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COMMUNICATIONS

A FUNDUS DYSTROPHY WITH UNUSUAL FEATURES

(Late onset and dominant inheritance of a central retinal lesion showing oedema, haemorrhage and exudates developing into generalised choroidal atrophy with massive pigment proliferation)

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IN AN earlier study (Sorsby, 1940) attention was drawn to the polymorphism of the dystrophies of the macula. It was shown that when such genetic affections as "family choroiditis" (Doyme, 1899, 1910), the central fundal disturbances in elastosis dystrophica (angeoid streaks—Doyme, 1889; Plange 1891; Grönblad, 1929;

Böck, 1937-38; and Prick, 1938) and central choroidal sclerosis (Sorsby, 1939) are excluded, the residual group of macular dystrophies of an atrophic character, generally associated with the names of Stargardt and Behr, cannot be regarded as a sharply defined clinical entity. Evidence was brought forward for the existence of a variety of additional types: exudative, heavy pigmentary, and "inverse retinitis pigmentosa." It appeared from the literature (Mazzi, 1934 and Waardenburg, 1936, 1938) that there was also the possibility of a haemorrhagic type but the evidence was regarded as unconvincing. It was also suggested that Doyme's choroiditis was a variant of the "exudative type," and that each of the four main forms of macular dystrophy—the atrophic, exudative, pigmentary, and inverse retinitis pigmentosa types—showed subsidiary variants in different families. As to the age of onset of these affections, it was shown that Behr's classification of lesions as occurring at birth, early in childhood, adolescence, early adult life, and at the beginning of involution, and possibly also at old age, was distinctly schematic; there was nothing to support his suggestion that the lesions appeared at critical periods of life, for the age incidence of macular dystrophies was found to extend over a continuous unbroken range. The conception that these lesions are purely macular was shown to be too rigid, for in many cases considerable extension beyond the central area could be observed in longstanding cases. Moreover sharply defined peripheral and central lesions may be present in combination (Sorsby, 1941).

The present study based on five families brings out the existence of a genetic affection which manifests itself at about the age of 40 years. In the early stages there is oedema and a haemorrhagic-exudative reaction in the central areas; this progresses unto atrophy centrally, generally with some choroidal sclerosis and heavy pigmentation; ultimately the whole of the fundus shows a diffuse atrophic reaction. The affection is inherited as a simple dominant. It therefore establishes the existence of a haemorrhagic type of macular dystrophy, and confirms the view that macular dystrophies cannot always be regarded as localised lesions, but are occasionally, and possibly frequently, merely the starting point of a diffuse retinal or choroidal disturbance.

I. CASE RECORDS.

1. *The Randall family.*

(Pedigree Plate 1 and Figs. 1-5).

(1) MISS MARY RANDALL (IV, 1 in pedigree plate I) aged 39 years when first seen in May, 1946. Her vision in the right eye was 6/60 and in the left 1/60. Three years previously Mr. H. M. Armstrong, of Bedford, had found vision of

6/6 in the right and 6/12 in the left. The left fundus at that time showed a pale oedematous central area with a small haemorrhage on its outer side. An intensive general examination proved negative, and early in May, 1946, the patient was again seen by him as vision of the right eye had become blurred. The fundus appearances in this eye were now identical with those observed in the left three years previously. The picture in the left eye had changed considerably meanwhile; the central area had become largely scarred, as can be seen from Fig. 1*b*. The changes in the right eye became more marked during the course of the succeeding two months. Fig. 1*a* shows that by July, 1946, the oedema had spread to involve the disc so that the picture was now one suggestive of neuro-retinopathy showing oedema, haemorrhages and exudates. Observed frequently since May, 1946, the changes in the left eye have not progressed to any extent, whilst those in the right eye are now (22 months later) assuming the appearances of atrophy (Fig. 1*c*). This patient's peripheral fields are full. Colour vision is good and there are no subjective symptoms of night blindness, or of poor dark adaptation. A provisional diagnosis of macular dystrophy of the exudative type made by Mr. Armstrong seemed reasonable, particularly in view of the family history. The patient held that the affection had appeared in her family over three generations, always coming on at about the age of 40. She stated that the women in her family are apt to be more severely affected than the men, and did not readily accept an assurance that there was no danger of blindness as distinct from central loss of vision. A full investigation of the family, which originally hailed from Bedfordshire, but is now scattered in that county, Northamptonshire and the South of England, was made possible by her ready collaboration.

Plate I shows the pedigree which extends over five generations with observed cases in the second, third and fourth generations. There is only presumptive evidence of the affection in the first generation, whilst the members of the fifth are all too young to show the affection. In Miss Randall's generation (the fourth) there is only one other affected member as yet, a second cousin, Mr. John Pritchard.

(2) JOHN PRITCHARD (IV, 24) is now aged 44 years. He was seen 15 months ago, when his vision was 6/6 each eye and the fundi were normal. Six months later he came complaining of sudden blurring of sight in the right eye. Vision was down to 6/36 in this eye, and ophthalmoscopically the picture was identical to that first observed in the case of Miss Randall. There was a central oedematous area with temporal and also nasal haemorrhages. The disc and vessels were normal. His fields were full and colour vision was good. He had not experienced any symptoms suggestive of night blindness throughout his life. Unfortunately it has proved impossible to follow him up.

In the generation antecedent to these two patients five affected members were observed personally by one of us (A.S.). Records concerning two more have been obtained from Mr. E. H. Harries-Jones of Northampton, whilst three more who are now dead are reputed to have been affected. The sub-joined case histories 3-12 give the details concerning this generation.

(3) MRS. MABEL PRITCHARD (III, 12), the mother of J. P. (No. 2 above and IV, 24 in pedigree), aged 67 years. Her trouble started at the age of 40 years and has progressed slowly. Vision is 6/36 partly in each eye. As can be seen from the fundus drawings (Figs. 2*a* and 2*b*), there are massive pigmentary changes in both eyes extending well beyond the central area, particularly in the left eye. Apart from the pigmentary changes, there is a suggestion of patterned exudate on the nasal side of the right disc and peculiar "woolly" massive exudates temporally. In both the right and left fundi the choroidal vessels in the central

area are exposed, and there is a suggestion of incipient choroidal sclerosis. This patient, too, has not been conscious of any night blindness, and her colour vision is good.

(4) MRS. AMY MARTIN (III, 16). Aged 68 years, her fundi are not markedly dissimilar from those of her cousin, Mrs. M. P. (III, 12). The same massive pigmentary changes and patterned exudate are present, but there is also undoubted evidence of central choroidal sclerosis. Towards the periphery the choroidal vessels are exposed, but not definitely sclerosed. Vision is 6/60 in each eye. First symptoms developed at 41. She gets about freely, and by the aid of a magnifying glass can read big type. Fig. 3 shows the fundus of the right eye. The left (not drawn) is very similar.

(5) ALFRED RANDALL (III, 6), a member of the sibship including patients Nos. 5 to 9 (III, 6, 4, 3, 1 and 2 respectively), was seen in 1937, when drawings were made of his eyes (Figs. 4a and 4b). Vision was reduced to hand movements in each eye. His sight had failed at the age of 43 years and steadily got worse. At the time of examination, when he was 56 years, he could readily find his way about London. He died a year later from lymphatic leukaemia. His peripheral fields and colour vision were good. Both fundi showed extensive choroidal atrophy in the central and pericentral areas. There was much pigmentary reaction in the affected area and unmasking of the choroidal vessels peripherally. Distinct choroidal sclerosis on the temporal side of the right disc was present.

(6) MRS. ANNIE THORNTON, aged 71 (III, 4). This patient is totally blind. A full examination proved impossible. Twenty years ago she had trephine operations on each eye—apparently not for glaucoma, but for the relief of failure of sight, which began at about the age of 40 years. There is some post-operative iritis. An incomplete view of the fundus revealed an almost totally white background with massive pigmentary changes and narrow retinal vessels. The discs were somewhat pale, but showed no evidence of glaucomatous atrophy. Tension in each eye was normal. Fundus drawings could not be obtained, but the appearances are very similar to those seen in her sister, Mrs. E. C. (III, 3).

(7) MRS. ELIZABETH CLARK (III, 3). A frail old lady of 77 years, suffering from chronic glaucoma, which has not been treated. Her sight began to fail at about the age of 40 years and has deteriorated steadily. Fig. 5 shows the fundus of the left eye. Apart from glaucomatous atrophy, there is obvious choroidal sclerosis peripherally, and almost total atrophy of the choroid and retina centrally with massive pigment proliferation.

(8) and (9) JOHN RANDALL AND GEORGE RANDALL (III, 1 and 2), two elder brothers of the last three patients. Both these are now deceased. The elder of these two brothers was the father of our first patient. He died aged 67 years, and could see to get about the country until the end of his life. His trouble began at the age of 40 years, and he had to retire from business at the age of 52 years owing to "centre blindness." He was seen during the first world war by Mr. Harries-Jones, who found a central haemorrhage in one eye, followed in about two years by the same condition in the other. The younger brother (III, 2) was known to Mr. Harries-Jones as likewise affected.

(10), (11) and (12) (III, 7, 9 and 14). The three deceased members of this generation concerning whom only hearsay evidence is available.

ROSA RANDALL (III, 7) is reported to have died blind at about the age of 70 years. Her trouble began at about the age of 40 years and progressed steadily.

JOHN RANDALL (III, 9) died at the age of 57 years. His sight is stated to have been "slightly affected" from "centre blindness."

FLORENCE O'HARA (III, 14) died aged 72 years. She is reported to have "lost central sight" at 42 years, but could always see to get about.

In the generation antecedent to this, one member (II, 3) was observed by Mr. Harries-Jones, and two more are reputed to have been affected. These patients (13-15) are now all dead.

(13) GEORGE RANDALL (II, 3) is reported to have developed "centre blindness" at the age of 40 years. He lived until the age of 72 years and could "see

sideways." He used to get about comfortably in the village in which he lived. Mr. Harries-Jones writes concerning this patient: "I saw him about forty years ago at a doctor's surgery with very poor light, and found both retinae covered with pigmentary degeneration, and central vision practically nil."

(14) RICHARD RANDALL (II, 4). His daughter, Mabel (III, 12), states that his "central sight" went at the age of 40 years.

(15) MRS. SARAH BUTT (II, 5). Her daughter, Amy (III, 16), states that her mother became affected at the age of 48 or 49 years, when "her central sight went." She died at 65 years and was "four-fifths blind."

Concerning the first generation all that is known is that John Randall died late in life and had "perfect sight": his wife died at the age of 40 and was not known to be affected. A brother of hers, who survived to old age, is said to have been affected. Apart from the eye lesions this family is remarkably free from general disturbances, and in particular from cardiovascular and neurological affections. There is no instance of consanguineous marriages in this group.

Reconstructing the essential features of the affection as seen in this family the following points emerge:

(1) A fundus lesion has been observed over three generations. Transmission is not sex-linked, and the mode of inheritance fits in well with a simple autosomal dominant. This is shown by the following analysis:

Number of individuals aged 40 years and over.

Generation	Unaffected			Affected		
	M.	F.	P.	M.	F.	P.
II	1	2	3	2	1	3
III	2	3	5	4	6	10
IV	1	2	3	1	1	2
V	0	0	0	0	0	0
	4	7	11	7	8	15

(2) The affection begins at about the age of 40. Subjectively the first sign is blurring of vision. Objectively the course of the affection extends from a localised oedema of the central area associated with haemorrhages to a terminal phase in which choroidal vessels disappear and massive pigment proliferation is seen against a white background. Figures 1 to 4 show the successive stages beyond the initial slight and localised oedema at the macula. Figs. 1a and 1b illustrate the appearances in the same patient in whom there was a time lag of three years between the left and right eye: Fig. 1c shows the condition depicted in Fig. 1a after two years. Figs. 2a and 2b illustrate considerable extension

beyond the central area with exposure of the choroidal vessels, proliferation of pigment and the presence of woolly exudates in the patient in whom the affection had run a relatively mild course over 27 years. Fig. 3 shows a still further extension of the process with clear choroidal sclerosis. The time factor is approximately the same as in the preceding patient. Figs. 4a and 4b represent the fundus appearances after the affection had existed for some sixteen years. Here central vision was rather more affected and choroidal atrophy rather than choroidal sclerosis is evident. The lesion is still largely central, but though more localised and of lesser duration would appear to be more intense than in the preceding two patients. Fig. 5 may be taken as representing the terminal state: the choroidal vessels have disappeared centrally and are sclerosed peripherally. There is no suggestion of any haemorrhages or exudates, but massive pigment proliferation is present.

(3) The histological nature of the affection is dubious. The first objective signs would suggest a central retinal lesion. The intermediate and terminal stages indicate that the lesion is primarily choroidal. It is possible that the apparently retinal lesions first seen are the result of the slow cutting-off of the choroidal blood supply to the central area of the retina from underlying choroidal sclerosis.

(4) The available evidence therefore points to a genetic affection of a simple dominant mode of inheritance, beginning at about the age of 40 with a picture simulating central retinitis or possibly neuro-retinitis. The prognosis is, however, more serious than in a macular dystrophy, for in the course of time the whole of the fundus is involved from sclerosis and ultimately disappearance of the choroidal vessels. Though there is some variation in the rapidity of progress in different members of the family, it may be taken that blindness ensues in the course of thirty years or so.

2. *The Carver family.*

(Pedigree Plate II and Figs. 6-15).

In this family—mostly resident in Cumberland—affected members have been observed over two generations by one of us (M. E. J. M.). As can be seen from pedigree plate 2 there is a history that two more antecedent generations were likewise affected. The surviving members of the fifth generation are all below middle age. Twenty-seven members of the third and fourth generation of this family over the age of 40 years have been examined and 14 were found affected. All but one patient (IV, 35) dated their trouble to round about the age of 40. None of the

affected individuals is the offspring of consanguineous parents. The condition is known in the family as the "Carver eye" after the male member of the first generation. The family holds that only blue-eyed members are affected.

Fundus drawings (M.E.J.M.) of ten patients are available. For the sake of convenience four groups in this family may be described separately.

(a) *Anthony Hepburn and his children (III, 3 and IV, 8-16).*

(1) ANTHONY HEPBURN, aged 75 years. First noticed deterioration in vision at about 42 years. Objects appeared to be distorted. Now vision is hand movements at 1 ft. in each eye. As can be seen from Fig. 15, the fundus of the right eye shows a white reflex with some exposed choroidal vessels and scattered gross pigmentation, the latter being especially marked centrally. The retinal arteries are somewhat narrowed. The fundus of the left eye is essentially similar.

There are 4 sons and five daughters all of whom were examined; three sons and two daughters were found affected. (Patients Nos. 2-6 below.)

(2) NELLIE, aged 52 years, married Bedford (IV, 8). She had no trouble until about four years ago, when she began to notice that, despite correct glasses, she could not read. She is able to get about but has little central vision. R.V. 1/60, L.V. 2/60. As can be seen from Fig. 10, which shows the left eye, the macular area is heavily pigmented, surrounded by a white area of choroidal atrophy. At about the macula itself there is an oval red area, probably a hole. There is a small area of choroidal atrophy with exposed vessels below the main patch. The fundus otherwise looks reasonably healthy. Appearances in the right are only slightly less marked; there is, however, no suggestion of a hole at the macula.

(3) ARCHIE HEPBURN, aged 50 years (IV, 9). At the age of 48 years he noted that objects became much smaller in appearance and that blues were confused with greens. R.V. 6/18, L.V. 6/18 part. No defects in colour vision. As can be seen from Fig. 11, there is a generalised atrophic-looking fundus somewhat simulating retinitis pigmentosa sine pigmento. There are fine scattered pigment spots in the macular areas and there are peripapillary groups of small white spots along the upper branches of the retinal vessels, themselves rather narrow. The choroidal vessels show clearly at the periphery.

(4) JOHN HEPBURN, aged 47 years (IV, 10). The right eye has 6/6 vision and the fundus appears normal. The left eye is stated always to have been divergent, and the fundus shows a central atrophic and pigmentary lesion (Fig. 7).

(5) MARGARET HEPBURN, aged 46 years (IV, 11). Has not noticed much wrong with her vision. Both maculae show moderately fine pigmentation.

(6) JIM HEPBURN, aged 44 years (IV, 13). A few months ago he began to notice that he could only see part of an object with his left eye. Vision has gradually become worse so that he is now unable to follow his occupation. R.V. 2/60, L.V. 2/60. Definite paracentral scotomata. The right fundus shows a large atrophic area in the macular region (Fig. 9). There is some fine pigmentation, mainly marginal, and the choroidal vessels are exposed in this area. To the temporal side of this atrophic patch is a small jagged intensely red patch, probably a small haemorrhage. Otherwise the fundus looks healthy. There is a similar, but somewhat larger, patch of atrophy in the left macular area; this patch shows pigment centrally as well as at the margins.

(b) *Mrs. E. Lace and her daughter, Mrs. S. Hayes (III, 8 and IV, 20).*

(7) MRS. ELLEN LACE, aged 74 years (III, 8). Vision began to deteriorate at about the age of 45 years, and is now hand movements at 2 ft. Her fundi show massive central and peripapillary choroidal atrophy of a gyrate type. There

is considerable pigment disturbance. Peripherally the choroidal vessels are exposed and there are numerous atrophic areas (Fig. 14). She is not myopic.

(8) MRS. SARAH HAYES, aged 54 years (IV, 20). About 8 years ago (though probably earlier) her sight began to deteriorate. Vision with small minus correction is right 6/18, left 6/24. The whole of the fundus is "thinned" and patchy with fine and scattered muddy-looking areas (Fig. 13). There is peripapillary choroidal atrophy, not clearly delineated from the surrounding retina. The macular area is "muddy" with some fine pigmentation. The retinal arteries are narrowed.

(c) *John Batèy Murray (III, 19), his brother, Dryden Murray (III, 21), his sister, Jessie McLean (III, 23), and Dryden Murray's son, Jim (IV, 37).*

(9) JOHN BATEY MURRAY, aged 78 years (III, 19). The third member of a sibship of eight, of whom three are known to be affected and two more reputed to be so. He himself has never complained of his sight, and would not admit any visual defect. His fundus lesion (Fig. 8) was discovered during the routine examination carried out for this study. Vision is about 6/18 in each eye. The fundi show fine scattered pigment in the macular area, with patches of choroidal sclerosis in the perimacular and peripapillary areas. The rest of the fundus appears healthy. The retinal vessels are normal.

(10) DRYDEN MURRAY died in 1941 at the age of 73 years (III, 21). His sight began to fail at about the age of 45 years, and in 1940 he had only perception of light. There were some slight lens opacities and the fundus showed massive choroidal atrophy, some choroidal sclerosis and gross pigmentation occupying the whole of the central and peripapillary areas. The retinal vessels were somewhat narrow. Unfortunately no drawing was made.

(11) JESSIE MCLEAN, aged 71 years (III, 23). Sight began to fail at about the age of 40 years. Seen when aged 69 years, there was absolute glaucoma in the right eye. The left had perception of light only. The fundus showed massive choroidal atrophy centrally reaching out to the periphery with coarse pigmentation. Six months later she developed an attack of acute glaucoma in this eye, which also went on to absolute glaucoma.

(12) JIM DRYDEN MURRAY, aged 50 years (IV, 38), the son of Dryden Murray (III, 21). At the age of 36 years he began to notice that objects looked distorted with the left eye. The appearances observed four years later by Dr. J. A. Ross, of Carlisle, are depicted in Fig. 12a. A heavy exudative and atrophic reaction is present centrally. The same symptoms developed in the right eye two years later. Fig. 12b shows the fundus of the right eye at the present; the left eye is rather less heavily involved. In both fundi the whole background shows degenerative changes, most marked in the central areas. At the macular and the peripapillary areas the choroidal vessels are exposed, with evidence of sclerosis. Extensive pigmentary changes are present. Vision is grossly affected in the periphery as well as centrally.

(d) *Two further observed members, Annie Kirkpatrick (III, 11), and her nephew, John Ernest Murray (IV, 36).*

(13) ANNIE KIRKPATRICK, aged 65 years (III, 11). The patient has been short-sighted since childhood, but has not been able to obtain suitable glasses for some indefinite time. She has a moderate degree of myopia with astigmatism. Her fundi are similar in appearance to that of Anthony Hepburn (III, 3), illustrated in Fig. 9, though the condition is not quite so advanced.

(14) JOHN ERNEST MURRAY, aged 59 years (IV, 36). His mother, Ann Tyson (III, 17), died at about the age of 80 years. She is reputed to have been unaffected. (Her brother, John Batey Murray (III, 19), was also reputed to be unaffected, but was found affected on examination.) John Ernest Murray noticed deterioration in vision when he was aged 18 years, but served in the Army during the first world war. He states that his vision has not deteriorated since the age of 26 years. Vision in each eye is 6/18 and the fields are full. Fig. 6 shows the condition of the right eye. The left is similar. There is fine pigmentary disturbance and some few light-coloured whitish spots in the central area.

The essential features in this family are:

(1) A fundus lesion observed over two generations with a history of the affection in the two antecedent generations. As can be seen from Pedigree Plate II the mode of inheritance fits in well with a simple autosomal dominant. This is shown by the following analysis:

Number of individuals aged 40 years and over.

Generation	Unaffected			Affected		
	M.	F.	P.	M.	F.	P.
II*	1	1	2	4	2	6
III†	4	4	8	4	6	10
IV	3	7	10	5	4	9
V	0	0	0	0	0	0
	8	12	20	13	12	25

* On the assumption that II, 6 was affected, though recorded (on the history) as unaffected.

† On the same assumption for III, 17.

(2) With the exception of one patient (IV, 36), who dates his lesion to the age of 18 years and records no further deterioration after the age of 26 years, the patients all developed the affection at about the age of 40 years. In one instance—IV, 9—symptoms did not appear till the age of 48 years.

(3) The range of ophthalmoscopic appearances is rather more limited than that seen in the Randall family. The earliest stages—an oedematous-exudative reaction at the macula—have not been observed here. The intermediate stages of a pigmented macular lesion with exposure of choroidal vessels in the earlier forms and more extensive changes with atrophy—or possibly exudative reactions—in the somewhat later forms, are illustrated in most of the patients in the fourth generation. (Figs. 6, 7 and 9-13). For the preceding generation Fig. 15 may be taken to represent not only the patient to whom it refers, but also patients III, 21, III, 23, and III, 11. A milder course is observed in III, 8 and one still milder in III, 19. (Figs. 14 and 8.) Another exceptional feature in this group is that one patient (IV, 10) though already aged 47 years shows a lesion in only one eye (Fig. 7).

(4) Taken as a whole this family shows close parallels to the Randall family in so far as it gives the same mode of inheritance, an apparently similar lesion in the macular region, the same spread peripherally with exposure of the choroidal vessels, and

ultimately the same disappearance of these vessels leading to sub-total blindness.

3. *The Ewbank Family.*

(Pedigree Plate III and Figs. 16-18).

In this family the affection has been observed over two generations. The family is resident in London and the Home counties.

(1) RICHARD EWBank (II, 7) died blind at the age of 74 years. He had been a patient of the late Mr. R. P. Brooks, from whose case records it appears that he was treated for "maculitis." His trouble began at about the age of 43 years, and according to his son he was soon unable to read, but always retained some sight, *e.g.*, could play cards, do some gardening and go about unaccompanied.

(2) MAURICE EWBank (III, 10), aged 48 years. Seen by one of us (N. G.) in 1942, when he was 42 years of age. Vision with small minus correction was 6/6 in the right eye and 6/60 in the left. The left macula at that time showed mottling, apparently of recent onset. The right fundus was normal. Three years later the right eye had become "troublesome"; mottling of the macula was now present, with slight pigmentary changes at the upper border of the macula. The changes in both the left and right fundi have progressed steadily, and the present appearances are depicted in Figs. 16*a* and 16*b*. Definite choroidal sclerosis is present on the macular side of both discs, more marked in the left eye than in the right. In the right eye, which still has vision of 6/9 partly, the macula is mottled with some slight pigment reaction, and the choroidal vessels are exposed in the perimacular area; white dots are seen more peripherally. The appearances in the left eye are more marked, and both choroidal sclerosis and massive pigmentary changes are present centrally. There is considerable unmasking of the peripheral choroidal circulation with white dots, mainly equatorial in position. Colour vision, as tested by Ishihara plates, is good. There are no subjective symptoms of night blindness.

(3) COLIN EWBank (III, 11). Died in 1947 at the age of 46 years, apparently from tumour of the kidney. Symptoms developed at the age of 36 years, when Mr. Brooks found "central maculitis and neuro-retinitis." Vision was then right 6/5, left 6/9. Within six months it had declined to 6/18 part in the left eye. Seen by one of us (N. G.) in 1940, vision then was 6/36 partly in the left eye and 6/6 in the right. He complained that objects seen with the right eye now appeared distorted. Ophthalmoscopically there was a scar at the left macula and oedema at the right. When seen nine months later there was a haemorrhage at the right macula. Vision was deteriorating and was 6/18 two months later, and 6/60 four months subsequently. Sclerosis of the choroidal vessels could now be observed in the right central area. When last seen, towards the end of 1946, pigmentary disturbances towards the periphery were present.

(4) MRS. MARY WATERER (III, 12), now aged 43 years. Was seen at the age of 35 years, when vision was 6/6 in each eye, and the fundi showed glistening "colloid" bodies around the disc and macula. There were no subjective symptoms. In September, 1945, when she was 40 years of age, she came complaining that tiles did not appear straight. Vision in the right eye was 6/6 and in the left 6/9. The left macula appeared swollen, suggestive of an acute toxic choroiditis. Two years later haemorrhages and scar formation were present in the left central area, and vision in the left eye had declined to 6/60. The appearances now, one year subsequently, are shown in Figs. 17*a* and 17*b*. It will be seen that extensive "colloid" bodies are present around the disc, extending to well beyond the equator in both eyes. The right macula appears normal, whilst the left central area shows gross scarring and pigmentation. Vision in the right is still 6/6. The Ishihara test shows colour vision to be good. There is no history of night blindness.

(5) MRS. KATHLEEN HUGHES (III, 13). The daughter of Richard Ewbank by

his second marriage. She is now 41 years of age and was first seen nine years ago because of loss of vision in the left eye. The right fundus was then normal. The left showed oedema at the macula with small haemorrhages and scattered pigment; vision was 6/60. Over the course of a year the haemorrhages in the left absorbed slowly, but there was no return in vision. The right eye remained normal till 1945, when she was 38 years of age. Pigment changes were now present in the central area with a haemorrhage below the macula, and four months later there was a definite scar. The appearances now are shown in Figs. 18*a* and 18*b*. In the left eye there is chorio-retinal atrophy in the central area with a veil-like scar and gross pigmentation, whilst in the right eye gross pigmentary disturbances with some choroidal sclerosis and peripheral outlying white dots are present. Vision in both eyes is less than 6/60. Colour vision appears defective (Ishihara test) and there appears to be some night blindness.

(6) MRS. ISABEL JAGGER, aged 61 years (III, 3). The history obtained from her cousin, Maurice Ewbank, was that her sight became affected at the age of 58 years, and that "her present condition is similar to that of her sister, Florence." Seen at the age of 60, in 1947, by Sir Stewart Duke-Elder, she was found to have advanced central choroidal atrophy in both eyes, more marked in the right than in the left.

In the Ewbank sibship there are therefore four affected members in a total of six, the affection having been transmitted through an affected father to children of his two marriages to unaffected individuals. Pedigree Plate III gives further information as regards collaterals in this family. It appears that Richard Ewbank (II, 7) had two affected sisters (II, 3 and II, 5) and that these affected sisters have in turn transmitted the affection to some of their children. (III, 2 and III, 3; III, 5 and possibly III, 4.) The eldest member of the fourth generation is only 32 years of age, and the affection is not known to have appeared in any member of this generation as yet.

The range of ophthalmoscopic appearances seen in this family group covers early and intermediate stages only. Oedema and haemorrhages at the macula have been observed in Colin Ewbank and his two sisters as the earliest lesions. The first observed changes in Maurice Ewbank were mottling of the macula. Scar formation in the central areas have been seen in Colin and in Mrs. Waterer. "Colloid" bodies, widely scattered over the fundi, were the first signs in this last patient, and some white dots are also seen in both Maurice Ewbank and Mrs. Hughes, though in these patients they are probably of later origin. The appearances depicted in Figs. 16 to 18 are very largely those of the intermediate stages. Figs. 18*a* and 18*b* showing the present condition in the youngest member are obviously an earlier stage of the appearances depicted in Figs. 16*a* and 16*b*, which illustrate the fundi of the eldest surviving member. The appearances shown in Fig. 17*a* representing the right eye of the elder sister (III, 12) bear no resemblance whatever to those seen in the other illustrations; they are essentially a representation of widespread "colloid" bodies, but the appearances in her left eye (Fig. 17*b*) show that changes in the central area are fundamentally similar to the lesions seen in the

other members of the family. This widespread distribution of colloid bodies scattered over the fundus is unique, not only in this particular patient in this family, but for all patients recorded in this study. The appearances in Mrs. Hughes (Figs. 18a and 18b) bear considerable resemblance to those seen in the Randall family (Mrs. Pritchard and Mrs. Martin, Figs. 2 and 3), whilst those observed in Maurice Ewbank (Figs. 16a and 16b) parallel those seen in the Cranston sibship recorded below (Fig. 26).

It will be noted that the affection began at about the age of 40 years in all the patients in this family, except that in the case of Mrs. Hughes the left eye failed at the age of 32 years, and in her brother Colin at 36 years.

The transmission of the affection by an affected man to the children of two marriages suggests dominant inheritance. The occurrence in collateral branches supports this. Taking the family history on its face value, the following simple analysis emerges.

Generation	Unaffected			Affected		
	M.	F.	P.	M.	F.	P.
II	1	2	3	1	2	3
III	2	2	4	2	5	7
IV	—	—	0	—	—	0
V	—	—	0	—	—	0
	3	4	7	3	7	10

In this family the salient features are therefore :

(1) A fundus lesion observed over two generations in the children of two healthy mothers married to an affected man. The affection is also reputed to have occurred in two sisters of this man and their descendants, one of whom is known to be affected.

(2) In all patients onset was at about the age of 40 years, except that in one patient the first eye failed at 32 years, and in another patient aged 48 years, vision is still 6/9 part in one eye with an extensive central lesion.

(3) Oedema and haemorrhage at the macula were observed as the first ophthalmoscopic changes in at least 3 of the 5 patients. Choroidal sclerosis is an obvious feature in two cases. Widespread "colloid" bodies are a striking aspect in one patient.

(4) None of the patients studied is old enough to show the terminal stage of subtotal retinal and choroidal atrophy.

4. *The Kempster Family.*

(Pedigree Plate IV and Figs. 19-24).

This Hertfordshire family was reported in part in an earlier study (Sorsby, 1940), when it was given as an example of macular dystrophy with intense pigmentary changes. The salient features then recorded were the occurrence of heavy pigmentation in the central areas observed in three sisters aged 62, 60, and 50 years. Another sister, aged 53 years, showed a fundus lesion which bore little resemblance to those seen in the other members of the family; in her case there was an extensive area of peripapillary retinal atrophy with comparatively little pigmentary disturbance and but little central involvement, whilst towards the periphery there was some suggestion of choroidal sclerosis. In these four sisters the affection began at about the age of 40 years. A brother, then aged 55 years, was reported as having developed "slight choroiditis" in the right eye, and "macular choroiditis" in the left eye at the age of 47 years. The history then obtained recorded that the father died "practically blind" at the age of 63 years, his eye trouble having begun at about the age of 40 years; "nearly all his brothers were affected"; the son of one of the brothers was also said to be affected. The four sisters observed had one unaffected sister and four unaffected brothers.

This family has now been re-examined, and Plate IV shows the pedigree. It will be seen that cases have been observed over one generation only, the third. None of the members of the fourth generation has yet reached the age of 40 years. There are no surviving members of the second generation and only hearsay evidence concerning this generation and the antecedent generation is available.

In the third generation of ten sibs four of the five sisters and three of the five brothers are affected.

(1) ARTHUR KEMPSTER (III, 9), aged 52 years. He gives a history that the first trouble began at about the age of 34 years, when he noticed "spots in a blue sky" when looking with the right eye. This apparently did not get worse until about the age of 47 years, when both eyes rapidly failed. The fundi of the two eyes (Figs. 19a and 19b) are not particularly similar. The left eye shows a mottled macular reaction surrounded by a fairly well defined brown ring, outside which white dots are present. Towards the periphery white exudate-like reactions are present. In the right eye a central pigmented and exudative lesion shows a considerable amount of veil-like scar tissue centrally with a few exudates equatorially.

(2) MRS. ROSE GRAVES (III, 6), aged 50 years when seen in 1939. The right eye failed at about the age of 46 years, the left at 48 years. Her fundi in 1939 are shown in Figs. 20a and 20b. She now lives in Canada and could not be seen.

(3) MRS. ANN REDDING (III, 5), aged 53 years when seen in 1939. Her eye trouble began at about the age of 40 years. Her fundi at that time are shown in Figs. 21a and 21b. They were puzzling then owing to the perimacular and peripheral involvement with relatively little central lesion. She died a year after these drawings were made.

(4) JOSEPH KEMPSTER (III, 8), aged 54 years. The right eye was lost in a war injury in 1916. The left eye began to fail at the age of 48 years. Vision is down to 6/60. The earliest stages observed by one of us (N. G.) consisted of oedema, and subsequently haemorrhages at the macula. The present appearances—six years after onset of trouble—are depicted in Fig. 22. There is an extensive atrophic lesion centrally with exudate and pigmentary reactions peripherally.

(5) WILLIAM KEMPSTER (III, 4), aged 64 years. This is the brother who was reported to have shown "slight choroiditis" in the right eye, and "macular choroiditis" in the left eye at the age of 47 years. He could not be examined in 1939, and when seen recently he was dying from cardiac failure. He was too ill for any drawing of the fundus to be attempted, but a rapid examination showed a fundus lesion not unlike that seen in his sister, Mrs. Poulton (III, 2). Unfortunately an eye for histological examination could not be obtained.

(6) MRS. CAROLINE POULTON (III, 2), aged 69 years. Her sight began to fail at about the age of 40 years. In 1939, when she was 60 years old, her lesion was largely central with fairly heavy patches of atrophy outside the macular area (Figs. 23*a* and 23*b*). Now the extension peripherally is marked (Figs. 23*c* and 23*d*). A striking change is particularly noticeable in the right eye where a solid sheath of black pigment spreads from just temporally of the disc across the central area. In addition, there is unmasking of the choroidal vessels and some choroidal sclerosis.

(7) MRS. ALICE HALL (III, 1), aged 71 years. Her sight began to fail at about the age of 42 years. The fundus appearances in 1939, when she was 62 years old, are shown in Figs. 24*a* and 24*b*. It will be seen that at that time the lesion was essentially central and consisted largely of a heavy pigmentary reaction, fairly uniform and deep chocolate brown in colour. There was at that time little peripheral extension beyond some whitish dots mainly equatorial in position. Now, nine years later, the extension peripherally is considerable and choroidal sclerosis has become evident (Figs. 24*c* and 24*d*).

Of the three members of the family who are reputed to be normal, Frederick Kempster, aged 66 years (III, 3) was not seen. Eliza Wood, aged 56 years (III, 7) and Robert Kempster, aged 50 years (III, 10) were examined and found normal.

In the antecedent generation, the father, as already noted, died blind, at the age of 63 years, his trouble having begun at about the age of 40 years. It appears that he had two affected brothers and one affected sister; two brothers and two sisters are reputed to have been normal. It is also reported that a son of one of his affected brothers, and a daughter of the affected sister are affected. The information given also records that in the generation antecedent to this, the father and a brother were affected, and that this affected brother had an affected daughter. The essential features in this family are therefore:

(1) A fundus lesion observed in 7 out of 10 sibs. In all of them the affection began in the forties, except that it may have begun at the age of 34 years in one member (III, 9).

(2) There is a history of the affection in two antecedent generations, with direct inheritance on four occasions. There is no history of unaffected individuals transmitting the affection.

The following analysis is given with some reserve owing to the indefinite information on generation II.

Number of individuals aged 40 years and over.

Generation	Unaffected			Affected		
	M.	F.	P.	M.	F.	P.
II	2	2	4	3	1	4
III	2	1	3	3	4	7
IV	—	—	0	—	—	0
V	—	—	0	—	—	0
	4	3	7	6	5	11

The range of ophthalmoscopic appearances in this family extends from observed oedema and haemorrhage at the macula to extensive central and peripheral atrophy of the retina and choroid, but the eldest member of this family has not yet reached the advanced age observed in members of the first two families in whom sub-total retinal and choroidal atrophy was noted. The range of ophthalmoscopic appearances is, however, exceedingly wide. The left eye of Arthur Kempster (III, 9, Fig. 19*b*) is strikingly similar to the right eye of Mary Randall (Fig. 1*c*). The only eye of his brother, Joseph (Fig. 22), is likewise very similar to the fundi of Alfred Randall (Fig. 4*a* and 4*b*) and Gertrude Cranston (Fig. 26) recorded below.

(4) Only one member of this sibship (Arthur Kempster III, 9) complained of nightblindness. On Stilling's tables there was heavy colour defect in the four affected sisters.

(5) Of special significance in this family are the recorded changes observed in two members after an interval of nine years. They show extension of the central lesion towards the periphery. (Figs. 23 and 24.) -

5. *The Cranston Sibship.*

(Figs. 25 and 26).

The case records of two sisters, Gertrude and Edith Cranston, were published earlier as examples of central and peripapillary choroidal sclerosis (Sorsby, 1939). In both sisters, then aged 59 and 58 years, there was peripapillary choroidal sclerosis involving the macula and producing heavy pigmentary disturbances. The periphery was clear: the peripheral fields were full and the patients could get about quite well with central vision of 6/60.

(1) **EDITH CRANSTON.** At the age of 46 years she consulted Mr. F. A. Williamson Noble for difficulty in reading. Figs. 25*a* and 25*b* show the fundus appearances observed then. There was indefinite haze at the disc margin, and some pigmentary disturbances and haemorrhages in the central areas.

A diagnosis of central chorio-retinitis, possibly of tuberculous origin, was made. Vision with correction at that time was 6/12 in each eye. Seen 10 years later by one of us, the fundus appearances had changed greatly. There was evident peripapillary choroidal sclerosis and gross pigmentary changes at the maculae (Figs. 25c and 25d).

Fundamentally the same lesion was found in her sister :

(2) GERTRUDE CRANSTON, one year younger. Here the fundus lesion was rather more marked centrally and extended further out (Figs. 26a and 26b). The subjective symptoms were identical with those of her sister. Her trouble began in the early forties, and had progressed steadily.

The family history elicited at that time (and confirmed recently) showed no consanguinity in the parents and revealed no history of any other affected members. Their father died at the age of 49 years from "fatty heart," and their mother at 64 years from "consumption." Both appear to have had good sight. There were two elder sibs, a sister who died at 46 years of age from "cerebral haemorrhage" and a brother who died at 41 years from "consumption." They, too, appear to have had good sight.

The fundus appearances and late onset of the affection suggested the possibility that the original diagnosis of central and peripapillary choroidal sclerosis may have stressed an aspect of the affection rather than the picture as a whole. Re-examination in 1948 showed considerable deterioration in vision. The two sisters, now aged 69 and 68 years, can no longer go about on their own as their peripheral field has shrunk considerably. The central fundus lesions now show considerable extension peripherally. In both sisters much of the peripapillary choroidal sclerosis has been replaced by choroidal atrophy (Figs. 25e and 25f; 26c and 26d) whilst there is considerable extension of unmasking of the choroidal vessels with some sclerosis peripherally. There is, moreover, increase of intensely black pigment at the central areas. Similarity in ophthalmoscopic appearances of Fig. 26 in this sibship with Fig. 4 in the Randall group, Fig. 16 in the Ewbank family and Fig. 22d in the Kempster family has already been pointed out.

In this sibship the range of observed ophthalmoscopic appearances therefore extends from the early stage when the lesion suggested a central chorio-retinitis; subsequently there was peripapillary and central choroidal sclerosis, and this has now progressed to extensive central retinal and choroidal atrophy with peripheral exposure and some sclerosis of the choroidal vessels. Though a positive family history showing dominant inheritance is lacking, it must be borne in mind that the father died at the age of 49 years, and that information on preceding generations could not be obtained. This family group appears to begin with these two sisters, and definitely comes to an end with them as they are unmarried.

THE RANDALL FAMILY

(FIGS 1 — 5)

FIG. 1 (a)

Miss M. R. aged 41 years. Appearances in the right eye 10 weeks after first onset of subjective symptoms (when patient was 39 years of age). Note swelling of disc, oedema of the central area, haemorrhages and exudates.

FIG. 1 (b)

Left eye: appearances 3 years after onset of first symptoms (at 36 years). Note the time interval in onset of symptoms and lesions in the two eyes, and the pigmented proliferating scar in the central area.

FIG. 1 (c)

The same eye as depicted in (a) 22 months later.

FIG. 2 (a)

Mrs. M. P. aged 67 years, a cousin of Miss M. R.'s father. Symptoms first developed about 27 years ago. Right eye. Note gross pigmentary changes, a suggestion of patterned exudates on the nasal side of the disc, the peculiar woolly, massive exudate temporally, and exposure of the choroidal vessels.

FIG. 2 (b)

Left eye. Choroidal sclerosis is rather more obvious than in the right eye.

FIG. 3

Mrs. A. M., aged 68 years, a cousin of Miss M. R.'s father and also of the patient depicted in Fig. 2. The patterned exudate and choroidal sclerosis are more marked than in the fundi shown in Fig. 2. Symptoms first developed about 27 years ago.

FIG. 4 (a)

Alfred R., died at the age of 57 years, an uncle of Miss M. R. Appearances at the age of 56 years, some 13 years after the onset of the first symptoms. Right eye. Note extensive central atrophy and pigmentation.

FIG. 4 (b)

Left eye. Appearances are fairly similar to those in the right eye. Note extension of the lesion temporally.

FIG. 5

Mrs. E. C., aged 77 years, the eldest member of the R. family group, an aunt of Miss M. R. Symptoms first developed about 37 years ago. Note extensive central atrophy with pigmentation and fairly advanced choroidal sclerosis peripherally. (There is also coincidental glaucomatous optic atrophy).

THE CARVER FAMILY

(FIGS. 6—15)

FIG. 6

John E. M., aged 59 years. His mother (reputed to have been unaffected) was a cousin of Anthony H., depicted in Fig. 15. Right eye: the mildest central lesion observed in this group. Trouble is stated to have begun at the age of 18 without deteriorating since the age of 26. The fundus in the left eye is similar.

FIG. 7

John H., aged 47 years, a son of Anthony H. The right eye is as yet normal. The lesion in the left is fairly sharply localised to the central area. It is not known when this lesion developed, as the eye is divergent and amblyopic.

FIG. 8

John B. M., aged 78 years, a cousin of Anthony H., and 3 years older. Patient's vision is 6/18 and he was unaware of any eye trouble. Right eye: there is a fine pigmentary central lesion with considerable patchy choroidal sclerosis. Appearances in the left fundus are essentially similar.

FIG. 9

Jim H., aged 44 years, a son of Anthony H. The right fundus shows a sharply localised lesion with exposed choroidal vessels. Appearances in the left eye are rather more marked. Symptoms began a few months ago.

FIG. 10

Mrs. N. B., aged 52 years, eldest daughter of Anthony H. Note fairly localised central lesion. First symptoms about 4 years previously.

FIG. 11

Archie H., aged 50 years, a son of Anthony H. Right eye: the lesion is more extensive than in his sister, who is two years older. The patterned exudate is particularly striking. The left eye is similar. Symptoms appear to have developed 2 years previously.

FIG. 12 (a)

Jim D. M., aged 50 years. A son of a first cousin of Anthony H. Left eye at the age of 40 years, four years after onset of symptoms. There is an extensive exudative-atrophic reaction centrally

FIG. 12 (b)

Present appearances of right eye: pigmentary changes are present centrally and equatorially. The choroidal vessels are exposed peripherally with some choroidal sclerosis around the disc. Appearances in the left eye which failed two years before the right are now fairly similar.

FIG. 13

Mrs. Sarah H., aged 54 years, whose mother, Mrs. Ellen L. (fundi depicted in Fig. 14), is a cousin of Anthony H. Right eye: there is a diffuse "pepper and salt" atrophy of the central areas with fairly well defined macular lesions. The left eye is similar. First symptoms developed about 8 years previously.

FIG. 14

Mrs. Ellen L., aged 74 years, a cousin of Anthony H. and mother of Mrs. Sara H., depicted in Fig. 13. Both eyes show extensive central and peripapillary atrophy with exposure and incipient choroidal sclerosis peripherally. First symptoms developed about 29 years previously. There is no myopia.

FIG. 15

Anthony H., aged 75 years. The most severely affected member of the Carver family. Note extensive chorio-retinal atrophy with pigmentation and choroidal sclerosis. Note also similarity to Fig. 5 depicting the most advanced stage in the Randall family. First symptoms developed about 33 years previously.

THE EWBANK FAMILY

(FIGS. 16—18)

FIG. 16 (a)

Maurice E., aged 48 years. Right eye. Vision of this eye still 6/9 partly. The macula is mottled, the choroidal vessels are exposed and there is choroidal sclerosis on the temporal side of the disc. There is also a suggestion of patterned exudate peripherally. Symptoms in the right eye began 3 years previously, and 3 years before that, at the age of 42 years, the right fundus was normal.

FIG. 16 (b)

Left eye. Symptoms began 6 years previously. Vision is now 6/60. The appearances are essentially similar to those in the right eye, but are more exaggerated. Note similarity to Fig. 25.

FIG. 17 (a)

Mrs. M. W., aged 43 years, a sister of Maurice E. At the age of 35 years the vision was full in each eye and both fundi showed a patterned exudate or colloid-like reaction equatorially and peripherally as depicted in the illustration. Right eye: the macula is intact and vision is full.

FIG. 17 (b)

Left eye: there is a destructive central lesion. Symptoms first began 3 years ago; the central area was then swollen; haemorrhages were observed two years later, and vision is now 6/60.

FIG. 18 (a)

Mrs. K. H., aged 41 years, another sister of Maurice E. Right eye. Note the pigimentary reactions and choroidal sclerosis centrally with outlying exudates. Symptoms in this eye first began 3 years previously. Before that this fundus was known to be normal.

FIG. 18 (b)

Left eye. The lesion is more established. Symptoms first began 9 years ago. Note similarity to Fig. 2a and Fig. 23c.

THE KEMPSTER FAMILY

(FIGS. 19 — 24)

FIG. 19 (a)

Arthur K., aged 52 years, the youngest affected brother of Mrs. A. H., whose fundi are depicted in Fig. 24. Left eye: symptoms first began 5 years ago (? 18 years ago). A fairly characteristic macular dystrophy is present with patterned exudate peripherally.

FIG. 19 (b)

Right eye: symptoms began 7 years ago. In contrast to the right eye the central lesion does not suggest a macular dystrophy. Note similarity to Fig. 1(c).

FIG. 20 (a)

Mrs. Rose G. a sister of Arthur K. Right and left eyes: appearances seen in 1939. The lesions are essentially central, pigmentary in character with choroidal exposure and some retinal atrophy. The present condition is unknown.

FIG. 20 (b)

FIG. 21 (a)

FIG. 21 (b)

Mrs. Ann R., died aged 54 years, another sister of Arthur K. Right and left fundi: drawn at the age of 53 years. In contrast to the appearances seen in her two elder sisters the lesion was essentially peripapillary rather than central, and extended well towards the equator. Incipient choroidal sclerosis was evident.

FIG. 22

Joseph K., aged 54 years, a brother of Arthur K. Left eye: symptoms first began 6 years ago; the earliest ophthalmoscopic changes consisted of oedema and haemorrhages at the macula. Now there is extensive central atrophy with some patterned exudate and pigment changes peripherally. The right eye was lost in a war injury in 1916. Note similarity to Fig. 4 and Fig. 26.

FIG. 23 (a)

FIG. 23 (b)

FIG. 23 (c)

FIG. 23 (d)

Mrs. C. P., aged 69 years, another sister of Arthur K. Right and left eyes in 1939. (a) and (b) : Note pigmentary reaction centrally with considerable exposure of choroidal vessels, and peripheral extension. (c) and (d) : Right and left eyes in 1948. Note central atrophy, and extension peripherally, and similarity of Fig. 23 (c) to Fig. 4 and Fig. 26. Figs. (a) and (b) show appearances about 20 years after onset of symptoms ; (c) and (d) illustrate the changes 9 years later.

FIG. 24 (a)

FIG. 24 (b)

FIG. 24 (c)

FIG. 24 (d)

Mrs. Alice H., aged 71 years, the eldest member of the Kempster family. (a) and (b): Right and left eyes in 1939. There is a gross pigmentary reaction in the central area, with rather more peripheral extension in the left.

(c) and (d): Right and left eyes in 1948. There is now considerable extension with exposure of choroidal vessels, more exaggerated in the left where definite choroidal sclerosis is present.

Figs. (a) and (b) show the fundus appearances 20 years after symptoms first appeared. Figs. (c) and (d) illustrate the changes 9 years later.

THE CRANSTON SIBSHIP

(FIGS. 25 — 26)

FIG. 25 (a)

FIG. 25 (b)

FIG. 25 (c)

FIG. 25 (d)

FIG. 25 (e)

FIG. 25 (f)

Miss Edith C., aged 68 years, (a) and (b) : Right and left eyes at the age of 46 when symptoms first began. Oedema around the disc and in the central area with haemorrhages and pigment reaction were then present. (c) and (d) : Right and left eye : 10 years later choroidal sclerosis and pigmentary changes centrally were marked. (e) and (f) : Right and left : 22 years after onset of symptoms. The choroidal sclerosis is becoming replaced by an atrophic reaction. Extension peripherally is considerable.

FIG. 26 (a)

FIG. 26 (b)

FIG. 26 (c)

FIG. 26 (d)

Miss Gertrude C., aged 67 years, a sister of Miss E. C. (a) and (b): Right and left eyes in 1939, appearances are fairly similar to those seen in her elder sister 10 years after the onset of symptoms. The duration of the lesion was probably 2 or 3 years longer. (Note similarity to Fig. 4, Fig. 22, and Fig. 23c.) (c) and (d): Right and left eyes 9 years subsequently. The extension peripherally is marked and the choroidal sclerosis is being replaced by atrophy.

Pedigree Plate I.—*The Randall Family.*

Pedigree Plate II.—*The Carver Family*.

Pedigree Plate III.—*The Ewbank Family.*

- = affected, seen.
- ◐ = reputed affected and found so by the late Mr. R. P. Brookes and by Sir Stewart Duke-Elder. (II, 7 and III, 3 respectively).
- ◑ = reputed affected, not seen.
- = not seen, reputed normal.
- = died before reaching the age of 40 years.
- ◌ = present age is under 40 years, not seen.
- ◌ = present age is under 40 years, seen and found normal.

Pedigree Plate IV.—The Kempster Family.

II. DISCUSSION.

1. *Range of fundus reactions.*

Taken individually the appearances seen in most of the members of these five families would present nothing of special interest. The appearances shown in Fig. 1a are an almost daily occurrence which might well raise the issue of differential diagnosis between an arteriosclerotic and toxic neuro-retinitis. Those seen in the fellow eye (Fig. 1b) might suggest a central choroiditis that has run its course. The appearances in Figs. 2a and 2b might in turn suggest a diffuse choroiditis, and very much the same applies to those of Fig. 3, where the choroidal sclerosis might be regarded as consequent on an old chorio-retinitis. The appearances in Figs. 4a and 4b would be more difficult to interpret and are in fact almost identical with those recorded in an earlier study of two sisters showing central and peripapillary choroidal sclerosis. The final picture in the series (Fig. 5) would raise the possibility of advanced disseminated choroiditis.

In the second family the sub-total choroidal atrophy shown in Fig. 15 might raise a differential diagnosis of advanced choroidal sclerosis, atypical retinitis pigmentosa, and possibly disseminated choroiditis. Figs. 6 to 10 on the other hand would be regarded as illustrating a central choroiditis, whilst Figs. 11, 12 and 13 could, with some justification, be regarded as illustrating progressive stages of diffuse choroiditis. The appearances in Fig. 14 would raise the alternative diagnoses of myopic atrophy or gyrate atrophy. As most of these conditions are relatively common, the fundus appearances in individual cases would therefore raise no special diagnostic doubts. Underlying most of these diagnoses would be the assumption of an infective or toxic process, and such treatment as would be undertaken would be directed along those lines.

In the third family the appearances shown in Fig. 16 could pass for an example of choroidal sclerosis. Fig. 17 is more puzzling. The healthy disc and vessels suggest a diagnosis of fundus albi punctatus (Lauber, 1910) rather than retinitis punctata albescens; an alternative diagnosis would be diffuse "colloid" bodies, though the central lesion in the left eye leaves no doubt as to the nature of the affection. Fig. 18 is reminiscent of what has been described as macular dystrophy with heavy pigmentation. In two out of these three cases it is known that the earlier stages consisted of oedema and haemorrhage at the macula.

As for the fourth family, Fig. 19a might well represent a macular dystrophy of the mottled type complicated by outlying exudates. The veil-like film over the pigmentary central reaction seen in the left eye (19b) is more suggestive of the changes seen in the first

patient of the first family (Fig. 1c). Fig. 22 is almost a replica of the appearances shown in Fig. 4. Most of the remaining figures could be regarded as heavy central or diffuse chorio-retinitis.

In the last sibship, Fig. 25 *a* and *b* represent what may be regarded as fairly typical central chorio-retinitis; 25 *c* and *d* have been read to show choroidal sclerosis; whilst *e* and *f* are obvious examples of chorio-retinal atrophy. Likewise Fig. 26 *a*, *b*, *c*, and *d* show a similar difficulty in diagnosis.

2. Implications.

These considerations emphasise several points:

(1) Gross pigmentary disturbances are not always infective or toxic in origin. Attention to this has already been drawn in the earlier study on macular dystrophies. The present study is further evidence to the same effect.

(2) The earliest changes in a genetic affection may be haemorrhages and exudates identical in appearance with the lesions commonly observed in arteriosclerotic and metabolic disorders. It would therefore seem that as genetic anomalies are studied more intensively, the line of demarcation of the fundus appearances in these affections as from the more widely recognized non-genetic affections is becoming more blurred. The classical teaching that the abiotrophic fundus appearances take the form of the pigment changes of retinitis pigmentosa, atrophy as seen in gyrate atrophy, or macular dystrophy represented by mottling and atrophy, is clearly too limited.

(3) Apart from the wide range of types of reaction that the abiotrophic fundus anomalies may show—mottling, gross pigment changes, atrophy, "colloid" bodies, oedema, exudates, and haemorrhages—there is this significant consideration: these reactions are not all sharply demarcated from each other, but represent different phases in one and the same process. A reaction showing oedema, haemorrhages, and exudates may pass into a grossly pigmented scar and end in an atrophic lesion. The possibility that a particular fundus anomaly may be genetic in character is suggested not so much on the type of reaction—for almost any fundus reaction may be genetic in origin—as by the symmetry of the lesion in the two eyes—and even this criterion does not always hold good, for a genetic lesion may be asymmetrical and for a time unilateral.

(4) A lesion beginning as fairly strictly localised to the central area may extend relentlessly to involve the whole of the fundus. What may appear as a macular dystrophy with its relatively favourable end-result may actually be the starting point of a generalised dystrophy with a gloomy prognosis.

3. *A clinical entity.*

Apart from these general considerations it would appear that the present study also justifies the conclusion that to the relatively small group of clearly defined genetic fundus anomalies there is to be added one more possessing the following features:

(1) *Age at onset.* The affection begins at about the age of 40 years.

(2) *Subjective symptoms.* The first subjective symptoms are blurring of central vision in one eye followed by the same symptoms in the other eye within a matter of months, or perhaps a few years. It is not known whether the two eyes may be affected simultaneously. Central vision rapidly declines, but there is no involvement at this stage of peripheral vision or colour vision. There are no symptoms of night blindness early on or during the course of the affection.

(3) *Objective signs.* Objectively the first signs are oedema, haemorrhages, and exudates in the central area. These progress to scar formation with a varying amount of pigment proliferation, which may be exceedingly massive. The choroidal vessels become exposed and show some sclerosis. Over the course of years the process extends peripherally, choroidal sclerosis generally becomes more manifest and sometimes dominates the picture. During its spread peripherally, exudates—sometimes patterned—may appear and it is possible that widespread glistening “colloid” bodies may be a pointing sign. The end stage is widespread disappearance of the choroidal vessels exposing the sclerotic covered irregularly by proliferating pigment. The terminal stage produces practically total blindness. The polymorphism of the fundus reactions is such that any stage of oedematous and inflammatory fundus lesions as well as diffuse choroidal sclerosis can be simulated.

(4) *Course.* The full course of the affection spreads normally over about 35 years. The process may, however, be milder, or more severe, in individual cases.

(5) *Genetics.* Genetically the condition is probably a simple autosomal dominant.

The following summary table based on the first four pedigrees (excluding the Cranston sibship because of its incompleteness)

Number of individuals aged 40 years and over.

	Unaffected			Affected		
	M.	F.	P.	M.	F.	P.
Randall	4	7	11	7	8	15
Carver	8	12	20	13	12	25
Ewbank	3	4	7	3	7	10
Kempster	4	3	7	6	5	11
	19	26	45	29	32	61

shows the distribution of the affected in relation to unaffected and the sex incidence.

On the expectation of 50 per cent. ratio for a simple dominant, there would therefore seem to be an excess of affected over unaffected. The excess is, however, not statistically significant.

The excess is rather heavier in men. Of 48 men 29 were affected, whilst of 58 women 32 were affected. This excess of men over women is also not statistically significant, nor is it borne out by an analysis of those complete sibships that have been examined ophthalmoscopically. Extracted from the four pedigrees, the following data are obtained:

Complete sibships examined ophthalmoscopically.

Unaffected*			Affected		
M.	F.	P.	M.	F.	P.
5	5	10	13	11	24

* Excluding 3 women and two men under the age of 40.

Here there is no marked difference in sex distribution, but the discrepancy between the theoretical expectation as to frequency and the actual distribution is, however, wider, there being 24 affected individuals against 10 unaffected, a statistically significant difference. These ratios may, however, be loaded by the more ready submission to full examination by such sibships as are heavily affected. Until further data are available it would, therefore, seem best to assume a simple autosomal dominant mode of inheritance.

4. Relationship to other affections.

(a) *Doyne's Choroiditis*. The wide range of ophthalmoscopic appearances and extensive changes in their aspect in the affection recorded here has some features in common with the cases described by Doyne as "family choroiditis," or honeycomb choroiditis. In the families described by Doyne, and followed up by Tree (1937), the affection is also dominant and develops at about the age of 40 years. The characteristic appearance seems to be massive formation of white dots in the disc-macular area with only slight pigment proliferation. In some cases the choroidal vessels become exposed and possibly sclerosed, and haemorrhages may be seen during the course of the affection. But oedema and haemorrhages do not appear to be present during the early stages and extension peripherally does not appear to have been observed; in fact the process seems to be circumscribed by a circinate-like reaction, so that even in advanced cases the peripheral field is apparently not

involved. Histologically Doyne's choroiditis would appear to be a nodular hyaline degeneration of the pigment epithelium of the retina (Collins, 1913).

The final summary that Doyne gave of his cases would suggest that "white spots" and a strict localisation to the central area were the significant features. In his own words: "The condition may be summarised thus: It first appears in early adult life, but much more commonly later. It may either affect the disc neighbourhood, the macula neighbourhood, or the disc macula area. It consists of circular patches of exudation; these increase during the middle age, and at least, set up some irritation and pigmentary disturbance, for, though pigment is not always present, in some cases there is a good deal to be seen. During this stage the sight, though affected, is not grossly interfered with. In old age the condition passes into atrophy, with a corresponding degree of failure of sight."

It cannot, however, be excluded that the cases recorded as Doyne's choroiditis are actually examples of the affection reported here, and that in Doyne's cases (as in the first reports on the Kempster family and the Cranston sibship) a particular aspect has been stressed rather than the full picture. If the patterned reaction is indeed a constant feature in Doyne's choroiditis (and this would not appear to be the case) and if moreover Doyne's choroiditis does develop without preceding oedema at the macula, and in its later stages remains limited to the central areas (and the evidence on this is not conclusive) the affection described by Doyne would have to be regarded as a macular dystrophy of the "exudative type." It is, however, just as likely that the cases recorded by Doyne are instances of the affection described here, in which both the early and the late stages were not studied. The presence of patterned exudates in many of our patients is suggestive. The bare statement made by Doyne (1910) that he had had "two cases about eighty years of age, and they were almost blind" is likewise suggestive, as is also the remark that "the changes were different then, because the distinctive spots disappeared and the whole area [? central area or the whole of the fundus] became homogeneous and atrophic." It would appear that cases similar to those described by Doyne have been observed in the Leventino valley in Switzerland by Franceschetti (1948), whose brief note speaks of the presence of large hyaline bodies in a pre-senile macular degeneration with apparently irregular dominance. Until there is a fuller account of Doyne's choroiditis than is yet available, as also a histological study on the affection described here, the identity or otherwise of the two conditions must be left an open question.

(b) *Retinitis punctata albescens and allied conditions.*

Retinitis punctata albescens is an ill-defined entity. Even when the cases designated by Lauber (1910) as fundus albi punctatus are eliminated there is still left a rather heterogeneous mass. The group isolated by Lauber differs from retinitis punctata albescens in its congenital, non-progressive course, and in the fact that neither the disc nor vessels are involved; night blindness would, however, appear to be a constant feature. The stress laid by Doyne on "white spots" in his cases, the appearances depicted in Figs. 17 *a* and *b*, to a lesser extent in Figs. 6, 11 and 14, and to a slighter extent still in Figs. 1*a*, 2 *a* and *b*, 3, 18*a*, 24 *a* and *b*, 22 and 19*a*, raise the difficult question of the diagnostic significance of these "white spots." There is obviously no relationship between the condition recorded here and retinitis pigmentosa, even if the conception of retinitis pigmentosa is stretched to include "atypical" cases. The general absence of night blindness, the full peripheral fields almost until the end, the normal discs, and normal retinal vessels are quite conclusive. It is not improbable that the difficulty with "white spots" and "colloid" bodies and Drusen bodies arises from the fact that these are merely part of a wider picture, and the attempt to isolate clinical entities around these appearances has failed because of too narrow an approach. It may well prove that in a whole variety of affections the pigment epithelium reacts by the formation of non-pigmented hyaline excrescences; alternatively this reaction may be the basis of a wide range of ophthalmoscopic appearances.

(c) *Other ill-defined entities.*

The literature contains the following case reports of genetic fundus lesions that had become manifest at about the age of 40 years.

(1) Hutchinson (1875). Two sisters with central fundus lesions coming on at about the age of 57 and 48 years respectively.

(2) Leber (1916). A brother and two sisters with a central lesion setting in at the age of 50 years in the case of the brother, and at about 45 years in the sisters.

(3) Blue (1919). A macular lesion in a man affected at the age of 35 years, and a similar lesion in his daughter at the age of 12 years.

(4) Behr (1920). Two brothers, aged 43 and 53 years respectively, whose mother was probably also affected at the age of 50 years. These two brothers appeared to show a central lesion only.

(5) Clausen (1921). A man with a central lesion which developed at 41 years. Similar central lesions were found in three of his six children. They were 27, 19 and 15 years of age and their lesions had developed at 23, 10 and 13 years respectively.

(6) Cavara (1924). A macular lesion in three sibs; in two of them it developed at the age of 30 years and in the third at 40 years. In the youngest member the lesion was distinctly central; in the eldest member it had extended to engulf the whole of the disc-macular area.

(7) Mazzi (1934). A man who became affected with a central lesion at the age of 44 years had a son who showed a similar lesion at the age of 22 years.

Dominant inheritance is suggested by the cases recorded by Blue, by Clausen, and by Mazzi, but the age of onset in the second generation in each case would seem to exclude them from any affinity to the condition recorded here; moreover the lesion is recorded as central in position. The cases that might fit in best are those recorded by Hutchinson, Cavara, Leber, and Behr. Only in Behr's cases is there any suggestion of dominance; in the other three cases there is no information on either consanguinity, or of the affection being present in an earlier generation; and in none of these four cases is there any record on the evolution of the lesion.

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SUMMARY.

1. A description is given of five families which show an abiotrophic fundus lesion possessing the following features:

- (a) The affection is dominant.
- (b) It becomes manifest at about the age of 40 years.
- (c) It begins as a central lesion showing oedema, haemorrhage, and exudates, thus closely simulating a retinitis. In the course of years there is atrophy with pigmentation of the central area and extension peripherally. The choroidal vessels become exposed and show some sclerosis. Ultimately—generally within 35 years—the whole of the fundus becomes involved; the choroidal vessels disappear and the terminal picture is one of extensive choroidal atrophy with pigmentation.

(d) There is no night-blindness antecedent to the development of fundus lesions or during the evolution of the affection.

2. This affection is a clear-cut entity, with a prognosis graver than that of a macular dystrophy, for which the earlier stages may be mistaken.

3. The course of the affection would suggest that the lesion is primarily choroidal.

4. Two of the five families recorded here have previously been reported mistakenly as examples of macular dystrophy with heavy pigmentary reaction and of central and peripapillary choroidal sclerosis. The polymorphism of an evolutionary affection presents many diagnostic difficulties, and the mistaken diagnoses in these two earlier records is illustrative of these difficulties.

5. The classical teaching that abiotrophic fundus lesions are recognisable as such ophthalmoscopically owing to their mottled or atrophic appearance, their sharply defined contours and the symmetry in the two eyes, is valid only for extreme cases. It may indeed be doubted whether there are any ophthalmoscopic features in lesions of environmental origin that cannot be found in abiotrophic affections.

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APPENDICES.

1. The Randall Family.

GENERATION I.

(1) Mrs. John Randall, née Ellard. According to two of her grandchildren (III, 12 and III, 16), Mrs. Randall died at about the age of 40 years and was not known to be affected. Both state, however, that a brother who survived to old age was affected. The two other surviving grandchildren (III, 3 and III, 4) both agree with their cousins that their grandfather was not affected. There was no consanguinity.

GENERATION II.

(1) Mary Ann Randall. Died aged 85 years. She had good sight and was unmarried. (2) William. Unmarried. Died aged 79 years. Had good sight.

(3) George Randall. His grandson, George Randall (IV, 2), reports that at about the age of 40 years he developed "centre blindness." He lived till the age of 72 years and "could see sideways." Used to get about the village comfortably. Concerning this patient, Mr. E. H. Harries-Jones writes: "I saw him about 40 years ago in a doctor's surgery with very poor light and found both retinae covered with pigmentary degeneration and central vision practically nil." Had six children (III, 1-6). (4) Richard Randall. Stated to have been affected. According to his daughter, Mabel (III, 12), his "central sight" went at the age of 40 years. Had six children (III, 7-12). (5) Sarah married Butt. Died at 65 years. Reported by her daughter, Amy (III, 16), to have become affected at 48 or 49 years. Her "central sight went." She died aged 65 years and was "four-fifths" blind. Had four children (III, 13-16). (6) Kate married Carr. Died aged 92 years. Her sight was "perfect" according to her niece, Amy (III, 16). Was the mother of two children (III, 17-18). (a) A seventh child, John, died as a baby. His position in the family cannot be definitely determined, nor the position of (b) a twin that died in early infancy.

No member of this generation is alive to-day.

GENERATION III.

(1-6) The children of George Randall (II, 3). (1) John Randall died aged 67 years from renal failure after a prostate operation. He had retired from business as a corn merchant at the age of 52 years because of his eyesight, having developed "centre blindness" at about the age of 40 years. According to his daughter, Mary (IV, 1), he, like his father, could see to get about in the country and to look after his garden and outdoor work. Towards the end of his life his sight rapidly became worse. Mr. Harries-Jones saw him during the 1914-18 war and found "a central haemorrhage in one eye followed in about two years by the same condition in the other." Had two children (IV, 1 and 2). (2) George Randall was the editor of a local newspaper. According to his nephew, George (IV, 2), his sight became affected at about 45 years, but he carried on with his work until about 62 years. He died aged 64 years, after a prostate operation. He suffered from "centre blindness" and used telescopic glasses; his staff are said not to have realised that their chief could not read. His brother, Alfred (III, 6), reported that he underwent an extensive "mercury cure" which nearly killed him but produced no improvement in the sight. This patient was known to Mr. Harries-Jones as suffering from the same affections as the members of the family under his own care. He was unmarried. (3) Elizabeth married Clark. A frail old lady, aged 75 years, whose fundi show widespread lesions (Fig. 5). Her eyesight failed at the age of 40 years. She and her sister, Mrs. Thornton (III, 4), are known in the family as the most severely affected members. Is the mother of three children (IV, 3-5). (4) Annie married Thornton, is 71 years old. Very severely affected, possessing doubtful perception of light. Had a trephine operation on each eye at the age of 51 years by the late Mr. Nesfield, presumably not for glaucoma but for the relief of failure of sight which began at about the age of 40 years. Has two children (IV, 6 and 7). (5) William Randall, aged 70 years. Reputed to be normal and found so on examination. Has two children (IV, 8 and 9) and three grandchildren (V, 2-4), all reported to be normal and found so on examination. (6) Alfred Randall. Died from lymphatic leukaemia at the age of 57 years at the Westminster Hospital in 1938. Seen by one of us (A. S.) in 1937. His vision then was hand movements in each eye, and a diagnosis of central choroidal atrophy was made and the fundi were drawn. He gave a history of sight having failed progressively from the age of 43 years, but he could still find his way about London. He stated that his father had been likewise affected, and that only one of his five sibs had escaped the "family curse." It proved impossible at the time to follow this family up as the patient was unco-operative. He was unmarried. Whilst at the Westminster Hospital he was seen by the late Mr. A. D. Griffith, who reported that there were gross changes in the fundi "not at all connected, I should say, with the leukaemia." He regarded it as "a severe choroido-retinal atrophy such as follows luetic choroiditis." The blood Wassermann and Kahn were negative. This patient stated to one of us that he would not have any

treatment as he was sure to be "poisoned with mercury as his brother, George, had been."

(7-12) The children of Richard Randall (II, 4). (7) Rosa Randall. Unmarried. "Died blind" at about the age of 70 years, according to her sister, Mabel (III, 12). Trouble began at about the age of 40 years and progressed steadily. (8) Laura married Wrigley. Is alive and is 76 years old. Her sight is reputed to be normal, and her five children (IV, 10-14) are also reputed to be normal. (9) John Randall. Died at the age of 57 years of cancer. His sight had been "slightly affected" from "centre blindness." There was one son (IV, 15). (10) Gertrude married Cameron. Died at the age of 58 years. Is reputed to have been normal. Her three children (IV, 16-18) are also reputed to be normal. (11) Richard died at the age of 62 years. Reputed to have been normal, as are his five children (IV, 19-23). (12) Mabel married Pritchard. Is 67 years old. Reputed to be affected and found so on examination (Figs. 2a and 2b). Her trouble started at the age of 40 years. Has one son, John (IV, 24), who is affected.

(13-16) The children of Sarah Butt (II, 5). (13) Kate married Flatt. Died at the age of 30 years, reputed to have been normal, as are her two children (IV, 25 and 26). (14) Florence married O'Hara. Died aged 72 years. Lost "central sight" at 42 years, but could always see to get about. There were no children. (15) Lucy Ellen married Barrett. Is alive, aged 70 years, and is reputed to be normal, as are her two children (IV, 27 and 28). (16) Amy married Martin. Lost "central vision" at 41 years. Is now 68 years. Was not much handicapped till aged 60 years. Her fundi show a central lesion (Fig. 3). Has two children (IV, 29 and 30).

(17 and 18) Tom and Nellie, the children of Kate Carr (II, 6). This branch of the family is reported as normal and has not been followed up. Tom is 69 years, Nellie is 61 years.

GENERATION IV.

(1 and 2) Mary and George, the children of III, 1. Mary is the starting point of this study. Her fundi are depicted in Figs. 1a, 1b and 1c. A fuller account is given in the text. George, aged 27 years, reputed to be normal and found so on examination.

(3-5) Noel, Winifred and Muriel Clark, the children of III, 3. Noel was killed in the World War I, aged 22 years. Winifred, now aged 51 years, married Johnson. Reputed to be normal and found so on examination. Muriel, aged 47 years, married Burton. Reputed to be normal and found so on examination.

(6 and 7) Mary and Phillip Thornton, aged 33 and 31 years, the children of III, 4. Reputed to be normal and found so on examination.

(8 and 9) Dora and Margaret, the children of III, 5. Dora, aged 41 years, married Fleming. Reputed to be normal and found so on examination. Margaret Randall, aged 35 years, reputed to be normal and found so on examination. Is unmarried.

(10-14) Children of Laura Wrigley (III, 8). (10) died aged 30 years, unmarried. (11-14) Reputed to be normal. Have not been examined.

(15) Eric Randall, the son of III, 9. He is aged 46 years and is reputed to be normal. Not seen.

(16-18) The children of Gertrude Cameron (III, 10). (16) Died aged 10 weeks. (17 and 18) are 38 and 36 years of age respectively. Not seen.

(19-23) The children of Richard Randall (III, 11). (19) Died in childhood. (20) Is aged 40 years. His three younger sibs are younger by two years progressively. All reputed to be normal. Not seen.

(24) John Pritchard, the son of III, 12. When seen at the age of 43 years he was reputed to be normal and found so on examination. Six months later the right eye failed. He is discussed fully in the text.

(25 and 26) The children of III, 13. Lilian married England. Is aged 50 years. Has two children (V, 15 and 16). Winifred, aged 45 years, married Eldon. Has one daughter (V, 17). All reputed to be normal. Not seen.

(27 and 28) Ivor and Myfanwy, the children of Lucy Barrett (III, 15), aged 44 and 36 years. Reputed to be normal. Not seen.

(29 and 30) Joan and Albert, the children of Amy Martin (III, 16), aged 31 and 28 years respectively. Both reputed to be normal. Joan was found so on examination.

(31 and 32) The children of Tom Carr (III, 17), Freddie and Joyce. Reputed to be normal. Not seen.

GENERATION V.

None of this generation is beyond adolescent age and none is reported affected.

(1) David Johnson, the son of IV, 4.

(2, 3 and 4) A son, Robert, and two daughters of Dora Fleming (IV, 8), aged 8, 6 and 3 years respectively.

(5-8) The grandchildren of Laura Wrigley (III, 8), herself unaffected.

(9-10) Sheila and Barbara Randall, the children of IV, 15.

(11) Grandchild of III, 10.

(12 and 13) The grandchildren of Richard Randall (III, 11), himself reputed to be unaffected.

(14) The son of John Pritchard (IV, 24, himself affected), aged 6 months.

(15 and 16) John and Jean England, aged 25 and 21 years respectively.

(17) Daughter of Winifred Eldon (IV, 26), aged 16 years.

(18 and 19) Jean and John, the grandchildren of III, 17, himself reputed normal.

2. *The Carver Family.*

GENERATION I.

(1) Mr. Carver. The family ascribes the eye defect as originating with Mr. Carver, and the condition is known in the family as the "Carver eye."

GENERATION II.

(1) Dinah Carver married Hepburn. (2) William Carver. (3) Edward Carver. (4) Jane Carver, unmarried, died elderly. (5) Dan Carver. (6) Anthony Carver. (7) Dryden Carver. (8) Mary married Murray. Of this generation all but Edward, Jane and Anthony are said to have been affected.

GENERATION III.

(1-5) The children of Mrs. Dinah Carver-Hepburn (II, 1): Dan Hepburn (1), died at about 54 years of age, reputed to be unaffected. Catherine (2) married Wilson, died under 40 years, reputed unaffected. Anthony Hepburn (3), age 75 years. Lizzie (4), died under 40 years, reputed unaffected, and Dryden Hepburn (5), aged 65 years. Anthony reputed to be affected and found so on examination. Dryden is reputed to be affected.

(6-10) The children of Dan Carver (II, 5): John Carver (6), died at 78 years, a daughter (7) died at 16 years, Ellen (8) married Lacey; is 72 years of age, reputed to be affected and found so on examination, Emma (9) died in infancy, and Isabel (10) married Wright; examined and found normal; died at 62 years.

(11-16) The children of Anthony Carver (II, 6): Annie (11), Jane (12), Mary (13), John (14), William (15) and Dryden Carver (16). Annie, the eldest, married Duncan Kirkpatrick; she is reputed to be affected and was found so on examination; is now 65 years old. Jane married Dixon; she is now dead. Mary is in America; John Carver died under 40 years, William and Dryden are over 40 years, alive and in America.

(17-24) The children of Mary Carver Murray (II, 8): Ann (17), Mary (18), John Batey (19), Jane (20), Dryden (21), Maggie (22), Jessie (23), and another sister (24). The eldest, Ann, married Tyson, died at about the age of 80 years; she was reputed to be unaffected. Mary was unmarried and was reputed to be affected. John Batey was reputed not to be affected but was found affected on examination; he is now 78 years old. Jane died under 40 years. Dryden died at the age of 73 years; was reputed to be affected and was found so when examined some years ago. Maggie, married Wallace; was reputed to be affected; she is dead. Jessie,

aged 71 years, is reputed to be affected and was found so on examination; married to McLean. The youngest daughter is over 40 years; she is married to Cape.

GENERATION IV.

(1-3) The children of Dan Hepburn (III, 1): Mary Hepburn (1), aged 56 years, and Mrs. Spedding (2), aged 46 years, were examined and found normal. Archie Hepburn (3), aged 42 years, lives in Rochdale; not examined.

(4-7) The children of Catherine (Hepburn) Wilson (III, 2): Archie Wilson (4), died aged more than 40 years; Dinah (5) married Dawson, is now 69 years old and was found normal on examination; Harriet (6) married Hodgson; Reuben Wilson (7) is now about 65 years; examined and found normal.

(8-16) The children of Anthony Hepburn (III, 3): Nellie (8), aged 52 years, married Bedford; reputed and found to be affected. Archie Hepburn (9), aged 50 years, reputed and found to be affected. John Hepburn (10), aged 47 years, reputed and found to be affected. (11) Margaret, aged 46, patient No. 5 in the text. Emma (12) married Rudd, aged 45 years; found normal on examination. Jim Hepburn (13), aged 44 years, reputed and found to be affected. Annie Hepburn (14), aged 42 years; found normal. Dryden (15), aged 40 years, found normal. Mary (16), aged 37 years, found normal.

(17-19) The children of Dryden Hepburn (III, 5): Frank (17) is 38 years old, Douglas (18) is 33 years, and Graham (19) is 30 years.

(20-29) The children of Ellen Lace (III, 8): Sarah (20), married Hayes, is now 54 years old; reputed and found to be affected. Martha Lace (21), aged 52 years; found normal. Margaret (22), aged 48 years, married Prickett; reputed to be affected. Ellen (23), aged 45 years, married Jim Murray (IV, 38, himself affected), found normal on examination. Fred Lace (24), aged 44 years, Isabel Lace (25), aged 42 years, found normal. John Daniel Lace (26), aged 40 years, found normal. Dorothy (27), aged 38 years, married Wilson. Mary Irving (28), married Wilson, aged 37, found normal. Gordon Lace (29), aged 33 years, found normal.

(30) A son of Isabel Wright (III, 10). Died in the early twenties from tuberculosis.

(31 and 32) The children of Annie Kirkpatrick (III, 11): Leo (31) died aged 39 years. His younger sister, Nancy (32), is alive under 40 years.

(33 and 34) The children of Jane Dixon (III, 12): William (33) is 25 years old. Harriet (34) is a younger sister.

(35) A son of John Carver, aged under 40 years.

(36) John Ernest Murray, a son of Ann Tyson (III, 17), is reputed to be and found affected. He is 59 years of age.

(37-40) The children of Dryden Murray (III, 21): Mary (37), aged 54 years, married Dixon; found normal. Jim Dryden Murray (38), aged 50 years, reputed and found to be affected. He is married to Ellen Lace, now aged 45 years (IV, 23), herself normal. Emma (39), aged 43 years, married Parker; reputed normal. William Murray (40), aged 39 years when killed in the William Pit Disaster in 1947; was known to be unaffected.

(41-48) Eight daughters of Maggie Wallace (III, 22, herself reputed to be affected). Reputed that one daughter living in Scotland is affected. This branch of the family could not be followed up.

(49-54) The children of Mrs. Cape (III, 24): the eldest daughter (49), aged 64 years, married Bland and lives in Newcastle. James Cape (50) is 61 years old. William Cape (51), Harry Cape (52), and two younger sisters (53 and 54) are the other children. All are over 40 years of age, but none could be examined. They are reputed not to be affected.

GENERATIONS V.

In this generation there are no individuals who have as yet reached the age of 40 years.

(1 and 2) The two daughters of (IV, 2), aged 26 and 25 years respectively.

(3) A son of Archie Hepburn (IV, 3), aged 23 years.

(4 and 5) The two sons of Nellie Bedford (IV, 8) herself affected. The eldest, Anthony Bedford, died at the age of 24 years. His brother, Stephen Bedford, is aged 23 years.

(6-9) The children of Archie Hepburn (IV, 9) himself affected: Dennis (6), Jim (7), Eileen (8), Neil (9) are aged 25, 23, 15, and 7 years respectively.

(10-11) The children of John Hepburn (IV, 10) himself affected: Kathleen (10), Mary (11) are aged 19 and 10 years respectively.

(12-15) The children of Emma Rudd (IV, 12): Mary (12), Jean (13), Anthony (14), Howard (15), are aged 19, 13 and 10 years respectively.

(16) Ian, son of Jim Hepburn (IV, 13), himself affected, is aged 17 years.

(17-19) The children of Sarah Hayes (IV, 20) herself affected: Joseph (17) died at 26 years, John (18) is 26 years old, and Phyllis (18) is 14 years.

(20-26) The children of Margaret Prickett (IV, 22) herself reputed affected: Vera, Josephine, Brian, Mary, John, Ellen, and Fred, aged 26, 24, 23, 21, 19, 17, and 14 years respectively.

(27) Marjorie Lindsay Murray, aged 23 years, the daughter of Ellen Lace (IV, 23) and Jim Murray (IV, 38), himself affected, was found normal on examination.

(28) Mary Lace, the young daughter of IV, 24, aged 16 years.

(29) John Lace, son of IV, 26, is 14 years old.

(30) The son of Dorothy Wilson (IV, 27) is 11 years old.

(31) The son of John Ernest Murray (IV, 36), himself affected, is 33 years old.

(32 and 33) Nora, aged 27 years, and Raymond Dixon, aged 26 years, children of IV, 37.

(34-36) Yvonne, Margaret and Alan Murray, aged 5, 4 and 2 respectively, grandchildren of III, 21, himself affected.

3. *The Ewbank Family.*

GENERATION I.

Mr. Ewbank died in his fifties; is not known to have had any defect of vision. He married twice. All that is known of the first marriage is that there were children.

GENERATION II.

The information concerns the seven children of the second marriage.

(1) Sarah Ewbank, died aged 67 years, unmarried. Reputed to have been unaffected. (2) Cornelius Ewbank, died at 55 years, unmarried. Reputed to have been unaffected. (3) Josephine, married Adamson. Sight became affected in the early forties; was "practically blind" when she died at 60 years. (4) Susie, died at about the age of 20 years. (5) Rosa, married Steele. Sight became affected at about 35 years. Died "practically blind" at the age of 62 years. (6) Florence, died at 74 years. Reputed normal. No issue. (7) Richard Ewbank. Sight became affected at 43 years. He was seen by the late Mr. R. P. Brooks, who found "maculitis." The patient "was soon unable to read, but always retained some sight (e.g., could play cards, do some gardening and go about unaccompanied)." (Information given by his son Maurice, III, 10.) Died at 74 years. He was the father of the patients recorded here.

GENERATIONS III.

(1-4) The children of Josephine Adamson (II, 3). (1) Bert Adamson, died unmarried at 32 years. (2) Florence, aged 67, married Patchett. "Had severe haemorrhage in the eyes at 48 years; has peripheral vision only (cannot read or sew, but can play cards and gets about)." Has one son aged 32 years. (3) Isabelle, aged 61 years, married Jagger; no children. "Present condition similar to that of her sister Florence." Sight is said to have deteriorated at 58, but when seen by Sir Stewart Duke-Elder in 1947, when she was aged 60 years, he found advanced central choroidal atrophy in both eyes, more marked in the right than in the left. (4) Marjory, aged 54 years, married White; "Sight has been deteriorating for the past four years." Has one son.

(5-8) The children of Rosa Steele (II, 5), herself reputed affected. (5) Mary, now aged 55 years, married Cockayne. Sight has been bad for 20 years. Has four children. (6) Constance, aged 52 years. Reputed unaffected. Has one daughter.

(7) Wallace Steele, aged 50 years. Reputed unaffected. (8) Rosa, aged 46 years, married Grahame. Has two sons.

(9-12) The children of Richard Ewbank (II, 7, himself affected) by his first wife, who died aged 43 years and was unaffected. (9) Kenneth Ewbank, aged 54 years, is mentally defective, but is said to have no eye trouble. (10) Maurice Ewbank, aged 48 years, examined and found to be affected. (11) Colin Ewbank, aged 46 years, died from neoplasm of the kidney. Known to have been affected since the age of 36 years. (12) Mary, aged 43 years, married Waterer. Examined and found affected.

(13 and 14) The children of Richard Ewbank (II, 7) by his second wife. (13) Kathleen, aged 40 years, married Hughes. Examined and found affected. (14) Nora, aged 38, married Holland. Examined and found unaffected.

GENERATION IV.

(1) Bert, the son of Florence Patchett (III, 2); aged 32 years.

(2) The son of Marjory White (III, 4): Tony, aged 25 years.

(3-6) The children of Mary Cockayne (III, 5), herself reputed affected; Constance, aged 26 years, married Marshal, has one daughter; Nora, aged 23 years, married Dyer; twin brother and sister aged 17 years.

(7) Cynthia Stevenson, aged 14 years, daughter of III, 6.

(8 and 9) Gerald and Maurice, sons of III, 8, aged 21 and 19 years respectively.

(10) Denis, aged 29 years, the son of Kenneth Ewbank (III, 9).

(11-13) The sons of Maurice Ewbank (III, 10), himself affected. (11) Anthony, died aged 20 years. (12) Patrick, aged 17 years, and (13) David, aged 13 years.

(14-15) The children of Mary Waterer (III, 12), herself affected. (14) John Waterer, aged 9 years, and (15) Patricia Waterer, aged 4 years.

(16-17) The children of Kathleen Hughes (III, 13), herself affected. (16) Robin, aged 8 years, and (17) Wendy, aged 4 years.

(18-19) The two daughters of Nora Holland (III, 14). Elizabeth, aged 4 years, and Carolyn, aged 8 months.

GENERATION V.

(1) The baby daughter of (IV, 3).

(2) The baby daughter of Denis Ewbank (IV, 10).

4. *The Kempster Family.*

GENERATION I.

The grandfather of the observed patients is reported to have been blind. He is also reported to have had a blind brother.

GENERATION II.

The grandfather's brother is reported to have had an affected daughter. As for the grandfather's children there were 8, the order of whom is not known. Three out of five brothers are reputed to have been affected and one out of three sisters.

GENERATION III.

It is reported that two cousins of the present sibship are affected, the son of a paternal uncle, and the daughter of a paternal aunt. The sibship itself (III, 1-10) has been described in the text.

GENERATION IV.

(1) RUTH HALL, the daughter of Alice Hall (III, 1), herself affected, aged 30 years, unmarried; examined and found normal.

(2-5) The children of Caroline Poulton (III, 2), herself affected. (2) Ivy, married Collins, aged 32 years; reputed normal. (3) Gladys Poulton, unmarried, aged 31 years, seen and found normal. (4) Frances, married Cook, aged 29 years; reputed normal. (5) A son: premature stillbirth.

(6-9) The children of William Kempster (III, 4), himself affected. The eldest, a son, died at 21 years, was reputed normal. (7-8) Two girls died in infancy at

four weeks and six months. Joan Kempster, aged 24 years, unmarried, reputed normal.

(10-14) The children of Ann Redding (III, 5), herself affected. (10) Winifred, aged 35, reputed normal. (11) William Redding, aged 33 years, reputed normal. (12) Ann, married Puddephat, aged 31 years; reputed normal. (13) Dorothy, married Blunt, aged 28 years, reputed normal. (14) Percival Redding, aged 26 years, reputed normal.

(15-17) The children of Rose Graves (III, 6), herself affected. All in Canada. Rosemary Graves, aged 29 years, is reputed to be mentally defective; unmarried. Doris Graves, aged 27 years, reputed normal, unmarried. Robert Graves, aged 21 years, reputed normal; was seen in 1939, at the age of 12 years, and was then found normal.

(18) Thomas Wood, the son of Eliza Wood (III, 7), aged 25 years; reputed normal.

(19) Sidney Kempster, son of Joseph Kempster (III, 8), himself affected, aged 28 years, married, no children; reputed normal.

(20-23) The children of Arthur Kempster (III, 9), himself affected. (20) Herbert, aged 26 years. (21) Fred, aged 24 years. (22) Robert, aged 17 years. (23) John, aged 9 years. All reputed to be normal.

(24 and 25) The children of Robert Kempster (III, 10), Gwen, aged 18 years, and Margaret, aged 14 years, reputed to be normal.

GENERATION V.

(1 and 2) Ronald and Josephine Collins, aged 2 and 1 years, children of IV, 2.

(3) Michael Cook, aged 1 year, son of IV, 4.

(4-6) (4) Brenda, aged 8 years, Anthony, aged 5 years, Nita, aged 2 years, children of William Kempster (IV, 11).

(7-8) Harold and Sandra Puddephat, aged 8 and 6 years respectively, children of IV, 12.

(9) Stephen Blunt, aged 4 months, son of IV, 13.

(10) Stewart Redding, aged 14 months, son of IV, 14.

(11) Margaret Kempster, aged 12 months, daughter of IV, 20.

A THEORETICAL PLAN OF A METHOD FOR REMOVING NON-FERRO-MAGNETIC METALLIC INTRA-OCULAR FOREIGN BODIES BY MEANS OF ELECTRO-MAGNETIC FORCES.*

BY

P. M. ENDT *and* J. TEN DOESSCHATE

UTRECHT

THE removing of non-ferro-magnetic metallic intra-ocular foreign bodies (like copper, non-magnetic steel, etc.), always offers many difficulties to the ophthalmologist. For removing ferro-magnetic foreign bodies we have at our disposal very satisfactory methods which are all based on the principle of exerting electro-magnetic forces on the foreign body. Theoretically, however, it is possible

* A paper on this subject was read by the authors at the 112th meeting of the *Netherl. Ophthal. Soc.* on June 7, 1947. This paper did not contain the necessary physical foundations.