegant system is utilized by Topcon. With this system it is possible to photograph the frame number and the time in seconds, and various data concerning the patient next to the negative (Fig. 11). The data concerning the patient are photographed after being written on a plastic plate, which must be inserted into a slot.

The Eye Hospital in Rotterdam uses a somewhat similar system. A digital clock is photographed via a mirror system on the film next to the negative (Fig. 12 A + B). To start this timing mechanism, one can use one of three systems: manually, by foot, or through a micro-switch fixed to the syringe.

GASS et al. (1967) photograph a digital timer attached to the Zeiss fundus camera through a small mirror via the aspheric objective. The time is recorded on the negative in a far less disturbing way than in the Zeiss robot system.

The most sophisticated system, which we may call 'fluorescence by automatic pilot', has been designed by KLEINE & VAN RHIJN (1970). The injection

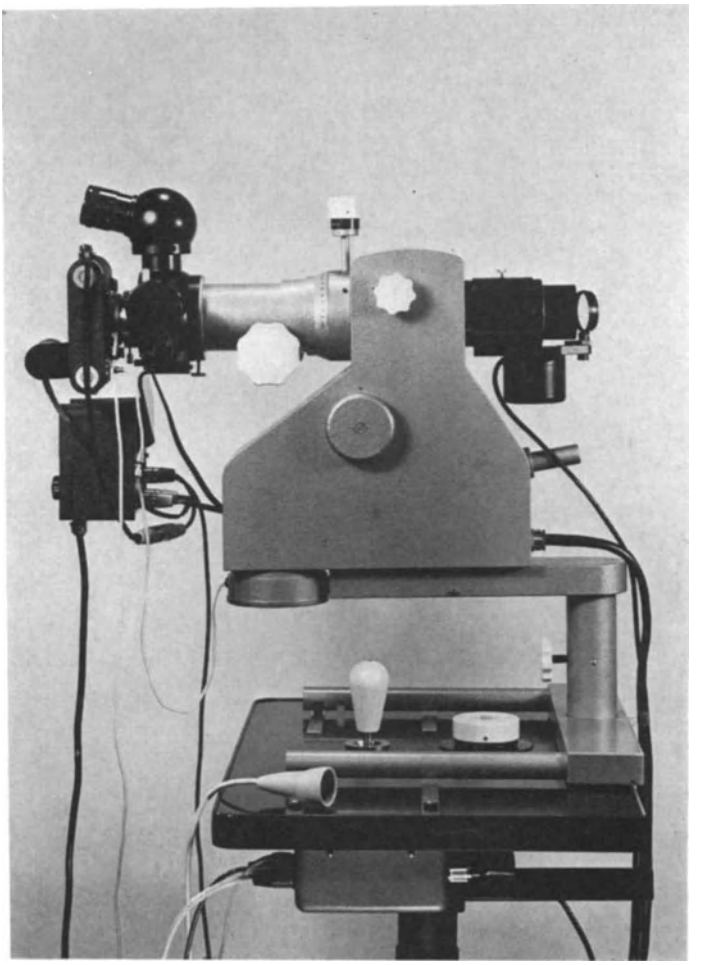

Fig. 10. A. Zeiss fundus camera with Allen stereo-separator in front of the aspheric objective, and timing device fixed under the robot camera.

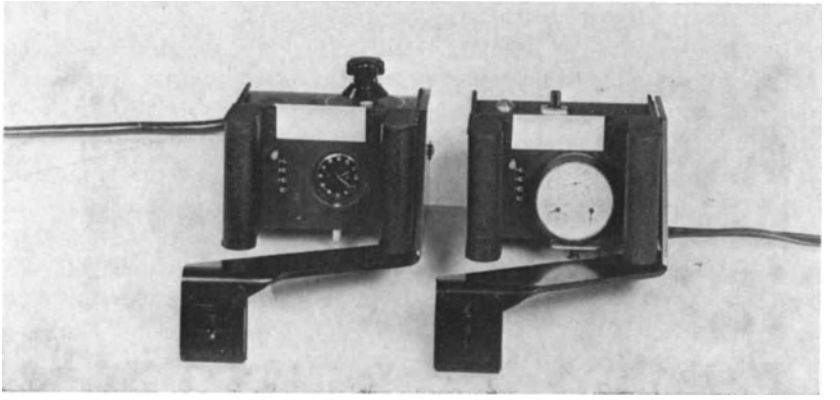

Fig. 10. B. Stopwatches photographed for timing.

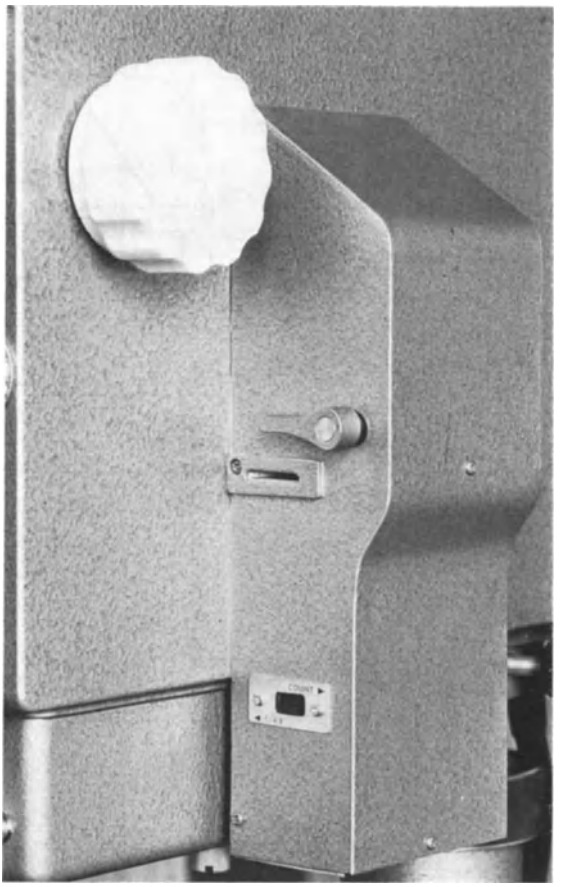

Fig. 11. Digital timer, counter and slot for data plate as used by Topcon.

of fluorescein, the timing and the photography is done more or less automatically. In this setup (Fig. 13) a cylinder of carbondioxide gas is attached to an empty syringe, which is connected to a sterile syringe filled with fluorescein. Between the flow meter and the empty syringe a T-joint is attached to a foot-switch. When the foot-switch is operated, the T-joint opens and the gas enters the empty syringe. One can dose the amount of fluorescein injected by way of the flow meter. Usually 3 cc of a 20% solution of fluorescein are injected in $1\frac{1}{2}$ seconds. A microswitch placed between the two syringes starts a tape recorder, which controls the camera throughout the photographic procedure.

Stereoscopic fluorescence angiography

If we use the ALLEN (1966) stereo-separator (Fig. 10A), it will be possible to

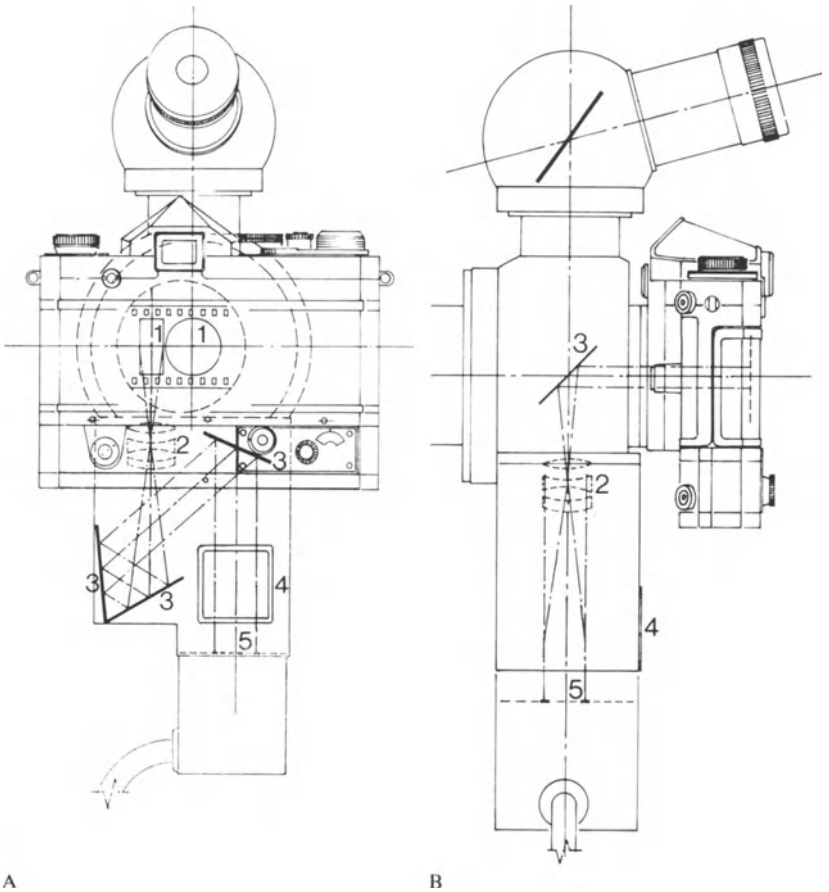

Fig. 12. Datarecording system as used in the Rotterdam Eye Hospital.
1. Image size and data recording. 2. Soligor lens 75 mm, 1: 3,5. 3. Surface mirrors. 4. Viewing window. 5. Digital data recording.

photograph stereoscopically the later phases of the procedure. The Allen stereo-separator is an accessory placed in front of the aspheric objective, which after an exposure changes its position automatically within one second, so that the second exposure is made from a slightly different angle. The time parallax is not an important factor.

In the early phases of fluorescence angiography it is essential to take the stereoscopic exposures simultaneously, otherwise one gets difference in retinal filling.

The best system is incorporated in the DONALDSON (1965) stereo-fundus camera, in which simultaneously two fluorescence exposures are taken. It is regrettable, however, that there is only one such camera in the world: the one DONALDSON uses himself!

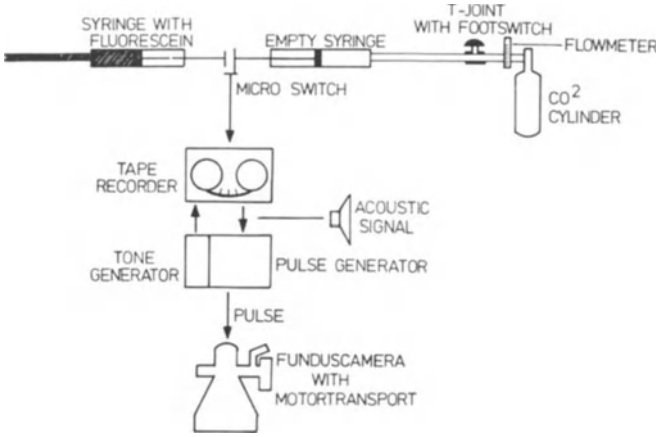

Fig. 13. Standardized fluorescence system as used by KLEINE and VAN RHIJN

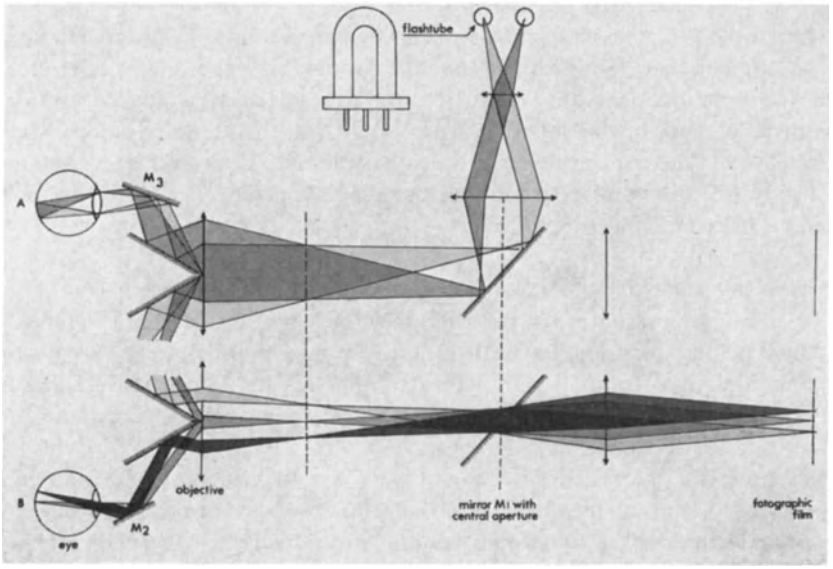

Fig. 14A. Diagrammatic drawing of the optical system as used for binocular fundus fluorescence angiography by KOOYMAN

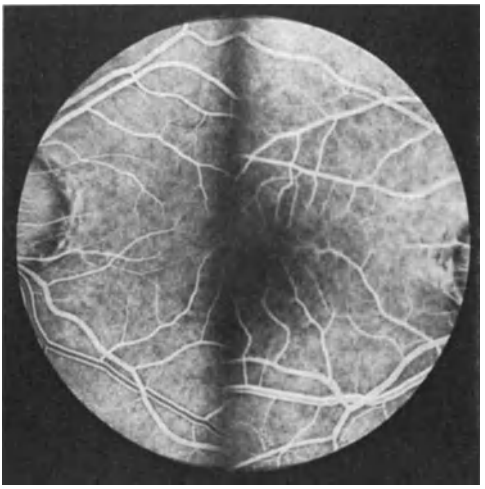

Fig. 14B. Fluorescence-angiograms of right and left eye taken simultaneously.

Bilateral fluorescence

KOOYMAN (1972) has developed a mirror system placed in front of the Zeiss aspheric objective, by which one can take fluorescence exposures of both eyes at the same time (Fig. 14). Light from the fundus camera is divided by two mirrors in front of the objective and is returned to both eyes by another set of mirrors. The pupillary distance must be adjusted. The two images overlap slightly, but this overlap is not disturbing. The apparatus is not easy to use, and is regrettably rather expensive.

The last camera I wish to discus is the Nikon fundus camera (Fig. 15). To all intents and purposes this camera will be very expensive, but the main advantage (or attraction) lies in the field of coverage of 45 degrees. This might be useful in cases of diabetic retinopathy, although the 15 degrees of field of coverage, which is gained, will in all probability result in loss of detail.

Starting the fluorescence procedure we use a frequency of one exposure per second, during the first 20 seconds, followed by one exposure every 3 seconds up to 30 or 35 seconds and one exposure every 10 seconds for the rest of the first minute. Normally we take the next photographs at 90, 160, 300 and 600 seconds. In patients suffering from vascular occlusions usually we don't go much further than about 5 minutes. In diabetic retinopathy, however, we extend that period up to 10 minutes. In cases of papilloedema the last photograph will be taken generally 15 minutes after the start of the angiogram. In cases of central serous retinopathy and juvenile disciform macular degenerations we may even go on up to 1 hour after injection of fluorescein.

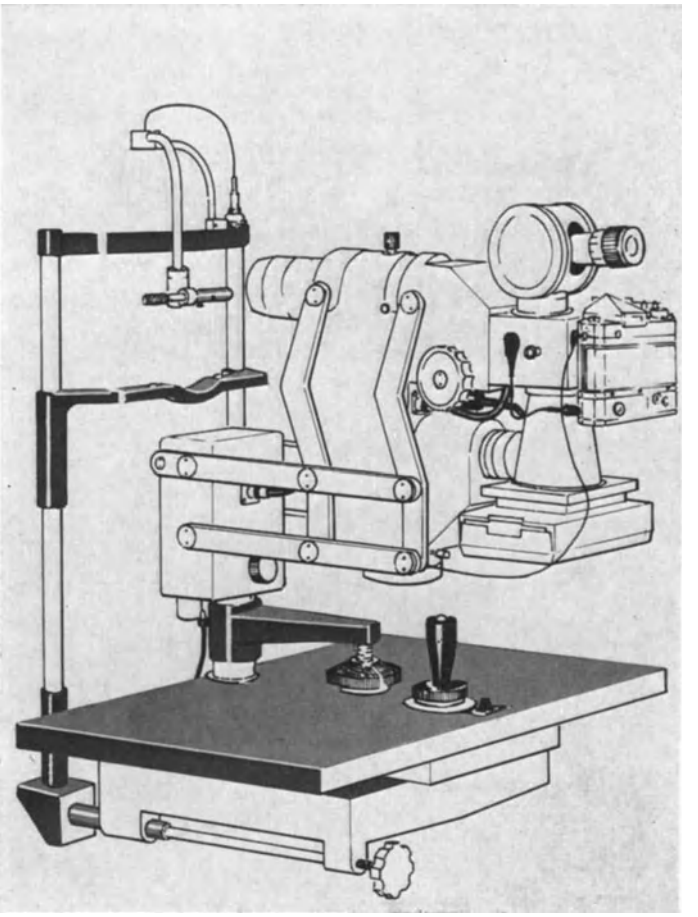

Fig. 15. Nikon Retinapan-45 wide angle fundus camera.

Fluorescence of the anterior segment of the eye

Several systems are available. The Zeiss photoslit lamp can be provided with a motor transport camera, a high intensity flash-unit and the necessary filters. A cheaper solution however is to modify the flash-units used in fundus fluorescence angiography and to install these on the photo-slit lamp. An even cheaper solution is the one proposed by CRAANDIJK & AAN DE KERK (1970), in which the blue exciting light from the fundus camera is used. (Fig. 16). Attached to the fundus camera is an external motor drive camera with a built-in yellow filter. The iris is photographed through an extension-ring of about 11 cm and an objective Luminar 63 cm, 1:4.5. Focussing is achieved by

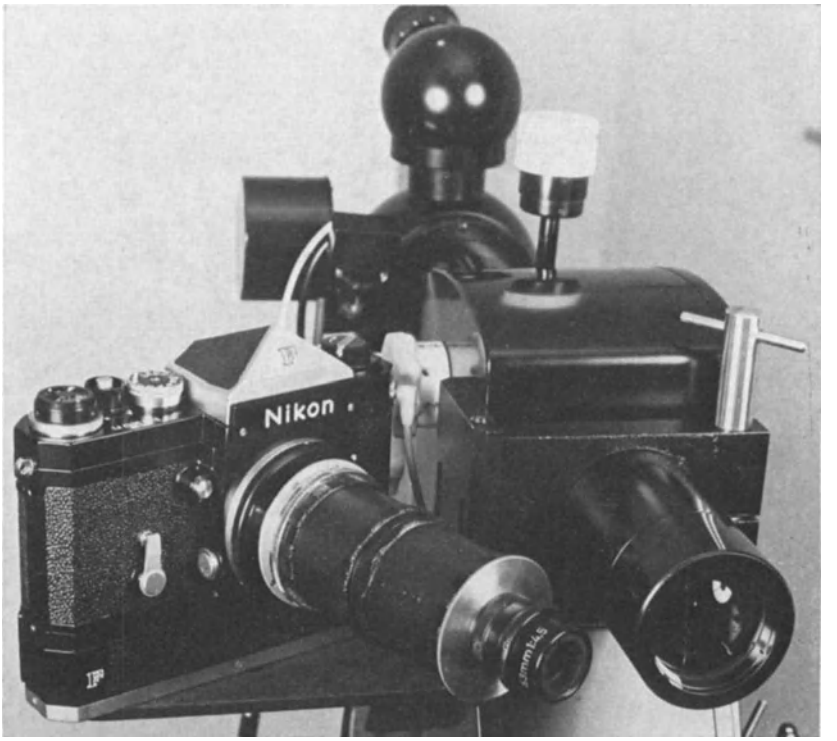

Fig. 16. Nikon motor drive camera, modified for fluorescence of the anterior segment of the eye, attached to the Zeiss fundus camera.

moving the fundus camera forward or backward while looking at the corneal reflexes. The costs for such a modification amount to an extension tube, the macro-objective, and an attachment which has to be made in a workshop.

4. FILMPROCESSING

Having removed the exposed film from the camera, the first question arising is, what do we want: almost instant results, but with a loss of quality, or a series of high quality photographs, but produced with a loss of time.

If we want quick results, we have to develop the film rapidly. This is the principle of ROSEN (1969) who develops his film in a Phentrace developer by Ilford in a dilution of 1: 5 at a temperature of 35 degrees (normal 18° to 20°). Developing takes 45 seconds. The development is arrested by an acetic acid stop-bath, after which the film is fixed for 40 seconds in an ammonium-thiosulphate rapid fixer. The film is then washed in a forced film washer at a temperature of 18 degrees. The fixer is eliminated in about 10 minutes. The film is then treated to a wetting-agent, washed and dryed in a heated drying cabinet in about three minutes. This implies that after about 15 minutes

one has dry negatives. However, if quality is important, the film has to be processed in a more normal way. Kodak Tri-X film will be developed in e.g., Microdol developer, diluted 1:1 during 15 minutes. The plus X film can be developed e.g., in Promicol diluted 1:2 during 15 minutes, both at a temperature of 20 degrees centigrade under constant movement. The fixing of the film takes in a normal fixing agent 10 minutes, in a rapid fixing-agent 2 to 3 minutes. The film has to be washed during half an hour. The drying can be done in a special drying cabinet, but one can also dry in the air. Before drying, the films must be treated with a wetting-agent in order to get rid of chalk marks.

5. INTERPRETATION OF THE FLUORESCENCE ANGIOGRAMS

One has a choice out of three possibilities: to interpret the negatives; to interpret the positives, either printed on paper or printed on flat-film; or to copy the negatives.

Interpretation of the negatives directly can be achieved with a magnifying glass on a film viewer, or can be done while projecting the negatives using a normal projector, or a daylight projector, or an overhead-projector. The latter has the advantage that one can interpret the whole series at the same time. With X-rays it is standard practice to interpret the negatives but with fluorescence angiograms it appears to be a trouble-some practice.

This implies that we have to make positive prints, either on paper or on flat film. If we print on paper, we can use the contact printing frame, in such a manner that one gets all 30 negatives with one exposure on the paper. The contact print must be developed, fixed, washed and dried. This procedure takes a lot of time, so it may be preferable to look for an apparatus that uses the activation-stabilization technique. Both the Agfa-print (Fig. 17) and the Ilfo-print serve our purpose. These processing machines develop and stabilize the photographs within seconds. It is, however, advisable to fix the photographs in a normal fixing-agent during several minutes, and wash and dry them afterwards. This ensures the durability of the photographs. The disadvantage of the contact prints on paper is the limited tone reproduction and the small size image. An advantage is the positive image. If we print on flat-film, the processing is similar to that of contact prints. The advantage over the contact prints are twofold, a much better tone reproduction and we can interpret the film on a viewer using a magnifying glass, or we can project the flat-film and combine it with the projection of colour slides.

Enlarging on paper

Our first advice is to use paper of standard size so that there is no need cutting the paper. Always use glossy paper. For enlarging one needs a special frame with a round mask cut into it. Again there is a choice of normal paper, Rapido-print or Ilfo-print paper. If you have development and printing done elsewhere, there is a chance that you do get back beautiful photographs, doctored and retouched, but useless for fluorescence interpretation!

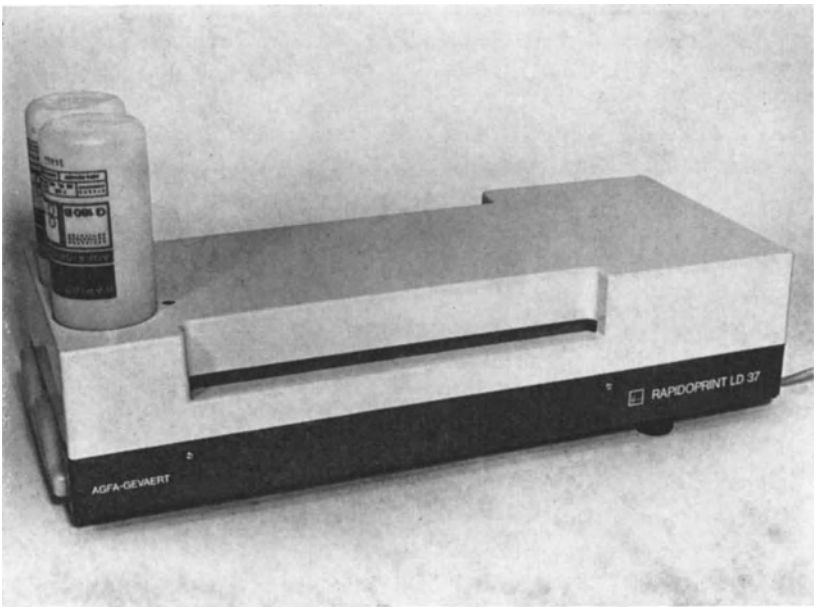

Fig. 17. Agfa Rapidoprint processing machine.

Copying of negatives

This system is used in the Rotterdam Eye Hospital.

The negatives are copied on black-and-white-film of high contrast. After processing they can be interpreted in the way already mentioned. The advantage of this system is that you can copy your films in daylight.

Still the best method seems to be enlarging on paper, since it offers an easy way of interpretation of fluorescence angiograms. Unfortunately enlarging and processing cost a lot of time and money. The enlargements are mounted on paper which gives us a complete series of fluorescence angiograms that can be filed as such. A disadvantage, at least for the large photographic departments, is the space consumption of this system. For people, who do not wish to do a lot of dark room work themselves, a further possibility is the use of direct black-and-white positive material, giving slides after processing. Kodak has developed a direct positive panchromatic film, type 5246, of a speed of 21 din. It can be obtained in tins of 30 metres. One has to wind these films on the spool of the casettes in a dark room. Kodak supplies a special developing set for use with this type of film.

6. APPARATUS NECESSARY FOR FILM PROCESSING

For developing one needs a multiple-spiral developing tank, such as made by

PATTERSON or KINDERMANN. The latter is more expensive, but more durable. The film must be wound on the spool in the dark room. The spool is placed in the tank, the lid is fixed and the tank is filled with developer, or any other bath one needs. The filling can be done in the light. After developing, fixing and washing, the film must be dried preferably in a drying cabinet. Thre are fairly cheap plastic drying cabinets on the market. For enlarging one needs an enlarger suited for miniature film. In order to develop the prints of the enlargements, one needs a few dishes and pinchers. Far quicker works a processing machine, such as the ones mentioned above: the Rapido-print or the Iifo-print.

7. NECESSARY HARDWARE FOR INTERPRETING FLUORESCENCE ANGIOGRAMS

The interpretation can be done with a normal, a daylight, or an overhead projector. There is a great choice of projectors on the market. There is one daylight projector worth mentioning, viz: the small portable model by KINDERMANN . Projection on a ground glass-screen can be done in daylight. In the dark an external screen can be used. The projector is fairly cheap.

Fig. 18. Philips overhead projector.

There are a number of fine overhead projectors made on the market by Philips (Fig. 18), Leitz and others. One has to be careful to project on an obliquely placed screen, otherwise one gets too much distortion.

8. FILING AND CODING OF FLUORESCENCE ANGIOGRAMS

Angiograms can be filed with the patient's record, but mostly separate filing in a special cabinet is preferred. Apart from filing angiograms on the patient's name, one can also file on diagnosis. A useful coding system has been developed by OOSTERHUIS. This system is in use in the eye clinics of Amsterdam, Rotterdam, Leyden and The Hague.

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ELECTRO-OPHTHALMOLOGY

ELECTRO-OPHTHALMOLOGY
I. EXAMINATION METHODS AND RECORDING PROCEDURES

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(*Rotterdam*)

ABSTRACT

A survey is given concerning the possibilities of examination methods for the registration of the electric responses of the visual system. Especially those methods are discussed, which can easily be applied with rather simple apparatus, or with the help of an EEG department, outside the great eye centres. The technical qualities of stimulator, amplifier and registration apparatus will not be mentioned in detail.

In electro-ophthalmology three phenomena can be measured rather easily, viz. the electro-oculogram (EOG), the electro-retinogram (ERG) and the visually evoked cortical responses (VECPs). The simplest to register is the electro-oculogram. It is the indirect registration of the standing potential of the eye. The electro-retinogram reflects the reaction of the retina, provoked through light flashes. The measurement demands more sensitive equipment. Finally, the visually evoked cortical potentials are the potentials which can be led off from the skull above the occipital lobes after light stimulation. These potentials are too small to be detected amidst the potentials of the electro-encephalogram (EEG). Special apparatus, the so-called averagers, are required to make the VECPs visible.

ELECTRO-OCULOGRAPHY (EOG)

Electro-oculography is the indirect measurement of the standing potential of the eye. The cornea is positive as compared to the posterior pole of the eye. This potential difference is almost entirely brought about by the deep retinal layers, viz. the photoreceptor layer and the pigment epithelium. In humans the standing potential cannot be directly recorded. This can only be done in an indirect way.

Electrodes are applied to both sides of the eye (Fig. 1). When the eye turns left, then the positive cornea approaches the left electrode, while the negative posterior pole of the eye comes closer to the right electrode (position B, Fig. 1). Between the electrodes a potential difference can be recorded. When the eyes turn the other way, the opposite occurs (position C, Fig. 1). The potential difference measured between the electrodes is not only dependent on

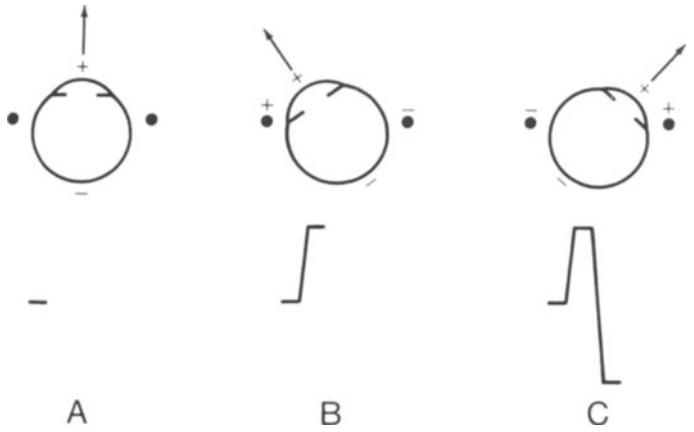

Fig. 1 Potential difference between two electrodes, placed at both sides of the eye (black dots), if the eye is turned to the left (B) and to the right (C). Actual registration against time is given in a schematic way.

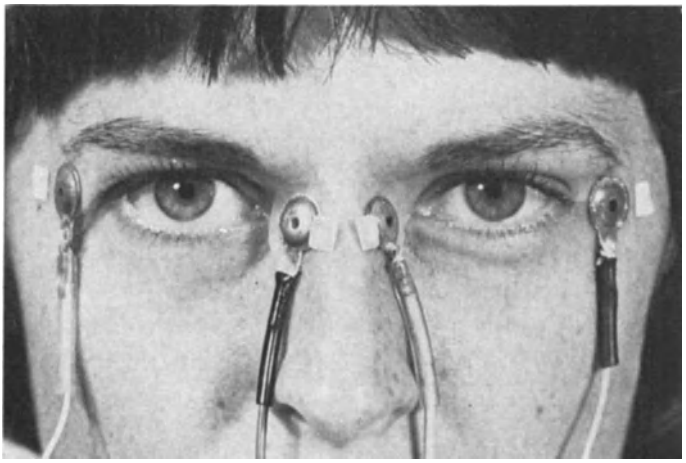

Fig. 2 Position of the electrodes for electro-oculography.

the standing potential itself, but also on the angle over which the eyes move, the resistance between electrodes and the skin and the position of the electrodes in relation to the eye. Even when the electrodes are always placed at the orbital rim (Fig. 2), differences will occur through the position of the eye in the orbita. In enophthalmus the distance between the electrodes and the potential generator is greater than that in exophthalmus.

Even when the measurement of the standing potential is standardized as much as possible, the variability is so great that a direct measurement has small value. Measurement of the increase of the standing potential, however, appears to be more valuable. It appears that the standing potential acquires a transient

increase when the eye, after a period in darkness, is suddenly exposed to a bright adaptation light. This is called the light rise in the EOG. The degree of this light rise appears to be a sensitive test for the function of the deep retinal layers (ARDEN & BARRADA, 1962 a; ARDEN, BARRADA & KELSEY, 1962 b).

The registration of the EOG is done as follows. The test is usually carried out in a sitting position. After the electrodes have been fixed, the patient has to look regularly and alternately at two fixation lights, placed in front of a large adaptive field at the right and left side. The actual registration is performed during approximately 15 seconds every minute. The light adaptation period, during which the standing potential increases, is preceded by a dark period, during which a steady state of the potential has to be achieved. The dark period has to be at least 12 minutes, the light period at least so long that the maximum light rise is passed.

Figure 3 shows part of an EOG registration in a normal subject and one in a patient with a pigment dystrophy. In this figure the last four minutes of the dark period and the first nine minutes of the light period are reproduced. The maximum value of the standing potential in the light period has to be divided by the steady state value in the dark. This is the light peak/dark trough ratio (LP/DT-ratio) of the EOG (ARDEN, BARRADA & KELSEY, 1962 b). Usually this ratio is greater than 2,0, with a lower limit of the normal range of 1,85. The normal eye of figure 3 has a ratio of 2,56, the affected eye showing only a ratio of 1,0 (no increase).

To standardize the measurement the following suggestions are given. The adaptive field for the light adaptation has to be large (90° visual angle) with a luminance of 1800 lux. Before the dark period, a standardized pre-adaptation period is advised. The angle over which the eyes are moved, i.e. the distance between the fixation lamps, has to be 30° to 40°; generally a 30° angle is used. The head has to be held as quiet as possible, so that it does not move together with the eyes. The fixation can better be red and of low luminance, in order not to interfere with dark adaptation. A single moving fixation light may also be used instead of two separate lights. Even if the measurement is standardized as

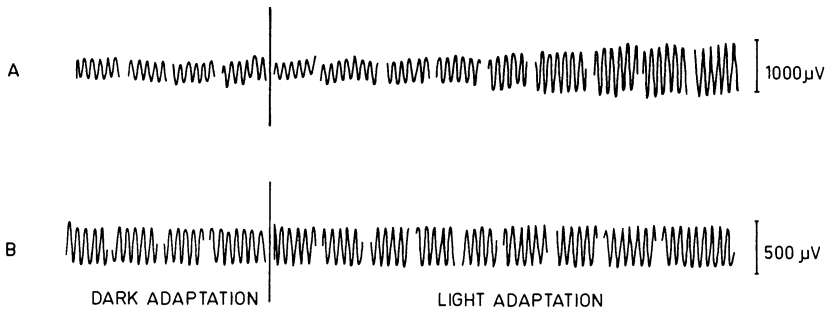

Fig. 3 Actual registration of an electro-oculogram (EOG) of a normal subject (A) and one of a patient with a pigment systrophy (B). A single moving fixation light was used.

much as possible, variations in the results may occur (KELSEY, 1967; VAN LITH & BALIK, 1970 a).

It is important that the patient keeps a steady pace as he watches the fixation lamps. This requires the cooperation and ability of the patient to do so. This means that a visual acuity of about 0.1 is required to distinguish the fixation lights properly. Extreme constriction of the visual field may also give problems in searching out the fixation lights. The youngest age at which an EOG usually can be made is about 5 years.

It is not necessary to dilate the pupils. The electrodes have to be placed on the orbital rim at the medial and lateral canthus of the eye, as shown in Figure 2. The same electrodes and electrode pasta can be used as in electrocardiography and electro-encephalography.

As the indirectly measured standing potential is relatively high, i.e. 250-2000 muV., a rather simple amplifier, such as an ECG amplifier can be used. An EEG amplifier with more possibilities (low and high frequency filters, higher gain, etc.) is however preferable. It is advisable to apply a long time constant of at least 1 second in order to eliminate distortions of the records (see Fig. 6). High frequencies may be cut down with the high frequency filter. This means that the use of a Faraday cage is not necessary.

For the registration itself one can choose between a thermo-writer, an ink-writer or a photographical registration with a polaroid camera from the screen of an oscilloscope. Rather expensive writers with high frequency range, like the ink-injector-system or UV-writers can be used as well, but are not indispensable. The optimum speed of the paper on which the EOG is registered is about 3 cm/sec.

ELECTRO-RETINOGRAPHY (ERG)

If a light flash is presented to the eye, a reaction potential will be the result. This potential variation is called the electroretinogram. It can be led off with the active electrode built into a contactlens. Various components can be distinguished in the ERG (Fig. 4). These are the early receptor potential (ERP), the late receptor potential (LRP) or a-wave, the bipolar cell layer potential (BP) or b-wave, and the oscillatory potentials (OPs) (DOWLING, 1970). Furthermore, there are slow DC-potentials. The ERP and DC components are not yet generally used for clinical purposes. Therefore these components will not be discussed in this paper.

After a light flash of high intensity a corneo-negative potential, the LRP, can be seen. It originates in the receptor cell layer. Directly after the LRP a positive deflection comes up, the BP, which is a reflection of the activity of the bipolar cell layer. This potential probably originates in the Müller cells. On the ascending limb of the BP small wavelets can be observed, the so-called oscillatory potentials (OPs). Their exact origin is not known, but is probably situated in the superficial retinal layers.

The simplest apparatus through which a light flash to the eye can be presented, is the Xenon discharge lamp. Frequency and intensity can be easily altered. It is

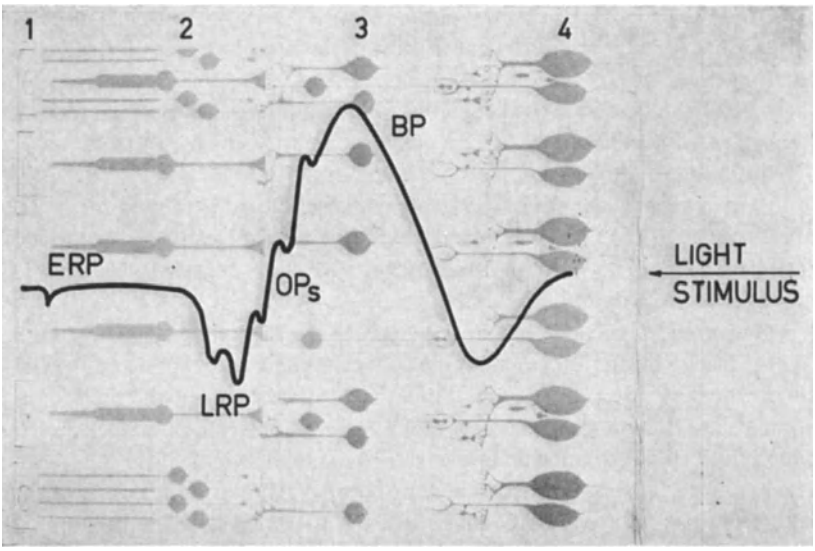

Fig. 4 Schematic representation of the various components of the electroretinogram. ERP: early receptor potential; LRP: late receptor potential; OPs: oscillatory potentials; BP: bipolar cellayer potential.
1: pigment epithelium; 2: photoreceptor layer; 3: bipolar cellayer; 4: ganglion cellayer.

more complicated to use an incandescent lamp (by example a halogen lamp) provided with a photoshutter or an electromagnetic shutter or a rotating wheel with holes. Most Xenon discharge lamps are placed into a lamphouse with reflector, which, when placed at 30 cm before the eye, subtends a visual angle of about 30°. By the direct image of the reflector, only the central part of the retina is illuminated. The rest of the retina will be illuminated by stray light. This unequal illumination of the retina is a disadvantage which can be avoided if the lamp is placed at the rim of a hemisphere like the adaptive lights in the Goldmann perimeter (VAN LITH, MEININGER & VAN MARLE, 1973). The intensity of the Xenon discharge lamps can be altered by means of varying the electric energy, which is expressed in Joules (J). Another and more accurate method to vary the stimulus luminance is placing grey filters in front of the lamp.

A stimulus of low luminance and low frequency presented to the eye in the dark, will evoke a response of the rod system. This response is called the scotopic ERG. High luminance stimuli against a bright adaptive background illumination will trigger the cone system: the photopic ERG. An adaptation light is necessary for suppressing the rod system. For this reason background luminance has to be at least 2000 lux, measured at the corneal plane. Instead of a background illumination, flicker light of high intensity and frequency may be used (KRILL, 1964). The retina will be light adapted through the stimulus itself. Moreover, the rods can no longer respond to a flicker of more than 20 flashes per second.

Because the cones are relatively more red sensitive, while the rods are more blue sensitive, a blue stimulus light triggers in the first place the rod system, red light the cone system.

The OPs can best be provoked with a white light flash of very high intensity (40-80 J) after some minutes of dark adaptation (YONEMURA, AOKI & TSUZUKI, 1962 a; YONEMURA, TSUZUKI & AOKI, 1962 b).

In Fig. 5 some examples of the scotopic and photopic ERG and of the OPs are presented. The OPs have been registered photographically, as they are too fast for a penwriter. The other recordings have been obtained with an EEG amplifier fitted with an inkwriter.

The scotopic ERG generally has no LRP. When the intensity of the stimulus light is increased, the BP becomes higher, while the latency time and the peak time become shorter. The latency time is the time between the start of the stimulus and the onset of the response. The peak time is the time between the start of the stimulus and the moment the maximum height of the response is reached. The maximum height of the scotopic BP may range from 200 to 400 muV. The photopic ERG consists of the LRP and BP. The photopic BP

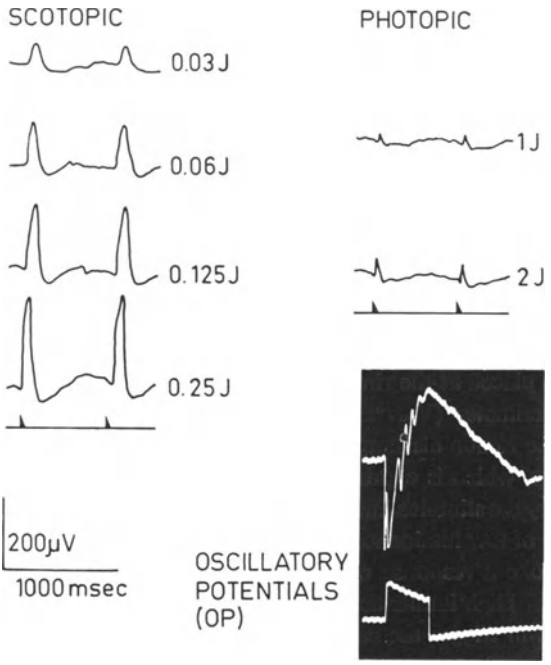

Fig. 5 Actual registrations of some components of the electroretinogram (ERG). The scotopic ERG made in the dark adapted state with stimuli of 4 intensities; the photopic ERG in the light adapted state with stimuli of 2 intensities (J. Joule).
Below the recordings stimulus indication.
OPs made with a stimulus of 40 J after 3 minutes of dark adaptation (calibration: 200 µV; sweeptime of the oscilloscope 20 msec).

is much smaller and faster than the scotopic BP. In normals the photopic BP reaches values of about 100 muV, the LRP of 50 muV.

The signal of the ERG is usually picked up from the cornea with a contactlens electrode and measured against a neutral electrode. This neutral or referential electrode can be placed at the earlobe, in the midline of the forehead or somewhere around the eye. Care must be taken, that in unilateral disturbances, a neutral electrode placed between both eyes, may pick up electric activity from the sound eye.

If it is not possible to place a contactlens on the eye, or if the patient cannot tolerate a contactlens, a skin electrode may be used as active electrode. This electrode has to be fixed as close to the eye as possible and always at the same

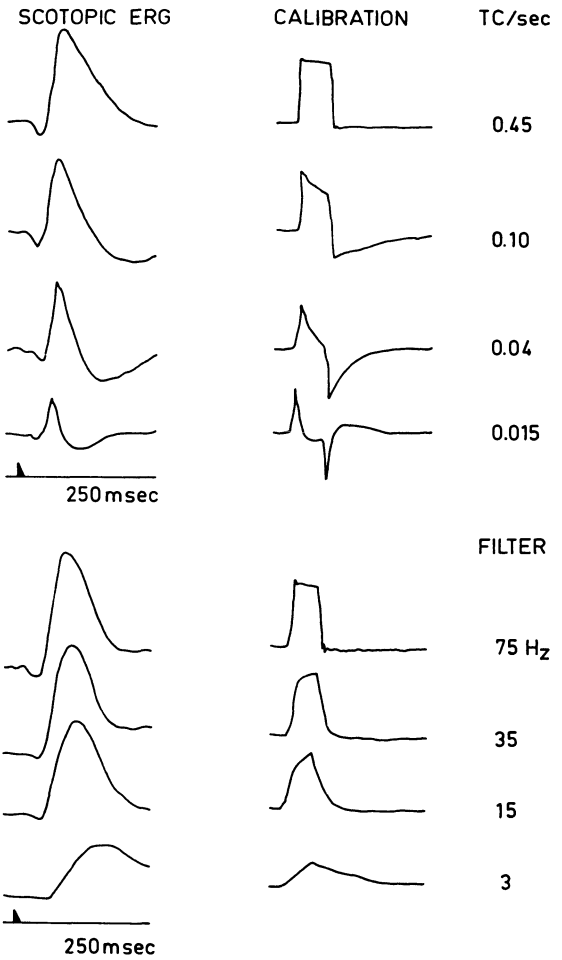

Fig. 6 Influence of time constant (upper recordings) and high frequency filter (lower recordings) on a block signal (calibration) and on the scotopic ERG.

position, for example at the lower lid. The amplitudes of the responses obtained with skin electrodes are about 25% of those obtained with a contact lens electrode. Moreover, they are less reliable. Commonly used types of contact lens electrodes are those of KARPE, HENKES, BURIAN-ALLEN and PAPST-ECHTE (SUNDMARK, 1962).

The amplification of an electrocardiograph is not sufficient to register the ERG. The gain in range of an EEG amplifier is required. Instead of an EEG amplifier, an oscilloscope with pre-amplifier can also be used. It must be possible to register responses of at least 25 muV. The time constant of the amplifier should be more than 0.3 seconds in order to get the scotopic responses more or less undistorted. The influence of the time constant on the response can best be shown, when using a block signal (Fig. 6). The shorter the time constant is, the more distorted the answer obtained from the amplifier. The same holds for the slow components in the ERG, viz. the scotopic BP. To obtain properly the fast ERG components (photopic BP and OPs) high frequency filters must be higher than 75 cps. The influence of lowering the high frequency filter is shown in Fig. 6. If 50 or 60 cps cable noise gives problems, a Faraday cage has to be used.

For the registration various systems can be applied. They have already been mentioned shortly in the section on EOG registration. As the ERG contains fast components, ink injector systems, UV-writers or photographical registration methods may be more profitable than ink-writers or thermo-writers. Photographic registration has the disadvantage that the results cannot be judged instantly. This is not the case when using a Polaroid camera (see Fig. 5, the registration of the OPs).

LOCAL ERG AND VECPS

The VECPs are mainly a representation of the fovea (VAN LITH & HENKES, 1970 b). The retinal periphery does not contribute substantially to these

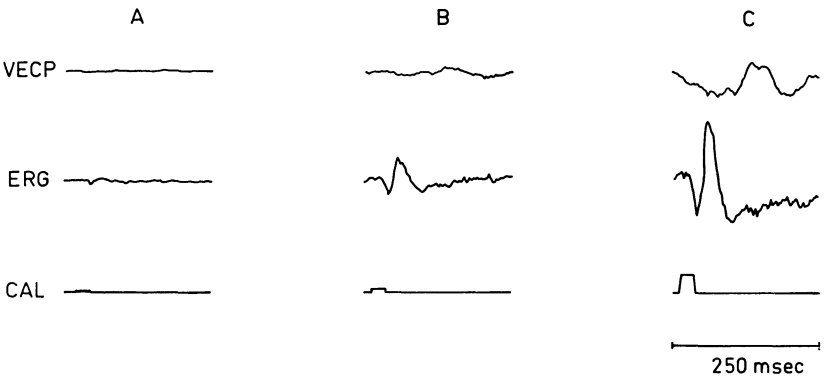

Fig. 7 The improvement of the signal-to-noise ratio by using an averager. VECP. ERG and calibration (5 microvolts) after 1 flash (A), 10 flashes (B) and 50 flashes (C).

potentials. In macular processes, therefore, it is of clinical interest to measure them, especially together with the local ERG of the fovea. Moreover, the VECPs are disturbed in affections of the conductive system.

For the registration of both the local ERG and the VECPs an averager is needed. With an averager the signal-to-noise ratio is improved, since the height of the signal (ERG or VECP) will increase with a factor $\sqrt{2}$ as compared to the random activity. (ARMINGTON et al., 1961). Using averagers responses of 10 muV can easily be seen amidst the noise. Even responses of 1 muV can sometimes be recognized. The effect of the averager is presented in Fig. 7. Even if we use one single flash of a 10° stimulus, presented to the centre of the light adapted retina, the ERG and VECPs are too small to detect, independent of the amplification used (see Fig. 7 A). If the ERG potentials and VECPs are averaged a small response can be seen after 10 flashes, while after 50 flashes the response becomes quite clear (Fig. 7 C).

The right and the left eye are stimulated the one after the other, as each fovea has its representation in both occipital lobes. The VECPs are lead off with skin (EEG) electrodes, fixed over the occipital lobes. Usually it is sufficient to place the electrodes in the midline. The electrode position is a the inion and 2 cm and 4 cm over the inion. However, it is more exact to place the electrodes at

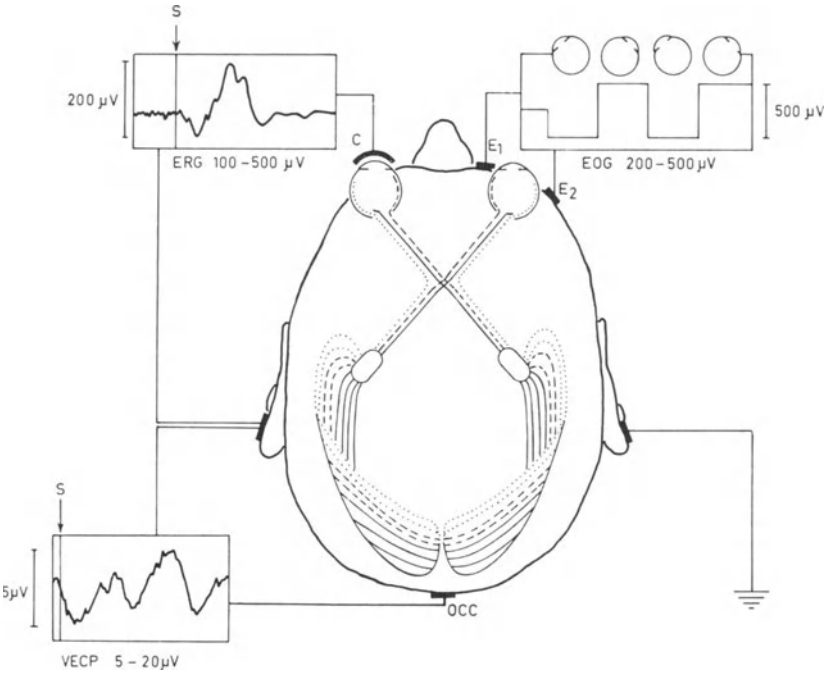

Fig. 8 The three electric phenomena which can be recorded from the visual system, E_1 and E_2: electrode position in the EOG; C: contact lens electrode; occ.: electrode position for the VECP; S: light stimulus.

fixed percentages of the inion-nasion distance (REGAN, 1972). In the Rotterdam Eye Hospital distances of 5%, 15% and 25% over the inion are used. One can measure between two electrodes (bipolar lead) or from one of the electrodes to an ear electrode (monopolar or referential lead). In intracranial processes electrode positions outside the midline, over the right and the left occipital lobe, may be profitable. These positions may provide us with information about displacement of the midline of the brain or about disturbances in the right or left hemisphere (JONKMAN, 1967).

The latency time of the VECP is much longer than that of the ERG, so that the photopic response comes up when the ERG has already vanished (Fig. 7). Height and wave-form of the VECPs show considerable interindividual variations. Therefore, they are generally not measured quantitatively, but estimated in the categories normal, lowered or absent. In optic nerve pathology the VECPs are generally absent or clearly lowered. In macular degenerations, however, the VECPs, evoked with light flashes, are only disturbed in rather severe cases.

New techniques with pattern stimulation, e.g. a checkerboard pattern, instead of light flashes will certainly provide us with more detailed information in the near future. In the context of this paper these techniques will not be dealt with. A review has been published recently by REGAN (1972).

In Fig. 8 the electric phenomena of the visual system which can be measured, are presented together. The EOG measured between two electrodes placed at both sides of the eye. The ERG, registered from the cornea to the earlobe. The VECPs are obtained from electrodes placed over the occipital lobes.

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ELECTRO-OPHTHALMOLOGY
II. INDICATIONS AND INTERPRETATION

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ABSTRACT

The disturbances of the visual system, for which electro-ophthalmological examination may be fruitful, can be divided into 5 categories. Opacities of the media will only lower the ERG responses by filter action. In pigment dystrophies and retinal detachments the EOG and all components of the ERG are lowered, while in retinal circulatory disturbances the ERG-potentials, originating in the deep retinal cell layers will remain intact. In disturbances of the conductive system the ERG has to be normal and the VECPs lowered. If the cause of a visual loss is beyond the level of the occipital cortex all electro-ophthalmological potentials will be normal.

Psychophysics, photography, ultrasonography and electro-opthalmology are examination methods which supplement one another in achieving the diagnosis of visual disturbances. In some diseases electro-ophthalmological examination may even be essential. In opacities of the media, psychophysics and opthalmoscopy or photography are not of great help when one wants to determine the advisability of an operation. In retinal degenerations and circulatory disturbances electro-ophthalmology gives the real function of the retina, independent of the extent of pigmentations, hemorrhages or exudates. In disturbances beyond the level of the retina, electro-ophthalmology is practically the only diagnostic aid.

Disturbances in which electro-ophthalmological examination may be significant can be divided into the following categories:

- Opacities of the media;
- Retinal degenerations and functional disturbances;
- Retinal circulatory disturbances;
- Disturbances of the conductive system;
- Amblyopia and visual loss with questionable etiology.

Since it would be impossible to treat all these subjects in detail, we shall limit ourselves to a discussion of their essentials on the basis of clear-cut examples.

METHODS AND NORMAL VALUES

All electroretinograms (ERGs) and visually evoked cortical potentials (VECPs) mentioned in this paper have been made with an averager. For this reason

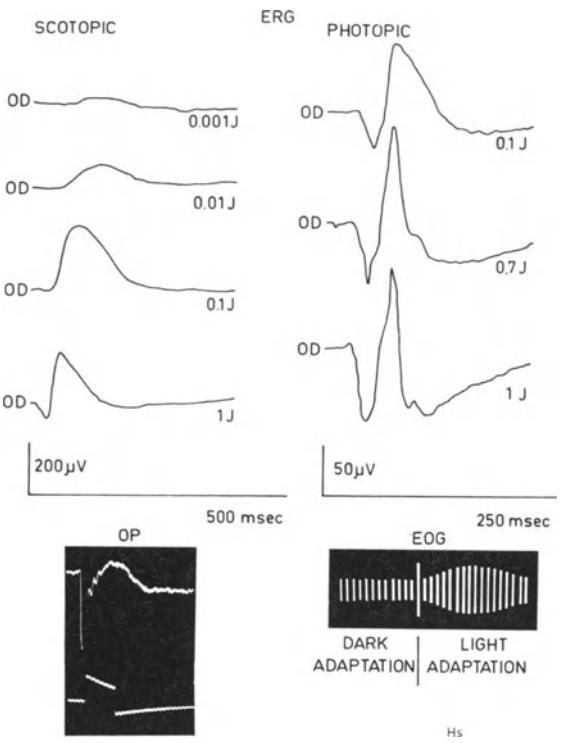

Fig. 1. Normal values. Averaged recordings of the scotopic ERG (7 counts) and the photopic ERG (70 counts). Single flash OP, photographically registered, calibration 200 muV. The EOG calibration of 100 muV is represented by the streak between dark adaptation and light adaptation.

the signal-to-noise ratio of the recordings, referred to here, is better than the one in the recordings made with an ordinary amplifier (ERMERS & VAN LITH, 1973). The electro-oculograms (EOGs) have been registered with a semi-automatic system (HENKES et al., 1968). The LP/DT-ratio has been measured. The oscillatory potentials (OPs) have been obtained with a single flash and registered from the screen of an oscilloscope with a polaroid camera (YONEMURA et al., 1962).

Fig. 1 represents the electric responses of a normal subject. On the upper left, the ERG responses of the rod system, also called the scotopic ERG, are shown. These responses have been obtained with blue light flashes, presented in four intensities against a dark background. With the three lowest intensities the scotopic ERG shows only the positive b-wave, the BP (bipolar cell layer potential). It reflects the activity of the bipolar cell layer (DOWLING, 1970). In the scotopic ERG obtained with the highest intensity and in the photopic ERG, the positive BP is preceded by the negative a-wave. The a-wave originates in the receptor cell layer and is also called the LRP (late receptor potential). The

photopic ERG (upper right) reflects the responses of the cone system and has been obtained with red light flashes against a bright blue background. The EOG (lower right) originates in the deepest retinal layers, viz. the photoreceptors, Bruch's membrane and pigment epithelium (GOURAS, 1968). The OPs (lower left) are small rhythmic wavelets riding on the ascending limb of the BP. Their origin lies in the superficial retinal layers. For routine recordings of the VECPs the reader is referred to the foregoing paper (ERMERS & VAN LITH, 1973).

The lower limits of the normal values in our set-up are:

Scotopic ERG		200 muV	
Photopic ERG	BP	100 muV	Ratio BP/LRP 2.0
	LRP	50 muV	
EOG	LP/DT-ratio	1.85	

OPs and VECPs are not calculated quantitatively, but divided into the categories normal, lowered or absent.

OPACITIES OF THE MEDIA

If the visual acuity is lower than 1/10, it may be difficult or impossible to make an EOG, as the fixation lights cannot be fixed properly. If the retina and the conductive system function normally the ERG and VECPs must also be normal independent of the degree of the opacity. One should be aware of the fact, however, that an opacity may be an effective light filter (SVERAK & PEREGRIN, 1968). Figure 2 provides an example. The scotopic ERG of the right eye has a

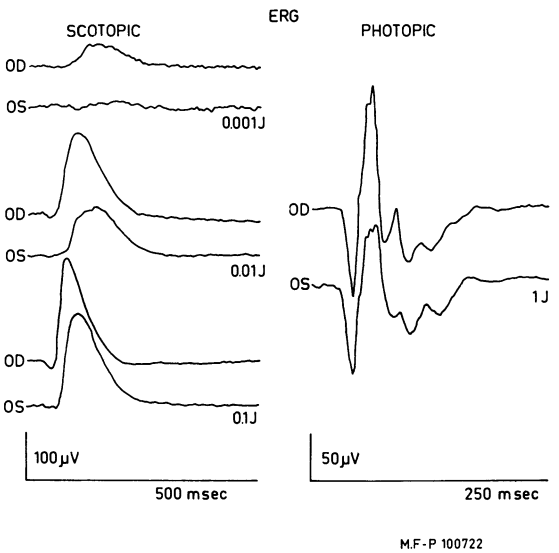

Fig. 2. Scotopic and photopic ERGs in cataract of the left eye. Scotopic ERG-calibration is 200µV instead of 100µV shown in this figure.

height of 340 muV, obtained with an intensity of 0.01 Joule. About the same response is achieved by the other eye, requiring in this instance an intensity of 0.1 Joule. A difference in pupil size may result in the same effect, since the retinal illumination is dependent on the pupillary area. The influence of opacities and pupil size on the photopic ERG is less than that exercised on the scotopic ERG. The reason for this is, that for the scotopic ERG only test light luminance is lowered, whereas for the photopic ERG both test light luminance and luminance of the adaptation light is lowered.

In opacities of the media electro-ophthalmology provides us with reasonable information concerning visual functions. If the retinal periphery is affected, the scotopic ERG will mainly be reduced whereas in diseases of the posterior pole the photopic ERG will be disturbed primarily. The VECPs make it possible to estimate the macular function and the function of the conductive system (VAN LITH, 1971).

RETINAL DEGENERATIONS AND FUNCTIONAL DISTURBANCES

From the electro-ophthalmological point of view retinal degenerations or pigment dystrophies can be divided into global degenerations and local degenerations. Global degenerations may be subdivided into rod-cone dystrophies and cone-rod dystrophies. The most important of the local degenerations are the macular diseases. Functional disturbances in which electro-ophthalmology is essential for the diagnosis are the hemeralopias and the achromatopsias.

The EOG and ERG are summation potentials of the illuminated and still functioning retina. Therefore they are more disturbed in the global degenerations than one should expect from the visual acuity, visual field and dark adaptation curve. Visual acuity only reflects the foveal function; in the dark adaptation curve made with total retinal illumination, the sensory threshold of the best part of the retina is determined. In local degenerations, the height of the electric potentials also reflects the properly functioning retinal tissue. That's why we seldom see significantly reduced EOGs and ERGs in pure foveal processes (JACOBSON, 1961). If they are reduced, then it is an indication that the disturbance extends over a larger area than the fovea proper.

Rod-cone dystrophies, hemeralopias and retinal detachment

Rod-cone dystrophies, such as the retina pigmentosa, are characterized by a strongly reduced or absent scotopic ERG and EOG. The photopic ERG is usually less disturbed (JACOBSON, 1961; GOURAS & CARR, 1964; BERSON et al., 1968 a; 1969 a, b; 1970). In Fig. 3 the EOG shows no increase at all during the light adaptation; the scotopic ERG only amounts to 10% of the normal value; the photopic ERG approximately 75%.

Since the reduction of the positive BP (b-wave) is accompanied by a reduction of the negative LRP (a-wave), it follows that a disturbance is present in the deep retinal layers. The EOG and ERG are much more reduced in the primary

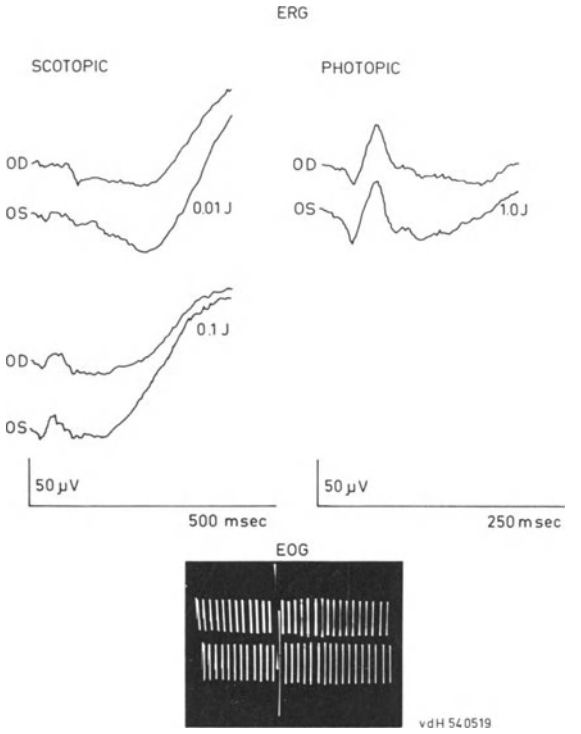

Fig. 3. EOG and ERGs in rod-cone dystrophy. Scotopic ERG 28 counts, calibration 50µV instead of 200µV; calibration of the photopic ERG and the EOG as in the normal.

hereditary rod-cone dystrophies than in the secondary dystrophies (measles, rubella) (JACOBSON, 1961). This is so in spite of the fact that the latter has many pigmentations while in the primary dystrophies pigmentations may even be absent (retina pigmentosa sine pigmento). In the group of hereditary dystrophies the electric responses of the recessive form are ordinarily worse than those of the dominant form. In the recessive form they are often absent (ARMINGTON et al., 1961), that is to say too small to be visible amidst the noise level ('non-recordable').

The very low electric responses found in the hereditary pigment dystrophies may be of importance in determining whether a patient suffers from the prognostically bad retina pigmentosa sine pigmento or from the non-progressive hemeralopia. The hemeralopias in general also have a lowered BP in the scotopic and photopic ERG (Fig. 4). The OPs are absent. The EOG and LRP, however, may be normal, indicating that the disturbance is situated post-receptorally (CARR et al., 1966 a, b; AUERBACH et al., 1969).

Retinal detachments, being a disturbance of the deep retinal layers, produce responses as found in the rod-cone dystrophies (RENDAHL, 1961). The height of the response is dependent on the percentage of the retina which is still functioning.

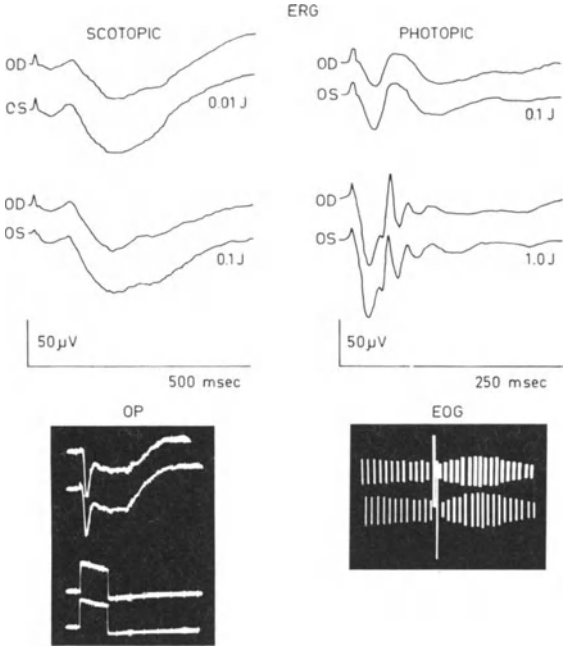

Fig. 4. EOG, OPs, and ERGs in sex-linked hemeralopia. Scotopic ERG 28 counts, calibration 50 muV. Calibration of the photopic ERG, OPs and EOG as in normal. The upward deflection at the beginning of each recording is a stimulus artefact.

Cone-rod dystrophies, achromatopsias and chloroquine retinopathy

In the cone-rod dystrophies the photopic ERG is more reduced than the scotopic ERG (BERSON et al., 1968 b, c; KRILL & DEUTMAN, 1973). Fig. 5 shows a scotopic ERG which is just at the lower limit of the normal range, while the photopic ERG has a value of only 25%. Also different from the rod-cone dystrophy is the relatively good EOG. This is reasonable as the EOG is mainly a reflection of the rod system. Later on, when the disease progresses EOG and scotopic ERG also become affected. This is the reason why in the progress of pigment dystrophies the differences between the rod-cone and the cone-rod dystrophies disappear. In the final stage of both diseases scotopic and photopic responses are absent.

If a patient is examined once it may also be difficult to make the differentiation between a cone-rod dystrophy and the achromatopsias. Ophthalmoscopically the cone-rod dystrophy may present itself only as a bull's eye. The achromatopsias on the other hand often show small macular alterations, too. The complete or total achromatopsia can be recognized, as it has an absolutely normal scotopic ERG and a totally absent photopic ERG. Moreover, the complete achromatopsias always have a nystagmus, whereas absolute colour blindness is generally

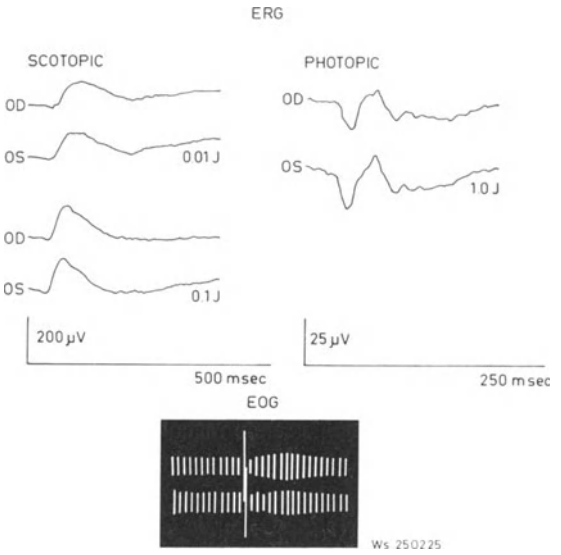

Fig. 5. EOG and ERGs in cone-rod dystrophy. Photopic ERG, 140 counts, calibration 25 muV. Calibration of the scotopic ERG and EOG as in normal.

known to have existed during a patient's entire life. Diagnosing partial achromatopsia is not that simple. The partial achromatopsia includes a large group of various serious colour defects. FRANÇOIS & VERRIEST tried to classify them. As some cone function may be left, they may resemble the cone-rod dystrophy (FRANÇOIS & VERRIEST, 1959, 1960). The typical bull's eye of the latter, however, can often be diagnosed by means of fluorescence angiography. Progression in the disease excludes the diagnosis achromatopsia.

The bull's eye of the cone-rod dystrophy resembles that of the chloroquine retinopathy (BUTLER, 1966; FRANÇOIS et al., 1972). Electro-ophthalmologically both diseases may be similar, too. More often than not, however, a disturbance of the EOG precedes the disturbance of the photopic ERG in the chloroquine retinopathy, while in the cone-rod dystrophy the reverse is seen.

It must be stressed that the EOG should never be the only examination method with which patients using chloroquine are checked. A disturbance of the EOG may be an early symptom in the chloroquine retinopathy, but sometimes the EOG remains normal in patients developing a chloroquine retinopathy. The EOG may only be a supplementary examination. An additional problem is that rheumatism and lupus erythematodes, the diseases for which chloroquine derivatives are used, may itself lower the EOG. This difficulty can be removed by performing an EOG before the therapy starts.

In the early stages the cone-rod dystrophy may also resemble some juvenile fovea dystrophies. A fast progression and relatively strong disturbance of visual acuity, colour vision and photopic ERG points to the more general retinal degeneration of the cone-rod dystrophy (KRILL & DEUTMAN, 1973).

In localized pigment dystrophies, such as sector dystrophies or posterior pole degenerations, the electro-ophthalmological responses are the same as in beginning generalized dystrophies. In general it can be said that the percentage of loss in retinal function will be reflected in the height of the responses (KRILL et al., 1970; BERSON & HOWARD, 1971). The localization of the degeneration in the retina determines whether the photopic ERG (more dependent on the posterior pole) or the scotopic ERG (originating in the retinal periphery rather) will be more disturbed. A difficult but interesting group for electro-ophthalmology is the group of macular degenerations. If the degeneration is limited to the fovea itself, a significant reduction in the photopic ERG, produced by global light stimulation, may not be expected (JACOBSON, 1961). This is generally the case with colloïdal and atrophic senile macular degenerations. The more difficult technique of the foveal-ERG with localized light stimuli or of the VECP with pattern stimulation must be used in these cases.

As the VECP, also after global stimulation, is mainly a representation of the 10° central retinal area, it should be a better graduator in macular diseases than EOG and ERG (VAN LITH & HENKES, 1970). An exact quantitative evaluation of the VECP, however, is not possible. Within the normal range a variability of at least 50% may be found, so that a significant reduction may only be found in seriously damaged maculas (JONKMAN, 1967).

When the retinal responses after global stimulation are reduced, then the disturbance spreads over a larger area than the fovea only. Examples are the disciforme macular degeneration and the severe myopic degenerations in the posterior pole. Lowered electric responses are also seen in the cone-rod dystrophy, the chloroquine retinopathy and the vitelliform foveal dystrophy, although ophthalmoscopically the abnormalities may be limited to the fovea. The juvenile fovea-dystrophies can usually be clearly distinguished from one another on the basis of the electric responses (DEUTMAN, 1971). The dominantly inherited vitelliform macular degenerations are characterized by an absent EOG, while the ERG may be totally normal (FRANÇOIS et al., 1967; DEUTMAN, 1969). The sex-linked juvenile retinoschisis has a normal EOG, a normal LRP and a lowered BP. The degree of disturbance is probably determined by the extent of the schisis and not by the foveal dystrophy itself. The recessively inherited foveal dystrophy of Stargardt has a normal EOG and ERG, as long as the disease is limited to the fovea. If the retinal periphery or perifovea participate in the dystrophy, the ERG responses will be lowered.

CIRCULATORY DISTURBANCES

The choroidal circulatory disturbances, just as the pigment dystrophies, cause loss of function, beginning at the pigment epithelium. This means that the EOG and all components of the ERG are reduced.

The retinal circulation provides only the ganglion cell layer and bipolar cell layer with blood, but not the receptor layer and pigment epithelium. Therefore,

EOG and LRP should be normal, OPs and BP reduced. For the EOG this is not always the case. It appears that after an occlusion of the central retinal artery the standing potential does not increase at all during the light adaptation (GOURAS & CARR, 1965; ARDEN, 1967). A good explanation for this has not been found, yet. The reduction of the BP in the retinal circulatory disturbances, while the LRP remains intact, causes the BP/LRP ratio to become lower. This appeared to be a very sensitive function test for the sufficiency of retinal circulation. Fig. 6 represents an occlusion of the central retinal artery; Fig. 7 a branch occlusion of the central retinal vein. In both cases the negative LRP is normal, while the positive BP is almost absent in Fig. 6, lowered in Fig. 7. It is clear that in both cases the BP/LRP ratio is reduced. In Fig. 6 the 'normal' left eye has a ratio of 1.8, the pathological eye one of 0.55, the branch occlusion reduced the ratio to 1.4, while the other eye has a ratio of 1.65. In Fig. 1 it can be seen that the ratio is also dependent on the test light luminance. In our routine test it should be higher than 2.0.

The BP/LRP ratio provides us with information concerning the retinal oxygenation, the height of the responses gives information about the total loss of function. Principally arterial occlusions, venous occlusions, hypertensive and diabetic retinopathies and arteriosclerotic diseases show the same alterations in

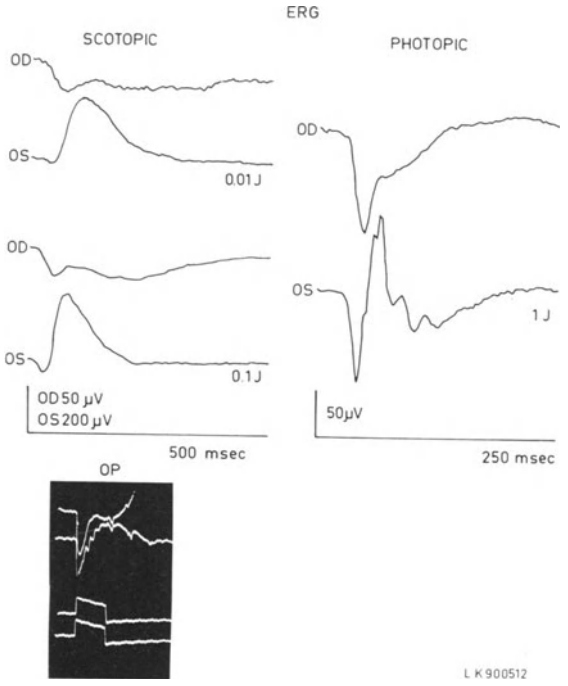

Fig. 6. OPs and ERGs in central retinal artery occlusion of the right eye. Scotopic ERG of the right eye 28 counts, calibration 50 muV. Other calibrations as in the normal.

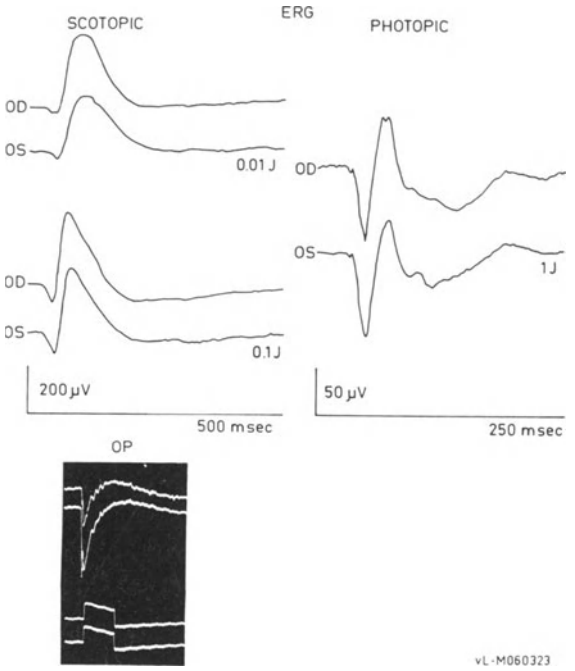

Fig. 7. OPs and ERGs in venous branch occlusion of the left eye. Calibration as in the normal.

the electric responses. The more branches or small vessels are occluded, the lower the responses will be, independent of the amount of hemorrhages and exudates (RIASKOFF, 1972). For the OPs this is not the case. The OPs are reduced in the early stages of the diabetic retinopathy and in the venous occlusions, while they may be undisturbed in senile and hypertensive alterations (SIMONSEN, 1968; TASSY et al., 1971; JAYLE et al., 1971).

When the BP is absent in central artery occlusions, the OPs are absent, too.

It is highly probable, that in future through a thorough analysis of the various waves in the ERG more data than described here can be obtained about retinal circulation.

DISTURBANCES OF THE CONDUCTIVE SYSTEM

These are the disturbances beyond the level of the bipolar cell layer, viz. in the ganglion cell layer, in the optic nerve and in the brains. The EOG and ERG are normal in these cases, while the VECPs are disturbed (DE HAAS, 1972). As already stated in the foregoing paper (ERMERS & VAN LITH, 1973) an EEG-amplifier will not be sufficient. For the recording of the VECPs, an averager is needed.

The clearest reduction of the VECPs is seen in optic atrophy and in optic neuritis. If the optic atrophy is in an advanced stage, then the VECP is totally

absent. An absent VECP can also be seen in the acute stage of the optic neuritis. Fig. 8 gives an example. While the ERGs of both eyes are normal, as well as the VECPs of the left eye, the VECPs of the right eye are almost absent. It is remarkable that in the optic neuritis the recovery of the psychophysical functions, such as visual acuity and visual field, is much faster than the recovery of the VECPs. It often happens that the VECPs are still absent, while visual acuity is restored to 100%.

The influence on the VECPs of a toxic disease or pressure on the optic nerve is not yet systematically investigated. The latter includes glaucoma and tumours in or around the optic nerve. From our material we are under the impression that the VECPs are disturbed most in optic neuritis, especially when compared to the psychophysical results.

In pressure on the optic nerve the VECPs are also severely disturbed. This may make it difficult to differentiate electro-ophthalmologically between an optic neuritis and a tumour before the optic chiasm. The toxic, as well as the hereditary optic diseases probably shows only lowered VECPs in advanced cases. When we measure the VECPs over the right and left occipital lobe separately, we can expect asymmetric responses in hemianopsias. This, however, appears not to be constantly present (VAUGHAN et al., 1963; JONKMAN, 1967; DE HAAS, 1972). This is probably due to the fact that the distance between the right and left occipital lobe is too small as compared to the distance between the electrodes and the occipital lobes through the scalp.

If the midline of the brains is displaced by a tumour, it may also cause an asymmetric response of the VECPs. The asymmetric responses, however, are

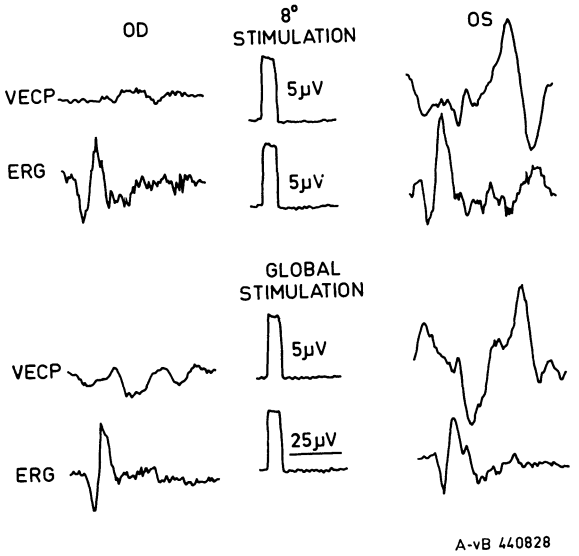

Fig. 8. ERGs and VECPs in an optic neuritis of the right eye. Stimulation 8° foveally and total retinal stimulation. Light adaptation.

not specific enough to make the registrations of VECPs an early diagnostic help for brain tumours (JONKMAN, 1967).

AMBLYOPIA AND VISUAL LOSS WITH QUESTIONABLE ETIOLOGY

In amblyopia no clear abnormalities can be found in the ERG. Most differences described in literature have to be attributed to differences in retinal illumination. This may easily cause differences in the VECPs between the normal and the amblyopic eye, too. It implies that up to now, the registration of the VECPs is of no help in diagnosing amblyopia. It can only exclude other diseases. Probably the registration of the VECPs with pattern stimulation will open new possibilities in this direction (REGAN, 1972).

For the same reason it is not possible at this moment to differentiate electro-ophthalmologically between a visual loss caused by an amblyopia or by psychogenetic abnormalities, aggravation or simulation. Only the optic neuritis with its low or even absent VECP can easily be separated from this group of low vision and normal fundus. In the electro-ophthalmological department of the Rotterdam Eye Clinic we are often confronted with patients referred to us because of having a visual loss with unknown etiology. The diagnoses which we may find are: retina pigmentosa sine pigmento or oligopigmento, juvenile macular degeneration, optic neuritis and pressure in or around the optic nerve. Most often, however, we obtain normal electro-ophthalmological results, which means that amblyopia, refractive errors, accommodation disturbances, psychogenetic reasons or simulation have caused the lowered vision. If we perform the examinations we have at our disposal in this department and the results are normal, then we may be pretty sure that no abnormalities before the level of the occipital lobe occur, except for the amblyopia.

Future developments

The possibilities in electro-ophthalmology have been so much extended over the last few years, that we usually do not apply all examination methods to one patient. Depending on the category of the disease a choice will have to be made which phenomenon can be measured best. Examination methods which we are able to use except for the registration of the EOG, ERG and VECPs with global retinal lightstimulation, include the registration of the ERG with foveal stimulation (F-ERG) or with a perimeter stimulus (ERTG = electroretinotopography) and the registration of the VECPs with local stimuli or pattern stimuli. The latter techniques require rather expensive apparatus, among others an averager. Moreover, they are not generally established to be applied outside the great ophthalmological centers.

The same holds good, in our opinion, for the examination of small children with supposed bad vision under general anesthesia. Once anesthesia is given, one should have the equipment to get as much information as needed. This includes determination of refraction, intra-ocular pressure, slitlamp examination, funduscopy, and if necessary photography, electro-ophthalmology, or

ultrasonography. Therefore it is not correct to carry out or even to talk about electro-ophthalmological examination under general anesthesia, as it is only part of the total examination.

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ECHO-OPHTHALMOLOGY

ECHO-OPHTHALMOLOGY: PHYSICAL PRINCIPLES AND DIAGNOSTIC VALUE

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1. INTRODUCTION

The frequency, or pitch, of the sound used in diagnostic systems is much higher (100 to 1000 times) than the limit of audibility. Therefore, this sound is termed ultrasound.

The use of ultrasound in medical diagnosis started about 20 years ago, and the first application in ophthalmology was published by MUNDT & HUGHES, 1956. As the title echo-ophthalmology indicates, ultrasound is mostly, and in ophthalmology exclusively, applied in reflection techniques. Hence, the source of acoustic energy is placed before the object and the ultrasound reflected by the outer and by the inner structures is registered. The reflections are caused by discontinuities in the acoustic properties, that may be completely 'missed' by optical means. The examination technique is very much like ophthalmoscopy with a pen light. A very important difference is, however, to be noted. In ophthalmoscopy light reflected from the whole illuminated field is observed by the examiner, whereas, with ultrasound the echoes can only be interpreted if the sound field is narrow compared with the dimensions of the object to be examined. In other words ophthalmoscopy yields a two dimensional picture, whereas echo-ophthalmology in its most simple form yields one-dimensional

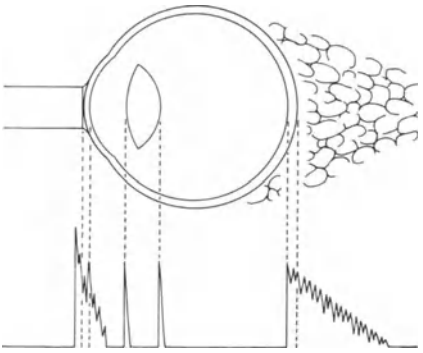


Fig. 1 Schematic drawing of the principle of one-dimensional echography (A-scan).

data, i.e. along the axis of the emitted sonic field (see Fig. 1). An advantage of this property is that the distance to the source and the relative direction of the observed echoes can be found rather accurately. In order to be able to make exact measurements of the distance from the source to a reflecting structure it is necessary to use pulsed ultrasound. Hence, the time between sound emitting pulses being longer than the time needed for the sound to travel to and from the most distant reflecting structure, all intermediate echoes can be observed and measured separately.

From the diagnostic point of view echo-ophthalmology is an extension of the diagnostic tools available to the ophthalmologist. Where the optical examination fails in cases of opaque or haemorrhageous media, the ultrasound technique yields extensive and reliable information, and tissue differentiation of neoplasms is possible within limits. Moreover, the orbital pathology can be examined as well. As compared with the röntgen examination techniques echo-ophthalmology has distinct advantages i.e. localization of pathology can be done rather accurately, without using marking techniques, or contrast material. Furthermore, the acoustic energy needed in diagnostic systems is low, so neither direct, nor cumulative damage to the tissue examined need be reckoned with. The damaging dose is of the order of 10 watts per square centimeter for continuous ultrasound applied over one minute (BAUM, 1956). This dose is about inversely proportional to the square roote of the time in minutes (THIJSSEN, 1974). However, it has been shown that the safety margin is at much higher intensities when using pulsed ultrasound. This is ascribed to the absence of standing waves in the latter case. The average intensity of diagnostic equipment is usually lower than one hundredth of the damaging dose for the one minute application mentioned above, and the pulses have a duration of the order of one millionth of a second. It can be concluded, therefore, that the danger of damaging the eye of a patient is absolutely absent.

The examination technique used generally is the manual application technique. The source of acoustic energy, called the probe, is applied at the globe or the eye lids of a patient by hand. This is the A-scan method, and due to its

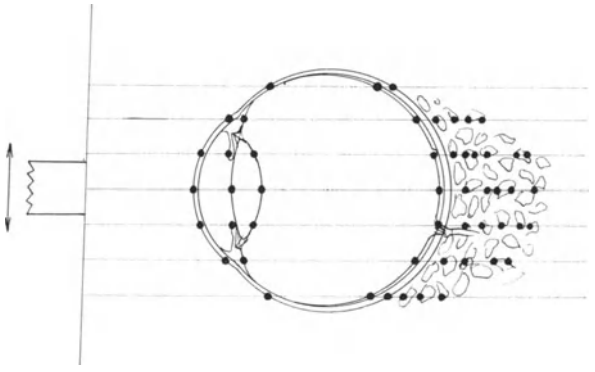


Fig. 2 Schematic drawing of the principle of two-dimensional echography (B-scan).

simplicity in method and equipment its wide practice is understandable. The more complicated, sonar-like, method of the B-scan, as illustrated schematically in Fig. 2, demands much greater financial investments and the examination technique is somewhat more laborous than the A-scan. Moreover, the B-scan equipment especially designed for ophthalmological diagnosis has hardly been commercially available up to now. So most B-scan systems have remained laboratory prototypes until, incidentally, 1973, the year of the second world congress on Ultrasonics in Medicine and Biology and the fifth SIDUO symposium. At this time three firms have combined A-scan and B-scan systems at the market. Two of these are hand-operated systems and, therefore, not suitable for exact quantitative (or 'gray scale') B-scan echography. New techniques making use of a computer and advanced display techniques are still under development.

The clinical questions that may be answered with an echographic examination can be deduced from the physical properties of the ultrasound. First of all echography is used in case of opaque media or haemorrhage, that is when inspection by optical means is impossible. It will be clear that this already includes many pathological and traumatic cases. Further, the location of a foreign body, or a luxated lens can be done echographically. Differentiation of intra-ocular and intraorbital neoplasms is possible within limits, when care is taken of reproducable adjustments of the equipment. Exact localisation and measurement of lesions can be done with the B-scan equipment. Biometrical measurements of the global dimensions can be carried out with an accuracy that permits the prescription of lens implants within one diopter limits.

This course is planned as an introduction to echo-ophthalmology with emphasis on the physical and technical backgrounds. The examination technique is so easy that it is not inconceivable that the naive examiner will be very disappointed by the uninterpretable echographic data when he has no insight to the pittfalls and limitations of the method. The presentation of the physics of ultrasound is a compromise between the exact mathematical and the completely verbal explanation and I would like to ask the forbearance of both the physicist and the physician for this duality.

The part describing the echographic diagnosis should be read with some reservation with regard to the pictures shown. Comparable results can be obtained with comparable equipment only. I hope, however, that the pictures are convincingly enough to stimulate the reader to go into the backgrounds of the echo-ophthalmology. The list of references contains a number of books that may be useful as a further introduction to the echographic diagnosis.

2. PHYSICS OF ULTRASOUND

a. General considerations

The physical proporties of ultrasound are not essentially different from those of audible sound, but some characteristics are more emphasized because their relative importance is larger. Ultrasound is a kind of 'radiation' transporting

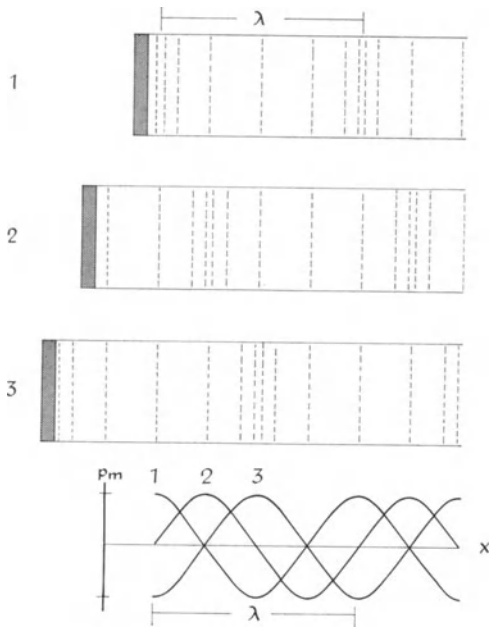


Fig. 3 Schematic drawing of the propagation of a pressure wave caused by a vibrating piston. Pm should be ξm.

mechanical energy from the source through a medium. The source is vibrating around a rest position and the molecules of the medium are brought into an oscillatory motion too. Due to the cohesional forces of the molecules this motion is transfered to neighbouring molecules and so on. Since the molecules remain oscillating around the rest position no transport of mass occurs. The binding forces in liquids and gasses are so weak that the oscillation mostly is transfered by collisions and the oscillations are performed only in the direction of the propagation of the sound, i.e. the longitudinal wave mode (Fig. 3). The speed of the sound propagation will depend on the inertia of the molecules, being expressed by the mass density of the medium (ρ), and on the elastic proporties of the medium, expressed by the adiabatic compression modulus (κ). Adiabatic means that the vibrational energy is transfered without energy loss (heat) to the surrounding medium. The elasticity theory yields the so-called wave equation for the propagation of a longitudinal mechanical vibration in a medium.

$$\frac{\partial^2 \xi}{\partial t^2} = \frac{\kappa \partial^2 \xi}{\rho \partial x^2} \tag{1}$$

ξ = local position of a molecule

It can be shown that analogous equations are valid for the local pressure p and the local velocity v. The fraction κ/ρ is defined as the square of the propagation velocity c, or

$$c = \sqrt{(\kappa/\rho)} \tag{2}$$

The general harmonic solution of the wave equation is:

$$\xi = \xi_0 \quad \sin 2\pi f\,(t - x/c) \tag{3}$$

f = frequency of the harmonic oscillation
t = time
x = distance from the origin
c = velocity of sonic wave propagation
the local velocity v of the molecules is obtained by taking the first derivative of equation (3). The momentary magnitudes of the pressure and of the velocity of a molecule are proportional

$$p = Z\,v \tag{4}$$

with p = pressure
Z = specific acoustic impedance
v = velocity of molecule
Equation (4) is sometimes called the acoustical Ohm's law. For longitudinal wave propagation in liquids, the specific acoustic impedance can be written in the following simple way:

$$Z = \rho c$$

The unit of acoustic impedance is *rayl*, with ρ in kg/m^3 and c in m/sec. The acoustic intensity can now be defined in a way that is analogous to the power dissipated in a resistance by an electric AC-voltage. Hence:

$$I = {}^1/_2\, p_m^2/Z \tag{6}$$

I = the intensity, i.e. the acoustic energy passing per second through the unit of cross section. So I is defined in watts per square meter, or W/m^2, p_m = maximum value of the momentary pressure, in newton per square meter, or N/m^2.
The macroscopic physical properties of the ultrasound are the velocity, c, and the frequency ,ν, . The frequency of a vibration is defined as the number of oscillations per second and is expressed in hertz (Hz).

The frequency is of course determined by the characteristics of the source, whereas the velocity is a medium constant. A third property that can be derived from the other two, is the wavelength, λ, of the propagated sonic wave, i.e.

$$\lambda = c/\nu \tag{7}$$

As can be deduced from equation (7) λ is given in meters, and it stands for the distance between homologous events in the wave (e.g. the pressure maxima).

The propagation of ultrasound generated by a hypothetical point source is like an expanding sphere with the source at its center. According the Huygen's principle the sonic wave from a flat acoustic source can be constructed by considering the flat source to be composed of a large number of point sources that are oscillating in conjunction (or in phase).
Such a flat acoustic source yields a flat wave front (Fig. 4). This subject is discussed further in the section 'the ultrasonic field etc.'. When a plane-progressive wave is passing from one medium to another two waves result, analogous to the well known laws of reflection and refraction of Snell for light. In solids the number of waves has to be multiplied by two because not only longitudinal but also transversal waves are present. The refraction of sound is illustrated in Fig. 5. It will be clear that θ_1 equals θ_2', whereas:

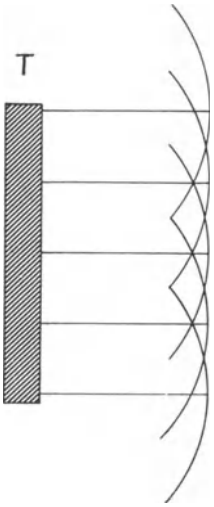


Fig. 4 Construction of the wave front of a flat acoustic source according to the HUYGENS' principle.

$$\frac{\sin \theta_1}{c_1} = \frac{\sin \theta_2}{c_2} \tag{8}$$

The fraction of the sound intensity that is reflected at the transition between two media is dependent on the difference, or discontinuity, of the acoustic impedance of the media. For a plane wave of normal incidence this fraction is defined as the reflection coefficient α_r and it is given by:

$$\alpha_r = \left[\frac{Z_2 - Z_1}{Z_2 + Z_1}\right]^2 \tag{9}$$

Where Z_2 and Z_1 are the specific acoustic impedances of the media 2 and 1, respectively. The fraction not reflected will be transmitted to the second medium to the transmission coefficient α_t is given by:

$$\alpha_t = 1 - \alpha_r \tag{10}$$

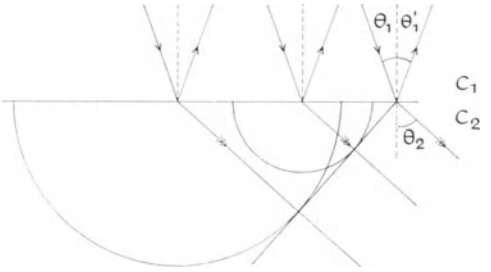


Fig. 5 Construction of the refracted sonic wave front according to the Huygens' principle. θ_1 equals θ'_1

From equations (9) and (10) it can be deduced that

$$\alpha_t = \frac{4 Z_2 Z_1}{(Z_2 + Z_1)^2} \tag{11}$$

With oblique incidence the values of the impedances must be divided by the cosine of the angle of incidence and of refraction, respectively, e.g.

$$\alpha_r = \left[\frac{Z_2 / \cos\theta_2 - Z_1 / \cos\theta_1}{Z_2 / \cos\theta_2 + Z_1 / \cos\theta_1}\right]^2 \tag{12}$$

The consequence of formula (10) is that when the acoustic impedances are equal, then $\alpha_t = 1$, so all the energy is transmitted to medium 2, whereas, in the case of an impedance 'mismatch' very little energy is transmitted. For instance a flat source of quartz is emitting in air, Z_1 equals 1.5×10^7 rayl, and Z_2 equals 430 rayl. From equation (10) it follows then that α_t is about 10^{-4}, or 0.01 %.

When the air is replaced by water, with a $Z_2 = 1.5\ 10^6$, α_t becomes about 0.1, or 10 %. In other words the acoustic energy is transmitted into water a thousand times more effectively than into air.

b. Ultrasound attenuation

Several reasons can be given why sound energy decreases when travelling through material. The first one is given above, i.e. the partial reflection at boundaries between two media. In biological tissues this type of attenuation may not only be present at boundaries between two kinds of tissue, but also within a single tissue. This occurs if the tissue is non-homogeneous. If the inhomogenities are large relative to the wavelength, so called specular reflections in various directions will occur, whereas, in the case of relatively small reflecting inhomogenities the sonic wave will be partially scattered in all directions (Rayleigh scattering). A second type of attenuation is due to conversion of vibrational energy into heat, i.e. absorption. In solids and in liquids the mechanisms of the absorption are known, but no general theory can be given for biological tissues. At least some evidence has been presented that heat loss does not play a major role in this attenuation. Since the fractional attenuation is

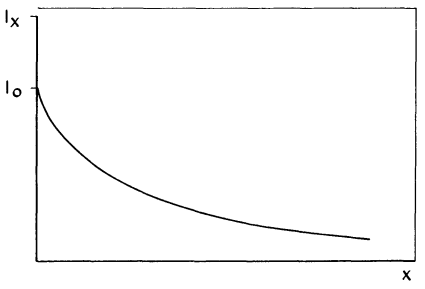


Fig. 6 Exponentially decreasing curve illustrating the attenuation of ultrasound, I_0 = intensity at the source, I_x = intensity at a distance x.

proportional to the path length travelled by the sonic wave, it can be shown that the attenuation is exponential (Fig. 6). Hence:

$$I_x = I_0 e^{-2\alpha x} \tag{13}$$

I_x = acoustic intensity at distance x
I_0 = acoustic intensity at the origin (x = o)
α = absorption coefficient, in nepers per meter
x = distance to the origin (e.g. the source)
The acoustic intensity attenuation is mostly expressed in a logarithmic form:

$$B = 10^{10} \log (I_x/I_0) = -2\alpha x\,(10^{10} \log e) \tag{14}$$
$$-8.7\alpha x = -\alpha^* x$$

B in decibels (dB)
α^* in decibels per meter (dB/m)
e.g. when $I_x/I_0 = {}^1/_4$, B equals −6dB, this is equivalent to an amplitude ratio of the ultrasound of $^1/_2$, since the intensity is proportional to the square of the amplitude. A third type of attenuation is due to the non-ideal shape of the sonic wave front. In other words a plane progressive wave is not realizable and a fraction of the sound energy diverges from the main 'beam'. Moreover a plane wave front is only present in good approximation in a restricted part of the sound beam emitted by a flat transducer and a cone shaped, diverging, beam yielding a spherical wave front is then present (see next section). The intensity decreases due to this geometrical property approximately inversely proportional to the distance from the source. Hence:

$$I_x/I_0(:)1/x^2 \tag{15}$$

Although neither the theoretical, nor the experimental evidence is very conclusive, the dependence of the absorption coefficient α^* on the frequency is mostly given by an inverse proportionality. It is, therefore, convenient to express the absorption coefficient in units per frequency unit: so

$$\alpha^{**} = \alpha^*/f \tag{16}$$

α^{**} in dB/m Hz, or in dB/m MHz.

Values of α^{**} for some ocular tissues are given in Table I. As can be seen the lens absorption is relatively high, moreover, the absorption may be much increased by a cataract. In ocular diagnosis it will be advisable for this reason to avoid passing a sonic beam through the lens.

TABLE I

Coefficient of absorption (dB/cm MHz)	
aqueous humour	0.3
lens (normal)	2
lens (cataract)	6
vitreous humour	0.3
soft tissues	0.8
orbital fat	1.0

c. The ultrasonic transducer

A transducer is a device converting one form of energy into another. So an ultrasonic transducer converts electrical energy into mechanical energy, i.e. ultrasound. Since most diagnostic applications are based on the pulse-echo

technique, the transducer is also used for conversion of mechanical energy back to electrical energy. The conversion is possible due to the piezoelectrical effect occuring in certain crystals (e.g. quartz) and in ferroelectric ceramics. In the latter type of material piezoelectricity is permanently induced by electric polarization during heating above the so called Curie temperature.

The transducer, when acting as a acoustic emittor, is excited by an electric voltage and vibrates like a mechanical oscillator. The resonance frequency of the crystal plate is dependent on its thickness. The transducers are cut or moulded in such a way that the thickness corresponds with an odd number times half the wavelength at the desired frequency. To obtain short pulses of ultrasound as required in echo techniques, a short electric pulse is applied. However, the transducer will then exhibit a damped oscillation of several periods. The acoustic pulse can be damped more rapidly by backing the transducer with a high absorbing medium. A scheme of such a probe is shown in Fig. 7.

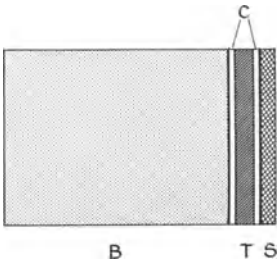


Fig. 7 Scheme of an acoustic probe. B = backing material. C = conductive layer, S = protective shield, T = transducer.

d. The ultrasonic field of a flat transducer

The ultrasonic field emitted by a flat transducer consists of two parts. The Fresnel zone (Fig. 8), or near field is characterized by a non-homogeneous distribution of the energy and by a nearly cylindrical shape of the beam. The distribution of energy in the near field is determined by interference. This can be understood when considering the plate to be composed of a large number of co-phasically vibrating point sources, which is again the Huygens' principle. It can be shown that for a circular transducer, with diameter D, the intensity along the axis of the beam is given in the near field by:

$$I_x = I_0 \sin^2 \left[\frac{\pi}{\lambda} \{ \sqrt{(x^2 + D^2/4)} - x \} \right] \tag{17}$$

x = distance from transducer
D = diameter of transducer
I_x = intensity at distance x
I_0 = maximum intensity

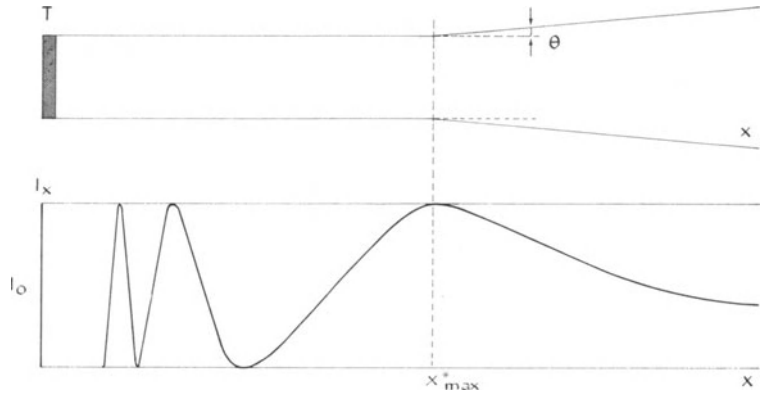


Fig. 8 Upper part: envelope of the first order sonic field of a flat transducer. D = diameter, θ = divergence angle, x_{max} = transition from Fresnel-zone or near field to Fraunhofer-zone, or far field. Lower part: intensity distribution along the beam axis x_{max} = last axial maximum.

From equation (17) it follows that the maxima are found at

$$x_{max} = \frac{D^2 - \lambda^2 (2n + 1)^2}{4 \lambda (2n + 1)} \qquad n = 0,1,2..... \tag{18}$$

Whereas, the minima occur at

$$x_{min} = \frac{D^2 - 4\lambda^2 m^2}{8m\lambda} \qquad m = 1,2..... \tag{19}$$

It follows from equation (18) that the most distant axial maximum is located at

$$x^*_{max} = \frac{D^2 - \lambda^2}{4\lambda}$$

this can be simplified to

$$x^*_{max} = \frac{D^2}{4\lambda} \tag{20}$$

with the condition that D^2 is much larger than λ^2.

The value of x^*_{max} for various frequencies and for propagation in water, with a velocity of 1500 m/sec, is given in Table II.

The axial intensity distribution is shown in Fig. 8.

The last axial maximum marks the transition from the Fresnel zone to the Fraunhofer zone, or far field. This Fraunhofer zone is characterized by the

TABLE II

Length of the near field (x^*_{max}) and the angle of divergence (θ) of the far field of a flat transducer (5 mm diameter) at various frequencies (ν) and valid in water of 34° C (c = 1500 m/sec)

ν (MHz)	x_{max}	θ
6	25	3.5°
8	33	2.7°
10	42	2.2°
12	50	1.8°
15	62	1.4°
20	83	1.1°

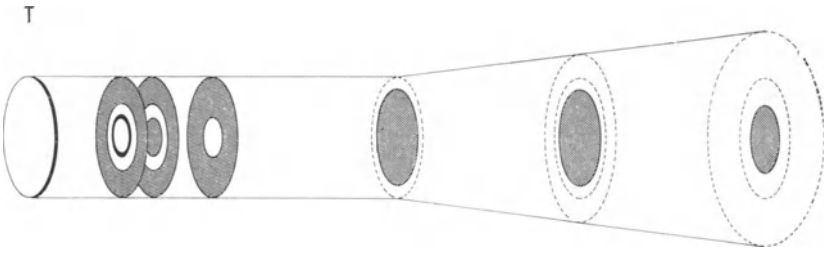


Fig. 9 Scheme of the off-axis intensity distribution, note the decreasing effective beam width in the far field.

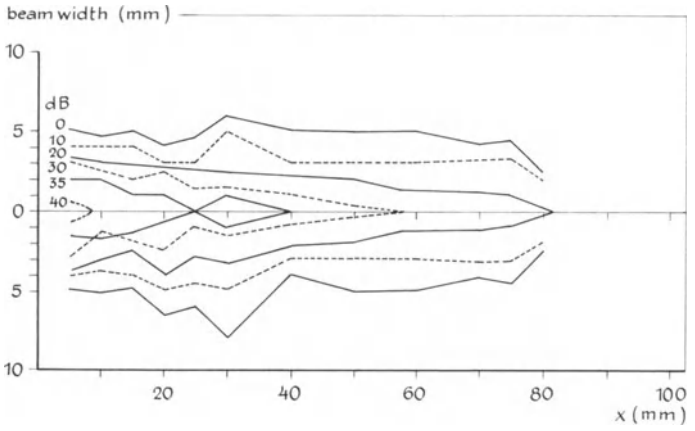


Fig. 10 Equal intensity contours of the sonic field of a 12 MHz flat transducer measured with a 3 mm steel ball.

absence of interference phenomena. The sonic beam is no longer cylindrically shaped but diverges (Fig. 8), so the intensity along the axis decreases continuously. The cone can be considered to originate in the centre of the transducer to a first approximation, in which case $\sin \theta = 2\lambda/D$, whereas theoretically $\sin \theta = 1.22\lambda/D$. The value of θ for the various frequencies as presented in table 2 indicates that the lower the frequency, and the smaller the near field, the greater the deviation angle of the far field.

The off-axis intensity distribution is rather complex as can be seen in Fig. 9. The number of maxima and minima in the beam sections decreases steadily from the transducer to x^*_{max}. It should be noted that due to the occurrence of minima in the near field, the possibility that small reflecting structures will be missed cannot be excluded. However, it can be shown experimentally that the minima are much less 'deep' when using pulsed ultrasound than with continuous ultrasound (Fig. 10).

The notion that the amplitude of echos that stem from structures in the near field may not be consistently interpretable should be kept in mind, nevertheless.

e. Resolution

Resolution can be defined as the shortest distance between two reflecting structures that can be detected with an echo system. Two kinds of resolution can be defined, as will be explained below, but it must be stressed beforehand that the actual value of the resolution is very much dependent on the reflectivity of the structures, and on the sensitivity setting of the system. Moreover, since the frequency of the transducer determines the length of the near field and the divergence of the far field, it will be clear that no single value answer can be given to the question of the resolution of a system.

The resolution in the direction of the wave propagation is called the *axial* or *depth resolution*. Structures with reflecting surfaces of at least of the order of the diameter of the beam in the near field will reflect energy from the whole section of the beam. Hence, interference phenomena will not then be involved in the echo amplitude. The amplitude of the echos will determine the depth resolution as illustrated in the left part of Fig. 11. It can be seen that with low reflectivity of the structures or low sensivity of the echo apparatus the depth resolution will be better than with high reflectivity or sensitivity. This is caused by the fact, that the number of periods of the acoustic pulse that can be observed depends on the amplitude of the echo and on the sensitivity setting. The depth resolution is also dependent on the frequency and the damping of the transducer. As follows from equation 7, the higher the frequency, the smaller the wavelength, so the smaller the 'base' of the echo for a particular number of periods. Since the damping determines the number of periods after a single electric pulse at the transducer, the importance of adequate damping for the depth resolution will be clear.

The axial resolution can be measured with an apparatus such as that shown in Fig. 12. Two thin nylon threads are attached in parallel in a micrometer or any other measuring device. The threads are moved apart until two echos can be distinguished.

The other kind of resolution is called the *lateral resolution*, which means the

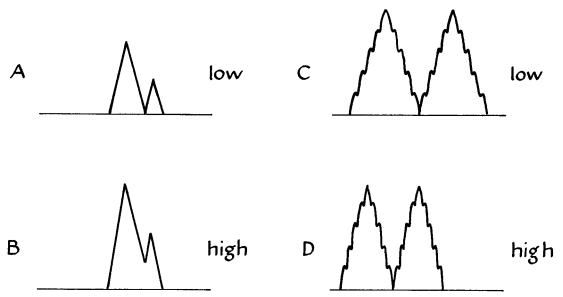


Fig. 11 *Left part*: echoes of low amplitude (A) yield a better depth resolution, than echoes of high amplitude (B), the base width of the latter is larger.
Right part: echoes from a high frequency transducer (D) yield a better depth resolution than echoes from a low frequency transducer (C), the base width of the latter is larger.

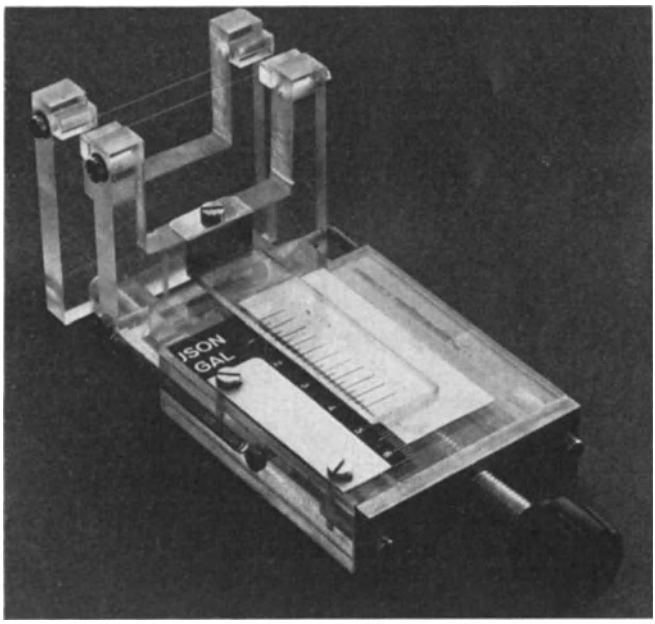


Fig. 12 Apparatus used for measurement of the resolution. The two u-shaped endings contain a 0.1 mm nylon thread. The distance between the threads can be adjusted with 0.1 mm accuracy.

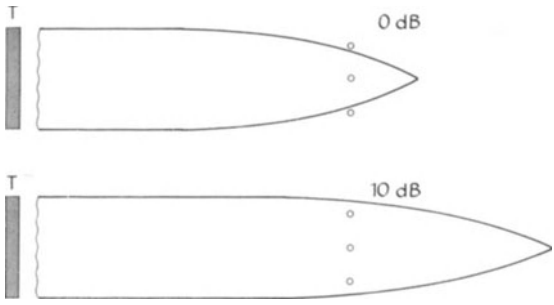


Fig. 13 *Upper part*: three point reflectors can be 'noticed' separately at the 0 dB sensitivity setting.
Lower part: the three point reflectors cannot be distinguished any more at a 10 dB higher sensitivity setting.

resolution normal to the direction of the beam axis. The lateral resolution is in the main dependent on the shape of the sonic beam, and, due to the energy distribution in a beam section, also on the sensitivity, or reflectivity.

In other words, the effective beam width is the main cause of a limited lateral resolution. This statement will be explained now with the help of Fig. 13. In

this figure the sonic beam is displayed as measured with a particular sensitivity setting of the echo system. Since the decibel is a relative measure (see equation 14) it is permissable to take one setting at zero when comparing two settings. With a higher sensitivity the beam is relatively extended because subthreshold echos at the 0 dB setting become suprathreshold at 10 dB. As can be seen in Fig. 13 the three point reflectors can be displayed separately with the 0 dB setting but not with the 10 dB setting.

The shape of the sonic beam can be changed by focussing using a curved transducer or an acoustical lens. The effective beam width can then be decreased in a limited part of the beam, but the divergence in the far field is increased thereby. The largest region of decreased beam width is obtained by focussing at the transition of the near field and the far field, in practice a beam diameter of about one half of the original is obtained. The lateral resolution can be measured with the same technique as illustrated for the axial resolution in Figure 12. However, now the threads are both placed at equal distance from the transducer. The transducer, or the meter, are moved in a direction normal to the beam axis, and the separation of the threads is changed until the echo amplitude decreases by a prescribed (e.g. 25%) percentage going from one thread to the other.

Physical conditions for optimum echo-ophthalmology

The choice of the frequency of the transducer is based on the conditions formulated for the axial resolution. The thickness of 0.55 mm of the cornea and the thickness of the retina are the bulbar dimensions to be dealt with. Hence, the axial resolution ought to be about one quarter of a millimeter. A common diagnostic probe will contain a transducer not damped too well, let us say in 7 periods. The velocity of the ultrasound in ocular tissue is about 1500 m/sec and it follows from equation (7) that

$$\nu = c/\lambda \tag{21}$$

Now the optimum frequency can be calculated. If one defines the axial resolution as the distance of 0.25 mm corresponding to a separation of two echo pulses equal to one half of the base width of a pulse, then one period will be 0.07 mm or 7.10^{-5} m, which yields with equation (19) a frequency of 20 MHz. The probes for ocular diagnosis are mostly in the range of 10 to 15 MHz. For orbital diagnosis a frequency of 6 to 10 MHz is commonly chosen. Since no condition based on geometrical properties can be given for the orbit, the choice is guided by the presence of a large attenuation in the orbital fat (Table I). According to equations 16 and 14 the logarithmic attenuation is inversely proportional to the frequency, so a relatively low frequency is advisable

The lateral resolution is determined by the diameter of the sonic field. In the near field the shape is cylindrical, whereas in the far field a cone shaped divergent beam is present. The transition of near field to far field should be situated not farther than the largest depth of the structures of interest. We can now calculate the diameter of the transducer yielding a near field of at least 50 mm length, which is suitable for ocular diagnosis. It follows now from equation 20, that

$$D = \sqrt{(4\lambda\, x^*_{max})} \tag{22}$$

For a 12 MHz transducer $\lambda = 0.125$ mm, x^*_{max} is set at 50 mm so $D = 5$ mm. The effective beam width of such a 12 MHz, 5 mm probe is about 4 mm which is rather large compared with the dimensions of the eye. The actual beam width for the concave and convex structures of the globe is however much smaller. In the most simple situation the ultrasound probe is applied paracentrally, so the plane progressive and cylindrically shaped wave arrives at the posterior retinal surface. (The small negative refractive power of the proximal sclera is neglected). The reflection is shown in Figure 14. A spherical concave mirror will reflect the plane wave into its focal point at r/2, with r being the radius of the sphere. A little geometry shows that the beam width arriving back at the probe has become three times larger. As can be seen from Figure 14 this implies that the effective beam width in this situation is one-third of the diameter of the applied sonic beam. The general formula for the effective beam width arriving back at the transducer from a concave mirror is given by (cf. FRANKEN, 1961):

$$D_e = \frac{D\, r/2}{L - r/2} \tag{23}$$

D_e = effective beam width
D = diameter of the transducer
L = distance from transducer to mirror
r = radius of mirror

It can be seen with this formula, that reflections from the macular zone will have a very small effective beam width. Assuming a radius of curvature of 0.5 mm, it appears that D_e becomes 5×10^{-2} mm, which causes an apparent attenuation of 52 dB. Hence, it can be concluded that the first posterior pole echo stems from the paramacular retina. Central application to the globe means through

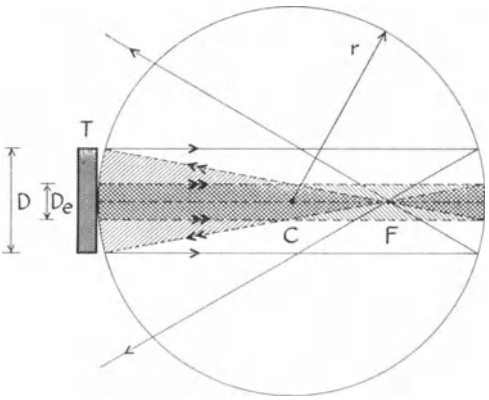


Fig. 14 Reflection of a plane progressive wave at a spherical surface (retina). D = diameter of the transducer, equal to the diameter of the sonic field, D_e = effective beam width, C = centre of the globe, F = point of focus, r = radius of the globe, T = transducer.

the lens, so the picture will be more complicated in that case. The acoustic lens power can be calculated with the formulas from optics. For a first idea the lens will be treated as a thin lens, so the image focal distance is given by:

$$\frac{1}{f_L'} = \left(\frac{c_0}{c_L} - 1\right)\left(\frac{1}{r_1} - \frac{1}{r_2}\right) \tag{24}$$

f_L' = image focal distance
c_0 = sound velocity in aqueous and vitreous (1530 m/sec)
c_L = sound velocity in lens (1640 m/sec)
r_1 and r_2 = radii of lens surfaces, measured from object space to image space. For the theoretical eye of Gullstrand $r_1 = 10^{-2}$ m, and $r_2 = -6 \times 10^{-3}$ m so it follows that:

$$f_L' = -53.5 \times 10^{-3} \text{ m} = -53.5 \text{ mm}$$

Hence, due to the large sound velocity in the lens, the acoustic lens power is negative.

The thick lens formula is given by:

$$\frac{1}{f_L'} = \left(\frac{c_0}{c_L} - 1\right)\left(\frac{1}{r_1} - \frac{1}{r_2}\right) + \left(\frac{c_0}{c_L} - 1\right)\frac{c_L\, d}{c_0\, r_1\, r_2} \tag{25}$$

f_L' = focal distance from the image principal plane
d = lens thickness, 3.6 mm

Now it is found that $f_L' = -52.5$ mm, so the thin lens formula is sufficiently accurate. The lens being situated 5 mm posterior to the cornea and the axial length of the eye being 25 mm, the effective beam width appears to be 0.29 times the diameter of the incident beam. However, it should be noted that this calculation is based on normal incidence, i.e. along the optical axis of the eye.

Oblique incidence, or paracentral passing through the eye lens generates a much lower figure for the effective beam width. It has been shown experimentally that the refraction of the lens increases considerably at the equator, so it must be stressed that the lens should be avoided as much as possible in ocular diagnosis.

3. THE PULSE-ECHO TECHNIQUE (A-SCAN AND B-SCAN)

The interval between two ultrasound emission pulses has to be within two limits. The lower limit is determined by the time that the ultrasound takes to travel to and from the most distant reflecting surface. The longest interval length is given by the properties of the oscilloscope (Fig. 15). With the repetition rate of the pulses too low, the brightness of the cathode ray tube becomes too low to yield a clearly visible trace. The interval length and therefore the repetition rate is made with a trigger system (Fig. 15) and this rate falls within a range of 50 to 2000 times per second. In purely diagnostic applications the lower rate limit is to be preferred, because the patient is examined with the least sonic energy then. As can be seen in Fig. 15 the trigger system starts the display oscilloscope via a time base control. Simultaneously, the pulse generator is activated and the transducer produces the acoustic pulse, receives the echoes, and the electrical potentials evoked by them are amplified and in most systems rectified. The resulting signal is fed to the vertical (y) deflection system of the

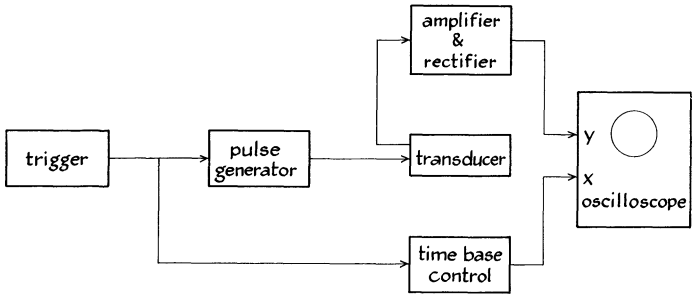


Fig. 15 Block diagram of the pulse-echo technique (A-scan).

oscilloscope. Since the trace on the oscilloscope screen is in fact a light point moving with constant velocity it will be clear that the echoes are displayed as vertical deflections at the proper distances from the starting point.

The real distances can be obtained by measuring the time interval between the starting point and the echo. This is mostly done by means of an electronic oscillator with a very stable frequency, e.g. by counting the number of periods of a 50 MHz oscillator the time can be measured with an accuracy of 20 nsec. The distance between two events is then found by multiplying this time by the sound velocity of the structure being examined.

An alternative method is to calibrate the time base of the oscilloscope at a particular sound velocity. The distance can then be read from the screen directly. However, when different velocities are involved in a single trace this method is not very suitable. A complication is the socalled zero point error, which is in fact the time elapsed between the trigger pulse and the acoustic pulse. Since both pulses are visible on the A-scan oscilloscope in a single broad waveform, the starting time of the acoustic pulse has to be determined by the multiple reflection technique or should be avoided in length measurements if possible (see section examination techniques).

The echo signal is called the radio frequency, or R.F. signal, and after rectification, the video signal. The R.F. signal should be used in exact length measurements, whereas, the video signal is used in diagnostic applications. The video signal is thus only an upward deflection of the oscilloscope trace containing the R.F. (rectified) oscillations. In order to simplify the picture, in most A-scan systems an electrical low-pass filter that smoothes the shape of the echo pulses can be used (Fig. 16).

The echo system as given so far is usually called the A-scan system in diagnostic applications. A more complicated system based on the principle of radar and sonar systems is called the B-scan system. The principle is explained with the aid of Fig. 17. The transducer is directed towards a structure yielding a front and a back surface echo. When moving the transducer along the structure the A-scan oscilloscope will continuously display two echoes with only variations in place and amplitude. In a B-scan system the amplitude of the echoes deter-

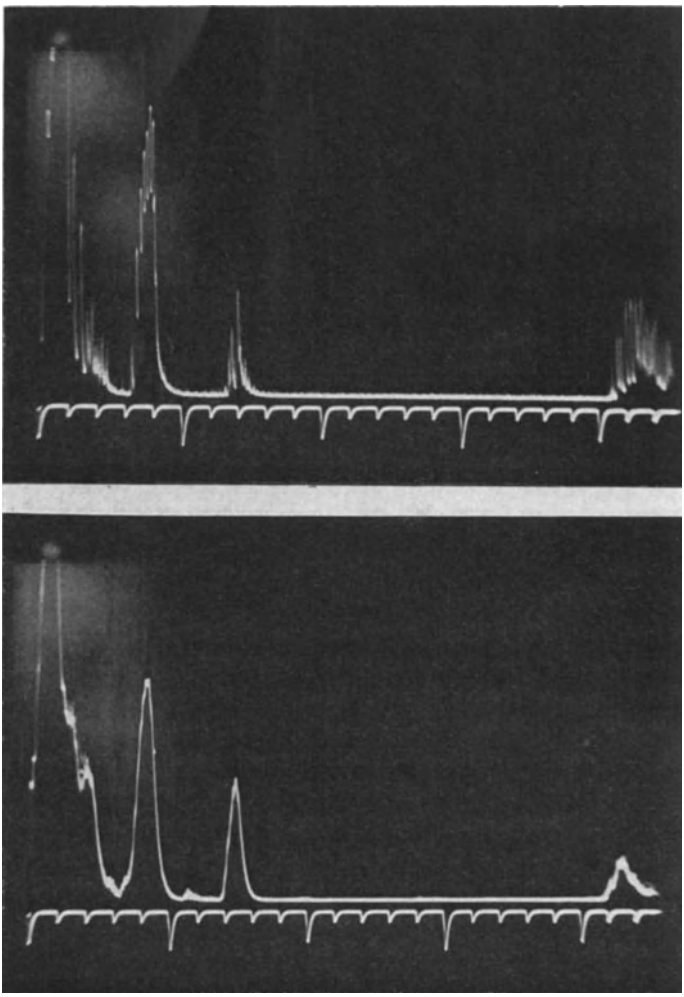


Fig. 16 Comparison of the video signal with low-pass filtering (lower part) and without low-pass filtering (upper part).

mines the brightness of the spot and when no echoes are present the trace is dark.

Moreover, the whole trace is displaced synchronously with the transducer in such a way that horizontal and vertical distances on the oscilloscope screen are proportional to the real distances. By this means the reflecting interfaces in a structure are displayed in a two dimensional picture. It should be stressed that in contrast with röntgen techniques the echo technique yields a sagittal section of the structure and not a lateral one.

The amplitude of the individual echoes, and the texture of an echo pattern contain the information for differential, or absolute, diagnosis. The pattern of

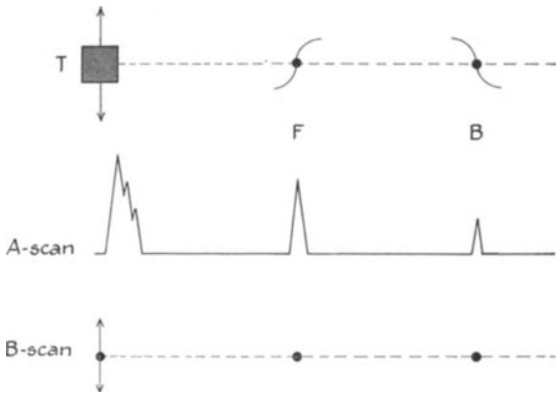


Fig. 17 Scheme of the B-scan technique. Above: T = transducer moving (linearly) along a structure. Echoes are received from the front (F) and back (B) surfaces, as displayed in the middle trace. Below: The B-scan oscilloscope trace is dark except at the occurence of an echo, the trace moves synchronously with the transducer.

a normal eye is shown in Fig. 18. However, it is essentially impossible to get a linear transformation from the echo amplitude to the gray scale on a photographic plate (cf. BAUM, 1971) and the range covered by the gray scale is too small to contain the whole range of echo amplitudes in a single B-scan picture. Modern techniques to convert the black and white B-scan displays to a three to eight color display either direct from the video signal, or indirect via iso-

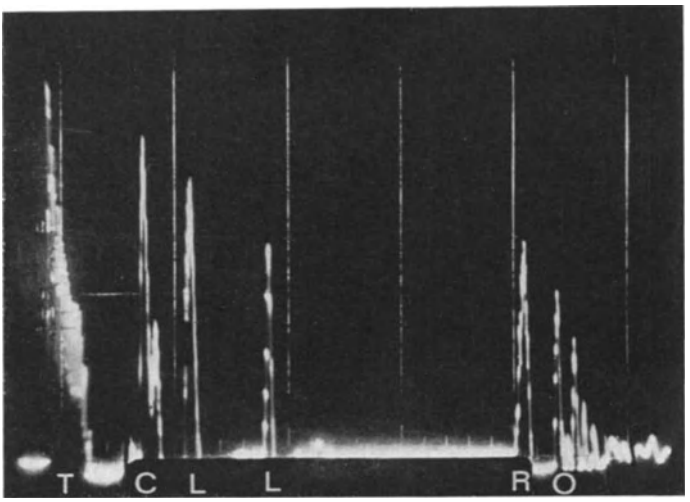


Fig. 18 Echopattern of a normal eye. From left to right: transducer pulse (T), cornea echo (C), anterior lens (L) echo, posterior lens echo (L), retina + sclera echo (R), orbital fat echoes (O).

densitometry of a black and white photographic picture are already a valuable step towards better interpretable B-scan pictures. At the moment the best way to perform an examination is to make A-scan and B-scan pictures simultaneously. By that means the most adequate position of the probe can be determined during the B-scan procedure and the A-scan pictures are taken at the same time, thus giving the best display of the amplitude information of the echoes. As will be shown later on, it is possible to mark the position of the probe on the B-scan picture, so the A-scan trace can be exactly localized afterwards.

Attenuation in the tissues to be examined is sometimes compensated for in diagnostic A-scan systems. The so called time varied gain control is a gradual increase in the amplification starting from the sound emission pulse.

Since the attenuation is in general not predictable and, moreover, not very strongly present in ocular diagnosis, this technique is not much applied. Special amplifiers are in use to obtain a large range of echo amplitudes that can be displayed in a single A-scan or B-scan picture. An amplifier with a logarithmic gain, which yields a relative compression of echoes of large amplitudes is most commonly used (see Fig. 19). This characteristic results in a decrease in the depth resolution, since closely spaced large echoes tend to form broad echo wave forms. In B-scan systems this degradation of the resolution can be partially reversed by differentiation of the echo signal, followed by a pulse shaper. This pulse shaper is useful because the differentiated signal does not display the amplitude information unambiguously and the standard pulses made by this system are optimum for the outlining of the anatomy or pathology on a storage oscilloscope tube. A special type of amplifier has been developed which has, according to the designers, a gain characteristic adapted to the tissue differentiation (OSSOINIG, 1971) by means of the A-scan method.

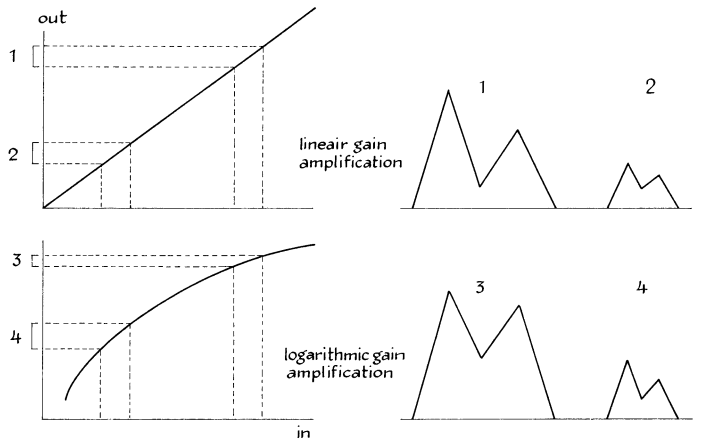


Fig. 19 *Upper part*: left: linear gain characteristic, right: resulting echo pattern. *Lower part*: left: logarithmic gain characteristic, right: resulting echo pattern. Note the relatively small difference between the amplitudes of the high echoes, i.e. decreased resolution.

Several characteristics of the A-scan and B-scan systems and of the probes used with these systems have to be examined to obtain reliable and reproducible data.

The *time base* of the A-scan apparatus can be calibrated by applying the probe to a perspex pillar equivalent with a specified distance in a 37° C saline solution. By this means the system is calibrated at the velocity of the ultrasound in the aqueous and vitreous humour.

The *zero point error* should then be corrected for also, this is done by applying the probe to a metal plate that yields at least two multiple echos. The mutual distance between the echoes is essentially constant because the ultrasound travels exactly the same distance several times. Most A-scan systems contain a very precise crystal oscillator (clock) that can be used to calibrate an adjustable metric scale (Fig. 20). The latter method has the advantage that non-linearities in the time base control, or in the oscilloscope deflection system are ruled out. Other characteristics of the A-scan system are dependent on both the electronic part and the transducer, so the necessary calibration procedures must be repeated for each probe.

The *frequency* of a transducer determines both the shape of the sound field (see section 'The ultrasonic field of a flat transducer') and the absorption. The frequency of diagnostic probes is mostly not much different from the value stated by the manufacturer, but if necessary the frequency can be measured by comparing the RF oscillations with the crystal clock.

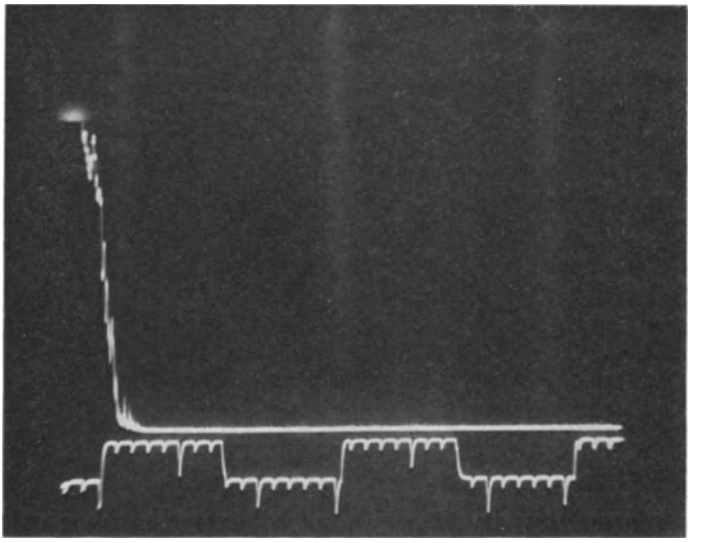


Fig. 20 Example of the calibration procedure of the metric scale of the A-scan system. The square wave is from a 50 kHz oscillator (20 μsec period time), a constant velocity of 1530 m/sec is calibrated, so one scale division equals one milimeter ocular tissue.

The *sensitivity* of an A-scan system is dependent on the intensity of the emitted sound pulse (which is often fixed), the amplification of the receiver, and the effectiveness of the transducer. The calibration of the sensitivity is carried out by the measurement of the attenuator setting yielding an echo of a particular magnitude. Several methods are in use, such as a glass block in water at 25 mm distance from the probe, a glass plate yielding multiple reflections, a metal reflector placed at a variable distance from the probe in a parafin oil bath. The most simple and elegant method is to use the distal sclera echo of a healthy eye to calibrate the instrument. According to TILL & NEUMANN (1971) the data from 18 eyes displayed a deviation of only 2 dB, hence, it can be concluded that a reliable standard has been found. The calibration procedure is the following then: for each probe to be used the attenuation (or amplification) relative to the maximum value is determined yielding a sclera echo of 10 mm, with direct application at the opposite conjunctival tissue and with careful adjustment of the beam axis through the centre of the eyeball.

This is indicated by a maximum of the distal sclera echo, thus ensuring a normal incidence.

The *depth resolution* of the system (cf. section 'Resolution') can be measured, but not adjusted. The only way to achieve a higher resolution with a particular A-scan apparatus, is to find a probe with a highly damped transducer or a transducer of a higher frequency. Most diagnostic systems are a compromise between the sensitivity and the length of the acoustic pulse (and thus the depth resolution). Therefore a better resolution is exchanged for a decreased sensitivity. A very simple method for measuring the depth resolution is to use two

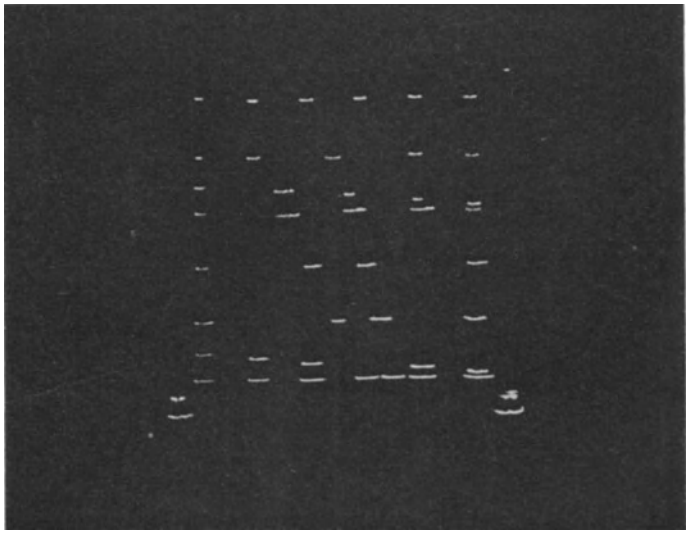


Fig. 21 Display of a 'figure' composed of 0.1 mm steel threads to determine the lateral and axial resolution of a B-scan system. Maximum distance 10 mm, minimum for lateral resolution 5 mm, minimum for axial resolution 0.8 mm.

thin nylon threads stretched between two plates yielding a V-shape. The probe is moved along the threads until the two echos are still just separately visible. It should be remarked that the calibration may depend on the sensitivity setting. The *lateral resolution* of the system is of great importance for the quality of the B-scan system to be used with the A-scan system. The lateral resolution will depend on the diameter of the transducer, on the frequency of the transducer (cf. section 'Resolution') and on the effective diameter of the sound field. The latter dependence means that both the distance from the probe to the reflecting surface and the sensitivity setting of the A-scan system are involved. The resolution can be measured with the two threads as mentioned above, but now the threads are both in a plane normal to the beam axis. A method suited for B-scan systems is displayed in Fig. 21. Several threads are stretched between two plates and the distances are chosen such that the lateral and the axial resolution can be examined up to 5.0 mm and 0.8 mm, respectively.

5. EXAMINATION TECHNIQUES

The A-scan examination is carried out by manual application of the probe (Fig. 22).

The patient is in the supine position, and his eyes are locally anaesthetized with a few drops of 0.2% novesine. The probe is acoustically coupled with the eye or with the eye lids by a drop of methylcellulose. Examination of the globe

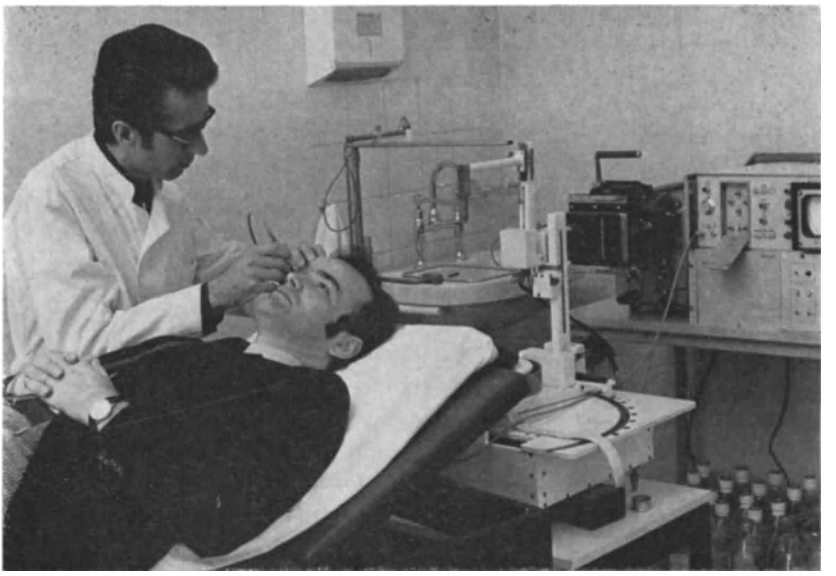


Fig. 22 Manual application of the probe and the position of the examiner with respect to the equipment.

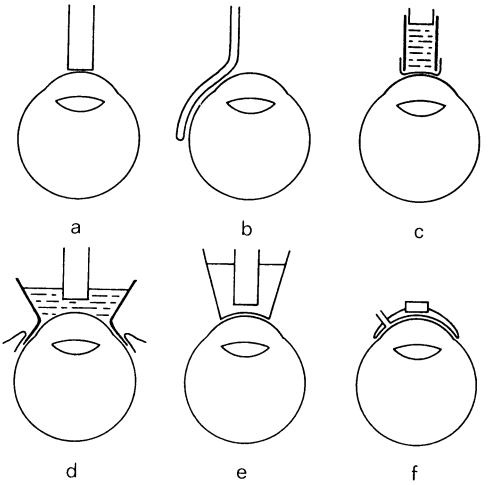


Fig. 23 Various kinds of transducer forms and attributes (THIJSSEN, 1974). a: normal contact method; b: curved flat-stalked probe; c: water stand-off; d: sclera-lens water bath; e: combined ophthalmoscopy-echography probe; f: suction-cup probe.

is always performed by applying the probe at the cornea or sclera, whereas, examination of the orbit is done by transbulbar of parabulbar application. With direct application at the globe, the cornea, the aqueous humour, the iris and the far periphery of the retina cannot be examined because of the broad pulse from the sound generation and the internal reflections within the transducer. The anterior part of the globe can be examined by using a water bath or intermediate water column as illustrated in Fig. 23 d, and c. The periphery of the fundus can be examined with a special type of probes. These probes are flat-stalked and can be brought beyond the eye equator (Fig. 23b). So, the sound travels the opposite way then from the posterior to the anterior part of the globe.

The examination is carried out systematically by applying the probe at different positions but always perpendicularly to the globe. The scheme for recording the information that is in use at our clinic is shown in Fig. 24. Since the probe is always applied in such a way that the axis of the sound beam passes through the centre of the globe, marking the position of the probe at the sclera is equivalent with marking the site of reflection at the fundus. We have chosen the latter method because it is quite analogous then with the record of the ophthalmoscopic examination. The probe is applied at the apex of the cornea and the various quadrants are explored from centre to equator in 5 mm steps corresponding approximately to the probe diameter. The large difference with ophthalmoscopy is that now all the information of the three dimensional object has to be indicated in the scheme. This problem is solved by indicating in the fundus picture only the presence of pathological echos and in a second picture the localization in depth. So the cross-sectional scheme of the globe and the orbit is used to indicate the meridional section and the localization in that section of the major site of pathology.

Naam pat.: Naam aanvrager:

Geb.datum: datum onderzoek:

Klinische diagnose:

Reden onderzoek

Trauma: ☐ ja ☐ nee

Röntgen foto: ☐ ja ☐ nee

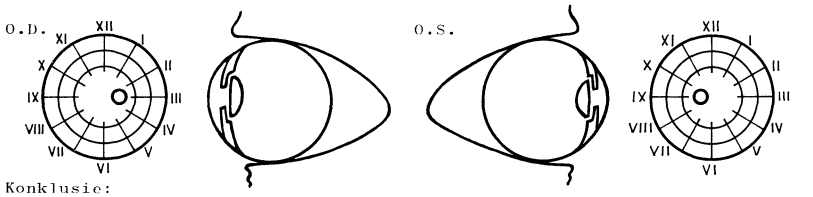
		degene-ratie	ont-steking	bloeding	cyste	tumor	corp.al.
bulbus	cornea						
	iris						
	lens						
	corp.cil						
	glasvocht						
	netvlies						
	ablatio						
orbita							

\+ indien zekerheid bestaat

\- indien diagnose niet vaststaat

A-scan. O.D. afst. cornea-achterz. lens ...mm; oogas ...mm; refr. ....D

O.S. ...mm; ...mm; ....D



Konklusie:

B-scan.

OD	meridiaan	OS
	6-12 uur	
	7- 1 uur	
	8- 2 uur	
	9- 3 uur	
	10- 4 uur	
	11- 5 uur	

Konklusie:

Fig. 24 Scheme in use at our clinic to indicate the A-scan data. The fundus projections are used to mark the incidence of the beam axis in fundo, the sagittal sections are used to indicate the localization of pathology in a meridional plane.

The B-scan examination has been principally explained in the section 'the Pulse-echo technique'. The ultrasound probe is moved by mechanical means along the eyes. The acoustic coupling is made by a water bath. The basin is formed by glueing a plastic drape around one eye or both eyes of the patient. We are currently using the following procedure to prepare the drape. In the center of one quarter of a large drape (3M-company, 1060) a small drape (3M-company, 1035) is glued with the non-adhesive side towards the large drape. Since the large drape is non-adhesive too, the two drapes are glued

together with a very thin double sided adhesive plastic leaf (Neschen, Gudy-P). Next an oval opening is made in the centre of te rectangular small drape. According to our experience the two drapes do not loosen within one hour of examination provided the saline solution that the basin is filled with is at room temperature. The skin of the patient is cleaned with a 70% alcohol solution and dried afterwards. Then the cover leaf of the small drape is removed and the drape is glued to the face of the patient starting in the centre, i.e. at the nose, next towards the corner of the eyes, and at last to the forehead. The result of this procedure is shown in Fig. 25, as can be seen the basin is completed by clamping the drape around a metal ring. The patient is resting with her head at a ring shaped cushion, and is fixating a small bulb straight above the centre of the B-scan apparatus. The B-scan system has been described elsewhere (THIJSSEN, 1971; THIJSSEN & BAKKER, in preparation). The mechanical move-

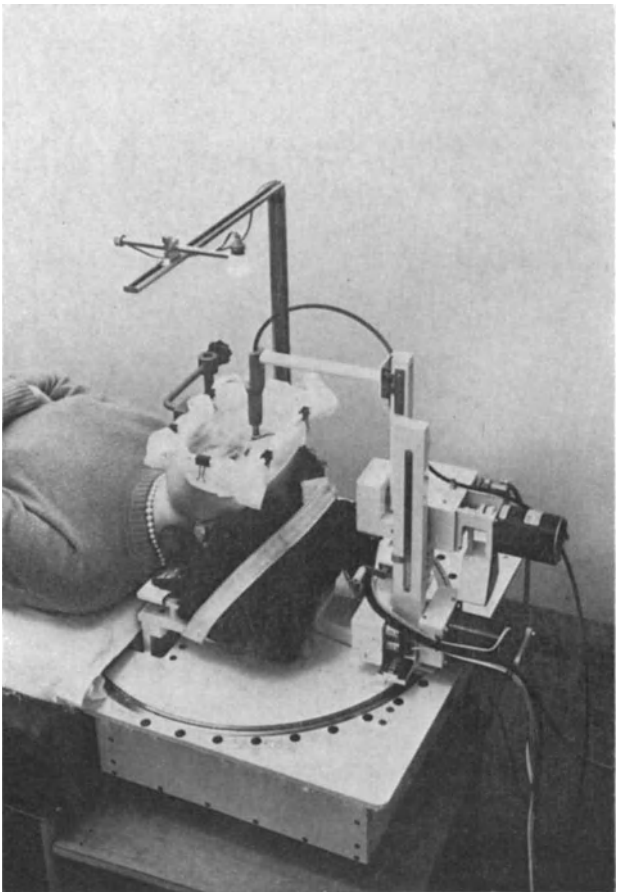


Fig. 25 The water basin made of plastic drape in use for a B-scan examination and the mechanical part of our B-scan system (THIJSSEN, 1971).

ment of the ultrasound probe can be made in three distinct ways, as illustrated in Fig. 26, i.e. linear scan, sector scan, and arc scan.

Fig. 26 Three principal scan modes.
a: the linear scan; b: the sector scan; c: the arc scan.

These are the simple scan modes, but most B-scan systems are able to perform compound scanning, e.g. linear-sector scan, or arc-sector scan. The simple scan modes yield a B-scan picture most rapidly. But as the eye media are rather curved the outlining is not complete, and it has been shown experimentally (Fig. 27) that the linear scan mode is a good choice for simple scanning. The linear scan mode displays distortion of the anatomy of all global structures equally, whereas the orbit is displayed the most reliably. The linear scan has still another advantage, i.e. the ability to perform binocular scan pictures, thus enabling differential diagnosis. Neither the arc scan nor the sector scan are very well suited for this purpose. Concluding that the linear scan mode is to be preferred, the choice of the secondary scan mode in compound scanning is not

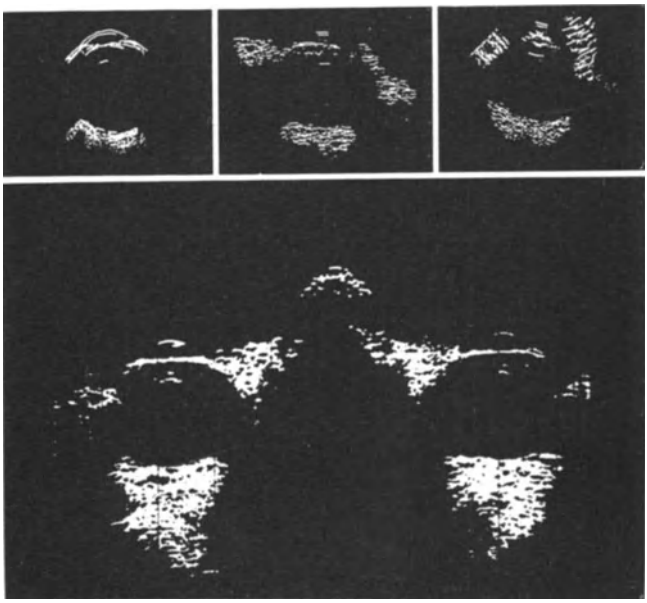


Fig. 27 B-scan picture resulting from the three simple scan modes (Thijssen and Gommers, 1973).
Upper part: left: arc scan, centre: linear scan, right: sector scan.
Lower part: binocular B-scan picture.

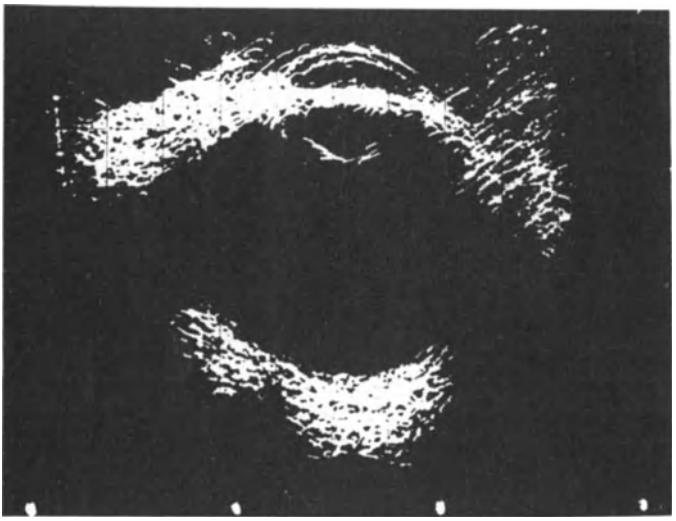


Fig. 28 B-scan picture resulting from a linear-arc compound scan (THIJSSEN & GOMMERS, 1973).

very crucial. Compound scanning is performed in order to get a more complete anatomical outlining. This is achieved by making excursions with the secondary scan mode at various positions arrived at with the primary scan mode. In this way a structure is 'hit' by the sonic beam several times and it will reflect a detectable echo when the beam axis is (nearly) perpendicular to the surface one or more times. The result obtained by linear-arc compound scan with our B-scan system is shown in Fig. 28.

The choice of the position of the scan plane relative to the eye to be examined is governed by the expected localization of the pathology. There are two reasons to make a series of scans, e.g. in case of unknown localization and in case of extensive pathology. Series of scans in parallel with the horizontal or vertical meridian are not adequate, because most of the acoustic energy will be reflected out of the scanning plane by the spherical structures of the globe. Meridional sections are therefore to be preferred.

6. LIMITATIONS OF DIAGNOSTIC ACCURACY

The two kinds of information present in an echo are the appearance of the echo and the absolute or relative magnitude of the amplitude of it. Although the sonic beam has a relatively large diameter, the echoes can only be interpreted as being reflected by a structure at the beam axis. So the first kind of misinterpretation stems from the effective beam width, and is, therefore, dependent on the sensitivity of the equipment and on the acoustic properties of the object being investigated. In the B-scan pictures a large effective beam width may cause substantial error in the outlining of curved surfaces and in the display

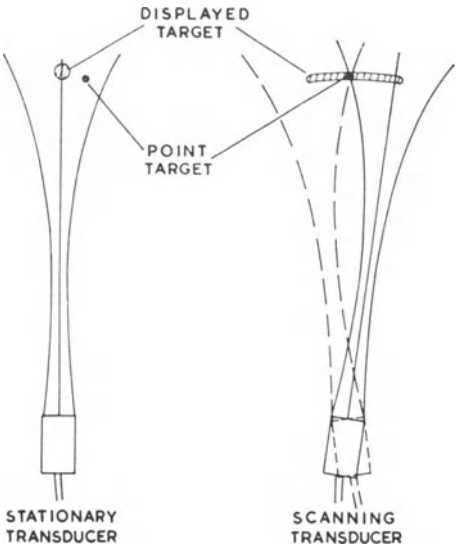


Fig. 29 Illustration of the lateral resolution of a sector scan. A point reflector is displayed as a curved line (KOSSOFF, et al., 1968).

of small reflectors. The case of a small reflector will be clear since the transducer will yield an echo, in passing, over a distance equal to the effective beam width. So a line is displayed instead of a point. This line will be straight with the linear scan mode and curved with the arc, or sector scan modes (see Fig. 29). The same kind of effect will occur when a flat or curved surface is scanned. Hence, the linear scan mode will flatten curved surfaces and the arc and the sector scan mode will display a flat surface concavely or convexly curved.

The axial resolution and the accuracy of length measurements are limited theoretically by the wavelength λ of the ultrasound (cf. section 'Resolution'). Because a single echo consists of several periods of the resonance frequency of the transducer the axial resolution will be worse than this theoretical limit. In most diagnostic equipment the axial resolution is better than 0.5 mm corresponding with 5 periods ($= 5\lambda$) of a 15 MHz transducer. The accuracy of length measurements is governed by the accuracy of calibration of the time base, by the read-out of the A-scan picture and by the accuracy of manipulating the probe at the central position i.e. the optical axis of the eye.

The accuracy can be of the order of a few percent of the axial length.

Within the eye, specular reflections occur from the transitions between the various media; this effect may cause multiple reflection artefacts, both axial and non-axial (Fig. 30). The amplitude information is obscured by various kinds of effects. The most important being the tendency of the surfaces of the global media to reflect the ultrasound like a smooth mirror. This implies that the echo amplitude is much decreased when the angle of incidence deviates from the normal. For this reason the need to search for the position of the probe yielding

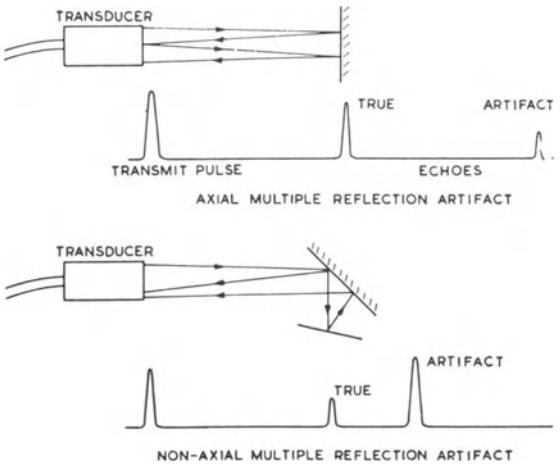


Fig. 30 Multiple reflection artifacts (KOSSOFF, et al., 1968).

the maximum echo amplitude of the tissue of interest should be emphasized. A second cause of unreliable amplitude information is the refraction by the eye lens, especially at its equator. The sonic beam is diverged and refracted obliquely, and therefore the echoes may return from reflecting structures too much off-axis. The eye lens causes still another artefact due to increased absorption in the case of a cataract. This is called the acoustic shadow effect, and it may be very prominent in the echo pattern of the orbital fat. In the B-scan picture the large absorption of the lens may cause an empty space or a 'pathological' texture of the echo pattern in the orbit. In general it can be said that the attenuation in proximal structures obscures the interpretation of the echo pattern of the more distal structures.

7. ECHO-OPHTHALMOLOGY

a. Introduction

The special physical properties of ultrasound permit the examination of lesions that cannot be examined by optical means. In other words, pathology that cannot be examined or classified visually will be the object of echographic diagnosis. The echographic data and the questions to be answered by an echographic examination are of various kinds. *Quantitative* data concern the information about the magnitude and texture of an echo pattern, by using this kind of information the type of lesion can often be characterized. *Topographic* echography is the examination of the location and the dimensions of a lesion. *Kinetic* echography is the study of changes and movements in the echo pattern after voluntary eye movements by the patient. The data from the kinetic examination will contribute to the quantitative information and may complete the diagnosis. *Biometry* is the exact measurement of the dimensions of the globe

for differential diagnosis, for correlation with the optical properties of the eye, or for calculation of the refractive power of a lens prosthesis.

Since quantitative echography may yield the most valuable diagnostic information, it may be emphasized once more that to ensure reproducible and comparable data the techniqual details of the equipment and its adjustments have to be carefully considered. This is likewise the reason why generalization about the echographic characteristics of various pathological conditions is hardly significant. Moreover, carrying out clinical examinations without knowledge of the physical and techniqual principles involved will produce a dissappointment regarding the usefullness of echography.

b. Quantitative echography

The pathology of the aqueous humour is in part similar to that of the vitreous and will not be discussed separately.

The cataract lens is often distinguishable from a healthy lens by the presence of two more echoes between the anterior and posterior lens echoes (Fig. 31). Up to now it seems implausible that any correlation is present between the amplitude of these intermediate echoes and the opacity of the cataract. It will be clear, however, that a cortical cataract will not produce intermediate echoes. In general the posterior lens surface echo is decreased in the case of a cataract, as well as the echo from the posterior pole of the globe. This is the so called acoustic shadow caused by the increased attenuation of a cataract. A secondary cataract is displayed as a sharp and high echo (Fig. 32).

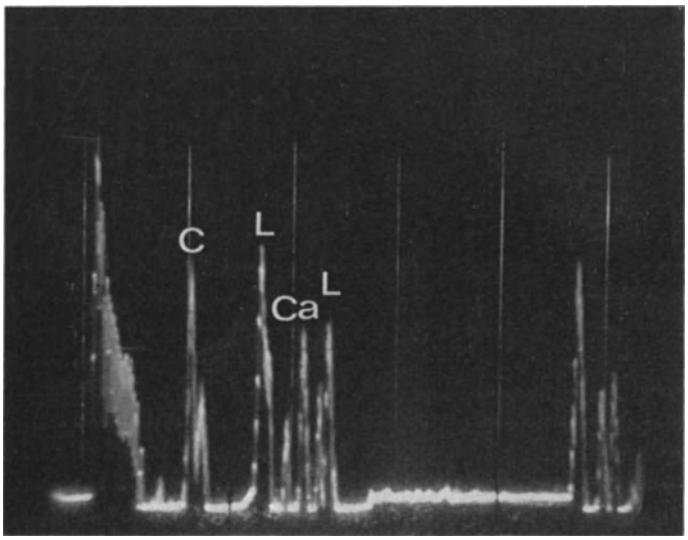


Fig. 31 A-scan picture of an eye with a nuclear cataract, displaying several echoes between the anterior and posterior echoes. C=cornea, L=lens, Ca=cataract.

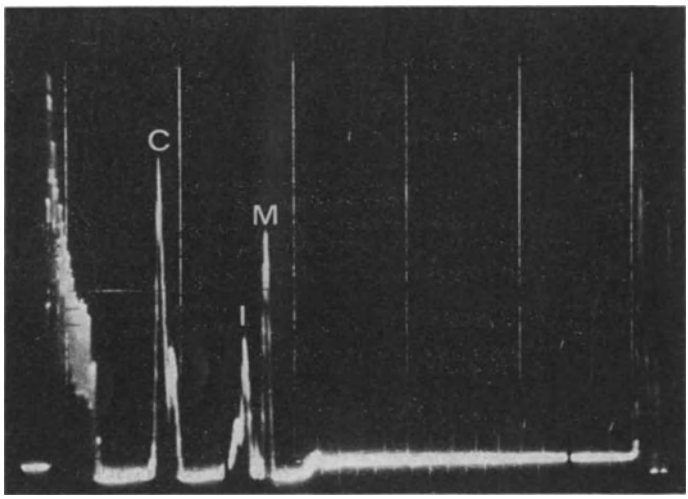


Fig. 32 Secondary cataract (M). C = cornea, I = iris.

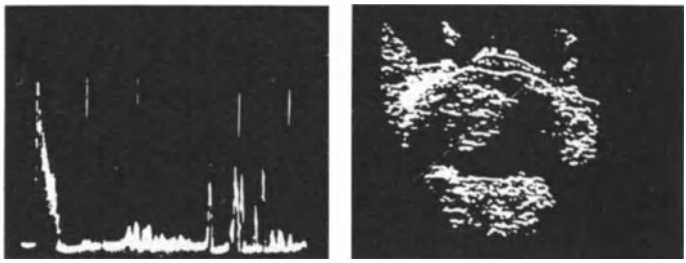


Fig. 33 Ciliary tumor of large extension. The A-scan picture is taken from the opposite limbus through the tumour (in the B-scan picture diagonally from upper right to lower left). Note the slow decrease of the tumour echoes and the high terminal spike, just before the retina.

The pathology of the ciliary body to be examined is generally confined to tumour diagnosis. An example is shown in Fig. 33, the tumour mass is characterized by a medium-size amplitude and regular echo pattern with slowly decreasing amplitude and a high boundary echo. The A-scan picture was taken diagonally through the picture at the right. No retinal detachment could be demonstrated.

A foreign body in the vitreous can be characterized by an echo with an amplitude about equal to that of the posterior global wall echo. This high reflectivity makes it possible to locate a foreign body even in the presence of a haemorrhage. A foreign body is further characterized by a small spatial extension, so it can be found in only a few positions of the ultrasound probe. It may be remarked that non-metallic, and röntgen negative, foreign bodies can be localized as well.

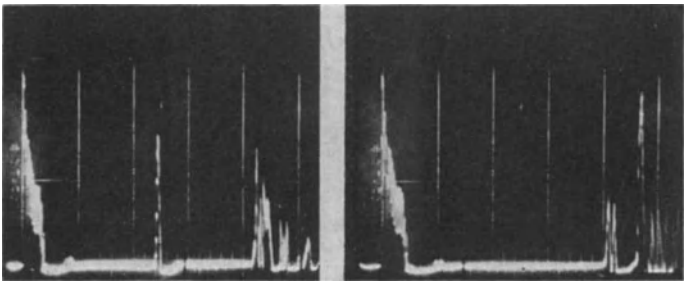


Fig. 34 Retinal detachment: left part: large isolated echo, right part: two echoes from a flat detachment with foldings.

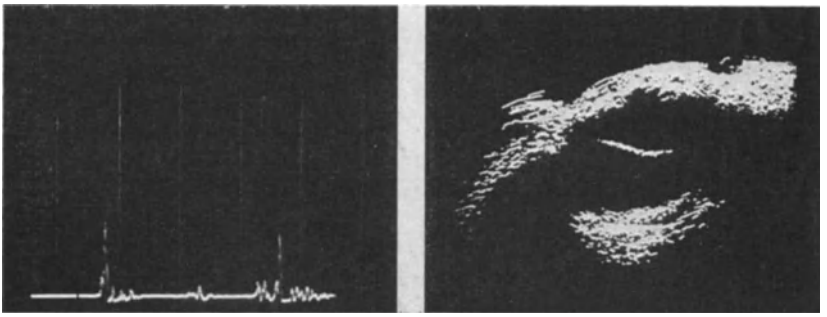


Fig. 35 Vitreous membrane: left part: the A-scan picture is taken vertically through the section displayed in the right part. The eye was atrophic and the vitreous membrane was detached anteriorly well as posteriorly.

Retinal detachments are shown in Fig. 34. In the left picture it can be seen that a detachment yields a large solitary echo. The amplitude of this echo is 6 to 29 dB lower than the sclera echo when both are separately adjusted at the maximum (this can generally not be shown in a single picture). The right picture shows a retinal detachment of the flat type with foldings yielding two or more echos of about equal magnitude.

A solitary echo with an amplitude of much more than 20 dB lower than the sclera echo is often to be ascribed to a vitreous membrane detachment. An example is shown in Fig. 35, this aphakic eye with corneal dystrophy displayed an anterior and posterior vitreous membrane detachment.

Choroidal detachments are very similar to retinal detachments, except for the presence of echoes of very low amplitude in the subchoroidal space (OKSALA, 1967).

The differentiation of retinal tumours from choroidal tumours is not obvious. POUJOL (1970) states that retinal tumours are characterized mostly by relatively high and irregular tumour echos as compared with those of a choroidal tumour. Moreover, the retinal surface echo will be lowered in the case of a retinal tumour due to the wrinkles and other irregularities of the retina. An example

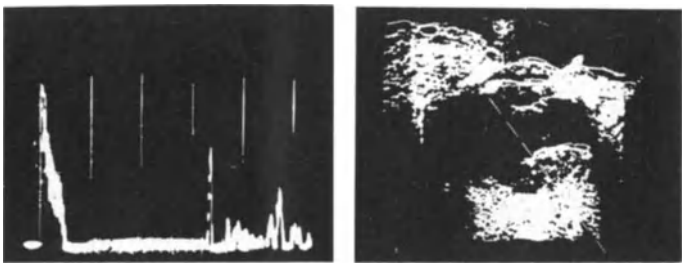


Fig. 36 Choroidal tumour. The A-scan picture displays the large anterior terminal spike, and the slowly decreasing amplitude of the tumour echoes. The trace in the B-scan picture indicates the direction of the A-scan.

of a choroidal tumour is shown in Fig. 36. The large anterior echo is clearly visible, as well as the small and regularly spaced tumour echoes. The direction of the probe application is indicated in the right picture by the striped line.

Intravitreal haemorrhage yields a pattern of irregular and often mobile echoes. The overall amplitude is dependent on the age of the lesion, a recent haemorrhage may yield a 20 to 30 dB higher amplitude than an old one. Thus the haemorrhage can be distinguished from an intraocular tumour by the texture, and additionally, often by the absence of boundary echoes.

Inflammatory opacities of the vitreous yield an echo pattern that is very similar to an old haemorrhage.

Orbital diagnosis is carried out most efficiently by differential diagnosis of the pathological and the normal orbit. The transbulbar and parabulbar orbital echo pattern is composed of gradually decreasing echoes. By using an amplifier with non-linear gain (e.g. logarithmic, see section 'The pulse-echo technique'), the echo amplitude decreases approximately linearly and therefore this property can be characterized by the angle, K, between the horizontal and the line through the echo peaks (Fig. 37). This method has been introduced by OSSOINIG (1969, 1971) and according to his experience an accuracy of better than 90% correctly diagnosed intraorbital tumours can be achieved. In general all tumours are characterized by a decrease in the angle, K, this means that the reflectivity of tumour tissue is less than that of the orbital fat. Further, if correct application is achieved the tumour will yield a proximal and a distal boundary echo (or 'terminal spike'). The scheme of tumour tissue differentiation given by OSSOINIG is based on the equipment which he uses (Kretztechnik, 7200 MA) and cannot therefore be generalized. With this reservation in mind the following differentiation can be found: a cavernous haemangioma produces a regular echo pattern

Fig. 37 Definition of the angle K, after OSSOINIG (THIJSSEN, 1974).

with a large angle K, a sarcoma and a meningioma yield a more irregular pattern with a small angle K, whereas, a serous cyst produces an empty space between the terminal spikes.

It has already been mentioned (cf. section 'The pulse-echo technique') that essential technical problems prohibit quantitative echography by the B-scan method. Although various authors (cf. BAUM 1971, DADD et al., 1973 and COLEMAN, 1973) obtain more or less consistent results with their systems, I have taken the view in this course that the accuracy of the A-scan method is much better and therefore the B-scan method is a completion of the diagnosis by providing accurate topographical and anatomical data.

c. Topographic echography

A topographic examination of a lesion can be carried out with the A-scan method. The great advantage of the B-scan method is however that the pictures display the lesion in an objective and instructive way. Two examples have already been given (Fig. 33 and Fig. 36). A serous retinal detachment can be seen in Fig. 38, the retina is attached to the globe at the blind spot, as can be deduced from the shape of the detachment. An organized vitreous haemorrhage is presented in Fig. 39. The blood is concentrated in the centre of the globe. The patient had an accident with a glass bottle and a splinter hit the eye at the limbus (at the left in this picture). A post-operative B-scan picture of a patient with an eye containing a cataract lens and a retinal detachment is shown in Fig. 40. The cerclage walls are clearly visible and no detachment could be found

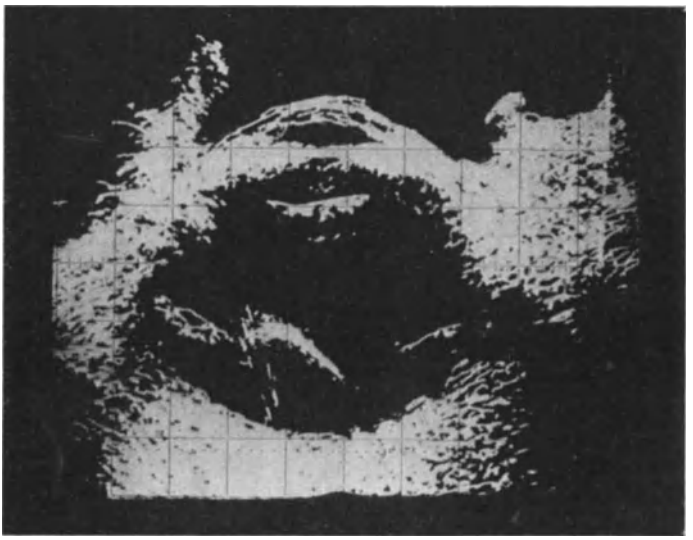


Fig. 38 Serous retinal detachment, note the inclination of the retina towards the blind spot.

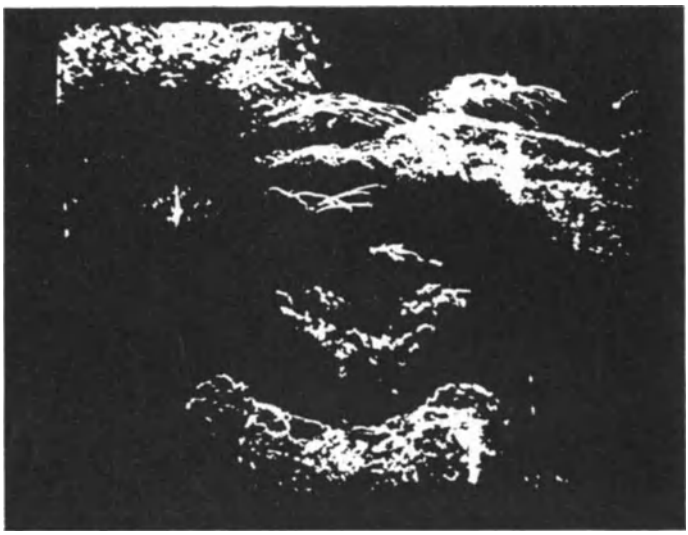


Fig. 39 Organized vitreous haemorrhage, traumatic. (THIJSSEN, 1974).

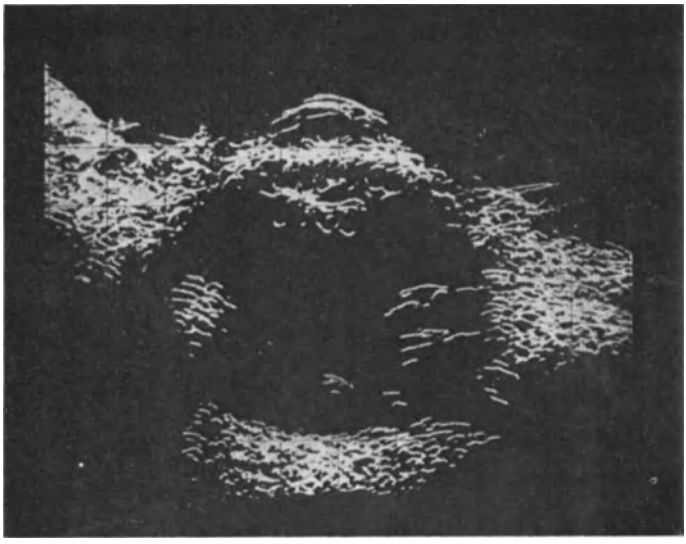


Fig. 40 B-scan picture of cerclage walls after retinal detachment surgery, cataract lens. No evidence of a detachment.

any more. In Fig. 41 a patient suffering from a unilateral exophthalmos is shown. As can be seen, the right orbit contains a nearly empty space, caused by a tumour of low reflectivity. This was confirmed by histological examination to

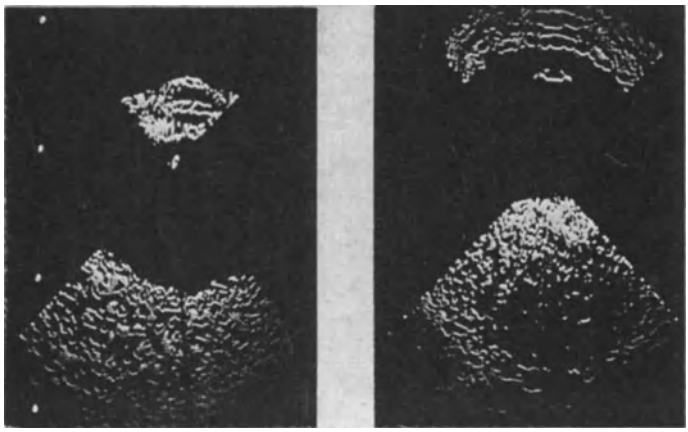


Fig. 41 B-scan pictures of both eyes and orbits of a patient with unilateral exophthalmos. The right orbit contains a space occupying proces of low reflectivity. Confirmed as carcinoma (THIJSSEN, 1974).

be a carcinoma in the orbital apex. Two more examples of topographic echography are shown in Fig. 42 and Fig. 43. The questions to be examined in these pictures could also be defined as functional biometry (see below). In Fig. 42 the right eye of a patient displayed a scleralization of the cornea. As can be seen the process had proceeded for a rather long time, because the thickness of the cornea amounted to 3 mm. The patient demonstrated in Fig. 43 suffered from retinal atrophy and high myopia. It will be clear from this picture that these complaints are caused by a posterior staphyloma.

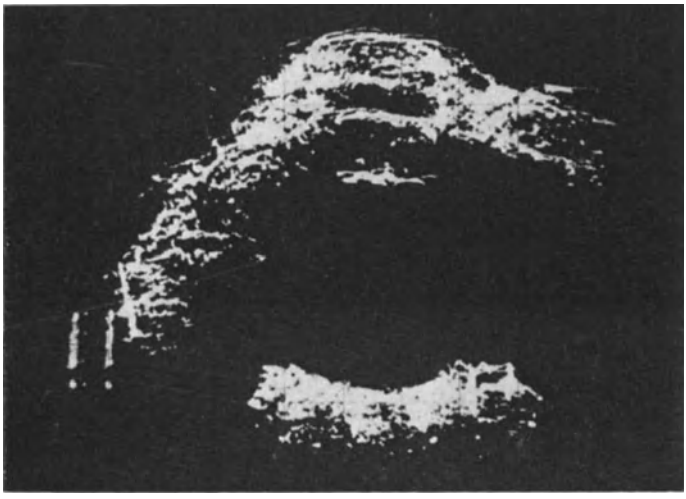


Fig. 42 Cornea scleralization, thickness of the cornea: 3 mm (THIJSSEN, 1974).

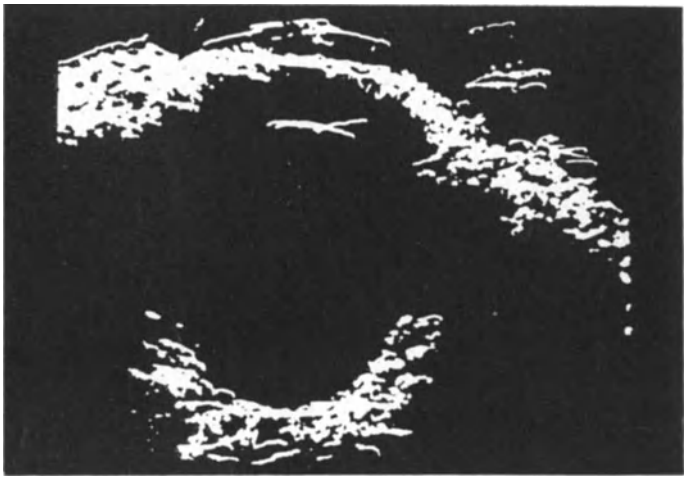


Fig. 43 High myopia and retinal atrophy. As can be seen a posterior staphiloma is present.

d. Kinetic echography

This kind of examination can be defined as a study of the after-movements of echoes from lesions with respect to the normal ocular pattern after a rapid eye movement by the patient. The idea was introduced by BUSCHMANN (1966), who used a suction cup containing a small ultrasound transducer. (cf. Fig. 23 f). OSSOINIG (1969) uses a normal diagnostic probe that is held steadily coupled to the eye. Some diagnostic results of OSSOINIG include: a retinal detachment displays oscillatory movements, visible at the A-scan oscilloscope like an 'unfocussed' echo. Foreign bodies in general show no after-movements. Also solid intraocular tumours are fixed. Orbital tumours are investigated by pressing the probe on the globe and examining the orbital echo pattern. Normal orbital tissue is compressable, hence, the echo patterns will be shortened. A solid tumour mass will resist the pressure of the probe. Most practitioners of echography do not have much experience with the kinetic method. However, the convincing results of OSSOINIG may be a beginning for incorporation of this method in echographic routine examination.

e. Biometry

Echographic biometry is the measurement of anatomical dimensions by measuring the time between echoes and converting this time into distance, provided the propagation velocity of the ultrasound in the tissue is known. The accuracy of echographic biometry is mainly dependent on the examination procedure, since adequate calibration of the A-scan equipment yields a theoretical accuracy of about 0.1 mm (see section 'Calibration procedures'). Direct

application of the ultrasound probe at the cornea is not advisable for two reasons if adequate axial length measurements ought to be made.

Firstly the zero point error, even when corrected for, introduces an unnecessary inaccuracy that can be avoided by a water stand-off, or a water bath (Fig. 20 c and d). Secondly, the pressure at the cornea will cause a nonreproducible deformation and thus another kind of inaccuracy. It may be concluded that a sclera-lens type of water basin will be the most adequate technique. The central position of the probe is also essential for accurate axial length measurements. This is achieved by manual positioning by the examiner, while the patient is fixating with his other eye. The indication that the position is correct can be found in the amplitude of the echoes. The probe axis is correctly aligned along the optical axis of the eye when the echoes of cornea, lens and posterior eye wall are simultaneously at a maximum.

Two kinds of biometry can be defined depending on the purpose of the measurements. *Anatomical biometry* is the measurement of anatomical dimensions of the globe in order to achieve a correct diagnosis of pathological conditions. Examples of this kind of biometry are:

The differential diagnosis of megalocornea and buphthalmos, and of microcornea and microphthalmos.

The diagnosis of glaucoma. HOLLWIG & BOATENG (1969) found a difference of 0.5 mm in the depth of the anterior chamber when comparing eyes suffering from wide angle glaucoma and narrow angle glaucoma, respectively.

The follow-up of progressive myopia and the differential diagnosis of axial and refractional myopia (cf. Fig. 43).

The measurement of the thickness of an opaque cornea before deciding on a cornea transplantation (cf. Fig. 42).

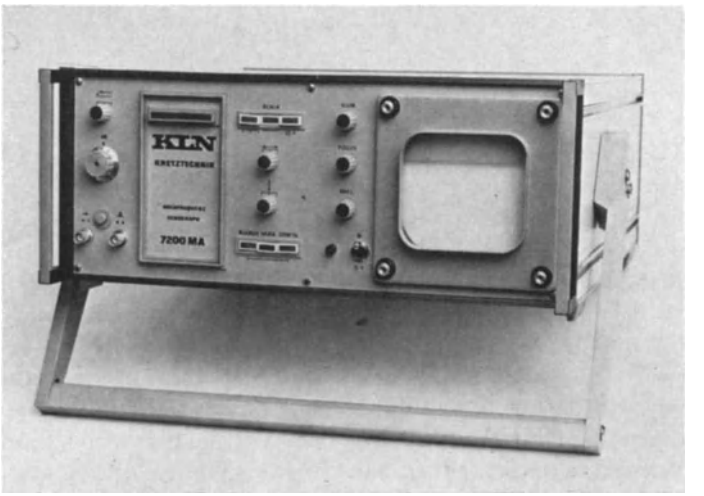


Fig. 44 Kretz, 7200 MA, A-scan system.

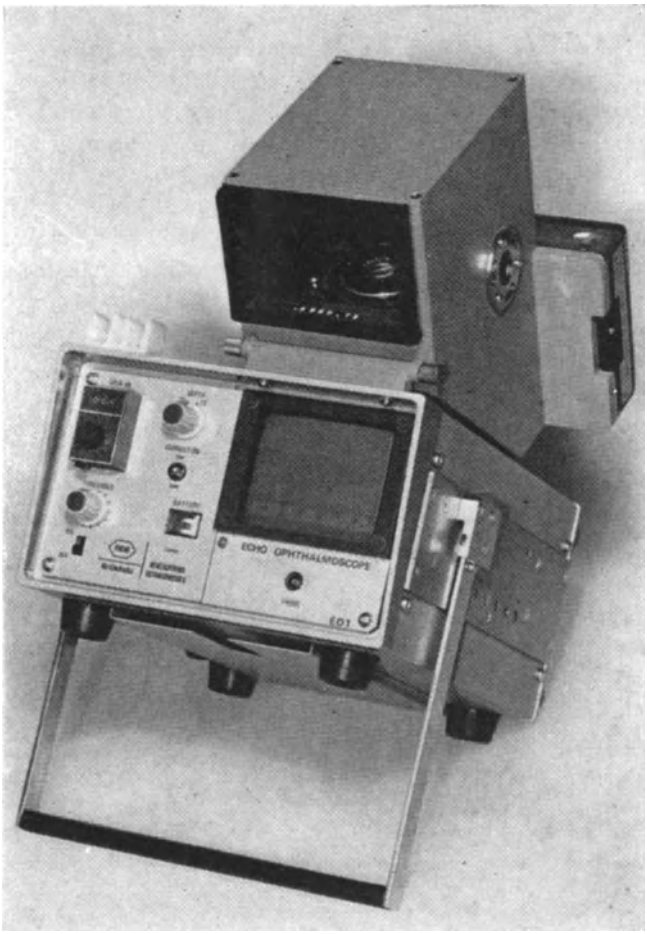


Fig. 45 Roche, Echo ophthalmoscope (A-scan).

Functional biometry is defined as the echographic measurement of the dimensions of the globe in order to calculate the function of the optical system of the eye. The dimensions to be measured are the depth of the anterior chamber, the thickness of the lens and the axial length of the eye. The velocity of ultrasound in the aqueous and vitrous humour is, according to most authors, about 7% lower than in the lens. For this reason it is necessary to add about 0.25 mm to the lens thickness, when the equipment is calibrated at a constant velocity of 1530 m/sec. The thickness of the retina is also added to the calculated axial length, since the first posterior wall echo stems from the retina and the photoreceptor cells are the most distal cells. Generally another 0.5 mm is added to the axial length to correct for this. Summarizing: if the equipment is calibrated at 1530 m/sec the axial length will be:

$$L = L' + 0.25 + 0.5 \qquad (26)$$

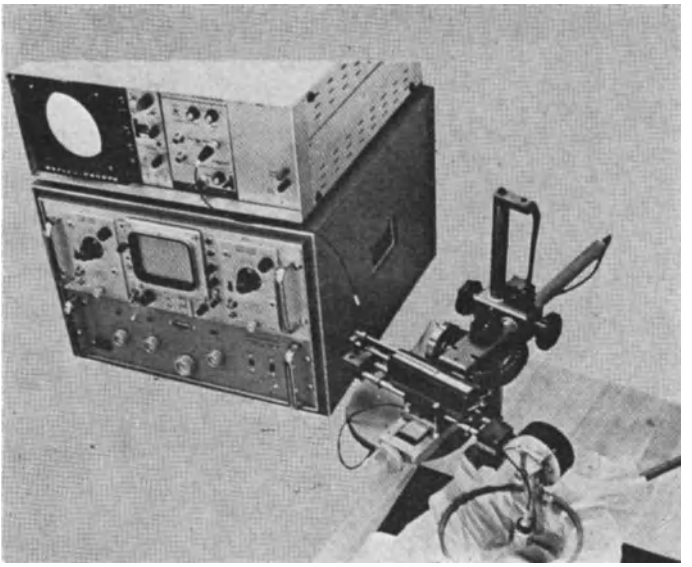


Fig. 46 Sonometrics, Ophthalmoscan (A + B-scan).

L = axial length in mm
L' = measured axial length in mm
When calibrated in time the axial length will be found by:

$$L = 1.530\,(t_2 - t_1) + (t_4 - t_3) + 1.640\,(t_3 - t_2) + 0.5\ (t \text{ in } \mu\text{sec.}) \quad (27)$$

t_1 = time of cornea echo
t_2 = time of anterior lens surface echo
t_3 = time of posterior lens surface echo
t_4 = time of echo from posterior eye wall

Additionally, the error of refraction and the refractive power of the cornea are determined. These data can be used in the calculation of the refractive power of the lens ('thin' lens) cf. THIJSSEN, 1974, OGUCHI & VAN BALEN, 1973, WORST & VAN DER HEIJDE, 1973.

$$D_L = \frac{1}{\dfrac{1}{\dfrac{n'}{L} - K} - \dfrac{d}{n'}} - \frac{1}{\dfrac{1}{D_c} - \dfrac{d}{n'}} \quad (28)$$

D_L = lens power
n' = index of refraction of aqueous and vitreous humour
K = refractive error of the eye at the top of the cornea
d = distance from top cornea to lens
D_C = refractive power of the cornea

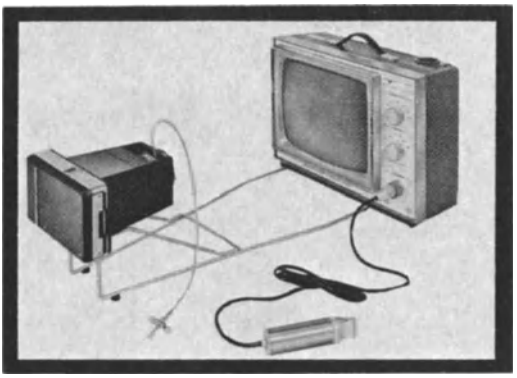


Fig. 47 Storz, Bronson-Turner ophthalmic B-scan.

The eye is considered as a single spherical surface for the relation of the axial length to the total refractive power, i.e. a reduced schematic eye. Equation 28 can be used for correlation studies of the refractive error and the lens power, or even for the calculation of the axial length from the refractive error in case of aphakia, since it can easily be shown with equation 28, that:

$$\frac{n'}{L} = K - D_C \tag{29}$$

Since the implantation of lens prosthesis has become routine in many clinics, the interest in accurate prescription of the refractive power has resulted in many papers giving the adequate optical calculations (cf. BINKHORST, 1972, LEARY, 1971, GERNET, and OSTHOLT, 1973).

It is possible to determine an emmetropizing power of the prosthesis, or an isometropizing power. The latter can be calculated only when the optical and biometrical data of the other eye are also measured. Because most implant lenses or not suited for an exact simulation of the optical properties of the real eye lens, isometropia results in a slight refractive error. By correcting this refractive error by glasses anisometropia is introduced again (about 1%). When the other eye has a considerable refractive error isometropia may be achieved by a combination of an ametropic implant lens and additional correction with glasses (cf. OGUCHI & VAN BALEN, 1973).

8. EQUIPMENT FOR ECHO-OPHTHALMOLOGY

The list of echographic systems as given in Table III may not be complete but the reader will find some technical specifications that can be usefull for a rapid comparison. The quotation marks in the table indicate that the information could not be found in the data sheet of the system, and could not be obtained in time from the manufacturer. I have also mentioned two industrial systems because these are portable A-scan systems with acceptable specifications.

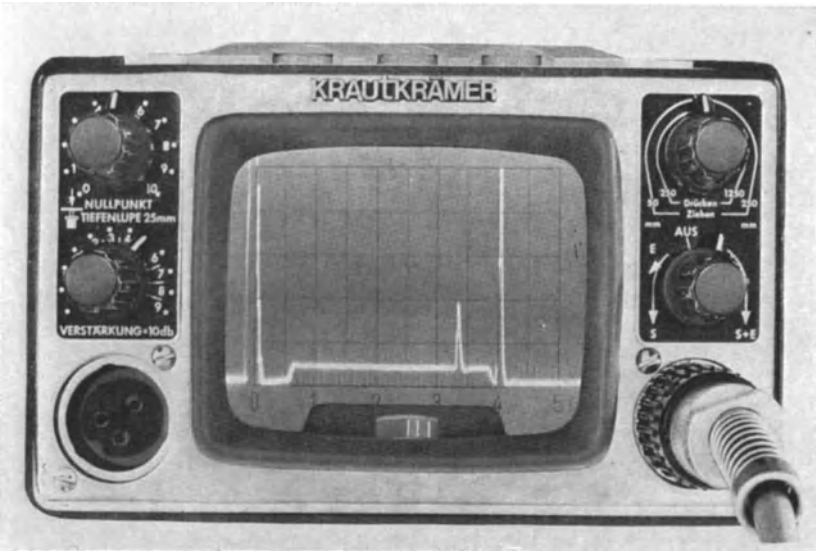


Fig. 48 Krautkrämer, USK 5, industrial A-scan.

TABLE 3

Equipment for echo-ophthalmology; technical specifications

Scan mode	*Firm*	*Type*	*Amplifier*	*Attenuator gain*	*Frequency range*	*Time base calibr.*
Diagn.	Alvar	Ophthalmox	linear	100 dB	6-10 MHz	yes
A-scan	Kretz	7200 MA	special	80	6-10	yes
	Roche	Echo ophthal-moscope	linear	70	6-10	no
	Smith Kline	Ekoline 12	?	80	1-11	no
	Toshiba	ZD-251	?	45	5-15	no
Industr.	EMEFCO	MK 4	linear	80	0,5-10	no
A-scan	Krautkrämer	USK 5*	logarith-mic	80	0,5-12	no
Diagn.	Sonometrics	Ophthalmoscan	linear	50	5-25	yes
A+B-scan	Syst.					
B-scan	Storz	Bronson-Turner B-scan	linear	?	?	no
A*+B-scan	Ultrasonic & Sci. Instr.	Ocular Sonograph	linear	120	5-25	no

* The A-scan is not manufactured by this firm.
* USK 5 has been replaced by a new model USM 2.

ACKNOWLEDGEMENTS

I am very much indebted to dr. Y. OGUCHI for his valuable suggestions concerning the section Biometry; to Mr. C. P. NICOLASEN for his excellent illustrations, to Mr. W. M. NABBE for his technical assistance and to Miss. D. SCHMIERMANN for her consientious preparing of the manuscript.

SYMBOLS

α = absorption coefficient (nepers/m)
α^* = absorption coefficient (dB/m)
α^{**} = absorption coefficient (dB/m, MHz)
B = intensity attenuation (dB)
c = velocity of sonic wave propagation
δ = symbol for partial differentiation (mathemical operation)
d = distance
D = diameter ultrasonic transducer (and sonic field)
D_c = dioptric power of the cornea
D_e = effective diameter of sonic field
D_L = dioptric power of the lens
f_L = image focal length of the lens
I_0 = maximum intensity (at the origin)
I_x = intensity at distance x
κ = adiabatic compression modulus
K = attenuation angle
λ = wavelength
L = axial length of the eye
ν = frequency of the ultrasound
n' = index of refraction of the vitreous humour
p = momentary value of local pressure
p_m = maximum value of local pressure
ρ = mass density
r = radius of curvature
R = refractive error (at the top of the cornea)
θ = angle
t = time
v = momentary value of local velocity
ξ = momentary value of local displacement
ξ_m = maximum value of local displacement
x = distance from origin (or transducer)
x^*_{max} = distance of last axial maximum of the field of a flat transducer
Z = specific acoustic impedance

Alvar, 6 bis Rue du Progress, 93107 Montreuil, Paris, France
Toshiba, 1-6 Uchisaiwaicho 1-Chome, Chiyoda-ku, Tokyo, Japan
KLN - Kretztechnik - Gesellschaft M.B.H., A - 4871. ZIPF, Tiefenbach 20, Austria
Roche Medical electronics division Hoffmann - La Roche Inc., Cranbury, N.J. 08512
Sonometrics Medical Instrument Research Associates Inc., 150 Causeway Street, Boston, Mass.
Storz Instrument Company, 3365 Tree Court Industrial Blvd. St. Louis Mo. 63122
Dr. J. & H. *Krautkrämer* - Gesellschaft, 5 Köln - Klettenberg, Luxemburger Strasse 449. W-Germany
Smith Kline Instrument Co. Ltd., Welwyn Garden City, Hertfordshire, England.
M. Falk and Company Limited, Emefco House, 107 Bell Street, Reigate, Surrey, England
Ultrasonic & Scientific Instruments,
P.O. Box 147, Station 'M', Toronto 21, Ontario, Canada

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