

## COMMUNICATIONS

### DOMINANT MACULAR DYSTROPHY\*

BY

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IN contrast with recessive macular dystrophy of the type described by Stargardt (1917), dominant macular dystrophy is not a well-recognized entity, nor are its features clearly defined. The present record of three families suggests that the affection may be symptomatically silent, or at any rate not particularly clamant, but that nevertheless it is sufficiently definite to be fairly readily diagnosed.

#### Case Reports

**I. M. FAMILY (Pedigree Chart I).**—In this family seven cases were observed in three generations in one branch, whilst a collateral branch showed two cases in two generations, the two latter presenting unusual features.

**Case 1, Percy M., aged 51 (III, 20, Pedigree Chart I),** the proband. Vision is hand movements in each eye and the trouble dates back to about the age of 40 when vision failed rapidly in a few years. He holds that he can see better in the dark than in daylight, and states that his colour vision has always been poor. In both fundi (Fig. 1, overleaf) the background is normal, except for a mottled pigmentary reaction in the central areas.

**Case 2, Mrs. Emma M., aged 83 (II, 9),** mother of Case 1. Her vision is 4/60 in each eye. This lady was a rather hostile witness; she knew that there was eye trouble in the family and seemed anxious to ascribe it to her husband's side rather than to her own. She failed completely on the Ishihara test, but was remarkably good in naming colours. Her fundi (Fig. 2, overleaf), like those of her son, show a macular lesion of the mottled type.

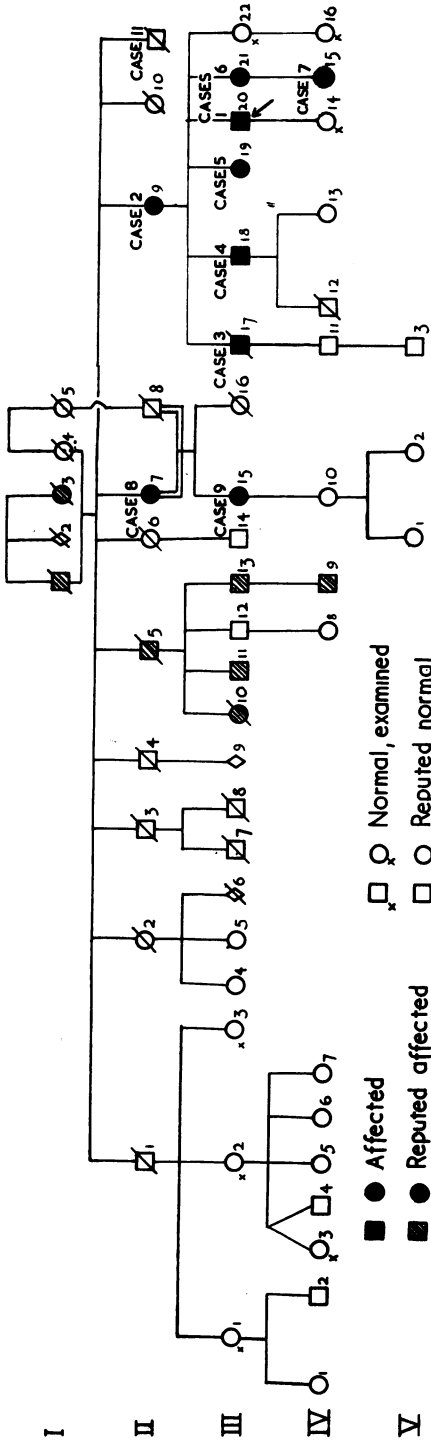
**Case 3, William M., died at the age of 59 in 1949 (III, 17),** brother of Case 1. Apart from the history obtained from the family, a B.D.8 blind certificate form was traced and showed that he was certified as blind from "macular choroiditis" in 1949 at the age of 54. The onset of the blindness was given as occurring at age 48 in the right eye, and at age 51 in the left.

**Case 4, Charles M., aged 56 (III, 18),** brother of Case 1. This man has myopia of 15 D in the right eye and 5 D in the left eye. He states that with correction his sight was good until about the age of 35 when he noticed that his colour vision was defective and that his sight began to fail. His vision is now perception of light in the right eye and 3/36 in the left. A dark-adaptation curve shows reduction of both cone and rod sensitivity. Both maculae show disturbances of the same type as seen in Case 1.

**Case 5, Mrs. Lilian W., aged 53 (III, 19),** sister of Case 1, gave a history of eye trouble beginning at the age of about 40. Vision was 6/60 in each eye; she failed entirely on the Ishihara test, and her fundi showed a loss of macular sheen. It was difficult to interpret the findings as she was undoubtedly an abnormal personality, and

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PEDIGREE CHART I.—The M. family.

the fundus lesion was minimal. Her history was, however, consistent with what is known of the rest of the family.

**Case 6, Mrs. E. B., aged 49 (III, 21),** a younger sister of Case 1. Vision was hand movements in each eye, with total colour defect on the Ishihara test; the patient had always been conscious of having defective colour vision. Her fundi (Fig. 3, opposite) are similar to those of the other affected members of her family.

**Case 7, Mrs. R. H., aged 24 (IV, 15),** daughter of Case 6. Vision is 6/12 in the right eye with correction (−2 D sph., −2 D cyl. at 150°) and 6/6 without glasses in the left. The patient is not conscious of any difficulty, but the Ishihara test showed green deficiency, and the fundi (Fig. 4, opposite) showed a lesion similar to that of her mother, perhaps not so well defined.

In addition to these seven cases, two further cases of defective vision were found in a collateral branch:

**Case 8, Mrs. Mary S., aged 86 (II, 7),** a sister of Case 2 (II, 9), the affected mother of the proband. Both fundi showed a central lesion considerably more marked than that seen in other members of the family. Fig. 5 (overleaf) shows the right fundus; the left eye is very similar. Vision was 1/60 in each eye (emmetropia), and her sight had been failing for over 20 years. Her father was reputed to have had similar trouble.

**Case 9, Mrs. Emily S., aged 61 (III, 15),** a daughter of Case 8, had a heavy central lesion (Fig. 6, overleaf). Vision was 3/60 in each eye with correction (−8 D sph.); her sight was reported to have failed fairly rapidly from the age of 33 years. She was unable to read any of the Ishihara plates.

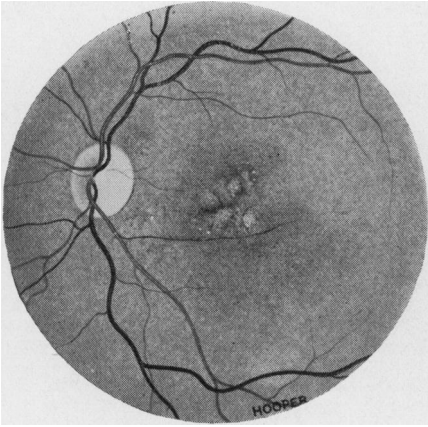


FIG. 1.

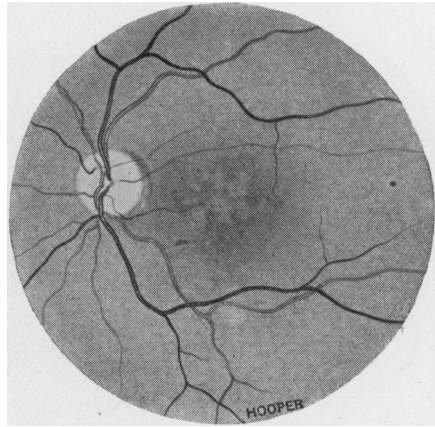


FIG. 2.

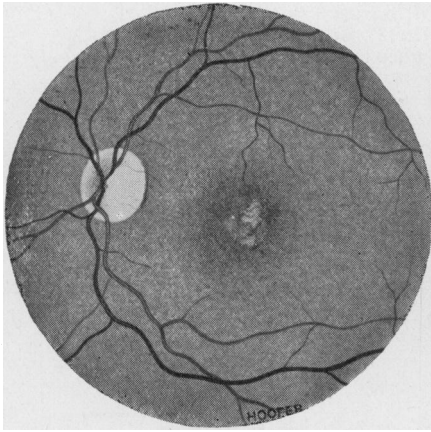


FIG. 3.

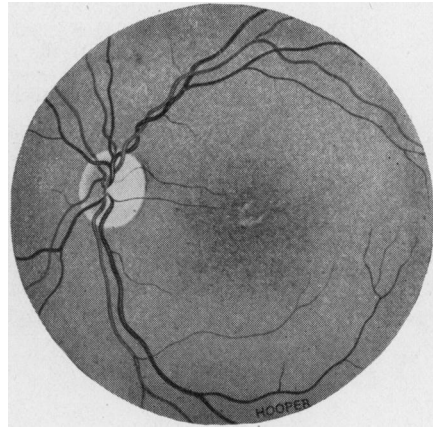


FIG. 4.

FIGS 1-4.—Macular lesions in the M. family (Pedigree Chart I), showing a man [Fig. 1, Percy M., aged 51 (III, 20), Case 1, proband], his mother [Fig. 2, Mrs. E. M., aged 83 (II, 9), Case 2], his sister [Fig. 3, Mrs. E. B., aged 49 (III, 21), Case 6], and his sister's daughter [Fig. 4, Mrs. R. H., aged 24 (IV, 15), Case 7].

Note the essential similarity of the reaction over three generations. The illustrations show the left eye; the right eye was similar in all cases. Vision is grossly affected in all except the grand-daughter, aged 24. All these patients show gross colour defects.

This family therefore shows clear evidence of the dominant transmission of a macular lesion over three generations. Excluding Cases 8 and 9, the lesion at the macula is similar to that seen in recessive macular dystrophy and could not be distinguished from it ophthalmoscopically. In the youngest member of this family the affection was silent, and the only subjective disturbance was the colour defect. The second generation in this group appeared to become conscious of failing vision at about the age of 40, but they had apparently all experienced difficulty with colour either in

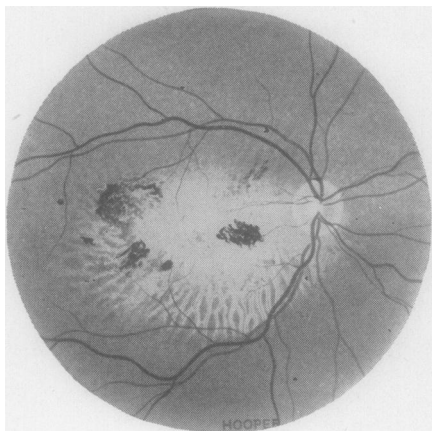


FIG. 5.

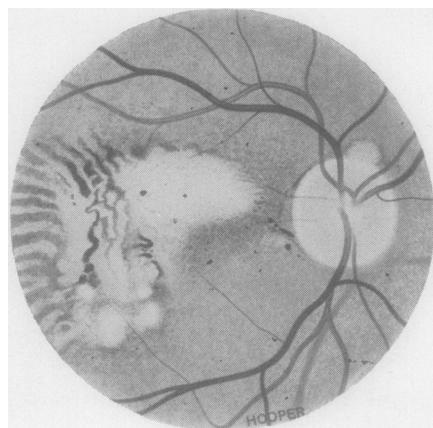


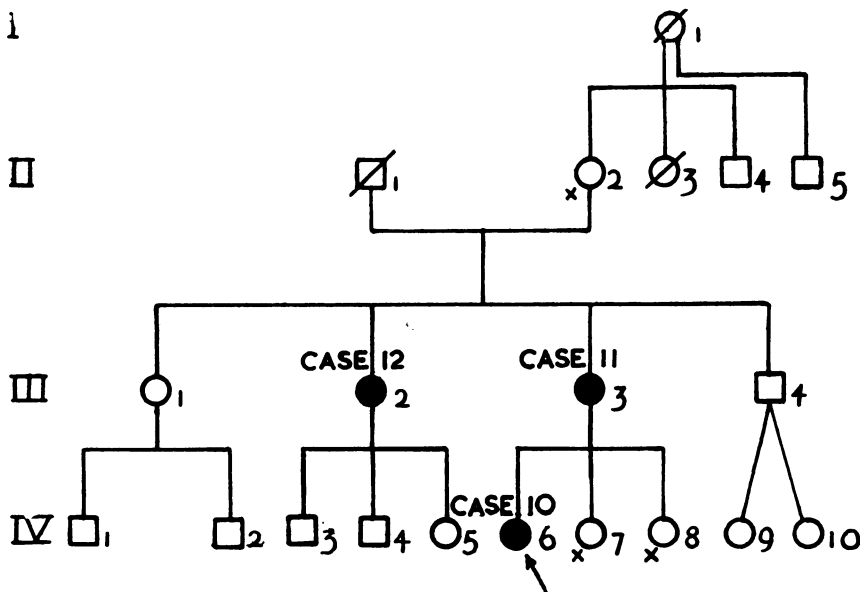
FIG. 6.

FIGS 5 and 6.—Macular lesions in a collateral branch of the M. family (Pedigree Chart I), showing a mother [Fig. 5, Mrs. M. S., aged 86 (II, 7), Case 8], and her daughter [Fig. 6, Mrs. E. S., aged 61 (III, 15), Case 9]. The mother here is a sister of II, 9 (Case 2, Fig. 2), the grandmother in the previous group.

The macular lesions are much more extensive and their interpretation is uncertain. The right eye is shown; the left eye was similar in each case.

childhood, or before the onset of the central visual disturbance. In the collateral branch the central lesion is so severe that one hesitates to regard it as a variant of macular dystrophy, but it is equally unsatisfactory to regard it as an entirely independent affection.

II. S. FAMILY (Pedigree Chart II).—In this family there are three affected members; the proband is a child aged 10. No consanguineous marriages.



PEDIGREE CHART II.—The S. family.

**Case 10, Carol S. aged 10 (IV, 6),** the proband, had vision 6/60 in each eye, not improved by glasses. Defective vision had been noted about 2 years previously in the course of a routine school examination. The dark-adaptation curves showed reduced sensitivity for both cones and rods. An anomaloscope test showed red deficiency; she was unable to read any of the Ishihara plates. The fundi (Fig. 7) show macular lesions indistinguishable from recessive macular dystrophy.

**Case 11, Mrs. Eva S., aged 36 (III, 3),** mother of Case 10, first noted trouble at about the age of 20. She does not regard herself as handicapped and is learning to drive a car. She is emmetropic and her vision is 6/18 in the right eye and 6/12 in the left eye. She knows that she is not particularly good at colours. An anomaloscope test showed red deficiency and she failed on all the Ishihara plates. The dark-

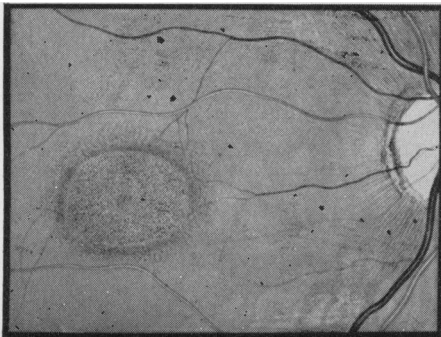


FIG. 7

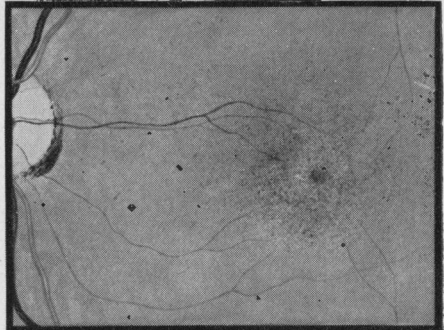
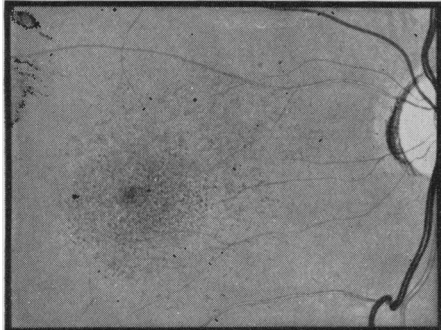


FIG. 8

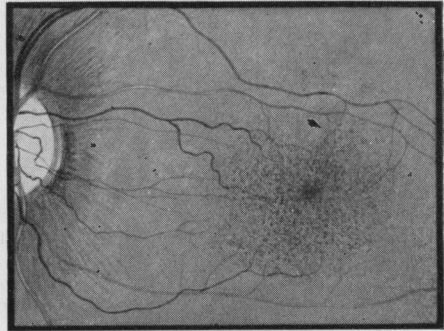
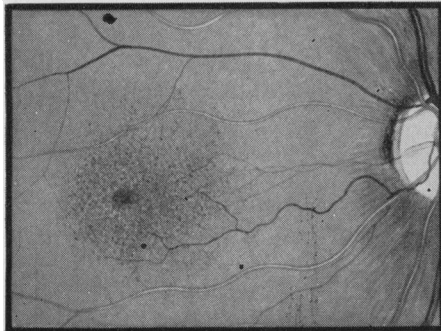


FIG. 9

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FIGS 7, 8, and 9.—Macular lesions in the S. family (Pedigree Chart II), showing a girl [Fig. 7, Carol S., aged 10 (IV, 6), Case 10, proband], her mother [Fig. 8, Mrs. E. S., aged 36 (III, 3), Case 11], and her maternal aunt [Fig. 9, Mrs. D. L., aged 39 (III, 2), Case 12].

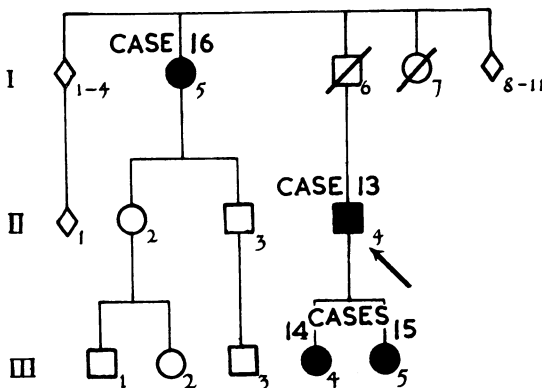
adaptation curve showed deficiency for both cones and rods. Her fundi (Fig. 8) show macular lesions similar to those of her daughter, though not so well marked.

**Case 12, Mrs. Doris L., aged 39 (III, 2),** and elder sister of Case 11. This patient is conscious of some trouble, but like her sister does not regard herself as seriously affected. She first became aware of some disturbance at about the age of 20. At school her eyes were passed as normal, but by the age of 30 she was known to have a fundus lesion. The anomaloscope showed green deficiency and her performance on the Ishihara test showed her to be green defective. Her dark-adaptation curve showed the same slight deficiency as that seen in her sister. Her fundi (Fig. 9) show a macular lesion similar to her sister's. Vision is 6/18 in the right eye, and 6/60 in the left.

In this family two sisters in the late thirties therefore show macular lesions which have been present for some years, possibly some 15 years or more, without reducing central visual acuity substantially, except in the left eye of the elder sister. Subjectively the one disturbance of which they are conscious and which could be demonstrated was a colour anomaly. The affected daughter of the younger sister shows, in contrast, not only the macular lesion and the colour anomaly, but substantial loss of visual acuity.

**III. H. FAMILY (Pedigree Chart III).**—In this family there are four affected members in three generations.

**Case 13, Albert H., aged 40, (II, 4),** the proband. When first seen the vision in the right eye was 6/18, in the left 6/12, not improved by glasses. He had been conscious of difficulty for the last 2 or 3 years. He had never experienced any nightblindness; the dark-adaptation curve showed a restricted cone component. Ophthalmoscopically there was a mottled reaction at the macula in each eye (Fig. 10, opposite). On the Ishihara test performance was poor, inaccurate responses being given to all plates except 2, 3, 7, and 15; the anomaly was therefore rather more than a red-green defect. The visual fields were full, but there was a central scotoma in each eye to white 1/2,000.



PEDIGREE CHART III.—The H. family.

Two years later central vision had declined to 6/36 each eye.

**Case 14, Shena H., aged 13 (III, 4),** a daughter of Case 13. When first seen the vision in the right eye was 6/6, and in the left 6/9, but the maculae were not above suspicion. The periphery of the fundus was rather albinotic. The visual fields, too, were full and no central scotoma could be detected. The dark-adaptation curve showed a normal cone component. She was not conscious of any difficulty, but on the Amsler chart (No. 4) there was a band of "scintillation" from the fixation point in each eye. On the Ishihara test her performance was almost identical with that of her father (Case 13), except that she failed on Plates 2 and 3 in addition.

She subsequently developed partial optic atrophy in consequence of a rapidly growing brain tumour which was later operated on successfully.

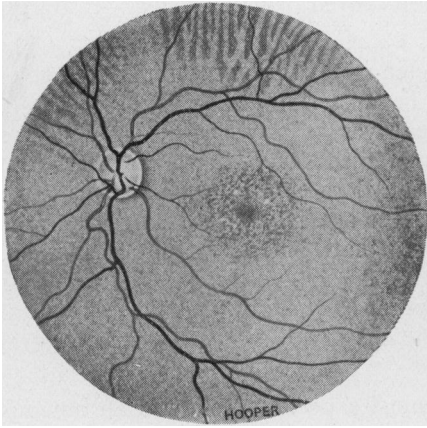


FIG. 10.

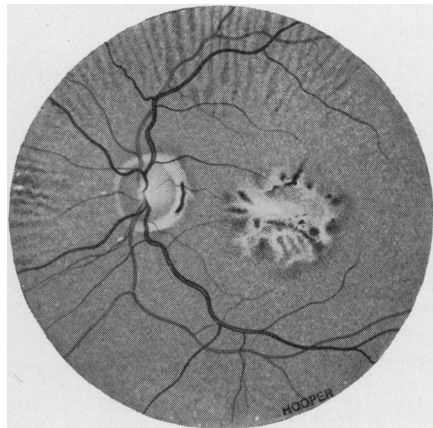


FIG. 11.

FIGS 10 and 11.—Macular lesions in the H. family (Pedigree Chart III), showing a man [Fig. 10, Albert H., aged 40 (II, 4), Case 13, proband], and his paternal aunt [Fig. 11, Mrs. R. S., aged 73 (I, 5), Case 16].

Cases 14 and 15, the two young daughters of II, 4 (Fig. 10), show macular mottling that is not above suspicion, and also gross colour anomalies with retained central vision.

**Case 15, Julie H., aged 10, (III, 5),** a younger sister of Case 14. Her vision was full; like her sister she was not conscious of any symptoms. Ophthalmoscopically the maculae were not above suspicion, and her performance on the Ishihara test was poor, almost identical with her father's.

**Case 16, Mrs. Rose S., aged 73, (I, 5),** a maternal aunt of the proband, Case 13. This patient was reputed to be affected and was found to have a gross central lesion in each eye (Fig. 11). Trouble first began at about the age of 40. Vision is now 6/60. Fuller information could not be obtained.

This family, which was difficult to follow up, does not appear to have had any other affected members. The proband's father, who died at the age of 43 from tuberculosis, was reputed to have had good sight. In this group four points of importance emerge:

- (1) The earliest subjective feature is defective colour vision.
- (2) The earliest objective feature is an indefinite macular lesion.
- (3) With failing vision there is evidence of cone disturbance.
- (4) The lesion is presumably progressive to something more than the usual mottling of the macula; the appearances in I, 5 recall the appearances in the collateral branch of the first family.

### Discussion

**(1) Dominant Macular Dystrophy as a Clinical Entity.**—These three families have these features in common:

- (i) A strictly localized central lesion, symmetrical in situation and extent in the two eyes.

(ii) An associated deficiency in colour vision—a red or green defect—is always present.

(iii) In the first family only one of the affected members is now under the age of 50. The history suggests that central vision began to fail at about the age of 40, but anomalies in colour vision were present very much earlier. In the one member under the age of 50—a young woman aged 24—the macular lesion and the colour anomaly are both present, without any loss of central visual acuity. In the second family two sisters both now under the age of 40 show macular lesions and the colour anomaly; and there is evidence that their central sight is failing, though so far only one eye has declined to 6/60. In the third family a colour anomaly appears again as the pointing symptom in childhood; failure of central vision does not apparently set in till about the age of 40; a gross atrophic central defect is apparently once again the end-stage.

(iv) In dark-adaptation tests no family against expectation showed an obvious cone deficiency as an early sign.

On the basis of these findings the suggestion emerges that dominant macular dystrophy is an affection in which the lesion is present ophthalmoscopically at some as yet undetermined age under 40—possibly many years before—and that colour anomalies are present simultaneously, or precede the onset of the ophthalmoscopic lesion. There is nothing to suggest that disturbance in the cone vision is an early diagnostic criterion.

Two features that do not fit in with these findings are:

(i) The severe central lesions observed in the two members of the collateral branch in the first family (Cases 8 and 9; II, 7, and III, 15), and in one member in the third family (Case 16; I, 5). Apparently in some cases the end-stage is not mere mottling but a distinct atrophic reaction.

(ii) The substantial defect in central visual acuity in the child in the second family (Case 10; IV, 6). Studied in isolation this child would justifiably be diagnosed as a case of recessive macular dystrophy (Stargardt's disease), even though the age at onset is rather below that commonly seen. Whether the lack of any history of fairly sudden loss of vision—as is seen in recessive macular dystrophy—and whether the rather early age at onset in this child are significant features in the differential diagnosis is uncertain. What is significant is that, if it be accepted that dominant macular dystrophy has a later onset and runs a milder course than recessive macular dystrophy, it must also be accepted that exceptions as to onset and severity do occur.

**(2) Differential Diagnosis from Total Colour Blindness.**—Dominant macular dystrophy needs to be distinguished from congenital total colour blindness (day blindness). Here the marked photophobia, the congenital nature of the affection, the frequently present nystagmus, the macular lesion (not always readily seen ophthalmoscopically because of the photophobia and nystagmus), and the extensive colour anomaly constitute an unmistakable picture. Dominant macular dystrophy has many of these features in a mild form, but there is nothing to suggest that there is any clinical, pathological, or genetic relationship between the two affections—if only because in con-



genital total colour blindness the cones are at fault and the mode of inheritance is recessive.

**(3) Differential Diagnosis from Other dominantly Inherited Macular Lesions.**

—The literature does not help much in establishing a clear clinical picture. There are a number of family records in which a macular lesion appears to have been inherited in a dominant manner. The earlier literature is reviewed elsewhere (Sorsby, 1940), and there are only a few further records (Damel, 1948; Dollfus, 1948; Falls, 1949). It is obvious that these records do not concern a well-defined entity, but cover several different groups such as:

(i) Best's disease (probably a congenital affection) in cases observed in a German family by Best (1905) and subsequently by Vossius (1921), Weisel (1922), and Jung (1937). Falls (1949) observed a similar lesion in an American family.

(ii) A widespread fundus lesion beginning as a macular lesion. Three such families are on record, and they all show that an initially macular lesion was merely the starting point (Tiscornia, 1926, and Damel, 1948; Sorsby, 1940, and Sorsby and Mason, 1949; Sorsby, 1940, and Sorsby and Davey, 1955). It is of interest that one of the sibships recorded by Stargardt (1917) as a recessive macular dystrophy [also showing outlying fundus reactions] proved at a follow-up in 1953 to consist of cases of a fairly widespread reaction [probably choroidal sclerosis] (Rosehr, 1954).

(iii) A true macular dystrophy—*i.e.* a strictly localized central lesion without peripheral spread. The cases of Morelli (1924), Halbertsma (1928), Berkley and Bussy (1949), and some reported by Behr (1950), and possibly others (such as Clausen, 1921) probably belonged to this group. Colour anomalies were recorded by Behr (1920) in some members of his M. family; Halbertsma (1928) stressed colour anomalies, but it is difficult to be sure of their association with a macular lesion. (Central scotomata for colour were of course frequently noted in all forms of macular lesions).

**(4) Outstanding Issues.**—It would seem that in future studies of dominantly inherited macular lesions special attention requires to be paid to three aspects:

(i) The limitation of the lesion to the central area without extension peripherally with increasing age;

(ii) The ophthalmoscopic appearances of such lesions; presumably they generally show as mottling, but occasionally extensive central atrophic scarring may be present;

(iii) The presence of colour anomalies—as distinct from central scotomata for colours—as a possible pointing feature of pathognomonic significance.

### Summary

Macular lesions, ophthalmoscopically similar to those seen in recessive macular dystrophy of the Stargardt type with its sharp localization, are recorded as presumably dominantly inherited.

In the first family the lesion was observed over three generations. The ophthalmoscopic appearances in the grandmother at the age of 83, and in

the grand-daughter at the age of 24 were fairly similar. Disturbances in colour vision were common to both these patients and apparently to other affected members of the family, but the degree of disturbance in visual acuity varied considerably; in the youngest member vision was still full. In a collateral branch of the family markedly more severe central lesions were observed in a mother and daughter.

In the second family an essentially similar lesion was observed ophthalmoscopically in two sisters and in a daughter of one of them. Here, too, colour anomalies were common to the three affected persons, and it was only in the child that central visual acuity was grossly disturbed.

In the third family a central mottled reaction was present in a man aged 40 when central sight was beginning to fail, and in his two daughters, aged 13 and 10 years, who showed full vision with mildly mottled maculae; all three showed gross colour anomalies. As in the first family, a severe central lesion was present in a member of a collateral branch.

The findings in these three families suggest that dominant macular dystrophy does not differ ophthalmoscopically from recessive macular dystrophy of the Stargardt type. The differences lie in the mode of inheritance and the mode of onset. As against the fairly sudden onset and rapid course of recessive macular dystrophy, the dominant variety of the affection has no sudden onset and may apparently be silent, or relatively so, over many years; in most cases it probably becomes subjectively manifest at about the age of 40 by decline in central visual acuity, though anomalies in colour vision are apparently present very much earlier. The dominant type appears to run a slower and milder course than the recessive type, and only exceptionally do severe disturbances occur early in life; it is apparently also exceptional that the macular lesion takes the form of a marked central scar. Whether anomalies in colour vision are a pointing symptom of pathognomonic significance still remains to be determined.

Differentiation from congenital total colour blindness presents no difficulties, though many of the features of dominant macular dystrophy are mild variants of some of the essential symptoms of day blindness. The differential diagnosis from a dominantly inherited fundus affection beginning as a central lesion is indicated.

Our thanks are due to Mr. S. H. G. Humfrey of Northampton for the great help he has given us in the study of the first (M.) family, who are under his care; we are also indebted to his associates, Mrs. N. M. Oughton and Mr. R. C. Jack, for their collaboration, and to Dr. Ruby Joseph for her help in investigating this family. We are obliged to Mr. Frank Law for kindly putting the second (S.) family at our disposal, and to Mr. D. W. A. Mitchell of the London Refraction Hospital for a similar service with the third (H.) family.

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## APPENDIX

## (1) The M. family

The following information additional to that shown in Pedigree Chart I is available:

*Generation I*

1. James H., died aged 57, reputed affected.
3. Mrs. B., a sister, reputed affected.
4. Wife of I, 1, reputed normal.
5. Sister of I, 4, reputed normal.

*Generation II*

1. Charles H., died aged 85, reputed normal.
2. Elizabeth H., (married name not known), reputed normal.
3. George H., reputed normal.
4. Thomas H., reputed normal.
5. Bill H., died aged 60, reputed affected.
6. Hannah H., reputed normal.
7. Mrs. Mary S., aged 85, affected, Case 8 in text (Fig.5).
8. Mr. S., husband of II, 7, and son of I, 5, dead, reputed normal.
9. Mrs. Emma M., aged 83, affected, Case 2 in text (Fig. 2).
10. Alice H., died young, reputed normal.
11. Mr. M., died aged 60, reputed normal.

*Generation III*

(1-3) Children of a man reputed normal (II, 1):

- |                              |  |
|------------------------------|--|
| 1. Mrs. Florence H., aged 74 | } All examined and found normal. Colour vision normal. |
| 2. Mrs. Nellie P. aged 68    |  |
| 3. Mrs. Lilian H., aged 61   |  |

(4-6) Children of a woman reputed normal (II, 2):

- |                   |                   |
|-------------------|-------------------|
| 4. Mrs. Lilian R. | } Reputed normal. |
| 5. Mrs. Edith F.  |                   |

(10-13) Children of a man reputed affected (II, 5):

10. Ada H., died aged 50, reputed affected.
11. James H., reputed affected.
12. Horace H., reputed normal.
13. George H.; some of the relatives thought this man had poor sight, they were more sure that his son's sight was bad.

(15-16) Children of an affected woman (II, 7):

15. Mrs. Emily S., aged 60, affected, Case 9 in text (Fig. 6).
16. Lilian S., died aged 2, reputed normal.

*(17-22) Children of an affected woman (II, 9):*

17. William James M., died aged 59, affected, Case 3 in text.
18. Charles M., aged 56, affected, Case 4 in text.
19. Mrs. W., aged 53, affected, Case 5 in text.
20. Percy M., aged 51, affected, Case 1 in text (Fig. 1).
21. Mrs. E., aged 49, affected, Case 6 in text (Fig. 3).
22. Woman, seen by Mr. Howard Reed and found to be normal but myopic.

*Generation IV**(1-2) Children of a normal woman (III, 1):*

1. Ethel H., reputed to have poor sight.

*(3-7) The children of a normal woman (III, 2):*

3. Lilian P., aged 42, normal. Vision in the right eye 6/60; in the left perception of light (myopia). This woman had cataract but normal fundi. Colour vision normal (Ishihara).
9. Son of III, 13, a man reputed to have a poor sight, was also reputed to have a poor sight himself.
10. Mrs. Emma M., aged 28, daughter of III, 15, an affected woman.
14. Doreen M., aged 17, daughter of III, 20, an affected woman. Refraction +2.25 D sph., 6/6 each eye. Colour vision normal (Ishihara).
15. Mrs. Rosemary H., aged 24, daughter of III, 21, an affected woman, is herself affected Case 7 in text (Fig. 4).

**(2) The S. family**

The following information additional to that shown in Pedigree Chart II is available:

*Generation I*

1. Mrs. N., later Mrs. B., mother of II, 1-5, nothing known about her sight.

*Generation II*

1. Walter H., died aged 57, husband of II, 2, and father of III, 1-4, nothing known about his sight.

*(2-4) Children of I, 1, by her first marriage:*

2. Elsie H., aged 64, refraction +3 D sph., 6/6 both eyes. Colour vision normal (Ishihara and anomaloscope).
3. Ethel H., died aged 60.
4. Frederick N., reputed normal.
5. Edwin B., son of I, 1, by her second marriage.

*Generation III**(1-4) Children of a normal woman (II, 2):*

1. Mrs. Violet D., aged 40.
2. Mrs. Doris L., aged 39, affected, Case 12 in text (Fig. 9).
3. Mrs. Eve S., aged 36, affected, Case 11 in text (Fig. 8).
4. Walter H., aged 30.

*Generation IV**(1-2) Children of a woman reputed normal (III, 1):*

1. Peter, aged 14.
2. Ian D., aged 9.

*(3-5) Children of an affected woman (III, 2):*

3. Michael L., aged 11.
4. Glyn L., aged 9.
5. Vanessa L., aged 1.

*(6-8) Children of an affected woman (III, 3):*

6. Carol S., aged 10, affected, Case 10 in text, proband (Fig. 7).
7. Margaret S., aged 7.
8. Theresa S., aged 6.

*(9-10) Twin daughters of a man reputed normal (III, 4):*

9. Patricia H., nothing known.
10. Christine H., was said to have a convergent squint and to wear spectacles. Nothing more known.

**(3) The H. family**

The following information additional to that shown in Pedigree Chart III is available:

*Generation I*

5. Mrs. Rose S., aged 73, affected, Case 16 in text (Fig. 11).
7. Miss Gertie H., "died of brain tumour".

*Generation II**(2-3) Children of an affected woman (I, 5):*

2. Vera . . . . . aged 52.
3. Ken S., aged 25.
4. Albert H, aged 40 son of a man reputed normal (I, 6), affected, Case 13 in text, proband (Fig. 10).

*Generation III**(1-2) Children of a woman reputed normal (II, 2):*

1. Stephen . . . . . aged 7.
2. Pauline . . . . . aged 5.
3. Peter S., aged 3, son of a man reputed normal (II, 3).

*(4-5) Children of an affected man (II, 4):*

4. Shena H., aged 13, affected, Case 14 in text.
5. Julie H., aged 10, affected, Case 15 in text.