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NOTES ON THE PIGMENTATION OF THE HUMAN IRIS.

By A. RUDOLF GALLOWAY, M.B., C.M., M.A., Aberdeen.

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IN the *Proceedings of the Royal Society* (B), Vol. 80, 1908, p. 85, C. C. Hurst has published a paper "On the Inheritance of Eye-Colour in Man." He therein states that there is distinct discontinuity between :

(1) "The eyes in which two kinds of pigments are present ; the one yellow-brown in colour, deposited on the outer or anterior surface of the iris ; the other, blue-black in colour, deposited on the inner or posterior surface of the iris." Such eyes he calls duplex.

(2) "The eyes in which the posterior pigment alone is present in the iris, the anterior pigment being absent." Such eyes he calls simplex.

At page 93 he states that "(1) simplex parents mated together give all simplex offspring ; (2) duplex parents mated together give either (a) all duplex offspring,

or (b) duplex and simplex offspring in the proportion of about 3 : 1 ; (3) duplex parents mated with simplex parents give either (a) all duplex offspring, or (b) duplex and simplex offspring in the proportion of about 1 : 1."

He adds "It is evident therefore that the simplex type, in heredity, behaves as a Mendelian recessive to the duplex type, which is dominant." "The unit characters concerned in the heredity of the duplex and simplex types of eyes are therefore presence (duplex) and absence (simplex) of anterior pigment in the iris, presence being dominant over absence, which is recessive."

From the above statements it follows :

1. That in studying the pigmentation of the human iris, the two surfaces— anterior and posterior—alone are of importance ; the stroma which is about ten times as thick as the posterior layer of retinal pigment epithelium is negligible.

2. That two kinds of pigments may be present in the human iris, the one yellow-brown in colour located on the anterior surface, the other blue-black in colour located on the posterior surface.

3. That Mendelian laws regulate the inheritance of these types.

Since the publication of the paper cited, I have, as occasion allowed, in the out-patient department of the Eye Institution in Aberdeen, where the annual attendance is over 20,000, taken notes of eye-colours and pedigrees which might throw any light on this question. My first difficulty was in finding any eye in which I could state, after careful examination in daylight and by focal illumination with magnification, that there was no anterior pigmentation. This difficulty still continues, and any such case noted in this paper must be taken to mean that no anterior pigmentation was seen at the examination. Several times I have thought that I had discovered a pure blue, or pure grey, or pure blue and grey parentage with no anterior pigmentation, but on careful examination traces of pigment were found in one or other parent.

My next difficulty lay in the immense number of different types of pigmentation. Only very few (each covering many grades) can be given in this paper, and these refer solely to the pedigrees of the families mentioned. This multiplicity of types probably accounts for the following differences from Hurst's observations as noted at pp. 86, 87 of his paper.

1. "Self-coloured duplex" eyes are often "spotted."

2. "Ringed duplex" eyes are often "spotted."

3. The pigment ring of "ringed duplex" eyes is often outside the pupillary zone, occupying an irregular middle zone, and also sometimes, in spots, a peripheral zone of the iris.

4. "Self-coloured duplex" eyes occur with no denser pigment ring round the pupil.

5. Eyes with grades of anterior pigmentation so low that they can be mistaken for "simplices" do occur.

6. "The lighter shades of blue, and coarser greys" are not necessarily "due to the greater density of age" (Hurst, p. 88). In the B family mentioned in this paper, II. 2, aged 9 years, has as densely grey eyes as her mother.

With regard to the first deduction from Hurst's observations concerning the two surfaces of the iris, it is necessary to mention that the two layers of importance developmentally and anatomically are (1) the stroma, consisting mostly of connective tissue, about ten times as thick as (2) the posterior retinal pigment epithelium. The latter is epiblastic, and the former mesoblastic in origin.

For facility of description, the area of the iris may be divided into three zones:

1. Pupillary zone—from the pupil to the lesser circle.
2. Median zone—from the lesser circle to the beginning of the outer or folded part of the ciliary zone (where there is sometimes a greater circle).
3. Peripheral zone, consisting of the outer or folded portion of the ciliary zone, and the periphery of the iris as far as visible.

As the other deductions from Hurst's observations with regard to the two different kinds of pigments, and their Mendelian inheritance, could not be proved or disproved without examining microscopically an iris, showing both, I took occasion to do so in the case of G. C., aged 70, whose right eye I removed on March 30th, 1910, for sarcoma of the choroid in the lower and inner equatorial region. The tumour had not advanced far enough to affect the globe beyond the site of the growth, there being no pain or inflammation, and the sight being only partially obscured. The iris was normal and healthy, with free movement, and was coloured in exactly the same way as that of the left sound eye of the patient. The colour note of the eyes made on March 22nd, 1910, was:

"At a short distance distinctly blue; narrow yellow-brown pupillary zones; median and peripheral zones blue."

"The *right* eye has nine dark brown spots of the apparent size of $\frac{1}{2}$ to $1\frac{1}{2}$ mm. dotted over all three zones, one distinct dark one (up and in) and three more hazy ones occur on the yellow-brown pupillary ring. There is also an irregular peripheral ring, consisting of separate grey spots free of anterior pigment; the median and peripheral zones generally show reticulations well except where the dark brown pigment spots occur.

The *left* eye has seven similar dark brown pigment spots varying from $\frac{1}{4}$ to 2 mm. in apparent size."

The presence of a yellow-brown pigment ring, of dark brown pigment spots, and of blue median and peripheral zones, apparently mostly free from anterior pigment, promised valuable information. The eye, on removal, was taken to the Pathological Department of Aberdeen University, where Professor Dean prepared a large number of serial sections. The globe was divided into an upper and

lower half, the lower containing the tumour. The upper half was used for the sections, which were cut antero-posteriorly from near the horizontal meridian.

Four figures will suffice to demonstrate the important appearances which may be followed all through the series of sections.

Fig. I. ($\times$ Zeiss A. unstained.)

Low power unilateral view of a section through the pupil, showing the dark brown posterior pigment epithelium, which increases in thickness near the pupil (behind the pupillary zone); in this region also, the *stroma* is seen to be thickly strewn with pigment cells, many rounded and full of pigment granules; towards the anterior surface these rounded pigment cells are less numerous, some appearing to have ruptured, while at the anterior surface, the pigment consists almost entirely of yellow granules, the cells apparently having distributed their pigment in a granular form, thus causing the pupillary ring. The anterior surface of this pupillary region is seen to be distinctly yellow in colour. In the median and peripheral regions of the iris, beyond the pupillary area, very few pigment cells are seen although in no part are they entirely absent; the anterior surface of these median and peripheral parts, which *to external examination before enucleation appeared blue and free from anterior pigment*, is yellowish and shows the presence of pigment granules, although more faintly than in the pupillary region. It will be noted also that near the pupillary margin, the dark brown posterior pigment epithelium passes suddenly and abruptly into the yellow colour of the anterior pupillary ring, also that the stroma of the pupillary margin has fewer pigment cells than the stroma behind the middle of the pupillary pigment ring. Towards the left limit of the field a dark brown anterior pigment spot is seen, as if some of the pigment cells had apparently passed through the stroma and located themselves on the anterior surface. In the stroma behind this spot, one or two disintegrated pigment cells appear with granular pigment around.

Fig. II. ($\times$ Zeiss A. unstained.)

Horizontal antero-posterior section through the pupillary margin.

At the mid-point of the section corresponding to the pupillary margin few stroma pigment cells are seen, while on each side in the parts corresponding to the stroma behind the pupillary pigment ring they are numerous. The yellow anterior surface is most distinct opposite the parts of the stroma which have most pigment cells.

Fig. III. ($\times$ Zeiss D. unstained.)

Horizontal antero-posterior section above the level of the pupil through the yellow-brown pupillary zone.

Note the dark pigment epithelium, and the stroma thickly strewn with pigment cells, which tend to disintegrate towards the yellow anterior surface, where pigment mostly in the granular form is seen.

Fig. IV. ($\times$ Zeiss D. logwood stain.)

Section through iris, showing the anterior pigment spot seen in Fig. I.

The spot is seen to be due to the presence of dark brown pigment cells of a similar nature to the stroma pigment cells, several of which, whole or dis-integrated, appear in the field: the logwood staining shows the structure of the iris tissues.

Professor Dean suggests that these stroma pigment cells are possibly connective tissue cells that have the power of movement. These sections appear to show that they tend to pass from the pigment epithelium layer forward through the stroma, to distribute pigment either in the shape of pigment cells or granules to the anterior surface of the iris. Whether this view be correct or not the sections lend no corroboration to the idea that there are two kinds of pigment, a blue-black behind, and a yellow-brown in front. All the appearances are compatible with the belief that only one pigment is present, which when heaped up in the form of pigment cells, is dark brown in colour, and is yellow when thinly distributed especially in a granular form. Moreover the dark brown pigment cells of the anterior spot are exactly similar in colour to the retinal pigment epithelium of the posterior surface.

It appears probable from the presence of yellow anterior granular pigment in all sections of the median and peripheral zones which were blue and apparently free from pigment, that many so-called pure blue eyes may have this anterior coating of granular pigment, which is revealed only microscopically*. Hence, in addition to the errors concerning two kinds of pigment, etc., another error in the classification of some blue eyes as having no anterior pigment would arise.

Therefore any theory, Mendelian or otherwise, which depends on the supposition that there are two kinds of pigments, with different loci, and that there is no stroma in the human iris, seems based on inadequate examination of the human eye.

Hurst's results so far as they go give approximately the anticipated Mendelian proportions, but as I have endeavoured to indicate in this paper the amount of anterior pigment is a continuous quantity, and nothing short of microscopic post-mortem examination will determine to what extent an eye does or does not possess it. Hurst suggests that half the "clear" or pure blue eyes classified by ordinary observers really possess anterior pigment and that this is the reason why the data collected by Galton do not support the Mendelian theory. If, as I anticipate, many of Hurst's "simplex" irides would show some anterior pigment on microscopic examination, it is evident that he has been singularly fortunate in discovering that the limit of his personal method of examination was that which coincides numerically with Mendelian theory. This coincidence is the more

[* In the case of the eyes of "clinically complete albinos" both in man and in lower forms of life a post-mortem microscopic examination will frequently show some posterior pigmentation, and occasionally some slight anterior pigmentation as well. On p. 85 of his paper Hurst states that in the albino pigment is entirely absent from both surfaces of the iris. EDITOR.]

remarkable in that he quotes the investigations of Davenport as leading to Mendelism in human eye colour, and thus as confirming his own work. Now Davenport collected his data in precisely the same way as Galton did, i.e. by aid of schedules with verbal definitions of eye colour and categories practically identical with Galton's scheme, and therefore, according to Hurst, leading to a wrongful classification of 50 % of the "clear" or pure blue eyes, i.e. eyes without anterior pigment. Yet Davenport—precisely like Hurst—finds his Mendelian quarter. It is thus fairly obvious that if both these authors are right and that if their papers actually confirm each other it must be practically of no importance where the limit is drawn between a "simplex" and a "duplex" eye,—for two different methods of observation which ought to lead to widely different numerical results are appealed to by both observers as confirming each the other's work!

During my search for pure blue parentages, I made the following note on February 22nd, 1910, "Very many blue eyes have a slight yellowish staining, sometimes arranged as a pupillary ring, at other times as a faint wash here and there preferably following the lines of the reticulations. This staining is usually visible only in bright daylight with focal illumination, and not in gaslight." To this, I have now to add the observation that if, after deciding that a blue eye has no anterior pigment, such an eye be rotated upwards, so that an oblique view of the iris surface with foreshortened pupil is obtained, a yellow sheen of anterior pigmentation will often be seen.

These observations account for the fact that I have not, as yet, met with a family from a pure blue or grey, or blue and grey parentage of sufficient size to be of any value to record. Even although many such pure blue or grey-eyed families were obtained, however, I question whether this would indicate any Mendelian inheritance with regard to iris pigmentation: the nearest approach I have been able to make is represented by the following pedigrees, which show some interesting points in inheritance of iris colour. On looking over the notes made when the various individuals of these and other families were examined, I am impressed with the frequency with which presence of the yellow staining of blue and grey eyes is mentioned as occurring in the *upper* parts of the irides. In light brown irides also, the upper parts of the irides are often darker brown (*vide* F. family, II. 3). I would suggest as an explanation of this interesting fact that the upper lid prevents the pigment from being bleached as quickly as in other unprotected parts. This would agree with the microscopic appearances of the sections given in this paper, which show the gradual disintegration of the pigment cells towards the anterior part of the iris.

It is probable that the greatest incidence of light takes place at the most prominent or convex part of the iris surface, at a little distance from the slightly funnel-shaped pupil. Hence the greatest pigment activity is seen there in the sections, and hence the frequency of the ringed pupillary type of pigmentation in light eyes, and the tendency to have darker pupillary rings in dark eyes.

Fig. 1.

Fig. 2.

Fig. 3

W^m Smith J^r del.

Fig. 4.

E. Wilson, Cambridge

SECTIONS OF THE EYE OF G. C. ILLUSTRATING
A. RUDOLF GALLOWAY'S MEMOIR.

REMARKS ON THE PEDIGREES OF IRIS PIGMENTATION.

A. Family :

This pedigree was constructed prior to April 1910, mainly on account of the large family of sixteen—from two blue-eyed parents II. 3, and II. 4. At that time, following Hurst's classification of simplex and duplex irides, I noted as having no anterior pigment those eyes which appeared to me to have none with focal illumination in good daylight. I have since found that many of these show the yellowish sheen of anterior pigmentation when rotated strongly upwards so that a foreshortened view of the pupil is obtained. This test was not applied either to the parents or children of this interesting family. It will be noted, however, that the mother II. 4 had a faint buff tint on the blue of the upper parts of each iris.

It would serve no useful purpose, therefore, to look for the manifestation of Mendelian phenomena in this family, although the proportion of 14 blues without visible anterior pigment to 2 with tells against this mode of inheritance. I feel that the classification of eyes into "duplex" and "simplex" according to the pigmentation of the iris, is an impossible one, and must lead to inevitable confusion.

It is interesting to note the inheritance, in the daughter III. 9, of the mother's brown spot of anterior pigment, and in the daughter III. 15, as a pupillary ring, of the mother's buff tinting*.

In the eyes of I. 3, faint buff tinting was at first noted, and on a second examination deleted. This yellowish sheen would probably appear on upward rotation in good light in this case also. Three of her sisters, I. 4, 5, 6, had anterior pigmentation well marked.

The mating of III. 3, a pure blue, with III. 4, a uniform rich dark self-brown, is interesting, and has resulted in no iris that is, or can ever become, self-brown. Three of the children have well marked pupillary rings when the parents had none, and IV. 6 is almost an albino. In the mating of II. 5 with II. 6, unfortunately the husband could not be seen, but again from dark brown eyes and almost pure blues there have resulted three with pupillary rings.

F. Family:

The chief points of interest in this pedigree—the mating of two blues which would be classified as pure blues with no anterior pigment by any non-professional examiner—are :

1. The occurrence of a son, II. 3, with brown irides with a complete coating of anterior pigment.

* For examination and report on III. 15 I am indebted to Major F. M. Mangin, R.A.M.C., Specialist in Ophthalmology, Aldershot Command.

2. The buff or yellowish tinting being confined to the upper parts of the irides in two members (I. 2 and II. 1), and pigment being rather more dense in the same regions in II. 3.

3. The appearance of pupillary circles in II. 4, while they are absent in the parents.

B. Family:

This pedigree is interesting:

1. From the mating of blue, almost free from visible anterior pigment, with very rare and peculiar dense grey, almost white, irides free from visible anterior pigment.

2. From the occurrence of the same peculiar white or light grey irides in three of the children, viz. II. 1, 2, 3.

3. From the appearance of pigment circles in four of the five children, the parents being free from them.

4. From the buff staining occurring in the upper parts of the irides of I. 1.

5. From the blue peripheral zones of II. 2. This appearance may partly be due to the fact that in this region the iris is thinner than elsewhere. In a clear yellow yellow-ammer—a *clinically* complete albino with pink eyes—which I have alive at present, this same grey colour occurs as a pupillary ring, where the iris is thickest, the median and peripheral zones being translucent and showing the red fundus reflex through them*.

6. From the absence of photophobia and other signs of albinism.

C. Family:

1. The eyes of I. 1, to any ordinary observer, are blue with no visible anterior pigment.

2. Mated with a blue with no visible anterior pigment, there appears the heterochromic iris of II. 1, showing a large deposit of anterior pigment.

3. Neither of the parents is ringed, but two of the children are, viz. II. 2 and 3.

D. Family:

1. The red pupillary ring of I. 1 corresponds, as is frequently the case, with the original reddish colour of the hair.

2. Red hair is more subject to change of colour, and is more closely connected with albinism than other colours.

3. The two children are verging on albinism and show variation in refraction, II. 1 being hypermetropic, and II. 2 myopic.

* This bird (*Emberiza citrinella* ♀) is now dead, and Dr Usher, who kindly examined the eyes, reports them to be entirely free of pigment, except in the posterior pigment epithelium of the irides, which is very lightly pigmented: see "Canary Breeding," *Biometrika*, Vol. VII. Plate II.

4. The pupillary rings of I. 1 are repeated in both the children.
5. Yellow staining on the blue irides of I. 2 occurs only in the upper and inner regions.

E. Family:

1. The blue eyes and reddish hair of I. 2 are probably connected with the appearance of an incomplete albino II. 2.
2. The examination of this patient II. 2, as detailed, combined with the microscopic examination of G. C.'s eye, has convinced me that it is quite impossible to say when any living person's blue eye is free from anterior iris pigment, and has led me to doubt that this ever truly occurs.

CONCLUSIONS.

1. The human iris cannot be held to consist merely of an anterior and a posterior surface, each, in certain eyes, exhibiting its own kind of pigment.
2. The stroma may contain pigment cells more especially in its deeper parts and granular pigment towards the anterior surface.
3. Pure blue, or so-called "simplex" eyes, which to any outward examination appear free from anterior pigmentation, may show stroma pigment cells, and anterior granular pigmentation when examined microscopically.
4. Hence the classification of "duplex" and "simplex" eyes is erroneous, and there is no discontinuity or Mendelian inheritance between them.

PEDIGREES OF IRIS PIGMENTATION.

All eyes that have been seen have been examined by myself, except III. 15, Fig. A.

The symbols used have been devised to indicate the main types of iris pigmentation occurring in the following pedigrees, but, as already mentioned, these varieties are so numerous that several grades of colouration must be included under some of the symbols.

The aim of these pedigrees is to indicate how complex is the problem of heredity of eye colour, when we pass from a mere rough appreciation of the extent of pigmentation, as provided by the ordinary verbal descriptions, to an analysis of its distribution throughout the iris.

APPENDIX, PEDIGREES.

Fig. A. (April, 1910.) I. 1, male, aet. 77. Poorhouse. *Hair*, black. *Eyes*, Right—brown with darker pupillary circles, three or four $\frac{1}{4}$ mm. darker brown spots in middle and peripheral zones; Left—greenish-brown with darker brown pupillary circles, four or five $\frac{1}{4}$ mm. brown spots in middle and peripheral zones. I. 2, male, seaman, aet. 55 at death. *Hair*, dark. *Eyes*, pale blue. I. 3, female, aet. 80. *Hair*, light brown. *Eyes*, pale blue, no pigment seen. I. 4, female, aet. 76. *Hair*, brown. *Eyes*, greenish-brown, large yellow-brown rayed pupillary circles, occupying pupillary and middle zones. Peripheral zone, bluish-green. I. 5, female, aet. 72. *Hair*, brown. *Eyes*, pale blue with small buff pupillary circles. I. 6, female, aet. 67. *Hair*, black. *Eyes*, green-brown. Brown pupillary circles, middle and peripheral zones, green. Right has one small ($< \frac{1}{4}$ mm.) brown tick inner peripheral zone. Left has one small ($< \frac{1}{4}$ mm.) brown tick outer middle zone. II. 8, female, aet. 34. *Hair*, dark brown. *Eyes*, green-brown. Brown pupillary circles: middle and peripheral zones, green. Right has 3 or 4 small brown dots inner middle zone. Left ditto outer peripheral. III. 33, female, aet. 7 (daughter of II. 8). *Hair*, light brown. *Eyes*, blue; buff mottling arranged in irregular pupillary and peripheral circles. II. 1, male, dead. Blue eyes. II. 2, female, dead. Brown eyes. II. 3, male, aet. 58. *Hair*, blond. *Eyes*, pale blue, no anterior pigment; reticulations well marked. II. 4, female, aet. 57. *Hair*, brown. *Eyes*, blue, each with faint buff tint especially upper part of left iris, which has also one $1\frac{1}{2}$ mm. brown pigment spot in lower pupillary zone. II. 5, female, aet. 55. *Hair*, brown. *Eyes*, pale blue with faint buff mottling on pupillary and peripheral zones. II. 6, male, aet. 51, trawler. *Hair* and *eyes*, dark brown. II. 7, male. *Eyes*, blue. III. 1, male, single, aet. 40, coachman. *Hair*, light brown—lighter on left side when young. *Eyes*, blue, no anterior pigment. III. 2, female, aet. 38. *Hair*, brown. *Eyes*, blue, no anterior pigment. III. 3, male, aet. 36. *Hair*, brown. *Eyes*, blue, no anterior pigment. III. 4, female, aet. 34. *Hair*, used to be auburn now brown. *Eyes*, rich dark self-brown, uniform colour. III. 5, female, aet. 34. *Hair*, brown. *Eyes*, blue, no anterior pigment. III. 6, male, aet. 32. *Hair*, dark brown. *Eyes*, greenish-blue with yellow rayed circles mostly in outer pupillary and middle zones (one in each eye). III. 7, male, aet. 32. *Hair*, black. *Moustache*, light brown. *Eyes*, pale blue, no anterior pigment. III. 8, female, aet. 29. *Hair*, dark brown. *Eyes*, pale blue with pupillary circles of buff. III. 9, female, single, aet. 30. *Hair*, dark brown. *Eyes*, blue—right has one $\frac{1}{2}$ mm. brown spot upper pupillary zone. III. 10, male, aet. 28. *Hair*, brown. *Eyes*, blue with no anterior pigment. III. 11, female, aet. ? *Hair*, brown. *Eyes*, blue with buff pupillary circles. III. 12, male, aet. 27. *Hair*, light brown. *Eyes*, blue, no anterior pigment. III. 13, female. *Hair*, black. *Eyes*, dark self-brown. III. 14, male, single, aet. 25, in Vancouver. *Hair*, brown. *Eyes*, blue. III. 15, female. *Hair*, light brown. *Eyes*, pale blue with buff pupillary circles. III. 16, male, soldier, Aldershot. *Hair* and *eyes*, brown. III. 17, male, died, aet. 9 mos. *Eyes*, blue. III. 18, male, aet. $21\frac{1}{2}$. *Hair*, brown. *Eyes*, blue, no anterior pigment. III. 19, male, aet. 19. *Hair*, brown. *Eyes*, blue, no anterior pigment. III. 20, female, aet. 17. *Hair*, light brown. *Eyes*, blue, no anterior pigment. III. 21, male, aet. $11\frac{8}{12}$. *Hair*, brown. *Eyes*, blue, no anterior pigment. III. 22, male, aet. 10. *Hair*, brown. *Eyes*, blue, no anterior pigment. III. 23, female, aet. 32. *Hair*, black. *Eyes*, greenish-brown, large pupillary circles of yellow-brown, and dots of same elsewhere, both zones. III. 24, male, died, aet. 31. *Hair*, dark brown. *Eyes*, dark brown. III. 25, male, aet. 30. *Hair*, dark brown, used to be light brown. *Eyes*, greenish-brown—well-marked pupillary circles of reddish-brown with rays meeting similar spots in peripheral zones—middle and peripheral zones dull green. III. 26, female, aet. 25. *Hair*, light brown. *Eyes*, blue. Right has two or three minute ticks of

yellow in peripheral zone down and out. Left very similar. Twin with III. 27. III. 27, female, aet. 25. Twin with III. 26. *Hair*, brown. *Eyes*, blue, both with very faint spots of buff staining. III. 28, female, aet. 23. *Hair*, dark brown. *Eyes*, self light brown. Right has one 1 mm. dark brown spot in peripheral zone down and out. Left ditto in pupillary zone upwards. III. 29, male, aet. 20. *Hair*, once black has now a slight reddish tint. *Eyes*, light brown, uniform yellow-brown pigment layer, no rings. Left has one $\frac{1}{2}$ mm. brown spot peripheral zone up and in. III. 30, female, aet. 16. *Hair*, brown. *Eyes*, light brown with darker pupillary circles. III. 31, male, aet. 14. *Hair*, dark brown. *Eyes*, light self-brown with one or two darker spots. IV. 1, male, aet. 12. *Hair*, light brown. *Eyes*, blue, no anterior pigment. IV. 2, female, aet. 10. *Hair*, light brown. *Eyes*, pale blue, very faint mottling of buff in sinuous lines. IV. 3, female, aet. 8. *Hair*, brown. *Eyes*, light brown with narrow pupillary circles of yellow-brown. IV. 4, female, aet. 5. *Hair*, light brown. *Eyes*, light brown, rather browner round pupils. IV. 5, female, aet. 3. *Hair*, light brown. *Eyes*, light brown, rather browner round pupils. IV. 6, female, aet. 2. *Hair*, light flaxen. Eyebrows and lashes the same—almost an albino. *Eyes*, pale blue, no anterior pigment. IV. 7, female, aet. $4\frac{1}{2}$. *Hair*, light brown. *Eyes*, blue, no anterior pigment. IV. 8, male, aet. 9 mos. *Hair*, light brown. *Eyes*, blue, no anterior pigment. IV. 9, female, aet. 4. *Hair*, brown. *Eyes*, pale blue with indistinct buff pupillary circles and other buff dots here and there. IV. 10, female, aet. 2. *Hair*, brown. *Eyes*, blue, no anterior pigment. IV. 11, male, aet. 2. *Hair*, light brown. *Eyes*, blue, no anterior pigment. IV. 12, male, aet. 6. *Hair*, brown. *Eyes*, brown with darker pupillary circles. IV. 13, male, aet. 5. *Hair*, brown. *Eyes*, blue, no anterior pigment, a greyish white ring in peripheral zone. IV. 14, male, aet. 2. *Hair*, light brown. *Eyes*, blue, no anterior pigment.

Fig. B. (March, 1910.) I. 1, male, aet. 33. *Hair*, brown. *Eyes*, blue, very faint stain of buff on upper part of each iris. I. 2, female, aet. 31. *Hair*, brown, used to be lighter. *Eyes*, very pale grey, almost white, no visible anterior pigment. By magnification the greyish-white colour of the iris is seen to be due to closely packed sinuous fibrous lines. II. 1, male, aet. 11. *Hair*, brown. *Eyes*, pale grey like the mother's, but with pupillary circles of yellow-brown, and one or two other ticks of the same colour here and there. II. 2, female, aet. 9. *Hair*, light brown. *Eyes*, dense pale grey all over except peripheral zones of blue, no visible anterior pigment. The grey irides very like the mother's, and quite as grey, verging on white. II. 3, male, aet. 8. *Hair*, brown. *Eyes*, the same pale grey, almost white irides but with median circles of yellowish-brown. II. 4, male, aet. 6. *Hair*, light brown. *Eyes*, pale blue, with faint pupillary circles of buff. II. 5, male, aet. 2. *Hair*, light flaxen. *Eyes*, blue, pupillary circles of grey, and other lines and spots of same, no visible anterior pigment.

Fig. C. (Feb. 1911.) I. 1, male, aet. 43. *Hair*, medium brown. *Eyes*, blue with rather darker pupillary circles. Touched with one or two minute ticks of yellow-brown; one brown pigment spot in *Right* periphery down and out of .25 mm. size, a smaller one up and out in median zone. I. 2, female, aet. 45. *Hair*, dark brown. *Eyes*, blue, no visible anterior pigment. II. 1, female, aet. 13. *Hair*, medium brown, rather reddish at tips. *Eyes*, blue. *Right* has a transverse heterochromic band formed by two distinctly red-brown patches of anterior pigment, one at each side of pupil, the outer one $4\frac{1}{2} \times 5\frac{1}{2}$ mm., widest at periphery, the inner one 3×4 mm., widest also at periphery. II. 2, female, aet. 11. *Hair*, red. *Eyes*, light blue, median irregular circles of reddish-yellow anterior pigment. II. 3, female, aet. 9. *Hair*, pale brown with reddish-golden tints. *Eyes*, pale blue with faintest possible staining of pale yellow in pupillary zones.

Fig. D. (March, 1911.) I. 1, male, aet. 37. *Hair*, used to be very fair, gradually got darker, now dark brown, almost black. Eyebrows and moustache light reddish brown, they have not altered. *Eyes*, bluish-grey with pale green tint in median and peripheral zones. Red complete pupillary rings, with rays stretching across median and peripheral zones. *Refraction*, $\frac{8}{10}$ with manifest hypermetropia of .5 D.: probable total hypermetropia of 1.5 D. I. 2, female, aet. 38. *Hair*, medium brown, used to be very fair. *Eyes*, blue, yellow staining in patches, one in each eye, at upper and inner parts only. Greyish hazy spots form irregular peripheral circles.

Refraction, hypermetropic astigmatism in each eye of about +2 D. cylinder, axis down and in. II. 1, female, aet. 8. *Hair*, yellowish flaxen. *Eyes*, pale blue, narrow yellow pupillary rings. *Refraction*, hypermetropia of 1 D. II. 2, female, aet. 5. *Hair*, pale yellowish-brown, a shade darker than II. 1. *Eyes*, pale blue, lighter than her sister's—faintest possible yellowish staining in irregular pupillary circles. *Refraction*, myopia - 6 D.

Fig. E. (April, 1911.) I. 1, male. Unexamined. *Hair*, light brown, darker than that of I. 2. *Eyes*, blue, darker than those of I. 2. I. 2, female, aet. 35. *Hair*, light reddish-yellow, used to be lighter. *Eyes*, blue-grey with irregular pupillary rings of yellow-brown, and one or two small separate ticks of brown in median and peripheral zones of each eye. *Refraction*, +1 D. II. 1. Two older and one younger children (than no. 2) with considerably darker hair and eyes. *Eyes*, blue. II. 2, male, aet. 10. Incomplete albino. Brought by his mother (I. 2) on account of sensitive eyes—photophobic in bright light—and difficulty with lessons. *Hair*, almost white, white eyebrows, lashes a shade darker—pale yellowish. *Eyes*, light blue, no pigment visible anteriorly, and would certainly pass all ordinary tests for absence of anterior iris pigment; but when the eyes are turned strongly upwards so that a foreshortened view of the pupils is obtained, a faint yellowish sheen appears over both irides, and this is more visible round the pupils than elsewhere. Both eyes have peripheral grey dots in irregular circles, no nystagmus, nor pink pupils. *Fundi*, distinctly albinotic, the choroidal interspaces being much paler than the choroidal vessels. *Refraction*, +2 D.

Fig. F. (April, 1910.) I. 1, male, aet. 58. *Hair*, very light flaxen—"white" in youth. *Eyes*, pale blue, very faint buff mottling here and there. He has four brothers and two sisters with blue eyes and one sister with dark eyes. I. 2, female, aet. 57. *Hair*, light brown. *Eyes*, slight buff or yellowish staining in upper part of each iris, seen only by focal illumination in bright daylight. II. 1, male, aet. 37. *Hair*, light brown. *Eyes*, blue, faint touch of buff upper parts of each iris. II. 2, male, aet. 35. *Hair*, dark brown. *Eyes*, pale blue, no visible anterior pigment. II. 3, male, aet. 33. *Hair*, brown. *Eyes*, light brown, left rather darker—diffuse brown anterior pigment—most marked at upper part of each iris, especially left. II. 4, female, aet. 31. *Hair*, light brown. *Eyes*, blue with pupillary circles of pale yellow-brown. II. 5, male, aet. 28. *Hair*, brown. *Eyes*, blue. Abroad, not examined. II. 6, male, aet. 20. *Hair*, brown. *Eyes*, blue, no visible anterior pigment.