

DEPOSITED BY THE FACULTY OF
GRADUATE STUDIES AND RESEARCH



LENS-RUPTURE

A New Recessive Gene in the Mouse

by

Moe Lionel Herer

A Thesis submitted to the Faculty of
Graduate Studies and Research, McGill
University, in Partial Fulfilment of
the Requirements for the degree of

Master of Science

TABLE OF CONTENTS

	Page
I. INTRODUCTION	
A. General Introduction	1
B. Review of Literature	
(1) The normal eye	2
(2) Reports on anomalies similar to lens-rupture..	3
II. EXPERIMENTAL WORK	
A. Materials and Methods	9
B. Genetics	
(1) The hereditary nature of lens-rupture	11
(2) Linkage Studies	13
(a) Test for linkage with albino	13
(b) Test for linkage with flexed-tail anemia.	14
(c) Test for linkage with waved ²	16
(d) Test for linkage with shaker ²	17
(e) Test for linkage with Agouti	18
(f) Test for sex-linkage	19
(g) Test for partial sex-linkage	19
(3) Conclusions	21
C. Observations on lens-rupture and normal eyes	
(1) Macroscopic	23
(2) Dissection	29
(3) Histology	34
III. DISCUSSION	
A. Genetic Data	36
B. Physical observations	37
C. Theories of Pathogenesis	37
D. Conclusions	41
IV. SUMMARY	43
V. ACKNOWLEDGEMENTS	44

VI. BIBLIOGRAPHY	45
VII. DESCRIPTION OF PLATES	51

1. INTRODUCTION

A. General Introduction

Lens-rupture, the eye anomaly discussed in this thesis was first observed in 1946 by Dr. F. C. Fraser in the F_2 of a cross between the albino A strain and an inbred albino stock homozygous for the flexed tail (f) gene.

Observations of the parent strains showed the flexed tail albino stock to be similarly affected.

The condition is termed lens-rupture because it involves extrusion of the nucleus of the lens, through a rupture in the lens capsule, into the vitreous chamber of the eye.

B. Review of literature

(1) The normal eye

Histogenesis of the eye in the normal house mouse and other mammals has been investigated and reported on by Chase and Chase (1941); Jordan and Kindred (1942); Mann (1928, 1937); Keeler (1927); Keeler, Sutcliffe and Chafee (1928); and Loeffler (1929).

A brief description of the normal mouse eyeball (Fig. 1) based on their reports is presented below.

The eyeball consists of three concentric coats enclosing a cavity filled with three of the four light refracting media. The coats are (1) an external fibrous sheath divided into (a) a proximal white part, the sclera and (b) a distal transparent part, the cornea; (2) a vascular and muscular middle layer divided into (a) a proximal part, the choroid, (b) a distal part, the iris, which controls the diameter of the pupil and (c) the ciliary muscle, with attached ciliary ligaments holding

the lens in place behind the iris; (3) an internal nervous coat, the retina which surrounds the proximal side of the vitreous body.

The refracting media are (1) the cornea, (2) the aqueous humor, which lies proximal to the cornea, and is contained in a space divided by the iris into the anterior and posterior aqueous chambers, (3) the large, crystalline lens, behind the iris, and (4) the vitreous body which occupies the proximal portion of the interior of the eyeball. The hyaloid artery which in the embryonic eye springs from the optic pit and supplies the lens usually degenerates shortly after birth, but may persist in normal mouse eyes as late as four months of age.

(2) Reports on anomalies similar to lens-rupture.

Genes causing pathological conditions in the eye are known in mice as in other mammals. No report has been found of a condition identical with lens-rupture. Conditions bearing some similarities to lens-rupture are well-known. In the sections below several of these conditions will be outlined.

Cohrs (1933) described a condition in the

house mouse which he had observed in histological preparations after the breeding stock had been killed off. He reported on three animals; one of the three had cataract and persistent hyaloid artery; all showed a loss of the layered structure of the retina, not similar to that occurring in lens-rupture mice. The retina was folded and irregular, and he mentioned the observation of a tear in the lens capsule (linsencapselriss). His illustration (Fig. 2) showed a hollow lens torn away from its ciliary supports.

Koch and Gowen (1933) reported a recessive gene in the house mouse in which they illustrate deformities in the shape of the lens and irregularities in the retina. The writer is at present endeavouring to obtain further information about the anomaly from the authors. (Fig. 3).

Smith and Barrentine (1943) reported a case of cataract in the rat, inherited as a dominant factor which involves irregularities in the shape and decrease in the size of the lens.

Bourne and Gruneberg (1939) reported a recessive gene in the rat responsible for degeneration of the retina beginning at three weeks of age. Later in

life, many of the animals develop lenticular changes which may lead to cataract. Persistent hyaloid artery occurs frequently in their cataract stock and not in normals. The illustration (Fig. 4) of their article shows an exaggerated bulging of the posterior curvature of the lens (posterior lenticonus) containing the lens nucleus pressed up against the posterior lens capsule, which is torn posteriorly. The authors' illustration makes it clear that the terminal lesion they refer to is the equivalent of the ophthalmological term hypermature Morgagnian cataract (a fluid cortical cataract in which a hard nucleus is floating). Gruneberg (1943) states that the condition described may be similar to that reported by Cohrs (1933) in the mouse.

Rochon-Duvigneaud (1928, 1943) reported cases of abnormalities of the lens in moles. The anomalies mentioned and illustrated included lenticonus anterior (Fig. 5), and lens-rupture with extrusion of lens matter as a posterior herniation. (Fig. 6).

No cases of hereditary lens-rupture have been reported as such among humans. Published reports on cases of rupture of the lens include papers by

Shoemaker (1910); Gonzalez (1919); Kaufman (1933); Osterburg (1936); Knapp (1937); Beisbarth (1937); and Ehrlich (1946).

Features commonly mentioned in these reports of rupture of the lens capsule among humans include observations of a lenticonus (posterior or anterior) complicated by the development of hypermature Morgagnian cataract followed by a rupture of the lens capsule resulting in expulsion of liquified lens matter and/or nucleus into either the aqueous or vitreous chambers of the eye. In some cases, glaucoma was observed after rupture of the lens capsule.

Ophthalmologists speculating on the factors involved in such ruptures have proposed the following factors - injury, glaucoma, degeneration of the layers of the posterior lens capsule, persistence of the hyaloid artery, developmental defects, Morgagnian cataract, and heredity.

Berens (1936) states that lenticonus in humans is an anterior or posterior conical protrusion of the lens substance covered by capsule or connective tissue; and that the posterior lenticonus variety is due to the traction

of the hyaloid artery or to fetal defects, or to rupture of the lens capsule.

Wolff (1935) states that lenticonus posterior consists of a protrusion of lens matter into the vitreous chamber and he emphasizes the hypothetical role of the hyaloid artery in such a process.

Stricker (1899) outlined 16 cases of lenticonus which had been observed and reported in humans. He discusses four cases in which the affected individuals demonstrated bilateral lenticonus from which he drew the conclusion that lenticonus is congenital. (present at birth).

Bach (1898) observed three cases of bilateral posterior lenticonus in rabbits and claims that a disturbance in the development of the lens is the cause of posterior lenticonus.

Ophthalmological techniques for observing the early stages of lenticonus in humans are inadequate for gathering data which will distinguish between cause and effect in the manifestations of the processes as similar as

lenticonus and lens rupture. Hypotheses therefore, based on these data, contribute little to the understanding of the true factors involved in humans. A final decision must be based on a histological study of the process of lenticonus in humans.

Ehrlich (1946) discussed a case of lenticonus in man described by Zavalía and Oliva (1939) in which two brothers developed uncomplicated anterior lenticonus at puberty, one unilaterally. Because the parents were cousins, Ehrlich believed that "this emphasizes the role of heredity in their report, ... although apparently it plays no part in any of the cases mentioned elsewhere in this paper."

Numerous cases of lenticonus (posterior and anterior) have been reported and described in man. References to these articles will be found in the Bibliography under the title reports on lenticonus.

II. EXPERIMENTAL WORK

A. Materials and Methods

The mouse strains used during the course of these investigations were the flexed-tail stock, the A stock and the BAGwa² sh² stock. Observations were made on normal and lens rupture mice at intervals throughout life.

A low power dissecting microscope was used for in vivo observations of normal and lens-rupture eyes. When non-albino mice were examined, one drop of 1% homatropine was applied to the cornea of each eye thus causing dilation of the pupil and facilitating examination of the vitreous segment of the eyeball.

Where post mortem examinations of mouse eyes were required, the mouse was killed by severing the spinal cord in the cervical region, macroscopic observations having been made and recorded immediately prior to death. The eyes of the freshly-killed mouse were instantly removed and fixed in Bouin's Picroformol.

For histological examination eyes were embedded in paraffin or celloidin and stained with Harris' haematoxylin and eosin.

For purposes of dissection, whole eyes were

removed from fixative and mounted on slides 1" square in soft paraffin (colored by the addition of carbon black) which was allowed to solidify about them. The eyes were then dissected under water on the stage of a binocular dissecting microscope and observations recorded. In some instances the dissections were photographed.

For measurements at the scleral-corneal junction, a standard microscope was used. (2X lens and 7X micrometer ocular).

B. Genetics

(1) The hereditary nature of lens-rupture

Reciprocal matings of lens-rupture mice with individuals from normal strains (A strain; BA²Agwa²sh strain) produced 11 litters totalling 64 (32♂:32♀) offspring, all phenotypically normal after 12 weeks of age.

Crosses among lens-rupture mice produced 53 litters totalling 301 (149♂:152♀) offspring of which 295 were affected by nine weeks of age; 6 (4♂:2♀) of the (in four litters) progeny remain phenotypically normal at 5 months.

170 (75♂:95♀) progeny were produced in 22 F₂ litters. Of these 41 (22♂:19♀) showed the character by 9 weeks of age. This is approximately the 1:3 ratio expected if the inheritance of the condition is controlled by a simple recessive gene. (E = 42.5 : 127.5; P = .8 - .9 - see table I).

21 backcross litters were produced totalling 160 (78♂:82♀) progeny of which 73 (39♂:34♀) were affected by nine weeks of age. The ratio of 73 affected; 87 normal progeny approximates the 1:1 ratio expected on the basis of simple recessive inheritance. (E = 80:80; P = .3 - .5 - see table I).

We therefore conclude that the lens-rupture

condition is the manifestation of a recessive gene and suggest that it be represented by the symbol lr. Based on matings of lens-rupture mice inter-se in which 295 of 301 offspring were phenotypically affected, we derive an expressivity value of 98% for the lens-rupture gene.

Table I

Data Used to Establish the Genetic Nature of the Lens-Rupture

	<u>Condition</u>			
Mating Class	Lr/Lr x lr/lr	lr/lr x lr/lr	Lr/lr x Lr/lr	Lr/lr x lr/lr
Normal ♂	32	4	53	39
Normal ♀	32	2	76	48
Lens-Rupture ♂	0	145	22	39
Lens-Rupture ♀	0	150	19	34
E* Lr/lr	64/0	0/301	127.5/42.5	80/80
Number of Litters	11	53	22	21
Total	64	301	170	160
χ^2 *	0	.119	.052	.612
P	.99	.7-.8	.8-.9	.3-.5

* Based on the expectancy that lens-rupture is inherited as a simple recessive gene.

(12.) Linkage Studies

(a) Test for linkage with albino (c)

Albino, lens-rupture mice were mated to non-albino, non lens-rupture mice and segregation of the two genes was followed in the F_2 and backcross generations. In the F_2 although there was a slight excess of the parental types, there was no significant deviation from the 9:3:3:1 ratio expected on the basis of random assortment. (Table II).

Table II

Segregation in the F_2 from crosses of

lr/lrc/c x Lr/LrC/C

<u>Phenotype</u>	<u>Number</u>	<u>E*</u>	<u>χ^2</u>	<u>P</u>
LrC	56	48.9	1.030	.3-.5
lrC	11	16.3	1.734	.1-.2
Lrc	12	16.3	1.144	.2-.3
lrc	<u>8</u>	5.4	<u>1.201</u>	<u>.2-.3</u>
	87		5.109	.1-.2

Similarly, in the backcross to the double recessive, a close correspondence to the 1:1:1:1 ratio expected on the basis of independent segregation was

* On the basis of random assortment

obtained. (Table III).

Table III

Segregation in the backcross of F_1 offspring from crosses of
 $lf/lrc/c$ x $Lr/LrC/C$ to $lrlrc/c$ mice.

<u>Phenotype</u>	<u>Number</u>	<u>E*</u>	<u>χ^2*</u>	<u>P</u>
LrC	22	22	.000	.99
lrc	23	22	.045	.8-.9
Lrc	18	22	.727	.3-.5
lrc	25	22	<u>.409</u>	<u>.5-.7</u>
			1.181	0.7-0.8

No evidence, therefore, was found for the existence of linkage between the lr and c genes.

(b) Test for linkage with flexed-tail anemia (f)

Flexed-tail, lens-rupture mice were mated to non flexed-tail, non lens-rupture mice, and segregation of the two genes was followed in the F_2 and backcross generations. In the F_2 there was no significant deviation found from the 9:3:3:1

* On the basis of random assortment

ratio expected on the basis of random segregation. (see Table IV).

Table IV

Segregation in the F_2 from crosses of lr/lr f/f x Lr/Lr F/F mice

<u>Phenotype</u>	<u>Number</u>	<u>E</u> *	<u>χ^2</u> *	<u>P</u>
FLr	24	23.6	.000	.99
Flr	8	7.8	.038	.8-.9
fLr	7	7.8	.097	.7-.8
flr	<u>3</u>	2.6	<u>.003</u>	<u>.95-.98</u>
	42		0.138	.98-.99

Similarly, in the backcross to the double recessive a close approximation was obtained to the 1:1:1:1 ratio expected on the basis of independent segregation. (See Table V).

* On the basis of random assortment

Table V

Segregation in the backcross of F_1 offspring from crosses of
 $lr/lrf/f \times Lr/LrF/F$ to $lr/lrf/f$ mice

<u>Phenotype</u>	<u>Number</u>	<u>E*</u>	<u>χ^2*</u>	<u>P</u>
FLr	10	9	.111	.7-.8
fLr	8	9	.111	.7-.8
Flr	6	9	1.000	.3-.5
flr	12	9	<u>1.000</u>	<u>.3-.5</u>
			2.222	.5-.7

(c) Test for linkage with waved² (wa^2)

Lens-rupture non-waved mice were mated to normal-eyed waved mice and behaviour of the two genes was followed in the F_2 generation. No significant deviation from the 9:3:3:1 ratio expected on the basis of independent segregation was found. (Table VI).

* On the basis of random assortment

Table VI

The F₂ from crosses of lr/lrwa²/wa² x Lr/Lrwa²/wa² mice

<u>Phenotype</u>	<u>Number</u>	<u>E*</u>	<u>χ²*</u>	<u>P</u>
Lrwa ²	50	48.9	.025	.8-.9
lrwa ²	16	16.3	.006	.9-.95
Lrwa ²	18	16.3	.181	.5-.7
lrwa ²	<u>3</u>	5.4	<u>1.061</u>	<u>.3-.5</u>
	87		1.273	.5-.7

No evidence was found for the existence of linkage between the lr and wa² genes.

(c) Test for linkage with shaker²(sh²)

Lens-rupture non shaker mice were mated to normal-eyed shaker mice and the segregation of the two genes was followed in the F₂ generation. No significant deviation was found from the 9:3:3:1 ratio expected. (see Table VII).

* On the basis of random assortment

Table VII

The F₂ from crosses of lr/lrSh²/Sh² x Lr/Lrsh₂/sh₂ mice

<u>Phenotype</u>	<u>Number</u>	<u>E*</u>	<u>χ²*</u>	<u>P</u>
LrSh ²	52	48.9	.196	.7-.8
lrSh ²	14	16.3	.324	.5-.7
Lrsh ₂	15	16.3	.030	.8-.9
lrsh ₂	<u>6</u>	5.4	<u>.066</u>	<u>.8-.9</u>
	87		.616	.8-.9

No evidence was found for linkage between the lr and sh² genes.

(e) Test for linkage with Agouti (Ag)

Non agouti lens-rupture mice were mated to non lens-rupture, heterozygous Agouti mice and the segregation of the two genes was followed in the F₂ generation derived by mating

Ag/ag lr/lr x ag/ag Lr/Lr

No significant deviation was found from the 3:3:1:1 ratio expected on the basis of independent segregation. (See Table VIII).

* On the basis of random assortment

Table VIII

The F₂ from crosses of lr/lrag/ag x Lr/Lr Ag/ag mice
i.e. Lr/lr Ag/ag x Lr/lr ag/ag

<u>Phenotype</u>	<u>Numbers</u>	<u>E*</u>	<u>χ²*</u>	<u>P</u>
AgLr	19	14.6	1.326	.2-.3
Aglr	5	4.9	.002	.95-.98
agLr	14	14.6	.024	.7-.8
aglr	<u>1</u>	<u>4.9</u>	<u>3.104</u>	<u>.05-.1</u>
	39	39	4.456	.2-.3

(f) Test for sex-linkage

Matings between lens-rupture females and normal-eyed mice from other strains (B Ag wa²sh²; A) produced six litters totalling 33 offspring. (15♂:18♀) all phenotypically normal after 12 weeks of age. Assuming that in mice the males are the heterogametic sex, and that the Y chromosome carries no allele of lr, it is concluded that the lr gene is not sex-linked.

(g) Test for partial sex linkage

* On the basis of random assortment

It has recently been demonstrated by Wright (1947) that wa^2 and sh^2 are factors exhibiting partial sex-linkage in the mouse, i.e. wa^2 and sh^2 are factors carried in the pairing segments of the sex(Y) chromosome. In her analysis, Wright treated the X and Y chromosomes as a factor pair.

Lens-rupture females mated to normal-eyed males produced normal-eyed offspring (Lr/lr). A Lr/lr male was backcrossed to lens-rupture females and produced 88 mice (49♂:39♀) in 13 litters. Treating X and Y as a factor pair, and on the basis of partial sex-linkage of the lens-rupture gene, one would expect significantly more than 50% of the lens-rupture offspring to be females. This, however, was not the case, and the backcross data (Table IX) shows that there was no significant deviation from the 1:1:1:1 ratio expected on the basis of random assortment of the two factors under consideration. We conclude that no evidence was found for partial sex-linkage of the lens-rupture gene.

Table IX

Segregation in the backcross of F_1 offspring from crosses of $lr lr \text{♀}$ x $Lr Lr \text{♂}$ to $lr lr \text{♀}$

<u>Phenotype</u>	<u>Number</u>	<u>E*</u>	<u>χ^2*</u>	<u>P</u>
$\text{♂} Lr$	20	22	.18	.5-.7
$\text{♂} lr$	29	22	2.23	.1-.2
$\text{♀} Lr$	14	22	2.91	.05-.1
$\text{♀} lr$	25	22	<u>.41</u>	<u>.5-.7</u>
			5.73	.1-.2

(3) Conclusions

Evidence has been presented to demonstrate the existence of a new mutant condition, lens-rupture in the house mouse, which is inherited as an autosomal recessive gene with 98% expressivity. (2% overlap)

The symbol designated to represent the lens-rupture gene is lr , its normal allele being Lr .

Lens-rupture was tested for its possible linkage relationships with the following:- albinism (c),

* On the basis of random assortment

flexed-tail anemia (f), shaker² (sh²), waved² (wa²), Agouti (Ag), and sex (XY) (See Table X.) There was no linkage demonstrated in these studies.

Table X

Lens-Rupture Linkage Studies

Locus Tested Against	X ² based on Independent Segregation	P based on Independent Segregation	Number of Mice	Number of Litters
Albinism (<u>c</u>)	B.C. 1.181	.7-.8	88	13
	F ₂ 5.109	.1-.2	87	11
Flexed-tail <u>f</u>	B.C. 2.222	.5-.7	36	5
	F ₂ 0.138	.95-.98	42	6
Waved ² <u>wa</u> ²	F ₂ 1.273	.5-.7	87	11
Shaker ² <u>sh</u> ²	F ₂ 0.616	.8-.9	87	11
Agouti <u>Ag</u>	F ₂ 7.373	.8-.9	54	8
Partial sex linkage	B.C. 5.730	.1-.2	88	13

C. Observations on lens-rupture and normal eyes

(1) Macroscopic

The eyes of the mouse are located at the sides of the head facing almost laterally with respect to the anterior-posterior axis of the body. In the descriptive terminology employed in this section of the paper, the eye and its components will be treated according to its position in the body, e.g.

towards the head = anterior

towards the tail = posterior

towards the dorsal surface = superior

towards the ventral surface = inferior

towards the brain = medial = proximal

away from the brain = lateral = distal

Where terms have been employed from medical terminology, e.g. anterior and posterior lenticonus, meaning distal and proximal lenticonus, no change from the medical wording has been employed.

Macroscopic examinations of the eye were begun at 14 days of age when the eyes of both lens-rupture and normal mice first open. The eyes of normal and lens-rupture mice are indistinguishable macroscopically, until an average age of four weeks, when the first visible manifestations of the lens-rupture syndrome become apparent. The value of four weeks of age for the time of visible onset of the condition, is based on examination of 143 mice.

However, it should be mentioned that as ability in recognizing the condition improved, there was a shift in time of first recognition of this condition from five to six weeks to three to four weeks. No evidence was obtained of the role of genetic drift in this shift of the time of onset.

In lens-rupture eyes, a small opaque whitish ring is seen to develop in the vitreous chamber, slightly postero-inferior to the pupil (4 weeks of age). Such a ring, demonstrated by dissection to exist within the lens is a type of cataract described as occurring with posterior lenticonus in humans (Berens 1936).

As this opaque ring becomes thicker and enlarges, a dense white mass, shown by dissection to be the lens nucleus, protrudes distally from the central portion of the ring, medial to the pupil (4-1/2 weeks of age). As the proximal opacity increases in area, the outline of the lateral border of the lens becomes visible distal to it, defined by numerous peripherally located vacuoles within the lens substance. (5-1/2 weeks of age). The lens appears quite cloudy at this stage, maximum cloudiness being concentrated at the lens periphery.

Shortly after this (at five to six weeks of age) a small, distinct white mass, histologically demonstrated to be lens nucleus, becomes apparent, medial and usually antero superior to the lens.

In some cases, under observation, it was found that the small white mass became situated in the anterior chamber.

In other cases the nucleus was observed to remain in the vitreous chamber, although its final position was quite variable.

In 52 of 246 mouse eyes over three months old (21%) the distorted lens was in the anterior chamber of the eye, having passed completely or partially through the pupil (See Table XI). Analysis of the data showed that the incidence of lens in the anterior chamber was not significantly different between sexes or from right to left eye within sexes. (See Table XII). Within males, the incidence of lens in anterior chamber was 24.5% in the left eye and 28.3% in the right eye; a simple χ^2 test based on the hypothesis on the equality of incidence in both eyes resulted in a P value of .7. Similarly, within females, a P value^{of} .3-.5 was derived. Testing incidence in males against incidence in females gave a P value of .3-.5. There were no significant deviations of incidence between eyes in either females or

males, and there was no significant difference of incidence between sexes (See Tables XI and XII). The lens in the anterior chamber is considered to be the terminal stage attainable in the lens-rupture syndrome. In a few cases, both the lens and white mass are observed to be in the anterior chamber of the eye (Fig. 7). There is a high variability between the final stages in the two eyes of a given affected individual.

Table XI

Incidence of lens in anterior chamber in mice eyes aged
three months and over

<u>Sex</u>	<u>Eye</u>	<u>Lens in anterior chamber</u>	<u>Lens in vitreous chamber</u>	<u>Incidence of lens in anterior chamber</u>	<u>Sex Incidence</u>	<u>Total</u>
♂	Left	13	40	24.5%	28/106 = 26.4%	53
	Right	15	38	28.3%		53
♀	Left	14	56	20.0%	24/140 = 17.1%	70
	Right	<u>10</u>	<u>60</u>	<u>14.2%</u>		<u>70</u>
		52	194	21.1%		246

Table XII

χ^2 analyses to test incidence differences of lens in anterior chamber between sexes, and between eyes within sexes.

<u>Incidence in*</u>	<u>Tested</u>	<u>Incidence in*</u>	<u>χ^{2**}</u>	<u>P</u>
♂ right eye	against	♂ left eye	0.14	.7
♀ right eye	against	♀ left eye	0.53	.3-.5
♂ eyes	against	♀ eyes	0.94	.3-.5

Measurements of the diameter of the corneal-scleral junction were carried out on 203 eyes in Bouin's fixative. By these measurements, the writer hoped to find whether there was a significant difference in the diameters of lens-rupture and normal eyes of various ages, with the idea that an increase relative to normal in the diameter of lrlr eyes would indicate any increased intraocular pressure (glaucoma) present. No significant differences could be found between normal and lens-rupture eyes. However, the writer feels that this technique may not have been sufficiently delicate to indicate changes in intraocular pressure, even if present.

* Based on values in Table XI

** Based on equality of incidence

Table XIII

Corneal-Scleral Junction Diameter Measurements (in mm)

<u>Age of Mouse in Days</u>	<u>Diameter in mm ($\bar{X}$)</u>		<u>Number of Mice</u>		<u>χ^2*</u>	<u>P</u>
	<u>lr</u> <u>eyes</u>	<u>Lr</u> <u>eyes</u>	<u>lr</u>	<u>Lr</u>		
1-20	3.846	3.737	22	15	.016	.9
21-40	4.254	4.300	15	10	.002	.95
41-60	4.675	4.775	7	15	.008	.9
61-90	4.525	4.863	54	5	.097	.7
91-110	4.724	4.781	12	2	.009	.9
111-300	4.850	5.078	38	8	.042	.8

*Based on equality of diameter values

The evidence derived from a study of the lens-rupture syndrome, concerning the macroscopic mode of expression of this mutation may be summed up in the following stages:

Approximate Age

1. Normal in appearance to 4 weeks
2. Small white ring in vitreous chamber about 4 weeks
3. Dense central mass within white ring about 4-1/2 weeks
4. White mass in vitreous chamber about 5 - 6 weeks
5. Lens and/or white mass in anterior chamber ...after 6 weeks

(2) Dissection

The techniques used for the following series of observations have been discussed in the section on materials and methods. The process described below is based on 168 dissections of lens-rupture eyes performed by the writer at various stages of the syndrome.

Lens-rupture and normal eyes display the same features at birth; a small lens, a very small anterior chamber and a hyaloid artery which originates at the optic pit and extends out to the proximal surface of the lens. The hyaloid artery bifurcates halfway to the lens and the branches subdivide several times and form a fine network over the proximal surface of the lens. (Figure 8 - normal eye 14 days old). (Figure 8a - lens-rupture eye 14 days old).

In normal mice, the lens increases in size until three months of age at which time it almost fills the vitreous chamber. (Figure 9). The hyaloid artery may persist normally in mice as late as four months of age, but usually disappears about four weeks after birth. A normal lens at three months of age is composed of a hard, fibrous, central nucleus contained in a homogeneous soft cortex, which is itself enclosed in a peripheral fibrous cortex zone just inside the lens capsule. (Figure 10).

At 2 1/2 - 3 1/2 weeks of age, the eyes of lens-rupture mice exhibit the first abnormal sign distinguishable by dissection. A small ring appears on the proximal surface of the lens, within the network of the hyaloid artery. (Figures 11,12). Soon a small, conical bulge (usually within the cone of the network formed by the hyaloid artery) becomes apparent in place of the ring on the proximal surface of the lens (2 1/2 - 3 1/2 weeks) (Figures 13, 14). This bulge may correspond to what ophthalmologists call posterior lenticonus. Dissection of the lens shows the nucleus to have become separated from the cortex and distortion of the remainder of the lens is also observed (Figure 15, 16). As the bulge appears the nucleus leaves its central position and moves proximally within the cortical substance, thus further distorting the lens, especially the medial periphery. (Figures 17,18).

As the conical bulge of the lens increases in size (Figures 19,20,21) it is seen to contain a definite mass, the lens nucleus which has moved back against the proximal lens capsule (Figure 22), (Stage III macroscopic - about 4 1/2 weeks of age). The medial periphery of the lens appears vacuolated subcapsularly, shown by gross dissection of the lens to be due to the

change in position of the lens nucleus.

The conical bulge of the lens may exert pressure on the retina, and cause variable signs of irregularity in it (Figures 23,24) (4 - 6 weeks of age). As the lens becomes distorted in shape due to the posterior bulging, it may be torn away from its supporting network of ciliary ligaments (3 1/2 - 5 1/2 weeks of age).

The lens capsule ruptures proximally at the apex of the lenticonus within the cone of the hyaloid artery network and lens matter (cortical substance - Figure 25) flows into the vitreous chamber soon to be followed by the lens nucleus (5 - 6 weeks; Figures 26, 27, 28). Grossly sectioned lenses at these stages show the progress of the nucleus through the proximal rupture of the lens capsule into the vitreous chamber (Figures 29,30). The lens nucleus may be extruded either to one side of the lens (usually anterosuperior) or directly into the retina in the region of the optic pit, where it may remain permanently embedded (Figures 31,27). In some mouse eyes the nucleus may be found in the anterior chamber after the rupture has occurred (Figure 32). After the lens nucleus has been extruded, the residual

portion of the ruptured lens is soft and irregular, and a gross dissection of the lens at this stage shows it to be void of any firm vestige of nuclear matter (Figure 33).

General observations of gross dissections of eyes indicate that the remainder of the ruptured lens is decreased in size, irregular in shape, and may be found in any of the following abnormal positions:-

1. Flowing through the pupil into the anterior chamber (Fig.34)
2. In the anterior chamber (Figure 35)
3. Floating free in the vitreous chamber (Figure 27)
4. Wedged in the vitreous chamber contents, retina, etc.

(Figure 31)

An analysis of the location of the lens in mice (Table 11) over three months of age showed the incidence of 1 and 2 (above) to be 21%; the incidence of 3 and 4 (above) being 79%.

Many variations of these basic patterns may be found, among which are the following:-

1. The lens may be unaffected (overlap) (Figure 36)
2. The lens may be pressed up and flattened against the iris so tightly as to give the impression of two iris in the eye. (Special case of Figure 37).
3. The lens capsule may be attached to the optic pit by a thick band of fibrous material (Figure 38).

4. The lens may be completely extruded from within the capsule (complete cortical liquefaction) so that only the capsule and nucleus can be seen in the eye. (Figure 37)

In the later stages of the process, the retina assumes numerous gross convolutions, the feature most commonly associated with the lens-rupture syndrome consisting of an increase in the depth of the optic pit with the surrounding retina raised into a ridge.

The hyaloid artery is found to be replaced in some affected mice (over 3 months of age) by a fibrous band. The hyaloid artery has not yet been found in normal mice older than four months.

The mode of expression of the lens-rupture mutation may be summed up in the following stages:-

- | | Approximate age |
|--|-----------------------------|
| 1. Normal in appearance | to three weeks of age |
| 2. Small proximal ring followed by formation of
small conical proximal lens bulge, hyaloid
artery present | 2 1/2 - 3 1/2 weeks |
| 3. Bulge increases in size, retinal distortion
starts, hyaloid artery present, lens torn away
from ciliary ligaments | about 3 - 1/2 - 5 1/2 weeks |
| 4. Lens capsule ruptures posteriorly, cortex and | |

- nucleus extruded, lens distorted, retinal optic
 pit deepened, retina distorted, hyaloid artery
 present about 5 - 6 weeks
5. Lens in anterior chamber or irregular in vitreous,
 persistent hyaloid artery invaded by fibrous elements,
 nucleus in vitreous or anterior chamber, retina
 distorted after 6 weeks

The ultimate expression of lens-rupture process
 within litters, as within individuals, is highly variable.

(3) Histology

Preliminary observations on the histology
 of the lens-rupture syndrome support the hypothesis that the
 first microscopic pathological changes occur in the fibres
 of the lens nucleus. At an average age of about 17 days,
 these fibres begin to become wavy in outline, and their normally
 homogenous substance takes on a granular appearance; a few
 days later the fibres of the lens nucleus become separated
 from one another by clear presumably fluid-filled spaces.
 The exact nature of the forces which lead to subsequent
 expulsion of the lens nucleus and hydropic degeneration of
 the main bulk of the lens as yet remains unclear.

In advanced stages of the lens-rupture syndrome,
 after the expulsion of the nucleus of the lens, the following
 histological observations apply:-

1. The main bulk of the lens relative to normal (Figure 39a) is highly distorted in shape (variable) (Figure 39b) and irregular in position (variable) (Figures 40, 41a, 41b).
2. The lens appears vacuolated throughout (advanced hydropic degeneration (Figures 42a, 42b) and is greatly decreased in size (Figures 43a and 43b).
3. The ruptured lens capsule may be firmly connected to the retina in the region of the optic pit by a thick fibrous band which has replaced the hyaloid artery previously found in that position (Figure 44).
4. The main irregularity of the retina in affected mice by comparison with normal (Figure 45) involves overall distortion (Figures 46, 47, 48, 49, 50, 51, 52); in some lens-rupture mice the retinal blood vessels are highly distended but this latter feature remains to be analyzed in greater detail.
5. In some instances, where the lens is found in the anterior chamber, it appears tightly pressed against the cornea, the anterior chamber being larger than normal (Figure 53).

At present the mode of action of the lens-rupture gene is being studied in a more detailed histological analysis of the syndrome.

III. DISCUSSION

A. Genetic Data

Investigation of genetic behaviour of the lens-rupture condition conclusively demonstrates that the genetic factor controlling the initiation of the process is an autosomal recessive gene with 98% expressivity in the present stock.

The lens-rupture gene was tested for possible linkage relationships with the following loci:- albinism (c), flexed-tail anemia (f), shaker² (sh²), waved² (wa²), Agouti (Ag), and sex (partial sex-linkage). No significant deviations from independent assortment were found in any of these crosses.

Because the numbers of mice obtained in the F₂ generations used in studying the relationships with the Agouti, waved², and shaker² loci were quite small, no positive statements can be made about linkage relationships of lens-rupture with these latter loci.

The genetic data therefore warrants the conclusion that the lens-rupture gene is an autosomal recessive gene not linked with the albino or flexed-tail anemia loci.

B. Physical Observations

The techniques utilized to study the syndrome have demonstrated that the outstanding features of the process are:- posterior lenticonus, rupture of the lens capsule, expulsion of lens material (nucleus and liquified cortex) into the vitreous chamber, distorted and convoluted retina, fibrous replacement of the hyaloid artery, hypermature cataract, and displacement of the lens.

Whereas certain of the above features have been described in other animals, no report has been found describing an anomaly identical with lens-rupture syndrome.

Measurements were made of the diameters of the scleral-corneal junction of normal and lens-rupture eyes in order to demonstrate if present the existence of glaucoma in lens-rupture eyes. No positive results were obtained, but the writer believes that this may be due either to insufficient numbers or to the use of a post-mortem technique; further studies should be carried out along this line, emphasizing in vivo observations.

C. Theories of Pathogenesis

Berens (1936) states that the lenticonus occurring in humans is a conical protrusion of the lens substance covered by capsule or connective tissue, posterior being more frequent than anterior lenticonus. He believes

that the posterior variety is due to the traction of the capsular remains of the hyaloid artery, to fetal defects or to rupture of the lens capsule. The concept of posterior lenticonus due to the rupture of the adult lens capsule is plausible, although apparently not the case in lens-rupture eyes. Berens mentions in addition that in posterior lenticonus in humans, as in our early mouse lens-rupture process, cataract is present as a bright refractile ring at the base of the conus. Wolff (1935) also considers that lenticonus posterior consists of a protrusion of lens matter into the vitreous either from the proximal pole of the lens or to one side of it. In the mouse-lens-rupture stock, there is no evidence to support the hypothesis that the lenticonus forms as a consequence of rupture of the lens capsule.

Stricker (1899) speculating on the nature of lenticonus, 16 cases of which had been reported in humans up to 1899, discusses four cases in which individuals were affected bilaterally. He considers these four cases to be congenital (present at birth). Dissection of eyes of lens-rupture mice one day old showed no lenticonus and consequently the condition is not congenital in our mouse stock.

Bach (1898) after observing three cases of posterior lenticonus in rabbits, claims correctly, but not

very helpfully that a disturbance in the development of the eye is the cause of posterior lenticonus. He says that during the development of such eyes, there is an anomalous formation of the lens, which remains in contact with the remnant of the foetal hyaloid artery. As the eye increases in size, he claims that the artery exerts tension on the posterior capsule, drawing it out, and finally rupturing it. (This is unlikely if, as in the mouse, the lens gets bigger in proportion to the eyeball.) At this time, the posterior cortical substance, following the direction of least resistance, diffuses itself posteriorly and forms a lenticonus.

These various concepts contribute little to a true knowledge of the formation of a posterior lenticonus. The writer believes that such a formation is composed of two phases: - first, an internal alteration of the lens, e.g. development of cataract, and secondly, alteration of the shape of the lens capsule in response to internal lens changes.

As for rupture of the lens-capsule, the writer believes that rupture comes about as a consequence of lenticonus formation, rather than as a cause of lenticonus formation (in the lens-rupture stock at any rate).

Several cases of spontaneous rupture of the lens followed by glaucoma (increased intra-ocular pressure) have been described in man. Presumably, the glaucoma was the result of blockage of the canals of Schlemm which normally drain the vitreous chamber. Up to now, no evidence has been found for the existence of glaucoma in lens-rupture eyes.

It can be stated that the rupture in mice occurs after primary lens development. That the lens-rupture condition is due to failure of the lens to form properly has yet to be demonstrated.

Duke Elder (1934) attributes all cases of rupture of the lens capsule to the aetiology of Morgagnian cataract; especially where spontaneous absorption of such a cataract occurs. However, as most of the stages in this process of spontaneous absorption of Morgagnian cataract in humans have not been histologically examined, it is fruitless to comment on his classification.

Conditions with features similar to those occurring in the lens-rupture process have been reported in many mammals. These features include lenticonus, rupture of the lens capsule, lens distortion, persistent hyaloid artery, cataract, and retinal irregularities. The writer suggests the possibility that there may be a common denominator in the patterns of these various conditions and believes it possible that mutations having similar effects, namely, the lens-rupture process have occurred in these animals, although several of the

conditions discussed have been reported as non-hereditary.

D. Conclusions

On the basis of the present research, the writer believes that the process of lens-rupture is as follows:- the gene acts to cause internal changes in the nature of the fibres of the lens nucleus. These changes are coupled with alterations in the nature of the lens cortex in the proximal region of the lens. As a result the nucleus becomes distinct within the lens, and the cortex becomes very pliable; the capsule responds to the forces acting on it i.e. the lens enlarges with the formation of a proximal bulge which ruptures when it exceeds its point of maximum stretch. As a result, both liquified cortical substance and the lens nucleus are released into the vitreous chamber. This causes irregularities to form in the retina and results in overall retinal distortion in advanced stages of the syndrome. The rupture of the lens capsule may occur within the cone of the hyaloid artery, in which case the hyaloid artery may be replaced by a fibrous band. It is possible that the canals of Schlemm which normally drain the vitreous chamber are blocked by the exuded cortex and glaucoma results. After the rupture, the distorted lens and/or nucleus may be forced through the pupil into the anterior chamber of the eye to produce the typical terminal pathology of the lens-rupture syndrome.

The writer believes the expression of the lens-rupture gene in mice depends on the genotype and age of the mouse, and some intrinsic physiological factors at the time of lens-rupture. That the physiology of each eye plays a specific role is evident from the variability of expression within the eyes of a single affected mouse.

It would be of interest to carry out investigations along the following lines:-

1. Further analysis of lens-rupture genetics should be directed towards establishing a known linkage for the lens-rupture gene as well as experimentally determining the mode of action of that gene.

The problem of the mode of action of the gene could best be attacked by histological and biochemical analyses. These studies might be coupled with an analysis of the relation of glaucoma and Morgagnian cataract to the lens-rupture process. It is indeed possible that this stock may serve as an aid to the ophthalmologist in solving the problems of glaucoma and cataract in man, in addition to serving as a supply of cataractous animals for medical students.

IV. SUMMARY

1. A new syndrome, lens-rupture is described in the house-mouse. The features of the syndrome include: - (1) cataract, and (2) lenticonus, (3) extrusion of the nucleus of the lens into the vitreous chamber of the eye following proximal rupture of the lens capsule, (4) retinal distortion and irregularity, (5) persistent hyaloid artery (6) displaced and distorted lens, and (7) extreme variability of expression.

2. The condition is termed lens-rupture and its expression is controlled by an autosomal recessive gene with 98% expressivity in the present stock. Evidence is presented to show that the lens-rupture gene is not linked to the albino (c) or flexed-tail anemia (f) genes.

3. The symbol lr is suggested to designate the lens-rupture gene, its normal allele being represented by either Lr or lr⁺.

V. ACKNOWLEDGEMENTS

I wish to express my thanks and sincere appreciation to Dr. J. Wallace Boyes, Chairman of the Department of Genetics, McGill University, for placing at my disposal the resources of this department and for his advice during the experiments.

I am indebted to and wish to thank Dr. F. Clarke Fraser, Department of Genetics, McGill University, under whose supervision and with whose aid this investigation was carried out, for his guidance, advice and enormous patience during the slow progress of this work.

I wish to express my gratitude to Mr. Donald H. Jolly, Department of Genetics, McGill University, for his help and advice on the photographic techniques employed in this work.

VI. BIBLIOGRAPHY

- Bach, L. 1898. Anatomische Studien uber Verschiedene Missbildungen des Auges. Graefe Arch Ophth. Vol. XLV, Pt. 1.
- Beisbarth, C. 1937. Spontaneous expulsion of cataract nucleus. American Journal Ophthalmology 20, 184.
- Berens, C. 1936. The eye and its diseases. W. B. Saunders Co. Phila.
- Bourne, M.C. and H. Gruneberg, 1939. Degeneration of the Retina and Cataract. Jour. Hered. 30, 130-136.
- Chase, H.B. and E. B. Chase, 1941. Studies on an anophthalmic strain of mice. I. Embryology of the eye region J. Morphol 68, 279-301.
- Cohrs, P. 1933. Vererbare Agnesie und Hypoplasie der Neuroepithelschicht der Retina bei albinotischen Mäusen. Arch. Augenheilk, 107, 489-500.
- Duke-Elder, W. S. 1934. Recent advances in ophthalmology.
- Ehrlich, L. H. 1946. Spontaneous rupture of the lens capsule in Anterior Lenticonus; American Journal of Ophthalmology 29; 1274 - 1281.
- Gonzalez, J. de J. 1919. Spontaneous rupture of Morgagnian Cataract. 2; 742.
- Gruneberg, H. 1943. Genetics of the Mouse, Cambridge University Press. London.
- Jordan, H. E. and Kindred, J. E., 1942. Textbook of Embryology, D. Appleton-Century Company.
- Kaufman, S. I, 1933. Morgagnian cataracts and their complications. Arch. of Ophth. 9; 56.
- Keeler, C.E. 1927. Rodless Retina, an ophthalmic mutation in the house mouse. J.E. 2. 46, 345-407.

- Keeler, C.E., Sutcliffe, E. and E. L. Chafee, 1928.
A description of the ontogenetic development of retinal action currents in the house mouse. P.N.A.S. 14, 811-815.
- Knapp, H.C. 1937. Spontaneous rupture of the lens capsule causing secondary glaucoma. Amer. J. Ophth. 20, 820.
- Koch, F.L.P. and Gowen, J.W. 1939. Spontaneous Ophthalmic mutation in a laboratory mouse. Archives of Pathol. 28, 171-176.
- Loeffler, L. 1932. Uber eine Mutation bei dei weissen Hausmaus und seine Bedeutung fure die menschliche Erblehre. ZIAV, 61, 409-446.
- Mann, I.C. 1928. The development of the human eye, Cambridge Univ. Press, London.
- Mann, I.C. 1937. Developmental Abnormalities of the eye, Cambridge Univ. Press. London.
- Osterburg, C. 1936. A case of ruptured Morgagnian cataract histologically examined. Acta. Ophth. 14, 471.
- Rochon-Duvigneaud, Andre. 1928. L'Oeil de la taupe et les problemes qu'il souleve. Ann. d'oculistique, Nov.
- Rochon-Duvigneaud, Andre. 1943. Les yeux et la vision des vertebres. Masson et Cie. editeurs. Paris.
- Shoemaker, W. T. 1919. Spontaneous rupture of the anterior lens capsule with rapid development of cataract. Amer. Jour. Ophth. 2, 348.
- Smith, S.E. and B. F. Barrentine, 1943. Hereditary cataract A new dominant gene in the Rat. Jour. Hered. 34, 28.
- Stricker, 1898-9. The Crystalline Lens System - Diseases in detail.
- Wolff, E. 1935. The Pathology of the eye, Blakiston's Publishing Company.

Wright, M.E. 1947. Two sex-linkages in the house mouse with unusual recombination values. Heredity 1, 349-55.

Zavalía, A.V. and Oliva, A.O. Consideraciones sobre dos casos de lentiglobos anterior. Arch. de oft. de Buenos Aires 14, 848.

Reports on Lenticonus

- Bach, P. 1898. Ed. Bupthalmus mit Lenticonus posterior.
Arch. F. Augenheilk. 35, 1 heft, 51.
- Bellows, J.G. 1944. Cataract and anomalies of the lens.
C.V. Mosby Co. St. Louis.
- Box, W.M. 1941. Spontaneous absorbtion of Cataract. Med.
Jour. Australia. 28, 451.
- Butler, T.H. 1930. Lenticonus posterior. Report of six
cases. Arch. Ophth. III, 425.
- Butler, T.H. 1932. Lenticonus posterior, Tr. Ophth. Soc. U.
Kingdom, 52;541.
- Dameļ, C.S. and A. Garbarino, 1942. Lenticono anterior.
Arch. de oft de Buenos Aires 17; 363.
- Doherty, W.B. 1943. A discussion of deformities of the shape
of the lens, with a report of a case of
posterior lenticonus. American Journal
of Ophthalmology 31; 457-60.
- Eisach, Dr. 1892. Ein fall von; Lenticonus posterior. Zehender's
Klin Monatsblatt. March.
- Feigenbaum, A. 1932. Origin of lenticonus anterior. Folia
Ophth. Orient. 1; 103.
- Friedman, B. 1931. The development of the lens, its significance
in the interpretation of lenticular opacities.
Arch. Ophthalmol. 6, 558-77.
- Gallo, L. 1942. Anterior Lenticonus. Proc. of the Sociedad
de Ophthalmogia del Littorae, Rev. Med.
Rosaria 32, 3889.
- Gullstrand, H. 1892. Ein fall von lenticonus posterior.
Nordisk Ophth. Tidskrift Centralblatt, 177.
- Harris, C.F. 1940. Bilateral anterior lenticonus. Northwest.
Med. 39, 219.
- Jano, Av. 1917. Posterior Lenticonus. Zeit. F. Augenheilkunde
38, 192-197.

- Jaworski, A. 1910. Ein fall von Lenticonus anterior und uber desseil. entstehen, Arch. F. Augenheilkunde 65, 313.
- Knapp, Dr. 1891. Posterior Lenticonus, Knapp's Arch. 22; 28.
- Knobloch, R. 1938. Abstr. on bilat ant. Lenticonus. Amer. Jour. Ophthalmol. 21; 476.
- Marbach, H. 1943. Sinal da gota de oleo na pupila microfaquia-lenticone anterior. Arquivos Brasilenos de oft 6; 119.
- Meyer, F. 1888. A case of posterior lenticonus, Archiv. fur Augen., heft I.
- Moulton, E.C. 1936. Anterior lenticonus. Trans. Sec. on Ophth. Amer. Med. Assoc. 87th session 261.
- Mitvalsky, J. 1892. Ein Neuer fall von Lenticonus Posterior mit theilweisen persistens der arteria hyaloidea. Centralblatt fur prak Augenheilkunde, Mars.
- Nordmann, J. 1938. A propos de l'histogenese de la cryst alloide. Arch. Anat. Hist. embryologie 25, 173-182.
- Patry, A, 1906. Sur l'histologie et l'etiologie du Lenticone Posterior. Geneve.
- Rauh, W. 1936. Anterior Lentiglobus. Zeit F. Augenheilk 89, 34.
- Rocha, H. and E. Coscarelli, 1943. Lenticone anterior, ophthalmos 3, 219.
- Rollet and Genet, 1913. Cataracte laiteuse overte spontanement dans la chambre anterieure. Rev. Gen. d'ophth. 32;1.
- Rones, B. 1934. Anterior lenticonus, Jour. Amer. Med. Assoc. 103,327.
- Schweinitz, G.E. and M. Wiener, 1919. Anterior Lenticonus. Jour. Amer. Med. Assoc. 73, 1191.

Szily, Av. 1884. Spontaneous rupture of the lens capsule -
cited by Ehrlich (1946).

Ter-Artuniantz, C.M; Kotilianskaya, R I, and M.B. Chutko,
1940, Abstr. on Lenticonus bilateral, Amer.
Jour. Ophth. 23; 959.

Tiffany, F.B. 1902. Anomalies and diseases of the eye.

Webster, 1874. Einfall von Lenticonus aus des prexis der
C.R. Agnew. Arch. fur Augen und Ohren,
Knapp, Moos. B. IV, 262.

VII. DESCRIPTION OF PLATES

Plate I.

- Figure 1:- Diagram of the normal mouse eye; cr. lens; c, cornea; i, iris; pc, ciliary muscle; r, retina; no, optic nerve; ch, choroid; s, sclera; cl, ciliary ligaments; aa, anterior aqueous body; pa, posterior aqueous body; v, vitreous body. (After Rochon-Duvigneaud - 1943).
- Figure 2:- Section through albino mouse eye showing pathological retinal neuroepithelium, a,b,c; persistent hyaloid artery, d; cataract, e; tear in the lens capsule. (After Cohrs - 1933).
- Figure 3:- Section through mouse eye showing deformity in the shape of the lens and irregularities in the retina (After Koch-Gowen - 1933).
- Figure 4:- Section through the eyeball of a cataractous rat showing retinal irregularity; displaced nucleus; softened cortex; persistent hyaloid artery; thickened anterior lens capsule. (After Bourne and Gruneberg - 1939).

Plate II.

- Figure 5:- Anterior lenticonus in the mole. (After Rochon-Duvigneaud - 1928).
- Figure 6:- Posterior lenticonus; posterior herniation of lens material in the mole. (After Rochon - Duvigneaud - 1928).
- Figure 7:- ♀, albino, lens-rupture, left eye, three months old. Note nucleus is the white mass in the anterior chamber, and lens is halfway through the pupil into the anterior chamber. (X9).
- Figure 8:- ♂, albino, normal mouse eye, right eye, 14 days old (X15).

Plate III.

- Figure 8a:- ♀, albino, lens-rupture, right eye, 14 days old (X15).
- Figure 9:- ♂, albino, normal mouse, left eye, 60 days old (X14).
- Figure 10:- ♂, albino, normal mouse lens, left eye, Gross dissection, 60 days old. Note hard central nucleus, contained in a homogeneous cortex, contained in a peripheral fibrous zone just inside the lens capsule, which has been distorted slightly by dissection. (X20).

Figure 11:- ♂, albino, lens-rupture eye, right eye, 18 days old. Note small ring on the proximal surface of the lens, hyaloid artery present. (X16).

Plate IV.

Figure 12:- ♂, albino, lens-rupture, left eye, 20 days old. Note hyaloid artery very small dot on proximal surface of the lens. (X16).

Figure 13:- ♂, albino, lens-rupture, right eye, 26 days old. Note small conical bulge of the proximal surface of the lens within the cone of the hyaloid artery (X16).

Figure 14:- ♂, albino, lens-rupture, right eye, 26 days old; small conical bulge (posterior lenticonus) within the cone of the hyaloid artery. (X16).

Figure 15:- ♂, albino, lens-rupture, left eye, 20 days old. (Fig. 12). Gross dissection. Note that the nucleus has become separated from the cortex. (X20).

Plate V.

Figure 16:- ♂, albino, lens-rupture, right eye, lens 26 days old (Fig. 14). Note a small posterior lenticonus peripheral degeneration of the cortex, nucleus displaced backwards into the proximal cortex. (X20).

Figure 17:- ♂, albino, lens-rupture, right eye, lens, 23 days old. Note proximal position of lens nucleus within lens. (X20).

Figure 18:- ♂, albino, lens-rupture lens, right eye, 22 days old. Gross dissection. Note peripheral irregularity in the lens cortex, rupture within the central portion of the lens cortex, proximal position of the lens nucleus. (X20).

Figure 19:- ♂, albino, lens-rupture, right eye, 4 weeks old. Note proximal bulge of the lens. (X20).
(Photograph by Dr. F. Clarke Fraser.)

Plate VI.

Figure 20:- ♂, albino, lens-rupture, left eye, 5 weeks old. Note enlarged lens volume, definite size increase of posterior lenticonus. (X14).

Figure 21:- ♂, albino, lens-rupture, left eye, 5 weeks old.
Note increased size of posterior lenticonus;
indications of artifact, i.e. small portion of
lens sectioned away; indications of beginnings
of posterior rupture of the lens capsule. (X14).

Figure 22:- ♀, albino, lens-rupture, left eye, 5 weeks old.
Gross dissection. Note posterior lenticonus,
cortical sutures, proximal position of the lens
nucleus. (X20).

Figure 23:- ♂, albino, lens-rupture, left eye, 6 weeks old.
Note lens has ruptured and has exerted direct
contact pressure on the retina. (X14).

Plate VII.

Figure 24:- ♀, albino, lens-rupture, left eye, 6 weeks old.
Note retinal irregularity, ruptured lens. (X14).

Figure 25:- ♂, albino, lens-rupture, right eye, 5 weeks old.
Note rupture of the lens capsule, at the apex of
the lenticonus. (X14).

Figure 26:- ♂, albino, lens-rupture, right eye, 7 weeks old.
Note irregularities in the retina, exuded
cortical substance in vitreous chamber. (X14).

Figure 27:- ♀, albino, lens-rupture, right eye, 80 days old.
Note nucleus in vitreous chamber, suture lines
indicating healing on the proximal surface of
the lens (X14).

Plate VIII.

Figure 28:- ♂, albino, lens-rupture, right eye, 8 weeks old.
Note rupture of the lens capsule. (X14).

Figure 29:- ♂, albino, lens-rupture, left eye, 8 weeks old.
Gross dissection lens at the rupture stage. Note
irregularities in the cortex, proximal lens
rupture and proximal position of the lens nucleus. (X20).

Figure 30:- ♀, albino, lens-rupture, right eye, 20 weeks old.
Note signs of healing in the cortex; extruded lens
nucleus. (X20).

Figure 31:- ♂, albino, lens-rupture, left eye, 12 weeks old.
Note lens wedged into the retina, lens nucleus
embedded in the retina, distortion of the retina
(X 14).

Plate IX.

Figure 32:- ♂, non-albino, lens-rupture, left eye, 5 months old, showing nucleus in the anterior chamber (X14).

Figure 33:- ♀, albino, lens-rupture, left eye, lens 3 months old. Note extruded nucleus which was in the vitreous chamber of the eye and pulpy lens (which was in the anterior aqueous chamber of the eye). (X20).

Figure 34:- ♀, albino, lens-rupture, left eye. (Fig. 33). Note lens flowing through pupil into chamber, nucleus floating free in vitreous chamber, irregularities of the retina (X14).

Figure 35:- ♂, albino, lens-rupture, right eye, 11 weeks old. Note lens in anterior chamber, nucleus in vitreous chamber, deep optic pit. (X21).
(Photograph by Dr. F. Clarke Fraser.)

Plate X.

Figure 36:- ♀, albino, lens-rupture, right eye, approximately 6 months old. Note:- this is an overlap eye. (X14).

Figure 37:- ♀, albino, lens-rupture, right eye, 7 months old. Note residual lens matter pressed against the iris resulting in this appearance of two irises, i.e. lower iris is flattened lens capsule. (X14).

Figure 38:- ♀, non-albino, lens-rupture, left eye, 5 months old. Note lens in anterior chamber, lens capsule attached to optic pit region by thick fibrous band of material. (X14).

Figure 39:- ♀, albino, normal right eye, 3 months old. (X21).

Plate XI.

Figure 39a:- ♀, non-albino, lens-rupture, left eye, 2 1/2 months old. Note displaced, distorted lens; retinal irregularity. (X21).

Figure 40:- ♀, albino, lens-rupture, left eye. Note vacuolated lens in anterior chamber (X21).

Figure 41:- ♀, albino, lens-rupture, left eye. 3 months old. Note gross malformations of the retina, distorted and vacuolated lens in anterior chamber, lens nucleus in vitreous chamber. (X21).

Figure 41a:- ♀, albino, lens-rupture, right eye, 2 1/2 months old.
Note displaced lens in the vitreous chamber. (X21).

Plate XII.

Figure 42:- ♀, albino, lens-rupture, right eye, 3 1/2 months old.
Note advanced hydropic degeneration of the lens;
retinal distortion, exuded cortical substance
wedged in beneath iris on left hand side of section
and enlarged anterior chamber. (X21).

Figure 42a:- ♀, albino, lens-rupture, right eye, 3 1/2 months old.
Note advanced hydropic degeneration of the lens;
retinal distortion and enlarged anterior chamber (X21).

Figure 43:- ♀, albino, lens-rupture, 3 1/2 months old. Note
advanced hydropic degeneration of the lens, enlarged
anterior chamber, decreased size of lens (X21).

Figure 43b:- ♀, albino, lens-rupture, right eye, 4 1/2 months
old. Note fibrous nature of the lens substance,
decreased lens size, enlarged anterior chamber.
(X21).

Plate XIII.

Figure 44:- ♀, non-albino, lens-rupture, 8 months old, left eye.
Note fibrous band from optic pit to the lens capsule.
(X110).

Figure 45:- ♀, albino, normal retina, right eye, 3 months old.
(X110).

Figure 46:- Normal mouse retina (After Keeler - 1927) Note
epithelial layer, A; rod layer, B; external
limiting membrane, C; external nuclear layer, D;
external molecular layer, E; internal nuclear
layer, F; internal molecular layer, G;
ganglionic layer, H; optic fibres, I; internal
limiting membrane, J.

Figure 47:- ♀, albino, lens-rupture, right eye, 4 months old.
(X112). Abnormal mouse retina.

Plate XIV.

Figure 48:- ♂, albino, lens-rupture, left eye, retina, 5 months
old. (X 112).

Figure 49:- ♀, albino, lens-rupture, right eye, 4 months old.
Note retinal irregularity, distorted and ruptured lens (X 21).

Figure 50:- ♀, albino, lens-rupture, right eye, 3 1/2 months old. Note retinal irregularity in the region of the optic pit; distorted lens (X21).

Figure 51:- ♀, albino, lens-rupture, left eye, 6 months old. Note retinal irregularity; distorted lens curvature. (X21).

Plate XV.

Figure 52:- ♂, albino, lens-rupture, right eye, 4 months old. Note retinal irregularities. (X21).

Figure 53:- ♀, albino, lens-rupture, left eye, 6 months old. Note lens in anterior chamber. (X21).

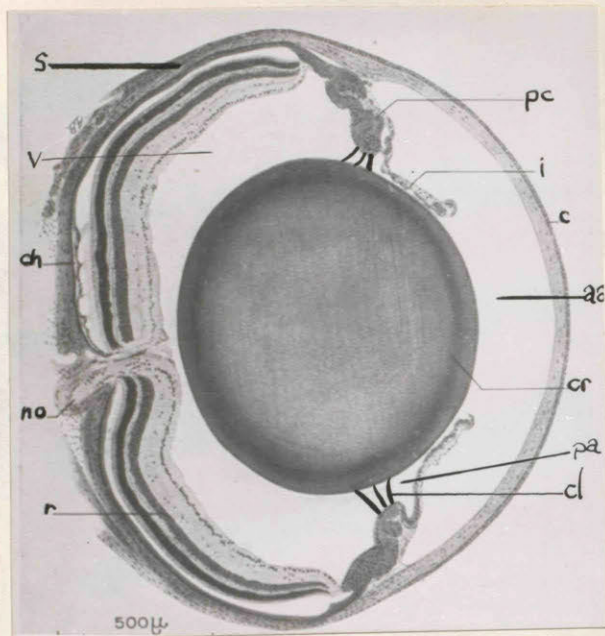


Fig. 1

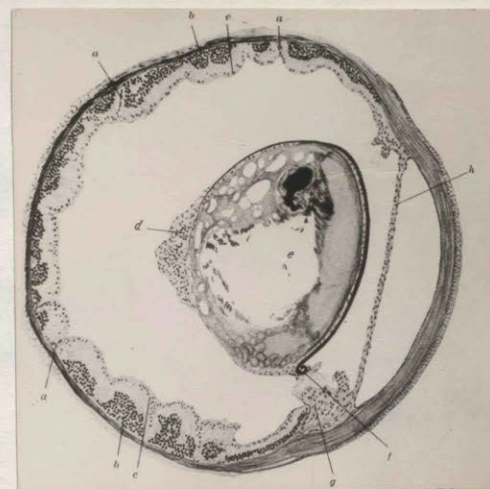


Fig. 2

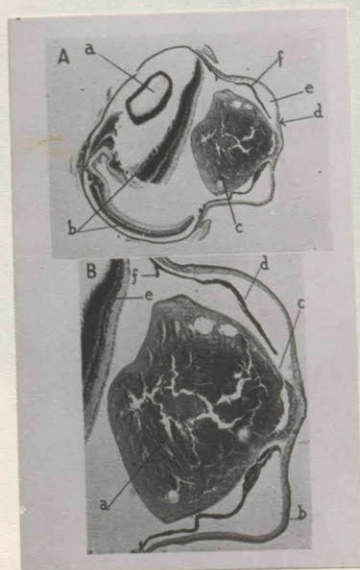


Fig. 3

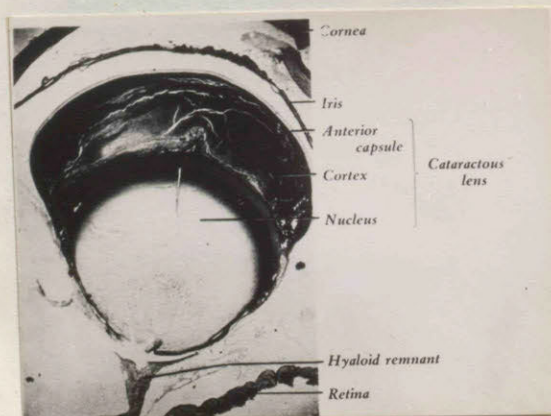


Fig. 4

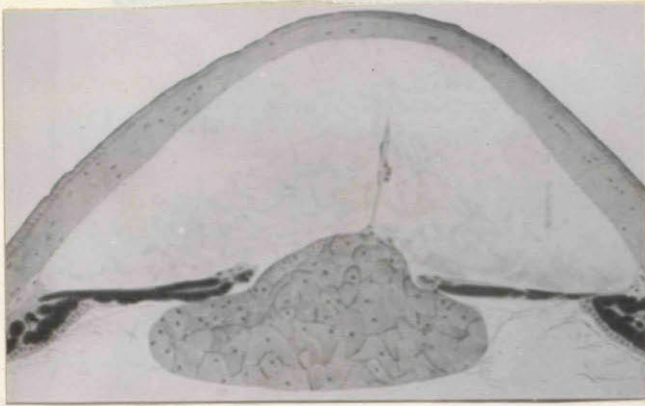


Fig. 5

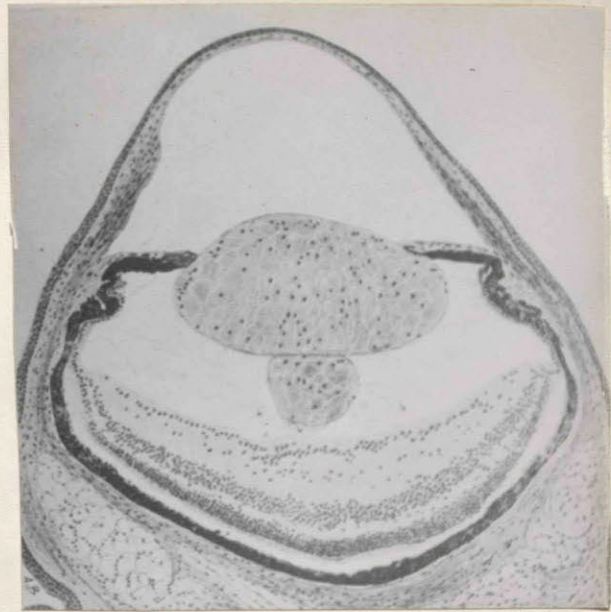


Fig. 6

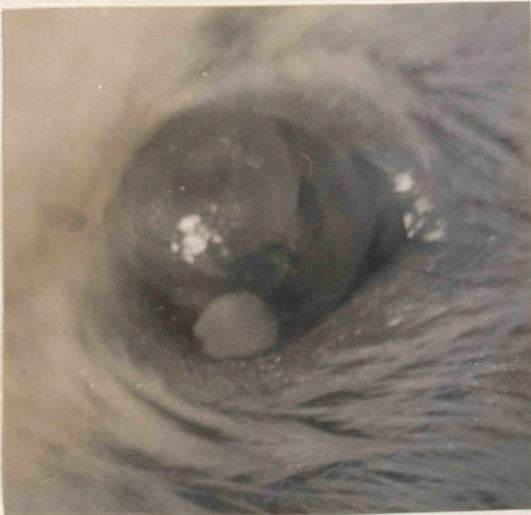


Fig. 7



Fig. 8

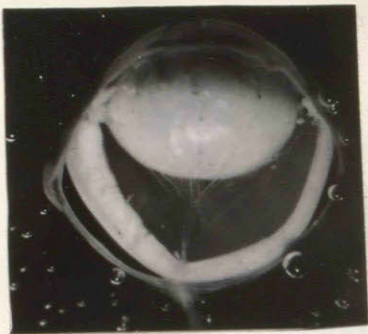


Fig. 8a

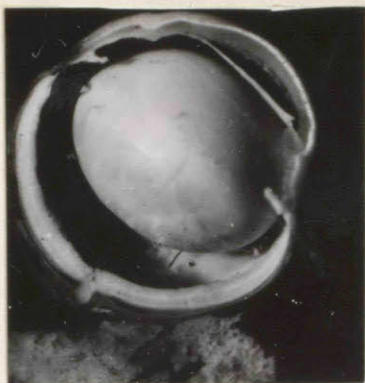


Fig. 9

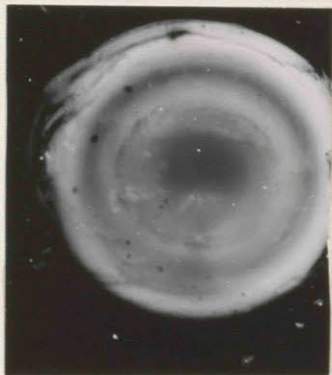


Fig. 10



Fig. 11



Fig. 12



Fig. 13

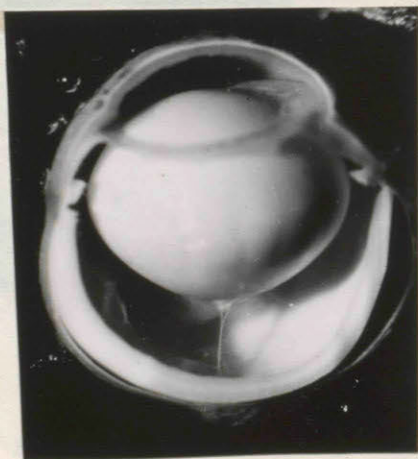


Fig. 14



Fig. 15



Fig. 16



Fig. 17



Fig. 18

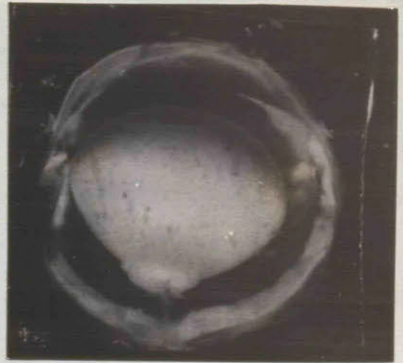


Fig. 19

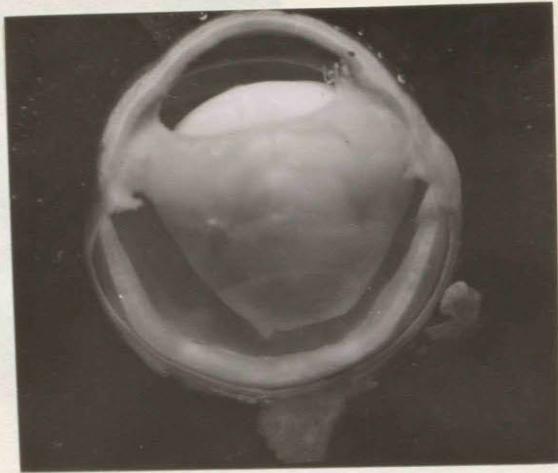


Fig. 20



Fig. 21



Fig. 22

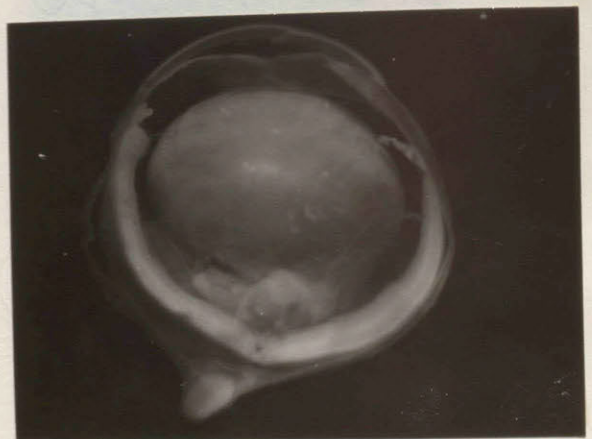


Fig. 23



Fig. 24

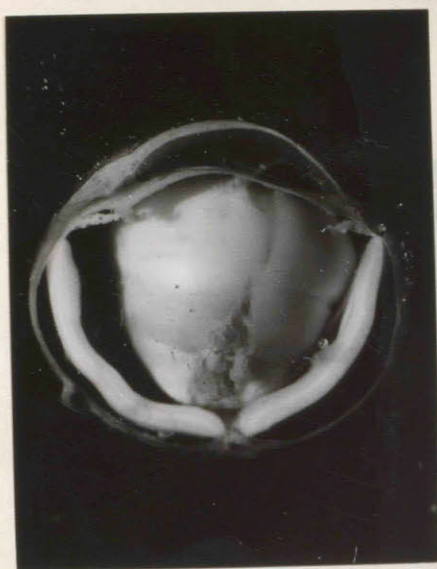


Fig. 25

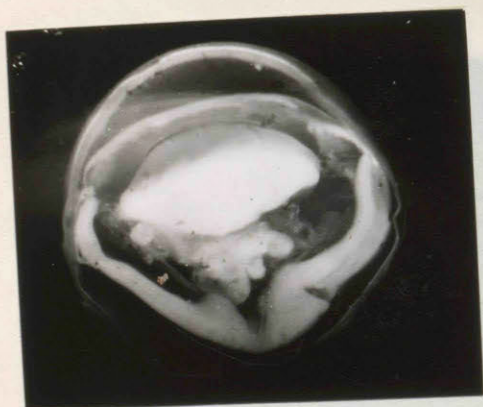


Fig. 26



Fig. 27

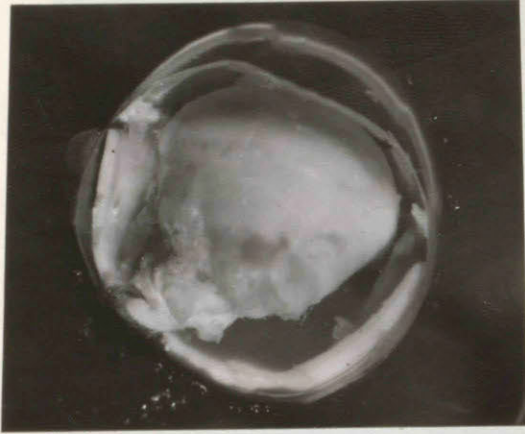


Fig. 28



Fig. 29



Fig. 30



Fig. 31



Fig. 32



Fig. 33



Fig. 34



Fig. 35



Fig. 36



Fig. 37



Fig. 38

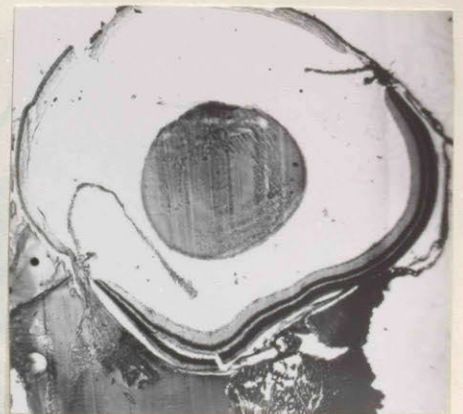


Fig. 39



Fig. 39a



Fig. 40

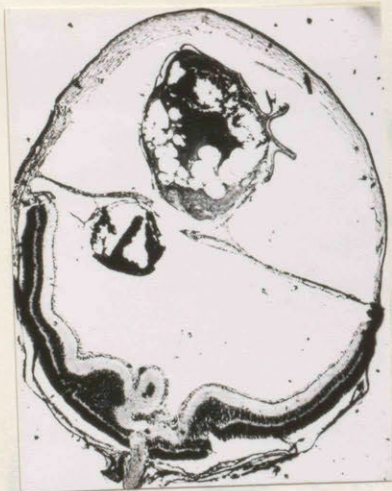


Fig. 41



Fig. 41a



Fig. 42

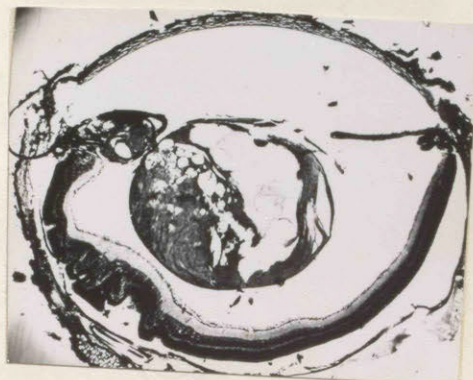


Fig. 42a



Fig. 43 a



Fig. 43b

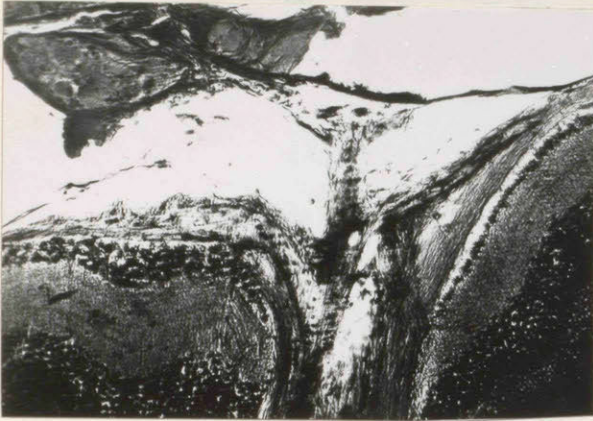


Fig. 44

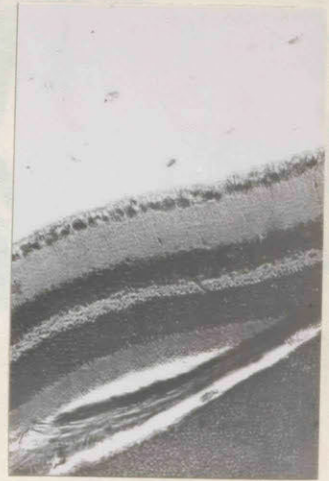


Fig. 45

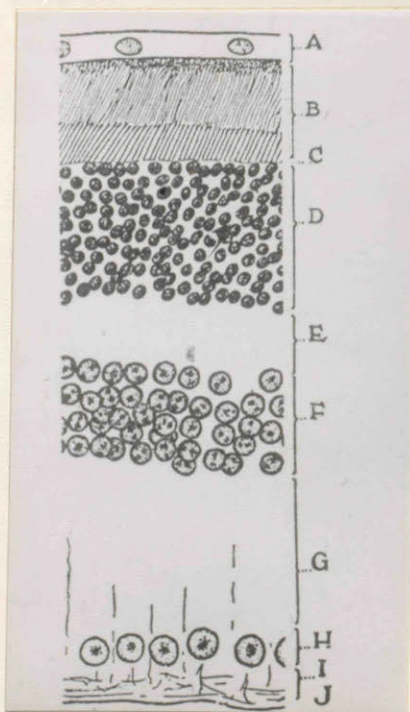


Fig. 46

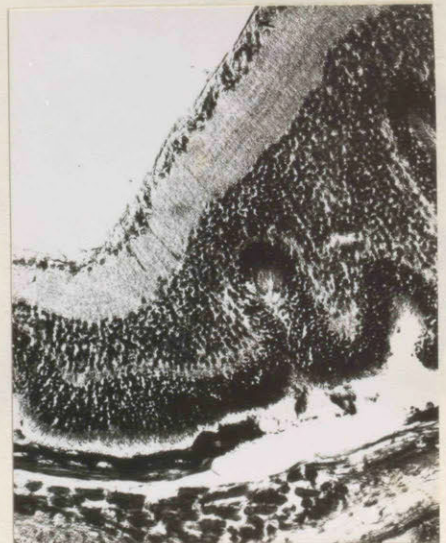


Fig. 47

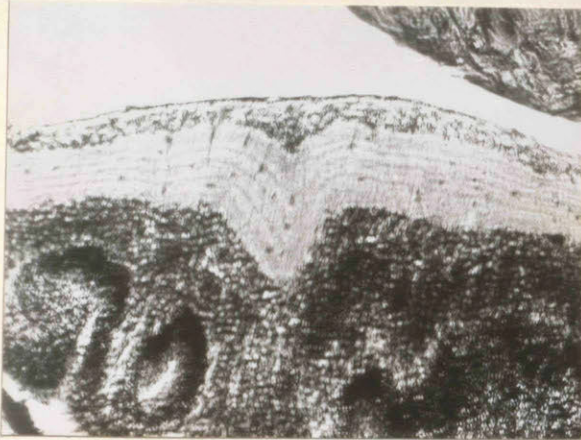


Fig. 48

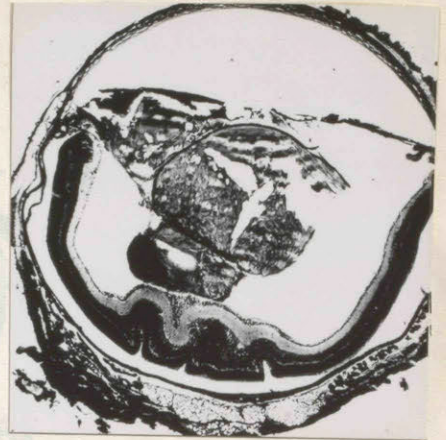


Fig. 49



Fig. 50



Fig. 51

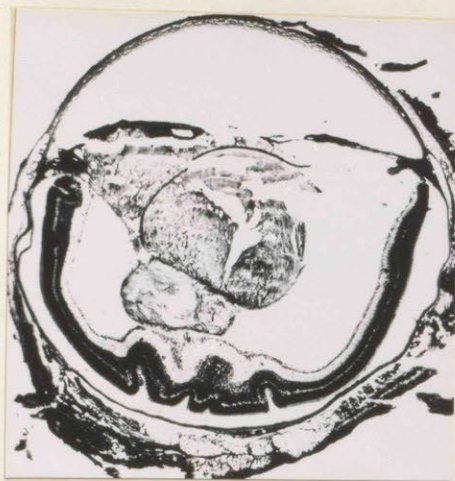


Fig . 52

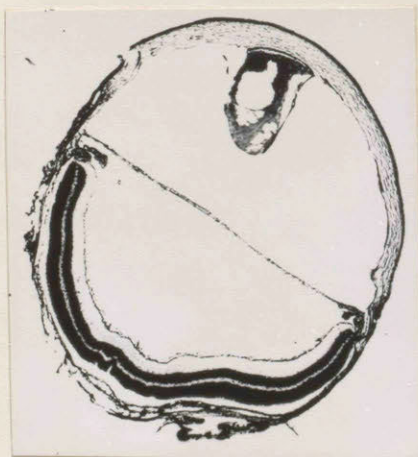


Fig. 53

McGILL UNIVERSITY LIBRARY

I x M

.1H421.1948



UNACC.

