Fundus in diseases of the vascular system

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THE FUNDUS IN
DISEASES OF THE
VASCULAR SYSTEM

by
Howard Slaughter

SENIOR THESIS
UNIVERSITY OF NEBRASKA COLLEGE OF MEDICINE
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CONTENTS

I. Introduction ............................................................................................................................. Page 1

II. The Ophthalmoscope ............................................................................................................... 2
   A: History ..................................................................................................................................
   B: Method of Ophthalmoscopic examination
      1: Indirect Method .................................................................................................................. 4
      2: Direct Method ..................................................................................................................... 5
   C: Types of Ophthalmoscopes used today .................................................................................. 7
   D: The Technique of Examination
      1: Indirect Method .................................................................................................................. 10
      2: Direct Method ..................................................................................................................... 11
   E: Measurement of distances on the fundus .............................................................................. 14

III. The normal fundus .................................................................................................................. 16
   A: The optic disc ......................................................................................................................... 17
   B: The retinal Vessels .................................................................................................................. 17
   C: Color of Fundus ....................................................................................................................... 18
   D: The Macula Lutea ................................................................................................................... 20

IV. Development and Congenital anomalies .................................................................................. 22
   A: Anomalies of the Choroid ....................................................................................................... 22
   B: Anomalies of the Retina .......................................................................................................... 25
   C: Vascular retinal Anomalies ..................................................................................................... 26
   D: Anomalies of Pigmentation ..................................................................................................... 27

V. Pathological Changes ............................................................................................................... 30
   A: Arteriosclerosis ....................................................................................................................... 33
1: Senile Sclerosis
2: Primary Sclerosis
3: Secondary Sclerosis

B. Retinitis
1: Stages
2: Types of Hemorrhages and Exudates observed in retinitis.

C. Hypertensive changes of the fundus

D. Diabetic Changes of the fundus

E. Syphilitic manifestation in the fundus

F. Tuberculose manifestation in the fundus

G. Periarteritic nodosal manifestation in the fundus.

H. Manifestations of Thrombo-angiitis obliterans in the fundus.

I. Manifestations of Raynaud's Disease in the fundus.

VI. Bibliography
INTRODUCTION

"The invention of the ophthalmoscope was one of the most beneficent achievements in modern medicine. It has made the interior of the eye accessible to investigation; blood-vessels and nerves, which in the rest of the body are exposed only by surgical manipulation, here lie unveiled before us and permit us to study their minutest variation. In ophthalmology, the ophthalmoscope has produced a complete revolution, since it has thrown light into the dark region of what was formerly called black cataract, and has acquainted us with the manifold morbid processes which lie at the root of this dreaded malady. Many of these processes, if diagnosed correctly and in time, would, at the present day, receive successful treatment. Furthermore, in general medicine the ophthalmoscope has become an indispensable aid to diagnosis, since many internal disorders produce characteristic changes in the fundus of the eye."

(1)
A: HISTORY

The first ophthalmoscope was invented by the English mathematician, Charles Baddage in 1847. The first in actual point of time, though not the first in point of admitted or even admissible priority. Baddage reported his discovery to Thomas Whorton Jones, the greatest ophthalmic authority in his county at that time and Jones reported against it. (2, 3v2)

W. Cumings, in 1846, a surgeon of London first showed that if the light is reflected into the eye from a source coinciding with the observer's eye, the human eye appeared luminous, and from the reflex visible through the pupil attempted to draw conclusions about the retina. However this work was not published for seven years. (3v2)

Meantime Helmholtz, in 1851, had elaborated his ophthalmoscope and had elucidated the optical principle governing the path of the rays into and out of the eye, and since his discovery was at once taken up intensively by von Graefe and the other leading ophthalmologists of the time: it is to von Helmholtz that the science of ophthalmoscopy must owe its inception. (3v2)
It was a very simple instrument wherein the light was partially reflected by three glass plates through which at the same time the observers could look. So with this instrument von Helmholtz in 1851 introduced the direct method of ophthalmoscopy: almost immediately afterwards, Ruete in 1852 evolved the indirect method. In this way all the essentials of the reflecting ophthalmoscope were rapidly incorporated within the first two years after its introduction, and the addition which have been made since represent merely minor details which render the instrument more convenient and practicable. (3v3)

Elkanah Williams while in Europe for training in ophthalmology the newly invented ophthalmoscope was the source of much experiment and discussion. He acquired a knowledge of its use in its modified form and was probably the first to bring an instrument to this country (1854) and to teach his America colleagues its wonderful revelations. He used an ophthalmoscope designed by Dr. Anagnostakis of Paris. It is said that he was also the first to demonstrate its use to the London ophthalmologists at Moorfield in 1854. (4)

The electric bulb gave a real impetus to
renewal of interest in ophthalmoscope examination. (3v2) Dennett of New York substituted direct (electric) light for light reflected from a separate source. (4) The electric ophthalmoscope came into general use the beginning of the twentieth century. (3v2)

B: METHOD OF OPHTHALMOSCOPIC EXAMINATION.

Indirect method of ophthalmoscopic examination; in this method the eye is made highly myopic by placing a strongly positive lens in front of the patient's eye. This places the punctum remotum between the lens and the examiner's eye. The details of the fundus can be seen so long as the observer can accommodate for the image formed at the punctum remotum. This forms a real inverted image of the fundus in the air between the lens and the observer which can be studied. The image is always magnified: with a plus 13 diopter lens employed the image is magnified about five times. If a stronger condensing lens is employed the image is smaller and brighter. If a weaker lens is employed the magnification is greater and the illumination less. (3v2 5)

This method is not used to any extent in the United States, but is used in some European
countries. With this method you get better view of the fundus in high muopia or astigmatic eyes since you don't add correcting lenses. (6) You also see the fundus clearer when opacities are present with this method if sufficient light is used. (1,3v2)

Direct method of ophthalmoscopic examination; A light is thrown into the eye by a mirror (either plane or convex), when the subject and the observer are separated by some considerable distance (e.g. 1 meter), an image of one point only of the retina can be seen when the observer's eye is in line with the source of light. The optical conditions are represented in Fig. 1. Since the whole
of the pupillary aperture of the subject's eye is filled by the cone of light from one point, no image of a retinal area is seen, but his pupil appears uniformly illuminated. If we consider the path of light emitted by two points (X,Y, Fig. II), it is evident that they form two diverging and parallel bundles. If the observer's eye is at 0, rays from these two points cannot enter his eye simultaneously: No clear image is therefore formed since light from one point only (Z) can be seen. It is only when the observer's eye is brought up so close to that of the subject that it enters into a region common to both beams, that rays from two points on the retina can enter his pupil; and the closer the two eyes are together the larger will be the number of those points and therefore the larger the available image. (3v1)

If the subject's eye is emmetropic an image of equal size to the object is formed on the retina of the emmetropic observer when his accommodation is relaxed; but if the subject is ametropic, such an image is formed in these circumstances only if a correcting lens equivalent to the amount of ametropia is placed behind the mirror of the ophthalmoscope in the anterior focal plane of each
eye, except in the case of very high myopia. (3+1)
The direct method of ophthalmoscopy gives an image of the fundus magnified about fourteen diameters. (6)

C. TYPES OF OPHTHALMOSCOPES USED TODAY.

The reflecting ophthalmoscope consists, in its essentials, of a perforated mirror with which light is reflected into the patient's eye. The observer's eye, being placed at the perforation, receives the light reflected back from the patient's fundus. Opacities in the transparent ocular media are seen as black shadows where they obstruct these returning rays, while the fundus itself is seen directly, providing the entering rays are focused upon it. It is seen in focus without the use of a lens if the patient's eye is free from refractive error. When such errors are present they must be corrected either by an effort on the observer's accommodation if the patient is hyperopic, or by the use of concave lenses in the ophthalmoscope if the patient is myopic. Various models of the ophthalmoscope provide various systems of lenses for this purpose but the principle is the same. (6)

The Electric of self-illuminated ophthalmoscope; In the self-illuminated ophthalmoscope derived from Dennett's original model, a microlamp
serves as the source of illumination, current being supplied by a dry cell or through a cord attached to the house circuit. The light from the lamp is collected by one or more convex lenses, and is reflected into the patient's pupil by a silver mirror or by the silvered back surface of a glass prism.

The model of May combines certain advantages which have caused its essential features to be adopted by most manufacturers. One convex lens is provided in a small capsule which fits over the lamp holder, and further condensing power is added in the glass rod through which light passes, the lower end of which is convex. The upper surface of this rod is cut obliquely, the oblique surface being silvered so as to reflect light through the sighthole, the lower part of which is covered by the upper end of the silvered surface. Through the upper part of this hole the observer views the fundus, proper lenses being rotated into place from a disc containing lenses of various refractive powers. (3v2)

Stereoscopic Ophthalmoscope; with the methods of ophthalmoscopy previously described, observations are made with one eye and judgment of depth must be made by means of the lenses employed,
or by the relation of objects in the fundus to each other and their apparent displacement during movements of the eye. With the stereo-ophthalmoscope of Gullstrand the fundus is viewed with both eyes through two eyepieces and a fairly reliable impression of depth is obtained. It is a large instrument giving a magnification of 32 diameters. Its use requires a certain experience in making the necessary adjustments. While useful in the study of certain lesions near the optic disc and macula, it is unsuitable for routine examination of the fundus as only a small area can be seen at one time.

(6) The Restricted Light or Nonochromatic Light in Ophthalmoscopy; the normal retina is transparent to ordinary white light. When a green filter of a filter of a certain type is employed which absorbs all red light, the retina itself becomes visible and certain fine changes in it may be observed. In such red-free light the yellow pigment of the macula is now seen and early changes in it may be detected. The course of the nerve fibers in the retina is also visible, and atrophy may be detected before pallor of the disc appears. The method is of especial value in detecting senile or cystic
degeneration of the macula. For the employment of red-free light an intense source of light is necessary, an arc-light being best. The green filters provided with some electric ophthalmoscopes are not of much use as the light provided by such instruments is usually insufficient.

With a yellow filter the column of blood in the vessels is seen as black against a yellow background, and finer vessels than may be seen with ordinary light are visible. The capillaries in the macular region and fine hemorrhages otherwise invisible may be seen by this method if the light source employed is sufficiently intense. (6)

The Slit Lamp Ophthalmoscope; in some conditions light reflected from opacities interferes with clear vision of the fundus, if the fundus is illuminated by a narrow beam of light from a pin-hole diaphragm or a small slit this minimizes the reflected light from the opacities and makes possible the view of the fundus when not possible under ordinary means. (9)

D. THE TECHNIQUE OF EXAMINATION.

The indirect method; the technique of examination in the indirect is: the examiner remains seated before the patient one meter away, and throws
the light into his eye from a large concave mirror of the ophthalmoscope; keeping his on the red reflex he interposes the condensing lens in the path of the beam of light close up to the patient's eye, and slowly moved the lens from the eye towards himself until the image of the retina is clearly seen. In order to bring the optic disc into view when the patient's left eye is being examined, he is asked to look at the surgeon's left ear. (3v2) When the periphery of the fundus is examined by this method the lens and ophthalmoscope are held stationary while the patient is asked to move the eye in various directions. (6)

The direct method; the technique of ophthalmoscopic examination in the direct method is:
The light is reflected into the patient's eye with the ophthalmoscope about 15 inches from the patient with a plus 8 lens placed over the sight hole. When examining the normal eye one sees a bright red reflex in the pupil at this distance. If the refractive media of the eye is not clear, this reflex varies from a dull orange to black. The observer brings his head nearer to the patient's eye continuing to observe the reflex. The opacities if any are localized, and vision of the fundus

11
is attempted by changing the lens over the sight hole. This is accomplished by rotating the milled disc. Vision of the fundus is attempted in this manner. Assuming the eye under observation to have no refractive error, one should theoretically employ no lens to observe the fundus. Due to the observer's own accommodation a minus 2 or minus 3 lens will have to be placed before the sight hole to get a clear view of the fundus. Instruct the patient to not look at the light, but at a point straight before him over the examiner's shoulder. (6)

After these preliminaries, the ophthalmoscope is brought almost to the patient's eye. At a distance of one inch or less, one should see the retinal vessels and the disc. (3v2) If a clear image is not obtained one of several conditions may be responsible. These are, the patient has a high refractive error, the observer's accommodation is in spasm and opacity of the media. (6)

In the patient with high refractive error, if the error is hyperopic, the observer usually makes the additional effort of accommodation necessary to obtain a clear image. If the error is myopic it is impossible to obtain a clear image.
without addition of a minus lens to correct the error. If there is high astigmatism a clear image cannot be obtained with spherical lenses, but many details can be seen. In eyes with high myopia or astigmatism a clear view by the direct method may usually be obtained by observing through the patient's own glasses or his proper correction in the trial frames. (6) The observer's accommodation spasm is unusually marked. This requires the addition of stronger minus lenses till the vessels are seen. (6) The observer can by practice relax his accommodation by leaving the non-observing eye open and training oneself to look into the distance. (5)

If the media are so opaque that insufficient light is admitted to illuminate the fundus, no change of lens remedies this situation but one should have become aware of it by his preliminary approach to the patient with the positive +8 lens of the electric ophthalmoscope using the direct method. (6) (5)

In the presence of such opacities one may employ the direct method with a slit of light or pinhole diaphragm light. These are of advantage here as much of the light reflected from the
opacities, which interferes with clear vision is eliminated. With these methods a view of the fundus is obtained in eyes with media so cloudy as to prevent observation with the ordinary instruments. (6) One may also employ the indirect method of ophthalmoscopic examination or increase illumination in the direct method. (3v2)

E. MEASUREMENT OF DISTANCES ON THE FUNDUS.

A convenient method of measuring distances on the fundus is in relation to diameters of the optic disc. The abbreviation commonly used is P.D., for papillary diameters. The average disc breadth is $1\frac{1}{2}$ millimeters. It is convenient to observe the reflex of an artery in the fundus, adding convex lenses till it first becomes indistinct and noting with which it is seen distinctly. Then a vessel on the nerve head or a detail of the lesion is similarly observed as stronger convex lenses are added. The difference in diopters is noticed. Three diopters of elevation as seen with the ophthalmoscope corresponds roughly to one millimeter of actual elevation. (1,3,5,6) There is also a means of measuring the diameter of the retinal vessels, optic disc or exudation by photographs of the fundus. Also a lens which can be superimposed on the
ophthalmoscope that has an area scratched into uniform square and this area is placed over the exudation and then compared to the disc. (3v2)
THE APPEARANCE OF THE NORMAL FUNDUS

The first actual description of the fundus of the eye beyond a doubt appeared in early periodicals which were being published at the time of the first employment of the ophthalmoscope in fundic observation. The men to first use the ophthalmoscope were Albrecht von Graefe of Berlin, Richard Liebriech of Konigsberg, Franz Cornelius Donders of Tilburg, Holland, Jaeger von Jaxthal of Vienna, Anagnostakis of Paris, and Heyman of Berlin. To them must go the credit of the description of the normal fundus. By 1854 detail description of recognized retinal hemorrhages were described. (7) In January 1854 the archive fur Ophthalmologic first appeared with Albrecht von Graefe of Berlin as editor. In 1855 the name of Ferdinand Arlt of Prague and Franz Cornelius Donders of Tilburg, Holland were associated with von Graefe (8). The first atlas was published in 1863 by Richard Liebriech. This was followed in 1869 by Edward Jaeger's inimitable "Atlas" representing pathological and normal fundi. This atlas was produced in color and the direct method of observation was employed. (4) It retains its authority to the present day. (8)

No amount of written description cannot
picture adequately the human fundus. The most amazing variations are apparent in health and disease. In the examination of the fundus the optic disc is the first point of orientation to be noted, the vessels should be noted next, then the general color of the fundus, and last the macular area should be studied. A description of these will follow in the above order. (9)

A. THE OPTIC DISC; it is circular to oval in shape and of a light pink color. The temporal half is normally paler than the nasal half and at the point where the central vessels enter the eye, near the center of the disc, there is often a pale or even white area. This is due to the thinning of nerve fibers in this area as they slope gradually into the depression surrounding the vessel. This is the physiologic cupping of the disc which varies greatly in different persons. The border of the disc shows a ring of white, representing the scleral edge. Often a ring of pigment or a crescent of pigment at the temporal side is seen just peripheral to the white ring. A white temporal crescent of sclera may be exposed with a ring of pigment outside of it. (6)

B. THE RETINAL VESSELS; the retinal vessels are
derived from the central artery and vein, which usually divide into two branches at or near the surface of the disc. These branches are above and below, and form a superior and inferior trunk. Each trunk usually divided into two, one of which sweeps up or down towards the nasal side. They divide dichotomously into innumerable branches. The nasal branches run much more radially than the temporal, which make a very decided sweep to avoid the macula. The retinal vessels as seen on the disc are easily distinguishable into arteries and veins. The former are of a lighter red with a definite shiny reflex running along the middle due to the reflection of light from the convex anterior surface. The veins are somewhat larger, usually in the proportion of 3 to 2, are of a darker color and usually show no reflex. The caliber of the vessel is even, no irregular abrupt changes in the size of the blood column.

C. THE COLOR OF THE FUNDUS; The appearance of the general fundus varies enormously within healthy limits. They are classified into three groups. Not all fundi will fall definite into this classification but may combine two of the three appearances described below.
The uniform Stippled Fundus has a uniform appearance and this is brought about by the fact that the layer of pigment epithelium contains so much and such dense pigment that the choroid beneath it is completely hidden from the eye of the observer. The tone of color is red, brown red, or black brown, according to the quality of pigment. (1)

The tessellated Fundus in this type the layer of pigment epithelium contains less coloring matter. Consequently it is possible to see through the almost transparent retina and to perceive the markings of the choroid. (12) The reddish choroid vessels are seen to form numerous anastomoses, and the pigment of the choroid is massed in the intervascular spaces between them. The vessels appear as bright bands on a dark background. (11)

In the albinotic type the layer of pigment epithelium contains little or no pigment so the markings of the choroid are again visible, but this membrane also has pigment so the markings of the choroid, forming a yellowish white background, upon which the choroidal vessels appear as dark bands. They can be distinguished from the retinal vessels by the absence of the light reflex, their
abundant anastomoses, and their deeper position.

(11)

The Pigmentation is usually densest about the papilla and in the region of the macula, so that even in an albinotic fundus the choroidal vessels are not usually visible in the macula, although they can be seen in the less pigmented places in the periphery.

D. THE MACULA LUTEA; the macula is situated about 3 millimeters or 2 disc diameters (2P.D) to the temporal side of the edge of the disc. In general, it is a small circular area of a deeper red than the surrounding fundus sometimes looking almost black. (5) The fovea is situated in the center of the macula. There is nearly always a foveal reflex, due to the reflection of light from the walls of the foveal depression. (9). This is most frequently seen as a silvery ring of light hiding everything behind it. The macular region is supplied by twigs from the superior and inferior temporal arteries, and by small branches coming straight from the disc. There is no retinal blood vessel actually at the fovea, and none can be seen ophthalmoscopically for a little distance around. (5)

A number of shimmery reflexes are often
to be seen upon the normal fundus. They are more frequently observable in younger subjects. In some instances these reflecting areas, which in appearance have been likened to the sheen observed on watered silk, follow the blood vessels. Such a retinal picture is peculiar to hyperopic children. Its presence, it is thought, is caused by the non-absorbent properties of the ganglionid cells of retina. Such reflexes are called retinal reflexes. (13)
DEVELOPMENTAL AND CONGENITAL ANOMALIES

Only those more commonly seen and those mentioned in the literature frequently will be discussed.

A. ANOMALIES OF THE CHOROID.

Coloboma of the choroid was first described by von Annon in 1830 and may be accompanied by complete or incomplete coloboma of the retina. \(^3,9\) They are divided into typical and atypical types.

Typical coloboma on ophthalmoscopic examination presents an area of striking appearance wherein the normal color of the fundus is replaced by the white background of the sclera. Situated downwards and slightly outward. The coloboma is usually oval in shape, the posterior and broader and frequently stopping short of the disc, but sometimes reaching forward beyond the limits of ophthalmic examination. On the other hand it may be small; it may be round or rarely transversely oval. \(^3v2\)

The edges are usually clean cut and are frequently pigmented, but sometimes fade off gradually. The floor of the coloboma is depressed below the level of the rest of the fundus, and may be ectatic, in whole or in part, a tendency which
may be so pronounced as to cause a bulging on the outside of the globe. Transversing the floor, or a portion of it, two types of vessels may be evident, which by their irregularity betray the presence of ridges and ectatic areas: retinal vessels which dip down into the coloboma as they pass from the normal fundus, and ciliary vessels, more tortuous and broader in appearance, lying at a deeper level. (3v2).

Colobomata of the choroid may exist at the entrance of the optic nerve. These rarely involve the nerve itself. They may resemble deep physiological excavation or even the more extensive ones, retro-bulbar cysts. They appear ophthalmoscopically as a white area occupying the posterior part of the fundus. The defect is rarely the same size as the disc, but is usually 2 to 4 times larger; and may be 20 times larger. It is generally round or vertically oval. (3v2).

A typical Coloboma of the choroid and retina are rare. Clinically they resemble in appearance the deformity of typical colobomata. (3v2). They differ only in their direction, not place as the typical coloboma. (6)
Macular colobomata have also been described. They are horizontally oval or round defects of a size varying from less than one to ten discs in diameter. The clinical appearance varies considerably. They are pigmented and non-pigmented types which may be associated with the presence of abnormal vessels. This is rare, however. Usually there is considerable visual defect. (3v2)

Choroideremia, a condition where the choroid as well as the pigment epithelium of the retina is completely absent except in a region around the macula, is a very striking condition. It is rare and was reported first in 1871 by Naather. (3v2) The retinal vessels are seen to pass over the white sclera while at the central area a small red spot marks the location of the macula. (6). This area of red may extend toward the periphery some distance. This patch of choroid always has an indefinite border in contrast to the sharp border of a coloboma. The discs retain their normal appearances; and the retinal vessels pursue their usual course, but the arteries are slightly contrasted. (3v2) This condition appears in this paper because a patient with such a fundus was recently seen at the University hospital.
B. ANOMALIES OF THE RETINA.

As mentioned before under anomalies of the choroid, retinal coloboma may accompany coloboma of the choroid either complete or incomplete. Also the retina shows other anomalies in nerve fibers and developmental of the macula. This was demonstrated anatomically in the retina of man by Virchon in 1856 without ophthalmoscopic observation, and since this instrument has come into use has been confined innumerable times. (3v2)

The medullated sheath of the nerve may extend beyond the lamina cribrosa. They appear ophthalmoscopically as white patches, the peripheral edge of which are radially striated looking as if frayed out. Usually the patches are continuous with the disc, occasionally they are isolated, but rarely far from the disc. Usually the retinal vessels are covered in places by the opaque fibers. (14). The macula is rarely involved. (3v2).

Anomalies of the macula appear under several forms. Absence of the macula is rare. It occurs in albinotic eyes and is also associated with other gross abnormalities of the other derivative of the optic vesicles. This was first
described by Birgmeister in 1907. (3v2)

Misplacement of the macula is rare. Both the optic disc and the macula may be displaced temporally so that the former lies in the pupillary line. This is also associated with vascular anomalies. (3v2)

Oguchi's Disease. First described by Oguchi in 1907 in Japan. (3v2) The clinical picture of the fundus is very striking. In the ordinary course of events the posterior region, and sometimes the entire fundus, is of a grey color, upon which the retinal vessels stand out with extreme clarity, one side of the vessel showing a bright white edge and the other a dark shadow. After some hours in the dark, however, the grey color is replaced by the normal red appearances. (9) Most cases have been described in orientals but it has been reported in the United States and elsewhere. (14) This rare disease appears here because of its frequent appearance in the literature.

C. VASCULAR ANOMALIES.

Absence of the retinal vessels has reported by von Graefe in 1854 in a well developed eye of a boy who was blind. (3v2)
Abnormalities in branching of the vessels are common. Instead of each papillary artery dividing into two main branches, a trifercation may occur, or several secondary vessels instead of two large ones may emerge upon the fundus. Similarly, the papillary vein may be formed by the confluence of three branches of the second order, a number of veins may arrive at the disc independently, or a circular venous anastomosis may be formed round the disc, or smaller loops or bifurcations with intercommunications may be found upon it. (3v2)

Abnormalities in the course of the vessels usually take the form of unusual tortuosity. This may be localized or generalized, occurring unilaterally or bilaterally, in either arteries or veins, or in both. Gause estimated that 70.7% of persons had abnormal vessels. Tortuosity is usually seen in hypermetropic eyes. The arteries may cross beneath the veins, or the veins beneath the arteries, or both sets of vessels may turn and twist about each other. (3v2)

D. ANOMALIES OF PIGMENTATION.

Melanosis of the eye is a condition wherein the pigment of the uveal tract is greatly increased. The fundus is black or chocolate colored,
the pigment being especially marked at the macula and in the region of the posterior pole, while on ophthalmoscopic examination the whole retina shimmers with numerous light reflexes. (3v2)

Melanosis of the retina alone may exist. Congenital melanosis of the retina is a hyperplasia of the pigment cells of the retinal epithelium. The condition is usually, but not always, unilateral and is non-progressive. It forms a characteristic picture usually affecting a sector-shaped area of the retina, the apex of the sector lying at the disc. Scattered over the retina are individual angular spots of a chocolate brown color sometimes isolated, but usually grouped together in various patterns. At times these are oval or circular; at times they are reminiscent of groups of sarcoi­ae, or they may be strung out in chains or ar­anged in quite irregular masses. (3v2)

Congenital pigmentation of the optic nerve and congenital pigmentation of the optic disc may be met with in four conditions: fleck-form pigmentation, a uniform pigmentation, in pigmen­tion pits and as melanomata. As such the pigment may be of two types, choroidal or retinal. In choroidal pigmentation the optic disc is sometimes
pigmented to a small extent usually in a fleck-form manner, an appearance which may considered normal. Retinal pigmentation may also be found in the nerve head derived from the retinal pigment epithelium. (3v2)

In Albinism the fundus has a characteristic orange-red color wherein the retinal and choroidal vessels are seen sharply defined against sclera, while the optic disc may be indistinguishable except as the point of confluence of the retinal vessels, although it frequently appears darker. (5, 6, 9, 13). The fovea is absent in albinos, so no foveal reflex or fundus reflex are seen. (12)
PATHOLOGICAL CHANGES

Retinal hemorrhage was described by Liebrich in 1854 but definite retinal changes were first observed in the living eye by Heymann in 1856. In the same year Liebrich gave an accurate description and ophthalmoscopic picture of the fundus changes of albuminuric retinitis. The first publication of retinal changes appear in the United States in 1856. In William Mackenzie's "A Practical Treatise on Diseases of the Eye" when discussing the objective symptoms of amaurosis describes "pigmentary decomposition in the vitreous humor, effusion of blood or exudation of lymph on the surface or in the substance of the retina, or between it and the choroid, varicosity of the retinal vessels, partial removal of the pigment in patches, separation of the retina from choroid in consequence of subchoroidal dropsy, etc." He did not relate these to any pathology elsewhere but only with the condition amaurosis. (16)

Retinal changes have been studied in great detail and give valuable information in diagnosis and treatment of many systemic diseases. (17)

This paper will be limited to those con-
ditions listed in Cecil's "Textbook of Medicine" under the heading of "Disease of the Vascular System" that have fundus manifestations recognizable by the ophthalmoscope and that appear in the periodical publications. These include the generalized conditions of arteriosclerosis and hypertension and the peripheral vessel lesions, Raynaud's Disease, Thromboangiitis obliterans, periarteritis nodosa and syphilitic and tuberculous arteritis and periarteritis.

In the study of pathologic changes in the retina reflecting disease entities of the systemic vascular disease it is necessary to consider the normal fundus in more detail.

The normal retinal vessel's caliber in the healthy young or middle aged adult is regular with no tendency of alteration of the lumen. The vessels are translucent even to permitting the blood column of the vein below the artery at the arterio-venous crossings to seem as a shadow. (18) The blood column allows the vessels to be visible; the deeper the vessels are situated in the retina the darker they appear. Also the amount and quality of the blood contained within the vessel wall also determine the color. Thus
in severe anemias, heart failure and hypercholes-
	erenia the vessels appear incompletely filled. (1,13)

The fundus of a young patient is charac-
terized by light reflexes of varying intensity, due
to smoothness of the retinal surface. (9) The
size of the reflex is constant if the fundus is nor-
mal and the same ophthalmoscope is used. (19)
The arteries have a brighter, more intense, narrower,
and more definitely defined than on the veins.
In lowered blood pressure the reflex broadens and in
elevated blood pressure it narrows. (6) (11) As the
vessels course at different depths the reflex is
useful in determination of the difference of level.
At any change of elevation no matter how slight the
reflex disappears where the vessel bends. (20)

Venous pulsation is normal and can be ob-
served best where the vein descends into the excava-
tion of the physiologic cupping. The blood con-
tained in the vein seems to be driven toward the
periphery with each stroke. The venous pulsation
is normal to the young but if present in the aged
or if absent when compression is applied to the
eyeball it suggests pathology. The arterial pul-
sation is normally not present. If present it is
The division of the fundi into definite types cannot always be done as superimposing of conditions occurs and confusion of types result. Some division must be made, so the lesions will be divided into definite lesions of the systemic vascular diseases, combined with description of retinal lesions frequently seen in systemic vascular diseases. These descriptions will be presented and then referred to in the description of the definite lesions.

A: ARTERIOSCLEROSIS.

This lesion is the commonest lesion of the systemic vascular system. In 1860 Henrich Mueller published a short description of arteriosclerosis of retinal vessels. He stated the caliber of the vessels is greatly narrowed or they are even obliterated at certain points. (20) In 1876 Gowers called attention to the association of retinal sclerosis with Bright's disease and increased arterial tension. To Hirschberg in 1882 belongs the credit of being the first to observe and recognize atheroma of the retinal arteries. (22) Marcus Gunn in 1891 gave a classical description and classification. (23) In this paper
a combination of the classification of H. Friedenwald and J. F. Gipner will be used.

A sclerotic change is preceded by angiospasm. Angiospasm is recognized by irregularity of the lumen of the vessels near the disc border on the nasal side especially (24) and if persistent for ten days organic changes in the vessels occur (25). Arteriosclerosis is divided into three headings; Senile sclerosis, Primary sclerosis and Secondary sclerosis.

Senile Sclerosis; the process of senile sclerosis is preceded by a condition recognized by the ophthalmoscope and called fibrosis. In most patients past sixty a more or less loss of translucency, thickening and narrowing of the retinal arteries is observed. It may be absent but as a rule most patients of this age show such changes. This condition is not accompanied by irregularity of the lumen of the artery but it appears so due to the change in the translucency of the vessel wall and thus not all of the blood column is seen. (18) The sclerotic vessel wall becomes visible. (26) This condition in the choroid shows through the retina as a mild sclerosis. Mild compression of the veins at the arterial crossing may or may not be
As this process advances evidence of sclerosis will be seen, irregularity of the caliber of the retinal vessels. (18) This is due to endothelial proliferation. (5). This condition is not always associated with hypertension but it may be an etiological factor in the production of retinal arteriosclerosis. (23).

As the arterial wall becomes thicker in arteriosclerosis the column of blood becomes narrower; so that the arteries appear small in proportion to the veins, in which the column of blood remains of normal size or may even be increased. (6). The ratio of the size of the blood column of the arteries to vein changes (normal 2 to 3) in arterial sclerosis so it may reach 3 to 5 or 1 to 5 in severe cases. Since thickening of the arterial wall is not uniform, the arteries, as judged by the column of blood, appear to vary in caliber, in some places being of normal breadth and in others very thin. At the arterio-venous crossings, the arteries indent the veins, this indentation being produced by arterial branches which appears very small but which in reality have greatly thickened walls. The light reflex seen on the arteries
becomes broader, so that the whole artery may have a shiny appearance (silver-wire arteries). The walls of the arteries and later of the veins become visible, due to atheromatous deposits in their walls, and appear as if ensheathed in a grey veil. The condition is a patchy one, affecting some vessels while other remain normal in appearance. The vessels of one eye may be effected while those of the other appear nearly normal. (18)

This type of sclerosis is not pathological if it occurs in a person of sixty years or more but since it occurs earlier in life (premature arteriosclerosis) or may not occur it is described here as a pathological condition. (6)

Primary Sclerosis; "By primary arteriosclerosis is meant an endovasculitis of patchy distribution which may affect but one or two of the retinal branches and may be present in only one eye," (18). This type of sclerosis is thought to be due to endothelial damage from circulating toxin in the blood. If due to syphilis or tuberculosis a perivasculitis may be present. (18). Syphilitic sclerosis, also classed as primary by some, probably should not be classified as an arteriosclerosis (19) so this condition will be discussed
fully under syphilitic fundus affections. The primary sclerosis of tuberculosis will be discussed here with the other primary arteriosclerosis of nonspecific origin, both having the same primary sclerotic pictures.

In primary sclerosis the caliber of the retinal arteries and veins are fairly normal for the most part, but the reflex stripe on the retinal arteries is unevenly exaggerated. At one or more points the lumen of the artery is markedly constricted and complete obliteration due to endarteritis obliterans which may be present. New vessel formation and collateral circulation are often noted. (18, 24). Beading due to fatty degeneration of the nodules of the subendothelial proliferation may be present and small macular arteries may show corkscrew tortuosity. These last named signs are rare and are only seen in advanced cases. (18). Where the vein is crossed by a thickened artery right angle compression is present. (24).

Secondary Sclerosis; In fundi where there has been a previous edema of the optic papilla due either to optic neuritis or to choked disc, there is present, when the edema subsides, perivascular
thickening of the perivascular and periphlebitis extends peripheralward as far as the extent of the previous edema. This is usually not much further than the secondary retinal branchings. The artery and vein peripheral to the perivasculitis may be entirely normal in caliber and appearance. This condition will be discussed here because this picture may be seen in the rare cases healed hypertension, but it is more commonly seen as the result of healed nephritis. Both the artery and the vein in the area of perivasculitis show uneven constrictions due to true sclerosis with endovascular changes. The degree of change depends somewhat upon the severity of the previous active inflammatory process of choked disc. (18)

Another form of secondary arteriosclerosis is noted in retinitis pigmentosa and primary optic atrophy, where the attenuation of the retinal vessels is secondary to the degeneration of the retinal elements. (9)

The description of arteriosclerosis that occurs in hypertension and syphilis will be discussed under these headings later.
B: RETINITIS.

It may be stated that the pathological changes in retinitis are essentially those of increased vascular permeability, those of disturbed tissue metabolism and in many cases those of arteriosclerosis. (27)

All grades of retinitis whether mild or severe run a characteristic course which Wagener divides into four stages. In the first stage of retinitis the disc is hyperemic and edematous, the edema spreading to the peripapillary retina while superficial striate hemorrhages and soft cotton wool exudates may be present near the disc. In the second stage the nerve is swollen higher and the edema becomes more widespread so as to involve the macular region. There are more hemorrhages and exudates many of which more deeply situated. (18). In the third stage evidence of recession of the edema in the peripheral retina is seen, black spots of pigment proliferation develop, the disc appears pale through the edema due to atrophy, the hemorrhages are deep, edema absorbing exudates and macular star figures develop. (18, 28).

Secondary sclerosis of the vessels around the disc
and choroidal sclerosis are seen. (29). The fourth stage, which is rarely seen, is characterized by secondary optic atrophy. The full disc has blurred margins due to cicatricial changes and perivasculitis and retinal pigment spots are seen. (18).

Types of Hemorrhages and Exudates observed in Retinis; superficial hemorrhages located in the nerve fiber layer are striated or flamed shaped. Deep hemorrhages appear as round or granular red spots in the fundus. Striated hemorrhages are usually seen in early stages of retinis, while granular hemorrhages are usually seen in the later stages. Massive hemorrhages with white exudate along the course of a tremendously distended vein whose blood flow has been obstructed by a sclerotic artery, forms the characteristic picture of venous thrombosis. When the central vein is thromboid the disc is edematous and all the veins are swollen and tortuous while massive hemorrhages and exudates are scattered throughout the fundus. Rarely are preretinal hemorrhages, which are chiefly macular, seen in cardiovascular-renal disease. (18)

Cotton wool exudates which appear as fluffy, soft, superficial white spots in the retina
are undoubtedly due to varicose, swollen, degenerated nerve fibers. They usually appear in the early stages of retinitis. Deep exudates are of three main types. (1) The massive serofibrinous exudation is found in all the retinal layers and even subretinal, causing flat detachments of the retina around the disc, or globular detachments of the lower retina. In acute retinitis it appears first as edema of the disc and of the peripapillary retina. In the later stages of retinitis as the retinal edema recedes, the exudative material becomes clumped. Cells collection associated with deep exudates are responsible for the formation of both macular stars, and the scattered punctate, edema-absorbing exudates. (18, 30). (2) Macular stars are the result of radiating traction folds, of the retina in the macular region since at the fovea the retina is more or less firmly attached to the underlying choroid. Along the lines of traction the retina is pulled relatively thin and is free of cells and exudates. (31). (3) Edema-absorbing exudates appear ophthalmoscopically as scattered small white, angular spots in the retina. (18) Hemorrhages and exudates of the types mentioned in-
cluding macular stars, may be seen in persistent choked disc, neuroretinitis of nephritis, and neuroretinitis of malignant hypertension. (30). Because they are common features of these conditions, their presence offers little and often no assistance in the ophthalmoscopic differentiation of cardiovascular-renal retinitis. (31)

Retinitis proliferous is the result of organization of vitreous hemorrhages. Although vitreous hemorrhages are usually completely absorbed they may become organized, giving rise to masses of fibrous tissue in the vitreous, vascularized by newly formed blood vessels derived from the retinal system. The lesions are usually situated near the disc and the blood vessels spring from that area. (5)

The ophthalmoscopic picture is that of floating, whirling masses which are seen originating from the retinal vessels near the disc usually and extending into the vitreous. The masses are of a whitish or grayish yellow color. Some of them contain newly formed blood-vessels, and they are sometimes so large that they extend outward, covering the retinal vessels for three to four disc diameters. Repeated vitreous hemorrhages, trauma,
chronic inflammation, and syphilis have been given as etiological factors. (9, 5, 6)

The amount of fibrous tissue varies from the most delicate strands and films supporting new-formed blood vessels especially common in Syphilitic cases, to dense bands and membranes stretching far forwards into the vitreous hiding the fundus. (5) More intense inflammation may lead to massive infiltration of the retina itself. Replacement of such exudates by glia and connective tissue results in the picture of retinitis exudativa intima or coaté retinitis. (6) There is usually a large raised yellowish white area or several smaller areas posterior to the vessels. It resembles conglomerate tubercle in its ophthalmoscopic signs. The vessels often show gross degenerative changes, and there is sometimes arterio-venous communications, with enormous dilatation of the veins. (5)

C: HYPERTENSION CHANGES OF THE FUNDUS.

Hypertension is the most common etiologic factor in the production of the retinal arteriolar lesions (32). Changes occur in all levels and all sizes of retinal vessels. (33).

The patient who is suffering from hyper-
tension if seen early can be seen passing through the stages of retinal hypertension signs (angi spasms), retinal arteriofibrosis, hypertension arteriosclerosis and the retinitis or retinopathy. (23)

Hypertension may be divided for convenience sake into 1-Mild benign hypertension, 2-Severe benign hypertension, 3-Malignant hypertension. (18) Clay and others state the angiospasm, the precursor of hypertensive arteriosclerosis, is manifested in the fundus as irregularity of the lumen of the vessels. (25). This is most commonly seen near the disc border on the nasal side of the retina. (34). After ten days of such spasm organic changes in the vessels occur. (25). The organic change mentioned is an increased fibrosis. As the fibrosis increases, there is added to the generalized reduction in caliber, areas where still further reduction in caliber is present, so that there is a generalized irregularity in the caliber of the retinal arteries giving the picture of hypertensive sclerosis. (18). Early the vein may be considered normal or relatively dilated and moderate venous compression is present at the arterial crossing. (34). The veins of the retinal participate to a greater degree than those of the rest of the body.
in these changes. (35). Hypertensive sclerosis can be differentiated from the primary and secondary sclerosis in the fact that all the retinal vessels are involved throughout their course and that no retinal branches are found to be normal in appearance even though the degree of sclerosis may vary in different branches. It is characterized by exaggerated retinal reflex, irregularities in the caliber of the arterial lumen, relative venous engorgement, and obliquely angled arteriovenous compression. Rarely does the arteriosclerotic process go on to endarteritis obliterans with new vessel formation as in primary sclerosis. (18). Increased tortuosity of the retinal vessels is present in hypertension sclerosis, but it is more frequent in advanced cases. (36). The arteriosclerotic changes are indicative of the patient's resistance to the hypertension. (37). These patients usually have a diastolic pressure under 115 millimeters, have little or no peripheral sclerosis, and have no signs of impairment of function in heart, kidney or brain. (18)

Severe Benign Hypertension; it is characterized by the presence of hypertensive retinitis. The fundus shows marked hypertension reti-
inal arteriosclerosis with hemorrhage and exudates. The hemorrhages and exudates may disappear with rest and medication but the retinal sclerosis remains unchanged. (30). Such patients show marked peripheral sclerosis, and show signs and symptoms indicating impairment of the heart, brain or kidneys. The diastolic pressure is above 115 millimeters. (18).

Malignant hypertension: Malignant hypertension in its earlier manifestations are identical with those associated with benign hypertension. Those symptoms referable to the central nervous system and cardio-vascular apparatus are more severe from the onset and the course is short. (38) Some believe it is the terminal stage of benign hypertension. Angiospasm with great irregularity of caliber and rapidly developing progressive arteriosclerosis is seen early. (25). The angiospastic changes in the retinal arterioles are indicative of the active and progressive nature of the hypertensive diseases. (30,37). The neuroretinitis of malignant hypertension may occur in young adults with severe, rapidly progressive hypertension, or it may be superimposed upon cases of chronic hypertension which have passed through the stages of hypertension scl-
erosis and hypertension retinitis to develop edema of the disc, which is characteristic of this severe type of hypertension. (18, 39). The swelling of the nerve head may reach such a marked degree as to resemble papilledema and retinal detachment on one or both sides may occur due to transudation of fluid beneath the retina. (6, 5). The neuroretinitis of malignant hypertension differs from the retinitis described for the malignant nephrosclerosis of Volhard and Fahr, not in appearance, but in the fact that it has often been observed in patients while the kidney function was entirely normal. Some authors describe a type of hypertension seen without retinal sclerosis. In these cases the eye-grounds are normal or at most show slight arterio-venous compression. This may disappear when the blood pressure returns to normal. This heading includes cases of essential hypertension, acute nephritis, mild toxemias of pregnancy, increased intracranial pressure cardiac decompensation with transitory hypertension, hyperthyroidism with high systolic pressure, etc. It is of special interest that individuals of advancing years with beginning hypertension usually show at the onset no retinal arteriosclerosis (especially women
at menopause.) (39)

D: DIABETIC CHANGES OF THE FUNDUS.

The condition of diabetic arteriosclerosis is included in Cecil's "Textbook of Medicine" under the heading of arteriosclerosis. However, besides those changes seen similar to arteriosclerosis other changes are seen in the blood vessels. Arteriosclerosis appears about ten years earlier in the diabetic patient and has the same ophthalmoscopic picture as senile arteriosclerosis. (6)

The early observers of the fundus noticed a type of fundus change in diabetes. Graefe states specifically that without an increase in blood sugar no sign of diabetes occurs in the eye. (40). The retinal vessels were suspected to play an important part in this phase of the disease, thus Hirschberg (1891) suspected that changes described as diabetic retinitis "may possibly be due to disease of the finest blood vessels." The diabetic retinitis referred to here by Herschberg was a central punctata retinitis which is frequently associated with diabetes. (40).

Diabetes injures the finer arterioles or venules of the retina, probably the latter. The injury is insufficient in degree in most cases to
bring about abnormalities that are visible with the ophthalmoscope, but when a visible abnormality is produced, it is characteristic. These characteristic lesions are not seen in similar form or distribution in any other disease. (41). There is a similar change in the finer arterioles or venules throughout the body. (38)

Gray believes that the first retinal lesions that occur in diabetics consist in yellowish-white spots near the macula, unaccompanied by hemorrhages. McKee's earliest observed sign was a loss of translucency of the arterial wall so that at joints of crossing the vein lying beneath the artery could not be seen, as is usually possible in normal subjects. A more frequent change was a slight deflection of the line of a vein where it was crossed by an artery. The angle of deflection was never pronounced as occurs in pure arteriosclerosis alteration in the breadth of a vein on the distal side of the artery, tapering while beneath the artery to regain its normal size beyond, was seen. At the crossing the fine white lines described by Gunn due to an increase in the fibrosis tissue of the vessel wall, were in evidence in many cases, but the appearance was limited and never extended

49
for any distance along the course of the vessels. Vessel changes in diabetes on the whole differ from other arteriosclerotic retinas in being less marked. (42). Occasionally this affection comes to young people and is not accompanied by visible evidence of sclerosis. (6). Parson states that the vessels are often normal, but a degree of vascular degeneration correlated with the age of the patient is not uncommon. (5).

The exudative lesions of diabetes are characteristic; irregularly scattered small, bright white spots around the macular region are the commonest manifestation. The snowy patches and stellate arrangement at the macula are usually absent. The white spots may coalesce into larger plaques with crenated edges. Punctate hemorrhages are freely scattered over the fundus; they are often round and deeply seated. The optic disc and remainder of the retina are generally normal. (5).

Wagener, Dry and Wilder (41) classified the retinitis of Diabetes into five stages.

The first stage or earliest and mildest type of retinitis in diabetes consist of tiny punctate hemorrhages which are situated usually in the vicinity of dilated terminal venules in the macular.
regions. These authors list this finding as the earliest to appear. Later in the disease these hemorrhages may be larger and more widely spread. Almost always, however, they are deeply situated and therefore more or less round in form. (Hemorrhages alone, no other lesion.) (41)

In the second stage, a later but still early staved a few shiny irregularly-shaped punctate exudates, are seen apparently lying in the deeper layers of the retina, either above or below the fovea centralis and usually in association with the minute hemorrhages just described. This picture has been called "central punctate retinitis". Similar exudates or areas of degeneration may later appear in any part of the retina, may assume a tendency to coalesce, and, in long-standing cases, may ultimately fuse in the macular region into large and necrotic looking plaques that seriously interfere with central vision. In more advanced stages the hemorrhages are very widespread, and many of them are large and of irregular form. (Hemorrhages with punctate exudates.) (11)

The third stage in which the general picture is that of the central punctate type of retinitis, larger, more edematous exudates may be scatt-
ered throughout the retina. These are called "cotton wool" exudates and lie in the nerve fiber layer of the retina; they probably are dependent on a complicating hypertension with angiospasm. In the other cases, these patches of exudates are more deeply situated, more yellowish in color, and more chronic in appearance than the typical cotton-wool patch. This is called a cotton-wool like exudate. It is assumed that the presence of the exudates indicates vascular injury of greater severity than is present in the typical, central punctate variety of diabetic retinitis. This group (third stage) includes both cotton-wool exudates and cotton-wool-like exudates. (Hemorrhages with both punctate and cotton-wool exudates.) (41)

In the first three stages the visible changes in the arterial vessels of the retina are not prominent. The arteries are normal or show at most a moderate degree of sclerosis. Angiospasm is absent except in some cases in which there are cotton-wool patches. The retinal veins, however are frequently mildly dilated. (41)

The fourth group includes that group of patients whose retina show marked abnormalities of the veins differing apparently from that seen in
any other disease. The veins are more or less uniformly dilated and appear cyanotic. In some nodular dilation with intervening constrictions are observed. Sections of the wall may be ensheathed in a layer of heavy, greyish-yellow infiltration and other sections of the vein appear to be obliterated. These venous lesions are usually associated with large and extensive areas of hemorrhages. This condition described may be implanted on a retinitis typical of the central punctate type, with or without cotton-wool-like patches, although it may represent a primary lesion. (Hemorrhages or exudates associated with visible lesions in the vein).(41)

The fifth stage includes those cases in which there is hemorrhages into the vitreous associated with this marked disease of the veins, it is rather common. As a result of or as a sequel to these hemorrhages, bands of scar tissue may form and newly formed vessels proliferate into the vitreous, giving the picture of retinitis proliferous. (41)

Diabetic retinitis is more commonly seen in severer cases of diabetes (43). By percentage the female shows evidence of diabetic retinitis
twice as often as does the male. (44). It rarely occurs in patients below fifty years and white retinal foci were found only in women under fifty with a blood pressure reading below 140 millimeters mercury according to Heinsus. (44) report on 221 cases.

Wolfe (45) in a differentiation of diabetes, nephritis or arteriosclerosis states five characteristics of a true diabetic retinitis. First, it rarely occurs in a young subject; second, the patches of retinal exudates tend to have sharp-cut edges, they are distributed in an irregular manner, and sometimes form an irregular ring around the macular region; third, small dark round retinal hemorrhages are very suggestive of diabetes. As such they lie in the deeper layers of the retinal. Other types of hemorrhages may be present and all of the retinal layers may be infiltrated or the hemorrhage may be subhyaloid or may occur into the vitreous; fourth, soft edged cotton-wool patches. Characteristic of renal disease are not present in diabetes; retinal edema is not marked and thus retinal detachment does not result; fifth, a star figure is uncommon. (45)

E: SYPHILITIC MANIFESTATION IN THE FUNDUS.

54
Syphilitic manifestation of fundus has caused much discussion. Early in the use of the ophthalmoscope Liebrich, Graefe and others described syphilitic retinitis. In 1874 Forster denied that syphilitic retinitis existed but observed and described a syphilitic choroiditis and choroideretinitis. He characterized this condition in the diffuse type of choroidoretinitis by the presence of a fine dust-like opacities in the posterior part of the vitreous, blurring and redness of the optic papilla, and by alteration in the macular region and blood vessels. (20v14).

Schobl also believed that the retinal lesion were due to a direct extension of the choroidal lesion. Jacobson divided diffuse syphilitic retinitis of the arterial type into three definite stages which are covered in this paper under syphilitic arteriosclerosis. These were: 1-Syphilitic hemorrhages (rare) characterized by opacities in the posterior chamber. 2- Syphilitic arteries. 3-Syphilitic perivasculitis. (20v14). The classification of the various syphilitic lesion have changed many times and is still in a state of uncertainty. The character of the early lesions do not allow them to be placed in a definite classification.
Taylor (46) as early as 1913 stated that arteriosclerosis of syphilis probably did not belong classified with other arteriosclerosis. Friedenwald (19) does not include syphilitic arteriosclerosis under his classification of arteriosclerosis. However in the same article the author (19) states, "Most luetics with arteriosclerosis show nothing in their retinal vessels distinctive of syphilis. In a number of cases of central nervous system syphilis, however, it was noted that the retinal vascular lesions were peculiarly scattered, one arterial branching showing marked changes, while its neighbor appeared perfectly normal and only one eye may be affected. A similar scattered vascular lesions are rarely seen in non-syphilitic individuals. We feel, therefore, that this picture while not pathognomonic of syphilis, is, nevertheless quite suggestive."

Some authors include this condition in their classification of primary sclerosis; but in any case it should be included in this paper as a lesion of the generalize vascular endovasculitis of syphilis. Syphilitic arteriosclerosis is an endovasculitis of patchy distribution which may affect only
one or two of the vessels of the retina and it may be present in only one eye. (19). It is sometimes compared to atheroma of the larger vessels of the body. The caliber of the arteries and veins are quite normal in appearance, but the reflex stripe is unevenly exaggerated. At one or more points along the arteries the lumina are markedly constricted and there might be present a complete obliteration due to endarteritis obliterans. In these areas new vessel formation and collateral circulation are often seen. (18). Circumscribed bulky white exudation may occur along large blood vessels to form white lines or the exudation may take place in the macula. (1) Beading of the vessels may be present. In the macular area the small arteries may show corkscrew tortuosity, but these are rare and seen only in the late stages. They might also be seen in the late stages of sclerosis from hypertension and indicate extensive endothelial proliferation. When the thickened artery crosses the vein the compression is usually at right angles. (18). This perivascular thickening is called perivasculitis. It is a process of sclerosis that follows partial or total occlusion, whereby the arterial wall
may be replaced, covered or lined on either side by connective tissue. (47).

Syphilitic choroidoretinitis as a rule attacks both eyes simultaneously and early there is frequently very small deposits in the vitreous which are not often sufficiently numerous to cause an obstruction to vision. During the initial stage of the disease there may be no changes discernible by ophthalmoscopic examination. Later, there is usually a definite blurring of the papilla which is often surrounded by a yellow halo. The first manifestation of syphilis that can be recognized by the ophthalmoscope as definitely syphilitic in etiology are usually dark spots scattered about the fundus. (13). This represents a healing stage of syphilitic choroiditis which has destroyed Bruch's membrane mating together the choroid and retina and in healing an atrophy occurs and the area contains proliferated pigment. (48). These dark pigmented spots tend to be round or oblong and their margins are fringed. This fringed appearance of the choroidal lesions is quite constant. These lesions, however, are not sometimes sufficiently characteristic to enable the examiner to make a diagnos-
is of the condition from the ophthalmoscopic finding alone.

After the disease is well established, yellowish white plaques appear. Soon these undergo atrophy and thus give to the fundus the appearance of being studded with light-colored patches. These patches vary in size and shape and are usually heavily bordered with pigment. The retinal vessels, as they cross the denuded areas, are also occasionally seen to be laden with pigment. Through the overlying retina the choroidal vessels, frequently bordered with pigment may often be seen. (13). This condition may also be accompanied by hemorrhage. (20).

The existence of syphilis of syphilis of the retina not accompanied by choroiditis has been questioned, however. Parson(5) describes a syphilitic retinitis but states it is often accompanied by disease of the choroid. If it occurs as a primary retinitis syphilitic endarteritis is a predominant sign. (5). This author does not describe choroidoretinitis, but his description of retinitis is very similar to the description described here under choroidoretinitis.

In acquired syphilis the disease usually
occurs one to two years after infection. (5). A condition sometimes described as salt and pepper fundus may be present. This is more common to congenital syphilis. Such patients often show a dusty or peppery discrete pigmentation of the retina at the periphery, associated with a tigroid condition of the fundus in this situation. (13). It is only distinguishable from what is often seen as a normal condition by the greater aggregation of the pigment. (5)

In certain cases of cerebral syphilis there may occur an optic nerve atrophy preceded by an optic neuritis, which often presents an unusual picture that may have characteristic elevation of the papilla which extends outside on the retina. (11). The elevation of the retina causes the margin of the papilla to be obscure. The peripapillary edema is a reddish-grey to a pure grey ring one or two papillary diameters broad and around the entire nerve. (49). An elevation of the papilla may not be present but any previous excavation may be filled by edematous tissue. (11).

Also associated with syphilis is optic atrophy. Primary or simple optic atrophy is char-
acterize by a pale or white nerve head, with well
defined borders. The physiologic cupping and a few
minute dark spots marking the pits in the lamina
cribrosa are usually visible. In some cases atro­
yphy in the nerve fiber layer of the retina pro­
duces a light-colored halo partially or completely
surrounding the disc. The vessels are usually nor­
mal though the artereies may appear small. This is
associated with Lues of central nervous system.
Secondary or postneuritic atrophy also occur in ex­
tensive neurosyphilis. The nerve head is paler than
normal or white, as in simple atrophy, but the disc
borders are indistinct and the physiological cup is
filled with tissue. White lines often accompany the
retinal vessels away from the disc. (5,6,13,49).
The pallor of the disc is not due to atrophy of the
nerve fibers, but to a loss of vascularity. (5).
Some authors do not consider vascular changes in the
nerve head as optic atrophy. There must be some vis­
ual changes before atrophy is considered present.

F: TUBERCULOUS MANIFESTATIONS IN THE FUNDUS.

Beginning about four years after the dis­
covery of the ophthalmoscope we find descriptions of
choroidal tubercles in the medical literature. Among
the investigators who are associated with the early observations are Jaeger, von Graefe, Liber, Marz, Bouchert, Gerlach, Fraenkel and Honer. These descriptions include two types commonly known as (1), the granulona or solitary tubercle usually associated with chronic tuberculosis, (2), choroidal miliary tubercle associated with miliary tuberculosis. (50).

In 1890 Michel emphasized the overwhelming importance of tuberculosis in the etiology of ocular disease. (35). Ocular manifestations are very rarely found among persons suffering from active and undoubted pulmonary tuberculosis. (51). The subject is usually an active young individual. One attack immunizes the organ against subsequent attacks. (52).

In the last few years much attention has been given to the tuberculous etiology of recurrent retinal and vitreous hemorrhages accompanied by a perivasculitis. Much of the experimental work points to the possibility of tuberculosis being a cause of such a picture although it is clearly shown it is one of a group of etiological factors. (53).

This type of fundus is included under the heading of Primary Sclerosis in this paper. Fried-
enwald (35) describes this lesion as: "One sees extensive lesions in the retinal vessels, small thrombosis of the retinal veins with the development of varices aneurysmal dilatations. Extensive perivascular infiltration is often present. There is not infrequently a small focus of choroiditis." (35). If the patient is followed recurrent retinal and vitreous hemorrhages may be seen. These may be absorbed and leave no evidence in the fundus, or they may be organised with connective tissue and blood vessels may invade the area, (tubercular retinitis proliferans.) (54). Stellate figures are sometimes seen in the macula in tuberculous choroiditis and retinitis proliferans. (55).

When the choroid is involved we find several manifestations by the ophthalmoscope. Vitreous opacities are present and sometimes very dense, fluffy white area not clearly seen and fading out into normal tissue are also seen. They are likened to balls of fluffy cotton or wool, and are thought to be tubercles. Primarily in the choroid, but they involve the retina to such an extent that the retinal vessels are obscured by the accompanying edema and exudate, but the vessels are not involved, and
and when the lesion heals, a rounded pigmented area remains, crossed by normal retinal vessels. The outstanding characteristic of these lesions is their slow progression and tendency to recur. (56). The tubercles usually select the tissue underlying the bifurcation of the retinal vessels. (51)

The situation of the tubercles are also characteristic. Due to the blood supply of the choroid the lesion may appear in the periphery of the fundus, this is most frequently seen, however, they may appear centrally. (20v12).

The solitary or granulomatous lesion of chronic tuberculosis warrants early diagnosis because by treatment the sight of that eye may be saved. The lesions usually appear unilaterally. (35)

The multiple lesion or choroidal miliary tubercle associated with late generalized miliary tuberculosis, usually appear only a short time before death and the patient dies of tuberculous meningitis. (5, 35)

G: PERIARTERITIC NODOSAL MANIFESTATION IN THE FUNDUS.

(Synonyms; Kussmaul's Disease, Kussmaul-Maier's Disease, Polymartitis Nodosa.)

The term periarteritis nodosa was given by
Kussnau and Maier in 1866 to a distinct pathologic entity characterized by the presence of nodular thickening of various sizes in the walls of the small and medium sized blood vessels and caused by inflammatory disease. In reality it is an arteritis or panarteritis involving all layers of the wall of the artery. The lesion may be a macular nodular or microscopic periarterial node. (57). Syphilis has been virtually excluded as an etiological factor. (58).

No complete description of the ocular manifestations had been described up to 1929. However in 1899 P. Muller gave a brief microscopic description. In 1929 Goldstein and Wexler gave the first full description of the lesion. They mention that the fundus had often been observed in numerous cases but not described. (57). The reason for this is that periarteritis is seldom diagnosed clinically because of the diversity of the symptoms, (59, 60) and the ocular lesion is not characteristic of periarteritis nodosa. (61)

In consideration of an ophthalmoscopic picture a few facts may be sighted;

1- King states the lesion of the choroid

65
and retina are not typical of periarteritis nodosa. (58,61)

2-Periarteritis attacks only those vessels of medium size or those with a well defined muscular coats. (61)

3-The retinal arterioles are not attacked. (61).

4-Choroidal vessels are attacked usually (57) and are attacked where they change their course more frequently. (61)

5-Since this is a generalized vascular disease one may see manifestation of kidney pathology and hypertension upon ophthalmoscopic examination. (60).

The ophthalmoscopic picture of the fundus will vary. A marked retinal arteriosclerosis of the primary type, arteriovenous compression and hemorrhages may be seen especially if complicated by hypertension. An apparently normal fundus with the presence of periarteritic nodules may be seen, or the nodules may appear as scattered white foci, and might even suggest tubercle formation. (57). Nodular formation may be seen at the lamina cribrosa. (61). An edema of the retinal and optic disc with or without hemorrhage and exudation may be seen.
(61,58). Extensive subretinal exudates may be traced to the choroidal disease. (61). Hemorrhages and cotton-wool spots may be present. (60). Secondary optic atrophy and diffuse pigmentation disturbance have been reported. (61)

If the picture is complicated with kidney damage manifestation or hypertension the picture is altered a great deal and is less characteristic than the uncomplicated cases. (57) Gruber states that there are no choroidal foci before the onset of renal disease. (57). All the authors do not agree with this statement, however.

II: MANIFESTATIONS OF THROMBO-ANGIITIS OBLITERANS IN THE FUNDUS.

Thrombo-angiitis obliterans is an inflammatory type of obliterative vascular disease affecting chiefly the peripheral arteries and veins especially of the males during early adult life. Von Winiwater described this condition in 1879 and Buerger in 1908 published a more detailed description and it has since borne his name. It is believed to be related etiologically to use of tobacco since tobacco may produce a transient vasoconstriction. It is more likely that this probably favors the extension of the disease rather than causing it. (38) About one half of the patient's are Jewish and seem to bear some relation to t.b. (62) Syph-
Ilis is not an etiological factor. (63)

Thromboangiitis obliterans shows no characteristic change in the fundi. (64). An article in which changes in the retina were seen before the development of thromboangiitis obliterans could not be found, unless vasospastic effects of the inhalation of tobacco smoke could be considered such a finding. This is a true idiosyncracy and is manifested by definite vasospasm seen in the fundus accompanied by a severe rise in blood pressure and definite evidence of peripheral vasospasm as manifested by reduced skin temperature in the extremities. (65, 66, 67). This of course is not considered an early sign of Buerger but must be considered if tobacco is considered an etiological factor. No statistic could be found in which this idiosyncrasy was found more frequently in Jews.

Toxic amblyopic is developed in excessive use of tobacco but it is not a vascular lesion that causes the symptoms. (5).

The nomenclature tends to some confusion in the literature. The synonyms used are presenile Grangrene, Buerger's disease, Endarteritis obliterans, thrombo-angiitis. In this paper the synonyms
used by the author of the references will be used.

Thromb-angitis has been related to angiospasm. Angiospasm had been observed by the early men using the ophthalmoscope, von Graefe, Liebrich etc. In 1866 a case was reported by Zehendorf. Greenwood discussed a case in 1904. (68). Some authors do not believe that thromboangiitis obliterans is related to angiospasm while others do. Gradle and Folk listed the causes of obstruction of the central retinal artery under ten headings but did not list thrombo-angiitis obliterans as a cause, but mentions endarteritis obliterans as an etiological factor. (69). Wageman reports a case of retinal angiospasm, which finally remained permanently closed after repeated attacks in a case of endarteritis obliterans. (68). Beach in a review of a number of cases lists endarteritis as a possible cause of retinal artery obstruction. (70). Juler also states Thrombo-angiitis obliterans may effect the eye. (71). Grasser describes involvement of the retinal arteries (bilateral occlusion) in a case of generalized thrombo-angiitis obliterans. (72). Juler in discussing Grasser case calls this so-called generalized thrombo-angiitis obliterans, typical Buerger's disease. (71). In any event if Thrombo-angiitis
obliterans has an ophthalmoscopic picture it is one of retinal spasm or retinal occlusion.

The retinal vessels if affected show evidence of changes. The arteries are exceedingly fine and attenuated manifesting definite light streaks, coppery in color. They branch at acute angles and indent and deflect the vein at the crossings. Completely fibrosed arteries may or may not be observed. An occasional tortuous corkscrew twig may be present. (72, 73).

The veins may be tortuous and dilated in small portions but narrower than normal vein, having a ration of 2 to 1 to the arterial caliber. The normal venous loops were lost. The venous blood column may show segmentation, and the flow may vary in rate. The cilio retinal vessels may be enlarged. (72, 73).

Changes in the fundi besides those finding of the vessels were described by Grasser in his report is as follows: The discs appeared edematous, the cupping was indefinite and the fine vessels evident. The macular areas were also edematous, blurred and with a faint cherry red fovea. Fairly large, round, and irregular hemorrhages were present throughout the fundi though more evident in the posterior
polar area. White fluffy areas of degeneration were distributed throughout the fundi. (72).

Retinal hemorrhages have been reported in Buerger's by Marchesani (71) and he states that these lesions are often found in thrombo-angiitis obliterans and were associated with the general disease (Gangrene of fingers and toes). Yasui Uyania (75) reports on two cases of young people with vascular interocular disease. "The outstanding pathological findings in one of the eyes were; equal involvement of both arteries and veins with marked thickening of wall etc. but there is no inflammatory change. There is some question if this is a true Buerger or not." He did not describe the ophthalmoscopic picture.

I: MANIFESTATION OF RAYNAUD'S DISEASE IN THE FUNDUS.

Raynaud's disease described by Raynaud in 1862 is the primary form of paroxysmal, bilateral cyanosis of the digits, with or without local gangrene. The attacks of cyanosis are produced by cold and relieved by heat. (38).

In reviewing the literature on Raynaud's disease, it is found that ocular complications occur infrequently. This vascular disease has no typical retinal lesion. Osler states: "I have looked
in vain for signs of constriction of the retinal vessels in several very typical cases." Raynaud himself described what he considered as an unusual fundi in two patients only. During an attack cyanosis of the hand he described retinal vessels as having very clear contour and were more definitely narrowed around the papilla than at the periphery; the central veins were dilated and elongated. (76).

Fourteen cases were found in the literature that described changes in the fundus. These include, Bland in 1889 (76), Morgan in 1889 (76), Fisher in 1902 (76), Batten in 1910 (77), Weis in 1912 (78), Blaun in 1913 (76), Barre and Duverger in 1923 (76), Shinkle in 1924 (79), Allen and Brown in reporting one hundred and forty seven cases mentioned one that possibly had a retinal manifestation (80), Applebaum and Turner in 1926 (81), Wagner and Gipner in 1927 (82), Dumphy in 1932 (76), Baillliart in 1936, 3 cases (77), Anderson and Gray in 1937 (83). In 1938 W. M. and E. W. Carpenter gave a report on the follow up of Anderson's and Gray's case (84).

A conclusion was drawn from these cases, as to the changes in the fundus; they varied great-
ly. In most cases an intermittent spasm was reported as the most common arterial finding, following repeated attacks of spasm partial or complete obstruction of the central retinal artery or one or more of the primary or secondary arteries was reported. Arterial tortuosity was reported in a number of cases. The arteries were generally described as considerably contracted, of a very clear contour indenting the veins at the arterial venous crossing. A similar appearance of them was often described. The veins were described as being normal or dilated to such an extent as to resemble aneurysm. The disc was described as being normal or discolored with a hazed border to a papillaedema of four diopters. Hemorrhages and exudates were commonly described.

The Carpenters describe the intermittent filling and emptying of the arteries and veins in their follow up report of the case of Anderson and Gray. A few of the authors describe viewing and intermittent attack of angiospasm. They varied from complete exclusion of the blood from the retina to the exclusion of it from some branch, or to a general narrowing of the arterial blood column. The
flow of the blood in the vein was reported segmented to a reverse of the direction of flow upon a pulsation in the general circulation. In one case the fundi was reported as normal but with ocular symptoms of pain and temporary blindness. The patient varied in age from 9 to 57 years, and included both male and female. The effect upon vision was very variable also, no change to complete loss of vision was noted.

For a description of the fundus during a vasospasm two articles will be referred to that are not related to Raynauds, but afford good description of vasospasm. Harbridge (25) in 1906 describes a spasm of the central retinal artery as follows: "The inferior temporal artery gradually became lessened in caliber until completely collapsed, followed rapidly by the inferior nasal and the superior arteries undergoing the same change; following quickly upon the arterial change, the veins underwent a similar process until the entire retinal circulation looked very much like ribbons against the fundus. The head of the nerve became pale; the fundus became somewhat hazy. After the fundus remained in this condition four
minutes, gradually the inferior artery began to fill quickly, followed by the others, immediately the veins began to fill, the inferior becoming enormously distended. Sight did not return synchronously with the filling of the vessel, but followed immediately after."

Bruner (85) in 1921 gave a description of a typical case. His description was similar to Harbridge. He described the arteries as contracted and thread-like and that the flow of blood ceased in the veins and appear granular.

Saunder (87) also agrees with the above description but states the arteries were reduced to thin white threads.
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