COMMUNICATIONS

GENERALIZED CHOROIDAL SCLEROSIS*

COURSE AND MODE OF INHERITANCE

BY

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At least two forms of choroidal sclerosis can be distinguished—the sharply circumscribed central areolar type, which has been discussed elsewhere (Sorsby, 1939; Sorsby and Crick, 1953), and generalized choroidal sclerosis, the subject of the present study.

The late stages of generalized choroidal sclerosis are unmistakable, for not only are the choroidal vessels throughout the fundus exposed, but they are converted into white streaks—a change perhaps more marked in some parts of the fundus than in others. A subsidiary feature, not always present, is the occurrence of pigmentation, generally at the extreme periphery and sometimes of the bone corpuscle type, but the appearance of the disc and the relatively healthy state of the retinal vessels—never showing the marked attenuation seen in correspondingly advanced retinitis pigmentosa—readily distinguish the condition from the retinitis pigmentosa group.

Elsewhere (Sorsby, 1939) the hereditary basis of generalized choroidal sclerosis has been recorded. The mode of inheritance is still undetermined, though dominance would appear likely from some family records of “atypical retinitis pigmentosa”, suggestive of choroidal sclerosis rather than retinitis pigmentosa. The present study is of interest for three reasons:

(1) it gives support to the view that the condition is inherited in a dominant manner;

(2) it brings out the earlier stages of the affection when the appearances are not at all pathognomonic;

(3) it records the terminal stages that merge on to the appearances of choroid-eremia.

PEDIGREE CHART I.—Cl. Family.

Case Records

I. Cl. Family.—Four affected members were observed in two generations (Pedigree Chart I). In the first generation there were five survivors of an initial sibship of

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seven, and three of these survivors were affected. They are all elderly. Their parents are reputed to have had good sight and were not consanguineous.

Case 1, Mrs. G. C., aged 71 (I, 2 in Pedigree Chart I), the proband. This patient, who is registered as blind, first noted trouble at the age of about 55. There is no history of nightblindness, and for the past 16 years vision has declined progressively to its present state of counting fingers in each eye. The right fundus is shown in Fig. 1; the left fundus is very similar. There is extensive choroidal sclerosis centrally and around the disc, with considerable extension of the same process towards the periphery. The larger choroidal vessels peripherally are, however, still not converted into white streaks. There is a peculiar generalized darkening of the whole of the fundus background. The tension rose on instilling a mydriatic and both discs showed glaucomatous optic atrophy. There is some mild narrowing of the retinal vessels. The patient was seen by Dr. M. Klein in 1950 when the condition appeared to be not very much milder than now. The glaucoma obviously contributed substantially to the decline in vision.

Figs 1-4.—Generalized choroidal sclerosis. Range of appearances in a woman aged 71 (Fig. 1), her elder sister (Fig. 2), a younger sister (Fig. 3), and the proband's daughter (Fig. 4)—all members of the family shown in Pedigree Chart I.

FIG. 1.—Case 1, proband, Mrs. G. C., aged 71 (I, 2). Right fundus, showing extensive choroidal sclerosis centrally and around the disc, with considerable extension of same process towards periphery. The larger vessels peripherally are, however, still not converted into white streaks. There is a peculiar generalized darkening of the whole of the fundus background. The disc shows an incidental glaucomatous optic atrophy. There is also some mild narrowing of the retinal vessels. The left fundus was essentially similar.

Case 2, Mrs. A. W., aged 78, an elder sister of Case 1 (I, 1). The patient would admit only minor visual disturbances, but her vision is 6/36 in the right eye, and 6/60 in the left, not improved. When seen by Dr. Klein in 1950 the vision was 6/9 in the right eye, and 6/12 in the left. The maculae then showed gross pigmentation. The present appearances are seen in Fig. 2 (opposite); apart from the pigmented paramacular reaction, there is considerable exposure of the choroidal vessels without any conversion into white streaks. There is also incipient generalized darkening of the fundus background. Colour vision was normal to the Ishihara test.

FIG. 2.—Case 2, Mrs. A. W., aged 78, elder sister of Case 1 (I, 1). Right fundus, showing, apart from a pigmented paramacular reaction, considerable exposure of choroidal vessels without any conversion into white streaks. There is also incipient generalized darkening of the fundus background. The left fundus is essentially similar.

Case 3, Mrs. G. T., aged 67, a younger sister of Case 1 (I, 5). This patient, too, would not admit any obvious ocular disability. Vision was in 6/60 the right eye, and 6/9 in the left, not improved. Fig. 3 (overleaf) shows the present appearances of the fundi. In the right eye (Fig. 3a) there is exposure of the choroidal vessels centrally, and some pigment stippling as well as some more massive pigment proliferation in the overlying retina. The left eye (Fig. 3b) shows ill-defined mottling in the central area with an exudative reaction, also ill-defined. When the patient was seen by Dr. Klein in 1950, the vision and fundus appearances were essentially similar. There is no history of nightblindness and colour vision is normal to the Ishihara test. There are fine corneal nebulae in each eye, probably the remains of an old phlyctenular keratitis.

Case 4, Mrs. D. W., aged 53, daughter of Case 1 (II, 2). Her vision was 6/12 in the right eye and 6/9 in the left. The fundus appearances are shown in Fig. 4 (overleaf). Both central areas are oedematous, and there is paramacular atrophy in the right eye (Fig. 4a). The lesion in the left eye (Fig. 4b) is less definite. There is as yet nothing to suggest choroidal sclerosis in either eye. In 1950 Dr. Klein found vision of 6/9 in each eye, and very much the same fundus appearances as now.

In this family, serious visual trouble does not seem to set in till late in life. Only one of the three sisters, all of whom are over 65 years, is severely handicapped. The late onset and the non-pathognomonic aspect of the early stages of the affection are brought out by the one affected patient in the younger generation (II, 2). On the basis of this group the following sequence of events seems likely:

- (1) A non-pathognomonic central oedematous-haemorrhagic lesion setting in at about the age of 50;
- (2) subsequent mottling of the central area with exposure of the choroidal vessels centrally;
- (3) later accentuation of these features with exposure of the choroidal vessels all over the fundus;
- (4) later still deepening into definite sclerosis centrally; presumably this sclerosis spreads towards the periphery.

FIG. 3.—Case 3, Mrs. G T., aged 67, younger sister of Case 1 (1, 5).

(a) Right eye: exposure of choroidal vessels centrally, and some pigment stippling as well as some massive pigment proliferation in overlying retina.

(b) Left eye: ill-defined mottling in central area with an exudative reaction also ill-defined.

FIG. 4.—Case 4, Mrs. D. W., aged 53, daughter of Case 1 (II, 2).

(a) Right eye: oedema in central area with patch of paramacular atrophy.

(b) Left eye: oedema and mottling in central area with patch of incipient atrophy.

PEDIGREE CHART II.—C—e Family.

II. C—e Family.—Some members of this family (Pedigree Chart II) were previously reported (Sorsby, 1940) as one of a group of families illustrative of macular dystrophy of types other than Stargardt's disease. The salient features then recorded in this family were:

(i) The occurrence of an extensive central lesion in the two eyes of two sisters aged 43 and 39 years. The ophthalmoscopic reactions were too diffuse to fit into the known picture of Stargardt's disease, and the genetic character of the disturbance was proved by disclosing other affected members in this family.

(ii) A similar but less developed reaction in a younger brother aged 34.

(iii) Extensive macular mottling—regarded as pathological in spite of retained central vision—in a boy aged 8 and his sister aged 5, the children of the youngest sister of the affected sibship, this sister being herself normal.

When this family was followed up again in 1950 the following developments were noted:—

(i) The unaffected sister, now aged 51, had begun to develop minor disturbances shortly after the original examination in 1933. She now showed central lesions similar to those previously shown by her sisters, and considerably more marked than those shown by her children.

(ii) Of the affected sisters, the younger now showed obvious sclerosis of the choroidal vessels in the central area.

(iii) The affected brother now showed a picture which was strongly reminiscent of retinitis pigmentosa rather than of the reactions hitherto observed in the family.

(iv) The two children—now young adults—showed obvious macular lesions with central vision still intact.

(v) Four further cases showing relatively early lesions were found.

In this family there was therefore a wide range of appearances: mottling at the macula, similar to that seen in Stargardt's disease but beginning very much earlier and clinically silent; a gross central reaction; central choroidal sclerosis; and a picture reminiscent of retinitis pigmentosa.

There were no consanguineous marriages. The personal details of these ten cases (with ages as recorded in 1950) were as follows:

Case 5, Mrs. S. E., aged 62 (II, 2). Trouble began at about the age of 47 and increased in severity, until she could not see to read, though she could get about without difficulty. Her chief complaint is that she has to look sideways to see objects. She is not conscious of being nightblind. The fundi show heavy mottling centrally with some exposure of the underlying choroidal vessels, more marked in the left. The choroidal pattern is also seen towards the periphery and there is some pigment disturbance (Fig. 5).

Figs 5-12. Generalized choroidal sclerosis. Range of appearances in collateral branches over two generations in the family shown in Pedigree Chart II.

FIG. 5.—Case 5, Mrs. Sarah E., aged 62 (II, 2). Heavy central mottling with some exposure of the underlying choroidal vessels; choroidal pattern is also exposed peripherally.

Case 6, Miss E. C—e, aged 60 (II, 6), a cousin of Case 5. This patient was first seen in 1933 at the age of 43, and is reported as Case 1 in the earlier study (Sorsby, 1940). Her vision has been defective since childhood and by the time she was about 25 she could no longer see to read. She was certifiably blind in 1933. There was a doubtful history of nightblindness earlier. The fundi showed heavy central mottling with exposure of the choroidal pattern throughout (Fig. 6, overleaf). By 1950 the sight had so deteriorated that she had difficulty in getting about and the fundi now showed considerable atrophy in the central area with exposure of the choroidal vessels (Fig. 6b) and pigmentation of the retinitis pigmentosa type towards the equator. Neither discs nor vessels suggested retinitis pigmentosa. When she was re-examined in 1954 at the age of 64, the bone corpuscle pigmentation had increased considerably at the periphery without very much change in the central area. The arteries were now attenuated.

Case 7, Miss H. C—e, aged 57 (II, 7), a sister of Case 6. When first seen in 1933 she was aged 39, and the history and subjective symptoms were similar to those of her sister, but the lesion was more advanced and more irregularly distributed. There was the same heavy mottling centrally and exposure of the choroidal vessels through-

out (Fig. 7*a*). When she was re-examined in 1950, both discs were atrophic and the retinal vessels distinctly narrow. The most striking change was the conversion of the central area into a mass of sclerosed choroidal vessels (Fig. 7*b*); 4 years later the central choroidal sclerosis carried heavy pigmentary reaction, and much bone corpuscle formation present towards the periphery.

FIG. 6 (*a, b*).—Case 6, appearances in a woman (II, 6), at the age of 43 years and 17 years later.

FIG. 7 (a, b).—Case 7, appearances in the sister (II, 7) of Case 6, at the age of 40 years and 17 years later.

Case 8, Edward C—e, aged 54 (II, 9), brother of Cases 6 and 7. When seen in 1937 at the age of 41 he was doing sighted work, though with difficulty, as his vision had been failing for some years. The fundi showed heavy central mottling, not so marked as in his sisters. When he was re-examined in 1950 at the age of 54, he showed exposure of the choroidal pattern both centrally and peripherally, with considerable bone corpuscle formation at the equator (Fig. 8, overleaf). Neither disc, nor retinal arteries, fitted into the diagnosis of retinitis pigmentosa, nor was there any definite history of nightblindness, though he was finding it more difficult to get

FIG. 8.—Case 8, Edward C., aged 54 (II, 9). Exposure of choroidal pattern centrally and peripherally with considerable bone corpuscle formation at equator; 4 years later central choroidal sclerosis more marked and retinitis pigmentosa reaction unchanged.

about at night than during the day; 4 years later the central choroidal sclerosis was more marked and the retinitis pigmentosa reaction unchanged.

Case 9, Mrs. Sarah C—n, aged 51 (II, 10), the youngest sister of Cases 6-8. When first seen at the age of 39 at the time of the original report (when her two sisters and her brother were known to be affected, and her two children were regarded as affected, though still possessed of good central vision), she was passed as normal. She gave at the time an indefinite history of some difficulty at night during the 1914-18 war, but regarded herself as a normally sighted person. Since then her sight has deteriorated, particularly in recent years, and she is now certifiably blind. Fig. 9 shows the fundus appearance in the right eye in 1950 at the age of 51; the left eye was

FIG. 9.—Case 9, Mrs. Sarah C—n, aged 51 (II, 10), mother of children affected early in life shown in Figs 11 and 12. She herself was normal at the age of 39 and possibly later. The fundi now show extensive central lesions of the atrophic-exudative type.

substantially similar. Both showed an extensive central lesion of the atrophic-exudative type; 4 years later the lesion had become more accentuated without any marked differences in appearance except for the presence of a small retinal haemorrhage near the disc in the right eye.

Case 10, Mrs. Muriel G., aged 30 (III, 4), a daughter of Case 5. The fundi show a picture not dissimilar to that originally seen in her mother's cousin (Fig. 6*a*). There is exposure of the choroidal vessels with scattering of pigment centrally.

Case 11, Edward R., aged 30 (III, 10), son of II, 4. His visual acuity was right 6/9, left 6/12. He served as a navigator in the R.A.F. from 1940 to 1946, and is not conscious of any trouble, but the fundi (Fig. 10) show evidence of a central disturbance. Towards the periphery there are some atrophic and pigmented patches.

FIG. 10.—Case 11, Edward R., aged 30 (III, 10). Central areas mottled, vision still almost full.

Case 12, Joseph C—e, aged 23 (III, 14), son of Case 8. This patient is not conscious of any trouble by day or night, and his visual acuity is 6/6, but the fundi show both localized exposure of the choroidal vessels centrally and considerable retinal reaction in the form of slight scattered pigment and more extensive white dot formation, being not dissimilar to the appearances seen in Case 13 (Fig. 11*a*).

Case 13, Bernard C—n, aged 30 (III, 16), son of Case 9, was first seen in 1933 at the age of 8, when a doubtful central lesion was present; 5 years later, though vision was still full, the existence of a central lesion was no longer in question (Fig. 11*a*, overleaf), 12 years later, at the age of 25, the vision was still unaffected, but the lesion had obviously progressed (Fig. 11*b*, overleaf). He is not conscious of any trouble by day or night.

Case 14, Betty C—n, aged 29 (III, 17), daughter of Case 9. At the age of 7, in 1933, she showed an ill-defined central lesion like her brother; 5 years later the lesion was better established (Fig. 12*a*, overleaf). In 1950, at the age of 24, there was considerable extension of the lesion (Fig. 12*b*, overleaf), though vision was still full and she was not conscious of any trouble by day or night. A dark-adaptation curve showed normal rod and cone reaction; 4 years later there was only a slight deterioration in the fundus appearance without any visual disturbances.

It is possible that II, 15 is yet a further case, for indefinite central lesions are shown by this man aged 45.

FIG. 11 (*a, b*).—Case 13, appearances in the nephew (III, 6) of Cases 6 and 7, at the age of 13 years and 12 years later.

FIG. 12 (*a, b*).—Case 14, Betty C-n, aged 24 (III, 17).

(*a*) Left fundus at the age of 12, a fainter macular lesion having been observed 5 years earlier.

(*b*) Same fundus 12 years later. Vision was and has remained normal.

Reconstructing these findings, the sequence of events is somewhat as follows:

- (1) Mottling in the central areas sometimes occurring in early childhood, but occasionally as late as the middle thirties.
- (2) An extensive central reaction suggestive of an inflammatory reaction, but showing marked symmetry as between the two eyes. At this stage—generally seen in the twenties and thirties—there is no obvious choroidal sclerosis.
- (3) This central reaction develops into a picture of choroidal sclerosis centrally with exposure of the choroidal pattern peripherally. Subsequently there is atrophy of the whole of the central area exposing the underlying sclerotic.
- (4) Bone corpuscle pigment reaction at the equator or towards the periphery was a feature in several cases and was particularly prominent in one case during the course of the disturbance, but it is clear from the subsequent course that this was merely part of a spreading generalized choroidal sclerosis.
- (5) Nightblindness is not a feature of the disturbance.

The course was more severe in the C-e family than in the Cl. family.

Discussion

(1) OPTHALMOSCOPIC COURSE.—Judging by these two families the earliest ophthalmoscopic signs of generalized choroidal sclerosis are non-pathognomonic central lesions—mottling or possibly oedema which goes on to the formation of an atrophic area with exposure of the choroidal vessels. Subsequently these vessels become converted into white streaks which extend towards the disc, so that the picture is now one of central and peripapillary choroidal sclerosis, flanked by an exposed choroidal pattern throughout. Further extension leads to the stage of generalized choroidal sclerosis. In some cases pigment reactions of the bone corpuscle type, generally at the equator, develop while the sclerosis is becoming generalized.

Case 15.—Bearing on the terminal stages of the affection, Fig. 13 (opposite), is relevant. Fig. 13 (a) represents generalized choroidal sclerosis and generalized darkening of the fundus background in a man at the age of 59; an account of the affection as seen in him and in his sister has been given elsewhere (Sorsby, 1939; Fig. 13a is Fig. 17 of the earlier publication). Fig. 13(b) shows the same fundus 16 years later at the age of 75. Where previously the choroidal vessels were merely exposed at the periphery, they are now converted into white streaks. The irregular pigmentation throughout the fundus has become rather more marked as has the narrowing of the retinal vessels. The most striking change, however, is the absorption of most of the choroidal vessels, which previously had already become converted into white streaks. There is now an extensive sector defect of choroidal atrophy. Presumably, if the patient were to live long enough, the whole of the choroid would become absorbed, giving a picture very similar to choroideremia, which is, of course, a totally different affection, both pathologically and genetically.

Reconstructing the course of generalized choroidal sclerosis on the basis of these three family groups, it would seem that non-pathognomonic macular oedema or mottling may be the starting point of a process that ends in almost total absorption of the choroid.

(2) SYMPTOMS.—It seems likely that the onset and course varies with different families. In the first family the affection began late and ran a mild

(a) Appearances at age 59. This illustration was published in 1939 when generalized choroidal sclerosis in this man and his sister was recorded.

There is generalized darkening of the fundus, exposure of the choroidal pattern throughout and choroidal sclerosis around the disc with pigment changes reminiscent of bone corpuscle formation. There is also some narrowing of the retinal vessels.

(b) Appearances at age 75. The choroidal vessels are now converted into white streaks throughout the fundus, with almost total atrophy down and out. The retinal vessels are narrower and the pigmentation no longer characteristic.

FIG. 13.—Case 15, Generalized choroidal sclerosis; appearances in a man at 59 years of age and 16 years later.

course; in the second there was considerable variation between different members of the family, some of whom were severely affected in their twenties. In both families there was little evidence that nightblindness was a feature of the condition.

(3) MODE OF INHERITANCE.—The occurrence of the affection over two

generations in the two families (in one of which a collateral branch was also affected), and the absence of consanguineous marriages, suggest dominant inheritance. The fact that all the affected members of the first family were women must be accepted as incidental in a family in which women predominated.

(4) DIFFERENTIAL DIAGNOSIS

(i) *From Dominant Macular Dystrophy*.—During the early stages the central fundus lesion simulates macular dystrophy. Only with the course of the affection—the appearance of sclerosed choroidal vessels—does the ophthalmoscopic picture become characteristic. Before then correct diagnosis is possible only by family—and not individual—diagnosis.

(ii) *From Retinitis Pigmentosa*.—Neither the early nor the late stages of choroidal sclerosis are likely to be mistaken for retinitis pigmentosa. Various intermediate stages—those showing exposed sclerosed vessels throughout the fundus especially when bone corpuscle pigment reaction is present—raise that possibility. Three features should help in differentiation:

(a) Generalized choroidal sclerosis will always show heavy central involvement—the central lesion being more marked than the peripheral disturbance—a sharp contrast to retinitis pigmentosa. It is further possible that a diffuse darkening of the fundus background is a fairly common aspect of the earlier stages of generalized choroidal sclerosis.

(b) The mode of inheritance is likely to be dominant in choroidal sclerosis against the commonly recessive inheritance of retinitis pigmentosa.

(c) Night blindness is absent.

(iii) *From Generalized Fundus Dystrophy*.—The early stages when there is a central oedematous-haemorrhagic reaction are probably indistinguishable from generalized fundus dystrophy recorded elsewhere (Sorsby and Mason, 1949). The characteristic onset at about the age of 40 and the clear dominant history should help. Exposure of the choroidal vessels centrally may occur, but there is no substantial extension towards the periphery. The end-stage is far less disastrous. It should, however, be noted that the ophthalmoscopic appearances in the family reported by Burn (1950) are not dissimilar from those seen in some of the members in the second family recorded here. Whether the two affections are related requires further elucidation.

(iv) *From Choroideremia*.—In this condition the choroidal vessels become exposed before becoming absorbed; conversion into white streaks is not a significant feature.

Summary

Two families are recorded. In the first the proband is a case of generalized choroidal sclerosis, and less marked changes are given in three more patients over two generations. In this family generalized choroidal sclerosis appears

to begin around the sixth decade, and is generally only slowly progressive. In the early stages there is a non-pathognomonic macular lesion. Subsequently there is exposure of the choroidal vessels, which later become converted into white streaks, this process extending from around the disc so that central and peripapillary choroidal sclerosis is seen. Later still, extension towards the periphery sets in. Generalized darkening of the fundus background is perhaps a frequent feature.

In the second family (in part reported previously as cases of macular dystrophy), ten cases are recorded in two generations and in a collateral branch. Here, non-pathognomonic central fundus lesions appeared in childhood and ran a relatively mild course. Serious trouble in this family generally began in the thirties, but was observed both earlier and later. Ophthalmoscopically, the range of appearances extended from these non-pathognomonic central reactions to central choroidal sclerosis spreading towards the periphery, in some cases associated with bone corpuscle pigment reaction at the equator.

A follow-up of a member of a previously reported family group shows that after the conversion of the choroidal vessels into white streaks there is absorption of these sclerosed vessels, so that the white surface of the sclera becomes exposed.

On the basis of these three family groups the events in generalized choroidal sclerosis probably follow this sequence:

- (a) Mottling of the central areas, reminiscent of macular dystrophy;
- (b) Extensive central reaction—oedematous, atrophic, or pigmentary proliferation—suggestive of the intermediate stages of generalized fundus dystrophy or of inflammation;
- (c) Exposure of the choroidal vessels in the central areas with conversion into white streaks—the beginning of a pathognomonic appearance;
- (d) Central lesion spreading towards the periphery so that the whole of the fundus shows generalized choroidal sclerosis with its characteristic appearance;
- (e) Absorption of the exposed sclerosed choroidal vessels, giving an appearance reminiscent of choroideremia.

In the course of the affection pigment proliferation of the bone corpuscle type may be a prominent feature in some cases. Generalized choroidal sclerosis at different stages may therefore be mistaken for macular dystrophy, generalized fundus dystrophy, central choroiditis, central choroidal sclerosis, choroideremia, and “atypical” retinitis pigmentosa.

The findings in the present study suggest that the affection is inherited in a dominant manner.

Our thanks are due to Dr. M. Klein for kindly putting at our disposal the notes that he had made on the first family in 1950, and to Dr. H. B. Dawson of Derby for information on a member of the second family.

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APPENDIX

CL. FAMILY.—Additional information to that shown in Pedigree Chart I:

Generation I

- (1) *Mrs. A. W.*, aged 78, Case 2 in text, one son.
- (2) *Mrs. G. C.*, aged 71, Proband, Case 1 in text, one daughter and one son.
- (3) *C. Cl.*, dead, no children.
- (4) *W. Cl.*, aged 68, was a bus driver, now retired, one son.
- (5) *Mrs. G. T.*, aged 67, Case 3 in text, one daughter and two sons.
- (6) *Mrs. M. V.*, aged 67, two children.
- (7) *S. Cl.*, died abroad, nothing known of any eye trouble
- (8) *Mrs. O. S.*, lives in Australia; reputed to have normal sight } No children.

Generation II

- (1) *V. W.*, aged 50, a myope of some 20 D; some nystagmus; lenses cloudy. Son of I, 1; no children.
- (2) *Mrs. D. Wa.*, aged 53, Case 4 in text } Children of I, 2.
- (3) *A. C.*, aged 50 }
- (4) *A. Cl.* Son of I, 4. }
- (5) *Mrs. H. Co.*, aged 40 } Children of I, 5.
- (6) *W. T.*, aged 30 }
- (7) *H. T.*, aged 28 }
- (8) Died young, sex unknown } Children of I, 6.
- (9) *Mrs. Ivy L.*, aged 45 }

Generation III

- (1) *Mrs. J. R.*, aged 30 } Children of II, 2.
- (2) *Peter Wa.*, aged 27 }
- (3) *John Wa.*, aged 18 }
- (4) *Nita Wa.*, aged 16 }
- (5) *Roger Wa.*, aged 15 }
- (6) *Linda Co.*, aged 6. Daughter of II, 5.
- (7) *Allen T.*, aged 8. Son of II, 6.
- (8) *Susan T.*, aged 6 } Children of II, 7.
- (9) *Christopher T.*, aged 4 }
- (10) *Robert L.* } Children of II, 9.
- (11) *Julia L.* }
- (12) *Sally L.* }

Generation IV (1) *R. R.*, aged 9. Son of III, 1.

C—E FAMILY.—Additional information to that shown in Pedigree Chart II:

Generation I

- (1) *Mrs. S. M.*, died aged 75; according to her daughter (II, 2), she acquired the habit of looking sideways at things in order to see them more clearly. She used to wear dark spectacles. Two sons and three daughters.
- (2) *William C-e*, had bad sight all his life, according to his daughters; he was not badly affected until late in life. Three daughters and two sons.
- (3) *Mrs. E. W.* (Previously *Mrs. R.*), died at 59, used to "look sideways at things" (according to II, 2); she died when her son (II, 15) was 17 and he could not remember her having trouble. Four sons and one daughter.
- (4) *Mrs. L. W.*, reputed normal. Two daughters and three sons.
- (5) *Rebecca C-e*, reputed normal, died during 1939-45 war, when over 70. No children.
- (6) *Mrs. R. S.*, reputed normal. Two daughters.

Generation II

- (1) *W. M.*, died young, reputed normal
 - (2) *Mrs. S. E.*, aged 62, Case 1 in text
 - (3) *Mrs. A. W.*, died aged 36 from nephritis, reputed normal
 - (4) *Mrs. R. R.*, died aged 37 of "cancer of chest", was reputed to have bad sight which started in her twenties. She looked to the side of objects in order to see them and took to wearing dark glasses. According to her husband "she was troubled by sunlight"
 - (5) *F. M.*, killed at the age of 20 in first world war
- } Children of I, 1.

- (6) *Miss E. C-e*, aged 60 in 1950, Case 2 in text
 - (7) *Harriet C-e*, aged 57 (in 1950), Case 3 in text
 - (8) *Joseph C-e*, examined in 1933 and found normal
 - (9) *Edward C-e*, aged 54, Case 4 in text
 - (10) *Mrs. Sarah C-n*, aged 51, Case 5 in text
 - (11) *Alfred R.*, died at 32 in the 1914-18 war
 - (12) *Gertie R.*, died at 29
 - (13) *Sidney R.*, died at 33
 - (14) *Ernest R.*, died at 27 of rheumatic fever in 1918
 - (15) *Wilfred W.*, aged 46, seen 20 January, 1951. Recently this patient has been having difficulty with reading blue prints in poor light. Ophthalmoscopic examination showed the areas between the upper and lower temporal arteries to be darkened by broken pigment; just temporal to the maculae there were several discrete white glistening spots; the vessels were normal but the discs were pale. The patient was not conscious of being night blind, but he was unable to do the Ishihara test.
 - (16) *Miss Susan W.*, nothing known
 - (17) *Miss Mary Ann W.*, nothing known
 - (18-20), deceased.
 - (21) *Miss Irene S.*, aged 43. Visual acuity: right 2/60, 6/6 with correction; left, 4/60, 6/6 with glasses. Central fields normal. Doubtful loss of lustre in central areas.
 - (22) *Mrs. L. P.*, aged 41
- } Children of I, 2.
 } Children of I, 3.
 } Daughters of I, 6.

Generation III

- (1) *Mrs. Gladys McK.*, aged 40
 - (2) *John M.*, aged 35
 - (3) *Mrs. Daisy C-k*, aged 34
 - (4) *Mrs. Muriel G.*, aged 30, Case 7 in text
 - (5) *Mrs. Joyce C-k*, aged 28
 - (6) *Bobby E.*, aged 26
 - (7) *Mrs. Marjory Q.*, aged 40
 - (8) *Stanley W.*, (SM)
 - (9) *Frederick T. R.*, aged 32, normal except for traumatic corneal scar in left eye
 - (10) *Edward R.*, aged 30, Case 8 in text
 - (11) *Joseph R.*, aged 28,
 - (12) — *C.*, normal as a child in 1933. Son of II, 5.
 - (13) Nothing known.
 - (14) *Joseph C-e*, Case 9 in text
 - (15) — *C-e*, nothing known.
 - (16) *Bernard C-n*, aged 25, Case 10 in text
 - (17) *Betty C-n*, aged 24, Case 11 in text
 - (18-25) Nothing known, Children of II, 11, 13, and 14.
 - (26) *Brenda W.*, aged 16, Twin brother died at birth. Nothing abnormal seen.
 - (27) Male deceased
 - (28) *Barry P.*, aged 15, fundi normal, heightened macular reflexes
 - (29) *Trevor P.*, aged 8, fundi normal, heightened macular reflexes
- } Children of II, 1.
 } Children of II, 2.
 } Children of II, 3.
 } Children of II, 4.
 } Children of II, 10.
 } Children of II, 15.
 } Children of II, 22.

Generation IV

- (1) *Margaret McK.*, aged 4
 - (2) *Pamela McK.*, aged 1
 - (3) *Gillian M.*, aged 1. Daughter of III, 2.
 - (4) *Roger, C-k*, aged 11, at a home for backward children at Bristol. "Damaged at birth"
 - (5) *Olivia C-k*, aged 7
 - (6) *Joan C-k*, aged 4
 - (7) *Russell G.*, aged 3. Son of III, 4.
 - (8) — *W.*, Manchester. Son of III, 8.
 - (9) *Lynn R.*, aged 3½
 - (10) *Christopher R.*, aged 1
 - (11) — *R.*, aged 5
 - (12) — *R.*, aged 2
 - (13) Nothing known, son of III, 13.
- } Children of III, 1.
 } Children of III, 2.
 } Children of III, 3.
 } Children of III, 10.
 } Children of III, 11.