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COMMUNICATIONS

A CONSIDERATION OF ANIRIDIA, WITH A PEDIGREE

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Introduction

Two or three patients in the family which is the subject of this enquiry had been treated in Addenbrooke's Hospital, Cambridge. On enquiry it was found that the defect was common in various related sibships, and although the affected people were living in villages scattered through the fen country between Cambridge and Peterborough, it was thought worth while to visit them all and record the condition of their eyes. In the future, members of such a family as this are less likely to remain domiciled in one locality, and an observer's task will be more difficult by virtue of the distances he will be obliged to cover to collect data from them all. The congenital abnormality shown in this particular family is a rare one. Few pedigrees of aniridia have been published in

recent years. Many which are widely quoted in authoritative text-books are unreliable and have been constructed from second-hand reports. Many of the pedigrees collected by Julia Bell¹ are small and with little exact relevant detail. Julia Bell² has appealed for the suppression of the most remarkable aniridia pedigree published, that of Risley³, in which aniridia is reported in 111 out of 119 relatives but it was confirmed in the case of one individual only.

Strictly speaking the term "aniridia" is not accurate as some vestiges of iris have invariably been found in eyes which have been sectioned⁴, even though in life no trace was visible on ordinary clinical examination. The more limited term "irideremia" has been occasionally used but has not found general acceptance amongst ophthalmologists. For general purposes aniridia may be defined as "the entire absence of the iris or of a portion too great to justify the term coloboma."⁵ Any fragment which does exist is functionally useless.

All living affected persons in this family have been visited in their homes and examined there. In some cases they have been brought to hospital for more precise examination with slit-lamp, etc. Refractive errors were determined in their homes with an electric ophthalmoscope. Intra-ocular pressure was estimated digitally. Almost all non-affected descendants of II 1 were examined and a search made for any slight or intermediate change in the iris.

Thirty-one patients were found with bilateral abnormality of the iris. The abnormalities varied in gravity and have been subdivided thus—

Four cases with coloboma of iris and/or hypoplasia of iris.

Ten cases with aniridia either partial or complete of both eyes.

Twelve cases with bilateral aniridia and ectopia lentis.

One case with partial aniridia in R. eye and coloboma in L.

Four cases were not examined. Generations I and II are dead, as is Case III, 18. Careful questioning of their children and relatives make it certain that these people suffered from aniridia, but one cannot say whether or not the lenses were dislocated. Aniridia itself is such an obvious abnormality that lay testimony can probably be accepted, especially where the person involved was one of the family circle.

It is apparent from inspection of the pedigree that the three varieties of abnormality follow no special pattern of distribution. Cases with ectopia of lens are sometimes children of parents with uncomplicated aniridia, and vice versa. Those with colobomata of iris (or hypoplasia of stroma) occur in sibships affected with

aniridia alone or with the graver condition of aniridia and ectopia lentis. A parent with coloboma is capable of transmitting the defect in a severer form to her children—IV 45 and V 8. The defects appear to occur in an unpredictable way amongst affected members. Unfortunately three of the colobomatous group have no children so that their genetic potentialities are not known.

Genetics

The defect is generally inherited from affected members of a family in a proportion of approximately 50 per cent. In this family 42 per cent. of the total descendants of II 1 are affected. Only 23 per cent. of the children of II 2 are affected, but the children of this 23 per cent. show an incidence of 62 per cent. Only affected members transmit the disease and normal children invariably have normal offspring. It therefore fulfils the conditions of a regular Mendelian dominant. In this family an affected person has invariably married a normal person and from this and the proportion of cases with aniridia we must assume the affected person is heterozygous—the mate in every case being homozygous for the recessive allelomorph. This may be illustrated by the following diagram⁶ :—

		One parent heterozygous affected		i.e. 50% heterozygous affected 50% normal
		Gametes	A a	
One parent normal	a		Aa aa	
	a		Aa aa	

Being a dominant character the trait becomes apparent in a heterozygote. There are no cases in this pedigree, or indeed in the relevant literature, of two heterozygotes for the condition marrying each other and it is therefore impossible to say what appearance a homozygote for the condition would present. It is possible that lethal genes would accompany the homozygote condition, as in the case of the yellow mouse quoted by Corner⁷ and in numerous experiments with the *Drosophyla*. There is no accompanying infertility in aniridia as there is for example in neurofibromatosis⁸, nor in this pedigree is there evidence of mental or skeletal defects. We must assume that in some ancestor of I the

VERTICAL OCULAR DEVIATIONS

Addenda et Corrigenda for MONOGRAPH SUPPLEMENT NO. XII.

- p. 9. After "These" in 8th last line *add* "and the other influences concerned."
- p. 10. After "oblique muscles" in legend to Illustration 1 *add* "assisted by the vertical recti."
- p. 16. *Add* to legend of Illustration 3, "The narrow lines, which are central, represent the green light."
- p. 17. In 9th line "inferior rectus" should be "superior rectus" and be followed by "See Illustration 3."
2nd para. *Substitute* "asymmetry" for "variation."
Last para. should precede 2nd para.
- p. 18. *Add* "the" before "opposite direction" in 12th line. *Omit* 2nd last para. "Change of gaze in a vertical direction" etc.
Illustration 6 No. 3 photo is inverted.
- p. 20. At end of para. marked (5) *add* "Illustration 5 (3) & (4)."
- p. 21. In 1st line *omit* "again" and after "is" *add* "another aspect of."
- p. 23. *Replace* last 2 sentences of 2nd para. by "This explanation is made more unlikely by the change to a downward rotation that occasionally occurs."
- p. 31. *Omit* last paragraph.
- p. 34. In 2nd last para. 8 lines from bottom of page, read "a contractive" *instead of* "an overaction."
- p. 35. In para. (3) *change* "up" to "vertically."
- p. 36. In 5th last line *change* "makes" to "may make."
- p. 37. In 1st line of legend *add* "muscle" after "oblique."
- p. 41. In 2nd line *change* "the roots" to "their roots."
- p. 42. In 14th line *change* "latter" to "later."
In 2nd last line of 4th para. *add* "a" after "due to."
2nd last para. should follow 1st sentence of 3rd last para. The next para. should be headed "DISCUSSION."
In last para. after "Chavasse" *add* "following Maddox and Peters."
- p. 47. 2nd column *should read*

- Sup. Rectus		
R. & L.	R.	L.
1	2	4
—	6	8
1	6	11
—	2	7
2	16	30
15-0		

- p. 48. *Instead* of "Secondary inhibitional paresis" after "3" *read* "Secondary underaction."
Add "apparently" after "is" at end of 3rd line.
- p. 49. *Add* "relatively" between "The" and "overacting" in 1st line.
 In 1st line of 5th para. *change* "overaction" to "contracture."
- p. 52. *Add* to legends of Illustrations 23 and 24, "The broad lines, which are central, represent the red light."
- p. 54. Opposite p. 54, legend of Illustration 26, *instead* of "(3) then up and out" *read* "(3) than up and out."
- p. 55. *Add* to legend of Illustration 28, "The narrow lines, which are central, represent the green light."
- p. 57. In NOTE *read* "palsies of the inferior recti" instead of "R.I.R. palsy."
- p. 61. "Illustration 34" should be "Illustration 29."
 Section 1 refers to section 6 of Illustration 29.
 Section 2 refers to section 2 of Illustration 29.
 Section 5 refers to section 3 of Illustration 29.
 Section 6 refers to section 4 of Illustration 29.
 Section 7 refers to section 5 of Illustration 29.
- p. 63. *Omit* sentence "Usually the inferior oblique is the affected muscle" in 3rd line of para. headed "(2) Primary or Congenital 'Overfunction'".
- p. 65. "Facial" should be "Fascial" in heading of section (c).
- p. 67. At end of 1st para. "Illustrations 29 & 30" *should be* "Illustrations 30 & 31."
 Under "Abduction in Elevation," "Diagram 32" *should be* "Illustration 33."
- p. 69. At end of 2nd para. "Illustration 31" *should be* "Illustration 32."
- p. 74. In 2nd last para. "illustration No. 8" *should be* "Illustration No. 10."
- p. 76. *Add* "(a)" before "Unioocular Macular Projection."
- p. 78. "Illustration 33 (1)" *should be* "Illustrations 29 (1) & (2)."
Add (b) before heading "The Division of Diplopia."
 "Illustration 33 (2)" *should be* "Illustrations 29 (2) & (35)."
- p. 81. "Illustration 33 (3)" *should be* "Illustration 29 (2)."
 In 2nd last line *change* "squares. A" to "squares; A, in Illustration 36."
- p. 82. "—0°5'" *should be* "5°0'."
- p. 83. At the end of para. starting "Shirley L." *read* "contracture" instead of "overaction."
- p. 89. *Add* "ipsilateral" before "superior rectus" in Jackson's reference. The words "Bielschowsky (1945) condemned this operation" should follow.

condition arose as a gene-mutation and thereafter, as in other alterations of the germ plasm, the defect was transmitted in accordance with mendelian principles as a regular dominant. Nothing is known of the cause of gene-mutations in human beings, or indeed of mammals generally, but in the insect world the normal production of mutations can be multiplied by means of thermal, X-ray stimulations of the germ plasm⁹. Plenty of records exist of aniridia arising without any known hereditary predisposition^{10, 11, 12} and in the case of a dominant of this type a new mutation must be postulated, especially where it is known that the defect is transmitted to approximately 50 per cent. of children¹³.

In recent years an attempt has been made to assess the mutation rate for various human abnormal conditions. J. B. S. Haldane¹⁴ began this work with a calculation of the mutation rate for haemophilia. Recently Mollenbach¹⁵ has estimated the mutation rate for aniridia, on the basis of his findings in Copenhagen, to be between 1:50,000 and 1:100,000.

The presence of three types of defect in one family without any apparent order in their incidence presents a difficult genetic problem. It is known that in hereditary defects a good deal of variability exists in different families and indeed in different sibships of the same family¹⁶. It may be that the iris form and structure are governed not by one but by many genes and that in the defects of varying gravity different numbers of genes are responsible. Waardenburg¹⁷ says "Since in the fruit fly *Drosophyla*—cytologically the most exhaustively studied animal—genes transmitting the colour of the eye or the appearance of the bristles have been found in every chromosome, it seems probable that the genes which determine normal structure and function of ocular tissues, and therefore those genes which determine their hereditary abnormalities, are distributed over several chromosomes." Environment can have no influence in a disorder where different primary defects occur in the same sibships and even between twins—IV 6 and 7. No consanguineous marriages are recorded in this pedigree. We must assume that "since there are families in which some have aniridia and others coloboma, whereas there are other families in which cases of coloboma occur in the absence of cases of aniridia, there must be distinct hereditary factors at work in the respective families, factors whose effects are quantitatively different."¹⁸ With a view to determining whether the abnormal gene (or genes) is linked with normal hereditary factors, blood and "taste-testing" examinations of several separate sibships were performed.

[A]

Case	III	2	—	A ₂
	IV	3		OIV
	IV	7		OIV
	IV	9		OIV
	IV	10		OIV

[B]

III	6	—	A ₂	pp.	M	rr
	Wife		O	P	MN	R _{2r}
IV	14	—	A ₂	pp.	M	rr
IV	15	—	A ₂	P	M	R _{2r}

[C]

III	7	—	A ₂	pp.	M	R ₁ R ₂
	Husband		O	P	MN	R _{1r}
IV	16		O	P	M	R ₁ R ₂
IV	17					(Not taken)
IV	18		A ₂	P	MN	R ₁ R ₂
IV	19		O	P	M	R _{2r}

[D]

III	10	A ₂	pp.	M	R _{2r}
	Wife	B	P	MN	R _{1r}
IV	21	B	P	MN	R ₁ R ₂
IV	22	B	P	M	rr
IV	23	A ₂ B	P	M	R _{2r}
IV	24	A ₂ B	P	MN	R _{2r}
IV	25	B	pp.	MN	rr
IV	27	B	pp.	M	R ₁ R ₂

[E]

III	16	P	MN	R _{1r}
	Husband	P	M	R ₁ R ₁
IV	44	P	MN	R ₁ R ₁
IV	45	P	MN	R ₁ R ₁
IV	46	P	MN	R _{1r}
IV	47	P	M	R _{1r}
IV	48	P	MN	R ₁ R ₁

Note: Affected cases are underlined.

Taste-Testing with PHENYL-THIO-UREA.

A.	*III	6	—	Taster
	Wife		—	Non-Taster
	*IV	14	—	Taster
	*IV	15	—	Non-Taster

B.*III	7	—	Taster
	Husband		Non-Taster
*IV	16	—	Taster
IV	17	—	Taster
IV	18	—	Taster
*IV	19	—	Taster

* Affected cases.

Taste-testing with PHENYL-THIO-UREA—*continued*

C. *III 10 — Taster	D.*III 16 — Non-Taster
Wife — Taster	Husband — Taster
All children — Tasters	*IV 44 — Taster
	*IV 45 — Taster
	IV 46 — Non-Taster
	*IV 47 — Non-Taster
	IV 48 — Not tested

* Affected cases.

These findings were scrutinized by Prof. R. A. Fisher, who thought there was slight statistical evidence of linkage to the ABO group. He considered greater numbers should be investigated and that the matter was worth pursuing. It was realized that even if linkage did exist the knowledge would be of no immediate practical value in a disability such as this which is present from birth (unlike Huntingdon's chorea where linkage with a known normal factor such as blood groups might enable a prediction to be made of those likely to develop the disease in later life¹⁹). Nevertheless it would be of some theoretical value as a contribution to the body of known linkages which must be enormously extended before substantial beginnings of a so-called chromosome map could be assembled for humans. At present a relatively complete map is a remote possibility, man being such a slow breeder and not available for controlled genetic experiments like the fruit fly *Drosophyla* from the intensive study of which so many facts have been learnt.

Embryology

No foetal eye affected with aniridia became available for study. It is obvious the disability is germinal: environment is not a factor of any importance, nor is it the result of any transplacental infection such as the foetal maldevelopments associated with maternal German measles²⁰. Many theories have been advanced to explain the mechanism of its production and no general agreement has been reached amongst investigators. Foetal eyes affected with aniridia are rarely examined.

The presence of an anterior polar cataract suggested to Treacher Collins²¹ that the defect was due to an abnormal and prolonged adhesion of the lens to the cornea (an analogous opacity is seen

after a perforated corneal ulcer). This would make it impossible for the iris to insinuate itself between these two structures. An anterior capsular cataract does occur in this pedigree, *e.g.*, III 9, but it is not generally present—in fact in the youngest members the lenses and capsules are quite clear. One would also expect such an adhesion to be accompanied by an opacity in the substantia propria of the cornea, but such an opacity is not found in this series.

The mesodermal theory in Ida Mann's words ²² suggests "the growth of the mesodermal iris is primarily abnormal and inhibits the normal forward growth of the ectoderm." Evidence has been adduced that colobomata of the iris are caused by the "abnormally long persistence of one, several or all the vessels which normally connect the circulus arteriosus iridis major with the terminal branches of the hyaloid vessel around the edge of the optic cup."²³ If all the vessels persist the growth of the iris would be impeded all the way round and the condition of aniridia result. The mesodermal iris which normally appears first would not perform the function of a scaffold along which the ectodermal elements could grow. Some support is lent to the mesodermal theory of genesis by cases IV 45, IV 44, IV 23; these have defects in the iris stroma only, with intact pigment layers beneath, suggesting at least that the defect is not due to ectodermal maldevelopment. These cases also have a marked proliferation of the pigmentary layers at the defective parts of the pupillary region, as though vigorous ectodermal tissue had attempted to close the mesodermal defect.

The ectodermal theory postulates that the rim of the optic cup which subsequently forms the neural layers of the iris does not grow forward at the proper time, that is at the 70-80 mm. stage²⁴. This theory would be more in line with the "organizer" hypothesis, whereby the optic cup is believed to have a "governing" function calling forth the lens²⁵. Evidence in its support is found in the ectodermal defects which accompany aniridia—absent fovea centralis, nystagmus, and anomalies of lens and retina. Nystagmus was found in 3 cases, choroido-retinal degeneration in 3 and (except for one case of nystagmus) all belonged to a sibship in which hereditary myopia was present—IV 2-13. In one case of nystagmus (III 9) a brisk foveal reflex could be seen on the R. side only, IV 13, a normal case in the same sibship had extensive peripheral pigmentation of the fundus in both eyes. The frequent incidence of ectopia lentis in this series may lend support to the ectodermal hypothesis, as this condition is thought to be due to a primary defect of the zonule, which results in a displacement of the lens when the ciliary ring opens out—the zonule being developed from tertiary vitreous and therefore an ectodermal structure²⁶.

Pathology

No first-hand facts can be given of the histology of the condition, as no eye in this family has become available for pathological examination. III 14 had the L. eye enucleated seven years ago, but no histological examination was made. The eye had been blind for many years and very red and painful for 5 months. Reports are not numerous in the literature, but all agree that a few tags at least of iris are found in every case of (clinically) complete aniridia²⁷. Treacher Collins²⁸ says "Microscopical examination of these cases seems to show that they are really predisposed to glaucoma, for not only do we find that the ciliary body terminates in a rudimentary iris, which if pushed forwards is quite sufficient to block the whole of the posterior surface of the ligamentum pectinatum, but that between this rudimentary iris and the lig. pect. there are abnormal adhesions."

Corneal opacities are stated to occur, but they were not seen in this series. Lenticular opacities were common but of no single type and supported no particular embryological theory. Opacities become more widespread and severe as affected patients grow older and ultimately cause incapacitating visual defects. It may be noted that generalized opacity of the lens occurs most early in two cases where they were dislocated, IV 3 and IV 6. Presumably the liability to cataract formation is due to impaired nutrition of the lens. The iris normally has some share in the interchange of fluids in the eye and its absence may be assumed to have a deleterious effect. If the ciliary processes are small or absent as they are sometimes said to be²⁹ this would further interfere with the fluid interchange. Possibly the absence of the constant contraction and dilatation of the iris may remove a normal stimulus and be responsible for a more sluggish circulation in the ciliary body, which would prevent a vigorous interchange of intra-ocular fluid.

The development of a generalized opacity may be accompanied by a swelling of the lens, with pressure on the iridial angle and the onset of secondary glaucoma—III 16. Why the presence of an ectopic lens greatly increases the tendency to glaucoma is not altogether clear. This complication does not appear to be especially common in families with congenital ectopia lentis without aniridia. It may be that the elongated fibres of the suspensory ligament permit very minute movements of the lens to take place, movements which are not always clinically visible, and these may set up a chronic irritation leading to glaucoma.

Some writers have found histological evidence of an absent fovea centralis³⁰, which is assumed to be the cause of the partial amblyopia and nystagmus frequently encountered in aniridia.

Clinical findings

A. CASES WITH COLOBOMA AND/OR HYPOPLASIA OF IRIS.

Mingled without apparent order amongst affected sibships are four cases exhibiting small colobomata and/or hypoplasia of the iris. These patients suffer no disability. Visual acuity is normal, with no tendency to formation of lens opacities nor of raised intra-ocular pressure. They occur in sibships with normal and aniridic brothers and sisters and in each case are themselves children of one affected parent. From one case it is evident that they may transmit the disease in a more severe form to their children, *i.e.*, IV 45 who is the least abnormal of all affected members of her sibship, having slight hypoplasia of the superficial layers of the iris stroma revealing in patches the deeper pigmented layers, has transmitted the malady in a more severe form to one of her six children—V 8. The other five children are normal. IV 23 has a R. pupil of normal size, but the superficial layer of the iris has gaps shaped like the petals of a flower, exposing the deeper pigmented layers. The L. eye has a dilated and very feebly reacting pupil with a coloboma of the superficial stroma of the iris at 5 o'clock in the pupillary margin, but the gap is filled in with a proliferation of the deeper pigmented layers. IV 45 has a coloboma of the pupillary margin of the iris at 9 o'clock in R. eye, with numerous areas of hypoplasia of iris stroma. The L. eye has a pupillary margin coloboma at 5 o'clock, the gap being partially filled with deeper pigmented layers. There are also areas of hypoplasia in the lower and temporal regions of the iris, with a small complete breach in the iris at 5.30 o'clock, forming a second very small pupil. He sees 6/5 comfortably with each eye and reads J.1. IV 57 has a small pupillary coloboma of the iris in each eye downwards and outwards, with areas of superficial hypoplasia just above and below the colobomata. His vision is excellent; he was accepted as A1 for the army and passed his eye test for the railway.

This tendency for colobomata and hypoplasia of the iris to occur in aniridic families is frequently noted in the literature. Licsko³¹ noted atrophic anterior layers of iris in the child of an aniridic woman. Theobald³² records a woman with an atypical coloboma iridis in each eye having a child with aniridia and congenital squint. De Beck³³, Cross³⁴, Foster⁵, Polte³⁵ and others have recorded cases of intermingled aniridia and colobomata. In general it may be said that colobomata tend to occur in predominantly aniridic families, but Snell's family³⁶ exhibit the reverse finding—colobomata occurring in 5 generations with two individuals with aniridia. Complications are less frequent in

colobomatous eyes, but they do occur: *e.g.*, de Beck³³ records development of bilateral cataracts in a man aged 30 years, so disabling as to require extraction.

V 8 has a partial aniridia in the R. eye and a large coloboma of the iris of the L. eye directed downwards and slightly inwards. Such a case has been described by Waardenburg³⁷. In this child the lower margin of the lens could be clearly seen in the red reflex, even though there is no displacement of the lens—presumably because in a child of this age the lens is relatively small, whereas later on when the lens grows larger, the edge is obscured by the sclero-corneal junction. (The lens margin can be seen all the way round in case V 3, aged 2 years.)

B. CASES WITH SIMPLE ANIDIRIA. (Ten cases.)

The two predominant symptoms are photophobia and poor vision. Photophobia is a source of greater discomfort in the younger patients. V 3 and V 8 are obviously very uncomfortable in ordinary light. IV 12 wears tinted glasses only in very bright light. IV 20 served in the Middle East for 3 years without any special discomfort. The ophthalmoscope light caused lacrymation to IV 16 but normally she was quite comfortable. The older members of this group appeared to suffer no discomfort except III 2 who habitually wore tinted glasses. He, however, had had a bilateral lens extraction. Hamilton³⁸ suggested that lack of photophobia was due to abnormal insensitivity of the retinal elements. It may be, as this family shows that the retina is sensitive at first and gradually becomes more accustomed to excessive light as the patient grows older. Significant also is the fact that the lenses of aniridic patients develop scattered opacities as the patients grow older.

In none of these cases does vision reach normal standards. The following table gives the salient features of these ten cases.

From this it appears that vision deteriorates as the patient grows older. Case V 3 had transparent lenses but was too young for determination of vision. Case IV 12, aged 14, had 1 dioptré of myopic astigmatism, but correction of this did not improve visual acuity. IV 20 had an error of +2.50 sph. each eye, but this correction did not improve vision. IV 12 had clear lenses, and IV 20 a small localized opacity in L. which probably did not interfere with vision, yet both had mediocre vision. As the ages progressed the lenticular opacities increased, with exception of IV 58, who had slight dusty opacities only in the centre of each anterior capsule. III 2 was aphakic, both lenses having been removed when he was 34 for mature cataract. III 16 had a completely opaque lens in her R. eye, and a slightly less opacity

Case	IRIS PRESENT	Lens opacities*	Tension	Vision	Refractive error	Vision with correction
V 3 (age 2)		Clear	N	?	—	—
IV 12 (age 14)		Clear	N	6/36 6/24	-1'00D. cyl. at 180°	Not improved
IV 20 (age 21)		—	N	6/24 6/18	+2'50 sph.	Not improved
IV 14 (age 28)		—	N	6/24 6/18	?	—
IV 58 (age 30)		—	N	Not taken	+6'00 D. sphere	Vision good
IV 47 (age 32)		—	N	6/36 6/36	+6'00 D. sphere	6/12 6/12
III 9 (age 46)		—	N	6/18 6/60	+3'00 D. sphere	—
III 6 (age 50)		—	N	5/60 6/60	?	—
III 2 (age 57)		Aphakic-lens extractions 22 years ago	N	H.M. Certified blind	Now +8'00D. sph. eye is essentially myopic	—
III 16 (age 62)		—	+ ±	Certified blind	?	—

(*) For details of lens opacities see case histories.

of L. III 7's vision has gradually declined: he was a soldier in the 1914-18 war. Thus it would appear that in the absence of lenticular changes vision is sub-normal from the beginning and that the opacities which accompany advancing years cause further gradual decline. Precisely why vision is poor in the absence of lenticular changes is not known. Some have produced histological evidence³⁹ that the macular area is abnormal, but no specimen from this series became available for pathological examination. A brisk foveal reflex was seen in a number of cases (see case histories). It has been pointed out by Alger⁴⁰ that the refraction of light both outside and inside the equator of the lens without the

iris diaphragm would cause a poor image and this lack of precision may deprive the macular area of effective stimulation in the early months of life when normal differentiation takes place.

Only in one case, III 16, was the presence of raised tension noted. The tension of the R. eye was higher than in L., but the rise was not marked. This is a small series, of course, and six of the cases are under 35 years of age. Nevertheless the findings are in striking contrast to those cases of aniridia complicated by ectopia lentis.

Although serious and incapacitating opacities of the lens in this small series have not developed until at any rate after the third decade, the literature records cases where a cataract showing "an expansion co-equal with the cornea" developed at 13⁴¹, and another patient at 15 or 16 years had both opaque lenses broken up by a needle⁴². Foster⁵ says that "Hirschberg watched a case from babyhood when the lens was clear and in place, until it was cataractous and shrunken and luxated at age of 10."

Glaucoma is generally accepted as a complication of aniridia. Foster⁵, reviewing the European and American literature at the end of the last century, found it present in 12 out of 164 cases. Julia Bell⁴³, however, says "it would appear that there is no marked liability to glaucoma in the aniridic patient." Treacher Collins^{44, 28, 45} repeatedly spoke of the greater predisposition of aniridic eyes to glaucoma, basing his opinion on histological evidence. Frost records a case in which one drop of homatropine precipitated an acute glaucoma (quoted in 38). In this family those with uncomplicated aniridia mostly have a hypermetropic error. From a survey of the literature this appears to be a common type of error^{46, 44}. This fact may account for the convergent squint present in V 8, and frequently noted by other observers in aniridia. De Beck³³, examining a lens after extraction from an aniridic patient, noted that its nucleus was excessively broad and thin. Patients suffering from traumatic aniridia are said to suffer from no defect of accommodative power⁴¹, but in this series it was noted that IV 58 with an error of +6.00 D. though only thirty years old, saw more satisfactorily with a second more powerful pair of glasses for close work, as did IV 47. IV 12 belongs to a sibship affected with myopia. This defect is not uncommon in aniridia families. Blair and Potter⁴⁷ have recorded two aniridic children of a colobomatous father, each child with high myopia and astigmatism. Foster⁵ records it as a common accompaniment of aniridia.

C. CASES WITH ANIRIDIA AND ECTOPIA LENTIS. (12 cases.)

In this family twelve patients have the additional primary complication of ectopic lenses as well as aniridia. The principal

features are briefly summarized in Table E. As in aniridia alone, photophobia is troublesome early in life. It is, for example, marked in IV 27 and her two brothers, IV 26 and IV 24, but in older patients the symptom is not complained of. Whether this is due to an acquired insensitivity of the retinal elements or to the development of corneal opacities is not easily decided. In general visual acuity is poorer than in uncomplicated aniridia, especially in such cases as IV 15, IV 19, IV 24, where the lower edge of the lens traverses the central portion of the large pupil and further interferes with the refractive system of the eye.

In each case the patient preferred, where he had the choice, to look through the phakic part of the eye, except III 7 who was helped by a +11.00 D. sphere correction in R. eye, even though the lens was not dislocated upwards as far as the centre of the cornea. The first three cases have a mixed astigmatism, myopia and hypermetropia "with the rule." IV 24 and IV 26 were slightly helped by the appropriate correction. IV 3, IV 6, and IV 7 were not refracted but had gross signs of myopia in the fundus, with marked evidence of retino-choroidal degeneration. In this sibship myopia was inherited from an affected aniridic father, III 2. IV 16 had a moderate hypermetropia; correction did not improve her distant vision, but was a considerable help with near vision. III 10 had a hypermetropic astigmatism; correction improved his vision slightly.

Cases V 24, 26, 27 and III 10 were examined with the slit-lamp. Cases IV 24 and 26 and III 10 showed the elongated fibres of the suspensory ligament below, placed regularly with no gaps and with a sturdy vitreous behind. IV 27 showed irregular fibres with a gap in the vertical meridian and a grossly degenerate vitreous behind. In IV 15 the suspensory ligament could be clearly seen with a loupe. The mixed astigmatism noted in cases IV 24, 26 and 27 could be explained by the weaker pull of the suspensory ligament below compared with the fibres laterally. None of these cases showed a highly myopic retracted spherical lens correctable with a -14.00 D. sphere, indicating complete absence of traction by the suspensory ligament⁴⁸.

Only in the two youngest were the lenses quite clear. Opacities developed in the second decade, but there was no regular gradation of density as the patients grew older. Dense cataracts were present in IV 3 and 7, whereas III 10, who is much older, had milky opacities present in both nuclei and a suggestion of lamination in the rest of the lens. On making a fundus examination one was conscious of a slight distortion in some cases, probably due to tilting of the lens. In no case was a coloboma of the lens observed. Tremulous lenses were observed in cases IV 24 and IV 3. Rayner

CONSIDERATION OF ANIRIDIA, WITH A PEDIGREE

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Case	Displacement of lens	IRIS	Visual acuity	Tension	Refractive Error	Lens opacities*
IV 27 Age 7		None	R. H.M. L. 6/36	++ +	Mixed astigmatism	—
IV 26 Age 11		None	6/36 with glasses 6/36 6/60 6/36	++ ++	Mixed astigmatism	—
IV 24 Age 15		None	6/24 6/36	+ ++	Mixed astigmatism	—
IV 15 Age 15		None	6/24 6/36	Normal	Not refracted	—
IV 19 Age 18			6/60 6/24	++ N	Not refracted	—
IV 7 Age 19		None	Blind	Normal	Myopia	—
IV 6 Age 21		None	Blind	++ +	Myopia	—
IV 3 Age 28		None	Blind	++ ++	Myopia	—
IV 16 Age 32		None	6/36 / 6/60	Normal	Hypermetropia	—
III 10 Age 44			6/60 with glasses 6/36 6/24 6/18+	Normal	Hypermetropic astigmatism	—
III 7 Age 49		None	1/60 with glasses 6/60 <6/60 H.M. <6/60 H.M.	Normal	Not refracted	—
III 14 Age 64			Blind	++ L. eye enucleated for glaucoma	?	—

(*) For details see case histories

Batten⁴⁹ has recorded a case of bilateral aniridia and ectopia lentis: the R. lens was opaque and the L. partially so at 21 years old. The patient had never seen with the R. eye, but saw with the L. till she was 13 years old. Glaucoma had already developed.

The most striking difference on comparing these 12 patients with the ten having primary uncomplicated aniridia is in the incidence of glaucoma. Seven patients with ectopic lenses have glaucoma, whereas only one of the aniridia patients has slightly raised tension and she is the oldest of the group. Here IV 27, aged 7 has bilateral glaucoma, with an atrophic cupped disc observed, though in some eyes it was difficult to see the disc clearly or at all. Presumably the development of glaucoma is encouraged by the presence of ectopic lenses, but it is not clear why this should be so. Families showing ectopia lentis alone as a hereditary abnormality do not normally have a very high incidence of glaucoma. It will be observed that in five of the seven cases of glaucoma here there is no clinical evidence of any iris tissue present, and this, with possibly the particular formation of the iridial angle, may be a contributory cause of the raised tension.

Miscellaneous findings

The ocular defect is not accompanied by any skeletal abnormality, as, for instance, arachnodactyly, which is sometimes associated with congenital ectopia lentis. There are, however, some miscellaneous defects in the family which may be noted here. IV 7 is excessively fat, with a lazy good-humoured temperament suggestive of a pituitary dysfunction. X-ray examination of the skull revealed "a sella of physiologically small type." His twin brother, IV 8, is normal in all respects. Whilst hypermetropia is the predominating refractive error in this family, one sibship is found in which myopia is inherited from an affected father.

III 2, IV 3, IV 6 and IV 7 are all certified blind. IV 10 has myopia in R. eye only. IV 2 has a small myopia and astigmatic error (with aniridia). IV 13 has about 3 dioptries of myopia in

Mental defect associated with aniridia is reported by Velhagen⁵¹, L. Polte³⁵, Stephenson¹⁰. No cases of subnormal intelligence were encountered in this family, either amongst normal or affected members. A particularly robust sense of humour is noteworthy in many members.

IV 24 has corneae measuring 9 mm. in diameter transversely, with slight ptosis and defective dental enamel. H. Page⁵³ mentions micro-cornea and microphthalmos in an aniridic family, as does A. H. Benson⁵⁴, whilst Hamilton³⁸ and Stephenson¹⁰ record defective dental enamel.

							II							
							2							
						L		L		L	L	L		
III	13	14	15	16	17	18	19	20	21	22	23	24	25	

None of the children of affected members has this lisp, nor from enquiries made does it appear to have been present in the case of II 2 or his wife. The mouths were not examined for any abnormal attachments of the tongue.

Treatment

(a) Cases with colobomata and/or hypoplasia require no treatment.

(b) In cases with aniridia the photophobia, in this family at least, appears to be adequately relieved by dark glasses. McKie Reid⁵⁵ has recorded a case where an adult with aniridia was relieved of his discomfort in bright light by wearing contact lenses with an artificial iris and a central pupil of normal size. His vision was improved to 6/9 by this treatment and troublesome photophobia abolished. This method may be applicable to adults, but in this series it is the children who complain mostly of discomfort. Alger⁴⁰ suggests tattooing of the cornea as being effective in cutting out peripheral light rays, thus abolishing photophobia and maintaining an effective stimulus of the macula, which may be necessary for its normal development. He records a marked improvement in a young girl whom he treated in this way. This method might be satisfactory in young children if a satisfactory technique of tattooing were employed.

For the glaucoma which develops in aniridia trephining may be tried, but there is little reason to suppose it is effective in reducing tension. Wiener and Alvis⁵⁶ bluntly say operative treatment is hopeless. In this series IV 12 had a prophylactic trephine at seven years of age (she is now aged 14 years), but no filtration bleb is visible. She has retained a normal tension, but so have other untreated cases. Hudson⁵⁷ records the case of a baby aged 7 weeks with aniridia and bilateral acute glaucoma, which was relieved by a paracentesis and subsequent trephine operations. Satisfactory intra-ocular pressure was established, but there is no record of the case being followed up. III 14, the only one in the uncomplicated aniridia cases with raised tension, has bilateral cataracts: it may be the development of cataract has been accompanied by some swelling of the lens which has helped to block the iridial angle with rudimentary iris tags.

Eyes with aniridia have an undoubted predisposition to early lens changes, as this series abundantly shows. If the opacities proceed to cause serious impairment of vision, ordinary extraction of the mature lens does not appear to be accompanied by serious technical difficulty or risk. III 2 had a mature lens removed from each eye without any complication and went back later for capsulotomy. There is no report in the literature of a series of extractions in aniridia. DeBeck³³ gives an account of extraction of lenses in two brothers, one with aniridia and the other with bilateral colobomata. Vitreous was lost and cyclitis occurred in each eye, but ultimate vision was good in one eye in each patient

—in each case the eye in which cataract had developed more recently, which led De Beck to suppose that undue delay in operating on an aniridic cataract might make the prognosis poorer. Foster⁵ wrote that “a number of operators have testified that a greater degree of cyclitis or other destructive inflammation attends their removal than is usually the case.” This may possibly be due to the aniridia eye being relatively less vascular in the anterior segment, having no iris framework for vessels, and in consequence, less able to absorb foreign protein from the lens and overcome any slight infection. The risk of complications should not deter an operator from attempting to remove an opaque lens. The patient has nothing to lose. Possibly an intracapsular extraction would be less likely to be attended by subsequent inflammation as there would then be no irritating lens protein left in the anterior chamber. Treacher Collins⁴⁴ records an extraction where the patient regained vision 6/24 with +16 D., and J.4 with +20 D. In younger patients the cataract may be broken up by a needle and will sometimes rapidly absorb⁴², but a rise of tension may occur necessitating repeated paracentesis⁵⁸.

(c) *Aniridia with ectopia lentis*.—As in uncomplicated aniridia, photophobia may be relieved by dark glasses. Tattooing the peripheral areas of the cornea would obscure the lens and make estimation of its later condition difficult. In this series an attempt was made to improve vision by correcting the refractive error. Where possible to make an accurate estimation, refraction through the lens was found to be a mixed astigmatism, due presumably to the unequal pull of the zonule fibres. Correction in a few instances, e.g., III 10 and IV 24, made a little improvement. In no case was the lens found to be highly myopic, which would be expected if the suspensory ligament were defective in its whole circumference, a condition sometimes found in familial ectopia lentis and congenital microphakia. In one case only, III 7, was it possible to improve vision by an aphakic correction, and this in spite of the fact that the lens came well down in the pupil.

It is difficult to escape the conclusion that it is the ectopia lentis in combination with aniridia which is responsible for the high percentage of glaucoma in this series. To prevent the development of glaucoma by an early attack upon the lens would therefore appear to be the most rational procedure. Development of opacities in the lens are not necessary to produce glaucoma. The presence of an atrophic and cupped disc on R. side and raised tension on L. in case IV 27 at the age of seven years suggests that treatment at the earliest possible age is indicated. As removal of the lens would be a very hazardous procedure, almost certain to be accompanied

by vitreous loss on account of the difficulty of getting behind an upwardly dislocated lens, the first measure should be a needling of the lens in the hope of rapid absorption. If this were successful the eye would then be in the position of aniridia only with its more favourable prognosis, and the awkward optical disabilities caused by a dual refractive system would be removed. It would be possible to make a simple aphakic correction without the intervention of the lower border of the lens. If raised tension should develop after absorption of the lens, a trephine could be tried.

Case Histories of Aniridia Family

I 2. This man's eyes are known to have been abnormal.

II 1. According to his eldest son, this man's eyes were affected with the family complaint, but he was able to work as an agricultural labourer till well over 70. When very old he could see to fell trees and, in fact, was never obliged to retire because of poor sight.

II 2. J. W. This man's vision began to deteriorate when he was about 58 years old. He had looked after a pumping station in the Fen country satisfactorily, but during the last 20 years of his life his vision was very defective.

III 1. Deceased. Had normal eyes.

III 2. W. G. W., aged 57 years. This man's vision was never very good. It began to deteriorate seriously about 30 years ago. In 1922 he was admitted to the Royal Eye Hospital for a R. extraction and needling, and the L. eye was operated on in the following year. The lenses were opaque but there is no reference to ectopia lentis.

There is no clinical evidence of the iris. Both eyes are aphakic: some posterior capsule is visible in both eyes. Tension—normal both eyes. Refraction—+8.00 D. sph. +2.00 D. cyl. at 180 deg. Both fundi show myopic crescents and some central retinal degeneration. L. eye has a marked divergent squint. Vision—hand movements only. Prefers to wear slightly tinted glasses.

III 3. Normal eyes and vision.

III 4. III 5. Both males which died in infancy. Their eyes were normal.

III 6. Mr. S. W., aged 50 years. This man was in the 1914-1918 war. He now works in a brickyard and rides a bicycle to his work. Does not wear glasses. He gets very slight photophobia in bright light.

R. eye:—Complete clinical aniridia present. Tension normal. Slight central anterior lens opacity present and a wedge-shaped opacity which appears to involve whole thickness of lens at 5 o'clock. Vision—5/60.

L. eye:—Very narrow strip of iris present on nasal side. Tension normal. Milky nuclear opacity of lens present and a wedge-shaped opacity at 5 o'clock, as in other eye. Vision 6/60.

Patient himself thinks his vision has not declined in recent years, but his brothers are quite sure it has. No abnormality seen in fundi, but foveal reflexes could not be seen on account of lenticular opacities.

III 7. Mrs. F. M. This woman is a housewife. She has brought up four children and still manages to do house work.

R. eye:—Complete clinical aniridia present, with upward dislocation of lens. Slight opacities present throughout lens. Fundus seen through aphakic area appears normal. Tension—normal. Can read J.10. Distant vision is 1/60, but with a +11.00 D. sphere vision improves to 6/60.

L. eye:—Marked divergent squint present. Complete clinical aniridia, with upward dislocation of lens. Moderately dense opacities present throughout lens. Fundus not seen through aphakic area on account of vitreous haze. Vision—hand movements only. Tension—normal.

III 8. Female baby which died in infancy: normal vision.

III 9. Mrs. H. W., aged 46 years. This woman, unlike her brothers and sisters, has worn glasses for many years. A very fine *vertical* nystagmus is present in both eyes.

R. eye:—A narrow fringe of blue iris is present round the whole circumference, with a gap between 4 and 6 o'clock. The iris has a dark pigmented fringe, which looks like proliferation of the ectodermal layers. A small central anterior polar cataract is present with a circle of less dense opacities on the anterior capsule, paracentral in position. Vision 6/18; wears about +3.00 D. spheres. Macular area seen on this side, with brisk foveal reflex.

L. eye:—A narrow fringe of iris, blue in colour, is present, except for a gap between 3 and 5 o'clock. A central anterior polar cataract present, with a paracentral ring of capsular opacities. Fundus normal, except that foveal reflex could not be observed. Vision 6/60.

III 10. Mr. S. W., aged 44 years. This man is not troubled in bright light. Beyond 5 or 6 yards away he cannot recognize anybody. Is an agricultural labourer.

R. eye:—Very narrow fringe of iris present on nasal side. Lens is dislocated upwards and slightly outwards. With slit-lamp regularly disposed fibres of the suspensory ligament could be clearly seen in the aphakic part of the eye. The lens showed a central nuclear milky opacity, with opacities surrounding this showing a tendency to lamination. Slight tremulousness of lens seen with slit-lamp. Tension—normal. Vision R. 6/60, improved to 6/36 with +1.50 D. cyl. at 170°.

L. eye:—Condition of iris and lens as described in *R. eye*. Lens slightly tremulous when viewed with slit-lamp. Tension—normal. Vision 6/24; with +0.75 D. sph. +1.0 D. cyl. 90° vision improves to 6/18+.

III 11. Female child which died in infancy. Eyes normal.

III 12. Mrs. P. M., aged 40 years. Slight hypermetropic error (+1.00 D. sphere), otherwise eyes are normal.

III 13. Mr. W. W., deceased. Eyes were normal.

III 14. Mr. E. W., aged 64. This man's vision has always been poor, but 10 or 11 years ago it became too bad for working. Prior to that he could work in the stockyard if cattle were brought to him, but he could not work in the fields.

R. eye:—A very narrow fringe of iris is present in the upper nasal quadrant, extending from 12 o'clock to 4 o'clock. The lens is ectopic, displaced directly upwards. Lens is opaque throughout, but less so in the upper nasal and upper temporal periphery. Lens is tremulous. A good red reflex is visible in aphakic part of eye, but no view of retina could be obtained as vitreous is hazy. Suspensory ligament could not be seen below. Tension—++ . Vision—perception of light.

L. eye:—This was enucleated seven years ago following five of pain and redness in the eye. It had been blind for many years. Unfortunately, a pathological examination of the eye was not made.

III 15. Mrs. M. A. G. Normal eyes and normal vision.

III 16. Mrs. E. T. Patient is a housewife who brought up five children. She saw fairly well until about seven years ago, when her vision began to fail. Earlier in life she was tried with glasses, but these did not help her.

R. eye:—Partial aniridia present. A narrow band of blue iris extends from 9 o'clock to 5.30 o'clock, with a deeply pigmented inner fringe. The lens is uniformly opaque, having a mother-o'-pearl appearance. There is good projection of light in the eye. Tension—slightly raised.

L. eye:—Divergent squint present. Has never been able to see much with this eye. Partial aniridia present: the iris is slightly broader than on *R. side*, being completely absent between 6 o'clock and 3 o'clock. Paracentral opacities are present posteriorly in the lower temporal and nasal quadrants of the lens. Slight hazy opacity is present throughout the lens. The fundus can be faintly seen through the lens and appears normal. The appearance is that of a hypermetropic eye. Tension—slightly raised.

III 17. Normal eyes.

III 18. Mrs. A. R., deceased. This woman had abnormal eyes, but whether she had ectopia lentis is not known. She died of carcinoma at age of 54, but

for some years before her death vision had deteriorated very much. She had a lisp.

- III 19. Mr. F. W. Normal eyes.
- III 20. Mr. A. W. Normal eyes. Has a lisp.
- III 21. Mr. Z. W. Normal eyes.
- III 22. Mrs. F. L. Normal eyes. Has a lisp.
- III 23. Mr. L. L. Normal eyes. Has a lisp.
- III 24. Mr. H. W. Normal eyes. Has a lisp.
- III 25. Mr. S. W. Normal eyes.

IV 1. Has normal eyes.

IV 2. Mr. J. W. Has normal eyes and good vision. Was recently discharged from the Army and now works as a signalman on the railway.

IV 3. Mr. W. G. W. This man was certified as blind at age of nine years. Prior to that he had been able to see to go to school. He is now a basket-maker.

R. eye :—No iris visible. Lens is displaced upwards and outwards into the upper temporal quadrant of the cornea. It is uniformly opaque. A good view of the fundus is obtainable through aphakic area: the retina shows extensive central degeneration. Disc is very pale. Tension—++ . Vision—no perception of light.

L. eye :—No iris visible. The lower part of the displaced lens is present in the upper nasal quadrant of the "pupil" and is uniformly opaque. It is also tremulous. The fundus cannot be seen through the aphakic area on account of a very hazy vitreous. Tension—++ . No perception of light present.

IV 4. Miss M. P. W. Eyes normal. Vision 6/5:6/5.

IV 5. Miss V. W., aged 24 years. Eyes normal, apart from chronic blepharoconjunctivitis.

IV 6. Mr. K. W. This man works in a blind institute as a basket-maker.

R. eye :—Complete clinical aniridia. Lens is displaced upwards. There is a very circumscribed dense opacity, central in position, involving the capsular and subcapsular tissues. Lateral nystagmus present. *R. disc* is pale and atrophic and the whole fundus has appearance of a very myopic eye. Tension—+ . Vision—approximately 1/60.

L. eye :—Complete clinical aniridia. Lens is displaced upwards and slightly nasalwards. Slight superficial central opacities of the lens. Vitreous is hazy on this side, but fundus appearance suggests greater myopia than on *R. side*. Tension ++ . Vision—1/60. Nystagmus present.

IV 7. Mr. R. W., aged 19 years. This boy is certified blind. He works at home, working in a small timber business. He is very fat, rather lazy, but generally very good tempered. X-ray of the skull shows a "sella of physiologically small type." He is just able to discern light and darkness.

R. eye :—No iris visible. The lens is displaced upward and slightly towards temporal side: it is opaque and of pearly colour. Inferior to the lens, through the aphakic part of the eye, a dense mass of connective tissue strands can be seen in the vitreous on the temporal side. The fundus cannot be seen. Tension—normal.

L. eye :—No iris visible. The lens is displaced upwards, its lower border reaching about half way down the vertical diameter of the cornea. Diffuse opacities prevent ophthalmoscopic examination through the lens. The retina can be seen through the aphakic area: gross retino-choroidal degeneration is present in the central area, and the eye is obviously a very myopic one. Tension—normal.

IV 8. C. W. This boy is a twin with IV 7, presumably a fraternal twin as there is little physical resemblance. Has a traumatic ptosis of *L. eye*, but otherwise his eyes are quite normal.

IV 9. P. W. This boy has just been discharged from the Marines. His eyes and vision are normal.

IV 10. F. W. No anatomical defect of eyes. *L. eye* is emmetropic, *R.* has 4 dioptres of myopia.

IV 11. C. W. Died at age of 5 months. Eyes were normal.

IV 12. G. W. This girl works as a hospital ward maid. Wears tinted glasses in very bright light. Bilateral trephine operation 7 years ago, but no filtration bleb can be seen.

III 16, Mrs. E.T.

R. eye, focal illumination.

L. eye, red reflex.

IV 7 (R.W.) R. eye, focal illumination.

L. eye, red reflex.

IV 27. R. eye, red reflex.

L. eye, red reflex.

V 8. M.S., aged 4 years, focal illumination.

R. eye :—No iris visible. Lens in normal position and quite clear. Tension—normal. Vision—R. 6/36: small myopic and astigmatic error present, but vision is not improved by this correction.

L. eye :—No iris visible. Lens in normal position and clear. Tension—normal. Vision—L. 6/24. No improvement with small myopic and astigmatic correction. Both fundi normal, but poorly pigmented. Near vision with both eyes together is J.4.

IV 13. S. W., aged 13 years. This girl has 3.0 dioptres of myopia. Both retinæ show numerous small pigmented spots in the periphery. A large arterial loop is present on L. optic disc, extending forwards into the vitreous.

IV 14. D. W. Says she has slight discomfort in bright light. Examination with ophthalmoscope causes some lachrymation.

R. eye :—No iris visible. Lens is in normal position. Scattered opacities are present on anterior capsule and in anterior cortex of lens, especially peripherally. Fundus normal; foveal reflex seen. Small hypermetropic error present. Tension—normal. Vision 6/24.

L. eye :—No iris visible. Lens clear and in normal position. Fundus normal: macular area normal, with brisk foveal reflex. Tension—normal. Small hypermetropic error present. Vision 6/18.

IV 15. Aged 15 years. Works on the land. Does not wear 'glasses. Cycles to his work.

R. eye :—No iris visible. Lens displaced upwards and slightly towards temporal side. Small grey opacities present in periphery of lens. View of fundus through the lens is distorted (? due to some tilting of the lens). Through the aphakic part the fundus appears to be normal: a good foveal reflex present. With a loupe the elongated fibres of the suspensory ligament can be clearly seen below the lens. Tension—normal. Vision—6/24.

L. eye :—No iris visible. Lens displaced upwards, with fibres of suspensory ligament clearly visible with loupe. Slight diffuse opacities present in lens. Disc visible through both lens and aphakic part. Foveal reflex not seen on L. Vision—6/36. Tension—normal. With both eyes can read J.4, holding print very close to eyes.

IV 16. Mrs. E. S., aged 32 years. Says she sees well, but is "a bit short-sighted." Not troubled by photophobia. She sees exceptionally well at night. Both corneal are small.

R. eye :—No iris visible. Lens displaced upwards very slightly. Very slight central anterior opacity of lens, with more marked paracentral opacity. Tension—normal. Vision—6/36. Reads J.12.

L. eye :—No iris, and lens dislocated as in *R. eye*. Slight paracentral opacity in lens anteriorly. Tension—normal. Reads J.14. Vision—6/60.

This woman has +3.00 dioptres hypermetropia in both eyes. Correction does not improve distant vision, but helps considerably for near work.

IV 17. I. M., aged 28 years. Normal eyes. Vision 6/6 : 6/6.

IV 18. I. M., aged 19 years. Normal eyes. Vision 6/6 : 6/6.

IV 19. Mr. O. M., aged 18 years. Works as farm labourer. Has very good physique.

R. eye :—Slight fringe of brown iris present above, extending from 9.30-3.30 o'clock, with a slight constriction at 1 o'clock. Lens is dislocated upward and slightly nasalwards, with lower edge of lens midway across the anterior chamber. Lens is slightly opaque throughout, with denser opaque dots in lower periphery. Vitreous slightly hazy. Fundus not clearly seen, but peripheral parts appear to be healthy. Tension—+ +. Vision—6/60.

L. eye :—Slightly wider fringe of iris present, extending from 7.30-3.0 o'clock. Lens dislocated upwards and nasalwards. A wedge-shaped opacity present in posterior part of lens between 4.5 o'clock but lens otherwise clear. Vitreous clear. Tension—normal. Vision—6/24. Reads J.6.

IV 20. Mr. W. W., aged 22 years. This man served in the army in the Middle East. He was not particularly troubled by photophobia.

R. eye :—An extremely narrow fringe of blue iris is present on nasal side between 2.5 o'clock. Lens in normal position. Fundus—normal. Tension—normal. Vision—6/24. Good foveal reflex seen.

L. eye :—Very narrow fringe of iris present except between 2.30-5.0 o'clock where there is complete absence. At 9 o'clock and at 12 o'clock there is a proliferation of pigmentary (posterior) layers of iris. There is a small dense localized opacity on anterior capsule in lower temporal quadrant of lens. Fundus—normal. No foveal reflex seen. Tension—normal. Vision—6/18.

Both eyes have a hypermetropic error of +2.50, but this correction does not improve vision.

IV 21. Miss N. W. Normal eyes.

IV 22. B. W. Normal eyes.

IV 23. D. W.

R. eye :—The green stroma of iris has five gaps in it, shaped like petals of a flower, revealing the pigmented deeper layers. Pupil is of normal size. Fundus—normal. Vision—6/6 and J.2.

L. eye :—There is a partial (pupillary) coloboma of iris at 4.30 o'clock. The gap in the superficial stroma is filled in with proliferated pigment layers, so that pupillary red reflex is quite circular. Pupil reacts very feebly to light. Fundus—normal. Vision—6/6 and J.4.

IV 24. S. W., aged 15 years. Marked photophobia in bright light. Sclerotics are "duck-egg" blue shade. Corneae are small (9 mm. horizontal diameter), some ptosis present and palpebral fissure small. (An attempt was made to take a Schiötz reading, but there was insufficient room to accommodate the base of the instrument between the opened lids. Dental enamel is defective.

R. eye :—Complete clinical aniridia present. Lens dislocated upwards. Elongated fibres of suspensory ligament clearly seen below with slit-lamp. Lens has diffuse slight opacities, but of no special distribution. Lens slightly tremulous and appears to be tilted backwards above. Tension +. Mixed astigmatism present, but will accept only -3.00 D. cyl. at 165 deg., with which he sees 6/24. This is the same as without glasses, but definition is better. Good view of fundus through lens and aphakic portion of eye. Fundus—normal.

L. eye :—Aniridia complete. Position and condition of lens as for *R. eye*. Tension ++. Mixed astigmatism present, but accepts -2.00 D. cyl. at 180°, with which he sees 6/36. Good view of fundus not obtained because of slight vitreous haze. Lens slightly tremulous. Elongated fibres of suspensory ligament clearly seen.

IV 25. J. W., aged 14 years Normal eyes.

IV 26. S. W., aged 11 years. Marked photophobia in bright light. Blue sclerotics present.

R. eye :—No iris present. Lens dislocated upwards. Lens clear but fundus difficult to see because of ? tilting of lens. Disc clearly seen through aphakic part of eye: fundus appears normal. Tension ++. Vision—6/36. Mixed astigmatism present. Sees J.14, holding print very closely to eye.

L. eye :—No iris present. Lens dislocated upwards as in *R. eye*, clear and slightly tilted. Aphakic portion clear, but disc difficult to see because of intervention of rim of lens. Tension ++. Vision—6/60, but improves to 6/36 with -2.50 D. cyl. at 180°. A mixed astigmatism is present, but the + constituent is not accepted. Vision is not improved on either side by correction of the aphakia. Sees J.14.

IV 27. J. W., aged 7 years. Schoolgirl.

R. eye :—Complete aniridia. Lens dislocated upwards. Lens and vitreous clear. An atrophic and cupped disc present, with no central vessels but all emerging from periphery of disc. Tension ++. Vision—6/60 and J.16, held very close. Mixed astigmatism present.

L. eye :—Complete aniridia. Lens clear, but dislocated upwards. *L. fundus* healthy. Tension +. Vision—6/36 and J.16. Vision not improved by correction (mixed astigmatism).

With the slit-lamp the elongated fibres of the suspensory ligament on each side could be seen very irregularly disposed and with a wedged shaped gap between 5.30 and 6.30 o'clock, suggestive of colobomata. The vitreous beyond was fluid and degenerate. A needling of *R. lens* was recently performed. This was followed by a lowering of intra-ocular tension, except for a transient rise lasting one day. The lens is now in process of absorption.

IV 28. W. W., aged 3 years. Normal eyes.

IV 29. Normal eyes.

IV 30-43. Normal eyes.

IV 44. G. W. T., aged 40 years. Is a carman. This man has no children, so that his genetic potentialities are not known.

R. eye :—Partial coloboma of iris present at 9 o'clock. Several areas of hypoplasia of stroma showing deeper pigmented layers in base of gaps. Some proliferation of posterior pigmented layers present in region of coloboma. One long strand of persistent pupillary membrane present. Lens and fundus normal. Vision—6/5.

L. eye :—Partial coloboma at 4.30 o'clock. Four small areas of hypoplasia of stroma, showing pigmented posterior layers of iris. One small area at 5.30 o'clock in which all layers of iris are absent and a good red reflex can be seen. Some

IV 45. Mrs. M. S. Left eye by focal illumination.

proliferation of posterior pigmented layers in region of coloboma. Lens and fundus—normal. Vision—6/6.

IV 45. Mrs. M. S., aged 38 years. This woman's eyes at a casual glance would pass for normal.

R. eye :—Normal except for a gap in the superficial stroma and proliferation of deeper pigmented layers at the pupillary margin, between 7-9 o'clock. Lens and fundus—normal. Vision—6/5.

L. eye :—A small area of hypoplasia of iris stroma at 6 o'clock, showing deeper pigmented layers. A few strands of stroma can be seen passing over the area. Three other smaller such areas are present in the lower temporal region. At the pupillary margin the stroma is deficient from 4-9 o'clock, with proliferation of posterior pigmentary layer. Lens and fundus—normal. Vision—6/12.

IV 46. Mrs. B. Normal eyes.

IV 47. Mr. J. T., aged 32 years. This man works in a sand-pit.

R. eye :—Cornea normal. A thin fringe of iris extends from 7.30 to 5 o'clock, with an area from 5 to 7.30 o'clock; completely without iris. The lens has a superficial paracentral opacity just below anterior capsule, and a deep opacity in the lower nasal quadrant. Fundi—normal. Tension—normal. Vision—6/36 with correction (+6.00 D. sphere) improves to 6/12.

L. eye :—Same distribution of iris as in the right eye. Deep lens opacity present in lower temporal quadrant. Fundus—normal. Tension—normal. Vision—6/36, with correction (+6.00 D. sphere) improves to 6/12.

There may be some impairment of accommodation present here, as he sees to read very much better with +7.00 D. The extra dioptré considerably impairs his distant vision.

IV 48. Mr. E. W. Normal eyes. Was a driver in the army.

IV 49-56. Normal eyes.

IV 57. Mr. W. R. This man is a lorry driver by trade. Was passed A1 for army and accepted for railway work.

R. eye:—Partial coloboma of iris down and out, with proliferation of pigmented posterior layers to fill the gap. Six small areas of localized hypoplasia of iris stroma. Lens and fundus—normal.

L. eye:—Partial coloboma of iris down and out, with same pigmentary proliferation as on R. side. Four areas of hypoplasia here in lower temporal quadrant. Lens and fundus—normal.

This man is not married and therefore his genetic potentialities are not known.

IV 58. Mrs. E. R., aged 30 years. Housewife. Sees well. Slight discomfort in bright light.

R. eye:—Small fringe of pale blue iris present extending from 10.30 to 4 o'clock, with notch at 1 o'clock. Lens not dislocated. A very faint central capsular opacity, with several flecks of thicker opacity present in inferior quadrants. Tension—normal. Fundus shows some small patches of old choroiditis in upper temporal quadrant. The anterior capsule of lens is flecked with numerous fragments of pigment, the usual legacy of an attack of iritis.

L. eye:—Fringe of iris extending from 8 to 1.30 o'clock. A slight central anterior capsular opacity present. Fundus and Tension—normal.

IV 59-75. All normal eyes.

V1 and V2. Normal eyes.

V3 D. W., aged 2 years.

R. eye:—complete aniridia. Lens is completely clear: equator of lens can be seen all round. Fundus appears normal, but disc and macular area difficult to see on account of child's restlessness.

L. eye:—As on R. side. A slight central opacity is present on anterior capsule of lens.

V4-7. Normal eyes.

V8. M. S., aged 4 years. This child is troubled by photophobia in bright light. She has a R. convergent squint, which has been present for two years.

R. eye:—Iris present, though narrower than normal iris and with a crenated pupillary margin, between 7.30 p.m. and 5 o'clock. Lens is not dislocated, but lower edge can be seen below. Fundus—normal. Vessels tortuous.

L. eye:—Large coloboma iris between 5.30 and 7 p.m. Lens in normal position and lower edge visible.

Precise vision not determined: each eye has a refractive error of +3.50 D. sph. and +1.00 D. cyl. at 90°

V9-V20. Normal eyes.

I am very much indebted to Mr. Esmond Recordon for introducing me to this family and for his generous encouragement and advice. Dr. R. R. Race very kindly did the blood examinations.

REFERENCES

1. BELL, JULIA (1932).—Treasury of Human Inheritance, Vol. II, Part V.
2. ——— (1934).—*Nature*, Vol. CXXXIII.
3. RISLEY, S. D.—Hereditary Aniridia. An Interesting Family History. *Jl. Amer. Med. Assoc.*, Vol. LXIV, 1915.
4. DUKE-ELDER, W. S.—Text-book of Ophthalmology, Vol. II, p. 1300.
5. FOSTER, M. L.—Congenital Irideremia. *Arch. of Ophthalm.*, Vol. XXVII, pp. 593-615, New York, 1898.
6. WAARDENBURG, P. J.—Modern Trends in Ophthalmology (Ridley and Sorsby), p. 119, 1940.

7. CORNER, G. W. (1944).—Ourselves Unborn. Terry Lectures. Yale University Press, p. 99.
8. COCKAYNE, E. A. (1933).—Inherited Abnormalities of the Skin, p. 32.
9. MANN, IDA.—*Trans. Ophthal. Soc. U.K.*, Vol. LIII, 1933.
10. STEPHENSON, S.—Irideremia in Two Brothers. *Trans. Ophthal. Soc., U.K.*, Vol. XVI, London, 1896.
11. DRINKWATER.—Quoted by Julia Bell. Treasury of Human Inheritance. Vol. II, part V, p. 530 (no original article).
12. SHROTER, P. Quoted by Julia Bell. Treasury of Human Inheritance. Vol. II, part V, p. 526.
13. COCKAYNE, E. A. (1933).—Inherited Abnormalities of the Skin, p. 31.
14. HALDANE, J. B. S. (1935).—The Rate of Spontaneous Mutation of a Human Gene. *Journal of Genetics*, Vol. XXXI, pp. 317-326.
15. MOLLENBACH (1944).—"Mutation as a Cause of Disease." *Acta Path. et Micro. Scand.*, Supp. 54. Article by Tage Kemp.
16. COCKAYNE, E. A. (1933).—Inherited Abnormalities of the Skin, p. 35.
17. WAARDENBURG, P. J. (1940).—Modern Trends in Ophthalmology (Ridley and Sorsby), p. 102.
18. BAUR, FISCHER and LENZ.—Human Heredity, p. 241.
19. FRASER ROBERTS.—Introduction to Medical Genetics.
20. CORNER, G. W. (1944).—Ourselves unborn. Terry Lectures. Yale University Press, p. 110.
21. COLLINS, TREACHER (1893).—*Trans. Ophthal. Soc. U.K.*, Vol. XIII, p. 128.
22. MANN, IDA (1937).—Developmental Abnormalities of the Eye, p. 240.
23. ——— (1924).—Coloboma Iridis and its Embryology. *Trans. Ophthal. Soc. U.K.*, Vol. XLIV.
24. ——— (1937).—Developmental Abnormalities of the Eye. P. 244.
25. CORNER, G. W. (1944).—Ourselves unborn. Terry Lectures. Yale University Press, p. 104.
26. MANN, IDA (1935).—*Glas. Med. Jl.*, Vol. CXXIV, p. 64.
27. COATS, GEORGE (1910).—*Ophthalmoscope*, Vol. VIII, p. 766.
28. COLLINS TREACHER.—*Trans. Ophthal. Soc. U.K.*, Vol. XIII, p. 133.
29. DUKE-ELDER, W. S.—Text-book of Ophthalmology, Vol. II, p. 1300.
30. LINBERG, J. G.—Treasury of Human Inheritance, Vol. II, Pt. V (Julia Bell), p. 531, and Holm's Case, p. 528.
31. LICSKO, A. (1927).—Treasury of Human Inheritance (Julia Bell), Vol. II, Pt. V, p. 524.
32. THEOBALD, S. (1888).—Treasury of Human Inheritance (Julia Bell), Vol. II, Pt. V, p. 525.
33. DE BECK, D. (1897).—A Family History of Irideremia and Coloboma Iridis. *Trans. Amer. Ophthal. Soc.*, Vol. VII.
34. CROSS, F. R. (1895).—Congenital Anomalies of Iris. Clinical Sketches, Vol. I, pp. 104-106.
35. POLTE, L. (1908).—Several Cases of Congenital Anomaly of the Iris. *Arch. of Ophthal.*, Vol. XXXIII.
36. SNELL, S. (1908).—Coloboma of Iris in Each Eye Occurring in Five Generations. *Trans. Ophthal. Soc. U.K.*, Vol. XXVIII.
37. WAARDENBURG, P. J. (1919).—Treasury of Human Inheritance (Julia Bell), p. 532.
38. HAMILTON, T. K. (1905).—A Family with Irideremia. *Ophthalmoscope*, Vol. II, pp. 481-488.
39. HOLM, E. (1921).—Treasury of Human Inheritance (Julia Bell), Vol. II, Part V, p. 528.
40. ALGER, L. G. (1945).—*Amer. Jl. Ophthal.*, Vol. XXVIII, pp. 730-735.
41. NUNNELEY, T. (1861).—Congenital Malformation of Eyes in Three Children of One Family. *Lancet*, Vol. II, pp. 569-570.
42. NUNNELEY, J. A. (1877).—Cases of Irideremia Totalis. *Lancet*, p. 754.
43. BELL, JULIA (1932).—Treasury of Human Inheritance, Vol. II, Pt. V, p. 470.
44. COLLINS, TREACHER.—*Ophthal. Rev.*, Vol. X, p. 101.
45. JULER, H. (1902).—Aniridia. *Ophthal. Rev.*, Vol. XXI, pp. 22-23.
46. BROOK-LÉWIS, J. (1926).—Aniridia in Four Generations. *Med. Jl. of Australia*, Vol. I, p. 489.

47. BLAIR, C. and POTTER, B. (1903).—Two Cases of Aniridia and one of Coloboma of the Iris in the same Family. *Trans. Ophthal. Soc. U.K.*, Vol. XXIII.
48. CLAPP, C. A. (1944).—*Amer. Jl. of Ophthal.*, Vol. XXVII, No. 7. (Included in Collected Reprints of Wilmer Institute of Ophthalmology).
49. BATTEN, RAYNER (1900).—Congenital Aniridia and Displacement of Lenses with Glaucoma. *Trans. Ophthal. Soc. U.K.*, Vol. XX, p. 192.
50. MOHR, W. (1895).—Treasury of Human Inheritance (Julia Bell), Vol. II, Pt. V, p. 527.
51. VELHAGEN, C. (1923).—Treasury of Human Inheritance (Julia Bell), Vol. II, Pt. V, p. 532.
52. TIFFANY, F. B. (1900).—*Jl. of Amer. Med. Assoc.*, Vol. XXXIV, pp. 1043-1044.
53. PAGE, H. (1874).—Transmission through Three Generations of Microphthalmos, Irideremia and Nystagmus. *Lancet*, Vol II, p. 193.
54. BENSON, A. H. (1878).—Congenital Irideremia of Both Eyes. *Brit. Med. Jl.*, Vol. II, p. 359.
55. REID, A. MCKIE (1938).—Case of Congenital Aniridia fitted with Pigmented Contact Glasses. *Trans. Ophthal. Soc. U.K.*, Vol. LVIII, p. 434.
56. WEINER and ALVIS (1939).—Surgery of the Eye. P. 134.
57. HUDSON, A. C. (1921).—*Trans. Ophthal. Soc. U.K.*, Vol. XLI, p. 274.
58. GIFFORD, S. (1926).—Congenital Aniridia. *Amer. Jl. Ophthal.*, Vol. IX, 1924.

INDUCTION OF AN EXPERIMENTAL TUMOUR OF THE LENS*

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It is a curious fact, hitherto ignored by pathologists, that neoplasms of the lens are unknown to ophthalmologists. It is often stated by students of cancer that any tissue or organ capable of cell division may be the site of a malignant neoplasm, yet the lens, as far as we know, in spite of the fact that mitoses occur in the subcapsular epithelium throughout life, never produces a cancer. This immunity may theoretically be due to various causes. It might be that the cells of the lens vesicle are inherently from the beginning resistant to malignant change. This would be strange since, if it were true, the lens would stand practically in a class by itself. It might also be that the presence of the capsule inhibits new growths of the lens, either by the tension it exerts or by its properties of a semipermeable membrane, preventing access of the required stimulus to the lens cells. That this is not the case is obvious, since lenses with ruptured capsules never become malignant. A third possibility is that the lens owes its immunity

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