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COMMUNICATIONS

THE DYSTROPHIES OF THE MACULA

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With a genetic note by H. GRÜNEBERG (London)

FAMILIAL occurrence of lesions in the fundus situated mainly or exclusively in the central area has been recorded independently by a number of early observers: Hutchinson in 1875, Lang in 1885, Liebrecht in 1895, Batten in 1897, Haas in 1898, Doyne in 1899, Dujardin in 1904, Best in 1905, and Stargardt in 1909. As long as they constituted isolated observations the intricate problem of the unity of the different appearances shown by the families recorded and the no less complicated problem of the relationship of these cases to those showing familial macular lesions with psychic or neurological disturbances (Tay-Sachs disease and cerebro-macular degeneration) did not arise. Inevitably, incidental observations tended to assume an exaggerated significance in early reports. Thus in Doyne's cases the "honey-comb appearance"—by no means a characteristic feature in some of Doyne's later cases—has dominated the discussions on this affection. Best's belief that in his cases the lesion was congenital and stationary has likewise tended to emphasize features which are probably not valid, but led Stargardt to differentiate his own cases as developing in childhood and showing a progressive course. These difficulties have become less real when subsequent

reports showed that many cases conform to the description given by Stargardt and such of the earlier observers as Batten and Dujardin.* A large group has these unifying features: (1) familial occurrence, (2) a bilateral fundus lesion confined essentially to the macular area, (3) onset at about 8-14 years of age, (4) progressive course leading to loss of central vision and no peripheral involvement.

The recognition of this clear-cut group still leaves the problem of the significance of such "atypical" cases as those of Doyne, of Best and of many other subsequent observers. What contact there is between the "typical" and "atypical" cases can be assessed only when the limits of the more clearly established entity are defined. In recording eight new familial groups, some of them showing considerable departures from the classical type of familial progressive macular degeneration, the literature is reviewed and an attempt is made to classify these affections in relation to each other, to the more recently recognised allied conditions, and to cerebro-macular degeneration. In reviewing the literature, isolated cases, *i.e.*, those in which the diagnosis has been made without a definite family history, have been discarded—except for incidental reference—as lacking conclusive validity for analytical purposes.

(1) The Clinical Varieties of Central Fundus Lesions of a Familial or Hereditary Type

There is a considerable variety of familial affections confined largely or exclusively to the central area of the fundus—some recognised only recently.

(i) *Congenital macular coloboma.*

Familial cases of this congenital and non-progressive lesion were first reported by Schott and by Clausen in 1921. Subsequent reports have come from Davenport (1927), Sorsby (1935), Evans (1937) and Niccol (1938). Direct dominant inheritance was noted by Clausen, Davenport and Sorsby. Sorsby's cases have the additional interest of an associated skeletal defect: apical dystrophy of hands and feet.

(ii) *Best's disease.*

So far the appearances described by Best in 1905 in eight members of one family have not been recorded outside the collateral branches of this particular family. The family originally

* Hutchinson's cases are best left out of any discussion on the subject. The description (devoid of illustrations) is not sufficiently explicit to enable a clear retrospective diagnosis. They can be claimed as examples of familial choroidal sclerosis, "Doyne's Choroiditis" or macular dystrophy.

studied by Best has been the subject of subsequent and exhaustive investigations by Vossius, Weisel and Jung; 22 members out of 300 studied are now known to be affected. Lloyd speaks of having seen isolated cases of Best's disease. Vision in this affection is frequently good, sometimes even 5/5, as the lesion is generally situated below the macula. In one case there was colour blindness which was almost complete. Best believed that two of his eight cases showed the lesion on one side only, but in a subsequent study Jung doubts these two cases, as the ophthalmoscopic changes fell within normal limits. Vossius holds that the lesion is not always congenital, but the evidence for this too is not found convincing by Jung. There is, however, no conclusive evidence that the affection is indeed congenital; it has not been observed as such and the assumption that it is congenital is based upon its non-progressive character and upon the personal histories which go back to childhood—in such of the cases in whom vision is poor.

(iii) *Macular dystrophy.*

In contrast to the two previous affections with their gross ophthalmoscopic lesions and their congenital or early onset, the macular dystrophies may show but mild disturbances ophthalmoscopically and develop in patients who previously had good vision. Behr's classification (1920) of the macular dystrophies has the merit of emphasising their abiotrophic character, for in addition to the group of probably congenital lesions described by Best and the cases developing in childhood as noted by Stargardt and other observers, Behr drew attention to cases developing in early adult life, at the beginning of involution ("pre-senile," at 45 years) and further argued that some cases of senile macular degeneration may be familial and represent the end of a series beginning with a congenital lesion and running through different forms making their appearance at the critical ages: at the second dentition (6-8 years), at puberty, at full adult life (20 years), at the presenium (45 years) and in senility. Behr could not advance any proof that familial cases do occur in senility, but this is now available in the families reported by Waardenburg (1936 and 1938).

Morphologically Behr admitted macular lesions ranging from mild changes to central disturbances generally covering an area of $\frac{1}{2}$ -1 D.D., though in one case an area 5 D.D. was involved. He emphasised the purely macular character of the lesion and held that any optic nerve involvement that may occur in these cases is an associated lesion and not part of the picture. None the less extension beyond the macular area is not uncommon and peripheral lesions have been reported.

Ophthalmoscopically the appearances seen in macular dystrophy show a wide range, the usual variants being fine pigmentary mottling which is easily missed, whitish dots with but little pigment disturbance, and atrophic areas. Central pigmentary changes of the retinitis pigmentosa type have been reported, and also appearances suggestive of retinitis punctata albescens.

In discussing the functional disturbances seen in macular dystrophy, Behr pointed out the frequent occurrence of colour anomalies and even total colour blindness. In cases of total colour blindness the macular lesion is generally not marked, but the existence of such lesions lends further support to the view that there is no sharp demarcation between the congenital type of macular lesion and the macular dystrophy of later onset.

(iv) *Doyne's choroiditis.*

The literature on this affection is sparse. Doyne drew his material from two families, recently more fully described by Tree (1937). Isolated cases have been reported by Holthouse and Batten (1897), Bickerton (1900), Morelli (1928) and more recently by Malbran and Adroque (1936) and Tanaka (1938). Foster (1932) described two brothers as doubtfully belonging to this group; these cases are more fully discussed below (K. family, p. 481). The affection is said to develop at about 40 years of age and is characterised by massive formation of white dots in the disc-macular area; pigmentation is slight and atrophic areas ultimately form. Haemorrhages may be present during the course of the affection, and occasionally, also, a honeycomb pattern.

(v) *Angeoid streaks.*

This too must now be regarded as a familial affection confined essentially to the central and paracentral areas. The recognition of the associated pseudoxanthoma elasticum (Grönblad, 1929) and of elastic tissue degeneration in the big systemic vessels (Böck, 1938; Prick, 1938) puts this affection in a category of its own: elastosis dystrophica, the ocular lesion being caused by degenerative changes (ruptures) of the elastic membrane of Bruch.

(vi) *Central choroidal sclerosis.*

The familial occurrence of central choroidal sclerosis has been the subject of a recent study (Sorsby, 1939). Here it is only necessary to emphasise that the early stages may simulate a retinal macular dystrophy.

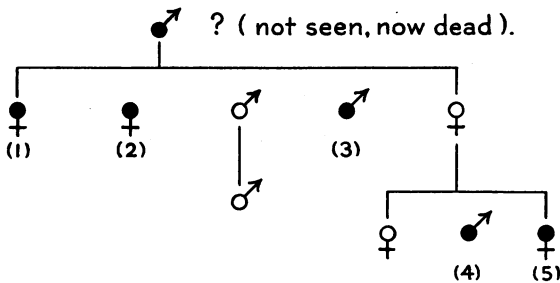
It is obvious that of these six forms of familial affections of the central area of the fundus, congenital macular coloboma, angeoid streaks and central choroidal sclerosis are clear-cut clinical groups, but in the three remaining affections the line of demarcation is

faint. The problem they raise is to what extent do these three forms—Best's disease, Doyne's choroiditis and the macular dystrophies with their considerable range of clinical appearances—represent different aspects of fundamentally the same retinal dystrophy, which in different families shows a different ophthalmoscopic appearance, and has a different clinical course and genetic behaviour. That extensive variations may occur within the same affection is well known from the behaviour of retinitis pigmentosa with its recessive and dominant forms, its early or late onset, and its mild or severe course in different families.

(2) Personal Observation

(i) *The C. Family.*

Family history.—Father had bad sight all his life; mother was normal. No consanguinity. Of the three daughters, two are affected, as is also one of the two brothers. The unaffected brother has a normal child, and the affected sisters are unmarried. The unaffected sister has three children, two of whom are affected.* The affected brother has no children.



(1) *Edith C.*, aged 43 years, when first seen in 1933. Vision defective since childhood, and continued steadily worse till about the age of 30 years. Lately she has experienced special difficulty at night. Vision: R: and L: > 6/60. Colour sense (Ishihara test): normal. Fields: full. No central scotoma. Emmetropic.

Ophthalmoscopic appearances (1933): Figures 1 and 2.

The macula and an area 3 D.D. shows extensive mottling with white and pigmented dots. The rest of the fundus is normal, and though the choroidal pattern is clearly seen, there is no suggestion of retinal atrophy peripherally. The appearances in the two eyes

* These children and their aunts were demonstrated before the Royal Society of Medicine in 1934. (*Proc. Roy. Soc. Med.*, Vol. XXVII, p. 694, 1934).

are similar except that in the right eye the choroidal vessels are exposed in the macular area and in the left eye no such vessels are seen in this region.

Re-examined in 1938, the appearances were essentially unchanged. There was no indication of any choroidal sclerosis.

(2) *Harriet C.*, aged 39 years (in 1933). The history and subjective findings are as for her older sister. Like her sister, she is emmetropic, is certified blind and works in a blind factory.

Ophthalmoscopic appearances (1933): Figures 3 and 4.

These are similar to those seen in the older sister, but the lesion is more advanced and rather more irregularly distributed. In the right eye the choroidal vessels are clearly seen in the macular area in which the pigment changes are tending to assume a more conglomerate distribution. In the left eye the appearances are not so fully developed and are intermediate between those seen in the right eye and the changes shown by the elder sister. There is no definite involvement of the retina beyond the central area.

Re-examined in 1938, the condition was essentially unchanged and like in the elder sister there was no evidence of any central choroidal sclerosis.

(3) *John C.*, aged 34 years. Vision: $> 6/60$ in each eye. No obvious difficulty at night. Is doing sighted work. Seen on one occasion only.

Ophthalmoscopic appearances: Similar to those shown by the elder sisters, though not so fully developed.

(4) *Bernard C.*, aged 8 years (in 1933). Not conscious of any eye trouble. Vision $6/6$ each eye. Hypermetropia (2.0 D.).

Ophthalmoscopic appearances: Doubtful departure from normal. Some loss of lustre at macular area with a few ill-defined whitish spots suggesting a worm-eaten surface.

Re-examined in 1938, the central area showed definite pathological changes. (Fig. 5.) The macular area itself showed several patches of gross pigment lying on an atrophic background. Surrounding these central changes were a number of white dots. The appearances in the two eyes were similar. Vision is now $6/9$. Not conscious of any visual defect.

(5) *Betty C.*, aged 5 years (in 1933). Not conscious of any eye trouble. Vision $6/6$ each eye. Hypermetropia (2.50 D.).

Ophthalmoscopic appearances in 1933 as in her brother, but less marked.

Re-examined in 1938 the macular lesion was well established (Fig. 6). It consisted of some heightened pigmentation over the central area without the gross pigmentary changes seen in her brother. In addition there were whitish dots surrounding this zone, not extending so diffusely as in the boy.

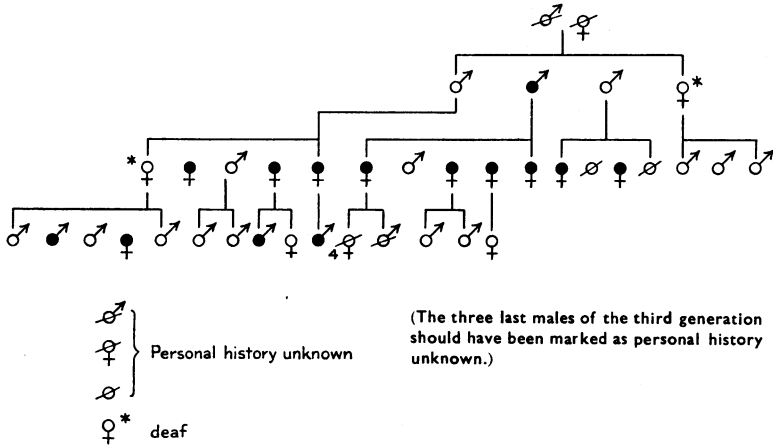
Remarks.—This group has the following points of interest :

- (1) Unusual mode of inheritance, probably irregular dominance.
- (2) Early onset of ophthalmoscopic changes in the children.
- (3) The extensive ophthalmoscopic changes seen in the end stage in the two aunts, emphasising the fact that macular dystrophies need not remain confined to the central area.
- (4) The onset of some night-blindness with the progress of the affection in the aunts.
- (5) Judging by the slow decline in central visual acuity in the children, the lesion is not rapidly progressive.

(ii) *The M. Family.*

Family history.—Mrs. M. (1) is the mother of John M. (2) and the maternal aunt of Bernard W.* (3). The mother of Bernard W. is said to have poor vision since childhood.

The family is extensive and the following tree, prepared by Bernard W. who is a male nurse, indicates the large number of members that are said to be affected.



If this tree is accepted on its face value, a doubtfully affected great-grandmother, transmitted the affection to one son and four of his daughters. Nothing is known of the children of one of the affected daughters, whilst the children of two other affected daughters are normal. Of the three unaffected members of the

* B.W. was demonstrated by Frederick Ridley before the Royal Society of Medicine in 1937. (*Proc. Roy. Soc. Med.*, Vol. XXX, p. 390, 1937).

second generation, the condition of the daughter's children is unknown, whilst her two (normal) brothers had affected daughters. In the fourth generation there are affected sons and daughters of an unaffected mother, and affected sons of affected mothers.

(1) *Mrs. M.*, aged 39 years. Trouble began at about the age of 20 years. Vision with correction : R : 6/24, L : 6/60. Patient was not seriously handicapped till after the birth of her only child (described below) eleven years ago. Vision has become worse recently with the onset of pregnancy; an affected sister who had two children (one being B.W. described below) is said to have experienced a similar deterioration of vision with each pregnancy. Hysterectomy was performed on the patient and there appeared to be some improvement in vision.

Ophthalmoscopic appearances: (Figs. 7 and 8). The lesions are more marked in the right eye than in the left. In both central areas there are whitish masses suggestive of exudate. They appear to be slightly raised on the surface and some of the patches are of a whiter and harder colour than others. The lesion in the right eye is bordered below by a sharply marked white streak with some pigmentary changes. The lesions appeared more quiescent after the termination of the pregnancy.

(2) *John M.*, aged 11 years (son of *Mrs. M.*). Is not aware of any visual defect. Vision with correction 6/9 each eye.

Ophthalmoscopic appearances: (Figs. 9 and 10). The lesions are confined to the central areas which are diffusely mottled. In the right eye, below the macula there is a circular patch 1 D.D., the upper part consisting of white dots and the rest showing a dense white mass suggesting organized exudate. In the left eye a more or less symmetrically placed circular area has essentially the same appearance as that seen in the right eye, except that the patch is more atrophic. The organized exudate at the lower pole is smaller than in the right eye.

(3) *Bernard W.*, aged 26 years (nephew of *Mrs. M.*). Patient was not aware of any eye trouble till 18 months ago. At the age of 24 years vision was 6/6 each eye, though even then the appearance of "a hole at the macula" was present in the right eye. Vision has since deteriorated to 6/60 in the right eye and 6/9 in the left. His mother, who apparently is likewise affected, had vision of 6/18 in each eye at the age of 52 years.

Ophthalmoscopic appearances: (Figs. 11 and 12). The left eye shows the same generalized mottling of the central area that is seen in *John M.* The right eye shows in addition an appearance suggestive of a hole at the macula. In contrast to the lesions seen in *Mrs. M.* and her son, there is nothing to suggest an exudative reaction in this patient.

Remarks:—

- (1) The ophthalmoscopic changes are unusual. Seen by themselves as isolated patients, Mrs. M. and her son would suggest, because of the exudative reaction, a diagnosis of either central choroiditis or of a central retinitis of an obscure type.
- (2) The more classical changes shown by B.W. emphasize the considerable variation possible within the same family.
- (3) There is preservation of fair vision in spite of extensive ophthalmoscopic changes.
- (4) The mode of inheritance is probably irregular dominance.
- (5) The severe ophthalmoscopic lesion without serious visual disturbance in the boy at 11 years of age cannot be regarded as evidence of a possibly mild course in view of the deterioration in sight observed in his uncle during the last eighteen months.

(iii) *The N. Family.**

Family history.—Parents are first cousins. They have normal vision. Father practically emmetropic: mother hypermetropic (+ 4.50 D. sph. + 0.5 D. cyl.).

Evelyn Mary N.: First seen at 12 years of age (in 1915). Vision said to have failed a few days before. Vision with correction (high hypermetropia) R: 6/12, L: 6/18. Nothing abnormal seen in fundus. Two years later "changes at both yellow spots." Drawings (Figs. 13 and 14) were made in 1928 at age of 25 years, *i.e.*, 9 years after changes first observed at maculae. The lesion in the right eye had become more pigmented, and was a little flatter, it having been definitely raised when first noted. The appearances in the left eye had not changed appreciably. Last seen in June, 1938, when vision in the right eye, which has steadily deteriorated, was 6/60 and in the left 6/18 (with correction, R: + 5.0 D. sph. \ominus 2.75 D. cyl., L: + 7.0 D. sph. \ominus 3.0 D. cyl.). The central area over a large extent is becoming atrophic; the left eye showed no obvious changes.

Kingsley N.:—First seen in 1914 at the age of 8. Vision with correction (+ 4.50 sph. \ominus 1.5 D. cyl.) was 6/18 in each eye. Round masses of exudate, mostly white in colour, were present at both maculae. In 1920 there was no change, apart from slight flattening of the exudate. In 1928—when the drawings (Figs. 15 and 16) were made—vision in each eye was 6/12, and the fundi showed a circular greyish area in the region of the old patches

* Not seen personally. Patients of Mr. Harold Grimsdale, to whom I am obliged for the clinical details.

of white exudate. Last seen in November, 1934, at the age of 28 years, when vision was R: 6/12, L: 6/9, binocularly 6/6 partly. The appearances had not changed substantially.

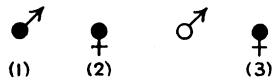
Two more members of this family have been examined. A brother now aged 35 is normal; vision with + 1.50 D. sph. is 6/4p. each eye. A brother of the father who had full vision with correction but showed (in 1913) a small whitish patch below the left disc "sharp and hard, ? retinal exudate."

Remarks:—

- (1) The ophthalmoscopic appearances in these two patients lend support to the existence of an "exudative" type of macular dystrophy illustrated by the M. family.
- (2) The preservation of good vision in one of the patients over a period of 20 years (between the ages of 8 and 28) is as noteworthy as the decline in visual acuity in his sister.

(iv) *The A. Family.*

Family history.—Mother married twice. No consanguinity in either marriage. There are three children from the second marriage, a twin boy and girl aged 4 years and a boy aged 6 months: they are normal. The affected children—3 out of a sibship of 4—come from the first marriage. Their father is dead; his sight is said to have been good.



(1) *Henry John A.*: Aged 17 years. Vision bad throughout school life. He had to attend at a school for partially-sighted children. Not getting worse. No night-blindness. Vision is less than 6/60 in each eye. Emmetropic. Heavy colour defect; in the Ishihara test misses all figures except those for red-green vision, on which he is uncertain. Fields full. No central scotoma.

Ophthalmoscopically (Fig. 17) there is an atrophic area at the macula about $1\frac{1}{2}$ D.D., bordered by finely scattered pigment.

The fundus immediately surrounding the area of the disc—macula region is normal, but towards the equator there are gross pigmented and atrophic areas, not suggestive of retinitis pigmentosa extending towards the periphery in a progressively diminishing manner. The disc and vessels are normal. The two eyes are fairly equally involved.

(2) *Florence A.*, aged 15 years. Like her brother she attended a school for partially sighted children. Not conscious of any

deterioration in vision. No night blindness. Vision: R and L: 6/60. Emmetropic. Colour sense (Ishihara test): normal. Field full. No central scotoma.

Ophthalmoscopically (Fig. 18), in each eye the macular area over 1 D.D. is atrophic with fine pigment disturbances. This is the most striking lesion, but scattered over the greater part of the fundus, more especially towards the periphery are numerous fine white and pigmented dots, some of them ghost-like in appearance. The disc is normal, but the vessels are rather narrow.

(3) *Kathleen A.*, aged 9 years, is the fourth member of the family. Her immediate senior, a boy aged 13 years, is normal. She herself has never seen well at school and is now attending a school for partially-sighted children. No night blindness. Vision: R: > 6/60, L: 6/60. Emmetropic. Colour sense (Ishihara test): normal. Field full. No central scotoma. Faint lamellar opacities are present in both lenses.

Ophthalmoscopically (Fig. 19), the macular area over 1 D.D. shows fine pigmentary changes of a pathological character. The immediately surrounding zone is normal. Beyond this the whole fundus shows fine mottling, and towards the equatorial region pigmentary changes strongly reminiscent of the "bone-corpuscle pigment" are present, some arranged along the vessels. The disc and vessels are normal.

All the three children are emmetropic.

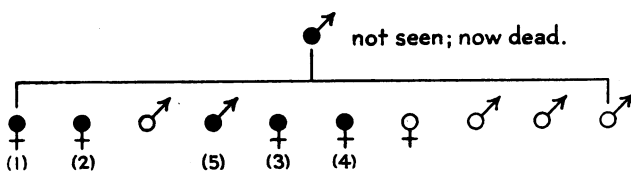
Remarks:—

- (1) In addition to the macular lesion with gross disturbance in the acuity of central vision, this group illustrates (a) peripheral involvement of the fundi and (b) appearances suggestive of retinitis pigmentosa as shown by the state of the arteries in the second child and the pigment changes in the youngest. The absence of night-blindness is noteworthy.
- (2) The fundus appearances approach those seen in cerebro-macular degeneration, but there are no neurological or psychic changes in this group.

(v) *The K—r Family.*

Family history.—Father died 20 years ago practically blind at the age of 63 years. The eye trouble began at about the age of 40 years. He was one of a large family and "nearly all his brothers were affected." The son of one of the brothers is also said to be affected. There was no consanguinity between the father and mother. There were 10 children, 5 sons and 5 daughters. Four of the daughters were personally examined and

are affected. The fifth daughter is said to be normal. Of the 5 sons nothing is definitely known of the eldest and another appears to be affected. The 3 remaining sons are the youngest members of the family, being 45, 44 and 42 years of age respectively.



(1) *Mrs. A. H.*, aged 62 years. Vision 1/60 in each eye. Sight began to fail about 20 years ago, but does not seem to have deteriorated lately. She has one daughter, aged 21 years, who is said to be normal.

Ophthalmoscopic appearances: (Figs. 20 and 21). There is some mild retinal arteriosclerosis, but the most striking lesion is an extensive area of retinal atrophy situated centrally in both eyes with massive pigmentary changes in the more central part of this atrophic area. There is some evidence of choroidal sclerosis deep to the pigmented patches. Towards the periphery there are a number of white dots situated deep to the retinal vessels.

(2) *Mrs. W. P.*, aged 60 years. Vision 1/60 in each eye. Sight had been failing for 20 years and became markedly worse after the birth of her third child. There are three daughters aged 24, 22 and 19 years respectively. They are said to be normal.

Ophthalmoscopic appearances: (Figs. 22 and 23). The lesion is similar to that in her elder sister, but is more strictly confined to the maculae. The peripheral white dots are far fewer. Some of the pigment is clustered around the vessels, but does not suggest the bone corpuscle pigment of retinitis pigmentosa; the arteries are normal. Here and there "exudates" are present.

(3) *Mrs. A. R.*, aged 53 years. Vision 6/60 in each eye. The trouble began about the age of 40 years and has steadily got worse. There are three daughters and two sons; all are said to be normal.

Ophthalmoscopic appearances: (Figs. 24 and 25). These bear little resemblance to those seen in her sisters. There is an extensive area of peripapillary retinal atrophy with comparatively little pigment disturbance. Towards the periphery there is some suggestion of choroidal sclerosis. The central areas themselves are not heavily involved.

(4) *Mrs. R. G.*, aged 50 years. Vision 3/60 in each eye. The right eye failed 4 years ago and the left 18 months ago. One of

her two daughters is mentally defective; her only son aged 12 years was examined and found normal.

Ophthalmoscopic appearances: (Figs. 26 and 27). There is a diffuse retinal atrophy as shown by appearances suggestive of "pepper and salt," but the most striking feature is the heavy central pigmented lesion with outlying dirty gray dots most marked in the right eye. There is a small haemorrhage a little below the disc at 7 o'clock in the right eye and there is some suggestion of an exudative reaction. Considerable retinal atrophy is further suggested by the map-like contours seen in the left central region.

(5) *W. K.*, aged 55 years. This patient could not be examined but there is a history of his having attended Moorfields Eye Hospital at the age of 47 years when the condition was diagnosed as slight choroiditis right eye and macular choroiditis left eye.

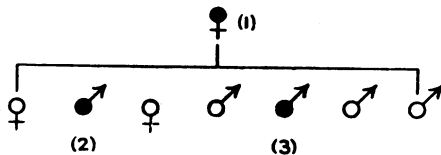
None of the four sisters examined showed any obvious contraction of the peripheral field. On Stilling tables they were heavily colour defective. None appeared to have night-blindness.

Remarks:—

- (1) In spite of the appearances in Mrs. A. R. it must be assumed that the lesion in this family is primarily macular, though there is considerable peripheral extension.
- (2) The striking feature in this group is the heavy central pigmentation. In two members of the family there is some "exudative" reaction.
- (3) The pigmentation does not appear to bear any relationship to retinitis pigmentosa, but is much more suggestive, if seen in an individual case, of an inflammatory lesion of the choroid.
- (4) The late onset in this family (after the age of 40 years) is noteworthy.
- (5) The history indicates dominant inheritance.

(vi) *The K. Family.*

Family history.—Parents not consanguineous. Father's vision R: 6/6, L: 6/60. (Right eye emmetropic; left high myopia). Mother illiterate, not conscious of any eye trouble—but fundi show pathological changes. There are seven children: five



brothers and two sisters. Two of the brothers are affected;* the other sibs are normal. The family is Jewish.

(1) *Mrs. K.*:—The central areas of the fundus show ill-defined whitish dots. These are more obvious towards the periphery. They do not constitute a marked lesion, but they cannot be regarded as normal. There is no retinal arterio-sclerosis.

(2) *Harry K.*, aged 37 years. Patient was not aware of any eye trouble until the age of 28 years. He went through his school career without any difficulty. There is no night-blindness and no colour defect. No central scotoma. Peripheral fields full. In February, 1931, vision was R: 6/24, L: 6/18. This had declined by one line within four months and deterioration has continued. Vision is now less than 6/60 each eye.

Ophthalmoscopic appearances: (Fig. 28). The discs and vessels are normal. A number of fine white dots are scattered over the fundi, lying on a more superficial plane than a diffuse grayish mottling of a rather gross character which is present over the greater part of the fundus, but most marked in the central areas, where slight pigmentary disturbances are seen in addition.

(3) *Mark K.*, aged 31 years. The patient first noticed eye trouble at about the age of 20 years. In 1931 his vision was R: 6/24, L: 6/12, which has deteriorated progressively and is now less than 6/60 each eye. The subjective findings are like those in his brother.

Ophthalmoscopic appearances: (Fig. 29). These are similar to those seen in his brother, except that the superficial whitish dots are not present and the grayish areas scattered over the fundi, but most marked centrally, are more defined giving a definite pattern. Some of these patterned figures show pigmentation. At the macula itself a number of white dots form a clear pattern.

Remarks:—

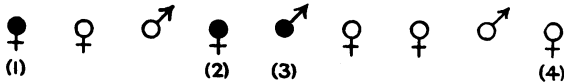
- (1) The patterned appearance in the two brothers in 1931 suggested the diagnosis of Doyne's choroiditis. The pattern has become less obvious with time, being lost in a more diffuse central degeneration.
- (2) The ill-defined changes in the mother suggest a dominant transmission, and perhaps also anticipation and a more severe course in her affected sons.

(vii) *The B. Family.*

Family history.—Parents not consanguineous. There were nine children. The third, a boy, is dead. The patient, the eldest

* These patients were demonstrated in 1931 by J. Foster before the Royal Society of Medicine (*Proc. Roy. Soc. Med.*, Vol. XXV, p. 90, 1932) as cases of ? Doyne's choroiditis.

in the family, is the only one who has visual trouble, but two other members of the family show fundus lesions.



(1) *Mrs. Marie B.*, aged 34 years when seen in 1934. Vision with glasses (low myopia) 6/60 each eye. Trouble dates back to the age of 17 years. There is no night-blindness. Fields full. With the Ishihara test there is gross colour anomaly, the patient being best on red and green. The patient has four children, three boys and a girl. Their fundi are normal.

Ophthalmoscopic appearances: In 1934 the central areas of both fundi showed numerous white dots of a gross type, diagnosed as colloid degeneration. Vision has not deteriorated further, but the ophthalmoscopic appearances have changed considerably. The pattern originally present has disappeared and the fundi show a metallic lustre in the central areas with considerable pigmentary changes (Figs. 30 and 31).

(2), (3), and (4). A sister and brother, the fourth and fifth members of the family, show white dots of the colloid type in the central areas of the fundi extending up to the equator. Their vision is full. The youngest member of the family is normal. The others have not been seen.

Remarks:—

- (1) The pattern, originally seen in *Mrs. B.* and now lost, as also the appearance of colloid bodies in a brother and sister, suggested the possibility of Doyne's choroiditis as a diagnosis.
- (2) The subsequent course involving the loss of a pattern illustrates the unreliability of the appearance in an intermediate stage as a criterion for diagnosis.

(viii) *The F. Family.*

Family history.—Parents normal. No consanguinity. There are eighteen children. Two daughters are affected,* the fourteenth and fifteenth in the family.

(1) *Helen F.*, aged 27 years when first seen in 1932. Vision was C.F. each eye. There is marked keratoconus, blepharospasm

* These cases were mentioned, but not described in an earlier paper. (*Trans. Ophthalm. Soc. U.K.*, Vol. LIV, p. 166, 1934).

and nystagmus. On the Ishihara test she is totally colour blind. She sees rather better in the dusk than in broad daylight.

Ophthalmoscopic appearances: There is fine mottling of a pathological character at the right macula. The fundus details of the left eye could not be clearly seen.

(2) *Rosina F.*, aged 29 years in 1932. Vision and the subjective symptoms are the same as in her sister, but there is no keratoconus.

Ophthalmoscopic appearances: The left macula shows an atrophic area. The right fundus could not be seen clearly, but there were a number of white spots scattered over the fundus.

Remarks:—

- (1) The fundus lesion is presumably congenital, as are the other symptoms.
- (2) As in most cases of total colour blindness with macular lesions, the ophthalmoscopic appearances are not marked.

Summary.

This group of eight families illustrates not only the extensive range of ophthalmoscopic appearances in macular dystrophy, but also the lack of uniformity as regards genetic behaviour, age of onset, course and effect on vision. As far as ophthalmoscopic appearances are concerned the children in the first group (family C.) illustrate the classical type of macular dystrophy, but the end stage seen in their aunts shows that the lesion can hardly be regarded as purely macular. The M. and N. families bring out a type not noted before, in as much as an "exudative" reaction has not been regarded as a manifestation of macular dystrophy. The A. family adds to a type which has obtained some recognition, for the literature records cases of "inverse retinitis pigmentosa," whilst the K—r family showing massive central pigmentary disturbances has an interest as a possible connecting link between the classical type and this "inverse retinitis pigmentosa" type and possibly also the "exudative" type. The K. family and the B. family illustrate the fine line of demarcation between Doyne's choroiditis and the macular dystrophies and in view of the present report of two familial groups showing an "exudative reaction," the line becomes finer still, and Doyne's choroiditis must be regarded as nothing more than a variant of macular dystrophy, showing a pattern of "exudates" at one stage in the course of its development. The F. family is yet a further illustration of the wide range of macular lesions seen in total colour blindness.

KEY TO ILLUSTRATIONS

Figs. 1-36 refer to case reports in the present paper:—

Figs. 1-6 concern the C. family; Figs. 7-12 the M. family; Figs. 13-16 the N. family; Figs. 17-19 the A. family; Figs. 20-27 the K—r family; Figs. 28-29 the K. family; Figs. 30-31 the B. family; Figs. 32-33 the F. family; and Figs. 32-36 illustrate three isolated cases. (For a summarised description of the reactions shown by these cases see p. 484).

Figs. 37-56 are illustrations taken from the literature to show different types of ophthalmoscopically observed reactions.

Figs. 37-41: Various appearances in which the lesion consists essentially of mottling of the central area.

Figs. 42-46: Various appearances of established atrophy at the macula.

Figs. 47-51: Unusual variants. Inverse retinitis pigmentosa, Doyne's choroiditis, rosette figure, and extensive perimacular involvement.

Figs. 52-56: The great range of ophthalmoscopic variants seen within several separate families.

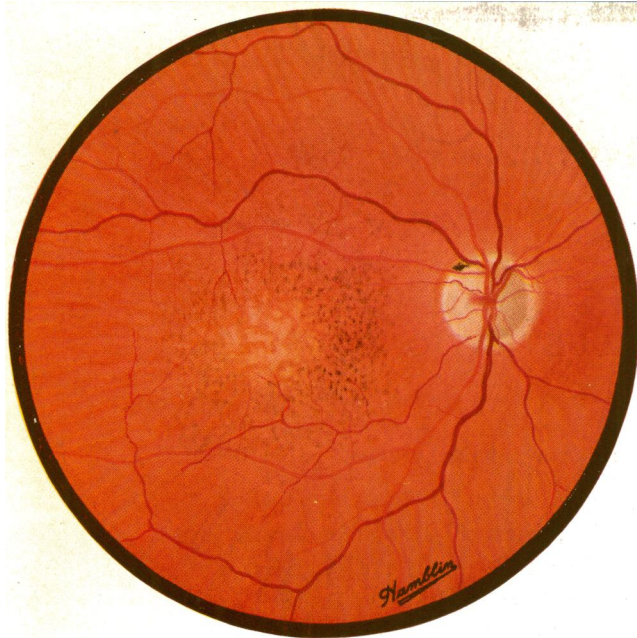


FIG. 7.

In the central area there are whitish masses suggestive of exudate. They are slightly raised and some of the patches are of a harder colour than others. The lesion is bordered below by a sharply marked white streak with some pigmentary changes.

Fig 8 shows the somewhat milder changes in the left eye. These drawings were made when the patient was 39 years old.

Figs. 9 and 10 show the appearances in the patient's son aged 11 years.

Figs 11 and 12 show the changes seen in the patient's nephew aged 26 years.

These three patients illustrate a wide range of lesions extending from fine mottling, to hole formation and "exudative" reaction.

Figs. 13 to 16 show the changes seen in a brother and sister of an unrelated family, and are further examples of the "exudative" reaction.

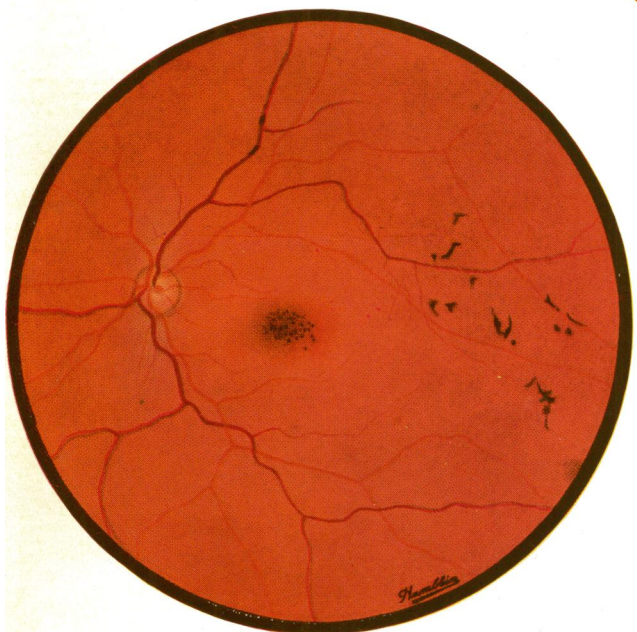


FIG. 1.

The macula and an area 3 D.D. show extensive mottling with white and pigmented dots. Choroidal vessels are exposed. The rest of fundus is normal and though the choroidal pat is clearly seen, there is no suggestion of ret atrophy peripherally.

Fig. 2 shows somewhat milder changes in the eye. These drawings were made when the pat was 43 years old.

Figs. 3 and 4 show essentially similar change the patient's sister, aged 39 years, whilst Fig and 6 show the early stages seen in a nep and niece aged 13 and 10 years respectively.

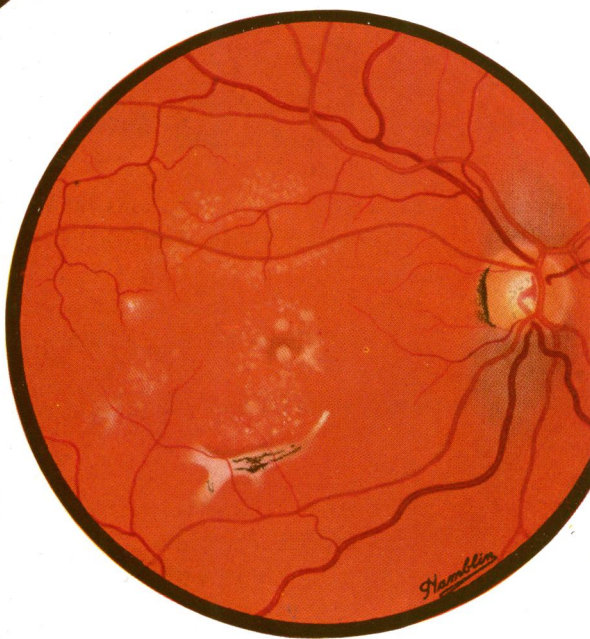


FIG. 19.

There is fine pigmentary mottling at the mac and some mottling peripherally beyond a narrow zone surrounding the central lesions. Characteristic "bone-corpuscle" pigment is present, the disc, arteries and veins are normal. Vision is 6/60; there is no night-blindness. The patient is aged 9 years.

Fig. 18 shows the changes seen in a sister aged 15 years, who shows a mottled, atrophic mac and peripheral pigment changes not suggestive of retinitis pigmentosa. The arteries are narrow.

Fig. 17 shows an advanced macular lesion with gross peripheral pigment changes in the brother aged 17 years.

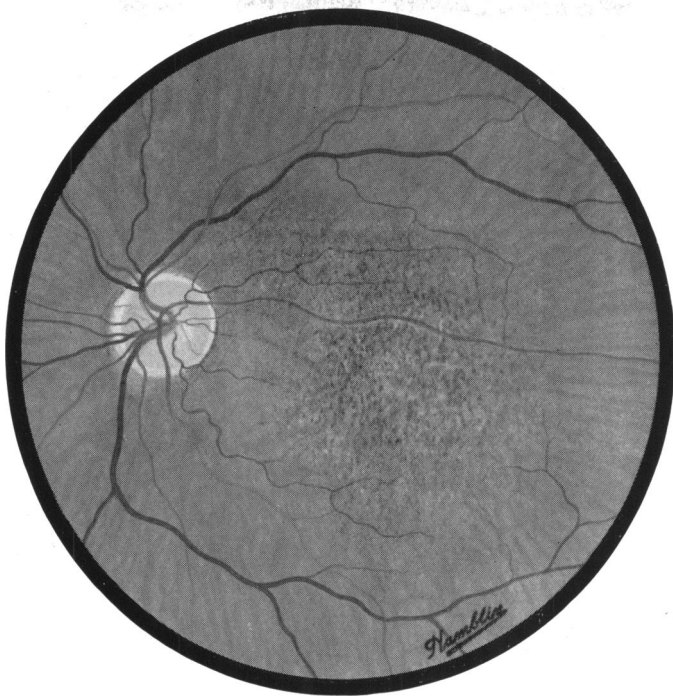


FIG. 2. For legend see Fig. 1.

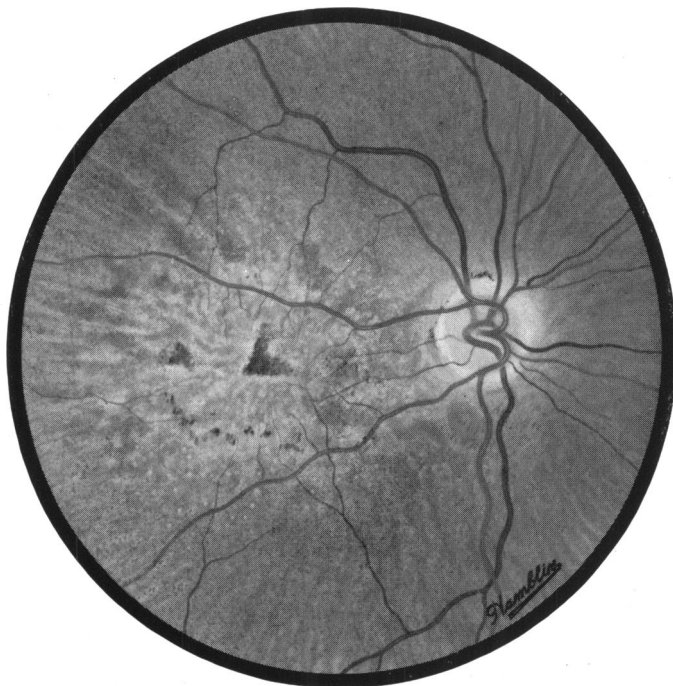


FIG. 3. For legend see Fig. 1.



FIG. 4. For legend see Fig. 1.



FIG. 5. For legend see Fig. 1.



FIG. 6. For legend see Fig. 1.



FIG. 8. For legend see Fig. 7.

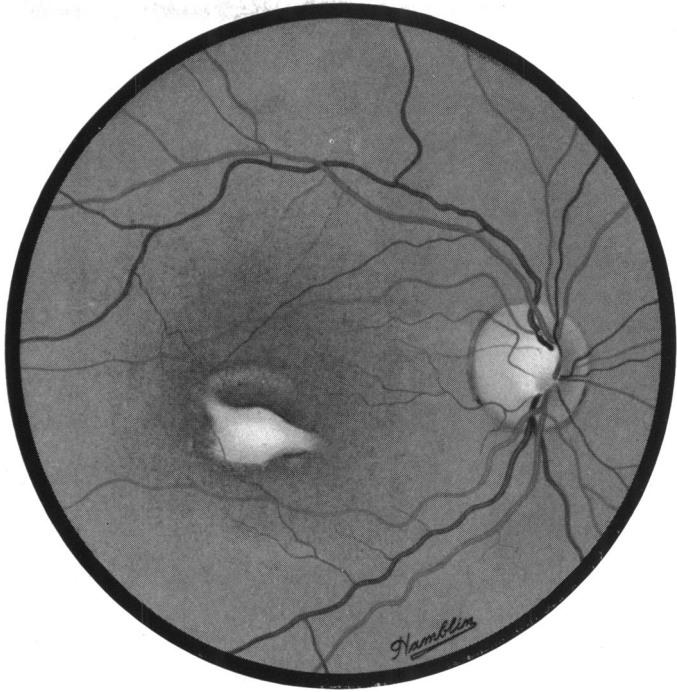


FIG. 9. For legend see Fig. 7.

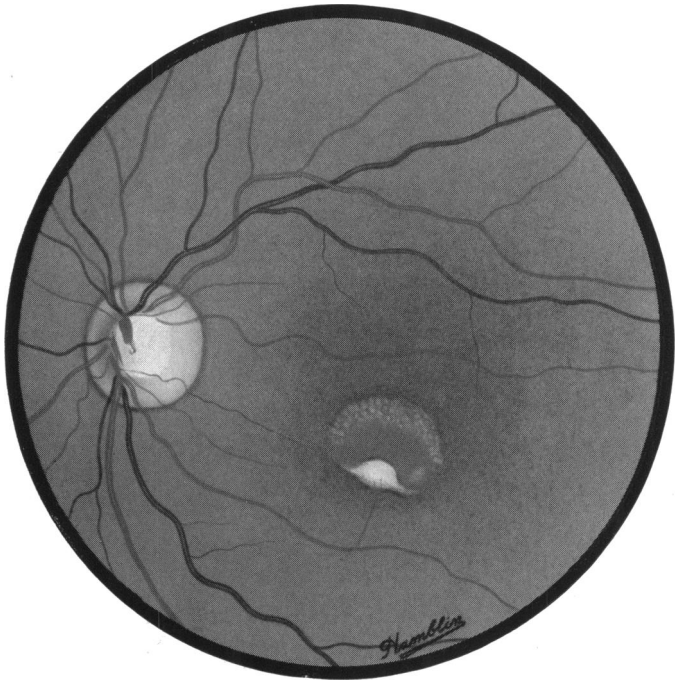


FIG. 10. For legend see Fig. 7.

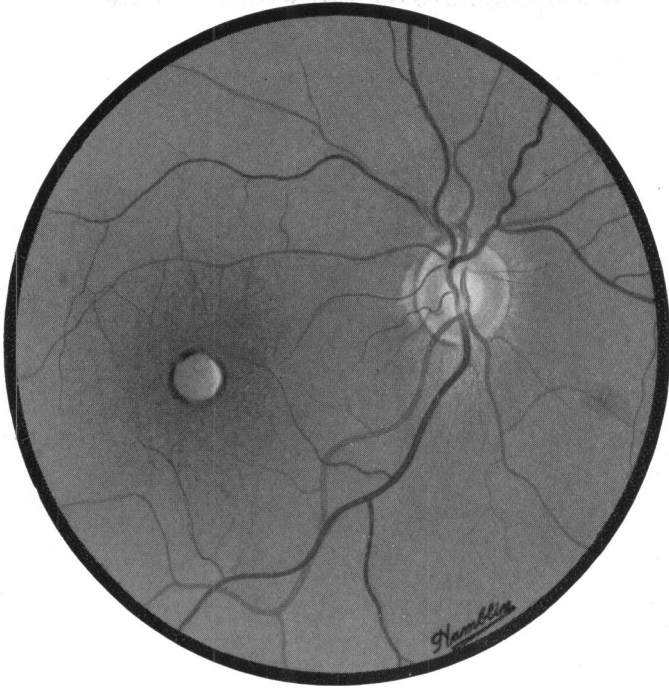


FIG. 11. For legend see Fig. 7.



FIG. 12. For legend see Fig. 7.

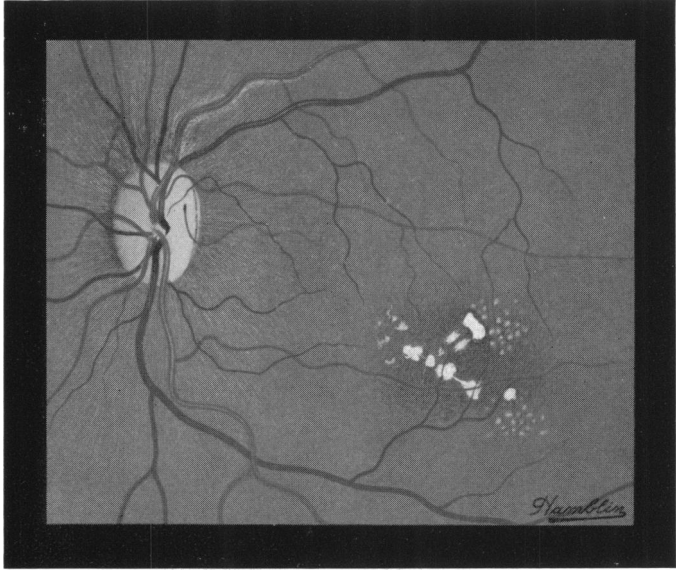


FIG. 13. For legend see Fig. 7.

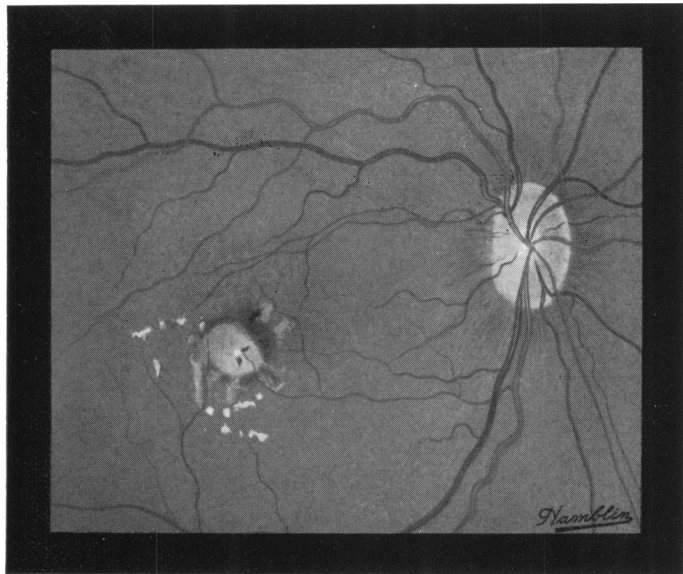


FIG. 14. For legend see Fig. 7.



FIG. 15. For legend see Fig. 7.



FIG. 16. For legend see Fig. 7.

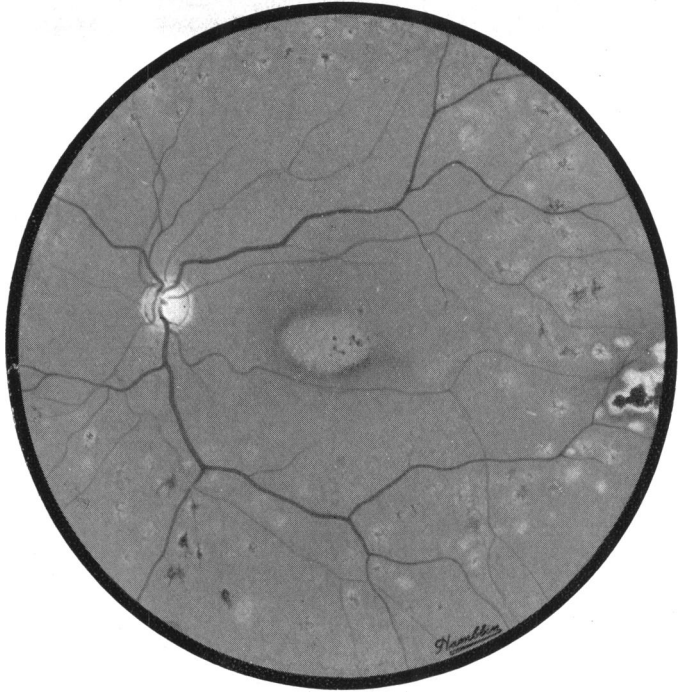


FIG. 17. For legend see Fig. 19.



FIG. 18. For legend see Fig. 19.

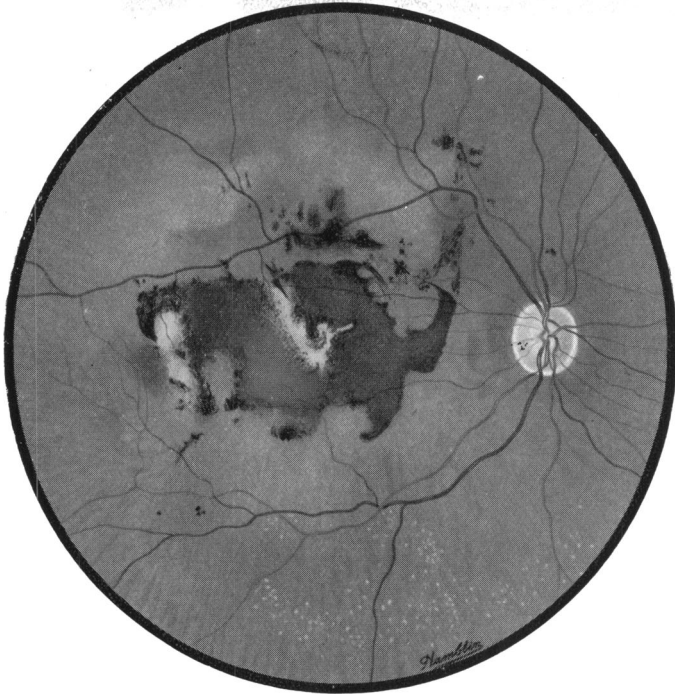


FIG. 20. For legend see Fig. 26.

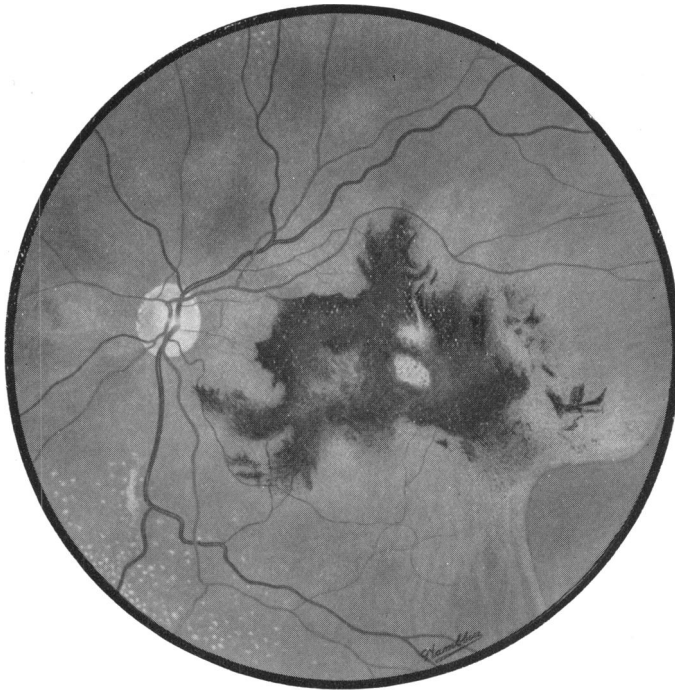


FIG. 21. For legend see Fig. 26.



FIG. 22. For legend see Fig. 26.



FIG. 23. For legend see Fig. 26.

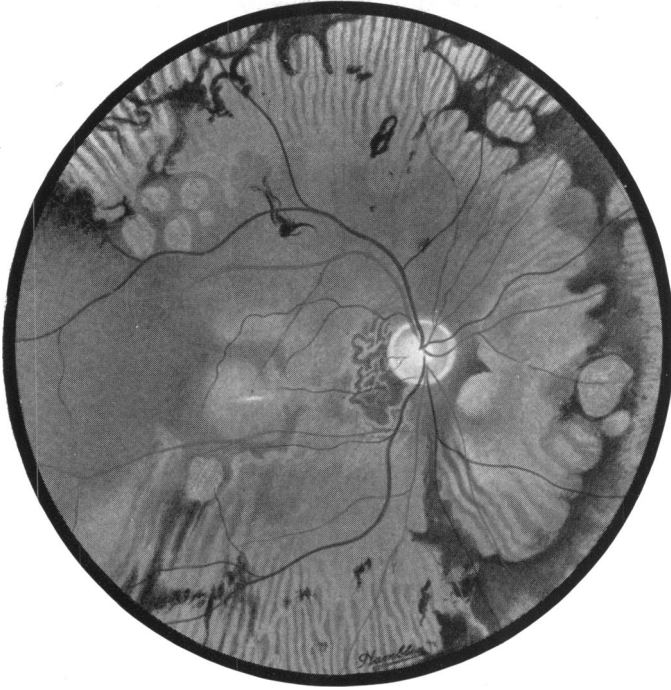


FIG. 24. For legend see Fig. 26.



FIG. 25. For legend see Fig. 26.

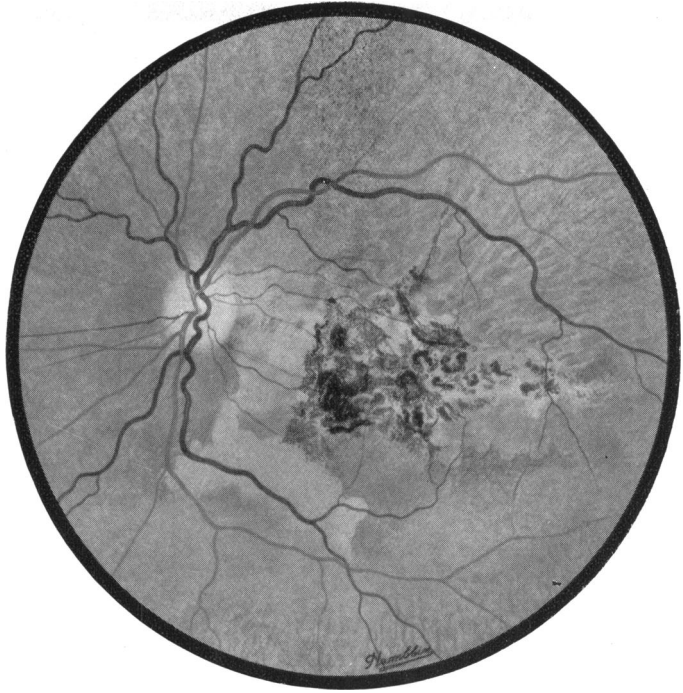


FIG. 27. For legend see Fig. 26.



FIG. 28. For legend see Fig. 29.

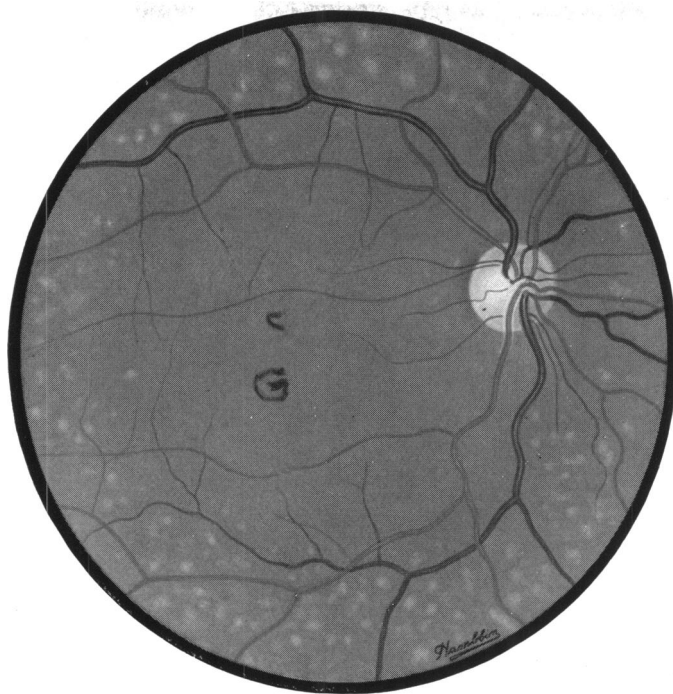


FIG. 30. For legend see Fig. 29.



FIG. 31. For legend see Fig. 29.



FIG. 32. For legend see Fig. 29.

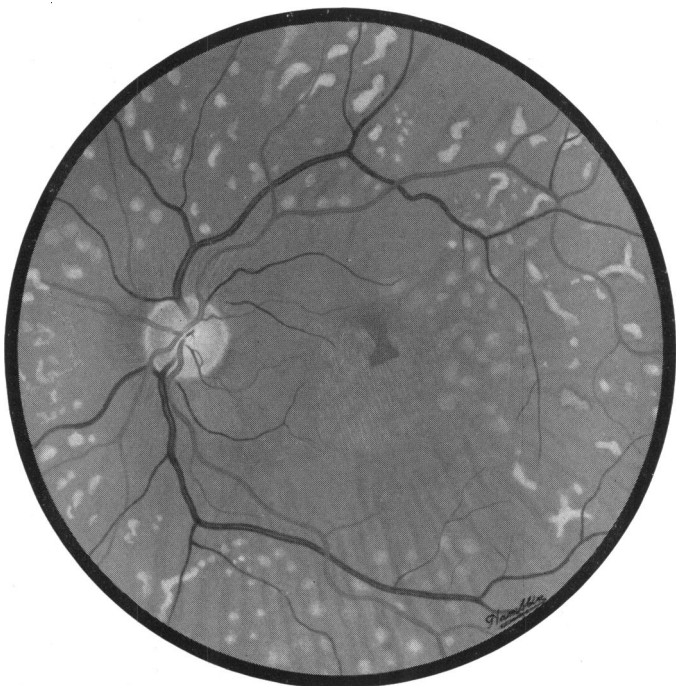


FIG. 33. For legend see Fig. 29

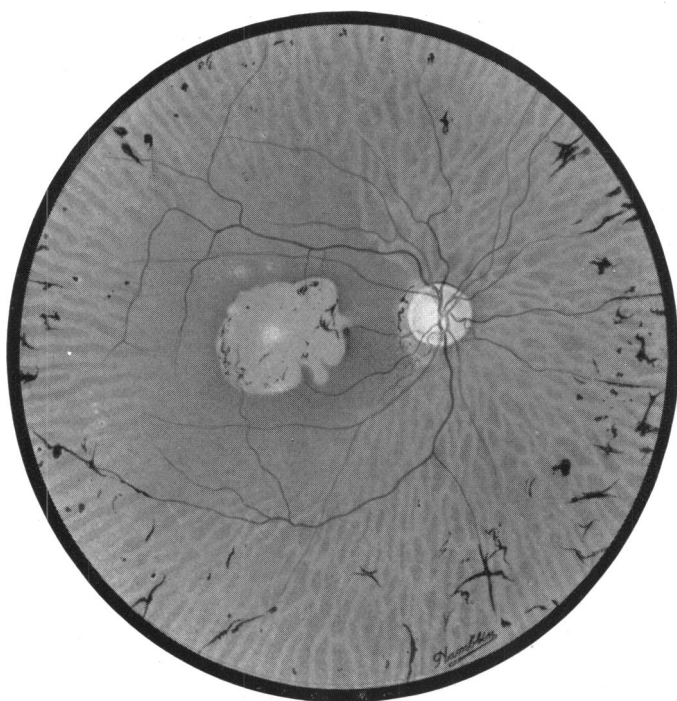


FIG. 34. For legend see Fig. 35.



FIG. 36

The right fundus of a patient of consanguineous origin. Essentially similar changes were present in the left eye. In addition to the macular lesion there is widespread retinal atrophy and incipient choroidal sclerosis. No other member of the family appears to be affected.

FIG. 26.

is heavy pigmentary disturbance in the central region over an area of more than 3 D.D., out-lying dirty-grey dots most marked towards the periphery. There is also a considerable degree of diffuse retinal atrophy. A retinal haemorrhage is present below the 7 o'clock position.

Fig. 27 shows the appearances in the left eye. The changes are less marked, but the suggestion of retinal atrophy is emphasised by the map-like areas seen in the central region.

Figs. 20-25 illustrate the appearances seen in the other three sisters. The changes seen in one of the latter (Figs. 24 and 25) bear but little resemblance to those seen in the three other sisters.



FIG. 29.

The patterned exudates characteristic of Doyme's choroiditis are most marked centrally, but also extend peripherally. There is some pigmentation. The patient is aged 31 years.

Fig. 28, illustrating the appearances in an older brother aged 37 years, shows a more advanced stage with the pattern becoming obscured. Ill-defined whitish dots were present in the central areas of the mother, whose visual acuity, in contrast to that of her sons, was unaffected.

Figs. 30 and 31 show somewhat similar appearances seen in a member of another family, two more members of which were affected.

Figs. 32 and 33 show the changes seen in a member of a third family of consanguineous origin.

FIG. 35.

Distinct and typical lesions are present: retinitis pigmentosa in the equatorial region spreading out peripherally and centrally, and macular dystrophy of the atrophic type with a central pigment but poorly reminiscent of retinitis pigmentosa.

