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COMMUNICATIONS

FAMILIAL PRIMARY GLAUCOMA IN ADULTS

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THE influence of heredity in the incidence of primary glaucoma—apart from racial factors—has attracted little attention, and comparatively few pedigrees of glaucomatous families have been recorded. The earliest reference to familial primary glaucoma I have been able to trace is by Benedict in 1842; since then a number of writers have published pedigrees of families in which members of several generations have been affected. This familial condition appears to be quite distinct from buphthalmia.

It has long been recognised that certain races, especially the Jews, the Egyptians, and some negro races, are particularly prone to glaucoma; a similar hereditary influence can be traced among the members of certain families, and the present article is a contribution to this group.

Elliot has suggested several possible means by which the hereditary influence may act; the eye may be of small size; the development, particularly of the angle of the anterior chamber, may be defective or arrested; there may be a predisposition to nervous or vascular crises; or the conditions of environment may be in some way responsible.

Priestley Smith considered that the most important factor was probably the smallness of the eye combined with normal or excessive size of the lens, and undoubtedly a maldeveloped eye may

well be predisposed to glaucoma; yet a study of the recorded cases of familial glaucoma does not appear to lend support to this theory; there is little or no suggestion that the affected eyes were smaller than normal.

Lawford, in a discussion of the hereditary factor, did not advance any new explanation for the condition, but stressed various other points, particularly that the descent is continuous, that it shows anticipation, that it is transmitted by both sexes, and that all forms of glaucoma may occur.

Defective development of the anterior chamber angle seems to offer the most probable explanation of the mechanism of familial predisposition; it explains why these cases often show no noticeable structural abnormality, and links them up with buphthalmia and juvenile glaucoma in a continuous series.

Against this very plausible explanation, however, is the fact that familial glaucoma and buphthalmia seem very rarely to be found together in the same family—far less frequently than would be expected if the two conditions differed only in degree.

It is very difficult to assess how far emotional, nervous or vascular crises may enter into the question; such crises certainly seem to be far more frequent in certain races, and in certain individuals, than in others, but they hardly seem to provide a very satisfactory explanation of a chronic familial condition, however reasonable they may appear as exciting factors in acute glaucoma, or in precipitating an acute attack in a predisposed eye.

The study of environment opens up another interesting field of speculation, but one in which it is difficult to form any definite conclusions. The brilliant sun of the tropics, and the prevalence of conjunctival disease such as trachoma, coupled with a low standard of life, have been blamed for the prevalence of glaucoma among the Egyptians, and the association of glaucoma with epidemic dropsy implies that nutritional and constitutional factors cannot be altogether disregarded; but again these are factors of racial rather than familial significance.

The most exhaustive study of familial glaucoma was made by Bell, in the Nettleship Memorial volume of the *Treasury of Human Inheritance* (1932).

In an analysis of 8,569 cases of primary glaucoma, Bell found 46 per cent. were males, and in 279 cases of familial glaucoma 52 per cent. were males, a difference which is hardly significant, although other writers, quoting small numbers of cases, have inferred that male cases predominate.

An analysis of age incidence is however of special interest; Bell found that the mean age of onset for the hereditary cases was twenty years earlier than for the general series; of the hereditary cases 52 per cent. occurred before the age of thirty years, while

only 3.6 per cent. of the general series did so. These differences are too great to be explained by the suggestion that cases occurring within one family tend to be recognised earlier than would otherwise be the case.

On the other hand there is a sharp distinction from buphthalmia, where 80 per cent. of the cases are congenital or are recognised within the first year of life. These figures suggest that the determining factors in buphthalmia, hereditary glaucoma, and non-hereditary glaucoma are separate and distinct.

Further, interesting comparison may be made between the relative liability curves for glaucoma at different age periods. As far as non-hereditary cases are concerned, the liability rises steeply to a maximum at the age of 60-70 years, but the liability to hereditary glaucoma remains more or less the same throughout life; that is to say, the incidence of hereditary glaucoma is approximately the same for each decade.

Another interesting conclusion reached by Bell was that the age of onset of the disease in the parents bears a close relationship to the age of onset in the affected offspring, the children tending to become affected about 10 years earlier than the parents did. These figures are difficult to compile with accuracy, however, since the onset of glaucoma at an early age naturally prejudices marriage and parenthood, and so introduces a complicating factor; of those who develop the disease before the age of thirty relatively few become parents.

At least it can be said that there appears to be some degree of "anticipation" in subsequent generations, although the available material is too scanty for definite conclusions.

With regard to the suggestion put forward by Priestley Smith, and endorsed by Elliot, that glaucomatous patients tend to have a small eye with an unduly large lens, and that such malproportion may be the essential mechanism in the production of hereditary glaucoma, Bell found little evidence to support this view; of 25 cases in which the corneal diameter had been measured, only two were below normal size; while of 32 cases where information was given as to the depth of the anterior chamber, 21 were noted as being deep or very deep, and in 13 of these 21 cases the onset of disease was before 19 years of age. These two factors—the early age onset, and the depth of the anterior chamber—suggest that these cases may be closely linked to buphthalmia.

Bell also found, in studying the transmission of the disease, that either parent was equally potent as a transmitter, but that the parent transmitting the disease was usually himself affected; that it was extremely difficult to declare any member of an affected family safe from the disease as long as he lived, and that the cases usually appear in otherwise healthy stock with no demonstrable association with any other disease or congenital defect.

Apart from the work of Bell—primarily intended as a study in heredity—very few collections of glaucomatous families have been published within the last thirty years. P. Calhoun (quoted by Zorab) published a full account of eight cases in the *Journal of the American Medical Association* in 1914, including pedigrees of cases previously published by Lawford, Howe, and Nettleship. H. T. Holland published a number of Indian cases, in which three generations were involved, in the *Indian Medical Gazette* (1924).

Zorab (*Trans. Ophthal. Soc. U.K.*, 1932), reported seven cases in one family, again involving three generations, and reproduced the pedigrees previously published by Calhoun, Lawford, Howe and Nettleship.

He came to the conclusion that males were more frequently involved than females, in the proportion of 25 to 10 (35 cases) and he suggested that whenever two members of the same family were found to be suffering from glaucoma simplex, all the members of the family of the same and succeeding generations should be examined.

In a discussion arising out of Zorab's paper Neame quoted a pedigree from his own cases where nine members of three generations appeared to be affected, four being males, and five females.

Another reference to the subject is made by Aphthomas (*Fasciculus Cestriensis*, 1934), who quotes two families, one showing eleven cases in two generations, and the other three cases in two generations. He again emphasises that glaucoma at an early age, or in two members of the same family, should be followed by examination of the others in the family. Aphthomas agrees that a small globe, or a small cornea, is not necessarily the only cause of familial glaucoma, and that familial glaucoma is not associated with any general disease. His cases did not support the contention that the condition was commoner in the male sex, but he found that transmission might take place equally by either sex.

Two families in which glaucoma simplex appears to be a familial condition have come to my notice; one in my own practice, and brief details of the second family have been placed at my disposal by the kindness of Mr. Foster Moore.

First Family.—This is a typical Lincolnshire agricultural family, of healthy stock, which has proved comparatively easy to trace since the members of the family have all settled and lived most or all of their lives close to their birthplace.

First Generation.—Mr. H— (the grandfather) went blind at an early age; nothing is known about the reason for this, but it seems probable that he had glaucoma.

Second Generation.—Mr. H— (the father) died at the age of 61

years, and had been totally blind for 9 years when he died. I have been unable to trace any record of his condition, and it is very doubtful whether he ever obtained any medical attention for his sight. It is known, however, that he often told his wife that he would lose his sight before middle age. His wife (the mother) died aged 84 years; her sight was very good up to the age of 80 years, and nothing more is known of her. The father had several brothers and sisters; several had poor sight and some "were operated on." One sister (Millicent) went blind at the age of 19 "and was never married."

Third Generation.—At the time of his marriage both Mr. H— (father) and his wife each already had one child; both these children were presumably illegitimate. Very little is known of the father's boy, George, but his sight is said to have been quite normal. The mother's girl, Mary, died two years ago, aged over 85 years, and had "perfect sight all her life." The legitimate offspring of the marriage were, in order:

(1) John; died 34 years ago, at the age of 49. He was blind when he died, but no information is obtainable as to the cause of the blindness. He never received any treatment or attention as far as can be traced. It seems probable that he had glaucoma. He left 8 or 9 children, and it is believed that they all had good sight.

(2) Elizabeth; died in 1911, aged 53 years; from cancer. She was blind when she died, but again there is no record of the cause. She left three children, all of whom have good sight as far as is known.

(3) Harry; died two years ago aged over 70 years. He "never had good sight." 34 years ago, when he would be 38, he attended the Nottingham Eye Infirmary complaining of his sight, but his records there cannot be traced. However, his sister-in-law wrote to me to say that she knows an operation on his eyes was proposed, but he refused to have one performed. A silk cord (presumably a seton) was put into the back of his neck but he went blind subsequently in spite of this. He had nine children, of whom four are living, and all had good sight except one, who has unilateral optic atrophy following a fracture of the skull.

(4) Addie Eliza; died in 1901, aged 24 years. She had perfect sight. It may be that she died too young for the family failing to manifest itself. She left one child, which died in infancy.

(5) Charles; is still alive, aged over 70 years. Dr. Christie Reid of Nottingham has kindly sent me particulars of him. He attended the Nottingham Eye Infirmary in 1923, after having been "treated" by several opticians. He was found to have advanced glaucoma cupping and raised tension in the right eye (120, McLean's tonometer), and R.V. $\bar{c}$ glasses = 6/18. The left eye

showed a cataract, a dilated pupil and L.V. = H.M. Left tension = +3. A peripheral iridectomy was performed on the right eye, but he refused operation on the left eye. In 1929 there is a further note: "R.V. = 6/9; tension 38 (McLean): L. E. i.s.q." He has 6 or 7 children; one has defective sight, but I have no information as to the cause.

(6) Joseph; is still alive, aged 71 years, and still has good sight. He has 6 children, all of whom seem to be unaffected. One of them was recently examined by my colleague Mr. W. A. Briggs, who found unilateral post-neuritic optic atrophy, but no evidence of glaucoma.

(7) Sarah Jane; died 16 years ago, aged 53 years. Her sight failed for some years before her death, but she was never medically examined. Her story is of considerable interest, and contains strong circumstantial evidence that she suffered from glaucoma. She was "treated" by a local sight-testing optician, and used to wear sometimes two and sometimes three pairs of glasses together, which was a standing joke in the family and is still well remembered. One day while walking along one of the country roads she was nearly killed by a car which passed close beside her, which she did not see. Presumably her visual fields must have been greatly reduced by then. This incident caused some local excitement and it appears to have brought home to her how defective her sight was. The same night she committed suicide by drowning herself in the Fosdyke. She left 5 children, all of whom had good sight. One of the sons has recently been under my care for severe tobacco amblyopia, but he showed no evidence of glaucoma.

(8) Died in infancy.

(9) Edric Edwin; is still alive, aged 65 years. He attended the Lincoln County Hospital in 1935, suffering from bilateral chronic glaucoma. The right eye was trephined by Mr. W. A. Briggs, but the iris failed to prolapse at the time of operation. It prolapsed under the conjunctival flap two days later, and was abscised at a subsequent operation. Before operation R.V. = H.M. L.V. = C.F. at 2 metres. He regained 5/60 in the right eye, but the left eye became worse and he was certified as blind in 1936, the condition of both eyes being very advanced before he presented himself for treatment, and his visual fields were very small. When last seen (1937) his condition was about the same.

(10) Died in infancy.

(11) Emma Caroline; is still alive, aged over 60 years. She came under the care of Mr. T. H. Cresswell at the Lincoln County Hospital in 1924 and was then suffering from fairly early chronic glaucoma in both eyes. She was kept under observation and

treatment by miotics until 1931, when the condition of the left eye began to deteriorate, and it was accordingly trephined, with complete iridectomy. This eye has remained satisfactory ever since, and in spite of the gradual development of some central senile lens opacity in the last year or two she still sees 6/9 with a suitable correction, and her left visual field is almost full. The right eye was kept under miotics until 1937, and it was then decided to trephine this eye too. It was trephined, with peripheral iridectomy, by Mr. Cresswell, and the convalescence was normal. Three months after the operation she presented herself for examination again with a history that the sight of the right eye had suddenly failed, and she was found to have developed a large choroidal detachment in the right eye, apparently quite spontaneously. There was no history of injury or unusual exertion, and no adequate explanation for this late complication has been found. The choroidal detachment persisted, and the eye remained soft for a period of about twelve months; I was then asked to take over her treatment upon my colleague's retirement. When I first saw her, about a year after the right eye had been trephined, her condition was as follows:

R.E. white; small thin trephine bleb above, draining to some extent; cornea clear, bright, no precipitates; anterior chamber very shallow, but definitely present, with deposits of fine iris pigment scattered over the posterior surface of the cornea and the surface of the lens and the iris; iris atrophic and somewhat depigmented; small free peripheral iridectomy above; small irregular pupil with numerous posterior synechiæ; small clumps of pigment on the anterior lens capsule; a few scattered lens opacities; some vitreous opacities; large dark rounded choroidal detachments on either side obscuring most of the fundus; disc not visible. Tension = -2. R.V. corrected = 6/36 with difficulty; visual field greatly restricted above and at either side, but fairly good below.

L.E. white; small trephine bleb above, draining well; cornea clear, bright, no precipitates; anterior chamber rather shallow; normal iris; free complete iridectomy above, small dotted developmental lens opacities with some early central sclerosis; vitreous clear; fundus—early glaucoma cupping and some retinal arteriosclerosis; L.V. corrected = 6/9; tension normal.

It was difficult to know what to do for the right eye. The detachments appeared to be quite definitely choroidal from their shape, size, and dark colour; they had been present almost unchanged in appearance for just over twelve months. They were quite translucent on transillumination. Their origin was mysterious; they were certainly not present until about three months after the

original operation, when they developed, apparently spontaneously, and they had not shown any tendency to resolution. At the original operation the trephine hole had perhaps been placed rather far back, and the operation had clearly been followed by a severe post-operative iritis with an unusual depigmentation of the iris, the pigment being freely scattered through the anterior chamber. It seemed possible that the original trephine hole had only just entered the anterior chamber, and that the small aperture might have become blocked by the pigment and inflammatory deposits set free during the post-operative iritis, resulting in almost complete closure of the operative channel with preferential filtration into the suprachoroidal space.

If left alone, it seemed clear that the eye must eventually degenerate from extreme hypotony, and the visual acuity and field were already so poor that the eye was of little use. At the same time operative interference with the original trephine hole seemed to be virtually impossible, while to perform a second separate trephine would have been technically very difficult and of doubtful efficacy. Mr. Foster Moore suggested that a cautery puncture might be tried, in the hope of draining the choroidal detachments and reattaching the choroid in the scar. I performed a cautery puncture in the lower outer quadrant over the most prominent part of the choroidal detachment, and a large quantity of pale straw coloured fluid was evacuated; the detachments disappeared and the visual acuity rose to 6/18, with a considerable increase in the visual field. About two months after the operation, however, the choroidal detachment reappeared on the opposite side and the condition of the eye has slowly relapsed almost to its former state. The patient is unwilling for any further operative measures in view of her age and the condition of the left eye.

The second family.—The records of this family have been very kindly placed at my disposal by Mr. Foster Moore.*

They cover six siblings out of a family of ten; it is said by Mr. E. D. S— that there were nine living members (one having died in infancy) and that he was the only one of the nine to escape glaucoma.

(1) Miss M. L. S—; a myope of about -6.0 D. The right eye was trephined by Mr. Rutson James in 1926, and the left eye by Mr. Foster Moore in 1932. Both fields show some early nasal loss, but the corrected central visual acuity in each eye was 6/6.

(2) Miss M. S—; visual acuity R.E. 6/9; L.E. 6/18; both eyes trephined in 1932. The left field shows early nasal loss and the right eye has very little nasal field.

* A paper on this family was published in *Brit. Jl. of Ophthalm.*, by R. R. James, Vol. XI, p. 438, 1927.

(3) Miss U. K. S—; visual acuity 6/6 R. and L.; extensive field loss in the right eye with moderate field defect in the left eye.

(4) Mr. E. D. S—; no sign of glaucoma; said to be the only unaffected sibling.

(5) Mr. L. S—; slightly hypermetropic; visual acuity 6/6 R. and L. The right eye was trephined by Mr. Rutson James in 1926, and the left eye by Mr. Foster Moore in 1933. The left field shows early nasal loss.

(6) Miss M. S—; chronic glaucoma in both eyes; both trephined in 1925; the right visual field shows a fairly extensive defect and the left visual field is very greatly reduced.

Summary and Conclusions

A survey of the scanty literature shows that familial glaucoma—a condition distinct from buphthalmia—appears to be a definite entity although comparatively rare. All forms of glaucoma may occur in affected families, but the chronic simple type seems to be the most frequent. The condition is transmitted by both sexes, and may involve several generations. There is some tendency to “anticipation” in succeeding generations. The sexes are about equally affected, males being slightly more commonly affected than females. The mechanism by which the hereditary influence acts is unknown; defective development of the angle of the anterior chamber seems to be the most probable means, but the statistics suggest that the determining causes of buphthalmia, hereditary glaucoma, and non-hereditary glaucoma are separate and distinct. There seems to be no association between hereditary primary glaucoma and buphthalmia. There is little evidence to support the suggestion that hereditary glaucoma is due to some degree of congenital microphthalmia with a disproportionately large lens.

Two glaucomatous families are described. The first family was probably affected through three generations, but no cases have yet been discovered in the fourth, although, curiously enough, several members of the fourth generation have defective sight; three which have come under observation, however, have been found to be suffering from quite unrelated eye disorders and to show no sign of glaucoma.

Of the third generation, of eleven legitimate children, two died in infancy; of the remaining nine, three were certainly glaucomatous and two more suffered from eye defects which were very probably glaucoma; two more had defective sight which may have been due to glaucoma, and two were unaffected. One of the two unaffected members died at the age of 24—too young for her condition to be certain.

Pedigrees

- No ocular defect as far as can be ascertained.
- ◐ Defective sight in adult life : cause unknown : ? glaucoma.
- ◑ Defective sight in early adult life : history suspicious of glaucoma.
- ◒ Defective sight with strong suspicion of glaucoma : proof lacking.
- Definitely known to be glaucomatous.

First Family

Second Family

One member of this family developed a spontaneous choroidal detachment about three months after sclero-corneal trephining, and this persisted unchanged for a year. It was (unsuccessfully) treated by a cautery puncture and is still present.

The second family comprises six siblings out of a family of ten, one of whom died in infancy. Of the nine living siblings, eight are said to be glaucomatous, and six have been examined. Of these five were glaucomatous, and one was unaffected.

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IRITIS (WHITE EYE) IN FOWLS

BY

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With an account of the Histological Changes in the Eye

BY

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Introduction

IRITIS in fowls, or "white eye" as it is called, is one of the manifestations of the disease-complex which is most commonly known as "fowl paralysis." The other manifestations are paralysis, leucæmia and the development of lymphocytomata. In this paper we are chiefly concerned with the changes in the eye, as these are usually the first to occur. The iritis is more commonly associated with paralysis, which it generally precedes, than with leucæmia and the lymphocytomata. The condition is widespread and it is thought to be transmissible and to be caused by a filtrable virus. Chickens are most susceptible and the disease-complex may appear in all breeds.

Cause.—We regard the condition as being one of the sub-acute or chronic manifestations of disease which arise in fowls as a result of the activity of the pathogenic developmental or mutation forms of the *Bacillus coli communis* which have their habitat in the intestinal canal. Climate, artificial feeding, confined space, incubation, intensive breeding, etc., lower the animals' resistance,