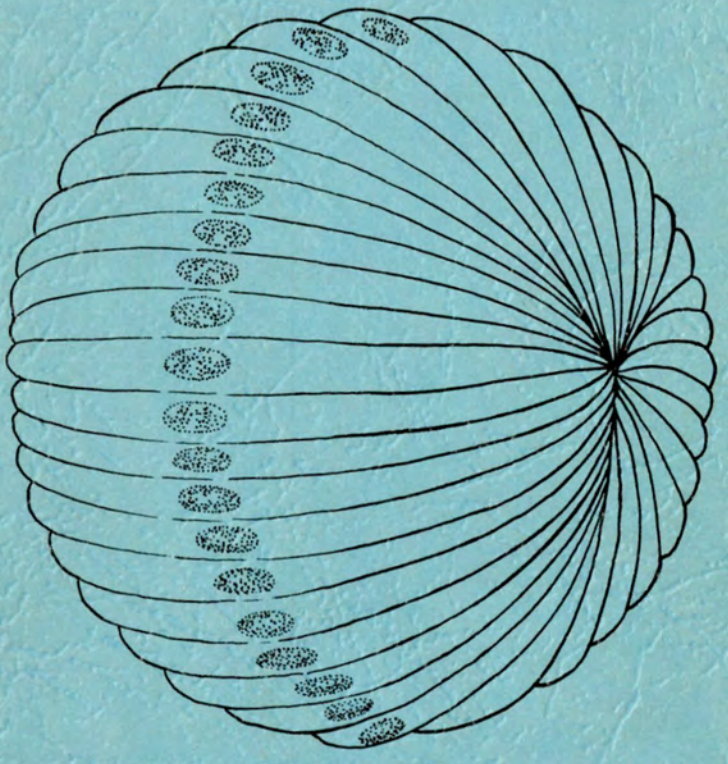
THE DEVELOPMENT OF THE EYE



American Academy of Ophthalmology
and Otolaryngology

THE DEVELOPMENT OF THE EYE

Anthony A. Pearson, Ph.D., *Editor*
University of Oregon Health Sciences Center
School of Medicine
Portland, Oregon

PART I
NORMAL DEVELOPMENT OF THE EYE
Anthony A. Pearson, Ph.D.
Emeritus Professor of Anatomy

PART II
ABNORMALITIES OF THE EYE
Richard G. Weleber, M.D.
Instructor in Ophthalmology

A SELF-INSTRUCTIONAL MANUAL
For Continuing Education in Ophthalmology
Planned as a Supplement to Section II of the
Basic and Clinical Science Course of the
American Academy of Ophthalmology and Otolaryngology
1974-1975

Printing Department
University of Oregon Health Sciences Center
Portland, Oregon
Printed in U.S.A.

NOTE TO THE READER

When information is presented in a large number of short, easy steps, the learning process is not only more efficient but also more pleasant. Information presented in this form becomes a self-tutoring course. As you read the questions in this manual, we suggest that you verify your answers. In this way the reader will constantly check his knowledge of the material presented.

The authors recognize that many readers studying this outline will be familiar with the technical terms used and that a definition of each term is not necessary. A large part of the material presented here may not be new to the reader and some of it is presented in the form of a review.

Some of the concepts of "program instruction" are used. It is assumed that the reader is already familiar with the structure and function of the adult eye and for the sake of brevity certain liberties in programing have been taken. The effectiveness of a programed outline, such as this, is improved with use and should never be considered a finished product.

The authors will appreciate your criticism and suggestions. We would like for you to call to our attention factual and typographical errors and the omission of relevant information which should have been included in this outline.

Formal courses in embryology are currently offered in some colleges and medical schools. Few schools, however, teach the complete developmental story of the eye. It is our aim to outline the basic concepts of the developmental anatomy of the eye and to familiarize the reader with the basic vocabulary. This is a work manual. It is not a complete text or source book nor does it replace books by authors such as Wolff (Last), Mann, and Duke-Elder, or standard textbooks of embryology. It is an adjunct to them. The objective is: The reader should be able to explain the concepts of eye development in his own words, and to relate this knowledge to the normal and the abnormal adult eye.

PREFACE

The physician should recognize that there are critical periods during prenatal life, at which time developmental arrests are more apt to occur. During these periods an organ will be more sensitive to the action of teratogenic agents, detrimental environmental factors and errors in metabolism. There is a definite need for a time table of development. The late George L. Streeter made a fundamental contribution to the timing of human embryos in a series of monographs entitled, "Developmental Horizons in Human Embryos". A significant question in human biology is summarized best in Streeter's own words:

> "Do the embryological parts progress independently in unrelated order, or do they fit into a precise system, each unit of which comes into existence in an accurately-timed sequence? If the latter is true, we should know from the developmental status of one organ, the status of all the other organs in that particular specimen. From the kidney alone, or from the membranous labyrinth, or from the shaft of the humerus we should be able to reconstruct the whole embryo."

If the developmental time table is interrupted, what happens? Is development like a game of pool where each ball is numbered and must go into a particular pocket in an exact sequence? Do the lines of the poet, Omar Khayyam, apply to embryology?

> "The moving finger writes; and, having writ, moves on: nor all thy piety nor wit shall lure it back to cancel half a line, nor all thy tears wash out a word of it."

A few years ago a knowledge of the physiologic, biochemical and genetic basis of normal and abnormal development was considered to be largely academic. Now, repair or prevention of many congenital anomalies is possible through modern surgery and medicine. What is considered to be academic today may be basic information for the physician of tomorrow.

One of the main problems in teaching is that of communication. Communication should be like a two-way street on which there is a free exchange of information and ideas between the teacher and the student. If the teacher regards his students as a row of empty bottles which he partly fills with information during each lecture, he loses the important ingredient of active student participation in making a response. This response is important in reinforcing what the student learns. It has been said that programed instruction is a modified form of the Socratic method. The story is told that Socrates on one occasion elicited from an ignorant slave boy the correct answer that a square placed on the diagonal of a square is double the size of the original square. Teaching at its best resembles a conversation between a good tutor and his student.

The secret of successful teaching lies in the procedure of presenting information and ideas in short easy steps which permits the student to learn one or a few new concepts at a time. Each concept should require the student to actively respond. He must answer a question, solve a problem, label a diagram or carry out some kind of activity. As soon as the student has given the answer, he should check his response with the correct answer. In this way the correct answer is reinforced in his memory. After learning a few new concepts the student passes on. New knowledge is added to the old so gradually that the student learns without strain or tiring effort. The material gradually becomes more difficult and the student goes from the simple to the more complex without a struggle. His confidence is bolstered by his learning experience. The student can learn at his own speed. He is not held back by the slow ones or intimidated by the rapid learners. Slowness is not necessarily bad in itself. There are many successful people who did not distinguish themselves either in school or college. Proponents of self-instructional methods claim that with this type of teaching, good students learn more rapidly and that poorer students receive higher grades than before. Within normal IQ limits, slow and fast learners often attain high levels of performance.

Of all the teaching machines designed by man none serve the student more effectively than the printed book. However, some books are exciting and others are dull. Why? Some stimulate the student while others discourage him. We have observed that many students emphasize selected words and phrases by overscoring or "hi-lighting" them with a felt pen using transparent colored ink. Hi-lighting increases the learning process. Certain drawings in this manual become more readily understood when shaded with colors. For this, red, blue, green and yellow pencils are suggested. Arteries should be colored - red, and veins - blue. Structures derived from neural ectoderm should be colored - blue, surface ectoderm - green, mesoderm - red, and entoderm - yellow. If additional labels are needed on drawings, the reader should add them.

ACKNOWLEDGEMENTS

This project has been supported by funds from the Oregon Heart Association, the University of Oregon Medical School, The Commonwealth Fund, and the Collins Medical Trust Fund through the Medical Research Foundation of Oregon.

Part I of this outline was written as a companion text to be used with the motion picture film, "The Development of the Eye". This film was produced by Sturgis-Grant Productions, Inc. for the American Academy of Ophthalmology and Otolaryngology under the technical direction of George W. Corner, M.D. and George K. Smelser, Ph.D.

We wish to thank Dr. Kenneth C. Swan, Professor and Chairman of the Department of Ophthalmology of this school and members of his staff for their helpful suggestions and criticism. The author was assisted by S. R. East, M.D., G. K. Roduner, M.D., L. R. Eidemiller, M.D., J. M. Keane, M.D., R. J. Stuart, Jr., M.D., L. F. Rich, M.D. and R.W. Sauter, B.A. in the preparation of earlier editions of this manual.

Our observations are based on the Human Embryological Collections of the Carnegie Institution and the University of Oregon Medical School. The collection of embryos at this school has been supported by funds from U.S.P.H.S. All developmental ages given are approximate.

We wish to thank Dr. Paul Henkind of the Committee on Continuing Education in Ophthalmology of the American Academy of Ophthalmology and Otolaryngology for his interest and encouragement during the revision of this manual.

The 90-Second True or False Quiz

1. The inner surface of the retina develops from that layer of the embryo which was continuous with the surface ectoderm (skin). T F
2. When the inner nervous layer of the retina is detached, it is almost transparent. T F
3. The term "fetal fissure" in the optic cup is more suitable for the "choroid fissure" because it may be confused with the choroid fissure in the brain. T F
4. The choroid fissure provides a short cut into the optic cup for the hyoid vessels and optic nerve fibers. T F
5. The optic cup develops as an invagination from the embryonic midbrain. T F
6. The lens like the retina develops from neural ectoderm. T F
7. The vitreous develops in the posterior chamber of the eye. T F
8. If the choroidal fissure should persist, it would lead to a coloboma of the iris. T F
9. In the embryo a canal develops in the vitreous body and in the adult it conveys the hyaloid artery to the lens. T F
10. The lacrimal gland develops from epithelial buds which grow from the upper part of the lacrimal sac. T F
11. The caruncle develops as an isolated part of the upper lid. T F
12. The semilunar fold (plica semilunaris) develops from the conjunctiva and it represents the nictitating membrane (third eyelid) in some animals.
13. The majority of white babies are born with brown eyes. T F
14. A tumor in the region of the facial colliculus may cause a lateral strabismus. T F
15. The trochlear angle even in early development is an acute angle. T F
16. The aqueous humor is produced in the posterior chamber of the eye. T F
17. In early development, the canal of Schlemm, which drains the aqueous humor, was an arterial channel. T F
18. Secretory preganglionic neurons in the carotid nerve synapse in ciliary ganglion. T F
19. An injury at birth causing an injury to the lower trunk of the brachial plexus may result in a Klumpke's paralysis with a Horner's syndrome. T F
20. The epicanthus develops as a fold of skin which partially hides the outer canthus. T F
21. If little pigment develops in the iris, the eye is blue or grey. T F
22. The optic nerve is formed by nerve fibers which grow from neuroblasts located in the optic cup to the forebrain. T F
23. Medullation of the fibers in the optic nerve begins in the brain and extends distally toward the lamina cribrosa. T F
24. This medullation reaches the lamina cribrosa at birth and gradually extends to the ganglion cells in the retina. T F
25. After successful cataract surgery, the cataract may eventually return. T F
26. An individual born with crossed eyes (esotropia) will have the same projection pattern of the optic radiations into the cerebral cortex as a normal individual. T F
27. It is normal for the eyelids to be held together (closed) by adhesions during part of the intrauterine life. T F
28. As the cornea develops its convexity becomes identical with that of the sclera. T F

29. The nerves which innervate the lens follow the hyaloid artery. T F
30. The cornea of brown eyed individuals contains a greater concentration of pigment granules than in blue eyed individuals. T F
31. Stimulation from the lens placode leads to the formation of the optic vesicle. T F
32. The differentiation of the fovea centralis is complete when the eyelids open. T F
33. The angle of the optic axes in the human embryo of two months is approximately 180°. T F

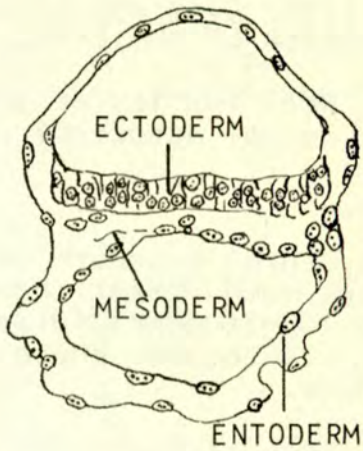
How True!

1. True. Through the invagination of the neural ectoderm and the evagination of the optic vesicle, this layer becomes the stimulus-receiving (nervous) inner lamina of the retina.
2. True. The pigment layer develops from the outer layer of the optic cup.
3. True.
4. True for lyaloid vessels. False for optic nerve fibers.
5. False. It develops from the forebrain.
6. False. It develops from surface ectoderm (skin).
7. False. It develops in the chamber posterior to the lens.
8. True.
9. True. A canal develops. False. The hyaloid artery disappears.
10. False. It develops from buds from the conjunctival sac.
11. False. It probably has an independent origin.
12. True.
13. False. They are usually blue.
14. False. The nucleus of the VIth nerve may be involved leading to a paralysis of the lateral rectus muscle.
15. False. In early development it is an obtuse angle and becomes acute later in development.
16. True.
17. False. It was a venous channel.
18. False. Fibers in the carotid nerve are postganglionic fibers and they do not synapse in this ganglion.
19. True. Sympathetic preganglionic neurons in the first thoracic nerve may be interrupted.
20. False. It is related to the inner canthus.
21. True. The eye becomes brown with the development of more pigment.
22. True.
23. True.
24. False. Normally the medullation does not extend into the retina.
25. False. When the lens is removed it will not grow back.
26. False (probably). In cross-eyed cats it has been shown that the projection pattern is not identical with the normal.
27. True.
28. False. They are not the same.
29. False. The lens has no nerve supply.
30. False. Normally there are no pigment cells in the cornea.
31. False. The reverse is true. The lens is dependent on induction from the optic vesicle.
32. False. The development of the fovea is not complete until after birth.
33. True.

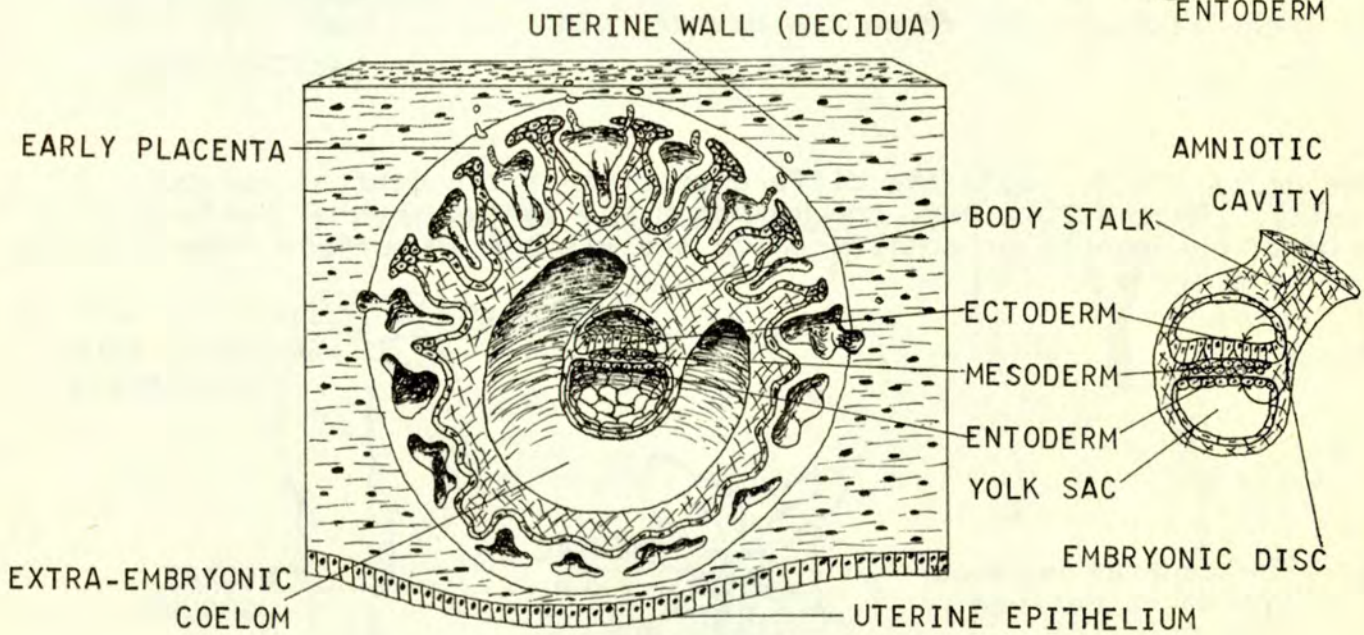
PART I

THE DEVELOPMENT OF THE EYE

1
The first major activity in the life of the embryo is the formation of a nearly flat plate of cells consisting of three germinal layers: ectoderm, mesoderm and entoderm. In the development of the eye, only ectoderm and mesoderm are of importance.

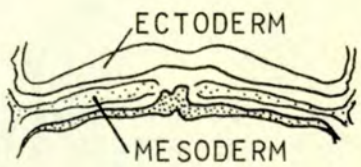


Q: Of the three germinal layers, only _____ and _____ are important in the development of the eye. (See answers at bottom of page.)

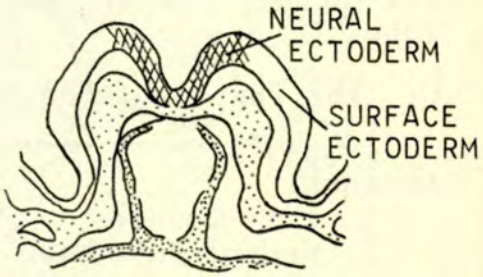


16 DAY OLD EMBRYO
PARASAGITTAL SECTION

2
The ectoderm may be divided into two types. The portion which will form neural structures is neural ectoderm, the remainder which will form the epidermal layer of the skin is surface ectoderm.

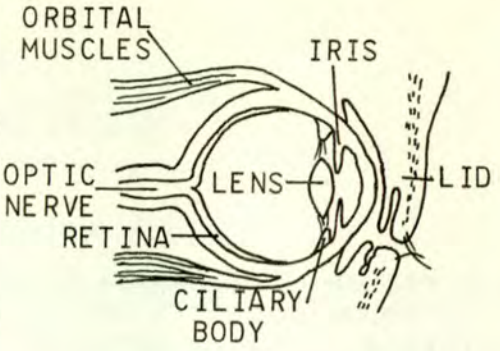


Q: Ectoderm is divided into _____ ectoderm and _____ ectoderm.



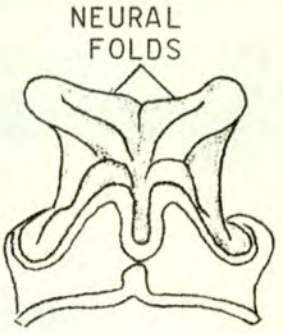
Answers:
1 Ectoderm, Mesoderm
2 Neural, Surface

3
In the embryo, the neural ectoderm of the brain wall will contribute cells for the development of:
the nervous retina which produces the optic nerve fibers,
the non-nervous retina which covers the ciliary body and iris and produces the muscles of the iris.



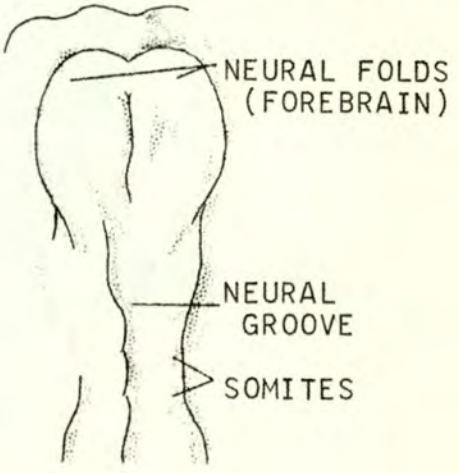
Q: What muscles of the eye are derived from neural ectoderm?

4
The neural ectoderm on either side of the midline grows much faster than the other layers, forming two longitudinal folds. These are the neural folds. Between these folds lies the neural groove.

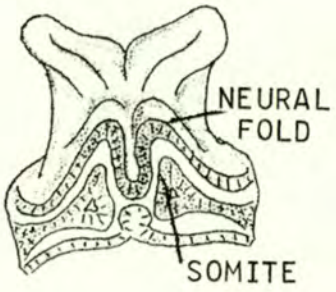


Q: What tissue layer forms the neural folds?

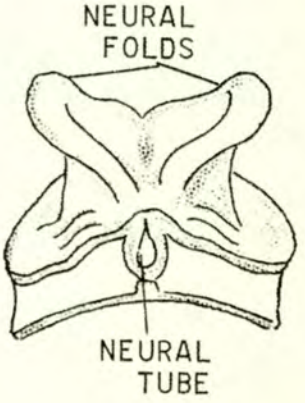
5
The neural folds begin the differentiation of the central nervous system. By the 20th day, the mesoderm has formed several pairs of primitive segments or somites which are visible in surface views of intact embryos.



Q: The central nervous system is derived from folds of _____ _____.



6
Possibly due to the more rapid enlargement of the exterior surfaces the folds begin to lean toward each other. As their edges touch, they fuse, and the groove between them becomes a tube, the neural tube.



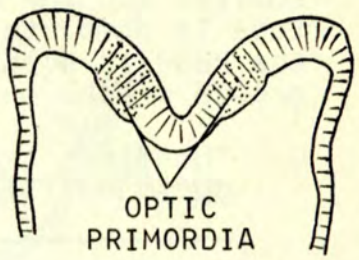
Q: The fusion of the neural folds forms the _____ _____.

Answers:

3 Iris Muscles
4 Neural Ectoderm
5 Neural Ectoderm
6 Neural Tube

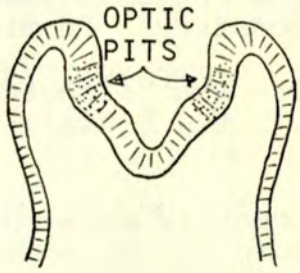
7
From now on, our interest will center on the cephalic end of the embryo, the region of brain formation.

This drawing of a cross section of the neural folds, in the region of the forebrain, shows thickenings, the optic primordia. The optic primordia are the first signs of the developing eyes.



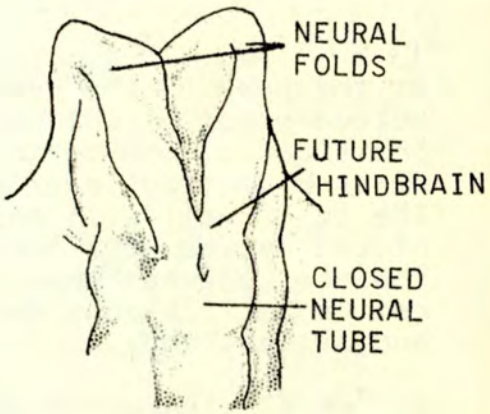
Q: The first signs of the developing eyes are the formation of the optic _____.

8
Soon, a shallow depression forms in each optic primordium. These are the optic pits.



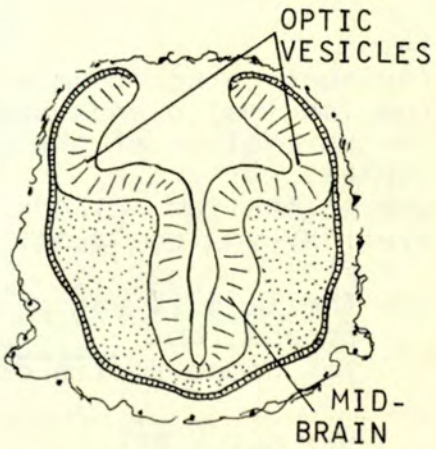
Q: The optic _____ form as depressions in the optic primordia

9
The rostral end of the neural tube has closed as far as the future hindbrain.



Q: The optic pits develop in the _____.

10
As the neural folds close, the forebrain in the region of the optic pits pushes away from the midplane to lie close to the surface ectoderm, forming the optic vesicles.

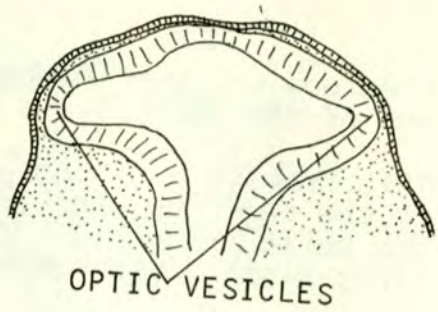


Q: The further invagination of the optic pits forms the _____ _____.

Answers:

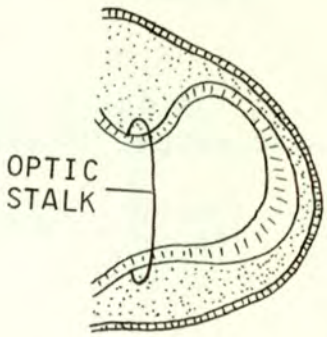
7 Primordia
8 Pits
9 Forebrain (Primitive)
10 Optic Vesicles

11
By the 25th day the embryo has 20 pairs of somites and the cephalic end of the neural tube is completely closed. On each side of the head is a bulge caused by the outward growth of the optic vesicles.



Q: The first stage in the development of the optic vesicle is the formation of the _____ _____.

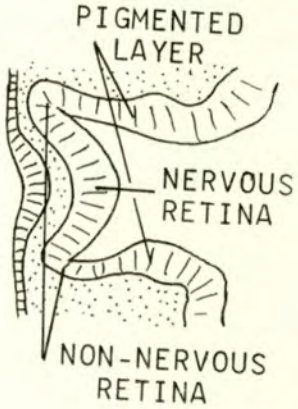
12
The region between the brain and the optic vesicle constricts forming the optic stalk.



Q: What structure connects the optic vesicle and the brain?

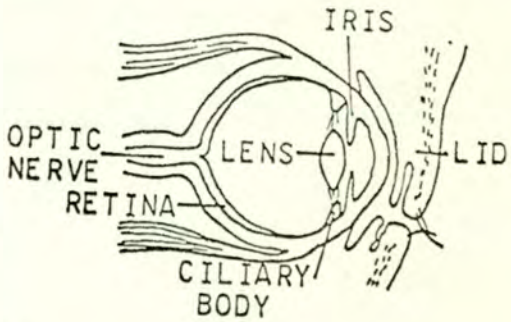
Identify structures in all drawings which are not completely labeled.

13
At the peak of the vesicle formation the neural ectoderm begins cellular differentiation. The sides of the optic vesicle will become the outer pigmented layer of the retina. The outer wall will become the sensory layer of the retina, the nervous retina. The area between these two, the non-nervous retina, will become the epithelium of the iris and ciliary body.



Q: What is formed from the outer wall of the optic vesicle?

14
The surface ectoderm will contribute to:
The lacrimal glands and ducts,
the epithelium of the conjunctiva and cornea,
the epithelium, glands, and cilia of the eyelids, and the lens.

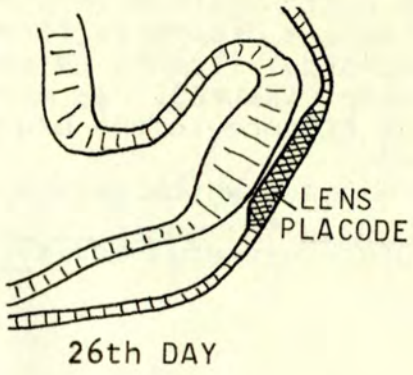


Q: The lens is unique in that it is formed from _____ ectoderm and yet comes to lie deep within the eye.

11 Optic Pit
12 Optic Stalk
13 Nervous Retina
14 Surface

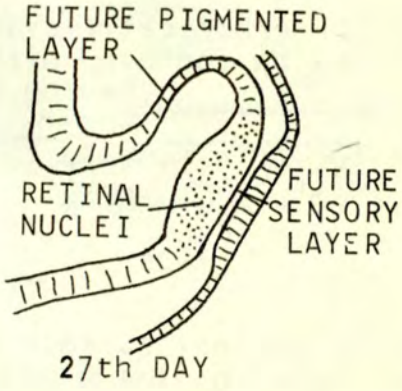
15
The surface ectoderm adjacent to the optic vesicle thickens forming the lens placode.

Q: The nervous retina develops in close relation to the surface ectoderm which forms the _____ _____.



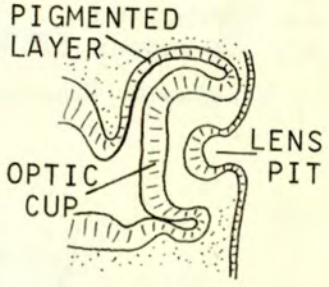
16
The retina begins differentiation into layers by the migration of cells toward the inner surface.

Q: The thickened area of neural ectoderm of the optic vesicle is the future _____ _____.



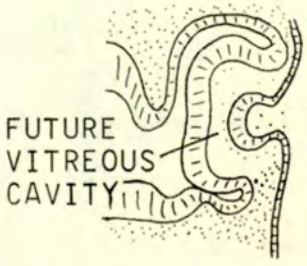
17
The sensory area of the optic vesicle pushes in toward the pigmented layer to form the optic cup. At the same time the lens placode invaginates to form the lens pit.

Q: The optic cup is formed by an invagination of the _____ _____ and the lens pit is formed by the invagination of the _____ _____.



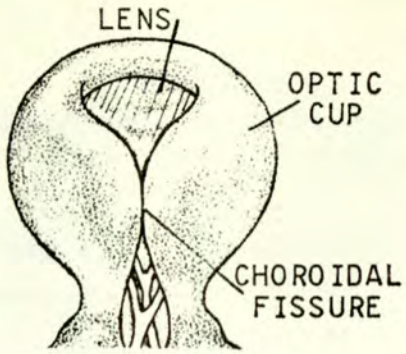
18
Between the lens pit and the optic cup, a space exists, the future vitreous cavity.

Q: The thickened plate of surface ectoderm overlying the retina is the _____ _____. Invagination of the optic vesicle forms the _____ _____.



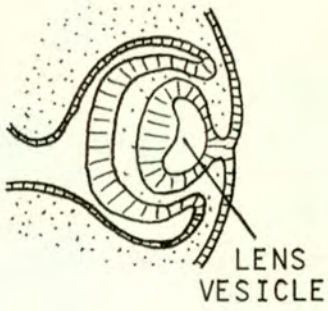
15 Lens Placode
16 Nervous Retina
17 Optic Vesicle, Lens Placode
18 Lens Placode, Optic Cup

19
As the optic vesicle invaginates to form the optic cup, a groove is formed which is called the choroidal fissure (also called fetal or embryonic fissure). It does not resemble the choroid fissure in the brain.



Q: The space which exists between the _____ _____ and _____ _____ is the future vitreous cavity.

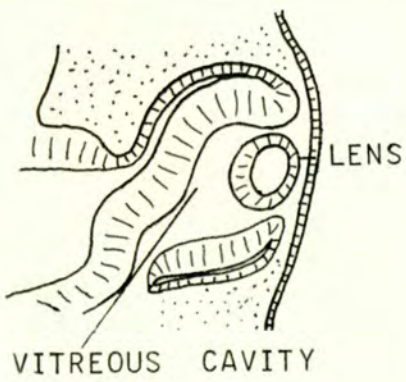
20
As the lens pit deepens, it forms a deep cavity which closes off to form the lens vesicle.

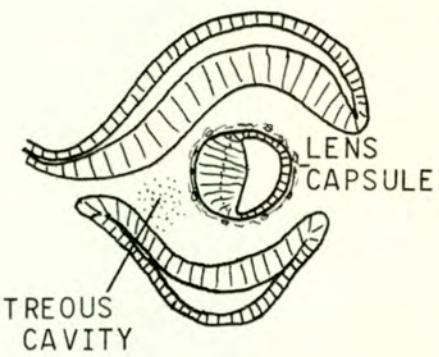


Q: The choroidal fissure of the optic cup should not be confused with a fissure in the _____ having the same name. The terms _____ and _____ are also names for this fissure in the developing eye.

21
As the retinal surface of the optic cup continues to invaginate, the space between it and the lens vesicle increases. At this time a capsule is forming around the lens vesicle.

Q: The germ layer from which the lens vesicle is formed is _____ _____ and it comes to lie deep within the _____ _____.

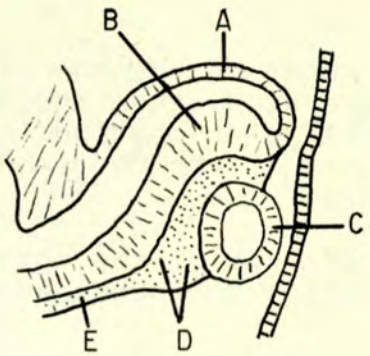




19 Lens Vesicle, Optic Cup
20 Brain, Fetal, Embryonic
21 Surface Ectoderm, Optic Cup

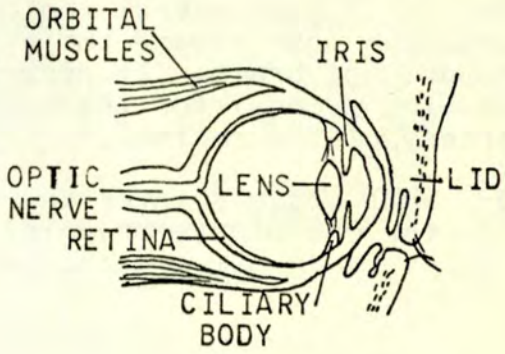
22
The structures formed thus far are as follows:
Pigment layer, from neural ectoderm
Retinal layer, from neural ectoderm
Lens, from surface ectoderm
Choroidal fissure, a groove in the optic cup
Vitreous cavity.

Q: In the figure, what are:
A_____, B_____, C_____, D_____, E_____?



23
Mesoderm will contribute to certain muscles, connective tissues and vascular tissues. The cornea, sclera, choroid, endothelium of the anterior chamber, extraocular and ciliary muscles are examples.

Q: What muscles are not derived from mesoderm?

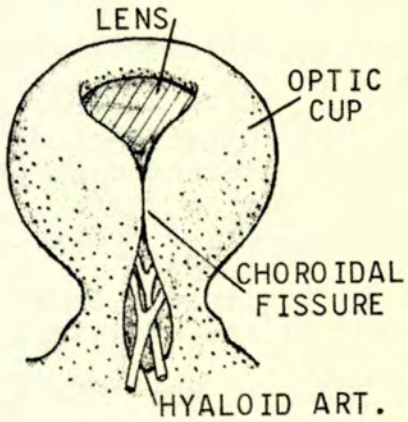


24
The muscles which arise from mesoderm are: The ciliary muscle which controls the shape of the lens; the orbicularis oculi muscle which closes the lids; the levator palpebrae which opens the lids; the extraocular muscles which move the eyeball.

Q: Identify the intrinsic muscles of the eye. From what germ layers are they formed?

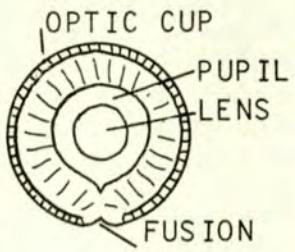
25
This is a drawing of the optic cup showing the choroidal fissure. The hyaloid artery which supplies the deep structures of the developing eye grows into the choroidal fissure.

Q: The space between the lens vesicle and the optic cup is the _____ _____.



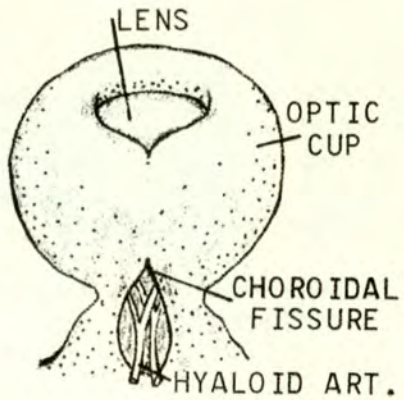
22 (a) Pigment Layer, (b) Retinal Layer, (c) Lens Vesicle, (d) Vitreous Cavity, (e) Choroidal or Embryonic Fissure
23 Iris Muscles
24 Ciliary Muscles--Mesoderm, Iris Muscles--Ectoderm
25 Vitreous Cavity

26
The edges of the choroidal fissure have been growing toward each other and now begin to fuse; the remaining circular opening in the optic cup is the pupil. The rim of the cup represents the region of the future iris.



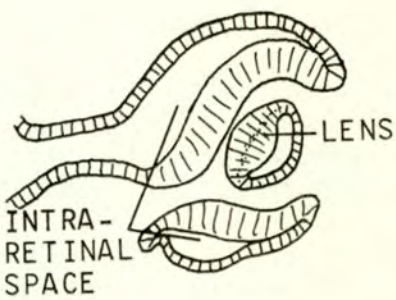
Q: The rim of the optic cup forms the _____ which surrounds an opening called the _____.

27
The fusion of the sides of the choroidal fissure begins in the central region of the fissure and proceeds both toward the rim of the optic cup and toward the brain. It never completely closes, leaving a canal for the hyaloid artery (central artery of the retina).



Q: What vessels enter the optic stalk by way of the choroid (embryonic) fissure?

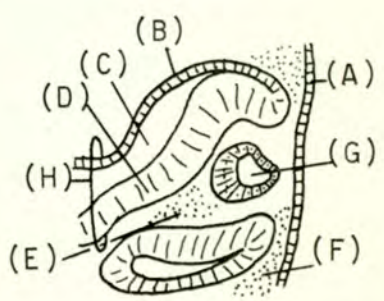
28
The space shown in this figure between the pigmented layer and the sensory layer of the retina is overly large due to tissue shrinkage. This space is the intraretinal space and is continuous with the third ventricle of the brain.



Q: The embryonic fissure fuses last in the regions of the rim of the _____ cup and the _____.

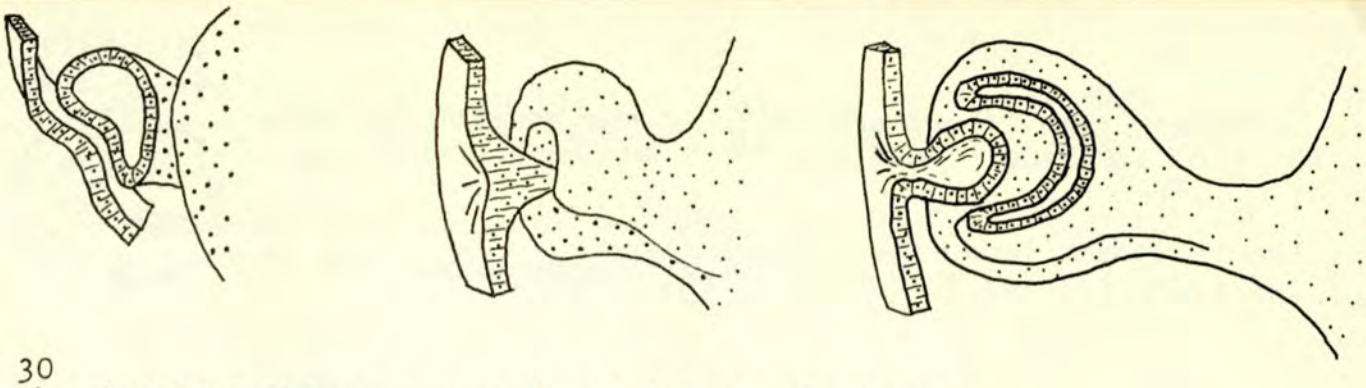
29
Shown in this sagittal section of the developing eye are:

( ) Intra-retinal Space
( ) surface ectoderm
( ) pigmented epithelium
( ) optic stalk
( ) retina proper
( ) mesoderm
( ) vitreous body
( ) lens vesicle

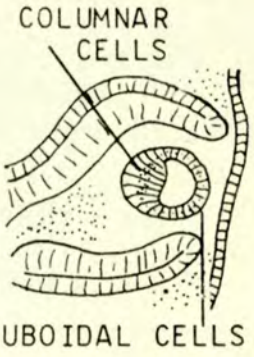


Q: Identify the labels in this diagram.

26 Iris, Pupil
27 Hyaloid Artery and Vein
28 Optic, Brain
29 C, A, B, H, D, F, E, G



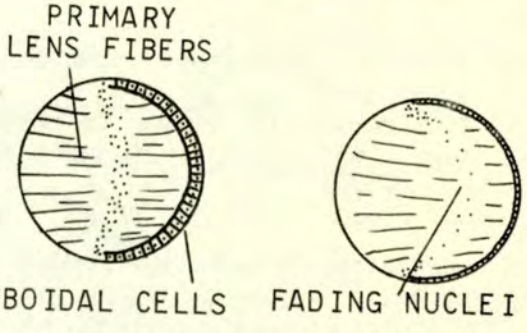
30
The diagrams above recapitulate the transformation from lens placode into the lens vesicle and the optic vesicle into the optic cup.



The anterior or more superficial part of the lens vesicle is made up of cuboidal cells, whereas the deeper, posterior cells, which are formed from the central part of the lens placode, are columnar. These columnar cells grow longer and form the primary lens fibers.

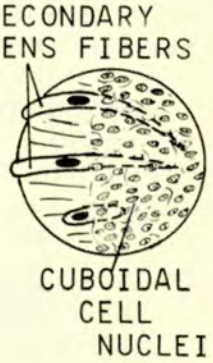
Q: The lens vesicle is now formed by _____ and _____ (type of) cells and is surrounded by a connective tissue _____.

31
The columnar epithelial cells (future primary lens fibers) elongate and completely obliterate the lumen of the lens vesicle. With continued growth their nuclei begin to fade. The lens remains roughly spherical in shape. The cuboidal cells remain as the "lens epithelium".



Q: The intra-retinal space is located between the _____ and _____ layers of the optic cup. This space is continuous with the _____ (a space) of the brain.

32
By the 7th week secondary fibers begin to proliferate in both directions from the equatorial region of the lens. These fibers originate from the cuboidal cells at their junction with the columnar cells. The nuclei of the cuboidal cells are shown here and the secondary fibers, as they extend forward, pass beneath the cuboidal cells. Their posterior ends pass backwards deep to the hyaline capsule of the lens.



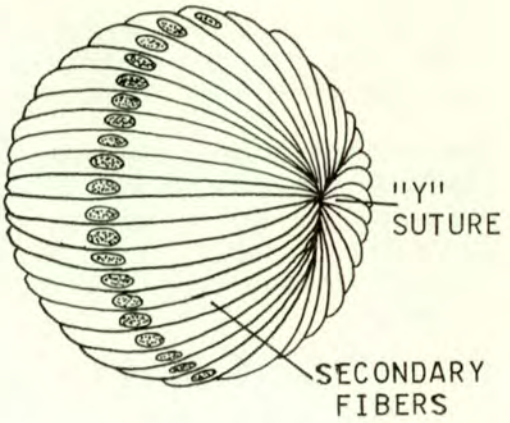
Q: The columnar cells of the lens vesicle give rise to the _____ lens fibers. These fibers eventually obliterate the _____ of the lens vesicle.

30 Cuboidal, Columnar, Lens Capsule
31 Pigmented, Sensory, 3rd ventricle
32 Primary, Lumen

33
The secondary lens fibers are thick at the equator but taper as their ends extend toward the front and back of the lens.

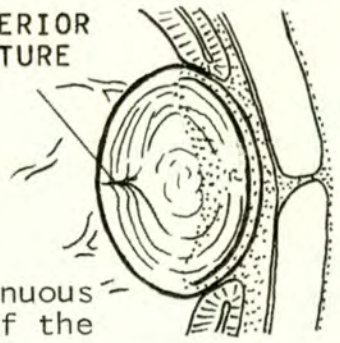
Q: The secondary lens fibers are a layer _____ (outside, inside) the primary lens fibers.

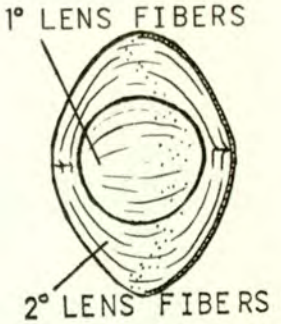
34
Secondary lens fibers do not become thin enough to meet other fiber ends at a single point and Y-shaped sutures result. Because of this arrangement no fiber ever becomes long enough to reach completely from pole to pole.



Q: The fact that the secondary fibers never become thin enough at their ends to all meet at one point, results in the _____.

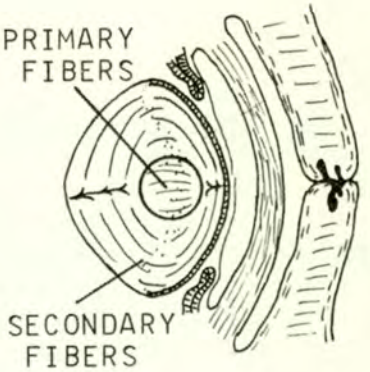
35
Since the secondary lens fibers are successively laid down on top of each other, with their thickest parts at the equator, the lens becomes less spherical. Note the posterior suture in the figure.





Q: The intraretinal space is continuous with the _____ _____ of the brain and is found between the _____ and _____ layers of the retina.

36
This drawing shows the shape of the lens at the 5th month. Note that the part of the lens formed by primary fibers remains in a spherical shape. The remainder of the lens is formed by secondary fibers.

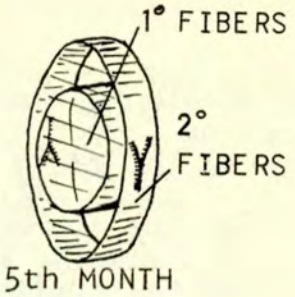


Q: In the lens vesicle the cuboidal cells give rise to _____ lens fibers, while the columnar cells give rise to the _____ lens fibers.

33 Outside
34 Y-shaped Suture
35 3rd Ventricle, Pigmented, Sensory
36 Secondary, Primary

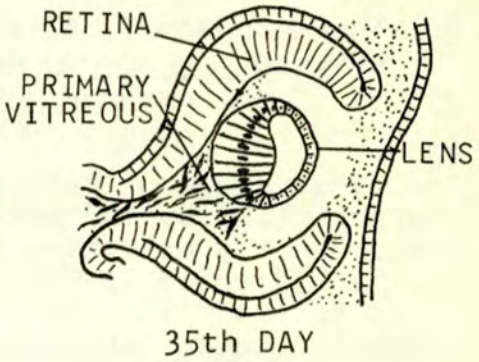
37
Shown here is a drawing of a section through the lens showing the primary and secondary lens fibers as layered entities.

Q: The characteristic shape of the adult lens is mainly due to the _____ lens fibers.



38
By the 35th day, the vitreous cavity is filled with mesodermal cells, fibers and secretions. The fibers and the secretions are formed by the lens and the retina. These, along with the mesodermal cells, make up the primary vitreous.

Q: The primary vitreous arises from which germ layers?

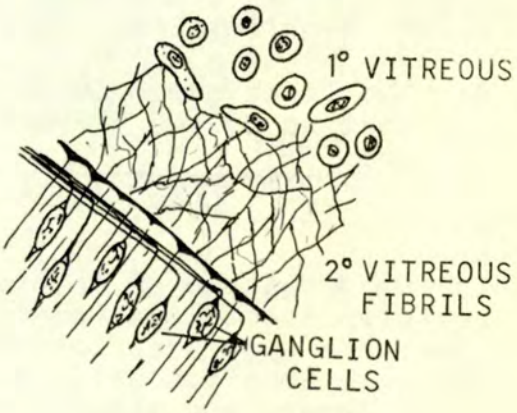


39
The mesodermal cells in the vitreous cavity will later form blood vessels and their associated connective tissues.

Q: The optic cup is connected to the developing brain by the _____.

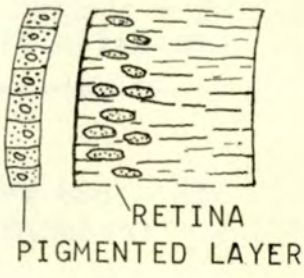
40
Cells lying in the retina give rise to vitreous fibrils so that a secondary vitreous is formed around the primary vitreous.

Q: The secondary vitreous is formed by cells of the _____.



41
By the 35th day, a few pigment granules are present in the pigmented layer of the retina.

Q: The pigmented layer develops from what germ layer?



37 Secondary
38 Mesoderm and Ectoderm
39 Optic Stalk
40 Retina
41 Neural Ectoderm

42
The development of the sensory retina may be divided into four steps or stages of differentiation according to Duke-Elder.

(1) The early differentiation into zones which takes place in human embryos during the 5th week (4 to 10 mm).
(2) The formation of temporary layers during the 6th to 11th week (10 to 68 mm).
(3) Cell differentiation and migration between the 12th and 24th week (65 to 230 mm).
(4) The final organization of layers (7th to 13th month).

Q: The mesodermal cells of the vitreous cavity primarily give rise to _____ and their associated connective tissues.

43
The first stage of retinal development in the optic cup is characterized by the differentiation of the nervous retina into two zones: a primitive zone (lying outermost in close relation to the pigmented layer); and a marginal zone (lying innermost close to the vitreous). Some cells eventually migrate from the primitive layer into the marginal layer.

Q: Neuroglia of the brain develop from _____ (germ layer), while microglia develop from _____ (germ layer).

44
In the second stage of retinal development, the original zone of primitive cells becomes divided into the inner and outer neuroblastic layers by the migration of the nuclei of some cells. Between them is a narrow zone without nuclei which is a transient fiber layer (of Chievitz).

Q: The first stage in the development of the retina was characterized by the formation of two zones, which are _____ and _____.

45
In the 3rd stage of retinal development, there is a beginning of cellular specialization in the inner neuroblastic layer. At this time, the outer neuroblastic layer undergoes relatively little change. Ganglion cells develop from the deeper cells of the inner layer, and migrate into the marginal zone of the nervous retina.

Q: When the nuclei of the primitive zone have separated into two definitive layers, these layers are referred to as the _____ and _____ _____ layers.

42 Blood Vessels
43 Ectoderm, Mesoderm
44 The Primitive, Marginal
45 Inner and Outer Neuroblastic

46
During the 4th stage, all the layers of the adult retina can be recognized. The cells of Müller are supporting elements which resemble ependymal cells and have a vertical arrangement. These cells extend between the external and internal limiting membranes with which they are closely associated. The intermediate layer contains the bipolar cells which connect the outer receptor cells with the deeper ganglion cells. We can only speculate as to how the retina became inverted in the optic cup so that light has to pass through many layers before reaching the receptor cells.

47
The first elements to develop in the nervous retina are the ganglion cells which send their fibers to the brain. The receptor cells (rods and cones) and the bipolar cells form later.

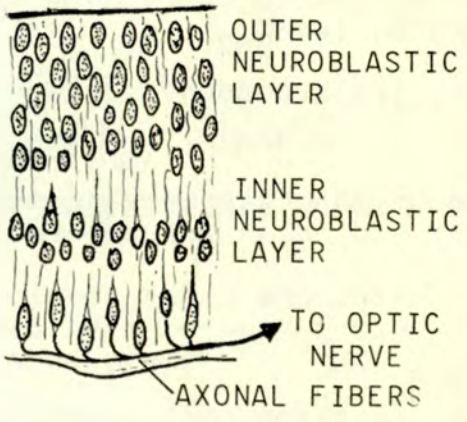
Q: The marginal zone is invaded by _____ _____ from the inner neuroblastic layer.

48
Each ganglion cell sends out a process which runs in the optic stalk toward the brain. These processes form the nerve fiber layer of the retina and the fibers of the optic nerve. This is the first fiber layer of the retina to be completely established.

Q: The first fiber layer to be established in the retina is formed by the processes of the _____ cells.

49
The ganglion cells send out fibers (axons) which grow slowly toward the optic stalk. When they enter the optic stalk and grow toward the brain they form the optic nerve.

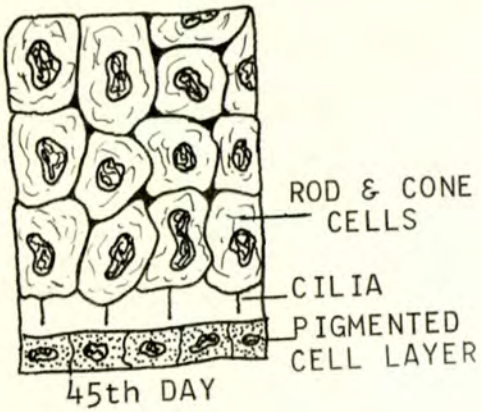
Q: The lens pit is formed from _____ (neural, surface) ectoderm.

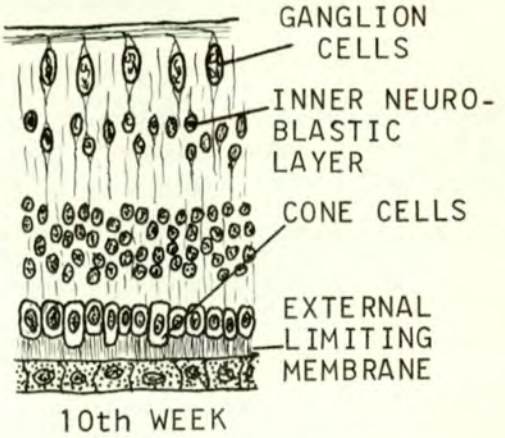


47 Ganglion Cells
48 Ganglion
49 Surface

50
By the 45th day the cells of the outer neuroblastic layer that will become rods and cones are ciliated. However, by the 10th week the cilia have disappeared on the future rod and cone cells and a few cone cells are protruding near the posterior pole of the retina.

Q: During the 3rd stage of retinal development cellular specialization begins in the _____ layer, but the _____ layer undergoes relatively little change.





51
There has been much controversy as to whether the Müllerian fibers of the retina give rise to the external and internal limiting membranes. It is probable that these membranes are the limiting membranes of the layer of cells which forms the primary optic vesicle. They further correspond to similar membranes which surround the neural tube.

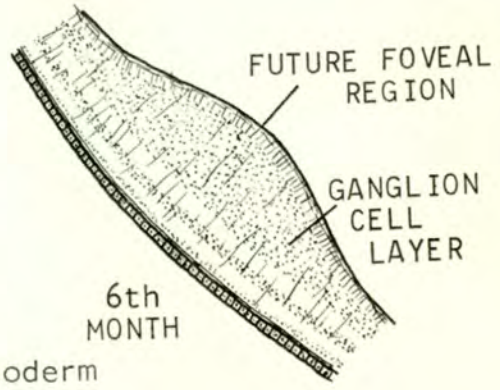
Q: The secondary vitreous is formed by cells of the _____.

52
About the 12th week, cone cells are present throughout the retina but rod cells are not fully differentiated at this time.

Q: Rods and cones develop from the _____ germinal layer

53
The ganglion cell layer of the retina now thickens in the region of the future macula. In the center of the macula, the fovea will soon develop. The fovea is the region of most distinct vision in the adult. In the adult rods are absent in the foveal region.

Q: The fovea develops in the center of the future _____.

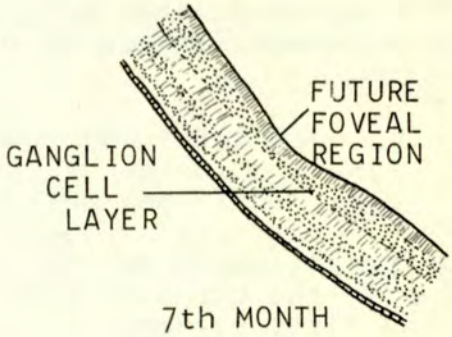


50 Inner Neuroblastic, Outer Neuroblastic
51 Retina
52 Neural Ectoderm
53 Macula

54
Differentiation of all parts of the retina is very rapid during the first 3 months of fetal life. At this time, the area which will become the future macula begins to lag behind adjacent areas in development. During the 8th month of fetal life differentiation again proceeds rapidly, however, unlike surrounding areas of retina it is not completed until 3 to 4 months after birth.

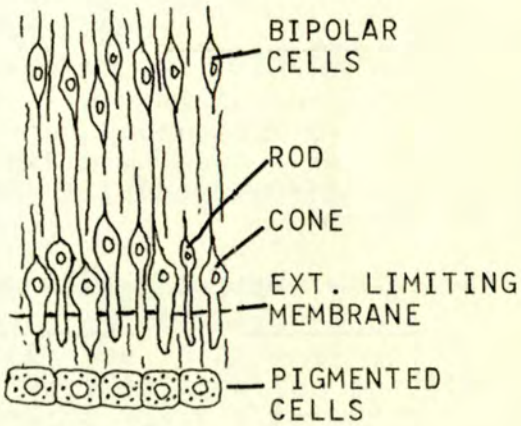
Q: The ganglion cell layer in the region of the future _____ thickens initially, but eventually this area is characterized by a thinning.

55
During the 7th month the ganglion cell layer in the region of the fovea thins causing a depression to appear, the fovea; however, it is not completely developed until after birth. Rods fail to develop in the region of the fovea.



Q: In the adult, the fovea contains _____ cells, but not _____ cells.

56
Rods differentiate from the outer neuroblastic layer during the 7th month, except in the region of the fovea. Horizontal cells also differentiate in the outer neuroblastic layer.



Q: The region of the fovea doesn't complete its development until _____ _____.

57
Also during the 7th month, the outer neuroblastic layer gives rise to the bipolar cells. The inner neuroblastic layer gives rise to the ganglion, amacrine, and Müller's cells.

Q: The outer neuroblastic layer gives rise to _____, _____ and _____ cells.

58
During the 7th month of fetal life the eye is sensitive to light.

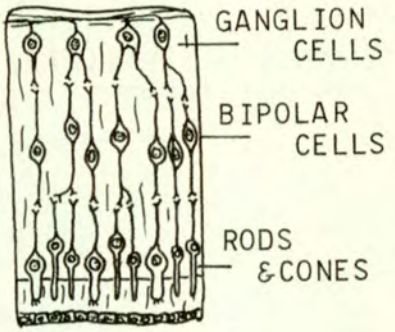
54 Macula
55 Cone, Rod
56 After Birth
57 Receptor, Bipolar, Horizontal

59
Form perception is acquired during the first year and color discrimination during the second year.

Q: Müller's cells arise from the _____ neuroblastic layer.

60
The bipolar cells serve as relays between the rods and cones and the ganglion cells which send the impulse to the brain.

Q: The region of the fovea completes its development (before or after) _____ birth.



61
The differentiation of the nervous elements of the optic system develop in the opposite direction of the path of the nerve impulses. Thus the first elements to develop are the ganglion cells sending fibers to the brain. The last to form are the receptor cells, the rods and cones.

Q: The _____ cells of the optic pathway are the first to differentiate.

62
At birth all layers of the retina are complete except in the region of the fovea.

Q: The inner neuroblastic layer gives rise to the _____, _____, and _____ cells.

63
Three factors are involved in the differentiation of the retina.

(1) Cells differentiate and migrate from superficial to deeper layers.

(2) The differentiation of layers proceeds from deep to superficial.

(3) Differentiation proceeds from the posterior pole to the anterior pole.

Q: Differentiation of the _____ pole of the retina lags behind that of the _____ pole.

59 Inner
60 After
61 Ganglion
62 Ganglion, Amacrine, Müller's
63 Anterior, Posterior

To recapitulate the development of the retina the following points should be remembered. During the early optic vesicle stage the nervous retina is located at the anterior pole of the vesicle adjacent to the lens placode. The retina at this time is represented by a single layer of columnar cells. In the optic vesicle, further development of the nervous retina results in the formation of two zones, the marginal zone and the primitive zone. The primitive zone, which lies adjacent to the chamber of the optic vesicle and deep to the marginal zone, contains cells which rapidly proliferate.

After invagination of the optic vesicle to form the optic cup, the marginal zone lies deep to the primitive zone and borders on the vitreous cavity. The marginal zone is devoid of nuclei but with further development cells migrate into it.

In the second stage of retinal development, the primitive zone divides into three layers; the inner neuroblastic layer, a transitory layer and the outer neuroblastic layer. The transitory layer is narrow and lacks nuclei; it is known as the transitory fiber layer of Chievitz. Further development sees the inner neuroblastic layer migrate into the marginal zone.

During the fourth week the cells of Müller become identifiable in the inner neuroblastic layer. By the end of the third month these cells have elongated and span the thickness of the retina.

The ganglion cells also arise in the inner neuroblastic layer and migrate across the marginal zone and come to lie next to the vitreous cavity. The acellular region between the inner neuroblastic layer and ganglion cell layer is now the inner plexiform layer. The remaining cells in the inner neuroblastic layer will become the amacrine cells.

From the outer neuroblastic layer the future horizontal and bipolar cells migrate across the transient fiber layer of Chievitz to the inner neuroblastic layer which now constitutes the inner nuclear layer. The transient fiber layer of Chievitz is obliterated by this migration. The region of the outer neuroblastic layer from which the horizontal and bipolar cells have migrated constitutes the outer plexiform layer.

The remainder of the outer neuroblastic layer constitutes the outer nuclear layer and in this layer the rods and cones will form.

Note to reader

In the last analysis the reader is the "doctor" and it is his responsibility to discover what points should be emphasized and what techniques serve his learning processes best. Coloring the diagrams in this manual will help the reader discover whether he completely understands the material presented. If the reader is uncertain as to the origin (germ layer) of a certain structure, leave this structure uncolored until the point in question has been resolved. It may be described later in the text.

64 (Continued)
Q: At birth the retina is ready to function. The layers of the completed retina are:

( ) Inner plexiform layer

( ) Inner limiting membrane

( ) Nerve fiber layer

( ) Ganglion cell layer

( ) Inner nuclear layer (Bipolar cell layer)

( ) Layer of rods and cones

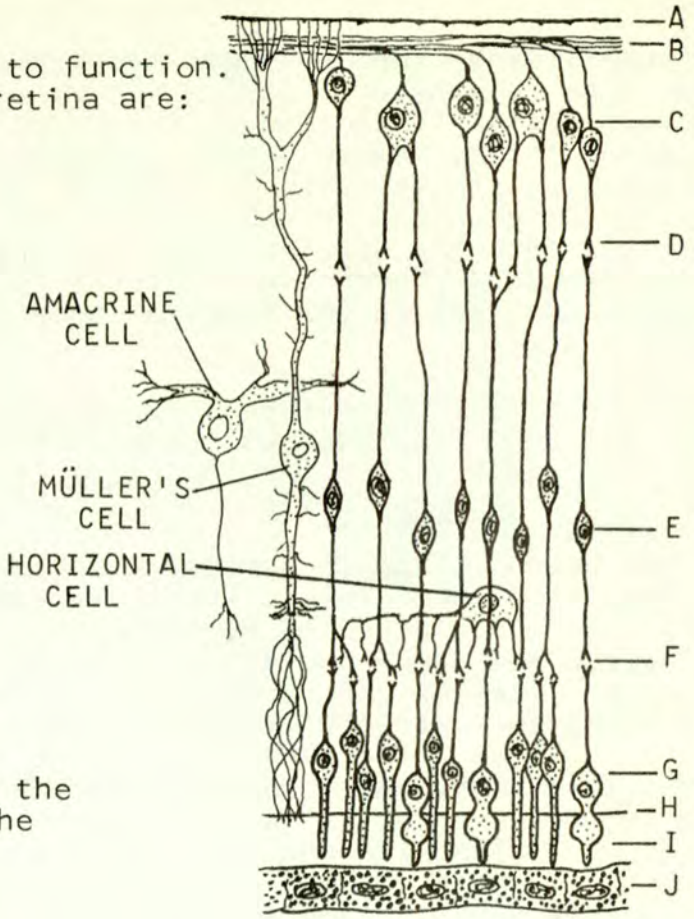
( ) Pigmented cell layer

( ) Outer plexiform layer

( ) Outer nuclear layer (Rod and cone nuclei)

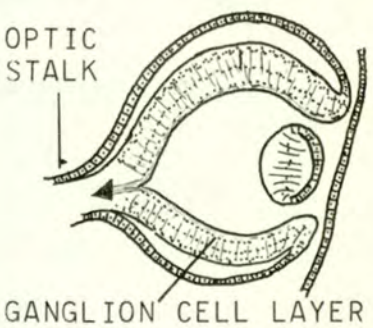
( ) Outer limiting membrane

Relate the structures labeled in the figure to the layers listed in the left-hand column.



65
During the 6th week the nerve fibers enter the optic stalk and grow toward the brain reaching it by the end of the 7th week.

Q: Which cell layer of the retina sends fibers (axons) to the brain?

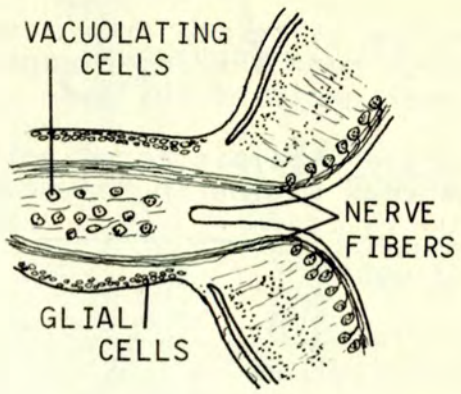


66
This drawing shows the optic stalk before the nerve fibers have entered it.

Q: The optic stalk and cup are extensions of the _____.

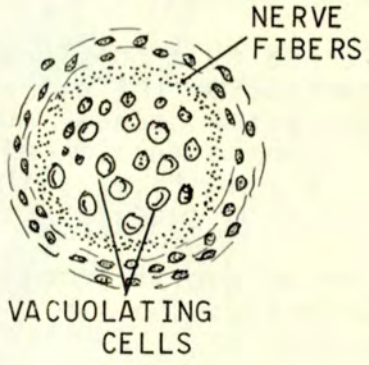
64 D, A, B, C, E, I, J, F, G, H
65 Ganglion Cell Layer
66 Brain

67
As the nerve fibers grow toward the brain, the optic nerve grows thicker and the inner cells vacuolate and disappear. The outer cells differentiate into the glial (supporting) cells of the nerve.



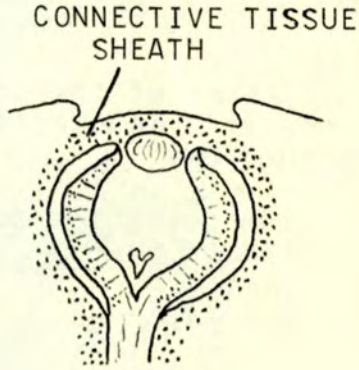
Q: The cells that support the nerve cells and fibers are known as _____ cells.

68
This drawing shows the optic stalk as it looks two days after the nerve fibers have begun to enter it.



Q: The optic stalk now contains fibers (axons) which are continuous with the _____ layer of the retina.

69
By the end of the 7th week a connective tissue sheath is forming around the optic nerve. This sheath (dura of the optic nerve) is continuous with the sclera of the eye and the dura of the brain.



Q: In the adult, the fovea contains _____ cells, but no _____ cells.

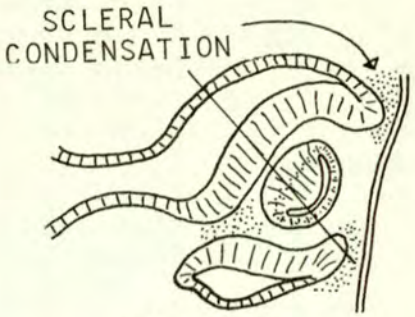
70
In the optic stalk droplets of lipid appear in the protoplasm of the glial cells surrounding the axons of the nerve fibers. These droplets condense to form a thin medullary sheath around each axon. This medullation progresses from the brain to the eye and isn't complete until the 9th month.

Q: The continuation of the dura of the optic stalk over the surface of the eyeball is the _____.

67 Glial or Supporting
68 Nerve Fiber
69 Cone, Rod
70 Sclera

71
The sclera is formed from mesenchyme which condenses near the front edge of the optic cup, and later encloses the eye.

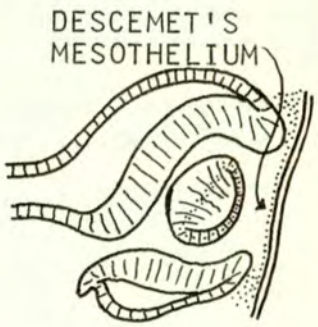
Q: Between the pigmented epithelium and the nervous retina in the developing optic cup is the _____ space.



37th DAY

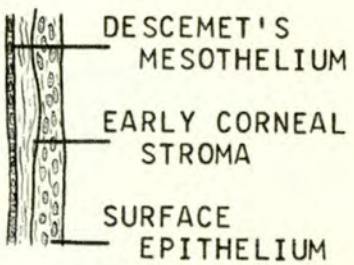
72
The cornea is a continuation of the sclera over the surface of the eye superficial to the lens. The posterior corneal surface is formed by a layer of mesothelium called Descemet's mesothelium. The surface epithelium of the cornea is derived from surface ectoderm.

Q: The sclera is formed by the _____ germ layer.



73
The stroma of the cornea is laid down between Descemet's mesothelium and the surface epithelium.

Q: The posterior surface of the cornea is formed by _____ _____.



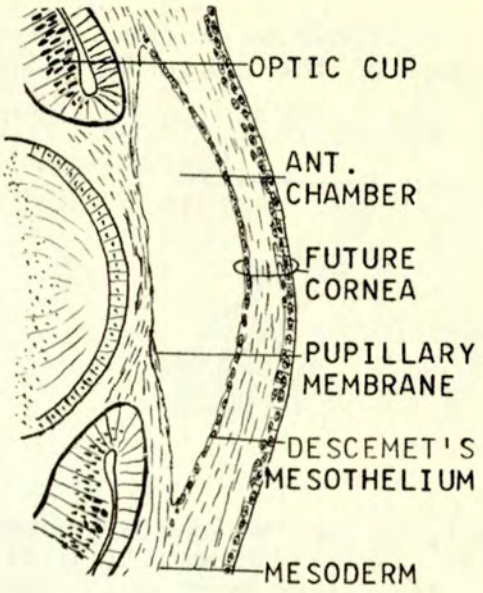
74
Another layer of mesoderm is laid down just deep to Descemet's mesothelium. This is the pupillary membrane, and it lies over the lens in the area of the pupillary opening, as its name implies.

Q: The corneal stroma lies between the _____ and _____ layers of the developing cornea.

71 Intraretinal
72 Mesoderm
73 Descemet's Mesothelium
74 Surface Epithelium, Descemet's Mesothelium

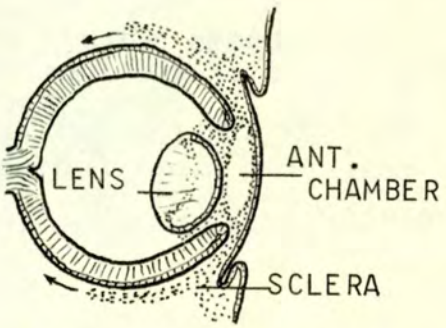
75
Descemet's mesothelium becomes separated from the underlying pupillary membrane, forming a space, the anterior chamber of the eye. Decemet's mesothelium is also called the endothelium of the anterior chamber.

Q: The anterior chamber lies between the _____ membrane and _____ mesothelium.



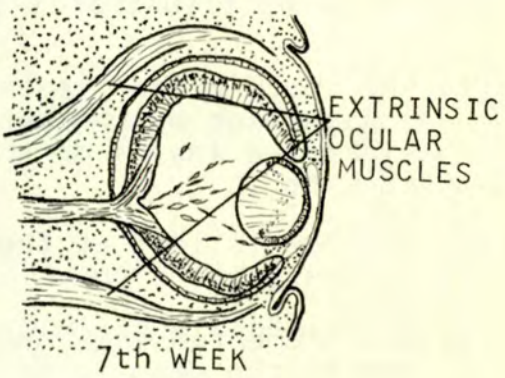
76
By the seventh week the sclera has developed around the eye about halfway and is extending posteriorly.

Q: The continuation of the sclera over the anterior surface of the eye is called the _____.



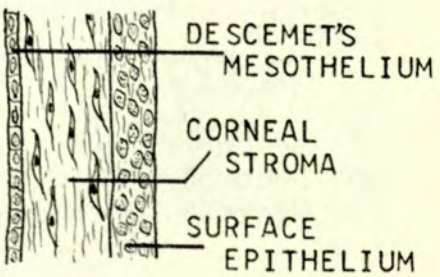
77
By this time condensations of mesoderm in the orbit are forming the extrinsic muscles of the eye.

Q: The lens vesicle develops from the lens _____.



78
Shown here are the posterior corneal surface (Descemet's mesothelium), the corneal stroma and the surface epithelium.

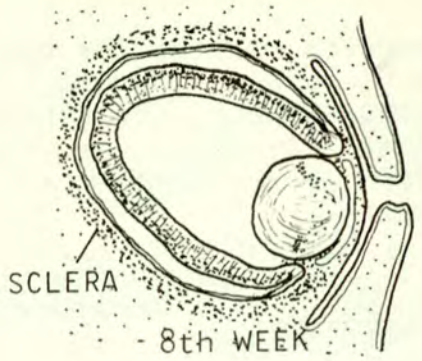
Q: Deep to the posterior corneal surface is a cavity, the _____ _____.



75 Pupillary, Descemet's
76 Cornea
77 Placode
78 Anterior Chamber

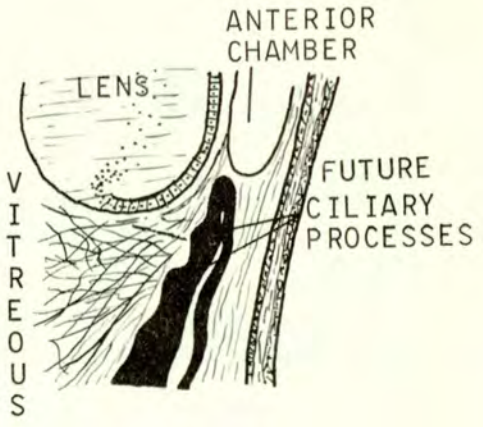
79
By the eighth week the sclera has formed all the way to the posterior pole of the eye.

Q: The sclera is formed by condensation of _____ (germ layer).



80
The folds or "wrinkles" shown here in the optic cup will form the ciliary processes. This thickened part will form the ciliary body of the adult eye.

Q: The Y-shaped sutures of the lens are a result of the fact that the _____ _____ do not become thin or long enough for all fiber ends to meet at a single point.



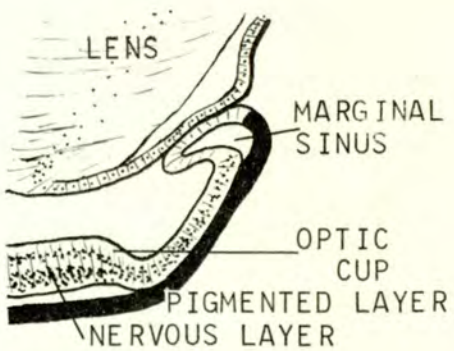
81
This drawing illustrates several points:

(1) The intraretinal space is becoming obliterated by the nervous and the pigmented layers of the retina growing together.

(2) A space is left at the rim of the cup, the marginal sinus.

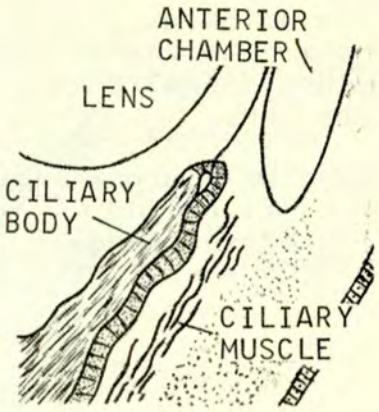
(3) The pigmented layer appears very dark due to the deposit of pigment.

Q: The marginal sinus is formed by the incomplete fusion of the _____ and the _____ layers of the retina.



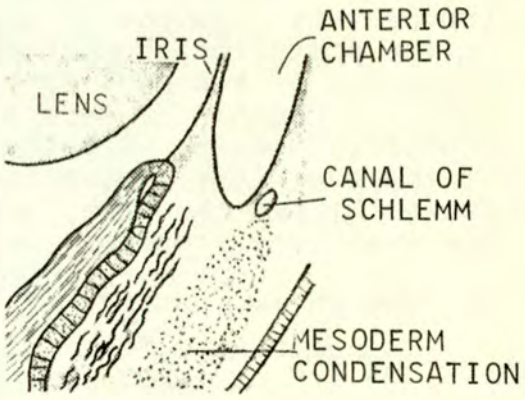
79 Mesoderm
80 Secondary Lens Fibers
81 Nervous, Pigmented

82
The ciliary muscle develops from the mesoderm in the region between the ciliary body and the sclera. The rim of the optic cup which extends far enough to partially cover the lens will form the epithelium of the iris.



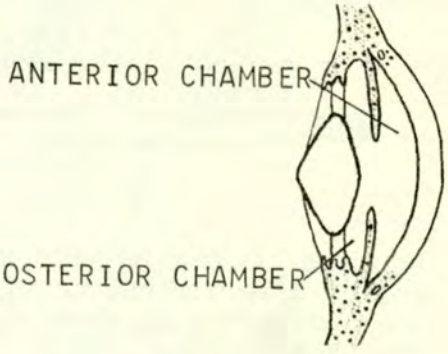
Q: The horizontal and bipolar cells of the retina migrate from the _____ neuroblastic to the _____ neuroblastic layer.

83
During the latter part of the 3rd month (embryos of about 65 mm.) a small plexus of venous channels appears among the fibers of the corneal-scleral condensation near the angle of the anterior chamber. This plexus drains into a vein which extends around the margin of the cornea at the peripheral edge of the pupillary membrane. This vein later stops carrying blood and serves to drain aqueous humor from the anterior chamber into the venous system. This will be called the Canal of Schlemm. By the 8th month of fetal life this outflow path connects with the scleral veins.



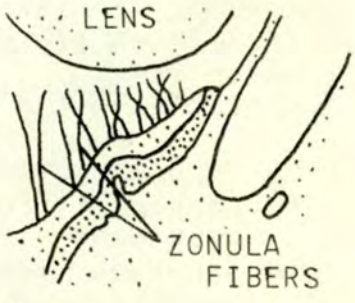
Q: The ciliary muscle is formed from the _____ germ layer.

84
Failure of the mesoderm of the angle of the anterior chamber to atrophy may result in blockage of the canal of Schlemm. The resulting increase in the intraocular pressure is termed buphthalmia or congenital glaucoma.



Q: The blood vessel formed at the margin of the cornea will become the _____.

85
Zonula fibers grow from the wrinkled ciliary body to attach to the lens. These fibers form the suspensory ligament of the lens.

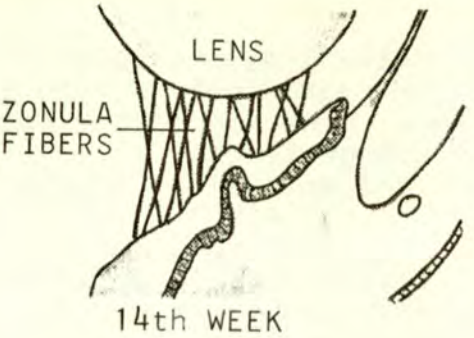


Q: Buphthalmia is similar to glaucoma in that the _____ _____ is increased.

82 Outer, Inner
83 Mesoderm
84 Canal of Schlemm
85 Intraocular Pressure

86
The wrinkles of the ciliary body as shown here have formed the definitive ciliary processes with zonular fibers suspending the lens.

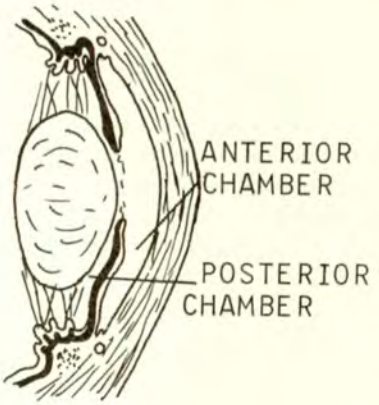
Q: The aggregate of zonular fibers is called the _____ _____ of the lens.



14th WEEK

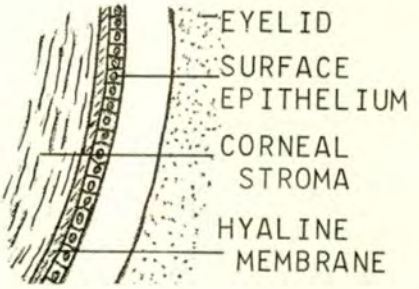
87
The space between the zonular fibers (suspensory ligament of the lens) and the iris is the posterior chamber of the eye. With the formation of the pupillary membrane, the anterior chamber is separated from the posterior chamber, however, with the subsequent atrophy of the pupillary membrane, communication between the two chambers is restored, through the pupillary opening.

Q: The three chambers of the eye are the _____ and _____ chambers and the _____ cavity.



88
A new membrane forms between the corneal stroma and the surface epithelium. This is the superficial hyaline membrane of the cornea (Bowman's membrane).

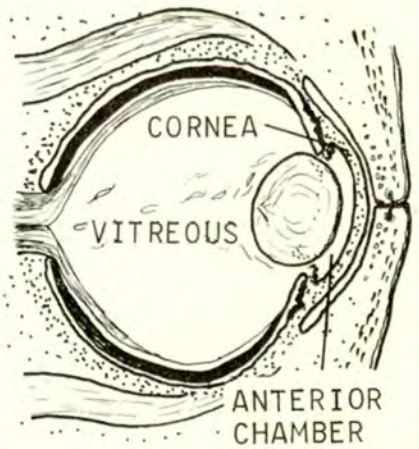
Q: The parts of the cornea are _____, _____, _____, _____ and _____.



14th WEEK

89
Because of the growth of the anterior chamber and of the cornea itself, the curvature of the cornea is beginning to differ from that of the eye as a whole.

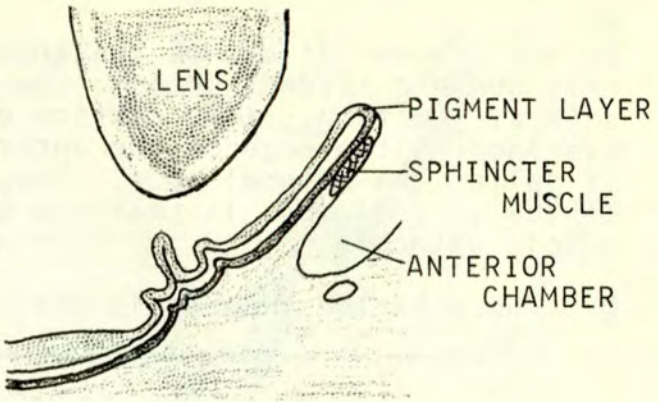
Q: The cornea has a radius of curvature which is _____ (greater, less) than that of the eye as a whole.



86 Suspensory Ligament
87 Anterior, Posterior, Vitreous
88 Surface Epithelium, Hyaline Membrane, Stroma and Descemet's Membrane & Mesoth.
89 Less

90
At the rim of the optic cup, which forms the iris, cells are forming the sphincter of the iris.

Q: The epithelium of the iris is formed by the rim of the _____ _____.

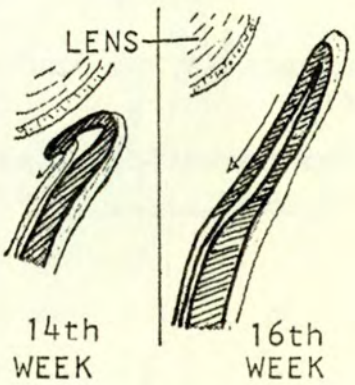


91
Pigmentation of the posterior layer of the iris begins at the rim of the retina (edge of the iris). This epithelial pigmentation does not result in the visible coloration of the eye. This coloration is brought about by stromal pigment cells. The ultimate eye color is dependent on the amount of this stromal pigmentation.

Q: The muscles of the iris are formed from _____ _____ (germ layer).

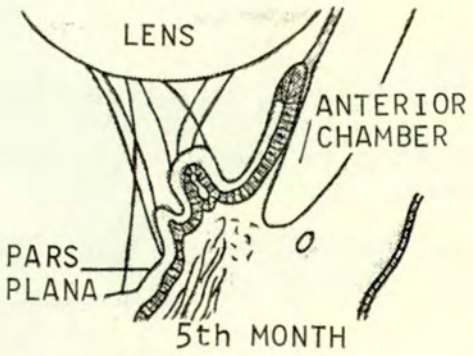
92
Here are two drawings apposed to show the pigmentation extending sequentially to the root of the iris. The left one shows the beginning and the right a more advanced stage of pigmentation.

Q: Eye coloration is due to the _____ _____ cells of the iris.



93
The ciliary body is made up of the ciliary processes and the ciliary ring (pars plana). The ciliary ring lies posterior to the ciliary processes.

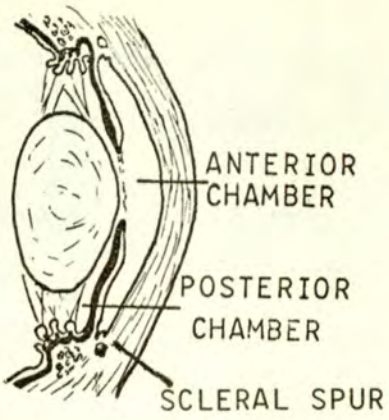
Q: Pigmentation is occurring in the _____ (superficial, deep) layer of the iris.



90 Optic Cup
91 Ectoderm
92 Stromal Pigment
93 Deep

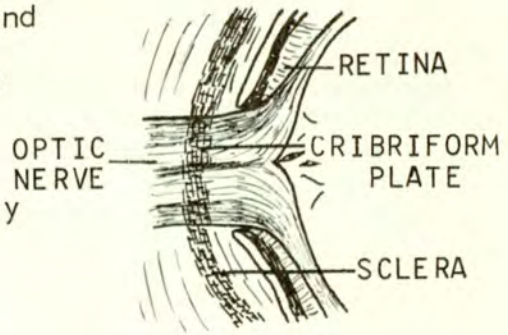
94
In the process of growth the anterior chamber enlarges and extends deep to the corneo-scleral junction. That portion of sclera overlapping the edge of the anterior chamber is called the scleral spur. The importance of the scleral spur is that the ciliary muscle attaches to it.

Q: The anterior chamber is drained through the _____ _____ _____.



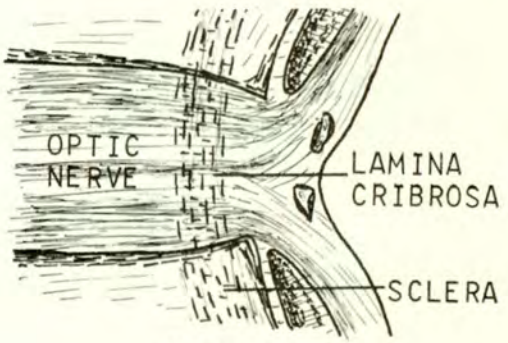
95
During the 5th month the sclera thickens around the globe. By the 6th month a network of scleral tissue has penetrated the optic nerve to form the lamina cribrosa (or cribriform plate).

Q: The ciliary body is made up of the ciliary ring and the _____ _____.



96
Shown here is the lamina cribrosa in an eye at term.

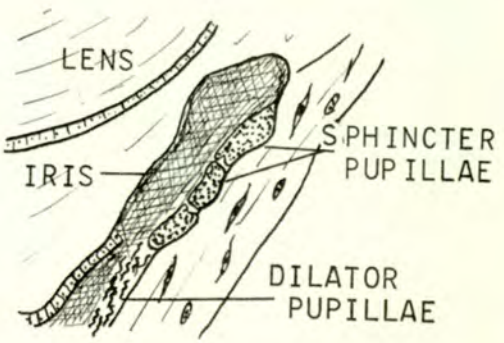
Q: The cribriform plate is a formation of _____ tissue.



TERM

97
The dilator pupillae fibers are formed in the pigmented portion of the iris a little removed from the rim of the optic cup.

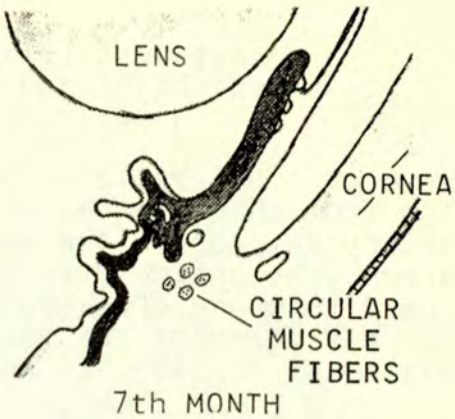
Q: The sphincter pupillae forms at the rim of the _____.



94 Canal of Schlemm
95 Ciliary Processes
96 Scleral
97 Optic Cup (Iris)

98
The pupillary membrane begins to atrophy and the circular fibers of the ciliary muscle form in the ciliary body.

Q: The atrophy of the pupillary membrane allows communication between the _____ chamber and the _____ chamber.

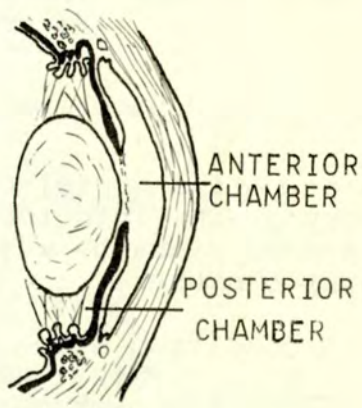


99
If the pupillary membrane fails to atrophy the condition known as persistent pupillary membrane exists, in which a variable amount of tissue extends over the pupillary opening.

Q: The incomplete obliteration of the intraretinal space results in the _____ _____ at the rim of the cup.

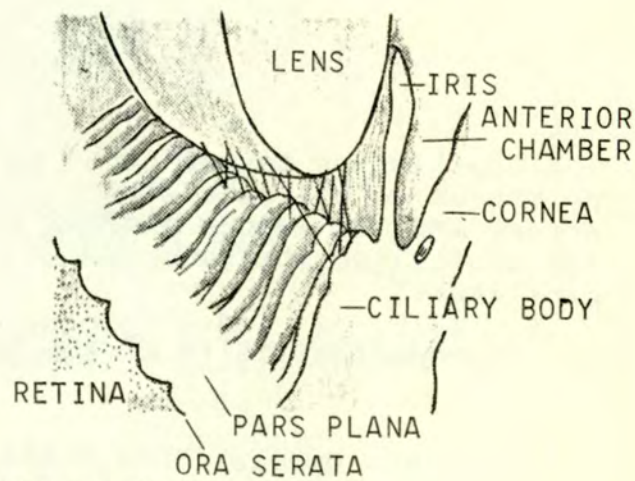
100
The shape of the anterior chamber in this view is nearly in its final configuration.

Q: The anterior chamber is bounded by the _____ anteriorly and the _____ posteriorly.



101
By the ninth month, the anterior edge of the functional part of the retina (pars optica) has receded, leaving a wide ciliary ring, the pars plana. The line separating the pars optica retinae from the pars plana is called the ora serrata.

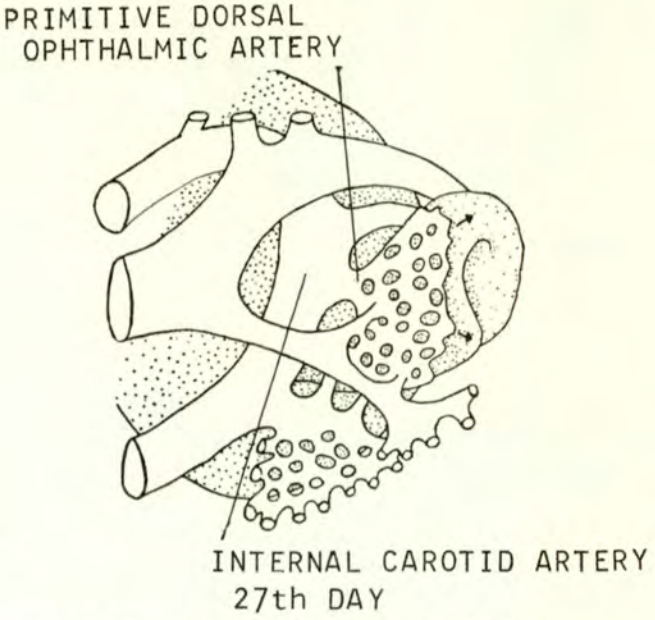
Q: The corneal stroma lies between _____ membrane and _____ membrane.



98 Anterior, Posterior
99 Marginal Sinus
100 Cornea, Iris
101 Descement's, Bowman's

102
Several small vessels leading from the internal carotid artery develop in the mesoderm around the optic vesicle on the 27th day. (See frame 142 for a diagram of the vascular system of the eye at term.)

Q: The ora serrata is a line separating the _____ _____ from the _____ _____.

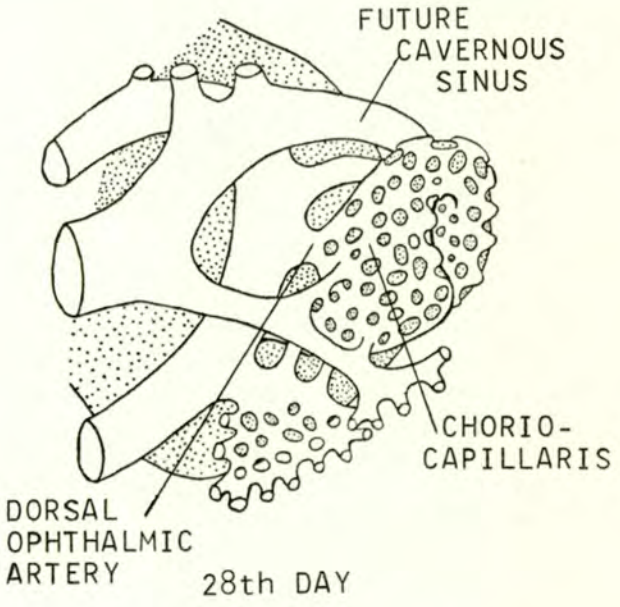


103
The arterial plexus which forms is the primitive dorsal ophthalmic artery.

Q: What is the main artery which gives rise to the vessels of the eye?

104
The primitive dorsal ophthalmic artery drains into the future cavernous sinus by way of the venous plexuses.

Q: A condition known as _____ _____ exists when the pupillary membrane fails to atrophy by birth.



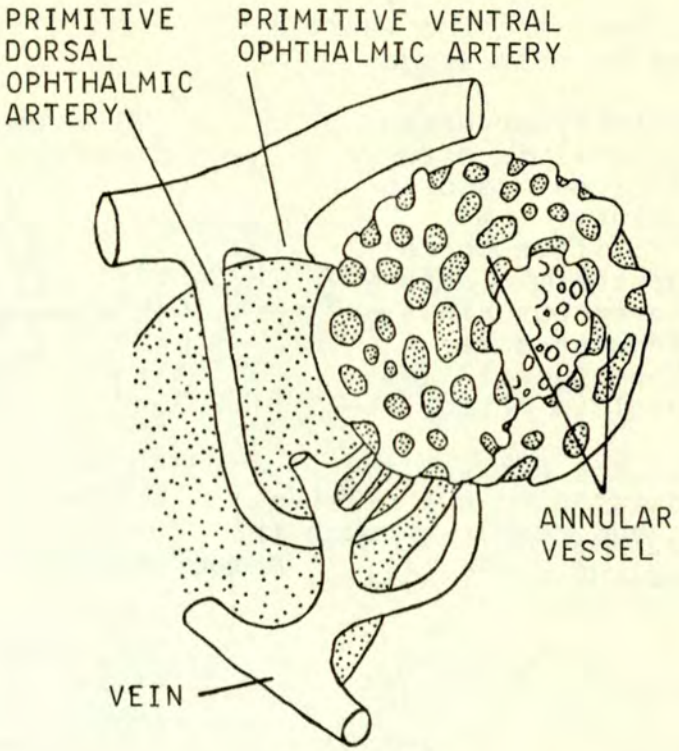
105
The capillaries between the primitive dorsal ophthalmic artery and its venous drainage are called the "chorio-capillaris".

Q: The cuboidal cells of the lens give rise to _____ fibers.

102 Pars Optica, Pars Plana
103 Internal Carotid Artery
104 Persistent Pupillary Membrane
105 Secondary Lens

106
When the branches of the primitive dorsal ophthalmic artery have developed to the front of the optic cup, some of them anastomose along the rim to form the annular vessel. This vessel also receives branches from the hyaloid and primitive ventral ophthalmic arteries.

Q: The capillary system between the arteries and veins of the eye at this stage is called the _____.



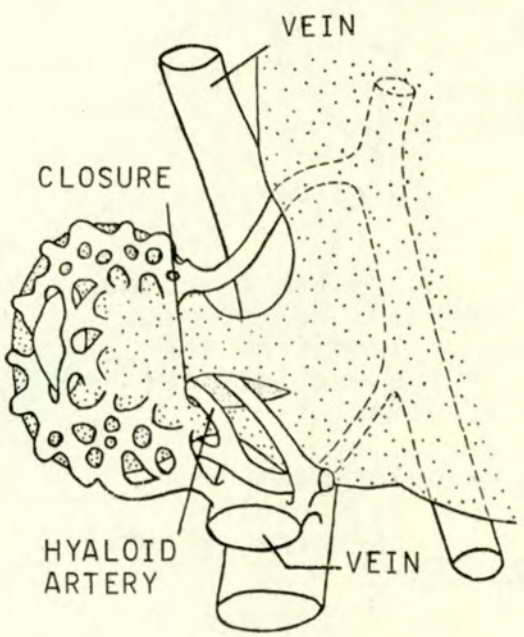
32nd DAY

107
When the internal carotid artery disappears behind the stalk, another vessel can be seen branching from it leading to the far side of the cup. This is the primitive (temporary) ventral ophthalmic artery, which will later disappear.

Q: The annular vessel is formed by anastomosing branches of the _____ artery.

108
As the choroidal fissure closes, the network of arterial vessels is trapped inside the cup. One branch connects with the ophthalmic artery through a small opening in the stalk behind the cup. This is the hyaloid artery, which will also disappear later in development.

Q: The lens is roughly spherical in shape when the _____ fibers first grow in length.



33rd DAY

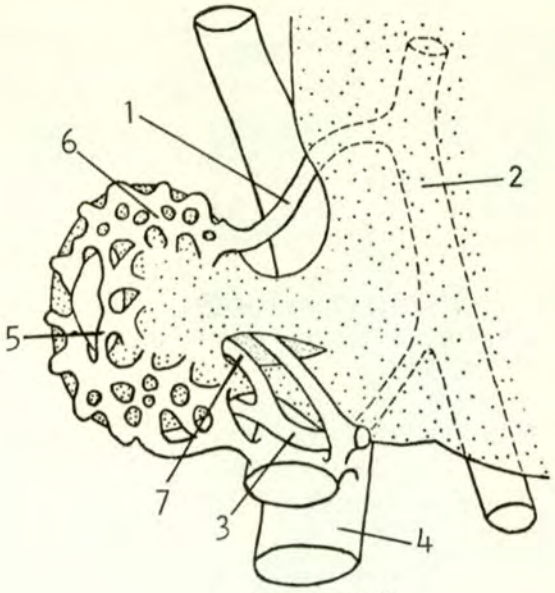
Color arteries - red.
Color veins - blue.

106 Chorio-capillaris
107 Primitive Dorsal Ophthalmic
108 Primary Lens

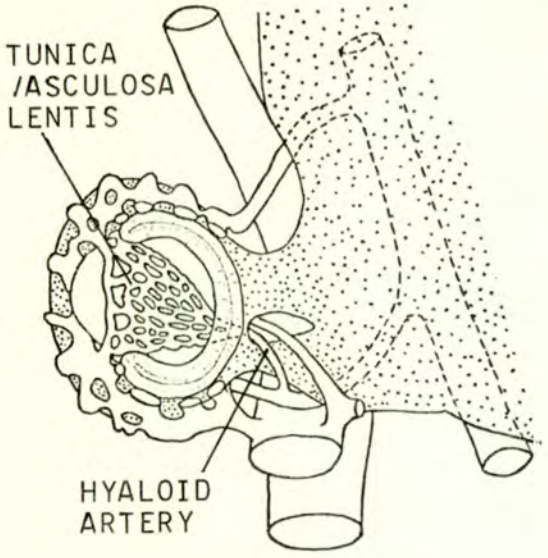
109
Shown here are the vessels formed by this stage:

(1) Primitive ventral ophthalmic artery
(2) Internal carotid artery
(3) Primitive dorsal ophthalmic artery
(4) Cavernous sinus
(5) Annular artery
(6) Chorio-capillaris
(7) Hyaloid artery

Q: In the embryo, the developing eye receives blood mainly through the _____ and _____ arteries.



33rd DAY



33rd DAY

110
The network of vessels at the forward extremity of the hyaloid artery has formed a tunic around the lens, the tunica vasculosa lentis.

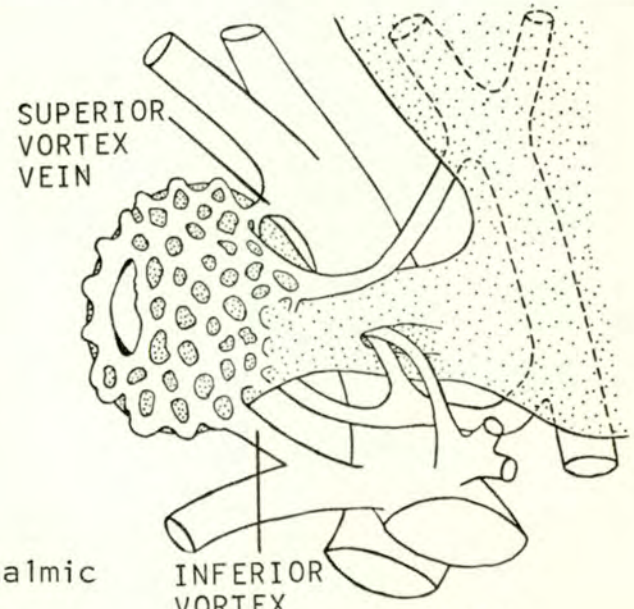
Q: The _____ artery enters the optic cup by passing through the optic stalk.

111
Before birth the vascular capsule of the lens normally undergoes retrogression. In certain forms of congenital cataract it may persist.

Q: The vascular capsule formed around the lens is called the _____.

112
As the venous system develops, the vortex veins are formed, which drain blood from the tissues of the eye into the ophthalmic veins.

Q: The vascular capsule of the lens is normally _____ (present, absent) at birth.



36th DAY

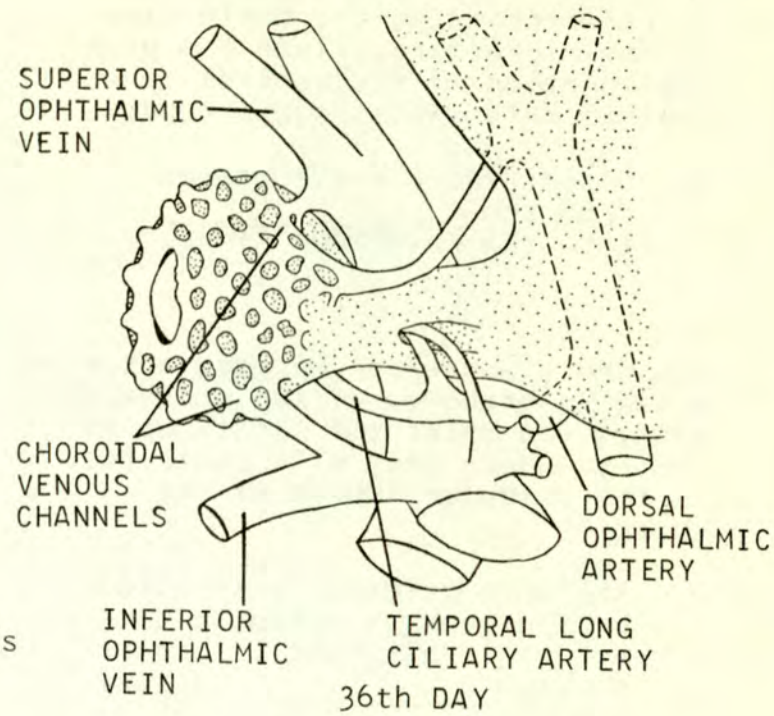
109 Dorsal and ventral ophthalmic
110 Hyaloid
111 Tunica Vasculosa Lentis
112 Absent

113
The superior and inferior ophthalmic veins receive blood from the vortex veins and drain into the cavernous sinus.

Q: What is the name of the artery inside the optic cup?

Note: Lymph is drained by perivascular channels around the capillaries and veins of the optic nerve.

114
The choroidal network of venous channels differentiates in the mesoderm adjacent to the pigment layer of the cup. Blood from the chorio-capillaris drains through this network into the vortex veins.



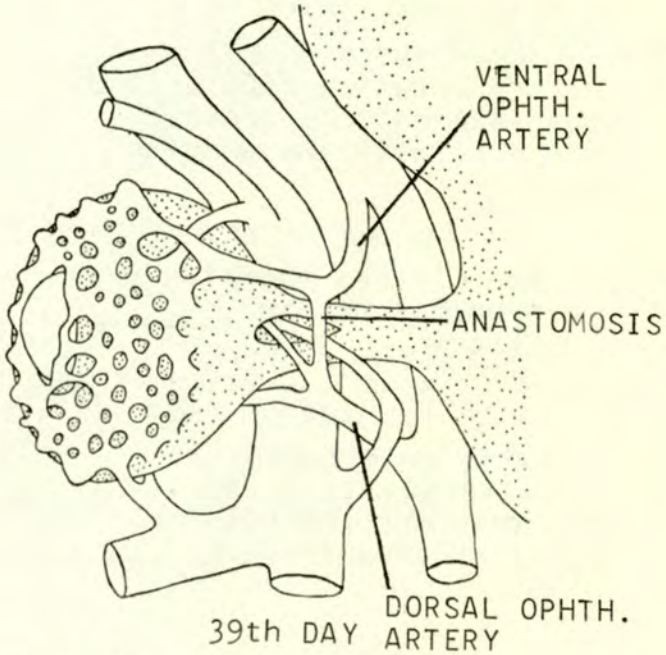
Q: After the 14th week the corneal stroma is bordered anteriorly by _____ and posteriorly by _____.

115
The temporal long ciliary artery is now present as a branch of the dorsal ophthalmic artery. It runs outside the optic cup toward the annular vessel at this stage.

Q: Blood draining from the eye passes through the _____ _____ into the ophthalmic veins.

116
The temporary ventral ophthalmic artery is anastomosing with the dorsal ophthalmic artery and its distal portion will become the nasal long ciliary artery. The remainder of the ventral ophthalmic artery will soon disappear.

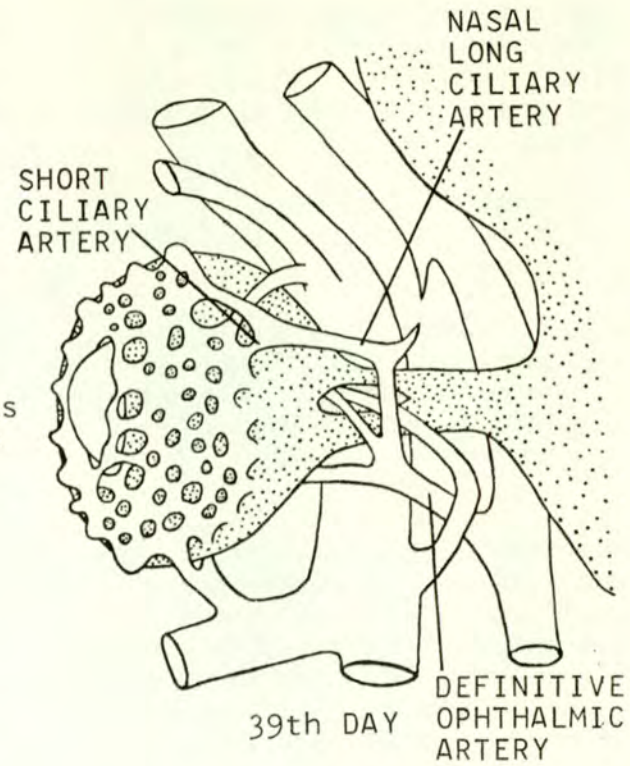
Q: The chorio-capillaris drains into the _____ _____ which drain into the ophthalmic veins.



113 Hyaloid
114 Bowman's Membrane, Descement's Membrane
115 Vortex Veins
116 Vortex Veins

117
The dorsal ophthalmic artery may be referred to as the definitive ophthalmic artery, since the proximal portion of the ventral ophthalmic artery has degenerated.

Q: Blood from the eye passes from the _____ _____ into the cavernous sinus.



118
The short posterior ciliary arteries arise as branches of the ophthalmic artery and enter the substance of the eye where they will contribute to the vascular lamina of the choroid.

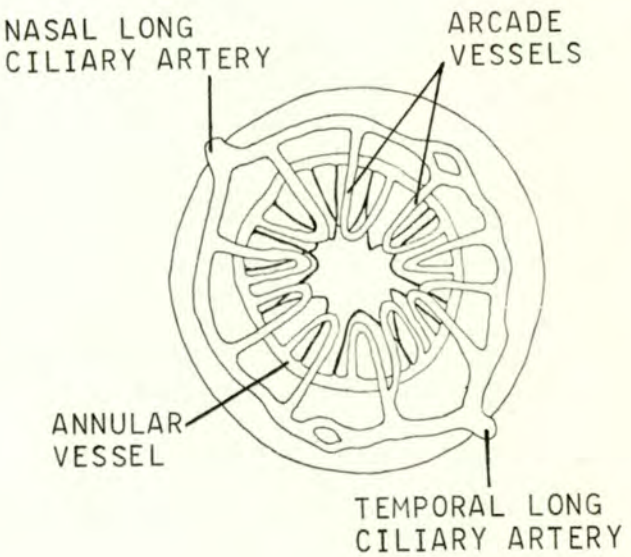
Q: The area originally supplied by the ventral ophthalmic artery is ultimately supplied by the _____ _____ artery.

119
The ciliary arteries are nearly in their adult configuration in that they all arise from the ophthalmic artery at this time.

Q: The _____ vessel surrounds the rim of the optic cup.

120
The nasal and temporal long ciliary arteries come around the globe to form arcades and unite with the annular vessel.

Q: The ciliary arteries are branches of the _____ artery

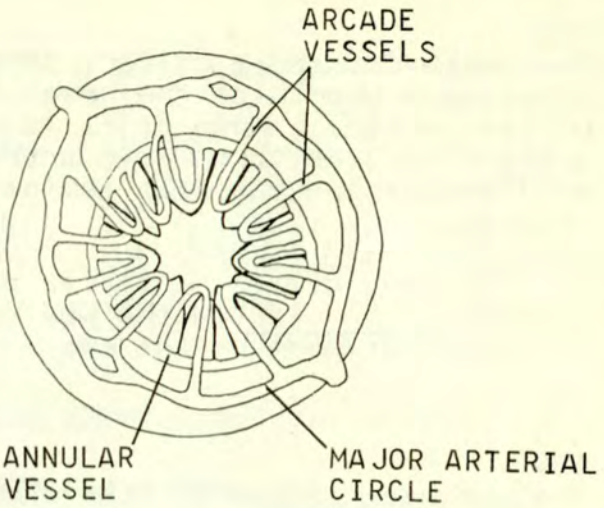


In early development it is difficult to differentiate arteries from veins structurally.

117 Ophthalmic Veins
118 Definitive Ophthalmic
119 Annular
120 Ophthalmic

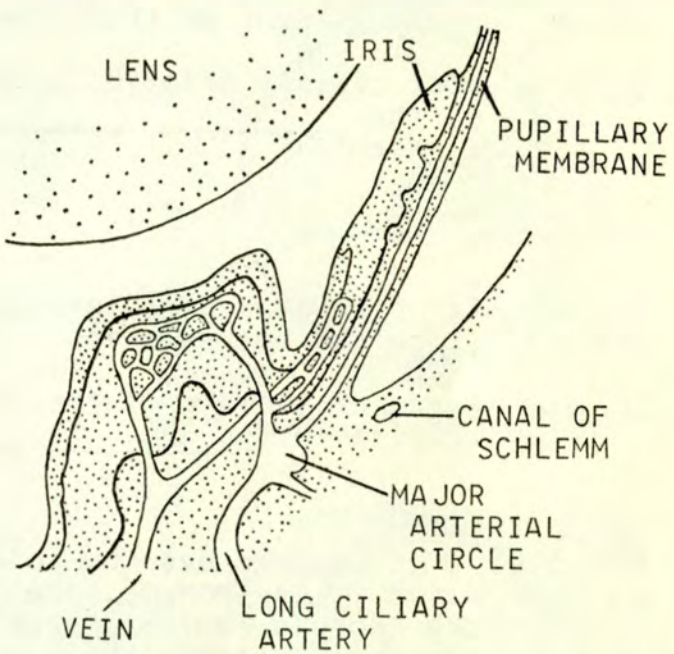
121
The long ciliary arteries unite near the annular vessel to form the major arterial circle of the iris.

Q: The short ciliary arteries are branches of the _____ and _____ long ciliary arteries.



122
The major arterial circle of the iris is located at the base of the iris.

Q: The major arterial circle of the iris is formed by anastomosing branches of the _____ arteries.



123
The arcades derived from the annular vessel and the major arterial circle of the iris are in the pupillary membrane at the base of the iris

Q: The long ciliary arteries anastomose at the base of the iris to form the ____ _____ _____ .

Some authors call the annular vessel an artery while others consider it to be a vein.

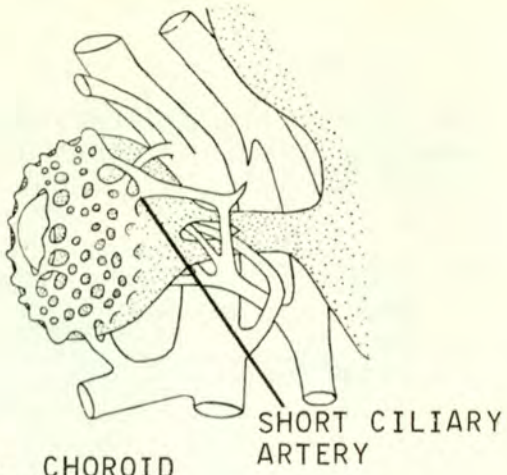
124
The long ciliary arteries are covered by sclera as it grows toward the back of the globe. In the adult the long ciliary arteries enter the back of the globe and encircle the eye deep to the sclera to reach the anterior of the eye.

Q: The arcades of the pupillary membrane are derived from the _____ and the _____.

121 Nasal, Temporal
122 Long Ciliary
123 Major Arterial Circle
124 Major Arterial Circle, Annular Vessel

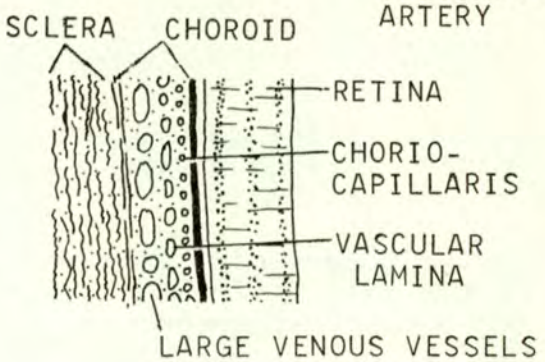
125
The posterior short ciliary artery is shown as a branch of the nasal long ciliary artery. However it is more often a branch of the ophthalmic artery. These will supply the vascular lamina of the choroid.

Q: The long ciliary arteries pass through the _____ on the way to the anterior part of the eye.



126
The vascular lamina of the choroid is situated between the chorio-capillaris and a layer of larger venous vessels present at this time.

Q: The short ciliary arteries give rise to the _____ _____ of the choroid.

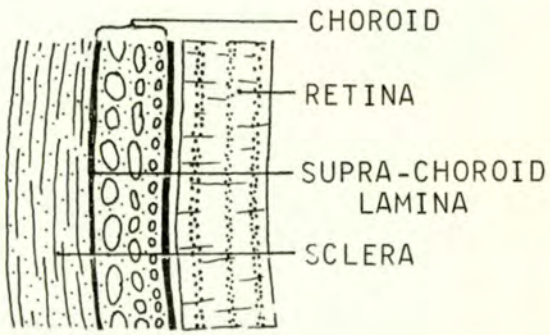


127
The vessels of the vascular lamina are mostly arterial in character, and drain into the vortex veins.

Q: The layers of vessels of the choroid, from inside out are the choriocapillaris, _____ _____, and _____ _____.

128
The choroid is covered over by sclera. A condensation of mesenchyme, the future supra-choroid lamina makes a line of separation between the two.

Q: The arteries which feed blood to the vascular lamina are the _____ _____ arteries.

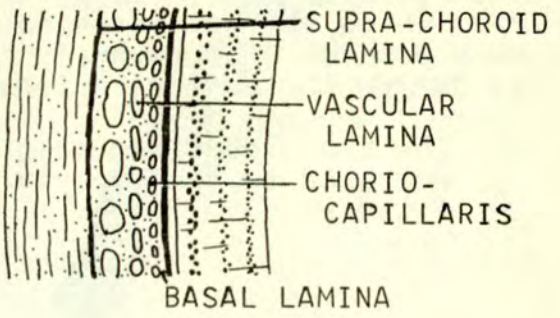


129
The supra-choroid lamina of the adult is a relatively thick layer of elastic fibers and chromatophores. The chromatophores are the last structures to differentiate in the choroid, and at this stage have not yet developed.

Q: The ciliary arteries are covered over by _____ in the adult eye.

125 Sclera
126 Vascular Lamina
127 Vascular Lamina, Venous Vessels
128 Short Ciliary
129 Sclera

130
In this view is seen the choroid with all the adult layers. From the outside in are:



(1) Supra-choroid lamina of elastic fibers at this stage.

(2) Vascular lamina, which includes both the arterial and venous layers.

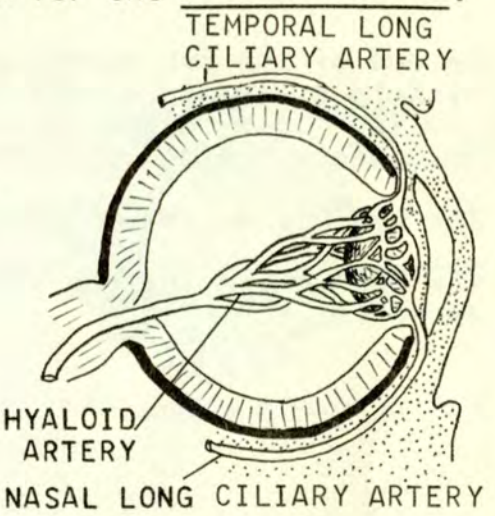
(3) Choriocapillary lamina, a layer of capillaries that nourish the outer layers of the retina.

(4) The basal lamina, located between the chorio-capillaris and the pigmented layer of the retina.

Q: The chromatophores provide pigmentation for the _____.

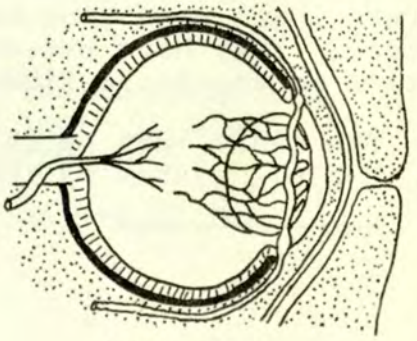
131
Arterial blood is fed into the anterior vascular capsule of the lens by both hyaloid and ciliary arteries. However, the job is taken over more and more by the ciliary arteries as the whole vascular system within the primary vitreous begins to atrophy and the annular vessel slowly disappears.

Q: Pigmentation in the choroid occurs in the form of _____ (type of cells).



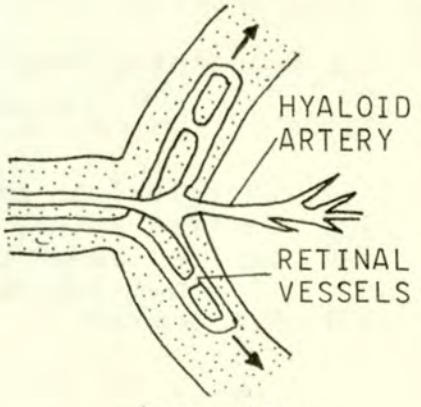
132
Since the optic cup continues to grow, the internal vessels and the primary vitreous appear to shrink. Circulation through these internal vessels diminishes and the branches break away from the hyaloid. This is the beginning of atrophy of the hyaloid artery.

Q: The vessel which supplements the function of the annular vessel is the _____ _____ _____.



133
Toward the end of the 4th month, two arteries which sprout from the diminishing hyaloid artery begin to vascularize the retina.

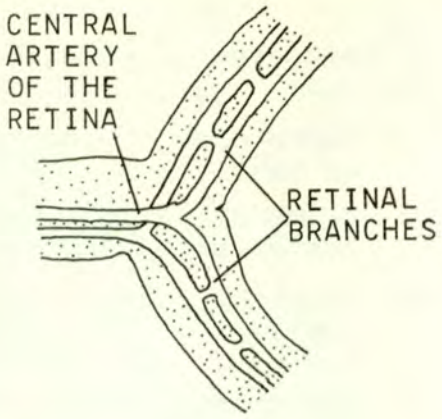
Q: The hyaloid artery degenerates from the center of the _____ _____.



130 Choroid
131 Chromatophores
132 Major Arterial Circle
133 Primary Vitreous

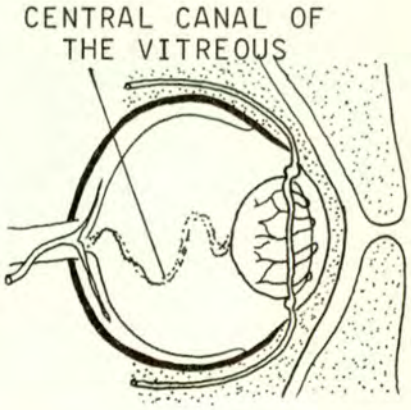
134
The hyaloid artery atrophies only to the point from which retinal arteries have grown. When this process of atrophy is completed the artery is called the central artery of the retina.

Q: The hyaloid artery originally gained entrance to the eye via the _____ fissure.



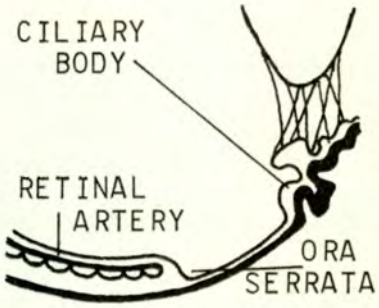
135
By the end of the 8th month, atrophy of the hyaloid system is almost finished. Left in its place is the central canal of the vitreous (Cloquet's canal).

Q: The hyaloid artery is renamed the _____ _____ when the portion inside the vitreous atrophies.



136
Shown here are the branches of the retinal artery which were branches of the hyaloid artery. They have extended throughout the retina in the nerve fiber layer.

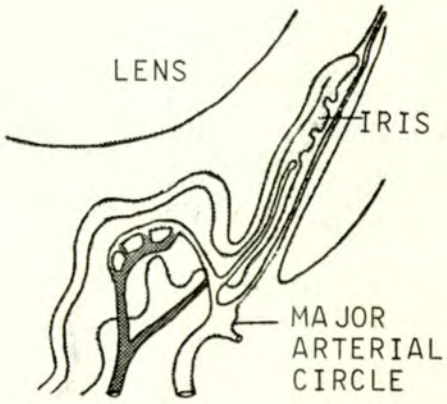
Q: The canal left by the atrophy of the hyaloid system is the _____ _____.



137
As the iris stroma thickens, branches from the major arterial circle enter it.

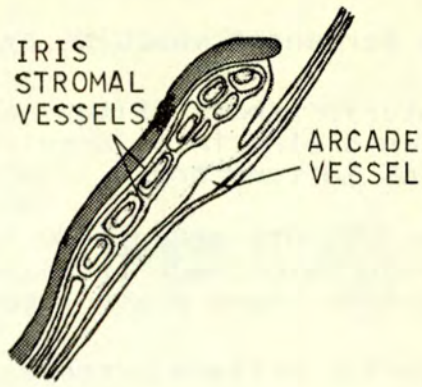
Q: The branches of the central artery come to lie in the _____ _____ layer of the retina.

134 Choroidal or Embryonic
135 Central Artery of the Retina
136 Central Canal of the Vitreous (Cloquet's Canal)
137 Nerve Fiber



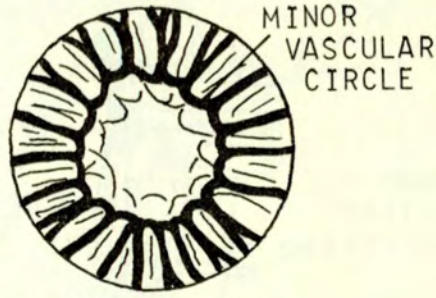
138
A number of small branches of the major arterial circle grow into the peripheral portion of the iris stroma and by the 7th month, several layers of vessels are distinguishable in the iris.

Q: The major arterial circle is formed by the _____ arteries.



139
The pupillary membrane atrophies as its blood supply diminishes. In the iris the minor vascular circle is formed by the apices of the arcades from the major vascular circle.

Q: The branches into the iris stroma are from the _____.



8th MONTH

140
The anterior ciliary arteries are derived from the muscular and lacrimal branches of the ophthalmic artery and begin to appear in the anterior portion of the orbit in the 4th month.

Q: The minor vascular circle is located near the rim of the _____.

141
The anterior ciliary arteries have branches which help to make up the major arterial circle.

Q: The anterior ciliary arteries are branches of the muscular and lacrimal branches of the _____ artery.

138 Long Ciliary Arteries
139 Major Arterial Circle
140 Iris
141 Ophthalmic

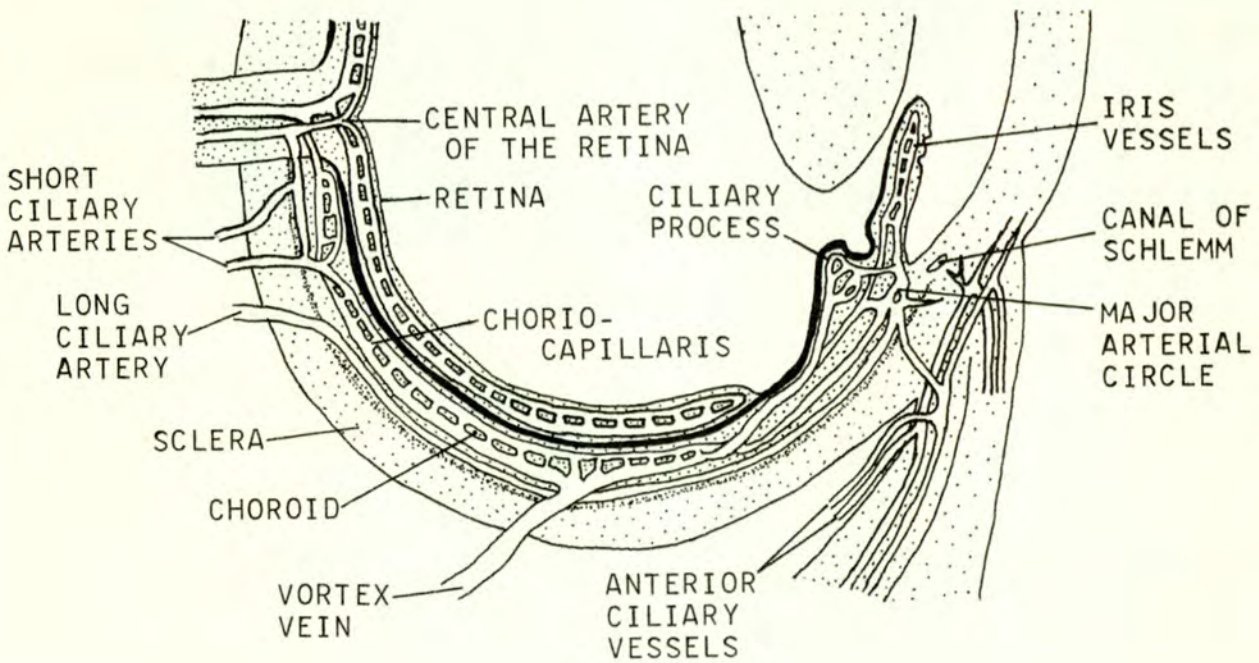
142
The permanent vascular system consists of:

Posterior short ciliary arteries leading into the choriocapillaris which drains into large veins in the vascular lamina of the choroid, which in turn drain into the vortex veins.

Long ciliary arteries which lead into the major arterial circle and thence into the iris vessels and the vessels of the ciliary processes and from there drain into veins which lead to the vortex veins.

Anterior ciliary arteries with branches into the major arterial circle and other extraneous branches.

The central artery of the retina supplying the retina.



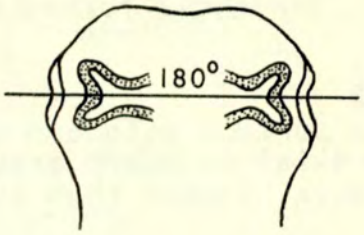
9th MONTH

Q: The arteries contributing to the major arterial circle are the _____ and the _____ ciliary arteries.

142 Anterior, Long

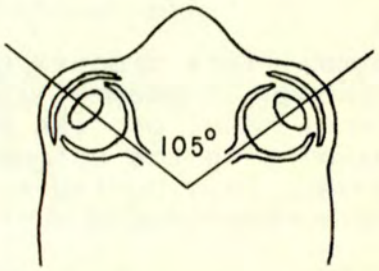
DEVELOPMENT OF THE OPTIC ADNEXA

143
In the development of the optic adnexa, the angle of the optic axes is about 180° at the end of the 2nd month.



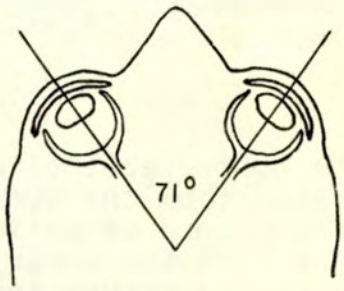
Q: In the retina, the region of the fovea does not complete its development until _____ _____.

144
The angle of the optic axes is reduced to 105° by the 3rd month.



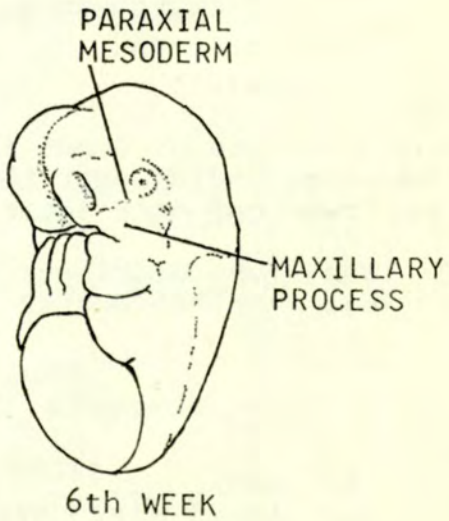
Q: In the primitive condition the direction of the eyes is _____ as in fish.

145
At birth the optic axes approaches 71°. In the adult this angle has further narrowed to about 68°.



Q: In the early embryo the optic axes is about _____.

146
The maxillary process extends to the opening of the nasal pit, touching the nasal processes. The maxillary mesoderm is in contact with the mesoderm surrounding the eye. The mesoderm surrounding the eye is referred to as paraxial mesoderm.



Q: The maxillary process develops from the _____ branchial arch.

143 After Birth
144 Lateral
145 180°
146 1st or Mandibular

147
The rapid development of the maxillary process probably plays a role in the swing of the eye in an anterior direction. This change in direction of the eyes is necessary for binocular vision.

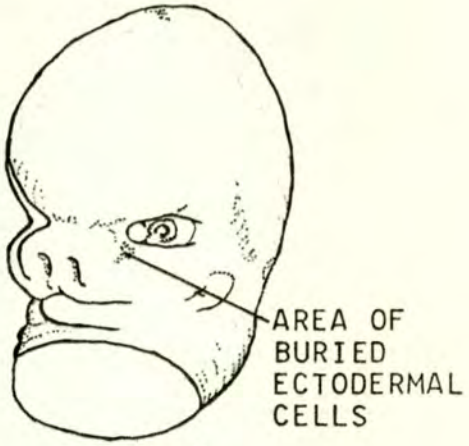
Q: The angle formed by the optic axes in the adult is about ____.

148
The surface ectoderm covering the maxillary mesoderm and the paraxial mesoderm around the eye is thicker where it lies in the groove between them (the nasolacrimal groove).

Q: The maxillary processes extend forward to the opening of the _____, touching the _____.

149
The maxillary process grows up and over the thickened ectodermal line fusing with the lateral nasal process and paraxial mesoderm, thus burying the ectodermal cells lining this groove. This buried ectoderm will form the nasolacrimal ducts and sac.

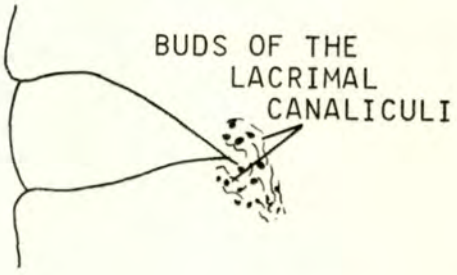
Q: The cornea forms the anterior wall of the _____ chamber.



7th WEEK

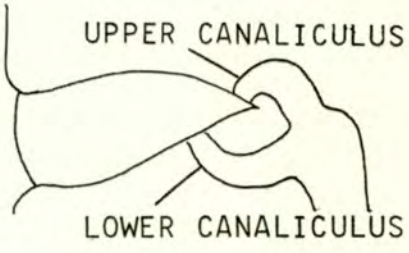
150
As the buried epithelial cells become separated from the surface ectoderm, forming a cord of cells, two buds develop from the upper end. These buds are the future lacrimal canaliculi.

Q: The _____ fuses with paraxial mesoderm and the lateral nasal process.



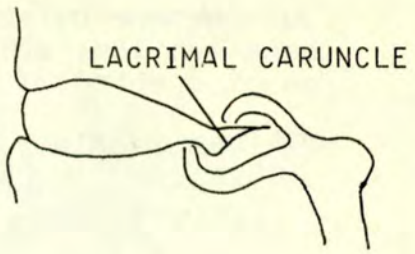
151
One canaliculus grows toward each eyelid, the upper ending near the inner canthus, the lower one more laterally.

Q: What type of tissue forms the nasolacrimal ducts?



147 68°
148 Nasal Pit, Nasal Processes
149 Anterior
150 Maxillary Process
151 Surface Ectoderm

152
It was generally believed that the lower canaliculus, as it enters the lower lid, cuts off a portion of the lid with its contained cilia, sebaceous glands, and sweat glands. This segment of the lower lid is known as the lacrimal caruncle.

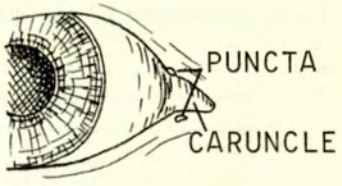


Q: The _____ canaliculus ends nearer the inner canthus.

153
It is now thought that the lacrimal caruncle has an independent origin. At the end of the 3rd month after the lids have fused it develops at the posterior surface of the medial part of the lower lid near its upper free border as a cellular proliferation of epithelium.

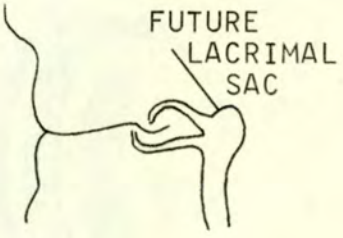
Q: Both the _____ ducts and sac are formed by surface ectoderm.

154
The openings of the upper and lower canaliculi are known as the puncta lacrimalia.



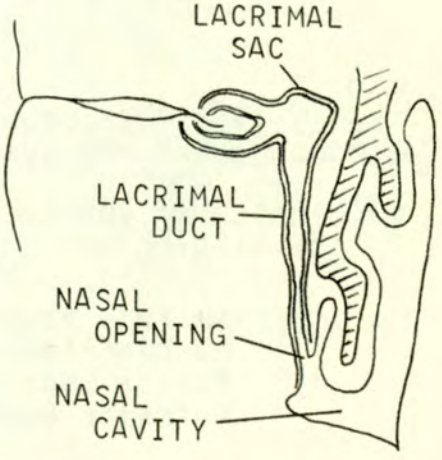
Q: The lacrimal caruncle was thought to be formed from a portion of the eyelid; now, however, it is believed to be of _____ _____.

155
The region of the ectodermal cord from which the upper and lower canaliculi first arise enlarges somewhat and will form the lacrimal sac.



Q: The canaliculi open as the _____.

156
The lower end of the nasolacrimal duct enters the inferior meatus of the nasal cavity.



Q: The upper and lower canaliculi drain into the _____.

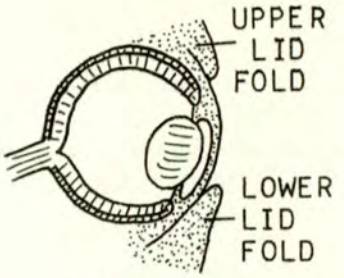
152 Upper
153 Nasolacrimal
154 Independent Origin
155 Puncta Lacrimalis
156 Lacrimal Sac

157
Just before birth these structures become patent by a process of canalization, which starts at the puncta and progresses toward the nasal opening of the lacrimal duct.

Q: The lacrimal sac is formed from _____ _____ (germinal tissue) which originally formed the floor of the _____ groove.

158
The growth of the maxillary process produces the lower lid fold. The upper lid is formed from paraxial mesoderm.

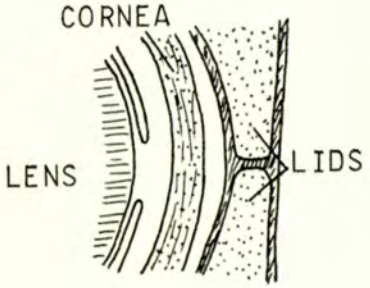
Q: Canalization of the lacrimal apparatus begins at the _____ and ends at the _____.

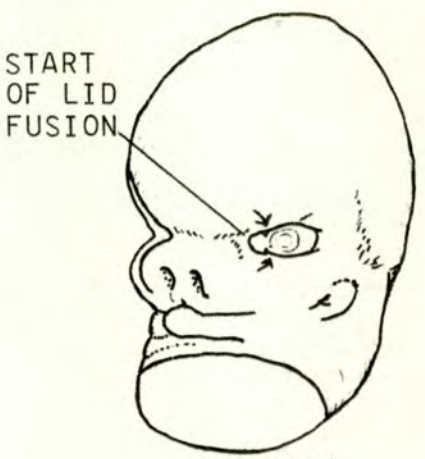


7th WEEK

159
This is a drawing of the growing eyelids. They fuse together, beginning at the inner canthus. The second drawing shows this fusion starting at the inner canthus (angle) of the eye.

Q: _____ gives rise to the lower lid fold, while the _____ gives rise to the upper lid.





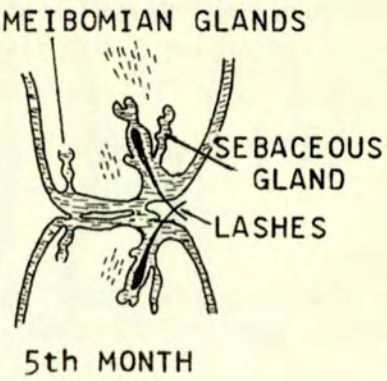
7th Week

160
The eyelids fuse about the 8th week, and remain so, until the inner structures of the eyelids are formed.

Q: Fusion of the lids begins at the _____ _____ of the developing eye.

157 Surface Ectoderm, Nasolacrimal
158 Puncta Lacrimalis, Inferior Meatus
159 Maxillary Process, Paraxial Mesoderm
160 Inner Canthus (Angle)

161
The eyelid adhesions begin to break down in the 5th, 6th, and 7th months. This is the result of several factors, two of which are: secretions from sebaceous glands of the lids which have formed by this stage; and cornification of the cells of this region lend to the process of breakdown.



5th MONTH

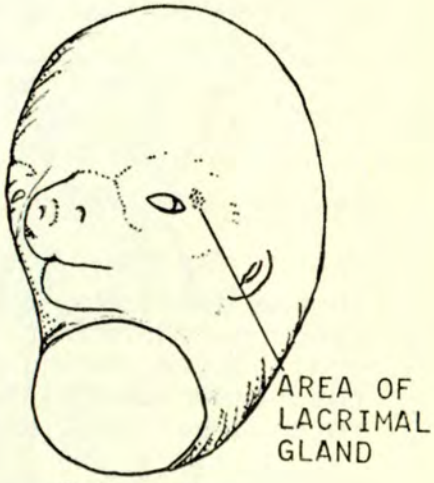
Q: The ciliary body is made up of the _____ ring, the _____ processes and the _____ muscle.

162
The conjunctival epithelium is derived from the ectoderm that is folded in during the formation of the lid folds. It covers the anterior surface of the globe and the inner surface of the lids in the adult.

Q: The major structures of the eye are formed by the time the _____ have separated.

163
In the 8th week several buds of ectoderm appear on the upper and lateral portion of the conjunctival fornix (sac), which will form the lacrimal gland.

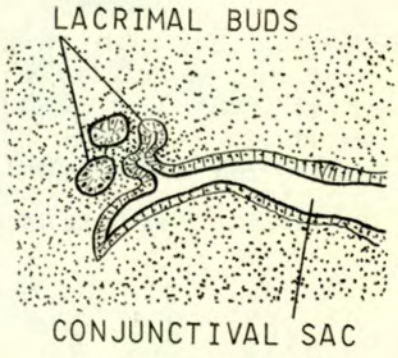
Q: The _____ lines the inner surface of the lids and the anterior surface of the globe. It is derived from _____ (germinal tissue).



8th WEEK

164
This is a drawing which shows the relation of the lacrimal buds to the conjunctival sac.

Q: The _____ of cells and the secretions from _____ glands are two factors which contribute to the breakdown of the fused lids.



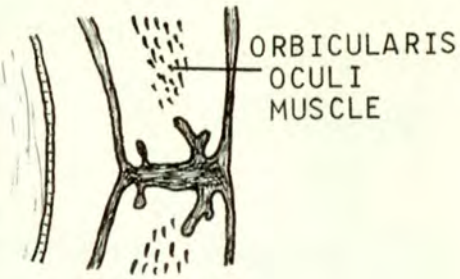
161 Ciliary, Ciliary, Ciliary
162 Eyelids
163 Conjunctival Epithelium, Ectoderm
164 Cornification, Sebaceous

165
The lacrimal buds divide a number of times to form the gland. The gland grows and develops acini. This process continues for some time after birth.

Q: The eyelids grow toward each other and _____ about the end of the _____ month of fetal life.

166
By the twelfth week the orbicularis oculi muscle has started to form in the eyelid.

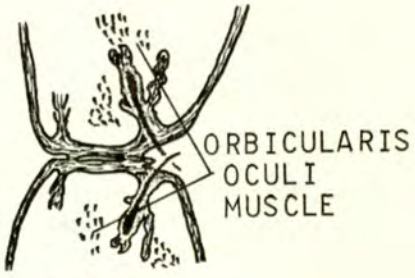
Q: The lacrimal gland is not completely developed until _____ _____.



12th WEEK

167
The orbicularis oculi muscle is well formed by the end of the twelfth week.

Q: The lacrimal gland develops from buds of the _____ sac.



5th MONTH

168
In the development of the lacrimal gland 5 to 8 cords of cells extend upward from the lateral part of the superior fornix of the conjunctiva during the 6th to the 8th week. During the 5th month the tendon on the levator palpebrae superioris separates the gland into superficial and deep parts.

Q: When do the eyelid adhesions break down?

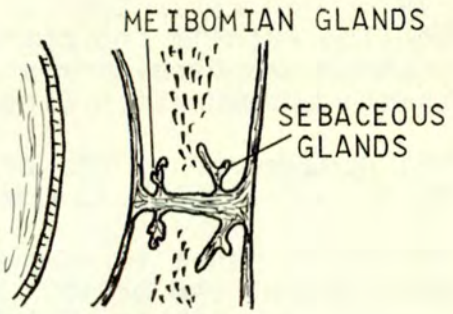
169
The new born child cries, but without tears. The lacrimal gland does not reach full development until 3 or 4 years after birth. After that the gland cells decrease in height until the age of 40. In later life the gland gradually atrophies. The time of weeping tears may vary from 20 to 104 days after birth.

Q: What gives rise to the lower lid fold?

165 Fuse, 2nd
166 After Birth
167 Conjunctival
168 About the 5th to the 7th Month
169 Maxillary Process

170
By the 12th week the sebacious and tarsal or Meibomian glands of the lids are beginning to form.

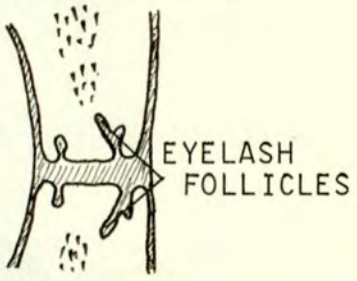
Q: The chorio-capillaris drains through the _____ veins which drain into the ophthalmic veins.



12th WEEK

171
The bulbs or follicles of the eyelashes begin to appear toward the end of the 9th week. Throughout differentiation the lower lid lags behind the upper in development.

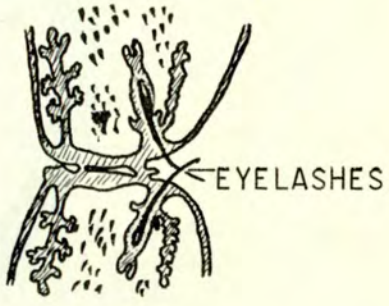
Q: Uveal chromatophores are thought to be of _____ origin, i.e. descendants of cells which have migrated from the neural crest.



12th WEEK

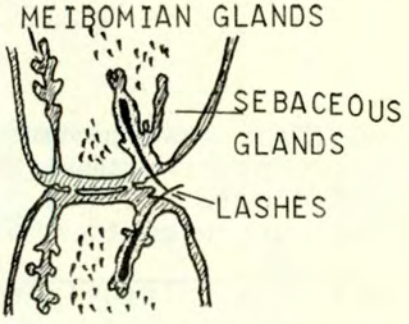
172
By the 5th month eyelashes can be seen as well as the beginnings of the glands of Zeiss.

Q: The tarsal glands of the eyelid are also known as _____ glands.



173
By the end of the 5th month, the Meibomian (tarsal) glands, the eyelashes and the sebaceous glands of the lash follicles are all well developed.

Q: Which eyelid develops more rapidly?



174
It should be emphasized that the eyes and optic nerves are outgrowths of the brain. The nerve fibers of the retina continue into the optic nerve and the optic nerve fibers continue into the brain.

Q: In man the eyelids have normally separated before _____.

170 Vorticose
171 ectodermal
172 Meibomian
173 Upper
174 Birth

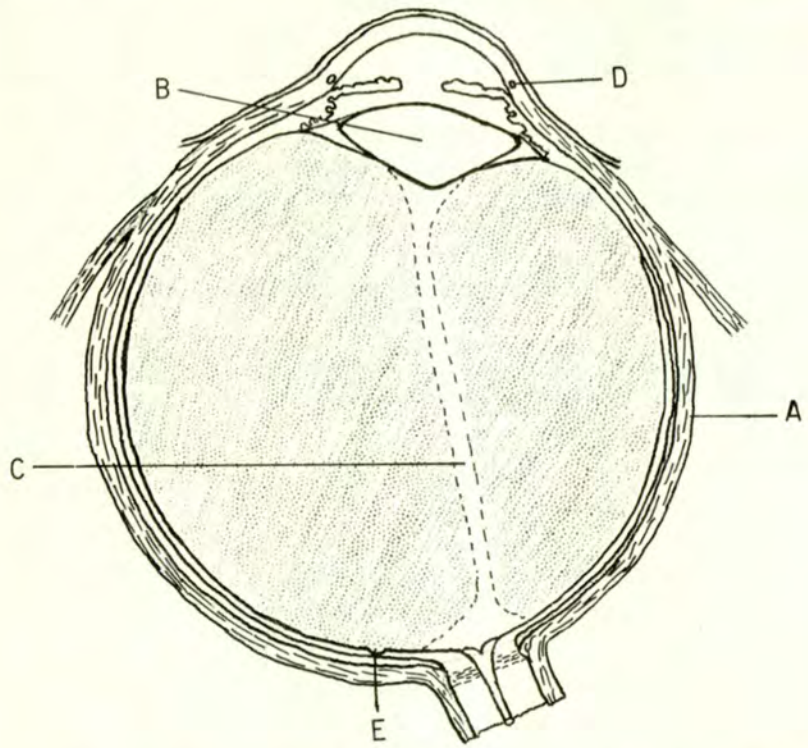
175
Developmentally the optic nerve resembles a tract of the brain more than a peripheral nerve. Its fibers do not possess a neurilemma sheath and when its fibers are cut they will not regenerate.

The dura mater of the brain is continuous with the sheath of the optic nerve which is continuous with the sclera.

The optic nerve is surrounded by sheaths from all three layers of meninges of the brain. Between the layers are spaces which are continuous with the subdural and subarachnoid spaces.

Q: What layer is absent in the optic nerve which surrounds individual fibers in a typical peripheral nerve bundle?

176



(A) From what primary germinal layer does this develop?
(B) This structure forms from _____ (germinal layer).
(C) Previously the _____ was found here.
(D) This used to drain _____ but now it removes _____ from the anterior chamber.
(E) This initially appears as a _____ of the nervous retina.

175 Neurilemma
176 (A) Mesoderm
(B) Surface Ectoderm
(C) Hyaloid Artery
(D) Blood, Aqueous Humor
(E) Thickening

177
The development of nervous function is related to the structural development and differentiation of the nervous system. Vision develops later than other sensory systems. A prematurely born baby may differentiate between light and dark, and pupillary responses can be obtained from a strong light.

Q: When do optic nerve fibers become myelinated?
_____.

178
During the sixth month of fetal life the visual area of the cerebral cortex becomes folded along its long axis. Huxley called this fold the calcarine fissure because of its relation to the calcar avis which is located in the interior of the posterior horn of the lateral ventricle of the brain.

Q: Is the optic nerve a typical peripheral nerve? _____

179
The white line of Gennari is visible to the unaided eye in fresh sections of the visual cortex and for this reason this region is called the area striata. The fibers of the optic radiation grow into the fourth layer of the visual cortex and help form the stria of Gennari.

Q: Are optic nerve fibers covered with a layer of neurilemma?
_____

180
Fibers from the lateral half of the retina grow into the optic tract of the same side, while those from the medial half pass through the optic chiasma and into the optic tract of the opposite side.

Q: What does calcarine mean? _____

181
The majority of the fibers of the optic tract terminate in the lateral geniculate body and a smaller portion passes to the superior colliculus and the pretectal area.

Q: When do optic nerve fibers reach the chiasma? _____

182
Neurons develop in the lateral geniculate body whose axons form the geniculocalcarine tract.

Q: Do peripheral nerves regenerate after injury? _____

177 Late fetal life
178 No
179 No
180 Spur-shaped
181 End of 2nd month
182 Yes

183
The pretectal area develops into an area concerned with light reflexes and the superior colliculus into a center for reflex movements of the eyes and head in response to optic stimuli.

Q: Do optic nerve fibers regenerate after injury? _____

184
The geniculocalcarine tract grows into the visual cortex which is located on either side of the calcarine fissure.

Q: Are the axons of the ganglion cells myelinated in the nerve fiber layer of the retina? _____

185
A point-to-point relationship develops between the origin of the optic nerve fibers in the retina and their termination in the lateral geniculate body.

Q: What forms the optic radiation? _____

186
Neurons in the geniculocalcarine tract develop a similar point-to-point relation between the lateral geniculate body and the striate cortex.

Q: Where is the calcarine fissure? _____

187
Nerve fibers from the medial half of the lateral geniculate body grow into the dorsal lip of the calcarine fissure, while those fibers from the lateral half grow into the ventral lip of that fissure.

Q: What become of the cells surrounding the nerve fibers in the optic stalk? _____

188
Nerve fibers from the upper retinal quadrants grow into the medial half of the lateral geniculate body, while those from the lower retinal quadrants connect with the lateral half of the geniculate body.

Q: What becomes of the cavity in the optic stalk? _____

183 No
184 Not normally
185 Geniculocalcarine tract
186 Medial side of occipital lobe
187 Become neurological cells
188 Obliterated

189
Macular fibers are represented in the caudal third of the visual cortex. Peripheral retinal areas are represented in more rostral positions.

Q: From what part of the embryonic brain does the optic cup develop? _____

190
In the course of development one structure may influence or induce the development of another structure, thus forming a link in a chain of developmental events. It has been shown experimentally with lower vertebrates that the development of the optic cup is influenced by the action of the underlying entoderm on the neural plate. Lens development in turn is caused by the induction influence of the optic vesicle. Without this stimulus the lens will not develop in a normal manner. The inducing agent is probably a chemical substance. At the time of the formation of the lens, the optic cup contains a large amount of ribonucleic acid. The lens in turn, acting with the optic cup, induces the development of the cornea. The optic cup and the lens probably influence the development of the vitreous body. In normal development induction takes place in definite regions at definite time periods.

Q: Without induction from the _____ the lens will not develop normally.

191
The visual projection cortex is called area 17. Area 18 develops around the area striata (17) and is called the parastriate area. Association fibers connect area 17 with area 18. The parastriate area (18) is located in the occipital lobe adjacent to area 17. Area 18 does not have a line of Gennari.

Q: The parastriate area is different from the striate area in that it lacks a _____.

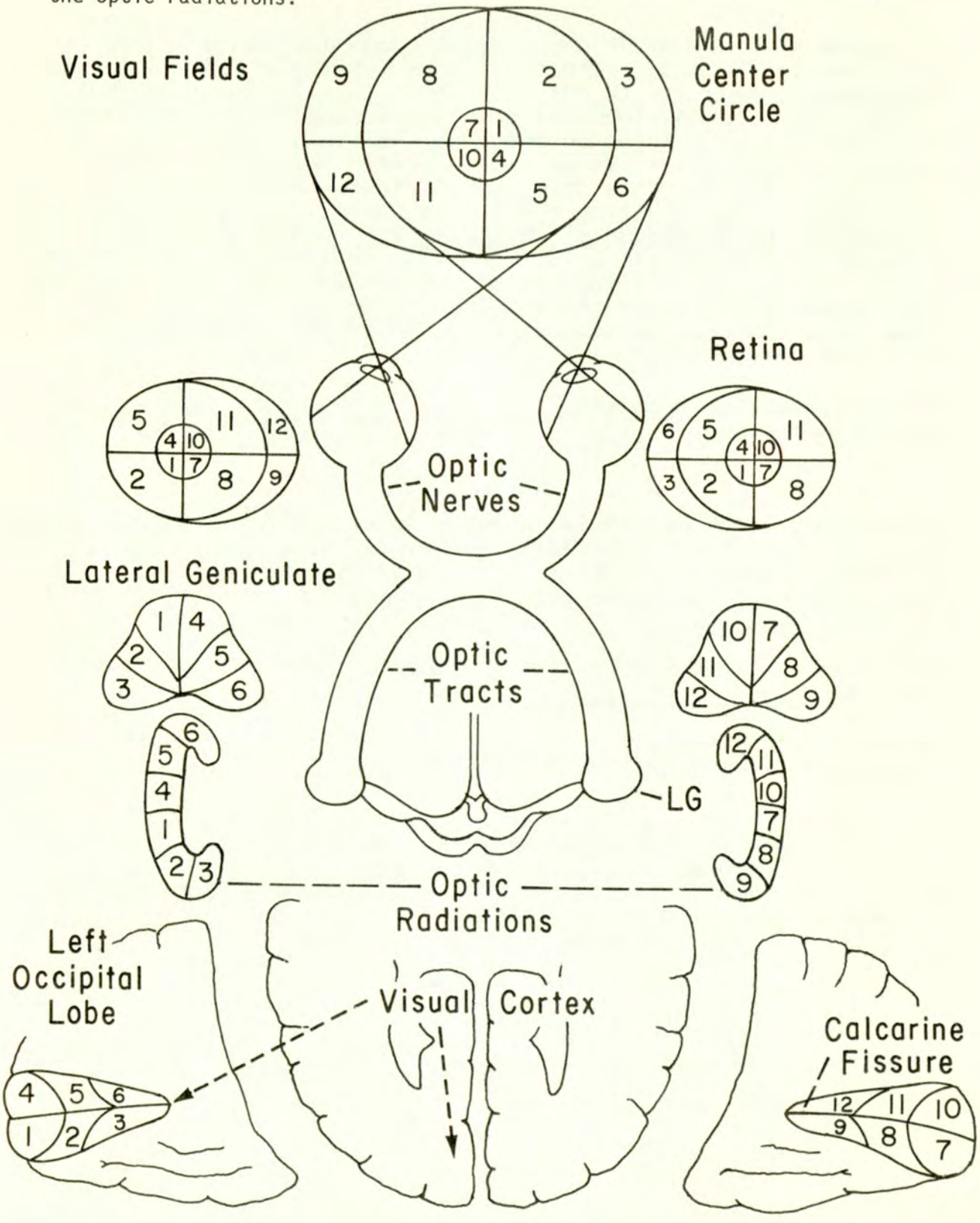
Q: Nerve fibers from the _____ halves of the retina cross in the optic chiasma.

Many double layers of myelin are wrapped around the optic nerve fibers by oliogodendroglial cells. Nodes of Ranvier and mesaxons are present. The myelin sheath helps insulate the axon and aids in the conduction of the nerve impulse.

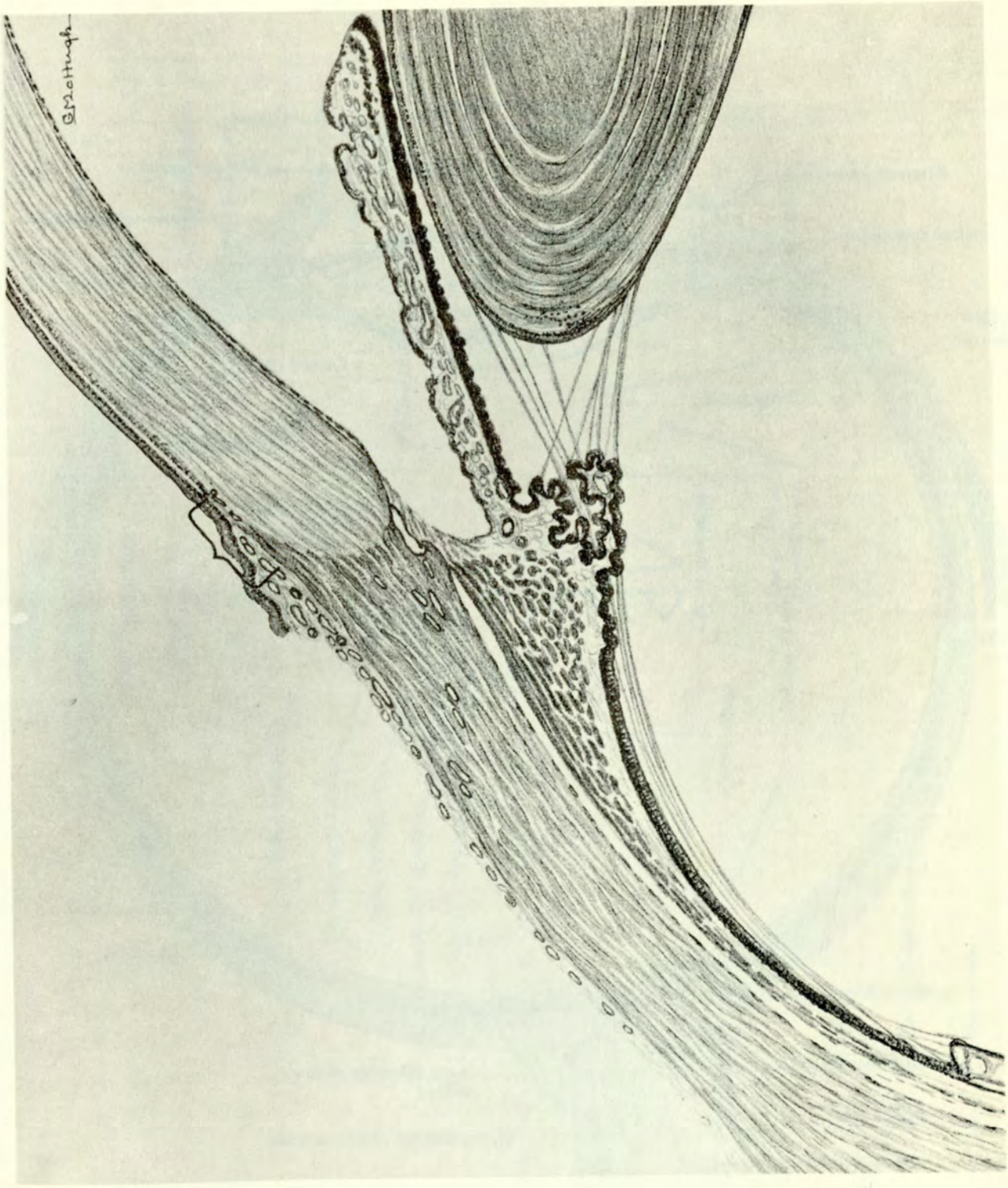
189 Forebrain
190 Optic vesicle

191 Line of Gennari
Medial

192
Color the 4 overlapping quadrants of the visual fields with 4 different colors. With corresponding colors show the way the visual fields are projected on the 2 retinae, the lateral geniculate bodies and the occipital lobes. Draw the path of the axon of a ganglion cell from the medial and lateral halves of each retina. Show the path of neurons in the optic radiations.

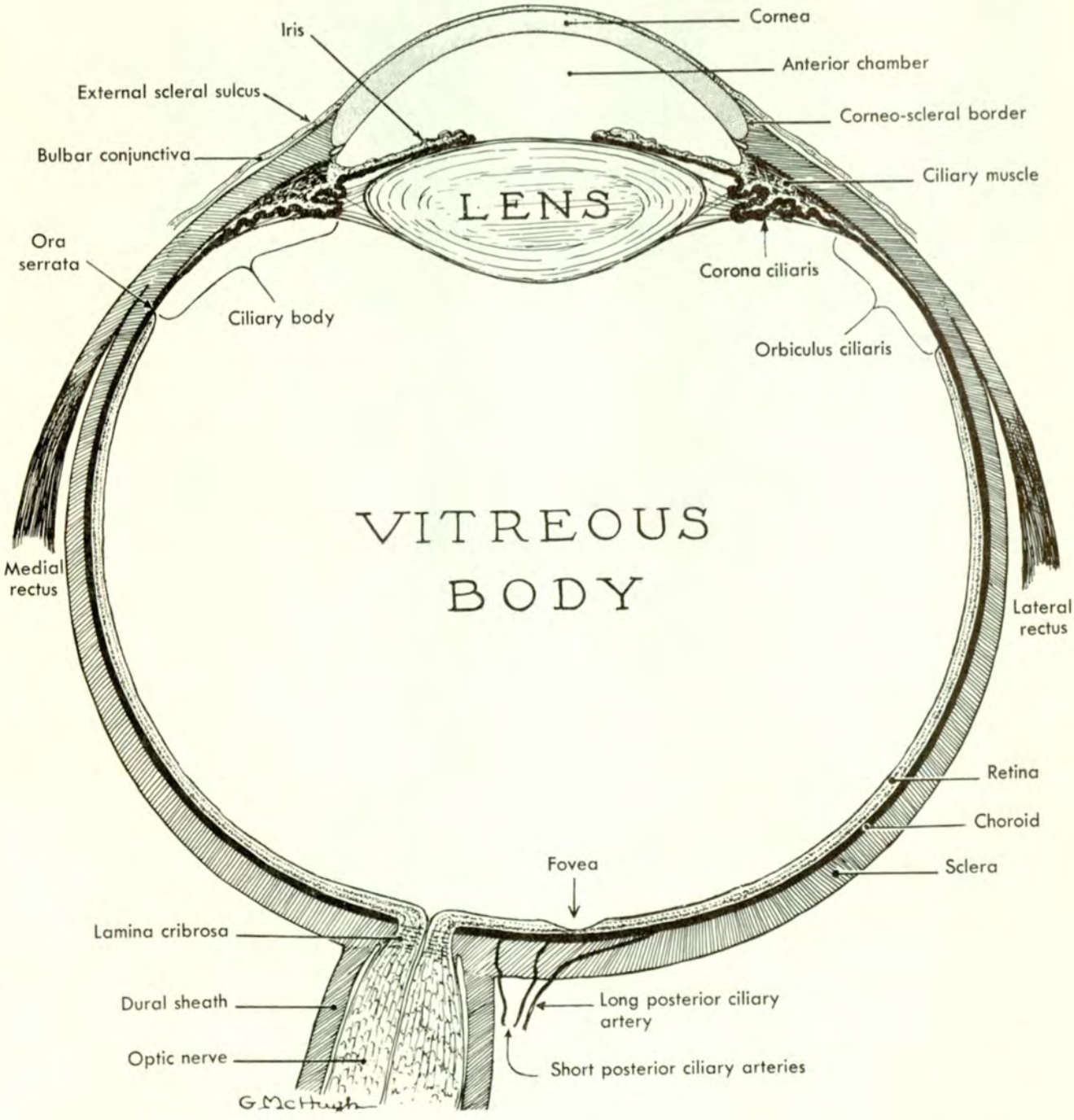


193
Identify and label structures shown in this drawing. Check answers with labels shown in 195. Color.



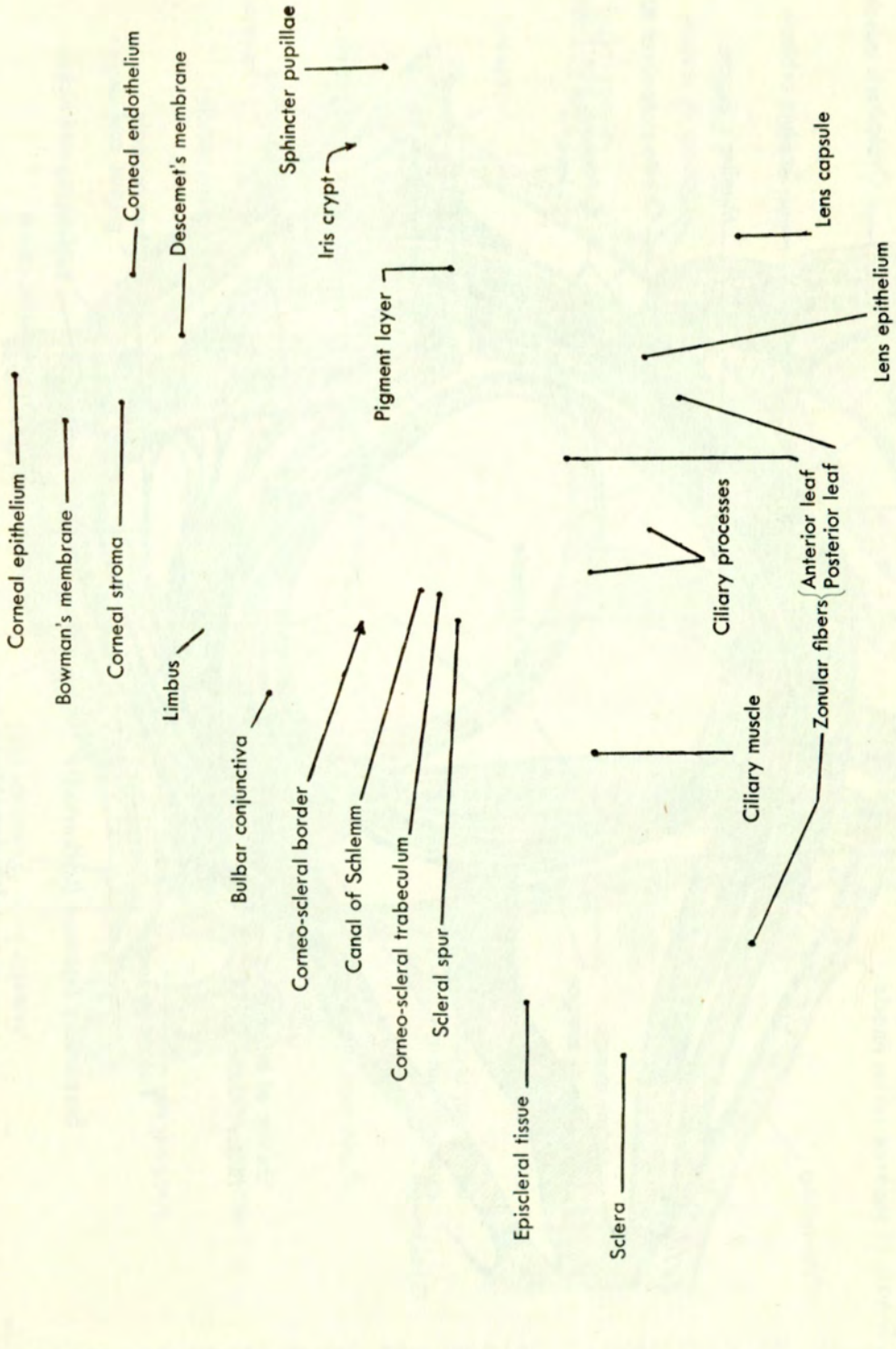
Anteronasal portion of a horizontal section of the right eye. (Courtesy of Bausch and Lomb)

194
Label all structures not identified in this drawing. Color. Horizontal section of right eye. (Courtesy of Bausch and Lomb)

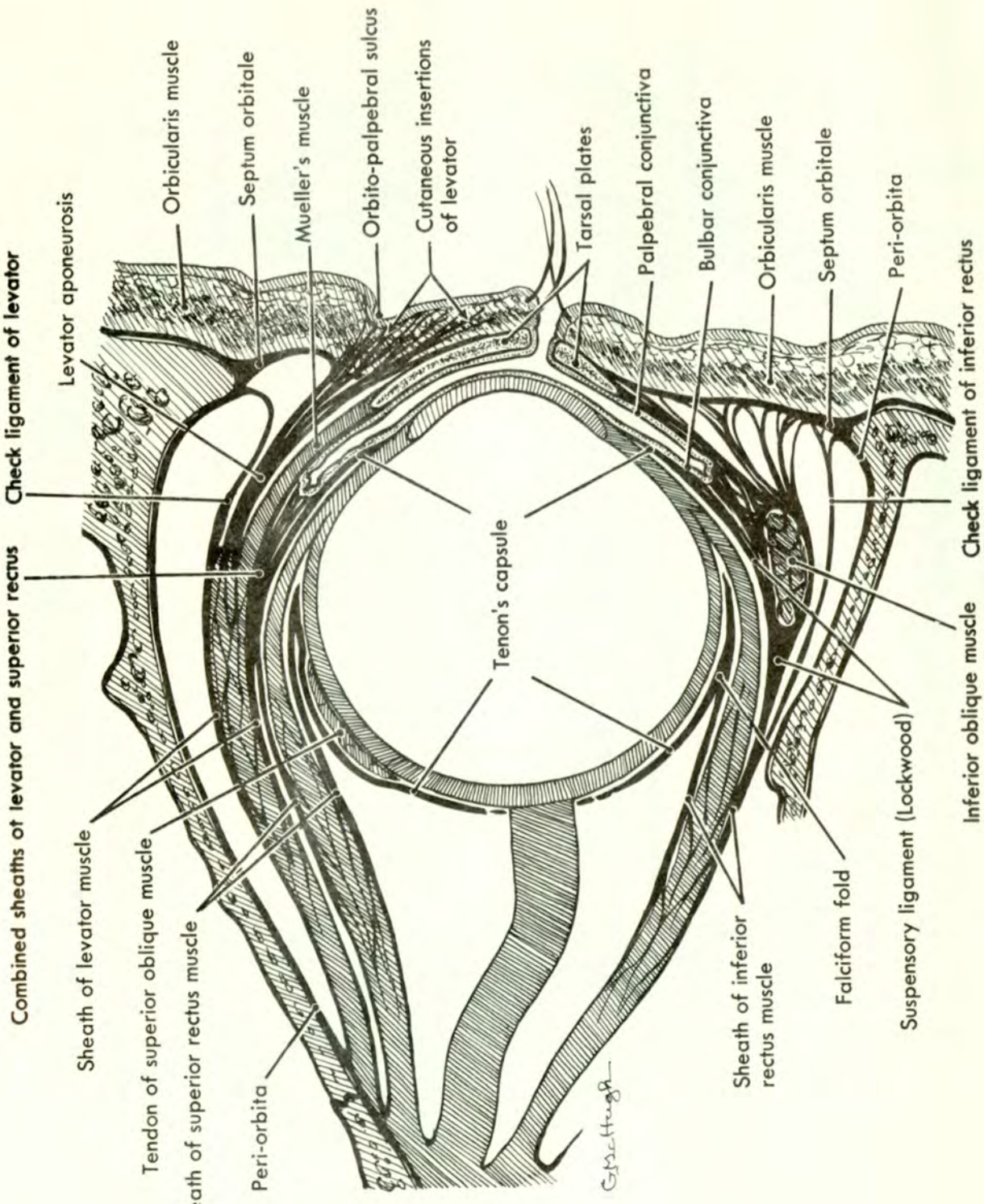


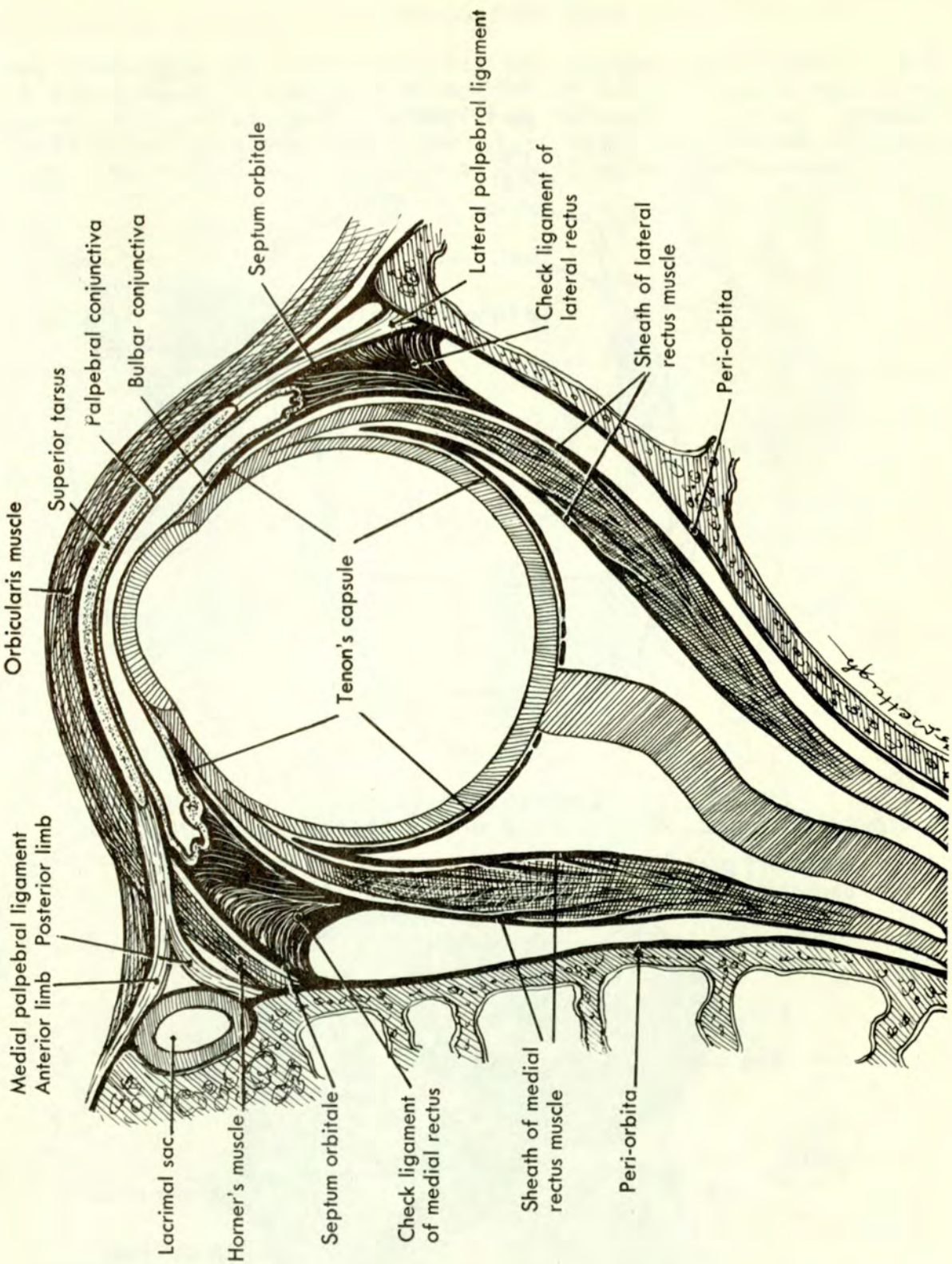
The illustrations obtained through the courtesy of Bausch and Lomb are from "The Human Eye" by P. C. Kronfeld, G. McHugh and S. L. Polyak.

Labels for drawing shown in 193.



A vertical section through the orbit. (Courtesy of Bausch and Lomb)

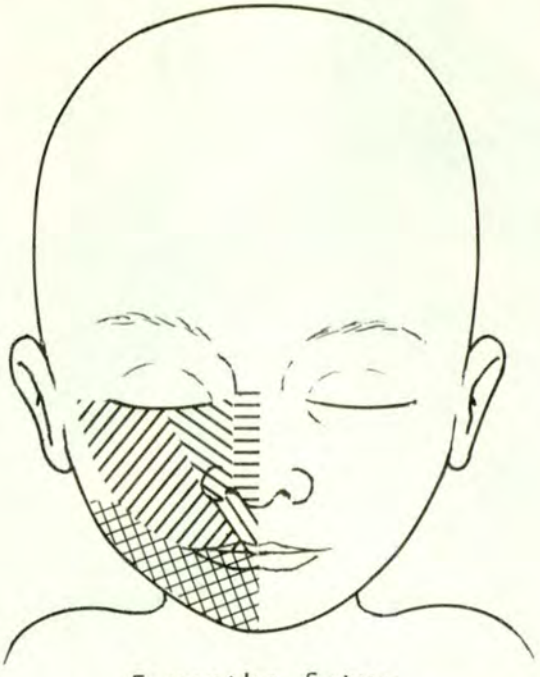




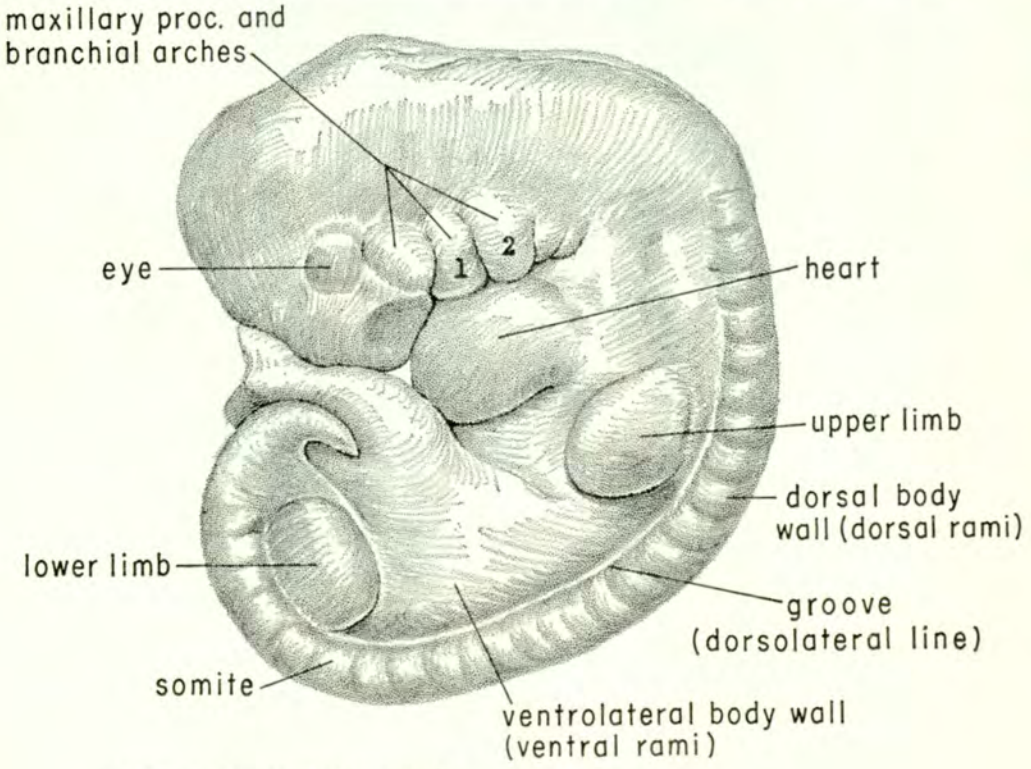
197
A horizontal section of the orbit. (Courtesy of Bausch and Lomb)

FACE DEVELOPMENT

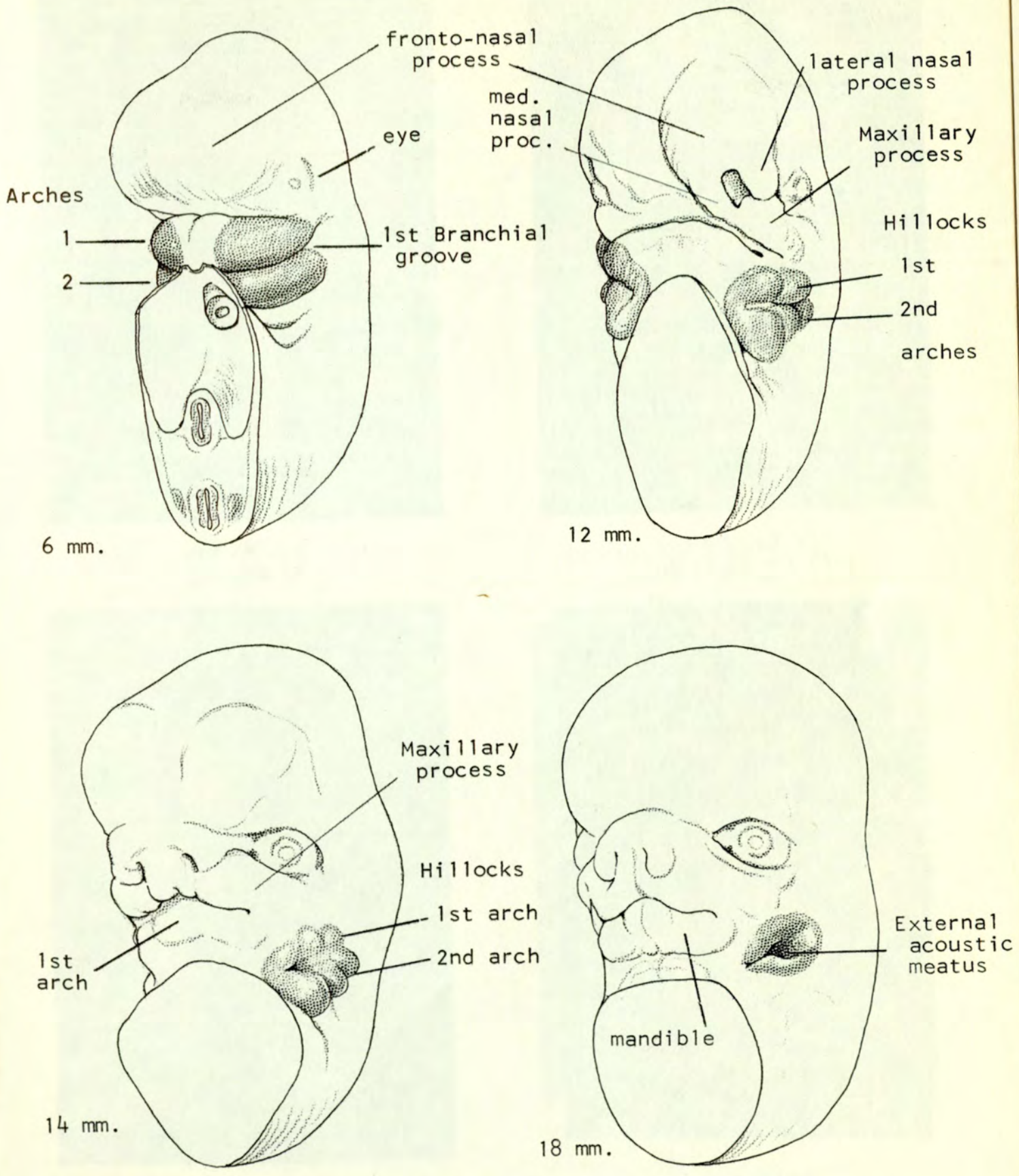
198 In the illustrations identify and color the component parts which contribute to the formation of the face. Observe the following: nasal pit, medial and lateral nasal folds, frontonasal process, mandibular (1st) arch, maxillary process, hyoid (2nd) arch, naso-optic furrow (naso-lacrimal groove or furrow), eye and eyelids.



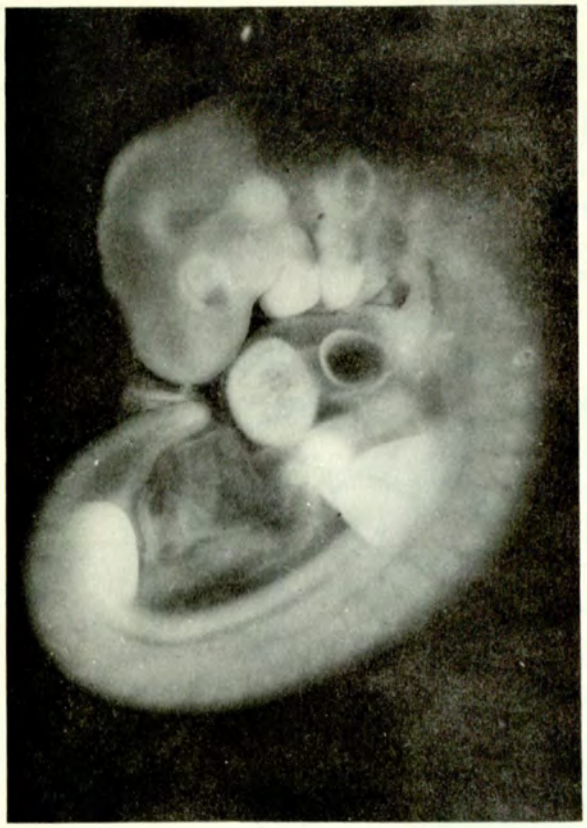
5 months fetus
Component parts of the face are differentially hatched.



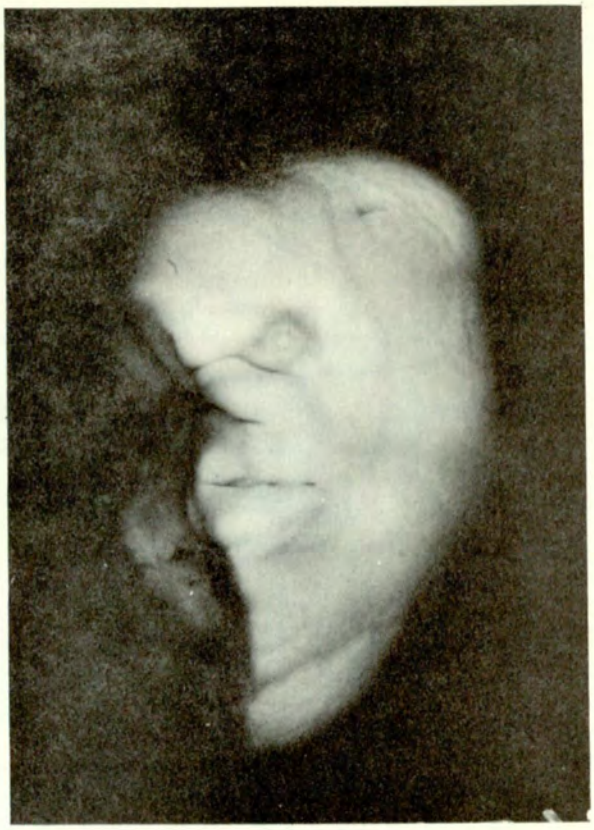
A 6.3 mm human embryo. × 15.



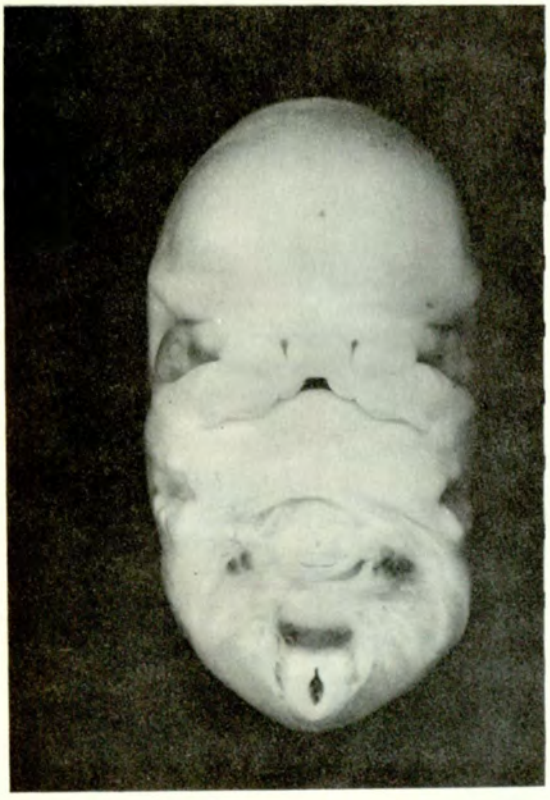
(after Streeter, 1922)



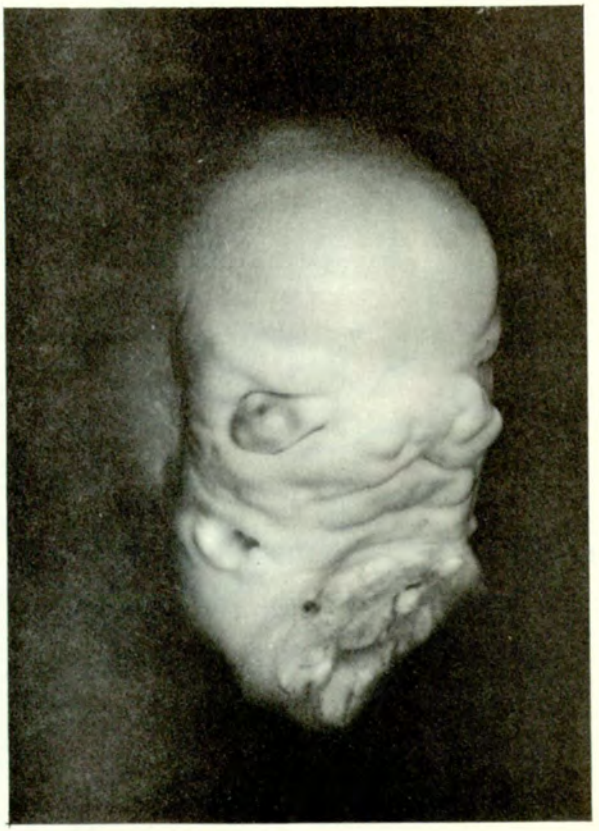
XIV 6.5 mm.
28 to 30 days ± 1.



XVI 11 mm.
33 days ± 1.

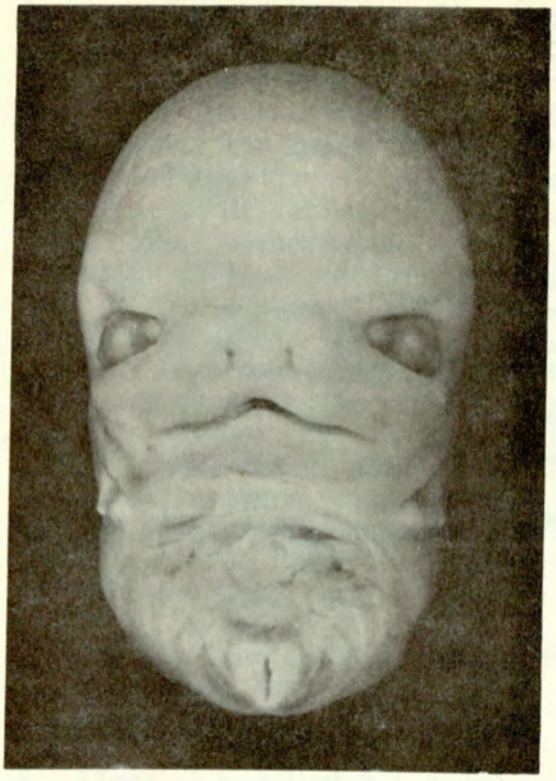


XVIII 14 mm.
37 days ± 1.



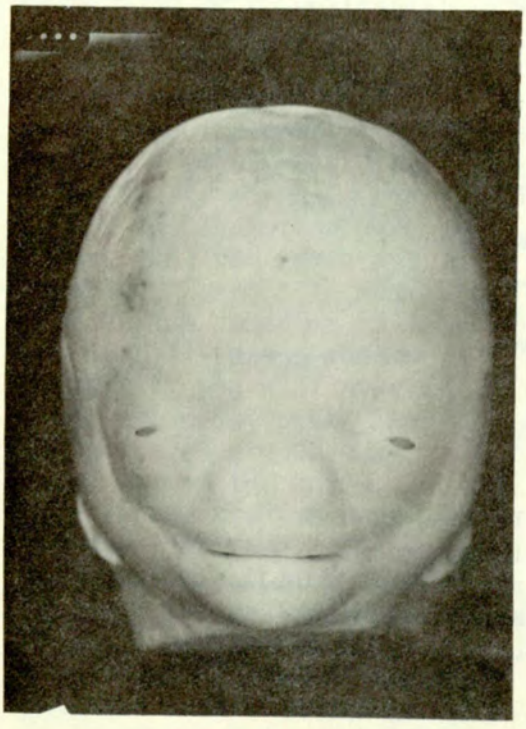
XVIII 14 mm.
37 days ± 1.

Courtesy of Professor Hideo Nishimura
Kyoto University



XIX 16 mm.
39 days ± 1.

XXI 20 mm.
42 days ± 1.



XXIII 33 mm.
48 days ± 1.

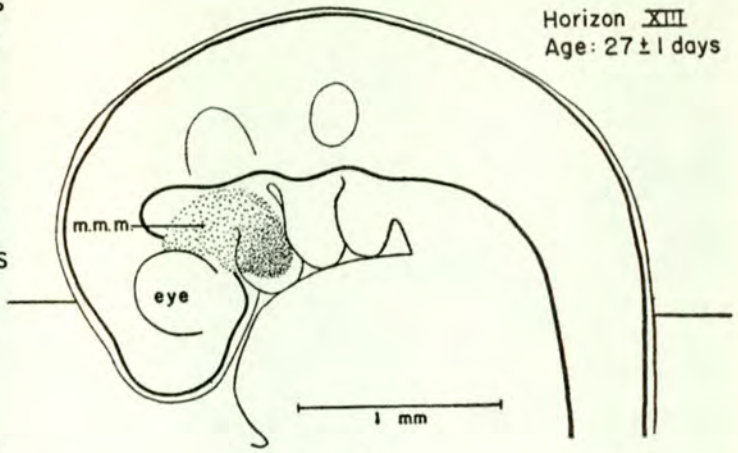
50 mm.
3 months.

Courtesy of Professor Hideo Nishimura
Kyoto University

201
In each orbital region in shark embryos, there are three preotic somites which give rise to the extraocular muscles. Typical somites have not been found in human embryos in the orbital region; however, since the orbital muscles and nerves in the shark are thought to be closely analygous to these structures in higher vertebrates, the eye muscles in man are usually assumed to be of somite origin. (See somites in frame No, 5.)

Q: All of the muscles of the body, with the exception of the muscles of the _____ and the myoepithelial cells of sweat glands, are derived from _____.

A: Iris, mesoderm

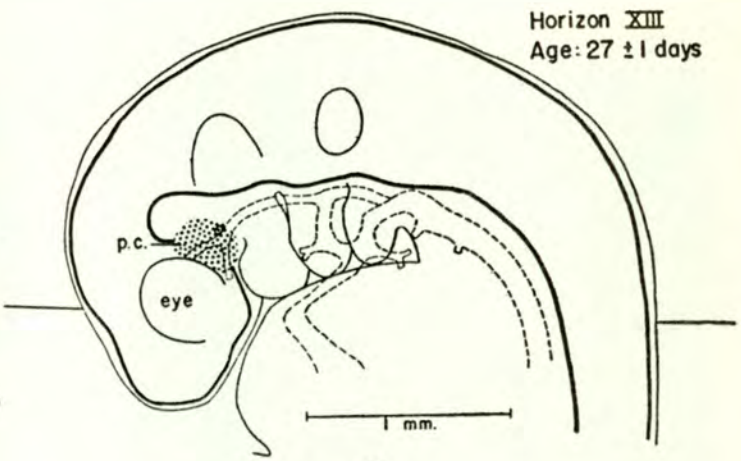


A

202
An early indication of the development of the orbital muscle is the condensation of mesoderm in the region of the developing eye. Figures A, B and C are diagrams based on reconstructions of human embryos about 4 to 5 mm. ± 1, CR length. Figure C is a diagram of a section through the brain and optic vesicle. The maxillomandibular mesoderm (m.m.m.) and the premandibular condensation (p.c.) have been superimposed on the left side. The level of fig. C is indicated in figs. A and B. (Figs. A-N from P. W. Gilbert, 1957, Carnegie Contributions to Embryology No. 246.)

Q: The voluntary muscles are mainly derived from the paraxial mesoderm which is segmentally arranged in _____.

A: Somites

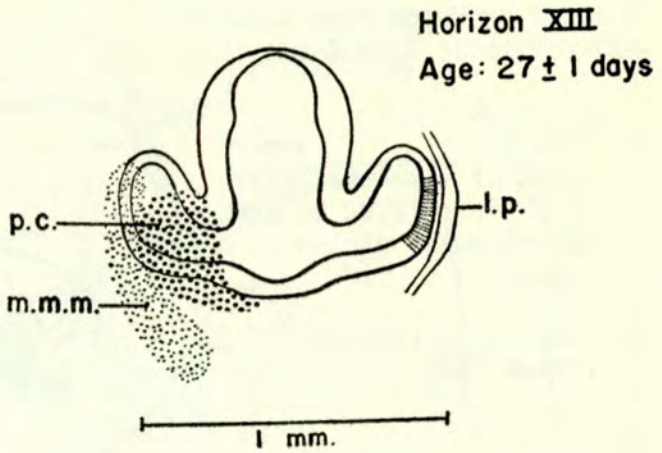


B

ABBREVIATIONS

a.p.c., anterior peripheral condensation
int., intermediate mass
i.o., inferior oblique
i.p.c., inferior peripheral condensation
i.r., inferior rectus
l.p., lens placode
l.p.s., levator palpebrae superioris
l.r., lateral rectus
l.v., lens vesicle
m.m.m., maxillomandibular mesoderm
m.r., medial rectus
n. III, oculomotor nerve
n. IV, trochlear nerve
n. VI, abducens nerve
p.c., premandibular condensation
p.p.c., posterior peripheral condensation
s.o., superior oblique
s.p.c., superior peripheral condensation
s.r., superior rectus
t., trochlea

203
In human embryos of about 6 to 7 mm. ± 1 (figs. D-F), the superior rectus (s.r.) extends forward from the premandibular condensation (p.c.). The primordia of the superior oblique (s.o.) and the lateral rectus (l.r.) appear as condensations of the maxillomandibular mesoderm and are connected by diffuse mesoderm called the intermediate mass (int.). As the head region expands in the early stages, the premandibular condensations are connected across the midplane by a transverse bridge of mesoderm. In embryos of about 7 mm. this bridge of mesoderm is interrupted and the two condensations are no longer connected. The significance of this is not understood.

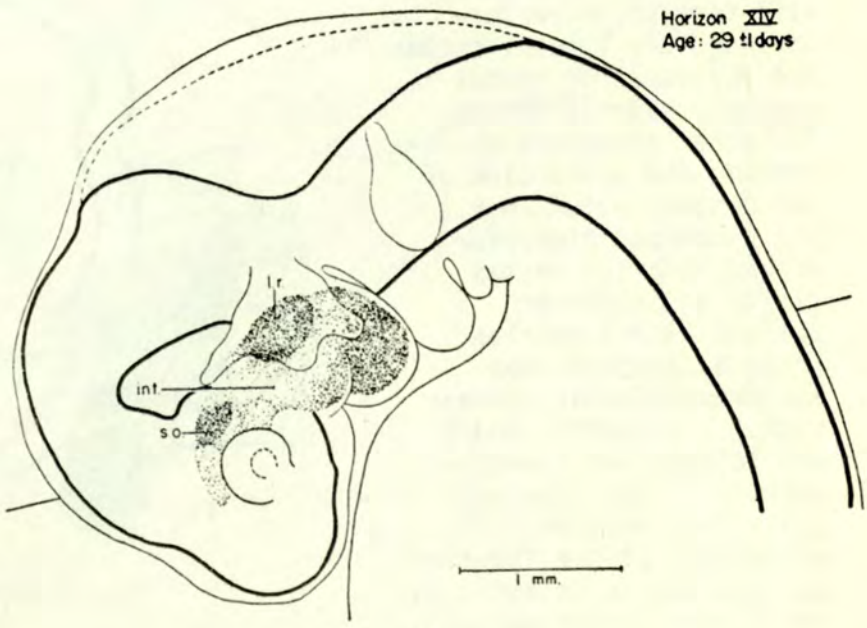


C

Q: The maxillomandibular mesoderm is related to the _____ branchial arch.

A: First or mandibular. Label this arch in fig. B.

204
Diagrams G through N are based also on reconstructions and sections of embryos. The position of the derivations of the maxillomandibular mesoderm and the premandibular condensation is shown in relation to the following: brain, eye, Vth nerve and mandibular arch. In addition to the superior oblique and lateral rectus muscle primordia, you will note 4 other condensations. These are situated around the outer rim of the optic vesicle and are known as the superior (s.p.c.), inferior (i.p.c.), anterior (a.p.c.) and posterior (p.p.c.) peripheral condensations. They anticipate the insertion points of the four rectus muscles on the eyeball and contribute to the formation of the sclera. The III and VI cranial nerves have now



D

grown into their respective muscle primordia. At this stage the lens vesicle has pinched off of the surface ectoderm. Figs. G, H and I are made from human embryos about 7 to 8 mm. ± 1.

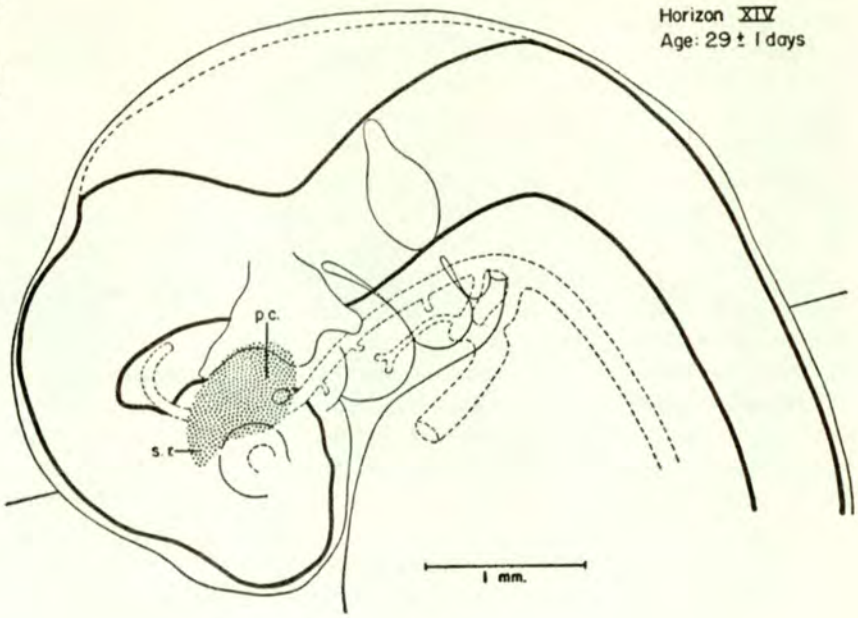
Q: The _____ process of the mandibular arch is related to the development of the orbit.

A: Maxillary (review frame 198)

205
In fig. I, derivatives of the maxillomandibular mesoderm and the premandibular condensation have been superimposed on the left side.

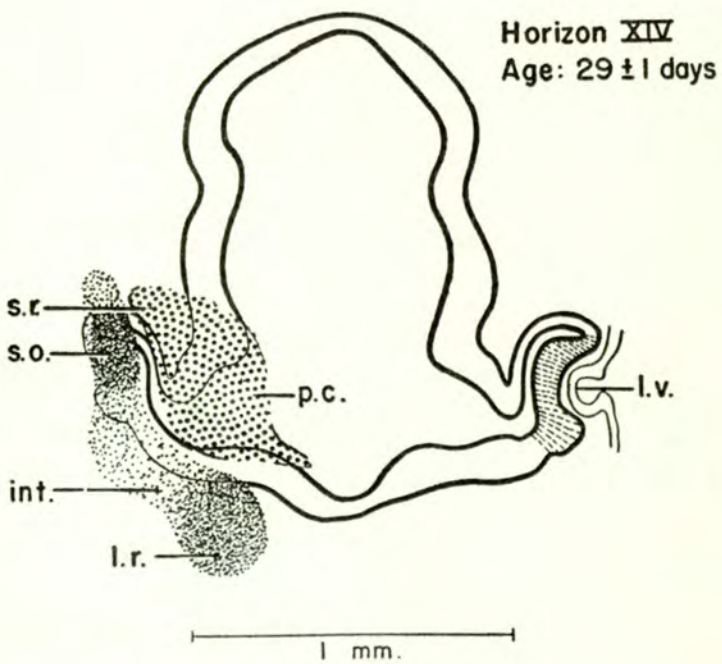
Q: Diffuse mesoderm is often called _____.

A: Mesenchyme



E

206
In figs. J and K note that the condensations, which will form the superior oblique, the lateral rectus and the superior rectus muscles, have elongated. Two other processes representing the primordium of the medial rectus (m.r.) and a common primordium of the inferior rectus (i.r.) and inferior oblique (i.o.) muscles (fig. N) project from the premandibular condensation. Figures L and M are lateral and caudal aspects of the premandibular condensation. The primordium of the inferior oblique muscle is attached for a time to the distal end of the inferior rectus. (Figures A to N from P. W. Gilbert.)

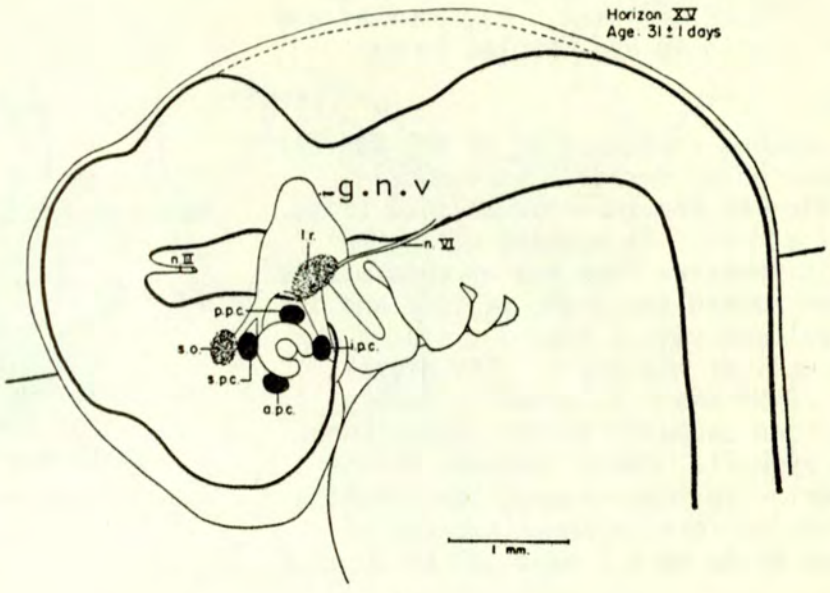


F

Q: From which germ layer does the ciliary muscle develop?_____

A: Mesoderm

207
The extrinsic ocular muscles in man arise from three independent but closely associated mesodermal condensations on each side of the head. The extrinsic eye muscles innervated by the IIIrd nerve arise from the pair of premandibular condensations. Small spaces may appear briefly in these premandibular condensations in embryos of about 26 to 28 days. These spaces have been regarded as rudimentary head cavities homologous with the premandibular head cavities in lower vertebrates. (g.n.v, ganglion of Vth nerve)

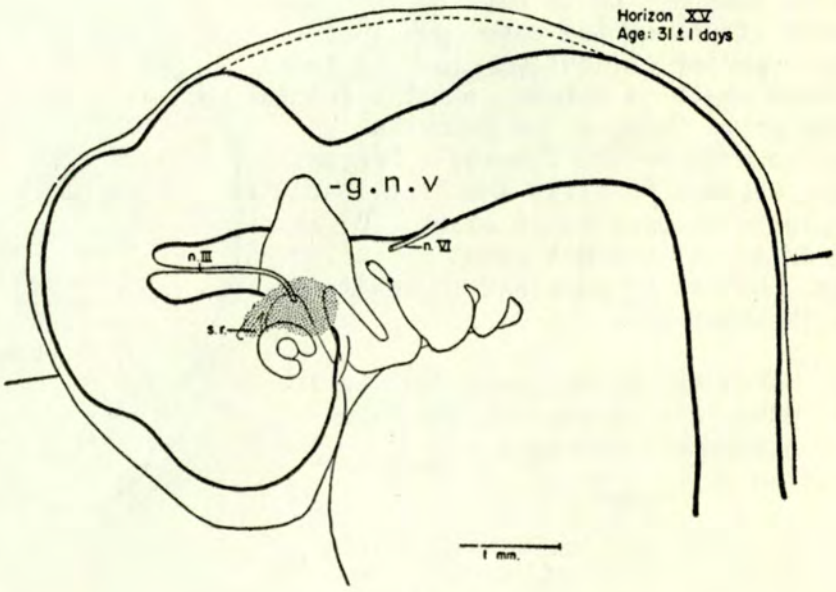


G

Q: Each premandibular condensation gives rise to _____ processes which represent the primordia of the four eye muscles which are supplied by the _____ muscle.

A: Three, oculomotor (Frame 206 & Fig. N)

208
Two condensations subsequently develop in the maxillomandibular mesoderm. The more caudal and medial condensation is the primordium of the lateral rectus muscle and it is found in embryos of about 27 ± 1 days (4 to 5 mm.). It grows cranially to reach the periphery of the optic vesicle (figs. G and J).



H

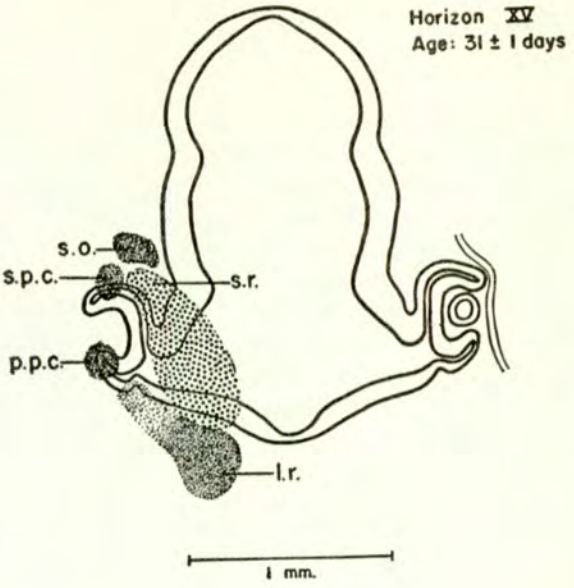
Q: Do definite somites occur in the development of the human head?

_____

A: Occipital somites develop at the base of the head. No, somites are related to eye muscles in man.

209

The second condensation of the maxillomandibular mesoderm is the primordium of the superior oblique (figs. G, I and J). It appears above the optic vesicle. One end of this muscle grows toward the optic vesicle and its caudal end swings toward the developing wall of the orbit. Its distal end bends sharply, grows laterally and then caudally to its insertion on the eyeball. About the bend in the superior oblique tendon, the trochlea begins to form in human embryos of about 40 to 48 ± 1 days (21 to 30 mm.).



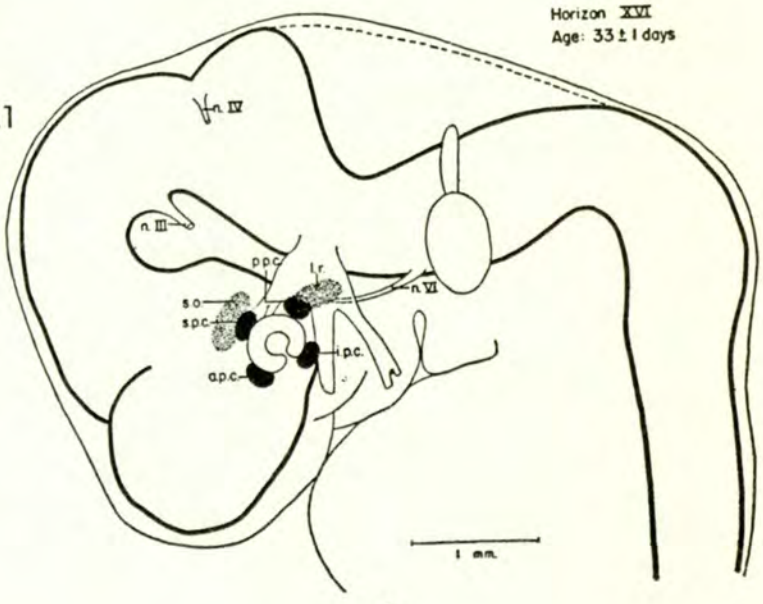
I

Q: Trochlea in Latin means _____.

A: Pulley; the superior oblique was formerly called the trochlear muscle.

210

It is interesting to note that in the early stages of the development of the superior oblique muscle, the trochlear angle is obtuse. As the frontal bone grows forward the trochlea is pulled with it and the angle becomes more acute. At first the trochlear angle is obtuse, being about 120° at 39 days. It becomes about 95° at 45 days, 80° at 47 days and in adult man it is about 55°.

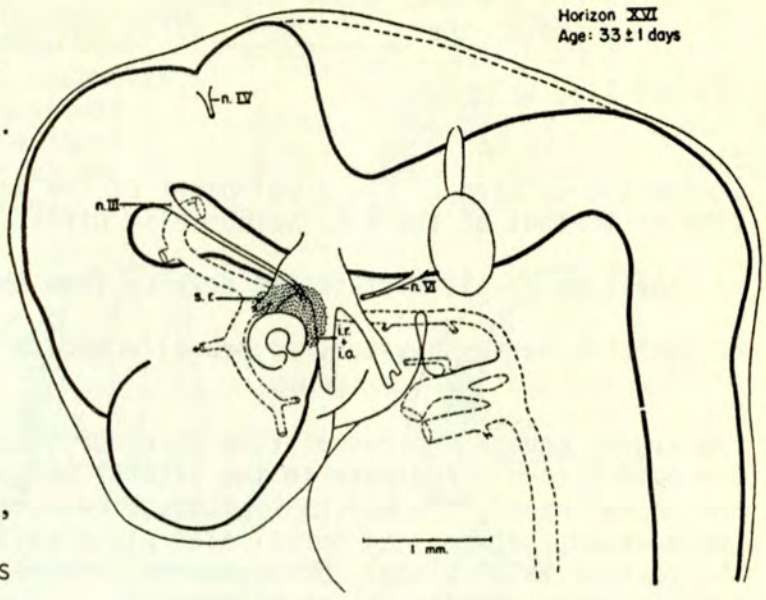


J

Q: Which two eye muscles develop in primordia located in the same mesodermal process?_____ and _____

A: Inferior oblique and inferior rectus

211
In human embryos of about 6 to 7 mm. (28 to 30 days) four peripheral condensations appear in the maxillomandibular mesoderm about the periphery of the optic vesicle. The primordia of the four rectus muscles grow peripherally toward these condensations and insert into them. These peripheral condensations contribute to the formation of the sclera (figs, G, I and J).

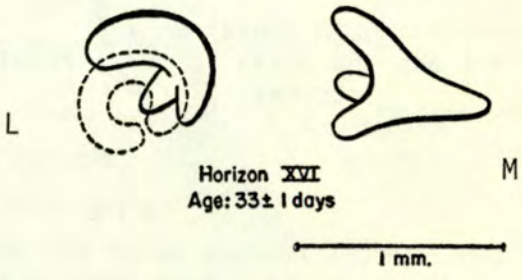


K

Q: With greater growth of the muscle primordia peripherally toward their insertions than centrally toward their origins, would you expect more or less variations in muscle insertions than in their origin? _____

A: More

212
The primordium of the superior rectus muscle (fig. N) splits into two muscular sheets of mesoderm. The dorsomedial layer becomes the levator palpebralis superioris in embryos about 22 to 30 mm. (42 to 48 ± 1 days) and it grows forward into the upper eyelid. Muscle fibers begin to appear in the superior rectus by the end of the 6th week.

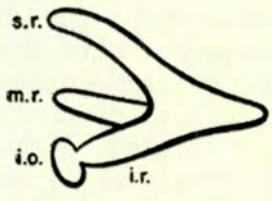


L M

Q: Failure of the levator palpebralis superioris to separate from the superior rectus would lead to a condition known as _____.

A: Congenital ptosis

213
The eye muscle nerves grow from the brain into their respective muscle primordia in approximately the following sequence: oculomotor (4 weeks), abducent (4.5 weeks) and trochlear (5 weeks). The horizons of Streeter are stages of human development. Various stages (horizons) are indicated by Roman numerals (Carnegie Contributions to Embryology Nos. 85, 197, 199, 211, 230, 244 and 259).



N

Q: With respect to the eye muscle nerves, the fibers of the _____ nerve are crossed, those of the _____ nerve are partially crossed and those of the _____ nerve are uncrossed.

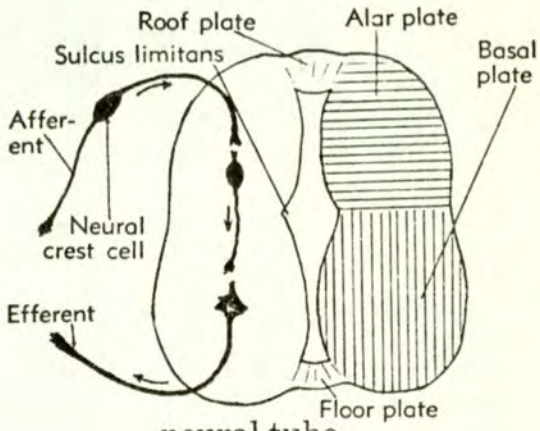
A: IV, III, VI

214
In man the pattern of the development of the extrinsic eye muscles is very similar to that of the cat, marsupials, birds, reptiles and sharks.

Q: The eyes of all vertebrates develop from the _____.

A: Central nervous system, or neural ectoderm

215
The caudal end of the neural tube develops into the spinal cord. A groove in the lateral wall of the neural canal, the sulcus limitans, indicates the boundary between the dorsal alar plate and the ventral basal plate. Motor neurons of the spinal nerves develop in the basal plate. Sensory nerves grow from the spinal ganglia into the afferent centers of the alar plate. The gray matter of the alar plate will become the dorsal horn and the ventral horn will develop in the basal plate. (A. T. Rasmussen, 1943, Outlines of Neuro-Anatomy, figures courtesy of Dr. Theodore Rasmussen.)

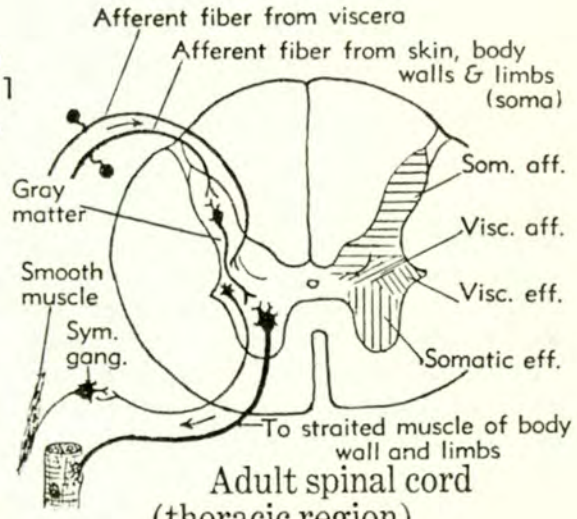


neural tube

Q: The ventral horn contains _____ neurons and the dorsal horn is related to _____ neurons.

A: Motor, sensory

216
A functional system is made up of all the neurons of the body which have certain anatomical and physiological characters in common so that they react in a common mode. A typical spinal nerve contains four functional systems, namely: somatic afferent (sensory), visceral afferent, visceral efferent (motor) and somatic efferent. The only neurons in spinal nerves concerned with the innervation of structures related to the eye are visceral motor (efferent) neurons. Their cells of origin are located in the visceral efferent (or intermediolateral) cell columns in the upper thoracic levels (T1-3±1) of the spinal cord. (Figure from Rasmussen.)



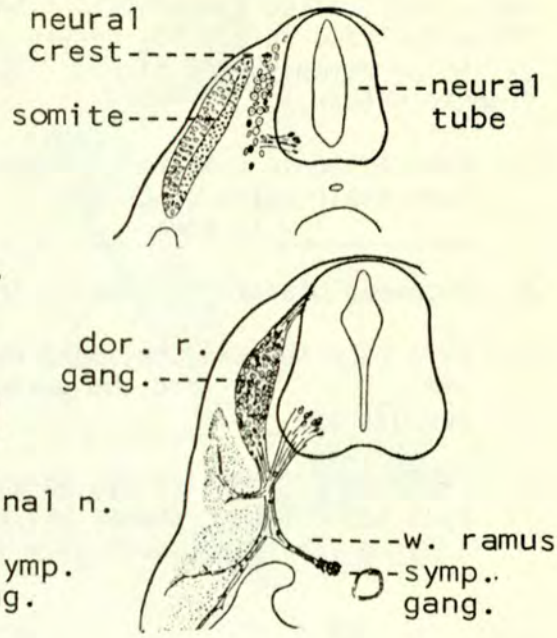
Adult spinal cord (thoracic region)

Q: In Latin, afferent means _____ and efferent means _____.

A: ad - toward and fero - I carry, thus carrying toward; ex - out and ferro - I carry, thus conveying away from.

217

The neural crest develops as a longitudinal band of cells on each side of the neural tube. Some of these cells differentiate into neuroblasts and sheath cells. Certain of these neuroblasts form the dorsal root ganglia of the spinal nerves and other migrate to a more ventral position where they differentiate into the chain ganglia of the sympathetic trunk. (Figs. of embryonic spinal cord, modified from Streeter, 1912, Human Embryology, Keibel and Mall, Lippincott Co.)

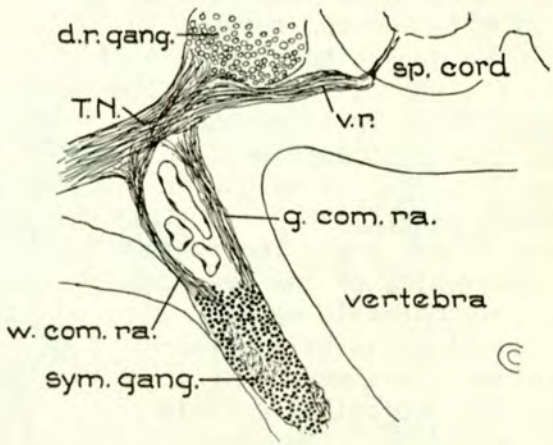


Q: Like the neural tube, the neural crest is formed from _____.

A: Ectoderm

218

Spinal preganglionic neurons are thinly myelinated and pass from the spinal nerve to the sympathetic trunk in the white rami. Postganglionic are nonmyelinated (unmedullated) and pass from the sympathetic trunk and chain ganglia to the spinal nerves for the innervation of sweat glands, arrector pili (hair) muscles, and blood vessels. (Figure from Pearson et al., 1960, Anat. Rec., 138)



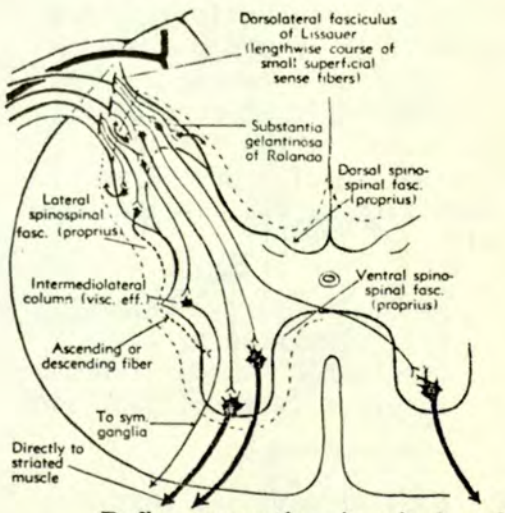
Q: In contrast to the innervation of the striated voluntary striated muscles, the innervation of the structures listed in the frame above are _____.

A: Involuntary

219

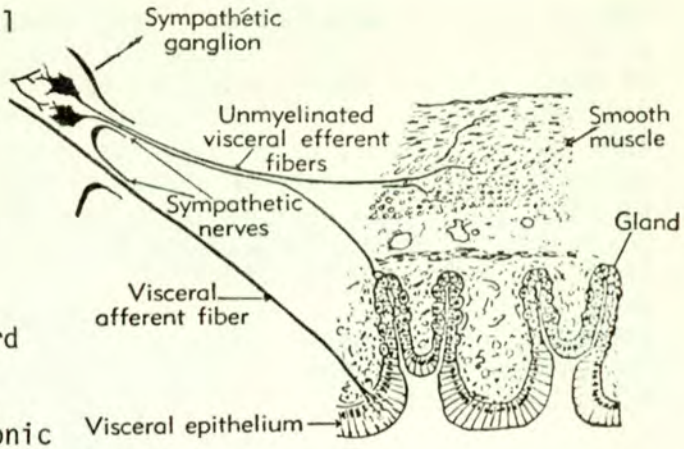
The visceral motor neurons constitute the autonomic nervous system. The autonomic nerves to the orbit are concerned with:

1. Vasomotor control of orbital structures.
2. Control of the intrinsic muscles of the eye (dilator and sphincter pupillae, and ciliary muscle).
3. Innervation of the smooth muscles of the lids and orbit and
4. Innervation of the lacrimal gland.



Reflex connections in spinal cord

Visceral motor neurons in thoracic spinal nerves are called sympathetic fibers. Those included in cranial nerves are called parasympathetic fibers. (Figure from Rasmussen.)



Q: Preganglionic sympathetic neurons have their cells of origin in the _____ in the _____.

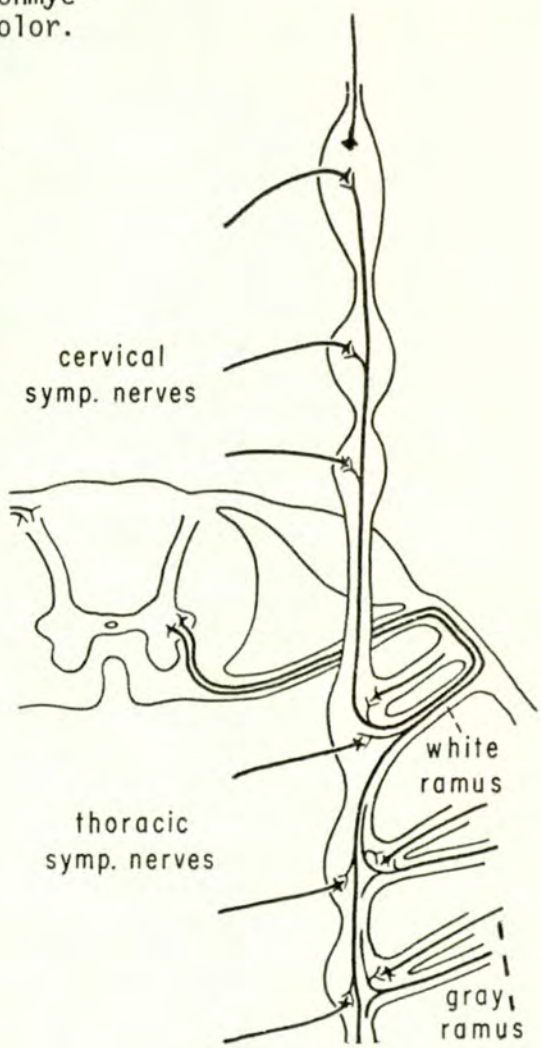
A: Intermediolateral column, spinal cord

Q: As a rule the preganglionic neurons are _____ and the postganglionic neurons are _____.

A: Myelinated (medullated), nonmyelinated. Myelinated fibers appear white. Unmyelinated fibers are more grey in color.

220

An autonomic nerve pathway is usually made up of a two-neuron chain. A preganglionic neuron has its cell of origin in the central nervous system and it terminates in an autonomic ganglion. The postganglionic neuron has its cell of origin in an autonomic ganglion and its fiber terminates in the organ innervated. In the innervation of the eye, preganglionic sympathetic neurons leave a spinal nerve by a white communicating ramus which is connected to a sympathetic chain ganglion and trunk. The preganglionic axon passes up the sympathetic trunk to the superior cervical sympathetic ganglion where it is in synapse with a postganglionic neuron. Other postganglionic neurons pass to the spinal nerves for the innervation of blood vessels, sweat glands, etc. in the body wall.

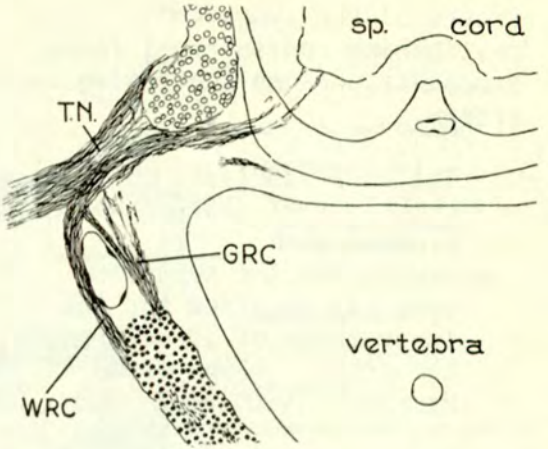


LABEL THIS DRAWING

Q: What structures in the orbit are innervated by postganglionic neurons from the superior cervical ganglion?

_____

A: Dilator pupillae muscle, tarsal muscles of the eyelids, blood vessels



221
Preganglionic fibers from the upper thoracic nerves pass up the sympathetic trunk to the superior cervical ganglion. Certain post-ganglionic neurons arising in this ganglion form the internal carotid nerve (plexus) which follows this artery and its branches to supply structures in the head. (Fig. from Pearson, et al., 1960, Anat. Rec., 138.)

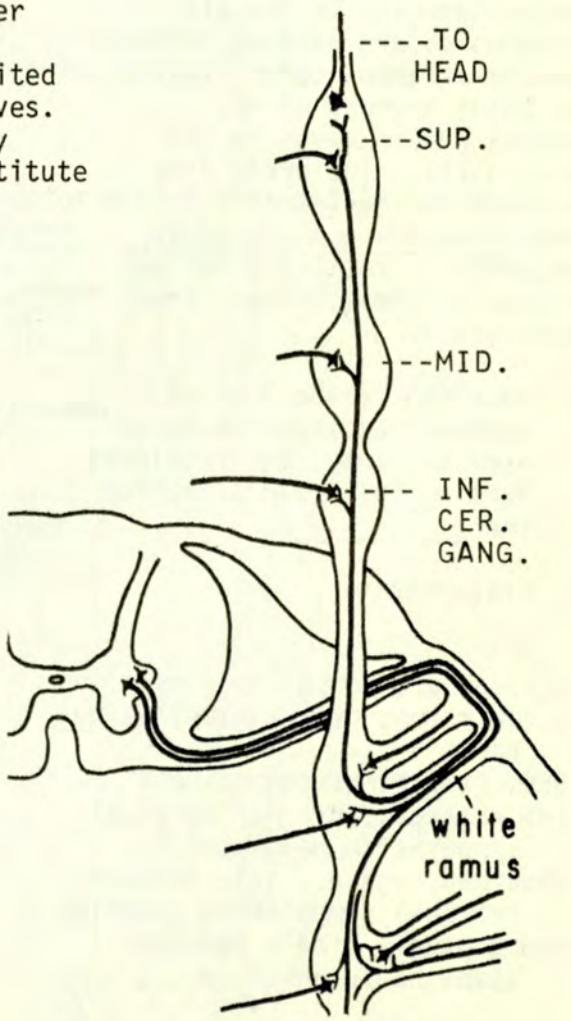
Q: Postganglionic neurons for the innervation of sweat glands, arrector pili muscles (hair), and vasoconstrictors of the face, have their cells of origin in the _____.

A: Superior cervical ganglion

222
The chain ganglia are connected to each other by the sympathetic trunk and to each spinal nerve by the gray rami. White rami are limited to the thoracic and upper lumbar spinal nerves. The chain ganglia in the neck region usually fuse into 3 ganglia on each side which constitute the superior, middle and inferior cervical ganglia.

Q: Would an injury to the nerves forming the brachial plexus interrupt the preganglionic neurons going to the superior cervical ganglion?_____
Would this involve the eye?_____

A: In some cases, it could



223
The preganglionic neurons for the innervation of the upper extremity and the head and neck are limited to the upper thoracic nerves. Preganglionic nerve fibers for the eye and orbit are usually limited to T1-3±1, however, there are occasional individual variations.

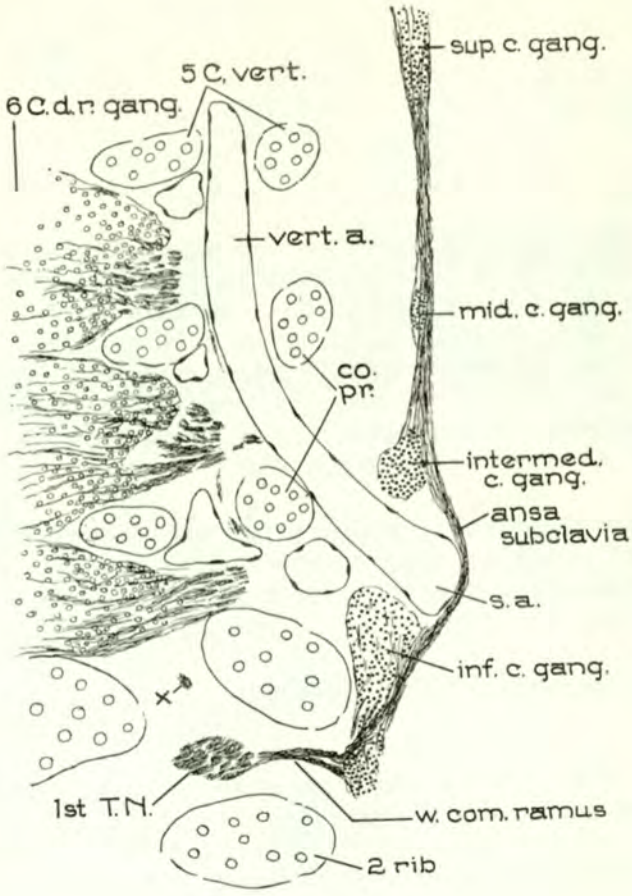
Q: Are preganglionic neurons found only in spinal nerves?_____

A: No, certain cranial nerves are involved.

224
Fibers of the sympathetic trunk pass behind and in front (ansa subclavia) of the subclavian artery.

Q: The ansa subclavia contains _____ neurons which synapse with _____ neurons in the superior cervical ganglion for the innervation of structures in the orbit. (Fig. from Pearson, 1960, Anat. Rec., 138)

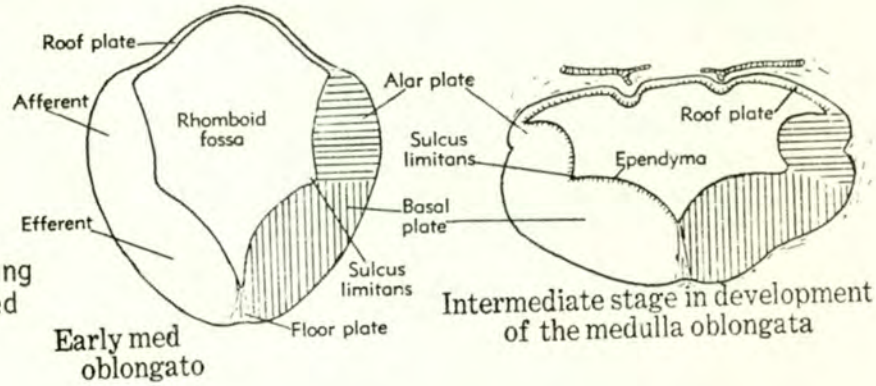
A: Preganglionic, postganglionic



225
The brain stem develops from that part of the neural tube which is just rostral to the spinal cord. Its lateral walls are divided into two longitudinal plates, alar and basal, by the sulcus limitans. As in the spinal cord, centers develop in the alar plate which are related to ingrowing afferent nerve fibers. The motor neurons of the cranial nerves delop in the basal plate. The brain stem contains the nuclei of the cranial nerves and the motor and sensory tracts and centers related to them. (Figs. from Rasmussen.)

Q: When the cerebellum and cerebral hemispheres have been cut away, the remaining part of the brain is called the _____.

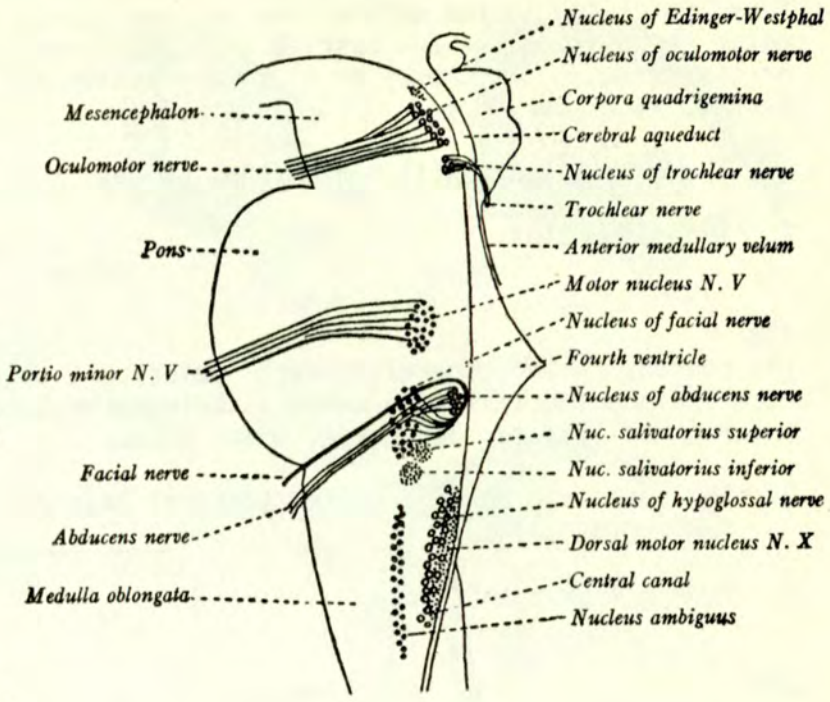
A: Brain stem



d.r..gang., dorsal root ganglion
g.com.ramus, gray communicating ramus
GRC, gray ramus communicans
inf.c.gang., inferior cervical sympathetic ganglion
intermed.c.gang., intermediate cervical sympathetic ganglion
mid.c.gang., middle cervical sympathetic ganglion
s.a., subclavian artery
sup.c.gang., superior cervical sympathetic ganglion
sym.gang., sympathetic chain ganglion
T.N., thoracic nerve
v.a. or vert. a., vertebral artery
v.r., ventral root
w.com.ra., white communicating ramus
WRC, white ramus communicans

226

In this diagram of a lateral view of the brain stem, note that the nucleus ambiguus, the facial nucleus, and the motor nucleus of V form an interrupted column of cells. These neurons supply muscles derived from mesoderm of the branchial arches. Muscle masses derived from the first (mandibular) branchial arch are supplied by the Vth nerve and those muscles derived from the second (hyoid) arch are innervated by the VIIth nerve. (Fig. from Ranson's Anatomy of the Nervous System, 1959, W. B. Saunders Co.)

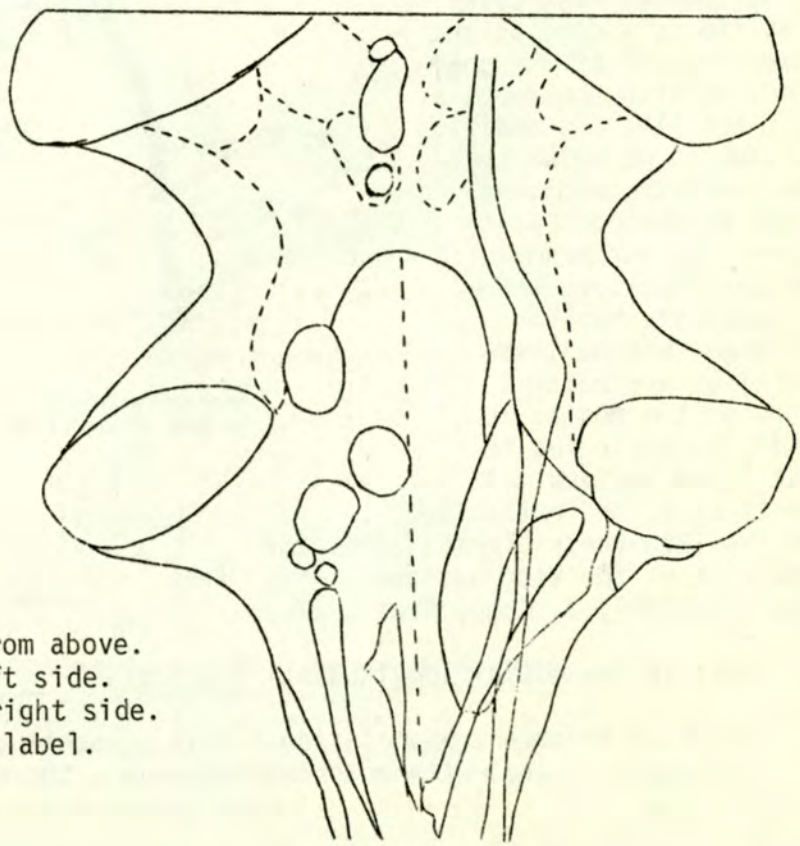


Q: The above nuclei (V, VII and X) are special visceral motor neurons and they innervate _____.

A: Muscles of mastication, muscles of facial expression (including the orbicularis oculi), muscles of the larynx, pharynx, etc.) (from nucleus ambiguus).

227

In a similar diagram, note that the somatic motor nuclei of the IIIrd, IVth,



Outline of brain stem from above.
Motor nuclei are on the left side.
Sensory nuclei are on the right side.
Identify nuclei, color and label.

VIth, and XIIth cranial nerves also form an interrupted column of cells. They lie closer to the wall of the central canal. They are called somatic motor neurons because the muscles they supply were thought to be of somite origin. (see f.114, Crosby et al., Correlative Anatomy of the Nervous System, MacMillan Co.)

Q: The hypoglossal (XII) nerve supplies the _____.

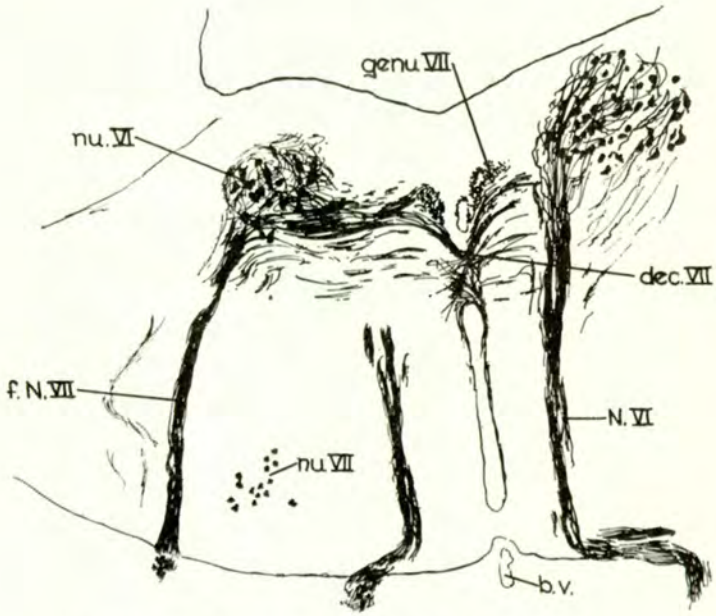
A: Tongue muscles

228
The neurons in the general visceral motor cell column in the brain stem include the following nuclei: Edinger-Westphal, superior and inferior salivatory, and dorsal motor of X.

Q: The autonomic nervous system (general visceral motor) is made up of all the _____ and _____ neurons.

A: Pre- and postganglionic

229
The abducens nerve is a bundle of about 6 to 7 thousand myelinated nerve fibers which arise from a cluster of neuroblasts which are part of the somatic motor column. They lie in the floor of the pons near the medial longitudinal fasciculus. Its fibers emerge at the lower border of the pons in line with the roots of XII and III. In addition to the large motor-type neurons, the abducens complex includes scattered smaller neurons which constitute the parabducens nucleus. Through this nucleus impulses are relayed through the medial longitudinal fasciculus to the IIIrd nucleus. A small swelling in the floor of the IVth ventricle indicates the position of the VIth nucleus. (Fig. from Pearson, 1947, J. Comp. Neur., 87.)



A cross section through the brain stem of a newborn at the level of the VI and VII nerves.

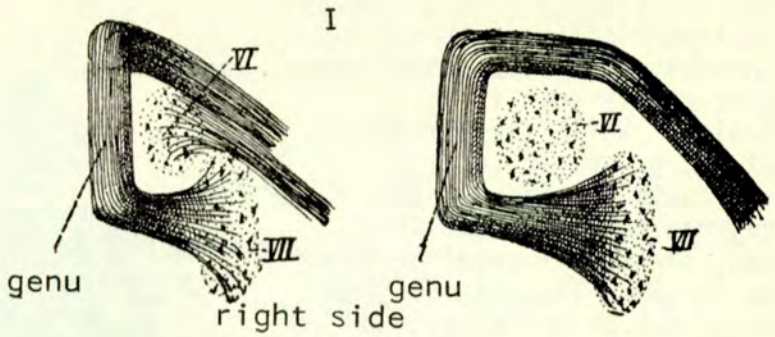
Q: What is the medial longitudinal fasciculus? _____

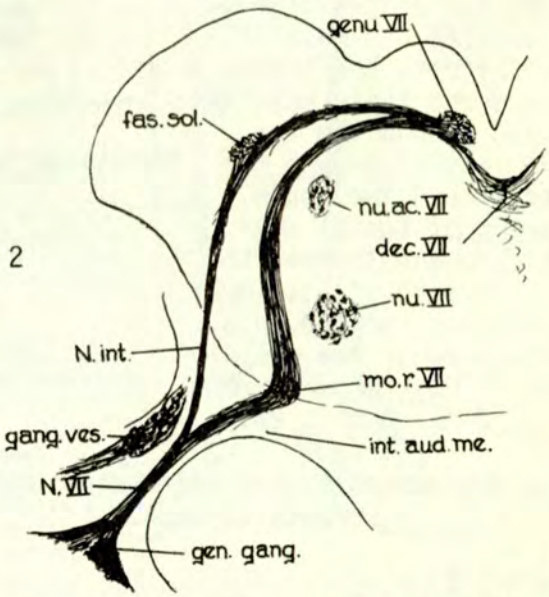
A: It is an important association bundle connecting centers like the vestibular nuclei with motor nuclei, e.g., the eye muscle nerve nuclei.

The special visceral motor fibers of VII arise from a group of neuroblasts beneath the floor of the IVth ventricle in the pons. The axons of the motor nucleus of VII grow rostral to loop around the nucleus of VI. Later the nuclei of these nerves migrate to new positions. The nucleus of VI shifts in a rostral direction, and the neuroblast of VII moves caudad and laterad. The root of the facial nerve bends around the abducent nucleus and thus the genu of the VIIth nerve is formed. This migration of neuroblasts to a new position has been regarded as chemotaxis, neurotropism, or neurobiotaxis. (Fig. 1, modified from Van Gehuchten; figs. 2 and 3 from Pearson, J. Comp. Neur. vols. 85 & 87; fig. 4 from Streeter, Anat. Rec. v. 2.)

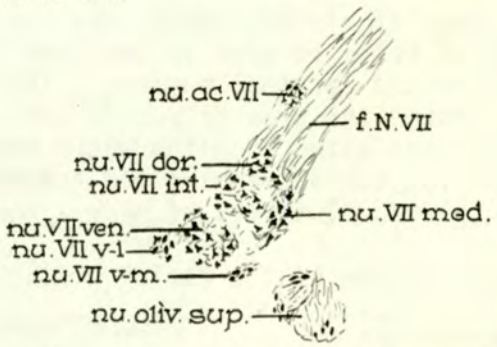
Q: What would be the clinical signs of an ependymona involving the region of the facial colliculus?

A: This lesion would involve the nucleus of VI and the genu of VII. There would be a flaccid paralysis of the muscles of facial expression with an inability to close the eye and a paralysis of the lateral rectus muscle (internal strabismus).

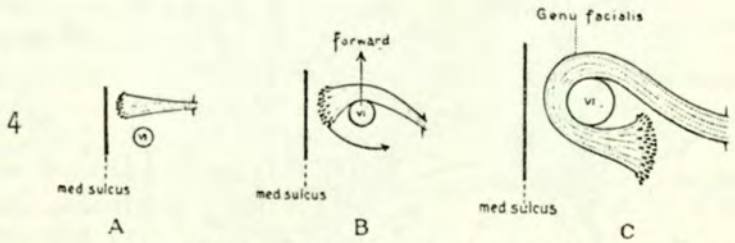




2 diagram drawn from cross sections of the brain stem of a human fetus

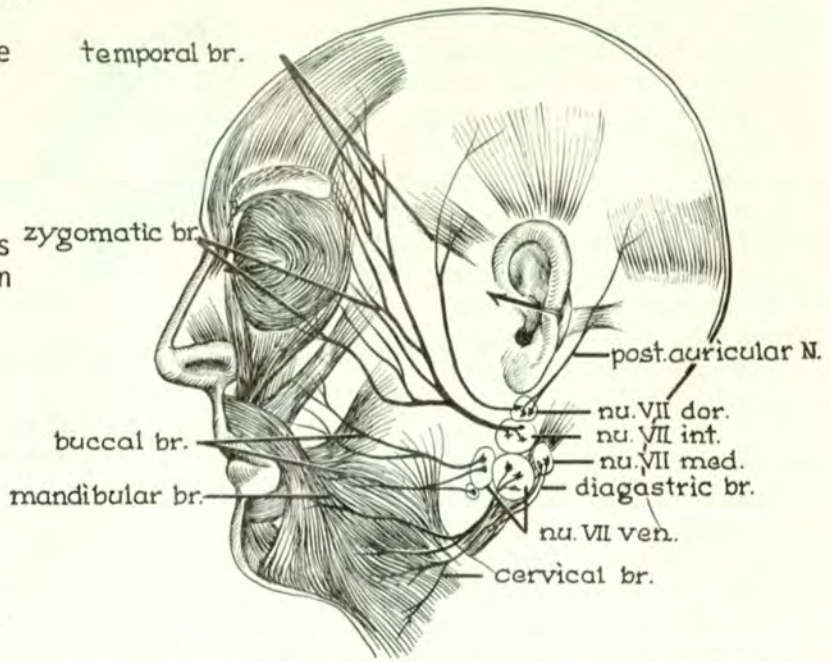


3 The special visceral motor nuclei of the facial nerve of a man



4 Diagram illustrating the development of the genu of the facial nerve in the human embryo. The drawings show the right facial nerve and its nucleus of origin, in three stages: the youngest, A, being the 10 mm. embryo, and the oldest, C, the new-born child. The relative position of the nucleus of the Abducens nerve is represented in outline. Its nerve trunk could not be shown, as the structures are represented as seen from above.

231
The cells which form the motor nucleus of VII are arranged into several groups which are more easily seen in fetal brains. While the position of the groups of cells in the facial nucleus in the cat are not identical with man, the experimental studies by Papez on the cat have been helpful. We can postulate that the dorsal group probably supplies the muscles around the ear, the intermediate group those muscles above and around the eye, and the ventral groups the muscles around the mouth. Each group of facial muscles is thought to have the cells of origin of its lower motor neurons located in a definite part of the facial nucleus. (Fig. from Pearson, 1946, J. Comp. Neur., 85.)



A diagram of the facial nucleus projected on the side of the head.

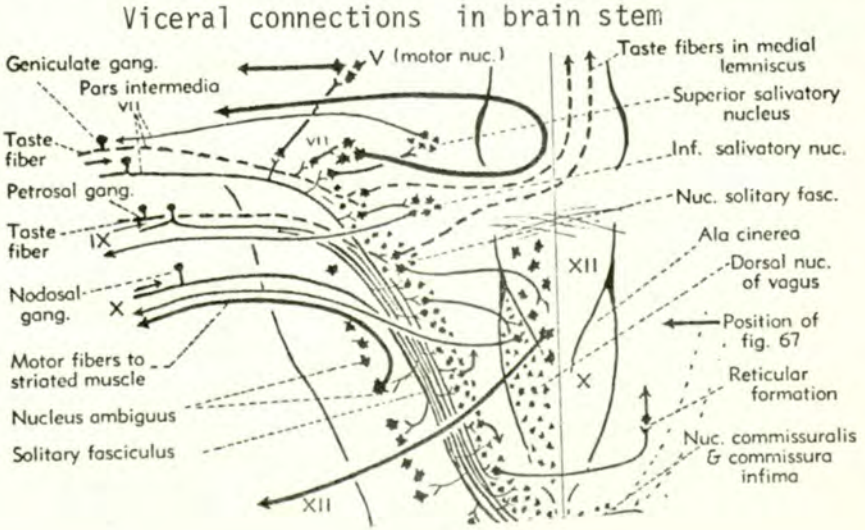
Q: The muscles of facial expression develop from mesoderm from the _____ branchial arch.

A: Hyoid (2nd)

232
A small group of visceral motor neurons have their cells of origin in a cluster of cells related to the superior salivatory nucleus and are sometimes called the lacrimal nucleus. Their axons join the motor root of VII, proceed through the greater superficial petrosal nerve and the Vidian nerve to the sphenopalatine ganglion where they synapse with postganglionic neurons supplying the lacrimal gland (secretory and vasodilators). (Fig. from Rasmussen, 1943, Outlines of Neuro- Anatomy)

Q: Would a lesion of the facial colliculus result in a dry eye? _____

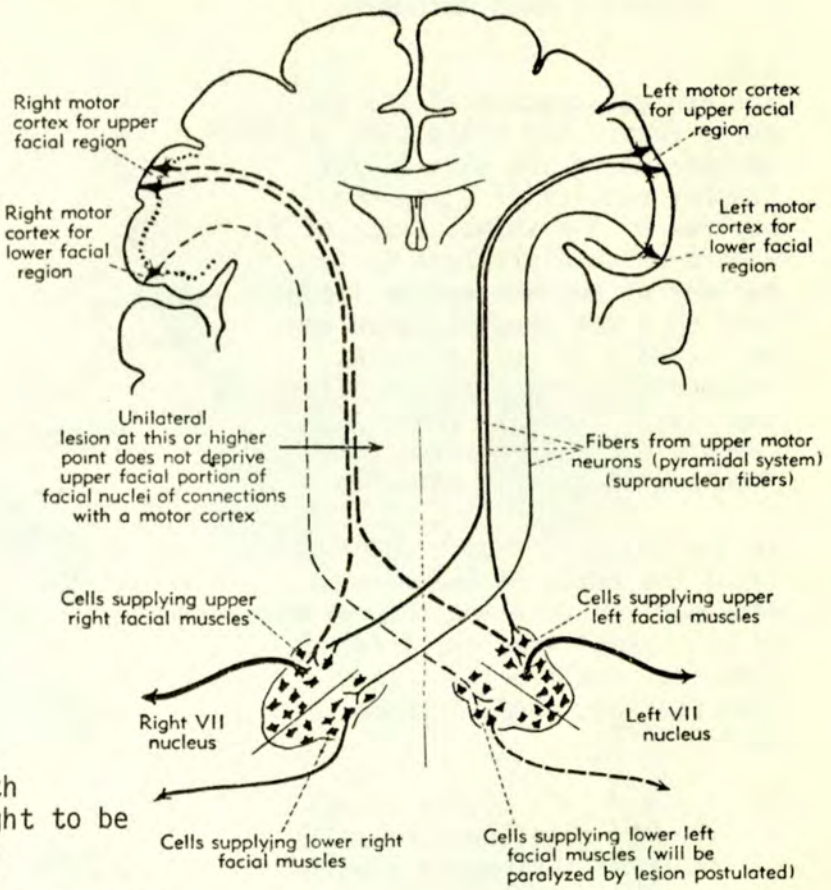
A: (probably) no



233

A lesion of the cortico-bulbar neurons may cause a paralysis of lower facial muscles without affecting the muscles around and above the eyes. That is, the muscles which close the eye may be unaffected while those muscles around the mouth may show distinct paralysis. The lower facial muscles may receive an upper motor neuron innervation only from the opposite side, while the upper facial muscles may be under the control of both cerebral hemispheres. Also, there is a partial crossing of the fibers of the facial nerve in the brain stem. That is, the upper facial muscles may receive lower motor neurons from both sides of the brain stem, while the lower facial muscles may have only a unilateral innervation. The structural differentiation of the mimetic muscles and the branches of the facial nerve are relatively complete at birth and postnatal changes are thought to be slight. (Fig. from Rasmussen.)

Diagram to illustrate one reason for certain muscles not showing paralysis in unilateral supranuclear (upper motor neuron) lesions, while others do, using the facial nerve as an example

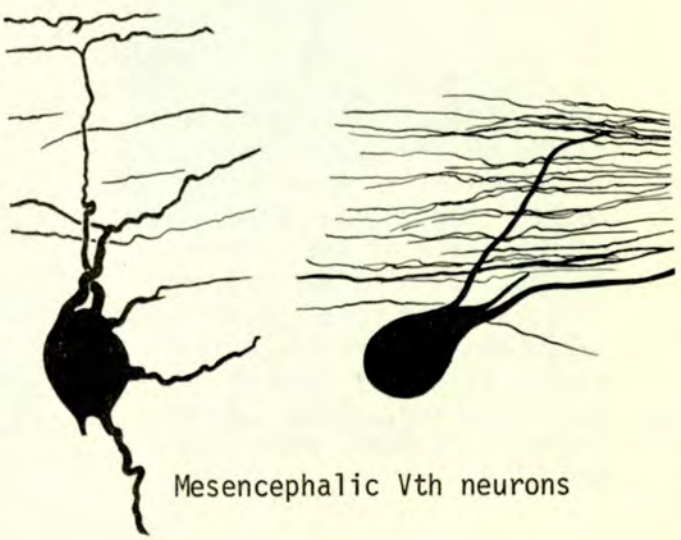


Q: Give two tests for the function of the motor nucleus of VII. _____, _____.

A: Close the eye, show the teeth

234

The development of the trigeminal (V) nerve is closely related to the development of the first branchial arch. From ganglion cells in its semilunar ganglion afferent fibers grow into the brain stem at the level of the pontine flexure. The mesencephalic nucleus of V is made up of large ganglion-like cells and are thought to be sensory. They are proprioceptive neurons which join the motor root of V and are distributed chiefly to the muscles of mastication. General somatic afferent fibers from the cornea and the skin of the face have their cells of origin in the semilunar ganglion. (fig. from Pearson)



Mesencephalic Vth neurons

Q: General visceral motor neurons innervate _____ and special visceral motor neurons innervate _____.

A: Smooth muscle, glands, heart muscle, etc.: muscles developed from branchial arch mesoderm.

235

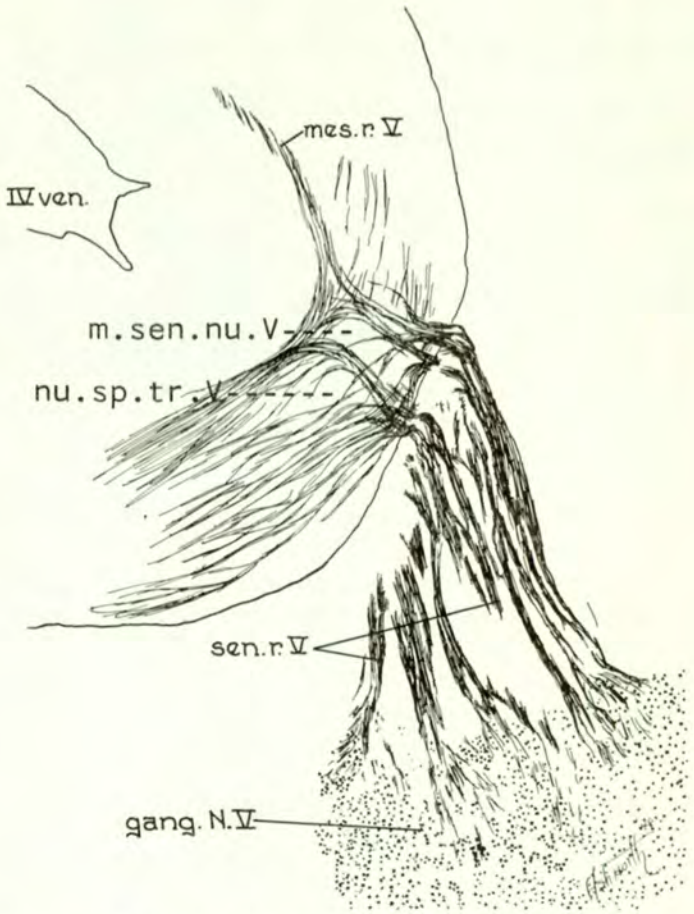
The central process of the Vth nerve enters the brain stem and terminates in the main (chief) sensory nucleus of V and the nucleus of the spinal tract of V. Fibers which distribute to the nucleus of the descending (spinal) root of V are thought to be concerned with stimuli of pain, temperature, and gross tactile impulses. The main (chief) sensory nucleus receives only impulses of tactile stimuli.

In the adjacent figure color and label the areas of the main sensory nucleus of V and the nucleus of the spinal tract of V (descending root fibers). (Fig. from Pearson, 1949, J. Comp. Neur., 90.)

Q: Are the cell bodies of all sensory ganglion-like cells found in peripheral ganglia?

_____

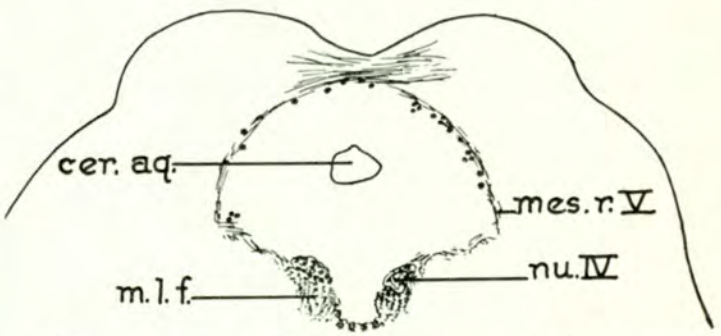
A: No. Exceptions are mesencephalic Vth cells and ganglion cells of retina.



A sagittal section through the medulla oblongata and pons

236

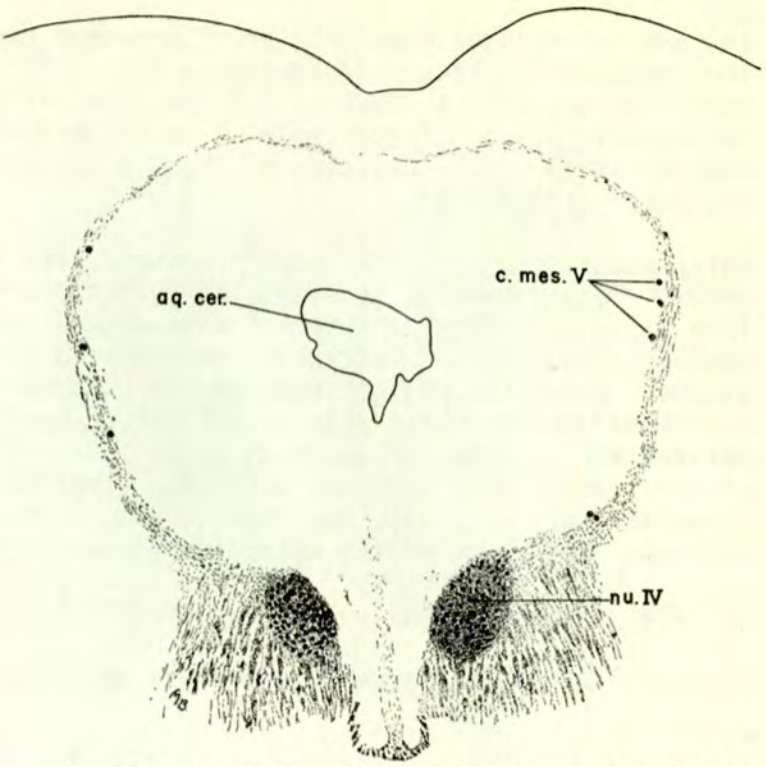
The trochlear nerve is a bundle of about 3,400 myelinated fibers which grows from as many neuroblasts in the trochlear nucleus. This nucleus is embedded in the medial longitudinal fasciculus at the level of the inferior colliculus. Its rostral end lies in close relation with the IIIrd nucleus and its more caudal cells may form an isolate group. (Figs. from Pearson, J. Comp. Neur., 78 and 91.)



Transverse section through the dorsal part of the mesencephalon

Q: The turning of the eye from the median plane is abduction. The abductor muscle (lateral rectus) is supplied by the _____ nerve.

A: Abducens (Latin, to lead away)

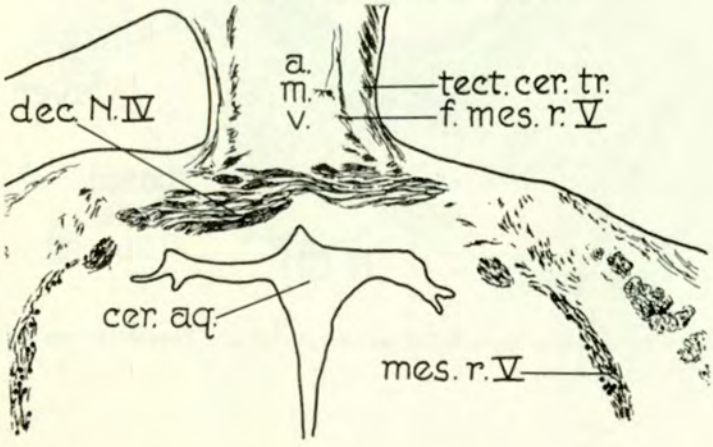


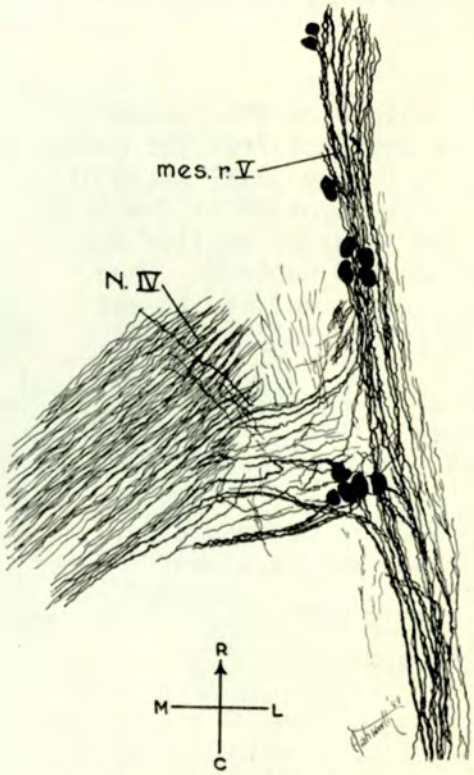
A transverse section through the mesencephalon of a 5-month-old fetus

237
Cells of the mesencephalic Vth type occur along the course of the trochlear nerve within the brain and occasional cells of this type occur within the trochlear nucleus. The axons of these cells join the trochlear nerve and are thought to carry proprioceptive impulses. The fibers of the IVth nerve cross in the anterior medullary velum just below the inferior colliculus. It seems likely that the trochlear nucleus has migrated along the ventricle to be nearer the oculomotor nucleus to which it is functionally related. The trochlear root is thought to follow the path of this migration. (Fig. from Pearson, 1949, J. Comp. Neur., 90.)

Q: What is unusual about the trochlear nerve? _____

A: It is the only motor nerve to rise from the dorsal surface of the brain stem. Also, it is completely crossed.





the mesencephalic root of V and the trochlear nerve

238
In some vertebrates even more primitive than the sharks, e.g., lampreys, the trochlear nucleus is formed by a cluster of neuroblasts located dorsal to the sulcus limitans and the decussation of the IVth nerve may be incomplete. The forces leading to the migration of these neurons and the story of the crossing of these and other cranial nerve fibers are poorly understood.

While anomalies of the extraocular muscles are rare, they occasionally occur. Some anomalies are variations in the origin or the insertion. They may result from an abnormal cleavage of the common premuscular mesodermal masses. A muscle may be replaced by a band of connective tissue. When both oblique muscles are abnormally developed, a condition may result in which there is a voluntary propulsion of the eye. The patient may be able to luxate an eyeball at will (Fink, 1951). Vestiges of a retractor muscle in man have been reported, but they are rare. A congenital ocular palsy may result from an error in development in the nucleus, the course of the nerve itself, or in the muscle.

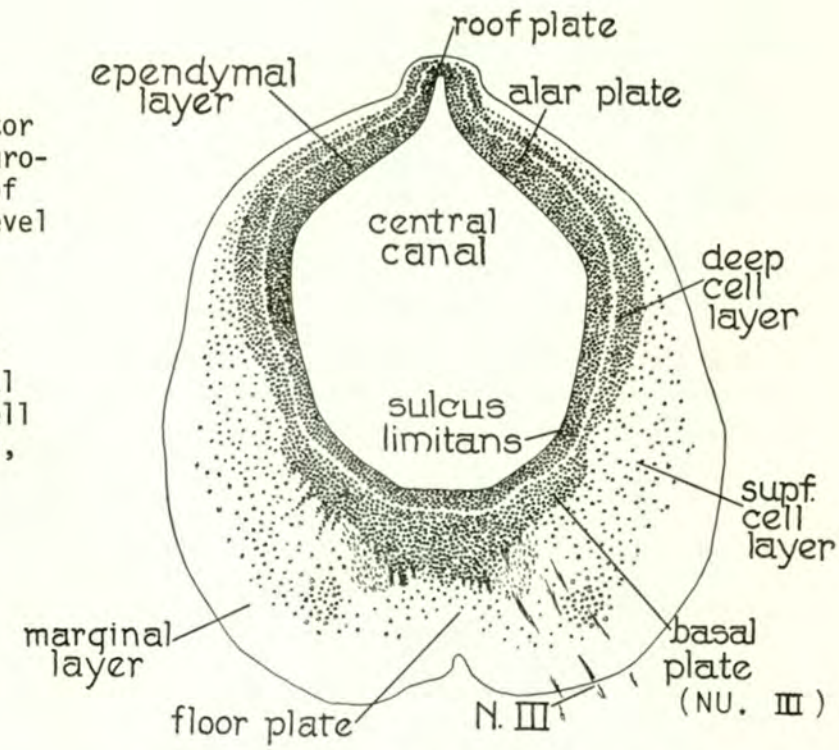
Q: What animals normally have a retractor bulbi muscle? _____

A: Large herbivora, some reptiles and amphibia.

239
The nucleus of the oculomotor nerve develops from the neuroblasts in the basal plate of the mesencephalon at the level of the superior colliculus and the red nucleus. They are closely related to the medial longitudinal fasciculus. They form the rostral end of the somatic motor cell column. (Fig. from Pearson, 1949, J. Comp. Neur., 91.)

Q: Somatic motor neurons as a rule are under _____ control.

A: Voluntary

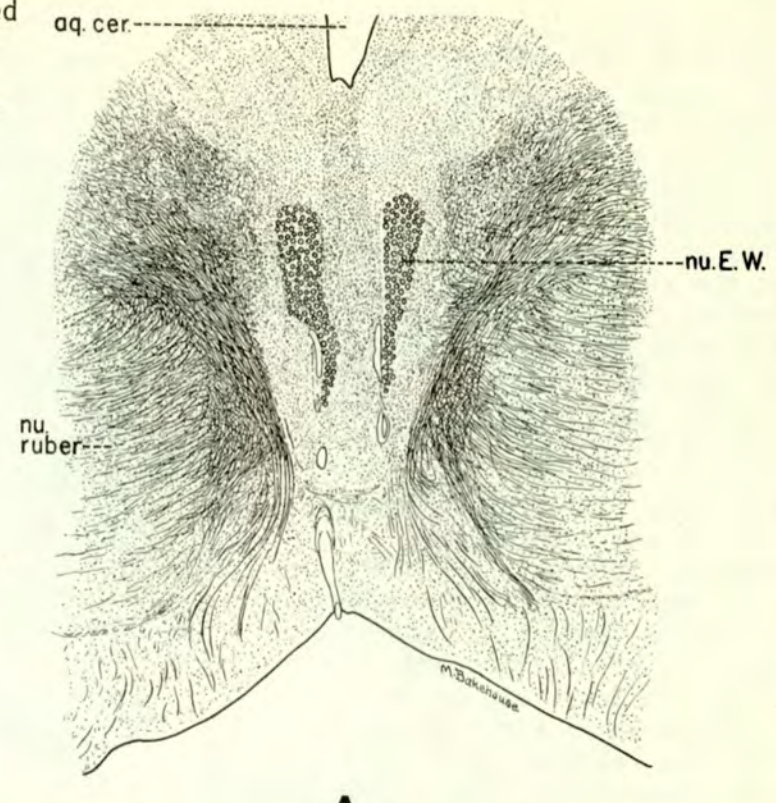


Transverse section through the mesencephalon of a 7-week (20 mm CR) human embryo

The oculomotor nucleus is formed by several clusters of medium-sized multipolar neurons located just rostral to the nucleus of IV. The III, IV and VI nerves are large when compared with the size of the muscle they supply. The III nerve contains about 24,000 fibers which would indicate that there would be at least this number of neuroblasts in the nucleus of III. These somatic motor cells of III (figs. A-D) are grouped into a large lateral column on each side which is subdivided into dorsal (nucleus lateralis, pars dorsalis) and ventral (nucleus lateralis, pars ventralis) groups. In cross sections the lateral nuclei of the two sides form a V-shaped mass partly closed at the bottom by fibers crossing the midline. Axons from neuroblasts in the caudal two-thirds of the nucleus are thought to be crossed and uncrossed.

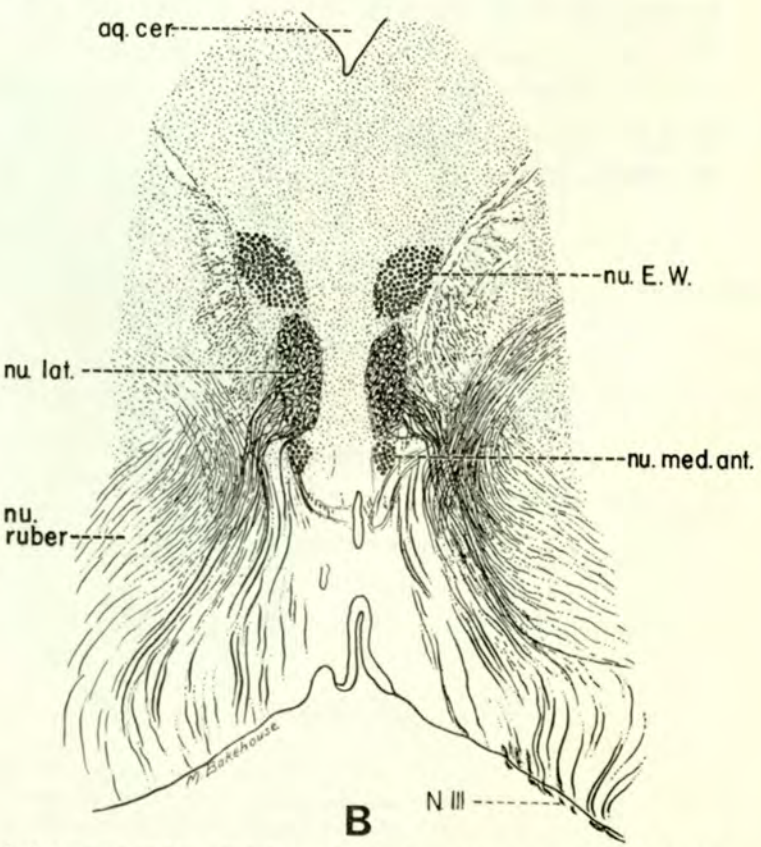
Q: Each eye muscle nerve nucleus is connected to the other eye muscle nerve nuclei and the vestibular nuclei by the _____.

A: Medial longitudinal fasciculus (f.l.m.)



A

A transverse section through the mesencephalon of a 5-month-old human fetus at the rostral end of the oculomotor nucleus

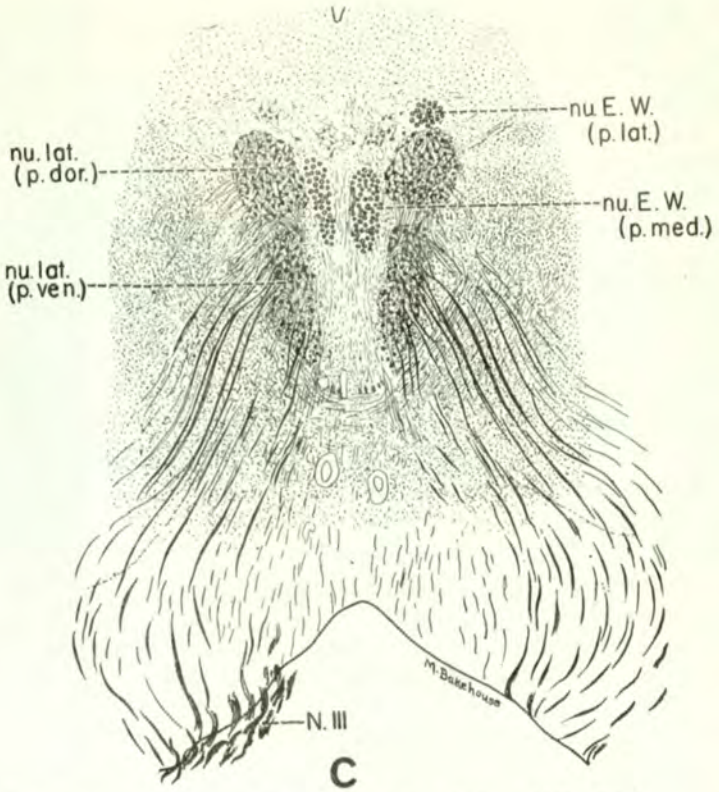


B

A transverse section slightly caudal to the middle of the rostral third

241

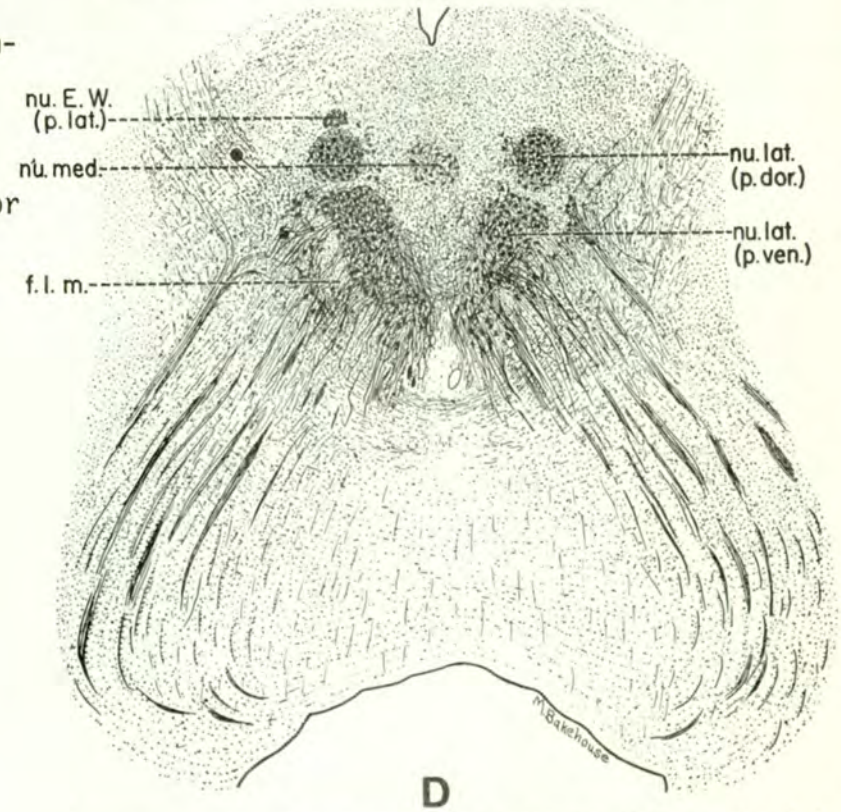
In the middle third of the III nerve cell column there is a group of medium-sized somatic motor cells in and near the mid-plane region. These form the nucleus medianus (nu. med., fig. D). They are often referred to as the central nucleus of Perlia. The axons of these and related cells are thought to innervate the medial rectus muscles and may be concerned with convergence. Discrete lesions in the nucleus of III are rare. Research in localization has been of more academic interest than clinical importance. The evidence collected from animal experiments is conflicting and difficult to relate to the IIIrd nerve in man. (Figs. A-D from Pearson, 1944, J. Comp. Neur., 80.)



A transverse section through the middle of the middle third

Q: The IIIrd nerve innervates all of the extrinsic eye muscles except the _____ and _____.

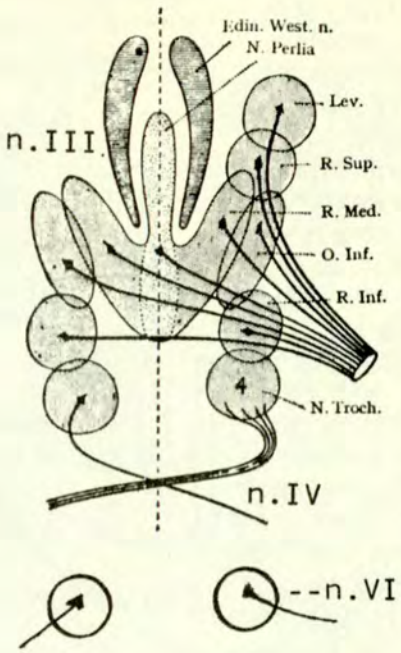
A: Lateral rectus, superior oblique



A transverse section of the mesencephalon at the level of the junction of the middle and the caudal thirds of the oculomotor nucleus. Note that a process of a cell of the mesencephalic V type is directed toward the oculomotor nucleus

242

Each eye muscle is probably innervated by a well-defined group of neuroblasts. A number of investigators have tried to localize these cell groups according to the muscles innervated in both dorso-ventral and craniocaudal directions. In a cranial to caudal arrangement, these muscles are represented thus: levator palpebrae, superior rectus, inferior oblique and inferior rectus. (Fig. modified from Brouwer.)

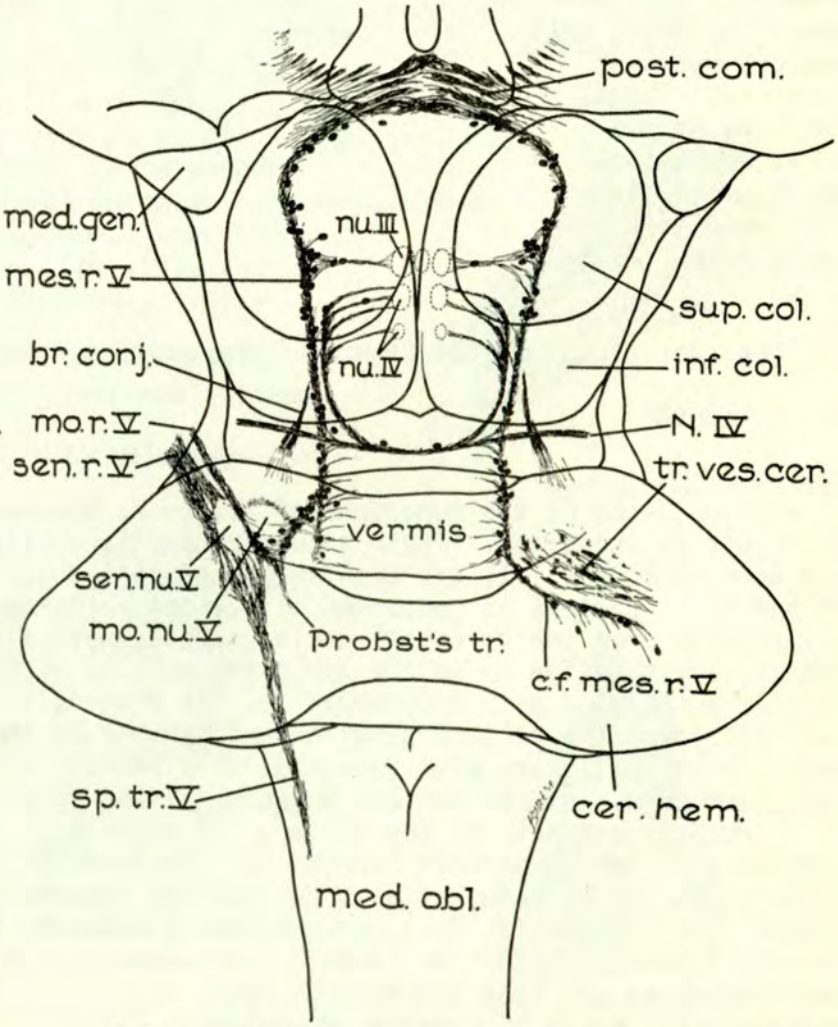


Q: Cells of the mesencephalic Vth type are believed to be concerned with stretch receptors in the _____ and _____ muscles.

A: Extrinsic eye, masticatory

243

It is thought that the epilemmal grape-like endings in the extraocular muscles are proprioceptors. The cells of origin of these sensory fibers are not concentrated in any one locality. They are probably the cells of the mesencephalic Vth type which are located along the central and peripheral course of the IIIrd nerve, within the oculomotor nucleus itself, and among the cells of the mesencephalic nucleus (V) which sends processes through the oculomotor nucleus and nerve. In addition, branches of the ophthalmic division of V communicate with the III, IV and VI cranial nerves. The route taken by proprioceptive fibers from the lateral rectus muscle are more difficult to explain. (Figs. from Pearson, 1949, J. Comp. Neur., 91.)

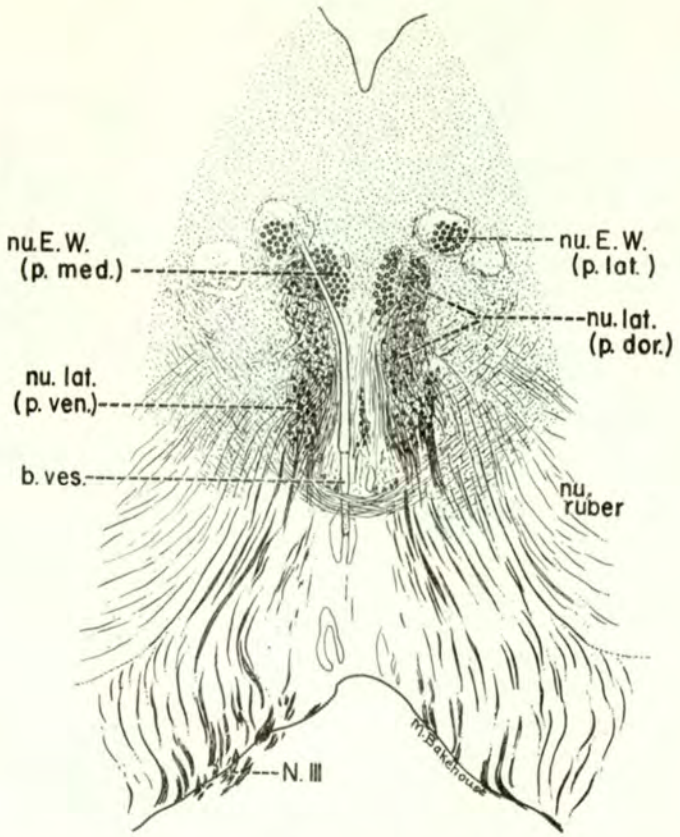


A diagram of the dorsal view of the brain stem of a 3.5-month human

Q: The pupil will constrict with an increase in light intensity and in conjunction with _____ in near vision.

A: Accommodation

244
The smaller general visceral motor neurons of the IIIrd nerve have their cells of origin in the Edinger-Westphal nucleus and are located in the rostral portion of this complex. They are preganglionic neurons and they terminate in the ciliary and episcleral ganglia. When followed caudad in serial sections, this group splits into a larger dorsal group, the E. W. nucleus proper, and a smaller ventral group (nu. med. ant) nucleus medianus anterior. Caudal portions of the E. W. nucleus may be formed by isolated clusters of cells (figs. A, B, C).



A transverse section near the rostral end of the middle third

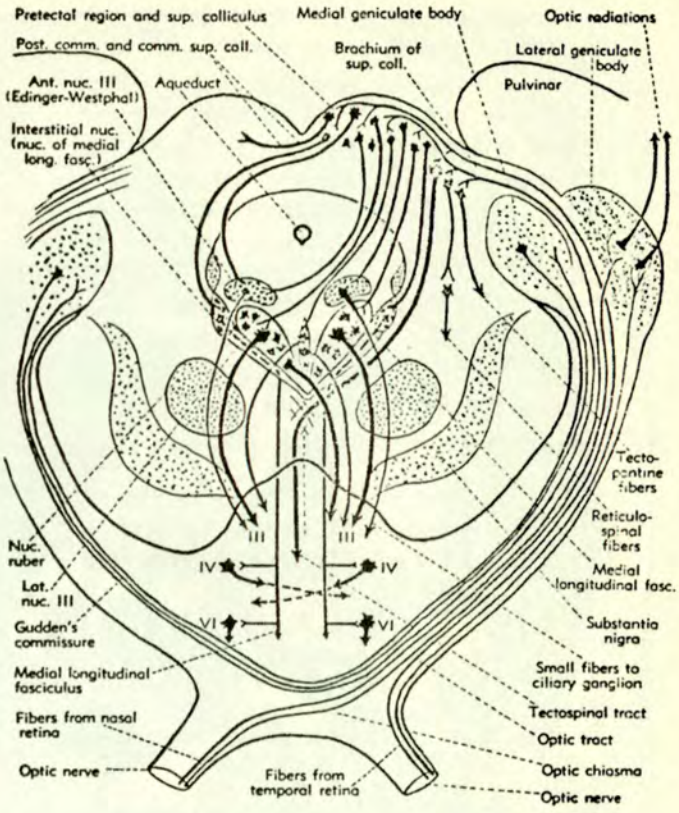
Q: The constrictor muscle fibers of the pupil develop from _____.

A: Ectoderm

245
Conclusive proof of the functions of the E. W. nucleus has been difficult to establish. Their axons are small, difficult to stain and hard to follow. It has been suggested that the rostral portion of the E. W. nucleus is concerned with light reflexes and receives stimulation from the pretectal nuclei. Postganglionic neurons from the ciliary ganglion go to the sphincter muscles of the pupil. When this is associated with accommodation, the preganglionic neurons are said to bypass the ciliary ganglion and synapse in the episcleral ganglion on the sclera with postganglionic neurons which go to the sphincter muscle of the pupil. Neurons arising more caudally in the E. W. nuclei terminate in the ciliary and episcleral ganglia and synapse with postganglionic neurons for the innervation of the ciliary muscle. (Crosby et al., Correlative Anatomy of the Nervous System, 1962, MacMillan Co.) (see Figs. Rasmussen, 1945, Principal Nervous Pathways, MacMillan Co.)
Read Crosby et al, 1962 and Peele, 1961, Neuroanatomic Basis of Clinical Neurology.

Q: Destruction of the pretectal nuclei, or the rostral portions of the Edinger-Westphal nucleus would interrupt the _____ reflex but would not interfere with _____.

A: Light, accommodation.
This is called the Argyll Robertson pupil. (A.R.P. - accommodation reflex is present: - pupillary reflex is absent.)
Fig. from Rasmussen's Outlines of Neuro- Anatomy, 1943.



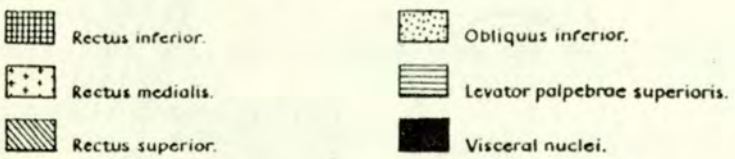
Optic tract and reflex connections in midbrain.

246
The adjacent diagram from Warwick is based on his experiments on primates. There appears to be a dorso-ventral as well as a rostro-caudal arrangement of the oculomotor neurons. (Read Warwick, J. Comp. Neur., 98, 1953, and Walsh and Hoyt, Clin. Neuro-Ophthal., 1969.)

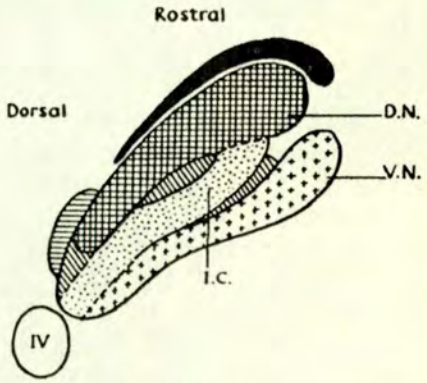
Q: The visceral motor neurons in the cranial nerves form the _____nervous system.

A: Parasympathetic (part of autonomic nervous system)

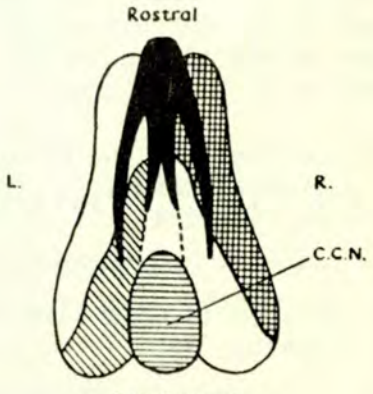
Note that the motor cells of the levator palprebralis superioris are located caudal and dorsal to the midline. The superior rectus muscle may be innervated by motor cells located in the contralateral nucleus.



Diagrams showing the representation of the right extra-ocular muscles in the oculomotor nucleus of the monkey. D.N. = dorsal nucleus, V.N. = ventral nucleus, C.C.N. = caudal central nucleus, I.C. = intermediate column, *IV* = trochlear nucleus.



Right lateral aspect.



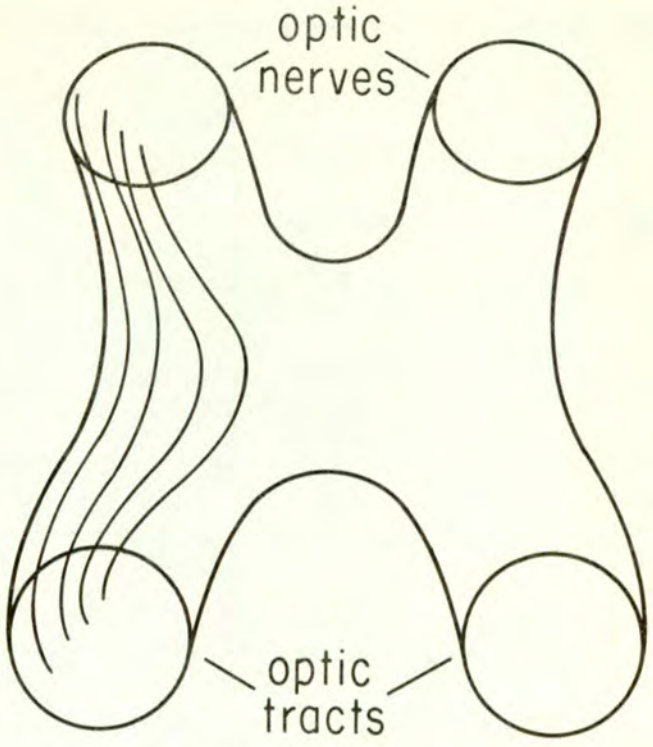
Dorsal aspect.

Read Gray's Anatomy, Ed. by Warwick and Williams, 1973.

247
The majority of fibers in the optic nerves have their cells of origin in the ganglion cell layer of the retina. Whey they reach the chiasma the fibers from the temporal half of the retina, including the temporal half of the macula, pass into the optic tract of the same side. There they join the crossed nasal fibers from the optic nerve on the other side. (Figs. modified from Hoyt, 1964, Neuro-Ophthal. Symp., J. L. Smith, Ed.)

Q: Fibers in the optic nerve which do not arise in the ganglion cell layer are _____.

A: Efferent (origin in the brain



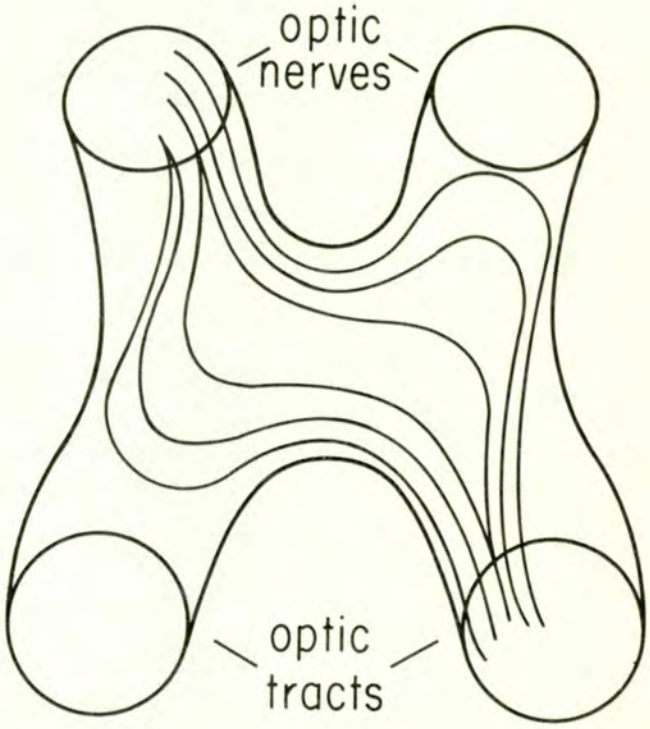
OPTIC CHIASMA

248
The fibers of the nasal half of the retina, including the nasal half of the macula, cross the mid-plane and continue in the optic tract on the opposite side. Some of the crossed fibers form loops, perhaps a centimeter, which extend for a short distance into the optic tract of the same side before crossing in the chiasma. Other fibers form loops which extend toward the optic nerve on the other side before they reach the optic tract. The fiber loops from the macular region are more flattened and occupy approximately two-thirds of the central region of the chiasma.

Q: Is the optic nerve a typical cranial nerve?_____ Will it regenerate if it is cut?

_____

A: No, it is more like a brain tract. No.



OPTIC CHIASMA

249

The position of the eyes in portraits of a famous Indian princess would suggest that she had an imbalance in her ocular muscles. It is assumed that her right eye is in the primary position (looking straight forward) and that her left eye is turned abnormally toward the temporal side (an external strabismus). This is shown both in the oil painting in the National Portrait Gallery in Washington and the line engraving in the British Museum. (Fig. from an engraving by Simon Van de Passe, courtesy of Trustees of British Museum.)

Q: This condition could be explained on the basis of an underaction (weakness or undevelopment) of the _____ muscle or an overaction (neurogenic or myogenic in origin) of the _____ muscle on the left side. Name this Indian princess._____

A: Medial rectus, lateral rectus, Pocahontas

250

Fink is of the opinion that muscular anomalies occur more frequently than is usually recognized. Whitnall states that these anomalies are by no means rare and that the number recorded in the literature may be misleading. In the dissecting room variation in ocular muscles are difficult to identify. and in life the anomaly may be compensated by the action of other muscles and often is not recognized. It is interesting to examine eye muscle anomalies in the dissection room, but it is more important to recognize them before the time of an operation and anticipate the situation.

Q: Many cases of congenital squint may be explained on the basis of _____.

A: Anomalous muscles

251

According to Fink, muscle anomalies may be classified as:

a) muscle absence.
b) abnormal development (including rudimentary muscle formations)
c) congenital palsies
d) abnormal development of adjacent fascia

Q: Anomalies of the eye muscles can be explained on the basis of errors in development resulting from the abnormal cleavage of the _____.

A: Premuscular mesodermal condensations

On this page and the next page write examples of the kind of new material which you consider appropriate for this manual. Include illustrations and questions with answers. Send a copy of this to A. A. Pearson. If your material is selected for inclusion in the next edition of this manual, a free copy of the new edition will be sent to you.

INDEX OF PART I

62. Vascular lamina
63. Suprachoroid lamina
64. Vascular lamina
65. Choriocapillary lamina
66. Bruch's basal
67. Central artery of the retina
68. Cloquet's
69. Posterior (or short) ciliary arteries
70. Long ciliary arteries
71. Anterior ciliary arteries
72. Central artery of the retina
73. 180
74. 68
75. Nasolacrimal ducts
76. Sac
77. Puncta lacrimalia
78. Maxillary process
79. Paraxial mesoderm
80. Cornification of the cells
81. Secretions from sebaceous glands
82. Ectoderm
83. Globe
84. Lids
85. Conjunctival sac (fornix)
86. Ectoderm
87. Tears
88. Tarsal
89. Outside
90. 2
91. Choroid (embryonic) fissure
92. Pigmented

The photographs of human embryos were obtained through the courtesy of Dr. Hideo Nishimura, Professor of Anatomy, Faculty of Medicine, Kyoto University, Kyoto, Japan. The Roman numerals refer to developmental stages (developmental horizons of Streeter).

Other self-instructional manuals on ear and heart development are available from the same author.

ADDENDUM

Review Questions on Part I: Normal Development

In the development of the eye, only ___1___ and ___2___ are of importance. The latter of which is further subdivided into neural and surface ectoderm. The central nervous system is derived from folds of ___3___ while the somites are formed from ___4___. The ___5___ are the first signs of the developing eye and occur as thickenings of the wall of the forebrain. The optic pits form as shallow depressions in the ___6___; further invagination forms the ___7___. Lacrimal glands, ducts, the epithelium of the conjunctiva, and cilla are all formed from ___8___. The surface ectoderm over the developing retina thickens forming the ___9___. Invagination of the optic vesicle forms the ___10___. As the optic vesicle invaginates a groove is formed called the ___11___. The space between the lens vesicle and the optic cup is the ___12___. Five structures that are formed from mesoderm are: ___13___, ___14___, ___15___, ___16___ and ___17___. The ___18___ muscles are derived from ectoderm. The hyaloid artery gains entrance to the optic stalk through the ___19___. With the closure of the embryonic fissure, the rim of the optic cup surrounds the ___20___ opening. The deep columnar cells of the lens vesicle form the ___21___, while the more superficial cuboidal cells form the ___22___. The ___23___ are responsible for the ultimate shape of the lens and the sutures that develop. The optic vesicle is connected to the developing brain by the ___24___. When the nuclei have separated into two definitive nuclear layers they are referred to as the ___25___ and ___26___ layers. The ___27___ cells of the optic pathway are the first to differentiate and the ___28___ are among the last. As the fibers of the ganglion cells enter the optic stalk and grow toward the brain they form the ___29___. The primary vitreous is formed from ___30___ and ___31___ (germ layers), but the secondary vitreous arises from cells of the ___32___. The fovea develops in the center of the future ___33___ and contains ___34___ cells but no ___35___. The outer limiting membrane of the retina lies between the ___36___ and the ___37___. The outer cells of the optic stalk form the ___38___ cells of the optic nerve. The dura of the optic stalk continues over the surface of the eye ball as the ___39___, which, at the very front, is continuous with the ___40___. The anterior chamber of the eye lies between the ___41___ and ___42___. The marginal sinus is formed by the incomplete fusion of the ___43___ and the ___44___ layers of the retina. The blood vessel formed at the margin of the cornea will become the ___45___. The suspensory ligament extends from the ___46___ to the lens. The three chambers of the eye are the ___47___ and ___48___ chambers and the ___49___ cavity. From anterior to posterior the layers of the developing cornea are: ___50___, ___51___, ___52___, ___53___ and ___54___. The cribiform plate is the area of the ___55___ perforated by fibers of the ___56___ nerve. Between the pars optica and the pars plana (ciliary ring) is a line called the ___57___. Both the primitive dorsal and ventral ophthalmic arteries are branches of the ___58___ artery. The ciliary ring, the ciliary crown (and its process) and the ciliary muscle form the ___59___. The circular vessel found at the rim of the optic cup is called the ___60___ vessel. At its forward extremity the

hyaloid artery forms a tunic for the lens called ___61___; this later atrophies. The long and short posterior ciliary arteries are branches of the definitive ophthalmic artery. The latter supply the ___62___ of the choroid. When the choroid has reached its adult configuration, it is characterized by the following layers from the outside to the inside: ___63___, ___64___, ___65___ and ___66___ membrane. The hyaloid artery is renamed ___67___ when the portion inside the vitreous atrophies, leaving in its place ___68___ canal. The main arteries of the adult eye consist of: ___69___, ___70___ and the ___71___ and ___72___. The optic axis in the early embryo is about ___73___ degrees, but it decreases to about ___74___ degrees in the adult. Ectodermal cells buried by the growing paraxial mesoderm will form the ___75___ and ___76___. The openings of the upper and lower canaliculi are known as the ___77___. Growth of the ___78___ produces the lower lid fold; the upper lid fold is formed from ___79___. The eyelid adhesions begin to break down for several reasons, two of which are ___80___ and ___81___. The conjunctival epithelium is derived from ___82___; it covers the anterior surface of the ___83___ and the inner surface of the ___84___. Buds appearing on the upper lateral portion of the ___85___ will form the lacrimal gland which is also derived from the ___86___. In the newborn infant, crying does not produce ___87___. A meibomian gland is the same as a ___88___ gland. The secondary lens fibers form a layer ___89___ (outside, inside) the primary lens fibers. There are ___90___ (number) Y-shaped sutures. The ___91___ permits the entrance of the hyaloid artery and vein into the optic stalk. The outside layer of the optic cup becomes the ___92___ layer of the retina.

ANSWERS

1. Mesoderm
2. Ectoderm
3. Neural ectoderm
4. Mesoderm
5. Optic primordia
6. Optic primordia
7. Optic vesicles
8. Surface ectoderm
9. Lens placode
10. Optic cup
11. Choroid (embryonic) fissure
12. Vitreous cavity
13. Corneal Stroma
14. Sclera
15. Choroid
16. Endothelium of the anterior chamber
17. Orbital and ciliary muscles
18. Iris
19. Choroid (embryonic) fissure
20. Pupillary
21. Primary lens fibers
22. Secondary lens fibers
23. Secondary lens fibers
24. Optic stalk
25. Inner
26. Outer neuroblastic
27. Ganglion
28. Receptor cells
29. Optic nerve
30. Ectoderm
31. Mesoderm
32. Retina
33. Macula
34. Cone
35. Rods
36. Layer of rods and cones
37. Outer nuclear layer
38. Glial
39. Sclera
40. Cornea
41. Pupillary membrane
42. Endothelium of cornea
43. Nervous
44. Pigmented
45. Canal of Schlemm
46. Ciliary body
47. Anterior
48. Posterior
49. Vitreous
50. Surface epithelium
51. Bowman's membrane
52. Stroma
53. Descemet's membrane
54. Corneal endothelium
55. Sclera
56. Optic
57. Ora serrata
58. Internal carotid
59. Ciliary body
60. Annular
61. Tunica vasculosa lentis

PART II

ABNORMALITIES OF THE EYE

I. Introduction

A. Definition of anomaly, congenital, variation, and normal

It is generally accepted that no two individuals or their organs are exactly alike. Within flexible boundaries we recognize individual characteristics as normal variations. It is difficult to separate the normal from the variations and the latter, in turn, from the anomalies. The effect of structure on function often provides aid in classification.

What is considered normal, i.e., theoretical normal, can only be an average, or at best, a mean between two extremes. This in itself may be rare. A variation usually signifies a slight departure from normal, often too minor to interfere with function. To be classified as an abnormality or anomaly a condition must be so different from the average that it is more than a variation and may interfere with the performance of the organ.

The manner in which these alterations occur is of further importance. If a variation in structure does not resemble any stage in normal development it is called an aberration. When development has proceeded along normal lines and has been slowed or halted at some point, it is termed an arrest.

Developmental defects, especially those of the lens, may occur at any time in life where new cells or tissues are constantly being formed. Included among these are congenital anomalies, which are present at birth and are due to abnormality in the intrauterine developmental processes.

For the sake of brevity this manual will cover mainly those genetic and developmental anomalies which are present at birth. Abnormalities which become manifest later in life will with few exceptions not be included, even if clearly genetic. Many good references exist for metabolic and hereditary eye disease of postnatal onset. These include GENETIC AND METABOLIC EYE DISEASE by Morton Goldberg, (1974), THE HEREDITARY DYSTROPHIES OF THE POSTERIOR POLE OF THE EYE by A.F. Deutman (1971), and CHORIORETINAL HEREDODEGENERATIONS by Franceschetti, Francois and Babel (1974).

This manual will not attempt to cover in great detail the rapidly expanding number of chromosomal and other dysmorphic syndromes. Only a few syndromes which illustrate the variety of congenital malformations of the eye will be included. Again, more complete coverage of these entities exists in recent texts such as RECOGNIZABLE PATTERNS OF HUMAN MALFORMATION by D.W. Smith (1970), MENTAL RETARDATION-AN ATLAS OF DISEASES WITH ASSOCIATED PHYSICAL ABNORMALITIES by L.B. Holmes, et al (1972), and SYNDROMES OF THE HEAD AND NECK by R.J. Gorlin and J.J. Pindborg (1964). A considerable part of the information presented in this text has been extracted from Ida Mann DEVELOPMENTAL ABNORMALITIES OF THE EYE (1957) and Duke-Elder SYSTEM OF OPHTHALMOLOGY, VOL. III PART 2, CONGENITAL DEFORMITIES (1964).

In agreement with current convention, the adjective rather than the possessive form of named diseases and syndromes will be used, e.g., Down syndrome instead of Down's syndrome.

Although retrolental fibroplasia can occur as a congenital defect (Karlsberg, Green, and Patz, Arch. Ophth. 89: 122, 1973) most cases are related to postnatal oxygen exposure and this entity will not be discussed. Also, arbitrarily, the embryopathies (rubella, syphillis, toxoplasmosis, cytomegalic inclusion disease, herpes simplex) will not be covered.

B. Causes of anomalies

The mechanisms of congenital deformities involve genetic and environmental factors and their interactions. Embryogenesis itself is under genetic control, through genetically determined aspects of cell growth, differentiation, proliferation, interaction, and programmed cell death or atrophy of certain embryologic tissues or structures. Environmentally caused anomalies are produced by influences, whether infectious, chemical or physical, acting on the fetus during intrauterine life. These agents are called teratogens.

The distinction between genetic and environmental factors has become rather vague and some authors attribute as many as 80% of congenital defects to the interplay of heredity and environment. The most frequently seen anomalies may be defects which are genetically predisposed but environmentally produced. Thus certain genetic traits in the presence of an environmental agent, will produce or allow abnormal development. Teratogens in this case affect only those individuals carrying a hereditary tendency or susceptibility, but have no influence on others.

C. Mechanisms of abnormal development which lead to anomalies (Perrin, E.V. and Finegold, M.J.: PATHOBIOLOGY OF DEVELOPMENT -- OR ONTOGENY REVISITED. The Williams and Wilkins Co., Baltimore, 1973)

According to James Wilson, the four manifestations which can result from deviations in development in utero are 1) death of the embryo or fetus, 2) malformation, 3) growth retardation, and 4) functional deficit. The last manifestation is the most difficult to establish and to link causally to a particular teratogenic agent or influence, whether genetic or environmental.

A few mechanisms in which development departs from normal will now be discussed. Eye abnormalities may result from developmental failure where the primordium does not appear or fails to develop to a significant degree. An example would be primary or secondary anophthalmos (congenital absence of the eye). Mentioned earlier was developmental arrest. Here, normal development of the eye does not occur because of suppression at some stage, as in congenital cystic eye. Overgrowth of the anterior segment with normal posterior segment appears to be the mechanism of abnormal development in megalocornea. Of classical importance are the failures in fusion such as colobomas, which may also result in microphthalmos. Failure of transitory embryologic tissue or structures to atrophy is responsible for a large number of eye anomalies. Indeed, persistence in some form of embryologic vascular elements which normally undergo atrophy is perhaps one of the most frequent types of congenital ocular abnormalities.

Another important mode of abnormal embryogenesis in man is failure of cell interaction, represented in the eye by agenesis of lens from failure of contact between optic cup and surface ectoderm over the forebrain region. Insufficient or inactive inductor tissue (the optic cup) or incompetent or unresponsive induced tissue (the surface ectoderm) may be the cause. Other modes of abnormal embryogenesis include excessive cell death, changed rate of proliferation (megalocomea or microcornea), impeded cell migration or interference of morphogenic processes such as invagination or evagination, reduced biosynthesis (through inhibition of synthesis of nucleic acid, protein or other essential substances), and mechanical disruption (destruction of tissues or growth interference through pressure, trauma or vascular insufficiency).

D. Period of development

Abnormalities may occur at any time in development. Generally, those appearing earlier result in the most pronounced deformities. If encountered early enough, such as in the germinal period (1st week), the defect leads to such gross changes that the conceptus rarely proceeds further. Those arising later, during the organogenic period (2nd-6th week), form most of the monstrous anomalies of the eye, e.g., cyclopia. The fetal period (3rd-9th months) is the time of origin of certain minor defects, growth retardation, some somatic mutations, functional deficits, and certain syndromes involving intrauterine diseases of the fetus.

II. The interplay of environmental and genetic factors

A. Etiologies of congenital anomalies

Until the fourth decade of this century, congenital defects were considered by many researchers as purely hereditary phenomena. At that time, it was discovered that the rubella virus could malform an embryo during intrauterine life, and other environmentally produced defects became known.

Now we recognize that abnormalities are seldom solely environmental or genetic in origin. Both causes may produce the same resultant manifestation, making it difficult to assign a cause to a given defect. The two are so inter-related that the environment (or even a single agent) may either modify a gene's expression, enchance its effect, suppress it or alter the gene through induced mutation to create new heritable characteristics.

The following (modified after James Wilson, 1972, and Neel, 1961) gives the breakdown of etiologies of congenital anomalies:

-20% known genetic transmission
-10% from chromosomal aberrations
-10% from viral or teratogenic origin, including radiation, chemicals and drugs
-60% of unknown origin

B. Environmental factors (Wilson, J.G.: ENVIRONMENT AND BIRTH DEFECTS, Academic Press, New York, 1973)

The most influential determinant in the character of a teratogen is the stage of development in which it acts. Many agents considered highly teratogenic in early stages have no effect on a fetus when given during later periods. The type

of malformation produced depends on an organ's susceptibility at the time of exposure. Each organ goes through its own susceptible stage, which in most cases occurs during the stage when the organ is rapidly differentiating. The genotype of an individual may determine the entire reaction of an organism to an environmental factor. And, of course, the amount of time an embryo is exposed to a teratogenic influence affects not only whether a defect occurs but also the extent of damage.

Recent evidence suggests that a specific factor acts on a particular aspect of cell metabolism. It may block or alter a single important biochemical mechanism, a fact which may explain why the time of exposure is so critical.

There are several teratogenic factors known to man and even more are suspected. They may act in many different ways: physically, chemically, infectively, metabolically, or nutritionally. A mother may harbor the agent and transmit it transplacentally such as in rubella, toxoplasmosis, syphillis and CMV (cytomegalovirus) or the fetus may be affected transamniotically, as with herpes virus or other intrauterine infections.

Mechanical interference with the embryo may easily produce deformities. Well known among this group are those malformations resulting from amniotic bands or puncture of the amniotic sac. Constrictions of the fetus by adhesions can cause lid and lacrimal apparatus deformities or severe malformations involving elements of the entire body.

Ionizing radiation exposure during pregnancy acts as a powerful teratogen having its greatest effectiveness in producing malformations during the organogenetic period--about 14th to 50th day in man. X-rays are most notorious in this category with gross malformations produced with as low as 50 R during a narrow period estimated from about the 15th to 21st day. During the second and third trimesters doses of 150 to 400 R will produce gross defects in development (mainly CNS: cerebral hypoplasia, microcephaly, cerebellar hypoplasias, etc.). The latter dose, 400 R, is also the LD 50 for man.

Growth retardation and functional defects may be more sensitive parameters of radiation damage than teratogenesis in man. Ultrasonic energy, low temperatures and atmospheric changes are suspected of increasing the frequency of defects. Hypoxia from lowered atmospheric pressure or dilution with other gases can be teratogenic.

Anophthalmos and cyclopia have been produced in animals by the presence or excess of certain metals, e.g., lithium or magnesium. Calcium or vitamin D deficiency can cause congenital cataracts. Perhaps the most dramatic example of a drug acting as a teratogen producing gross deformities is that of thalidomide. Aminopterin, a powerful antimetabolite, also is highly teratogenic.

The children of diabetic or prediabetic mothers are undoubtedly at a greater risk than those of normal mothers. Ocular anomalies such as cataracts, nystagmus, or strabismus are more often found in these cases.

As mentioned above infectious agents are potentially harmful, and maternal rubella is classic for this. For example, even in subclinical infections occurring during the 5th-6th week of pregnancy, a cataract may result in the child (this is when the primary lens fibers are proliferating). Conjunctivitis is a frequent

occurrence in cases of intrauterine infection. Gonococci, variola, or varicella, even though they are confined to the amniotic fluid, can be serious enough to produce corneal ulceration.

C. Genetic factors

With the exception of unpaired genes on the X or Y chromosome, the given hereditary characteristics of an individual are determined to a large degree by the combined effect of two genes on homologous chromosomes. Mendel stated: 1) the units of genetic material are particulate and segregate when gametes are formed (law of segregation), and, when these two pieces of genetic matter (one from each parent) combine in fertilization, 2) there is an equal chance for each of the separate units from one parent of joining with either of the units from the other parent (law of independent assortment).

Genes are coded in DNA triplets in a linear fashion on chromosomes. On a given chromosome a gene occupies a specific position known as its locus. A gene complement consists of two genes determining the same character, each of which is at the same locus but on separate homologous chromosome. When the two genes express different forms of the same trait, they are termed alleles. If the two similar loci on homologous chromosomes contain identical genes, the individual is considered homozygous for that trait. If the two genes are not identical then the combinant is termed heterozygous.

Chromosomes are paired in somatic cells, each of the pair being homologous to the other. In man the diploid or normal number of chromosomes is 46; however, there are 24 different kinds of chromosomes. Twenty-two are known as autosomes and two are called sex chromosomes, designated as the X chromosome and a shorter Y chromosome. While both sexes possess 22 pairs of autosomes, females possess in addition two X chromosomes and males possess a single X chromosome plus a Y chromosome.

Although not as important as the basic concept of the gene action (or failed action) the terms dominant and recessive have clinical significance. Often whether a gene may be referred to as either recessive or dominant depends on the diagnostic ability to detect the product of the gene, especially if gross disease is not evident. A given trait may be considered to have dominant inheritance if the trait is manifest with the abnormal gene in the heterozygous state. Dominant genetic disorders often are related to an abnormal structural protein produced by the defective gene, whereas in recessive disorders often the defective gene codes for an ineffective enzyme or, more rarely, no enzyme at all. Although oversimplified, malformations are often associated with dominant disorders whereas inborn errors of metabolism are usually recessive. Other features suggesting autosomal dominant inheritance within a family include direct transmission over two or more generations, half of the siblings in a generation affected, and both sexes affected in equal numbers. The term recessive describes a trait produced by a gene that must be homozygous to be expressed. A recessive trait will become apparent in offspring in three cases only: 1) if a homozygous affected person mates with a heterozygous carrier, statistically half of the offspring should be affected and the other half will be carriers (heterozygous unaffected); 2) if two unaffected heterozygous carriers mate, statistically 25% of the children should be homozygous normal, 50% should be heterozygous carriers, and 25% should be homozygous affected; 3) if two homozygous affected persons mate, all offspring will be affected.

Sex-linked inheritance involves genes on the X chromosomes rather than on autosomes. Males, possessing only one X chromosome, have no alleles on their Y to dominate or suppress a recessive gene on an X. Females carrying a disease-producing recessive gene on one X chromosome have another X, usually displaying a normal allele and are therefore heterozygous and unaffected. Through inactivation or "Lyonization" of randomly one or the other of the two X chromosomes, only one X is left active. Statistically one half of the cells will have inactivated the abnormal X and usually enough gene product will be produced to avoid the degree of disorder manifestations as is seen in the hemizygous male. However, statistically 50% of the sons of a carrier woman will be affected and 50% of the daughters will be carriers (if a female heterozygous for an X-linked recessive married a normal male). Affected males pass X-linked genes to all of their daughters (who with recessive traits are unaffected carriers) but never to their sons, since males pass only their Y chromosomes to their sons.

An imbalance of chromosomal material may give rise to gross anomalies. There are several kinds of these chromosomal anomalies, but they usually involve excessive chromosomal material, deleted chromosomal material, or more complex re-arrangement of individual chromosomal fragments. A detached part may re-attach itself to the same chromosome forming an inversion, or it may adhere to another chromosome which has sustained a break producing a deficiency in the one case and an excessive amount on the other (the translocation phenomenon). Non-disjunction of the chromosomes is due to an error in cell division where a chromosome pair fails to separate and both enter one daughter cell. One less than the normal number of chromosomes would be found in one daughter cell (producing for example, XO in Turner syndrome) and an extra chromosome would be found in the other (producing for example, trisomy 21 in Down syndrome).

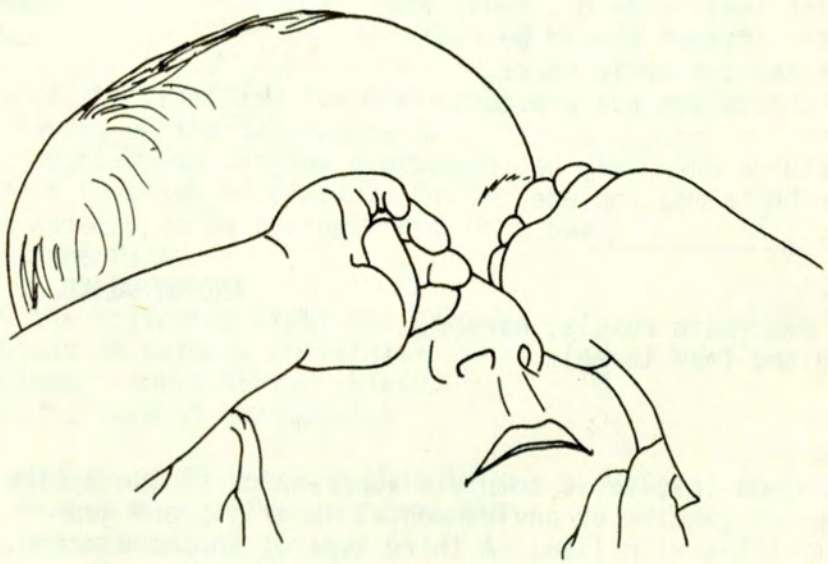
New dominant hereditary traits which appear for the first time in a pedigree are called mutations. Most of these are harmful to the individual but tend to be lost due to natural selection. In those dominant genetic disorders which are lethal or cause infertility or otherwise interfere with reproduction, eventually the incidence of the gene equilibrates with the mutation rate. Though mutations are new hereditary traits, they are not necessarily new genetic material. More precisely, they are usually modifications of genetic material that is already present.

Frequently misused as synonyms are the terms penetrance and expression. Penetrance refers to the percentage of individuals known to carry a given gene who actually manifest or show the effect. If a gene is known to produce a certain condition, but the trait frequently fails to appear at all in the presence of the gene, then it is said to have reduced penetrance. Variation in the quality or degree of manifestation of the gene is called expressivity. Thus a gene may exhibit a high penetrance and be expressed often, but the expression in a given person may be variable in manifestation or only partial in degree.

Pleiotropism refers to the situation where a single gene has multiple effects, often in separated areas, organs or tissues of the body, which may be quite variable in qualitative and topographic character. In this regard, pleiotropism must be differentiated from the effects of separate genes which in a particular family segregate together because of close linkage or proximity on the chromosome. No permanent association exists for different families between any two heritable alleles or traits if they are truly linked. It is the gene loci which are linked, not the alleles which occupy the loci, even though it is through the effects of the alleles or the presence of the trait that we recognize the loci.

All of these points emphasize the interaction of the genes and their environment. For this reason it is necessary to retain the distinction between a genotype, the genetic constitution of an organism, and its phenotype, the clinical appearance.

Traditionally, the study of monozygotic (maternal or identical) and dizygotic (fraternal) twins has been used to help separate hereditary from environmental factors. Since monoaygotic twins have the same genetic make-up, inherited traits will tend to be identical (show concordance) while degrees of difference (discordance) will be a measure of environmental influence.



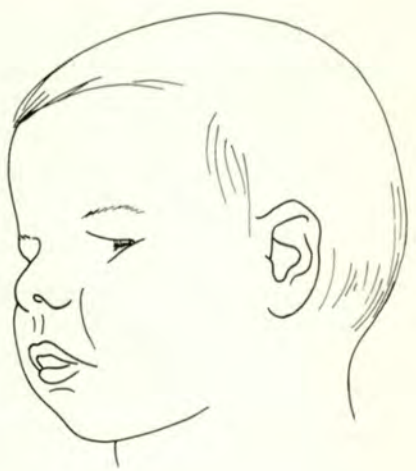
ANOMALIES IN ORGANOGENESIS

1
Defects of the entire eye have their origin before the closure of the embryonic fissure. This period of organogenesis, occurring early in embryonic life, is when the most pronounced anomalies occur.

Q: The fusion of the sides of the embryonic fissure begins at about the 30th day in the _____ region of the fissure and proceeds toward the _____ and the _____.

A: central, rim of the optic cup, brain

2
Anophthalmos is the complete absence of neuro-ectodermally derived eye tissues within the orbit. Primary anophthalmos, which is rare, is a failure of the optic pit to invaginate and form the optic vesicle. In this case, the neuro-ectodermal elements and those surface ectodermal structures stimulated by the optic vesicle (e.g., lens) are missing. The optic foramen should be rudimentary or absent and the optic nerve, chiasm and optic tracts are not present.



ANOPHTHALMOS

Q: Orbital structures which may be present in primary anophthalmos include _____, _____ and _____.

A: sclera, fat, extrinsic muscle, nerves, or lacrimal gland (any three).

3
Secondary anophthalmos involves a complete suppression of the entire forebrain. It may be genetic or environmental in origin and generally is not compatible with life. A third type of anophthalmos is termed degenerative or consecutive wherein the optic vesicle forms, but subsequently degenerates. This condition, present in a clinical setting, may be difficult to distinguish from microphthalmia.

Q: Anophthalmos will probably occur during which of the following periods of development: A. germinal (week 1), B. organogenic (weeks 2-6), C. fetal period (3-9 months). _____

A: B. Organogenic

4

Microphthalmos is a condition in which the essential structures are represented in the eye, but are very small and underdeveloped. Microphthalmos may result from either lack of proper development of the secondary vitreous and its influence on growth of the globe, or from failure of closure of the embryonic fissure and secondary arrest of growth of the globe. Clinically, extreme microphthalmos is often difficult to differentiate from true anophthalmos and the condition may be called clinical anophthalmos. Differentiation between microphthalmos and true anophthalmos can only be made by histological examination of the orbit.

BILATERAL MICROPHTHALMOS IN GIRL WITH HALLERMANN-STREIFF SYNDROME

Q: The absence of any clinically detectable gross eye structures in the condition of extreme microphthalmos often results in its classification as clinical _____.

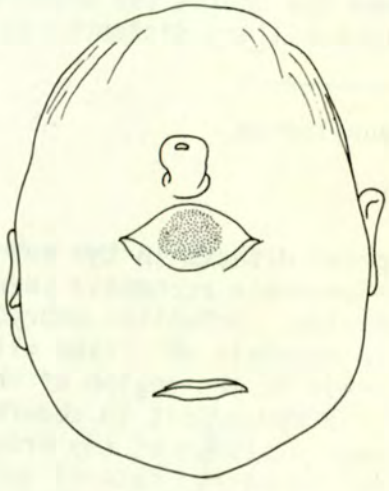
A: Anophthalmos

5

Malformation of the primitive forebrain may result in a fusing of the telencephalic and/or optic vesicles to varying degrees. Cyclopia refers to cases of complete fusion to form what appears to be a single eye in the middle of the face.

Q: Which of the following might one expect to be absent in primary unilateral anophthalmos: optic nerve, chiasm, optic tract, lateral geniculate?

A: All are absent or abnormal in that they are not formed of any elements from the anophthalmic side.

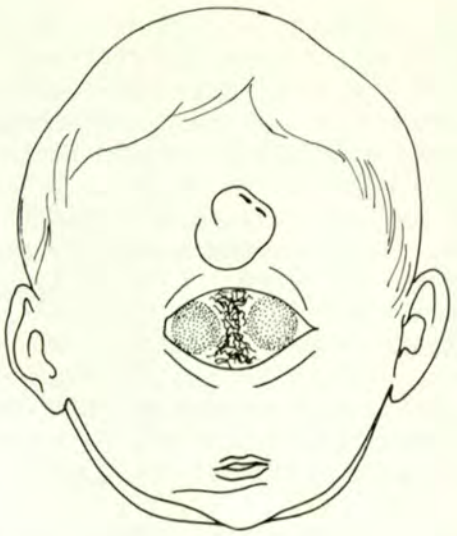


CYCLOPIA

6
The condition in which there is incomplete fusion of elements of the two eyes is termed synophthalmos.

Q: Cyclopia and synophthalmos in effect result from a fusion of the _____ vesicles.

A: Optic



SYNOPHTHALMOS

7
Hypotelorism refers to a less than normal distance between the orbits or a smaller than normal interpupillary distance. True hypotelorism may result from lack of development or involution of the tissues of the fronto-nasal process with subsequent narrowing of the angle formed by the orbits and shortening of the interpupillary distance.

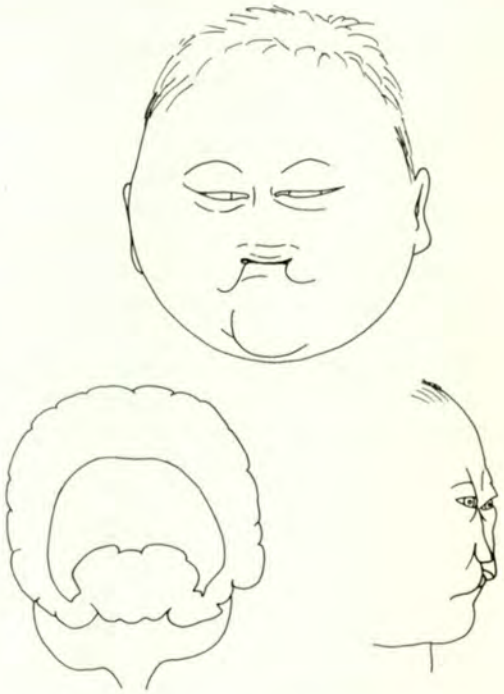
Q: A decrease in the normal distance between the orbits (as measured by interpupillary distance) is termed _____.

A: Hypotelorism

8
Often grave defects in the embryogenesis of the forebrain accompany severe forms of hypotelorism. Defective embryogenesis or ischemic necrosis of tissue with secondary fusion in the region of the lamina terminalis may result in abnormal or incomplete division of the prosencephalon into the paired lateral telencephalic or optic vesicles. This produces a spectrum of anomalies from holoprosencephaly to cyclopia. Chromosomal anomalies (such as trisomy-13 and deletion-18) have been reported to cause these severe forebrain anomalies.

Q: If marked, hypotelorism may be indicative of severe congenital malformation of the _____.

A: Forebrain



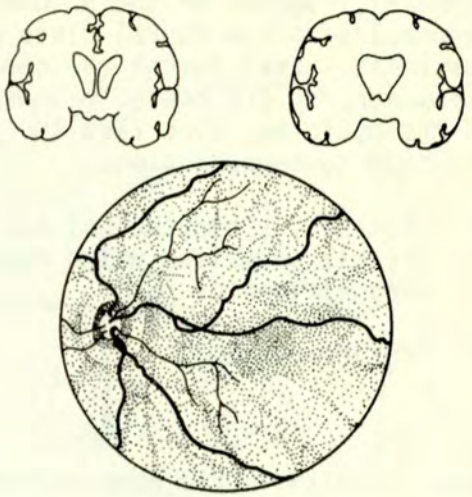
HOLOPROSENCEPHALY WITH EXTREME HYPOTELORISM AND SINGLE UNDIVIDED CEREBRAL VENTRICLE (LOWER LEFT)

9

Abnormal embryogenesis in the region of the ventral aspect of the lamina terminalis may also produce defects in the infundibular and chiasmic plate producing a constellation of features called septo-optic dysplasia or De Morsier syndrome. This syndrome includes bilateral congenital visual loss with hypoplasia of the optic discs, evidence of pituitary dysfunction +/or hypothalamic dysfunction, and agenesis of the septum pellucidum on pneumoencephalogram (P.E.G.).

Q: Defective embryogenesis of the floor of the third ventricle in the region of the infundibulum and chiasmic plate may result in _____ and _____.

A: Hypopituitarism, maldevelopment of the optic chiasms (or chiasmal defect).



SEPTO-OPTIC DYSPLASIA

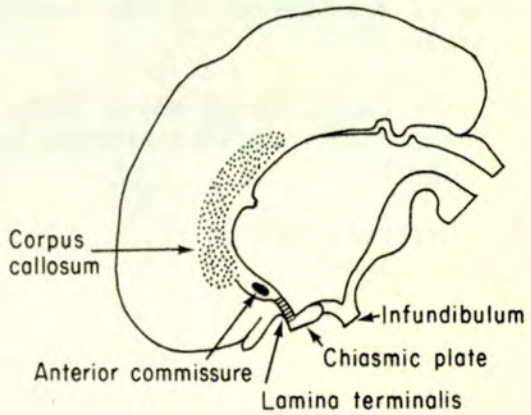
Upper left: normal ventricles
Upper right: single central ventricle with agenesis of septum pellucidum
Below: small hypoplastic optic disc with double-marginated rim

10

Chiasmal field defects (bitemporal visual loss have been reported in septo-optic dysplasia and probably result from loss of those optic nerve fibers which would normally cross in the abnormally developed chiasmal region. Retrograde loss of these crossing nerve fibers would also explain the hypoplastic optic disc and nerve. The later developing non-crossing fibers persist and contribute the bulk of the optic nerve and explain what binasal visual field remains. The electro-retinogram is normal.

Q: Hypopituitarism, in association with hypoplastic optic discs and agenesis of the septum pellucidum, has been termed _____.

A: De Morsier syndrome (or septo-optic dysplasia).



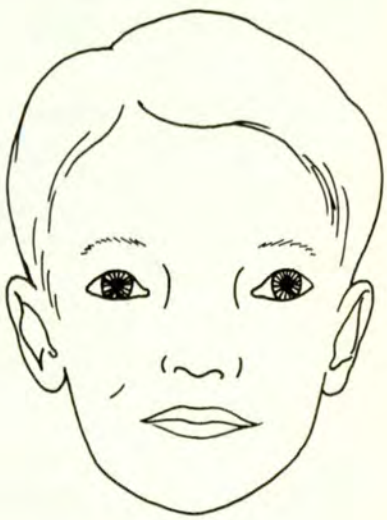
MEDIAN SAGITTAL SECTION OF BRAIN

11
There is experimental evidence in amphibians that disruption of the terminal fragment of the notochord or chorda-mesoderm results in an abnormally narrow neural plate and ineffective induction of the forebrain. Even though the neural ectoderm remains intact, the "template" in the neural ectoderm is spatially restricted and fusion of the optic vesicles results, producing anomalies ranging from cyclopia to synophthalmos.

Q: Cyclopia, synophthalmos and undivided single cerebral vesicle are all anomalies which result from fusion of the paired evaginations of the _____.

A: Prosencephalon

12
Hypertelorism is the name referred to the state when the axes of the orbits, in migrating during fetal development from 180 degrees toward the anterior position, do not reach the normal angle of 71 degrees at birth (or 68 degrees as an adult). Hypertelorism according to Walker (Duke-Elder, Vol III, Part 2, p. 1054) results from a primary defect in the development of bones of the first visceral arch allowing frontonasal elements to grow into the region normally occupied by the maxillary structures. Any condition or genetic defect which arrests embryologically the forward migration of the orbits will cause hypertelorism. Hypertelorism is measured as an increased interpupillary distance or as a radiographic measurement of the interorbital distances.



HYPERTELORISM

Q: The condition in which there is an increased distance between the orbits is called _____.

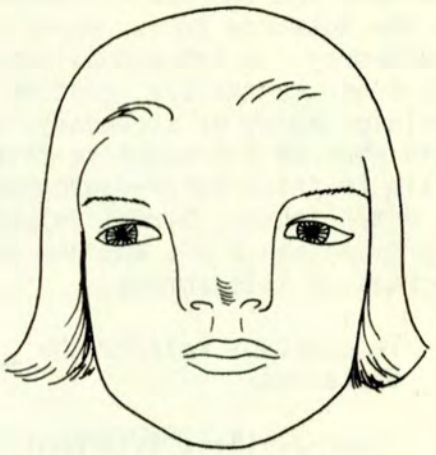
A: Hypertelorism

13

Conditions which are associated with hypertelorism include Waardenburg syndrome (which more frequently has telecanthus with lateral displacement of the puncti but may have hypertelorism in addition), Crouzon syndrome, agenesis of the corpus callosum, cranium bifidum occultum, frontal meningocoele, basal encephalocoele and congenital median clefting syndrome of face, nose and palate.
Exotropia, microphthalmia, peripapillary staphyloma, and optic disc anomalies (pallor, optic disc coloboma, optic disc pit, megalopapilla or optic nerve dysplasia) are features also associated with basal encephalocoeles (Goldhammer and Smith, Arch. Ophth. 93: 115, 1975).

Q: A mass present in the nose or nasopharynx in association with hypertelorism and/or median facial clefting may represent a(n) _____ and biopsy is (indicated, contraindicated).

A: Encephalocoele, contraindicated.



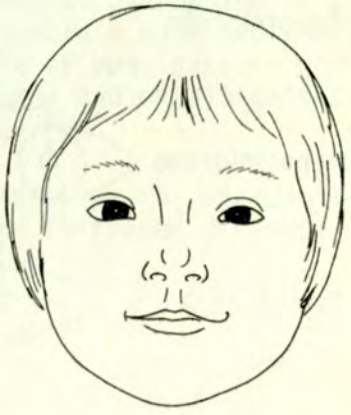
MEDIAN CLEFT FACE SYNDROME WITH HYPERTELORISM

14

Telecanthus, often mistakenly equated with hypertelorism, refers to an increased distance between inner canthi relative to inter-pupillary or inter-orbital distance. Telecanthus may or may not be associated with true hypertelorism. In primary telecanthus the interpupillary distance, and hence the interorbital distance, is normal. However, if associated with true ocular hypertelorism, the term secondary telecanthus may be used.

Q: Congenital visual loss, especially if associated with growth retardation or diabetes insipidus, demands careful evaluation of _____ for evidence of _____. Pneumoencephalogram may reveal agenesis of the _____.

A: Optic discs, hypoplasia, septum pellucidum



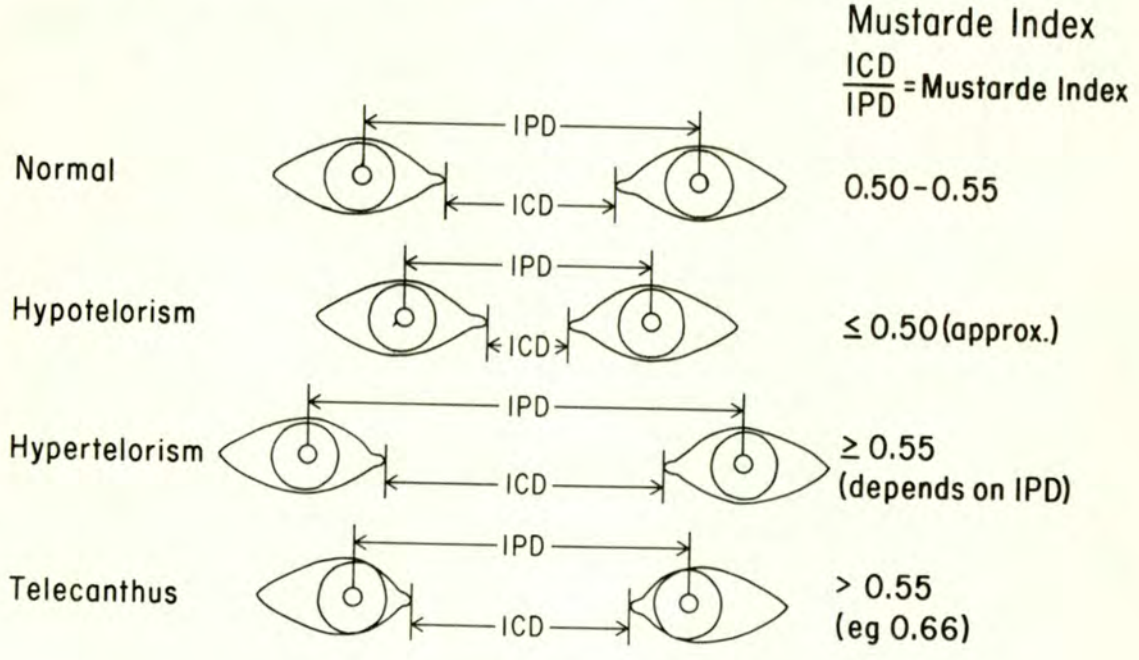
TELECANTHUS (MUSTARDE INDEX, 0.69)

Certainly the etiology and embryogenesis of telecanthus differ from hypertelorism. Telecanthus results from overgrowth in width of the fronto-nasal process, the tongue of tissue which forms the base of the nose and the medial canthal regions. One measure of telecanthus is the Mustarde index, which is the inter inner-canthal distance divided by the inter-pupillary distance. During early fetal life the inner canthi are relatively widely spread and there exists a certain degree of secondary "telecanthus" until about the 14th to 16th week of intrauterine development; at that time, the normal ratio of inter inner-canthal distance to inter-pupillary distance is established. Normal values from infancy to adulthood are approximately 0.50, whereas values over 0.55 indicate increasing degrees of telecanthus.

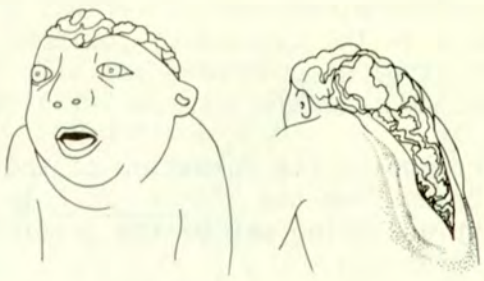
Q: Telecanthus relates the _____ to the _____ distances.

A: Inner-canthal, interpupillary

COMPARISON OF HYPOTELORISM, HYPERTELORISM AND TELECANTHUS



Anencephaly is a severe lethal malformation of the central nervous system which is of clinical importance because, if suspected, the presence in utero of such a neurally defective fetus can be detected through amniotic fluid alphafetoprotein measurement early enough to allow consideration of abortion (Lancet II, 197, 1972). Anencephaly is of embryologic significance in that the dorsal opening of the neural tube may represent a "secondary" event, not a primary failure of closure of the neural-groove. (For good discussion see Addison and Font, Amer. J. Ophth., 74: 972, 1972). Certainly it is difficult to imagine well formed optic vesicles (hence globes) forming from a primarily deranged forebrain. With the exception of decreased numbers of ganglion cell nuclei and fibers, the retinal elements are well differentiated in stillborn or late-aborted anencephaly. The optic nerves are thin and end a few centimeters behind the globes; the optic chiasm and tracts are absent. Studying an ancephalic 27 mm fetus, Ida Mann found normal retinal differentiation, including normal number of ganglion cells. She concluded that the marked reduction in ganglion cells evident at a later stage is secondary to retrograde degeneration from lack of connection of the ganglion cells with more central elements in the abnormally deranged brain. Frazer feels that between the 18 mm and 28 mm stage, the neural tube becomes blocked and the forebrain undergoes straightening of the normal cephalic flexion. Mechanical disruption of the vascular supply produces ischemic necrosis of the forebrain with secondary re-opening of the neural tube. This leads to failure of bony closure with rachischisis (congenital division of the spinal column) and cranioschisis (congenital failure of the skull to close dorsally).



ANENCEPHALY

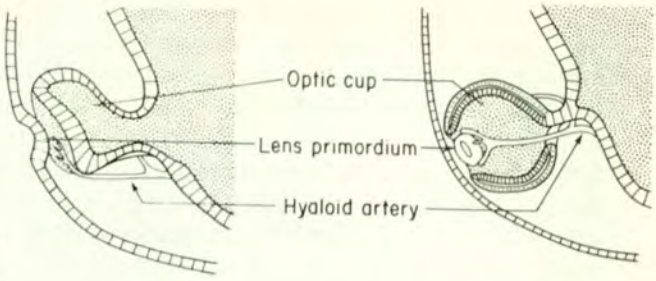
Q: An increased distance between the inner canthi relative to interpupillary distance is termed _____; whereas, an increased distance between the orbits is called _____.

A: Telecanthus, hypertelorism

17
After the optic vesicles have formed, many anomalies may occur before the optic cup stage. Complete or partial failure to invaginate (congenital cystic eye), failure to completely invaginate (congenital nonattachment of retina) and defects in the closure of the embryonic cleft (typical coloboma) are all anomalies in optic vesicle invagination.

Q: Following the formation of the optic primordium the _____ is formed by a budding out of the primitive forebrain.

A: Optic vesicle

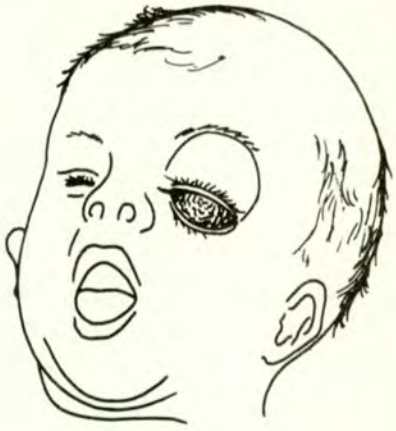


LEFT: THE BEGINNING OF OPTIC CUP INVAGINATION DURING NORMAL LENS VESICLE DEVELOPMENT
RIGHT: A FURTHER STAGE IN NORMAL OPTIC VESICLE INVAGINATION

18
Congenital cystic eye results when development does not continue past the formation of the outgrowth of the optic vesicle. According to Mann (1957), development may stop before invagination is complete and the eye may appear to be absent. An orbital cystic mass, especially if pulsatile, may be associated with a spheno-orbital encephalocoele.

Q: Prior to socket revision or excision of a congenital cystic eye, radiographic studies should be done to exclude a bony defect in the posterior aspect of the orbit, which might be from a(n) _____.

A: Encephalocoele

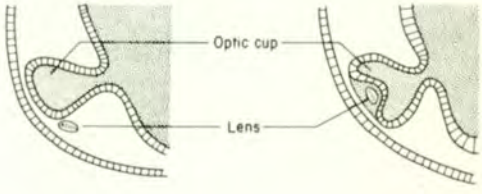


CONGENITAL CYSTIC EYE (Note prominent bulging of upper eyelid)

19
The presence of a lens in a microphthalmic or cystic eye is good evidence that during embryogenesis the eye had proceeded at least at one time, past the induction of the lens vesicle from surface ectoderm.

Q: The presence of lens remnants in orbital tissue rules out _____ or _____ anophthalmos but is compatible with the diagnosis of _____ or _____.

A: Primary or secondary
Degenerative (or consecutive) anophthalmos or colobomatous cyst (or microphthalmos).



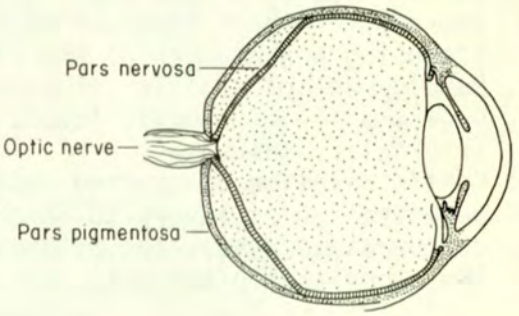
LEFT: CONGENITAL CYSTIC EYE WHERE THE LENS IS NOT CONTAINED WITHIN THE INVAGINATING OPTIC CUP
RIGHT: CONGENITAL CYSTIC EYE WHERE OPTIC CUP INVAGINATION DOES NOT GO TO COMPLETION

20
In anophthalmos or to a lesser degree microphthalmos, the lack of a normal growing eye causes failure of normal orbital growth.

Q: An anophthalmic or microphthalmic orbit will usually be (larger, smaller) than a normal orbit for age.

A: Smaller

21
As well as congenital cystic eye, congenital non-attachment of the retina may also be caused by an incomplete invagination of the optic vesicle. In this situation a gap which is normal up to the 3rd month, persists between the two layers of the optic vesicle. This is considered an anomaly of proliferation of the inner layer of the optic cup.

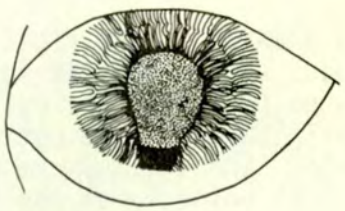


CROSS SECTION OF THE EYE SHOWING CONGENITAL NON-ATTACHMENT OF THE RETINA

Q: Would non-attachment of the retina be considered normal in early embryonic life?

A: Yes

22 (Review frames #26-27 in Part I)
Coloboma is the term used to describe a notch, gap, hole or fissure in any or all of the layers of the eye (e.g., retina, choroid, iris). Typical colobomas occur along the choroidal (embryonic) fissure, located in the inferior medial aspect of the developing eye, while those appearing elsewhere are atypical.



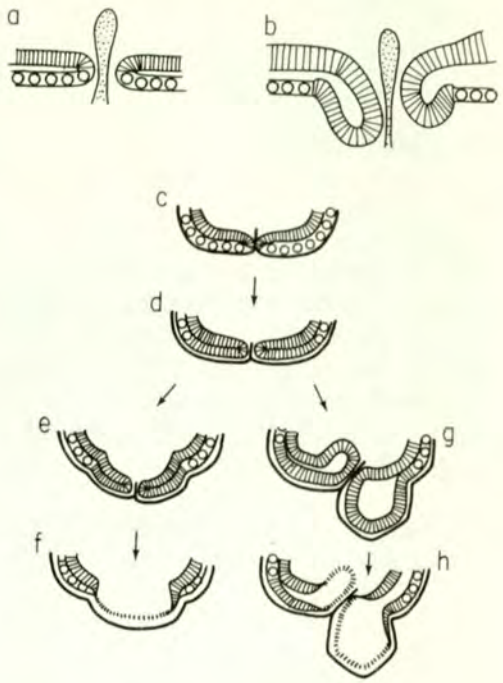
Q: The drawing at the right would be a(n) _____ coloboma of the iris.

A: Typical

23
Typical colobomata occur from events taking place during the 4th to 5th week (7 to 14 mm stage) when the cup is undergoing evagination and the embryonic cleft is beginning to close. Abnormal eversion of the inner (retinal) layer of the cup through the embryonic cleft interferes with normal fusion of the cleft margins. Completely closed sacks or distentions of retinal tissue may form and give rise to colobomatous cysts. More severe colobomatous defects probably result from earlier influences whereas later influences may result in only partial failure of closure of the cleft.

FORMATION OF TYPICAL COLOBOMA

a. Mesodermal tissue interposed between margins of embryonic tissue.
b. Excessive growth of inner (retinal) layer of optic cup, producing eversion of margin.
c. Normal closure of embryonic cleft.
d. Eversion of inner layer of fissure margins, producing non-closure of the cleft.
e. Development of ectatic coloboma.
f. Degeneration of ectatic layers to form an intercalary membrane.
g. Cystic dilation of everted retinal layers.
h. Degeneration of layers to form two colobomatous cysts, one within the eye and the other an orbital cyst.



(AFTER DUKE-ELDER)

Q: Typical coloboma can result from failure of _____, secondary to abnormal eversion of the rim of the (inner, outer) layer of the optic cup.

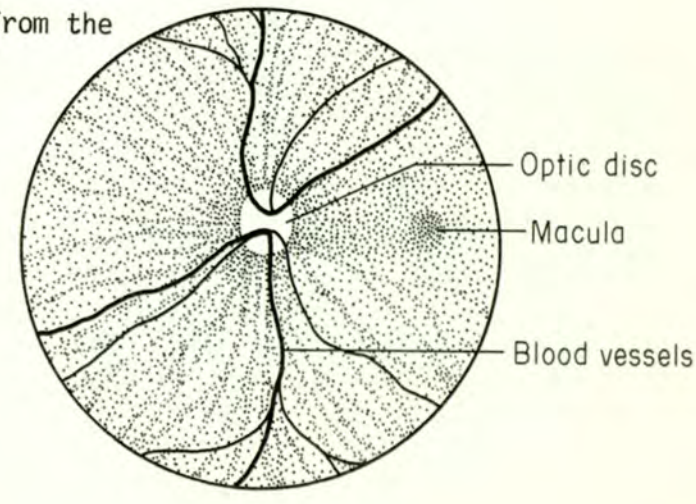
A: Closure of the embryonic fissure; inner

24

The drawing at the right shows a normal fundus (i.e., what is seen when viewing the posterior of the eye through the pupil) in which the optic disc, macula, retina, and choroid are complete. A typical coloboma of the fundus occurs when the choroidal fissure does not fuse completely. It may involve just the retina and choroid or all of the tissues associated with the fissure.

Q: The optic vesicle is formed from the _____ germinal layer.

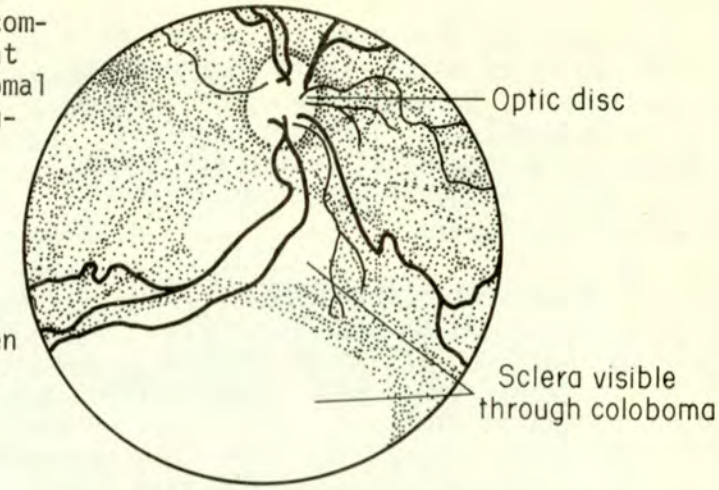
A: Neural ectoderm



NORMAL FUNDUS AS SEEN WITH THE OPHTHALMOSCOPE

25

Coloboma may be inherited as an incompletely penetrant autosomal dominant trait; however, X-linked and autosomal recessive inheritance has been documented in a number of families. Isolated sporadic occurrences are also reported. Several of the chromosomal syndromes (especially trisomy 13, the cat eye syndrome and less frequently trisomy 18) may have coloboma of the uvea, often in association with microphthalmia. It is of interest that in trisomy 18 the coloboma, when present, is usually posterior, often involving only the disc, whereas in trisomy 13 the coloboma is usually more severe, may be anterior as well as posterior, and more often is associated with microphthalmia. Uveal colobomas are also seen in association with cleft lip and/or palate. Lateral facial clefts may be associated with ipsilateral microphthalmos, uveal coloboma, congenital cystic eye, or coloboma of the lids (Gorlin and Pindborg, 1964).



BRIDGE COLOBOMA OF CHOROID

Q: A coloboma resulting from an improper closure of the choroidal fissure would be expected to involve the _____ portion of the eye.

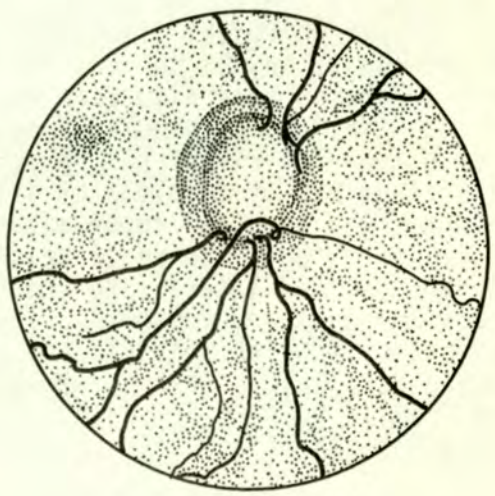
A: Infero-medial

26

Optic disc coloboma, often with microphthalmos, are produced at or just prior to the 18-20 mm stage, when closure of the posterior (or proximal) aspect of the embryonic cleft occurs. This is in contrast to earlier insults which generally cause more severe defects in closure. Optic nerve coloboma are often seen in several malformation syndromes, e.g., Cornelia de Lange syndrome and deletion of chromosome 18.

Q: An influence occurring late in the 6th week or early 7th week impeding fusion of the posterior aspect of the fetal cleft would produce a(n) _____, whereas earlier occurring influences might be expected to produce a (more extensive, less extensive) colobomatous defect.

A: Optic nerve coloboma, more extensive



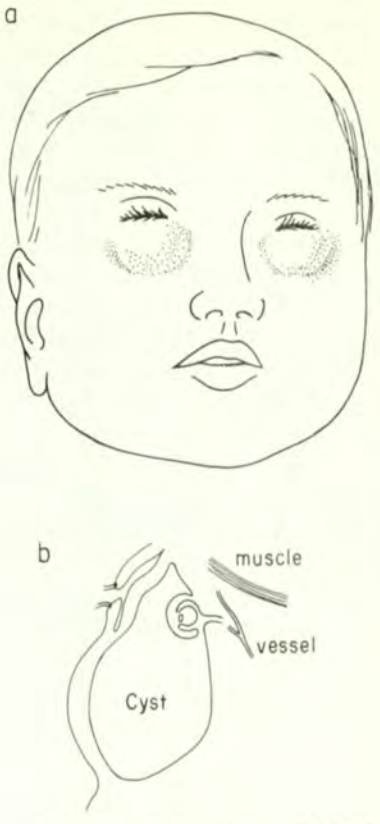
OPTIC DISC COLOBOMA (Note massive defect of disc compared to normal disc size in previous illustration)

27
Colobomas may give rise to congenital orbital cysts which simulate congenital cystic eye. Colobomatous cysts usually present a bulge of the lower eyelid; whereas, a congenital cystic eye tends to cause a bulge of both lids, particularly the upper.

a. BILATERAL MICROPHTHALMIA WITH COLOBOMATOUS ORBITAL CYSTS.
b. SAGITTAL SECTION OF MICROPHTHALMIC ORBIT WITH COLOBOMATOUS ORBITAL CYST.

Q: A unilateral congenital orbital cyst which presents a marked bulging of the lower lid is more likely a (congenital cystic eye, colobomatous orbital cyst).

A: Colobomatous orbital cyst

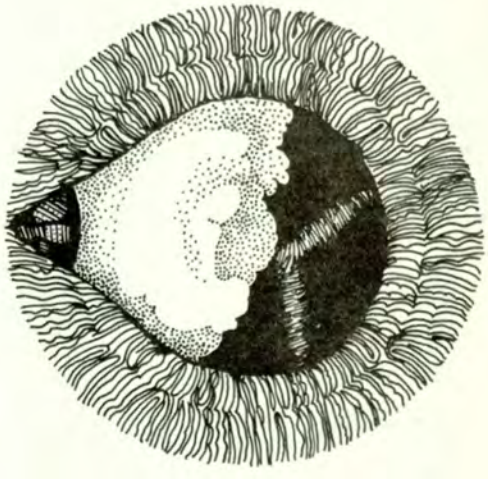


(AFTER IDA MANN, 1957)

28
Since the ciliary body, iris, and zonule are structures which are completely circular and are formed by the optic cup, a failure in the fusion of the anterior part of the choroidal fissure will result in defects of any of these structures. Iris colobomas have also been attributed to local failure of growth of ectodermal tissue from the rim of the optic cup. Other theories of etiology of iris coloboma and atypical colobomata include the abnormal persistence of vessels surrounding and anterior to the lens (capsulo-pupillary vessels). There are pedigrees in which aniridia has presented as atypical iris colobomata in some family members and as almost complete absence of the iris in others.

Q: A congenital cystic eye usually presents as a bulge through the (upper or lower) lid.

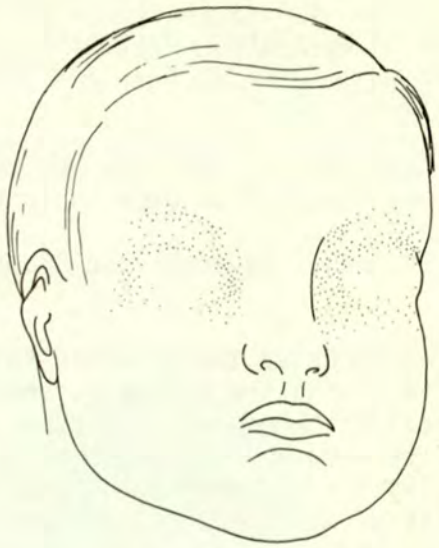
A: Upper (actually both but particularly the upper)



ATYPICAL COLOBOMA OF IRIS, LENS AND CILIARY BODY WITH ABNORMALLY PERSISTENT VESSELS AND CATARACT ADJACENT TO DEFECT

29

Cryptophthalmos, in most cases, is part of an autosomal-recessively inherited syndrome which includes mental retardation, cardiac anomalies, genitourinary abnormalities, cleft lip or palate, ear and nose anomalies, and syndactyly. The eyelids may be colobomatous or totally absent with skin-like tissue continuous over the surface of the eye; often there is no eyebrow formation. The globe is usually microphthalmic and the corneal thickness decreased, being replaced by vascularized fibrous tissue. Complete absence of the cornea is very rare but may occur in cryptophthalmos. The lens is defective or absent and the anterior chamber is small or non-existent, although rare cases have had normal anterior segments.



CRYPTOPHTHALMOS

Q: The term used for the multiple actions of a single gene producing different defects in separate regions or tissues of the body (as illustrated by the cryptophthalmos syndrome) is _____.

A: Pleiotropism

30

Absence of the conjunctiva occurs in cases of cryptophthalmos where the lid folds do not form. Consequently, there is no interposed conjunctiva between the eye and the skin. The skin is continuous over the eyeballs without the formation of eyelids.

Q: The absence of the conjunctiva is most likely caused by a fault in the differentiation of the _____ germinal tissue.

A: Surface ectoderm

31

The invagination of surface ectoderm to form the lens and the induction of the development of the cornea appear to result from induction by the optic cup. A failure in this induction process will bring about the absence of the above structures. Incompetence of the surface ectoderm overlying the optic vesicle with abnormal induction of lens, cornea, anterior chamber, and eyelid formation in conjunction with other anomalies occurs in cryptophthalmos. The many theories concerning the pathogenesis of cryptophthalmous are discussed in Duke-Elder, Vol. III, p. 829-834.

Q: The superficial (epithelium) layer of the cornea is formed from _____.

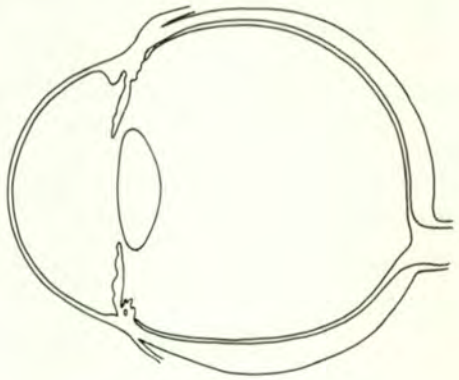
A: Surface ectoderm

32
Complete absence of the anterior chamber also occurs in gross microphthalmos, where the structures derived from the surface ectoderm fail to develop. The globe usually is spherical with a single retina-lined cavity. In severe forms of mesodermal dysgenesis and in persistence and hyperplasia of the primary vitreous (PHPV), the anterior chamber may be extremely shallow or clinically absent.

Q: Colobomas of the iris may be attributed to (one or several) causes and may result from defects in embryogenesis during (one or several) periods

A: Several, several (see 26 or Duke-Elder, Vol. III, Part 2, p. 577)

33
In megalocornea the anterior segment of the eye including the cornea is enlarged. Corneal thickness and curvature are usually normal. The lens may be normal or slightly enlarged. The zonules may be lax or stretched causing subluxation of the lens. Megalocornea is related to disturbed growth rates of the various parts of the optic cup ectoderm. The posterior part of the eye is not enlarged; however, the ciliary ring is. Megalocornea is not a result of raised intraocular pressure or glaucoma. Usually transmitted in a recessive sex-linked fashion, megalocornea, when associated with ectopia of the lens and pupil and late onset glaucoma, is inherited as an autosomal recessive trait.



MEGALOCORNEA

Q: The condition of enlarged cornea from birth in which the intraocular pressure is not increased is called _____.

A: Megalocornea

34
If an arrest in development occurs in the 4th to 5th month when the corneal curvature usually increases, microcornea may result. The eye is of normal size but the cornea has a diameter of 10 mm. or less. (A small globe with proportionately decreased overall size as well as a small cornea is termed nanophthalmos.) Mann (1957) says that 20% of patients with microcornea develop glaucoma in later life. Inheritance is often autosomal dominant.

Q: An overall small eye is termed _____; whereas a normal size globe with decreased corneal diameter is termed _____.

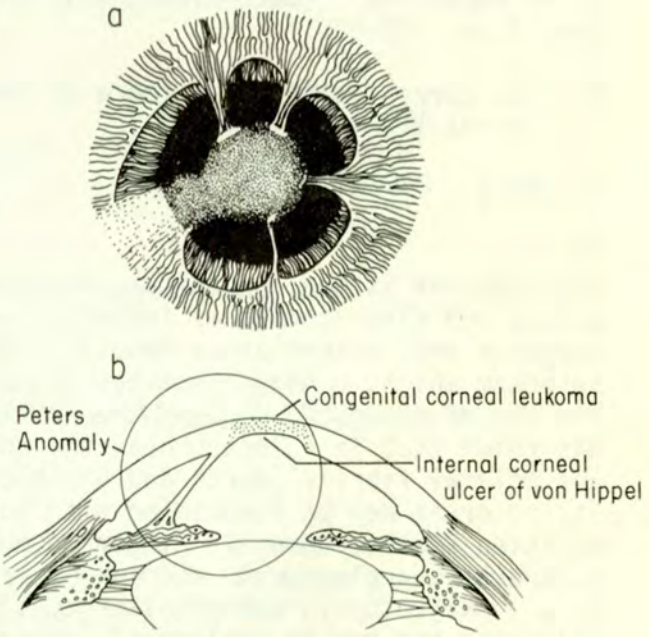
A: Nanophthalmos, microcornea

35
The most common congenital corneal anomalies are those involving an alteration in transparency. These opacities are of two types: inflammatory and developmental. Opacities due to intra-uterine inflammation, including both blood borne and transamniotic infection, are termed inflammatory opacities. Syphilis, smallpox and staphylococcus can be causative agents.

Q: The most common congenital corneal anomalies are related to alteration in _____.

A: Transparency

36 (Read frame #61 first)
Peters anomaly is a congenital corneal opacity with a central defect in stroma, Descemet's membrane and endothelium in association with an iris adhesion (often as a strand). Persistent hyaloid artery, persistent pupillary membrane and mesodermal dysgenesis (or anterior chamber cleavage syndrome) are often present. Anterior polar cataracts are common and glaucoma may occur. One theory presumes Peters anomaly to result from failure of complete separation of the lens vesicle on invagination from surface ectoderm. Such an explanation has often been used to also explain anterior polar cataracts, but it is difficult to imagine a normal fetal lens nucleus, which is usually the case, existing under these circumstances. Processes leading to inter-uterine formation of adhesions (infection or inflammation), defective development of Descemet's membrane, or defective anterior chamber cleavage seem better explanations.



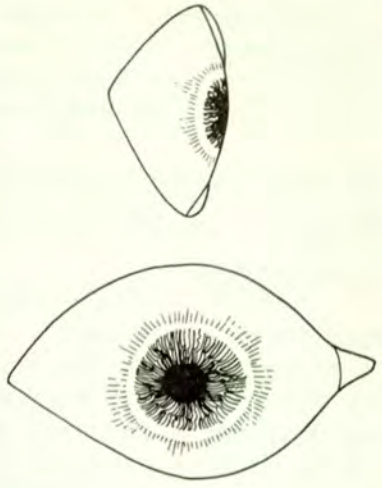
PETERS ANOMALY

a. Front view.
b. Cross section.

Q: In Peters anomaly one sees more frequently (cataract, glaucoma) whereas in Rieger anomaly or syndrome (cataract, glaucoma) is more common.

A: Cataract, glaucoma (although glaucoma must be watched for in both cases)

37
Up to the 4th month of fetal life, the cornea and sclera have the same curvature. If some factor arrests the relative increase in corneal curvature (which normally commences between the 3rd and 4th months), but general growth of the eye continues, cornea plana results. The cornea may be flatter than the sclera and the diameter of clear cornea is usually smaller than normal; usually the cornea-scleral limbus is indistinct (i.e., sclerocornea is usually present). Autosomal dominant and recessive families exist with more severe features in those families felt to be recessive. (Duke-Elder, Vol. III, Part 2, p. 505-508.)



CORNEA PLANA WITH SCLEROCORNEA

Q: The cornea is normally (more or less) convex than the sclera.

A: More

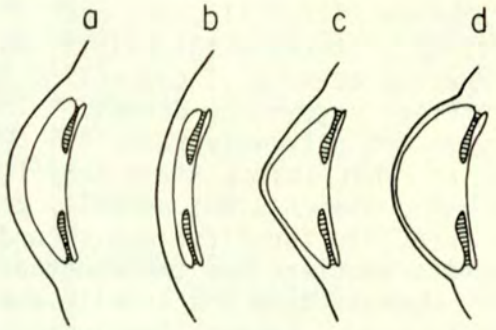
38
Sclerocornea is the congenital condition where the junction between sclera and clear cornea is indistinct or entirely absent. Duke-Elder suggests that sclerocornea results from a disturbance of the paraxial mesoderm which, beginning at the 16-20 mm. stage, normally grows between the rim of the optic cup and the surface ectoderm. Electron microscopy has shown that in sclerocornea, the cornea is a hybrid of both corneal and scleral fibrils (March and Chalkley, Amer. J. Ophth., 78: 54, 1974). Sclerocornea may be associated with cornea plana, other ocular abnormalities (Peters anomaly, Rieger anomaly, colobomata, microphthalmos, cataracts and glaucoma), and non-ocular congenital abnormalities (e.g., polydactyly, Dandy-Walker cyst). The condition is usually bilateral but may be unilateral (Howard and Abrahams, Amer. J. Ophth., 71: 1254, 1971).

Q: The condition where the curvature of the cornea is markedly flatter than normal and approaches that of the sclera is termed _____; whereas, _____ is the term used to describe the condition in which the sclera blends with and encroaches upon the substance of the cornea.

A: Cornea plana, sclerocornea

39

Keratoconus usually develops after birth in early adulthood or late childhood as an increase in the central corneal curvature with stromal thinning. Inheritance is generally thought to be autosomal with both dominant and recessive inheritance reported. Hammerstein (Albrecht von Graefes, Arch. Klin. Ophthalmol., 190: 292-308, 1974) has presented evidence indicating X-linked dominant inheritance. 6% of Down syndrome patients develop keratoconus, often later in life. Keratoconus has been reported often in association with Leber congenital amaurosis. Other syndromes less frequently associated with keratoconus include Ehlers-Danlos, van der Hoeve, Marfan, and Laurence-Moon-Bardet-Biedl syndromes. Keratoglobus is the term used to describe a more diffuse enlargement and thinning of the cornea.



a. NORMAL
b. CORNEA PLANA
c. KERATOCONUS
d. KERATOGLOBUS

Q: Three syndromes which are associated with keratoconus are _____, _____, and _____.

A: Down syndrome, Leber congenital amaurosis, Marfan syndrome, Ehlers-Danlos syndrome, van der Hoeve syndrome or Lawrence-Moon-Bardet-Biedl syndrome (any three).

40

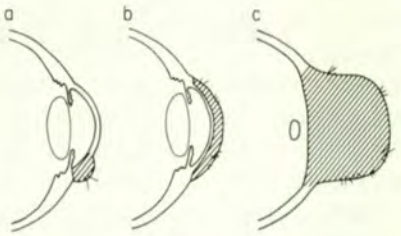
Megalocornea and keratoconus (keratoglobus) result in a deep anterior chamber, while cornea plana and microcornea result in an anterior chamber that is smaller than normal.

Q: _____ and _____ are two anomalies of cornea curvature while _____ and _____ are two anomalies involved with the size of the cornea.

A: Keratoconus, cornea plana, megalocornea, microcornea

41

Ida Mann (1957) classifies corneal dermoids into three types: I, limbal or epibulbar dermoid (most common); II, diffuse superficial corneal dermoid (which resembles sclerocornea clinically, yet easily distinguished histopathologically); and III, complete replacement of the entire cornea and anterior segment by dermoid. The latter two types are extremely rare; all can be classified as choristomas since they represent mesoblastic elements not normally present in the cornea. In the first and second type, Descemet's membrane and the endothelium are normal, whereas they are totally absent in the third type. (Mann: Developmental Abnormalities of the Eye, 1957, p. 357; Henkind, Marinoff, Manas, and Friedman: Amer. J. Ophth., 76: 972, 1973).



CORNEAL DERMOID (after Ida Mann)

a. TYPE I
b. TYPE II
c. TYPE III

Q: Sclerocornea can be differentiated from diffuse corneal dermoid (type 2) by _____.

A: Biopsy (histopathologically).

42

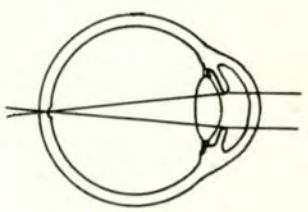
Defects in the curvature of the cornea, known as astigmatism, may result when the radius of curvature in one plane is different from that in another plane. This is so common that it is usually considered normal unless a marked difference in the radii of curvature exists. It is transmitted as an autosomal dominant and may be associated with keratoconus.

Q: A congenital corneal opacity with iris adhesion to a central corneal defect is termed _____; whereas a centrally displaced, thickened Schwalbe's line with iris processes is called _____.

A: Peters anomaly, Axenfeld or Rieger anomaly (or posterior embryotoxon).

43

Emmetropia is the state of refraction of the theoretically normal eye in which parallel rays of light will focus exactly on the retina when the eye is at rest. At birth, the eye is about 66% of its adult diameter and lengthens approximately 8 mm. by general enlargement of the globe.

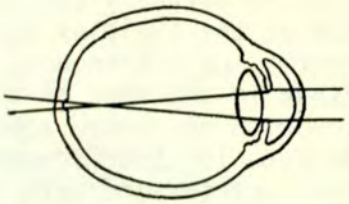


Q: Through what structures does light pass to reach the retina?

A: Cornea, aqueous humor, lens, vitreous

44

When the axial length of the eyeball is greater than normal, the rays of light focus in front of the retina resulting in the condition of myopia or "near-sightedness". This error in refraction can be due to a fault in the cornea, depth of the anterior chamber, refractive power of the lens, or in length of the eye. Lower degrees of myopia appear to be determined by multifactorial inheritance, although dominant transmission has been shown in some pedigrees. High axial myopia is usually autosomal recessive.

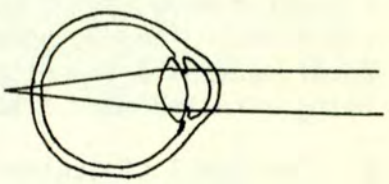


Q: In congenital high myopia, the length of the eyeball is _____ than normal so that light rays focus _____ the retina.

A: Greater, in front of

45

Hyperopia (or hypermetropia) is considered the opposite of myopia and is commonly called "farsight-edness". In axial hyperopia the length of the eyeball is less than normal allowing the rays of light to focus behind the retina. Inheritance, like myopia, is probably multifactorial for lower degrees of hyperopia although some families show autosomal dominant transmission. Autosomal recessive hyperopia, often severe, has been reported.

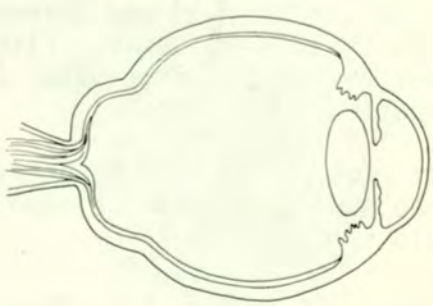


Q: A person with an eye which is shorter than normal has a condition of _____ and can see objects _____ but may have difficulty in seeing _____ objects.

A: Hyperopia, far away or at a distance, near or close

46

An ectasia is a localized dilatation, expansion, or distention of the ocular tunics without initial total discontinuity of the structures. A weakened or bulging area at the posterior pole of the globe, either at the optic disc, macula or both is termed scleral ectasia or posterior staphyloma. It is probably due to a delay in the condensation of the mesoderm in the posterior pole of the globe. Staphyloma or ectasia may also involve the anterior segment of the eyes.



POSTERIOR STAPHYLOMA

Q: A dilatation in the posterior pole of the eye most likely is caused by a defect in _____ _____.

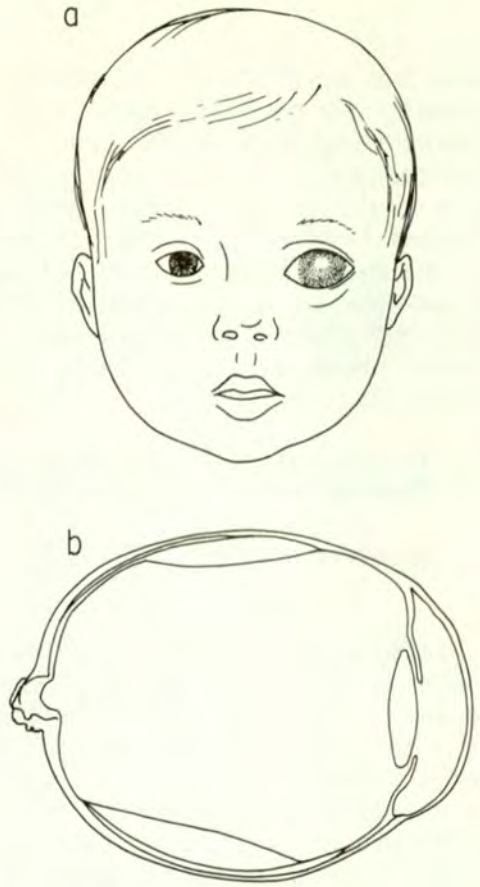
A: Mesodermal condensation.

47

Congenital glaucoma refers to a condition in which there is an increase in intraocular pressure probably due to a defect in development of the angle of the iris. There may be abnormal persistance of embryonic mesodermal tissue in the area of the trabecular meshwork with decreased aqueous outflow. Another theory holds that congenital glaucoma occurs from interference with the normal process of cleavage between the group of cells that represent the anlage of the trabeculum and the base of the iris. Still another theory relates the decreased aqueous outflow to abnormal insertion of the ciliary muscle into the trabecular meshwork (Maumenee, Tr. Amer. Ophth. Soc., 56: 507, 1958; Amer. J. Ophth., 47: 827, 1959). Buphthalmos is the marked distention of the eyeball caused by abnormally high pressure occurring during fetal development or early childhood when the elasticity of the eye is greatest. Congenital glaucoma generally shows autosomal recessive inheritance, with males being affected more often than females.

Q: The canal of Schlemm in early development was a _____.

A: Vein



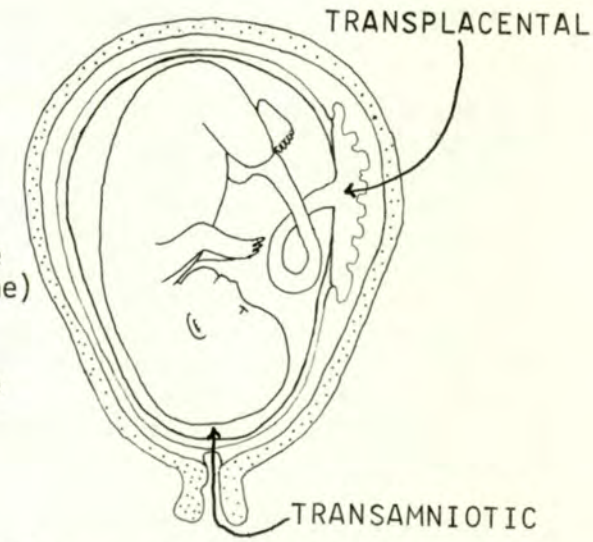
a. BUPHTHALMOS, CLINICAL APPEARANCE
b. BUPHTHALMOS, CROSS SECTION

48

Some organisms appear to be able to penetrate the epithelial adhesions which close the lids when the fetus is in the uterus. Two avenues of infection are transmission across the placental barrier (as in blood-borne virus diseases) and transmission through the amnion itself. Either of these avenues may lead to congenital (intrauterine) conjunctivitis.

Q: At what period in intrauterine life are the eyelids normally closed with adhesions?

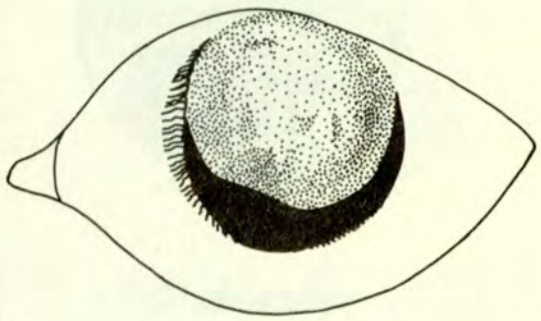
A: About 8th week to 6th month



AVENUES OF INTRA-UTERINE INFECTION: TRANSPLACENTAL OR TRANSAMNIOTIC

49

When the iris is entirely missing, or is represented by tags or a small stump, the condition is termed aniridia. Aniridia is associated with poor vision, strabismus, photophobia, nystagmus, corneal nebulae, ectopia lentis, cataracts, glaucoma, hypoplasia of the optic nerve, and often incomplete macular development. Since the iris and macula are differentiating at the same time, it is theorized that these two defects represent an arrest in the differentiation of the optic cup ectoderm. Another theory for aniridia is primary failure at the 65 to 88 mm. stage when growth of ectoderm anterior to the rim of the optic cup normally forms the iris. Even more attractive is the theory that the defect is related to aberrant development of the paraxial mesoderm at an earlier stage, 20-25 mm. Aniridia is often inherited as a strongly penetrant autosomal dominant trait. When aniridia occurs as a sporadic event and is severe (with other congenital anomalies), there is a significant risk (33%) of a patient developing Wilm's tumor (Fraumeni and Glass, JAMA, 206: 825-828, 1968).



ANIRIDIA WITH SMALL SEGMENT OF IRIS PRESENT NASALLY AND LENS SUBLUXED SUPERIORLY. NOTE COLOBOMA OR NOTCH OF LENS INFERO-NASALLY.

Q: The pigment epithelium of the iris is formed from _____, and the macula develops from _____ germinal tissue.

A: Neural ectoderm, neural ectoderm

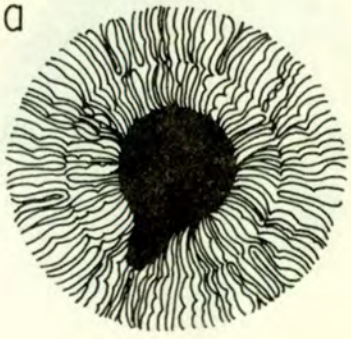
50

A partial iris coloboma is a perforation in all layers of the iris and occurs in three different types: (1) a notch-coloboma, affecting only the pupillary margin (figure a); (2) a hole or holes (pseudo-polycoria) in the iris (figure b); (3) iridodiastasis, a defect located near the periphery of the ciliary margin of the iris (figure c).

Q: A coloboma of the iris could be caused by failure of the _____ fissure to close or to a persistence of the fetal _____ system.

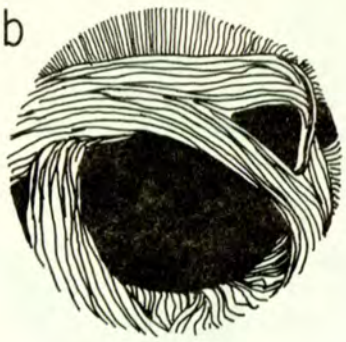
A: Choroidal, arterial (vascular)

a



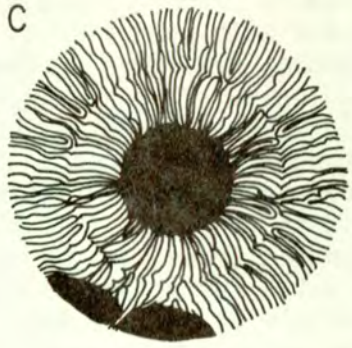
NOTCH-COLOBOMA

b



PSEUDO-POLYCORIA

c



IRIDODIASTASIS

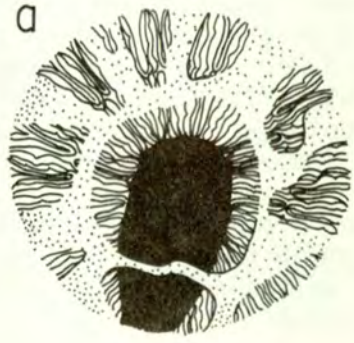
51

An incomplete coloboma of the iris typically involves a defect in one or more, but not all of the layers of the iris. It is considered to be of three types: 1) where both the stroma and pigment layers are defective but with mesodermal tissue from pupillary membrane stretching over the defect (bridge-coloboma); 2) where there is a defect in the stroma but not the pigment layer; 3) where there is a defect in the pigment layer but not in the stroma.

Q: The stroma of the iris is derived from the _____ germinal tissue.

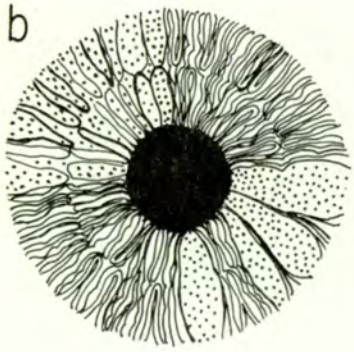
A: Paraxial mesoderm

a



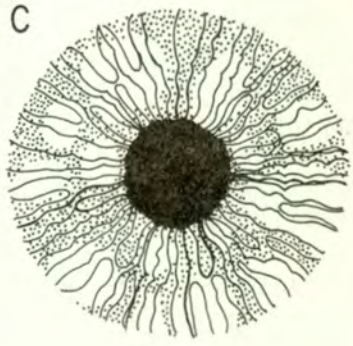
BRIDGE-COLOBOMA

b



STROMAL DEFECT

c

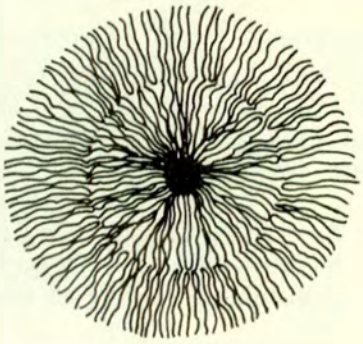


PIGMENT LAYER DEFECT

52
Microcoria (congenital miosis) appears as a small pupil which does not react to light or dilate during accommodation. It is due to an absence of the dilator muscle with the sphincter muscle being normal. This results from an arrest in the last phase of iris ectoderm differentiation, the sphincter muscle having already developed during the 4th to 6th month.

Q: The intrinsic iris muscles of the eye are derived from _____.

A: Neural ectoderm



MICROCORIA

53
The lack of a sphincter muscle as an isolated anomaly is very rare, since a defect in the neural ectoderm at this early stage is usually associated with widespread anomalies.

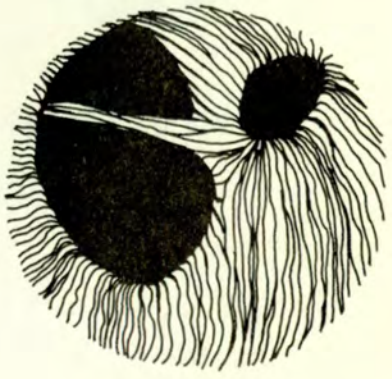
Q: The sphincter muscle is normally differentiated (before or after) _____ that of the dilator muscle.

A: Before

54
A condition in which more than one pupil is present is termed polycoria. Duke-Elder reserves polycoria for an iris hole surrounded by a sphincter. Generally what occurs are holes in the iris without a surrounding sphincter, better termed pseudo-polycoria. Pseudo-polycoria has been inherited as an autosomal dominant trait and may be associated with anterior chamber angle anomalies and glaucoma.

Q: A heterozygote with pseudo-polycoria would transmit the abnormal gene to _____percent of his offspring.

A: 50



PSEUDO-POLYCORIA

55
Anisocoria is the condition in which the pupil of one eye is smaller than the other. A difference of 20% in size is considered significant. Autosomal dominant inheritance is reported.

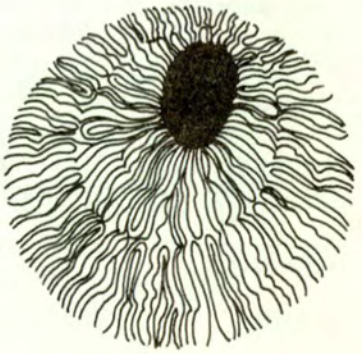
Q: Aniridia in a child, without a family history of similarly affected relatives, demands diligent search for evidence of _____.

A: Wilm's tumor

56
The anomaly of the position of the pupil is called corectopia. A slight deviation in the location of the pupil is common, but occasionally it may be greatly displaced and irregularly shaped. As an isolated defect or in conjunction with heart disease, it may be inherited as a dominant characteristic; recessive inheritance has been reported in association with ectopia lentis.

Q: Corectopia is an anomalous _____ of the pupil.

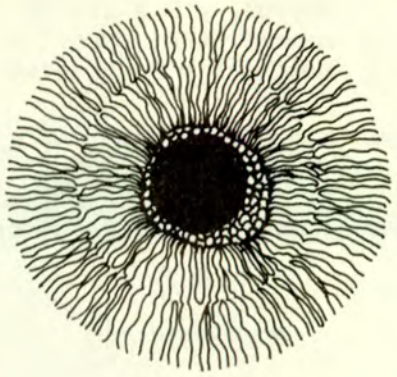
A: Position



CORECTOPIA

57

The pigment epithelium on the posterior aspect of the iris normally forms a double layer which just barely intrudes itself into the pupillary margin as the pigment ruff. This eversion may be accentuated with the pigment layer folding over the anterior surface of the iris. This is thought to result from an imbalance of growth between the mesoderm and ectoderm. The condition has been called ectropion of the uvea, but this is a misnomer, because it affects the retinal pigment epithelial and not the uveal layers of the iris.



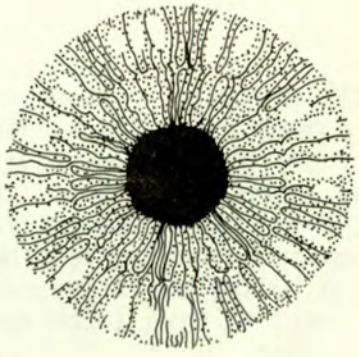
ECTROPION OF PIGMENT BORDER OF IRIS

Q: In ectropion of the uvea the _____ is affected.

A: Pigmented epithelium of the iris

58

In hypoplasia of the iris there is an underdevelopment and a translucency of the stromal tissue. In marked hypoplasia, the ectodermal pigment and sphincter are easily visible. When there is hypoplasia of the peripheral stroma, there may be associated Brushfield spots. Brushfield spots may be seen in 24% of normals, usually peripherally situated; whereas, the spots, as seen in 85% of Down syndrome patients, are commonly in the midzone of the iris. Histologically, Brushfield spots represent aggregates of fibrocytes in the superficial or anterior stromal layer, often with rarefaction beneath or behind this density (Donaldson, Arch. Ophth., 65: 26, 1961).



BRUSHFIELD SPOTS

Q: _____% of normals exhibit Brushfield spots; whereas _____% of Down syndrome patients have this anomaly.

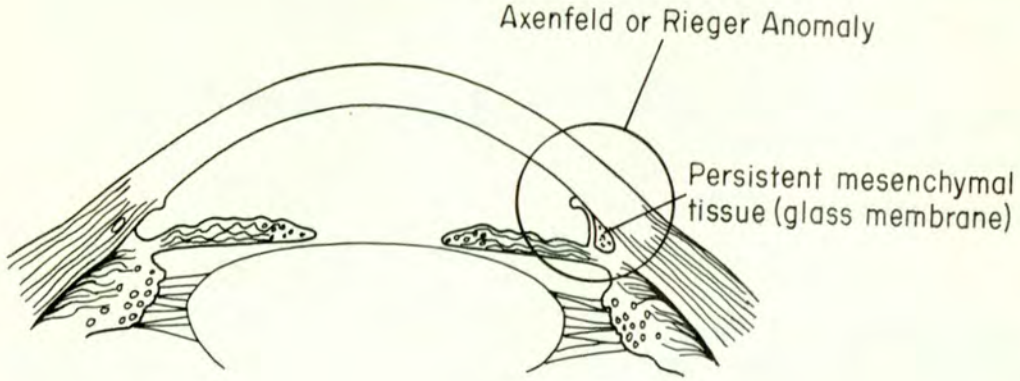
A: 24%, 85%

59

Hypoplasia of the anterior stromal leaf of the iris, prominent iridocorneal processes, and a centrally displaced, thickened Schwalbe's line (posterior embryotoxon) comprise Rieger anomaly, a form of mesodermal dysgenesis frequently associated with glaucoma (see frame 61).

Q: Rieger anomaly consists of _____, _____ and _____.

A: Iris hypoplasia, iridocorneal processes bridging trabeculum, posterior embryotoxon (prominent, often centrally displaced Schwalbe's line).

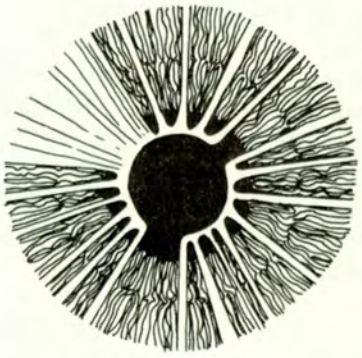


60

Hyperplasia of the iris, more rare, amounts to persistence and thickening or hypertrophy of the superficial mesodermal layer of the iris (the iridic part of the lamina irido-pupillaris), which normally atrophies leaving at most only a thin, wispy pupillary membrane. It is believed to have a dominant mode of transmission.

Q: The pigment cells of the retina are derived from the outer layer of the _____.

A: Optic cup



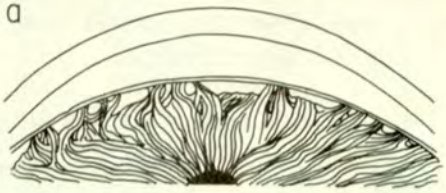
HYPERPLASIA OF IRIS

61 (See frame #59)

Rieger syndrome may represent the more complete expression of the same genetic defect as Rieger or Axenfeld anomaly. The complete syndrome includes hypoplasia of the anterior stromal leaf of the iris, posterior embryotoxon (or increased prominence of Schwalbe's line, often with central displacement), iris strands bridging the angle, dental anomalies (hypodontia, oligodontia or anodontia), and skeletal anomalies (e.g., syndactyly, supernumerary digits, thumb anomalies). Maxillary hypoplasia, small or absent teeth, hypertelorism, strabismus, macrocornea and microcornea have been reported. Pupillary abnormalities (corectopia, pseudopolycoria, ectropion pupillae, and dyscoria) and glaucoma are frequent. Cataracts occur. Inheritance is autosomal dominant with high penetrance (95% according to Alkemade, 1969) but extreme variability of expression. (For further reading see Hoskins and Shaffer, J. Ped. Ophth., 9: 26, 1972; Falkenstein and Henkind, Amer. J. Ophth., 76: 462, 1973; and Henkind, Siegel, and Carr, Arch. Ophth., 73: 810, 1965.)

RIEGER ANOMALY (after A. von Szily)

a



GONIOSCOPIC VIEW

b

FRONT VIEW

Q: If one suspects the diagnosis of Rieger syndrome or mesodermal dysgenesis, one must examine siblings and parents for subtle signs including _____, _____ and _____. Inheritance is _____.

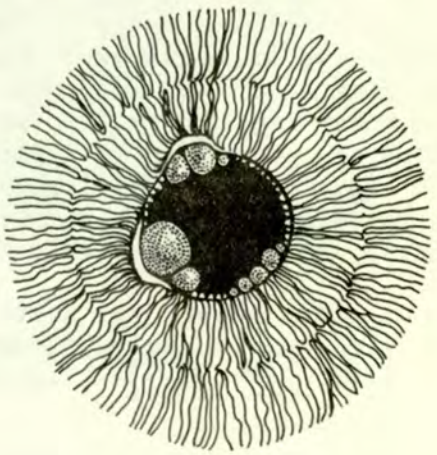
A: Gonioscopic angle anomalies (should also include tonometry), dental anomalies, skeletal anomalies, autosomal dominant

62

Congenital iris cysts are of two types, pigmented and non-pigmented. The pigmented types are thought due to localized dilatations of the marginal sinus which have either become free in the anterior chamber or have insinuated themselves among the stromal fibers. The non-pigmented types are more common, but also more complicated. They vary extensively in size, shape, and location within the iris. How these anomalies develop cannot be stated with certainty at this time.

Q: The increased prominence of Schwalbe's line, often with anterior displacement, is called _____.

A: Posterior embryotoxon (or part of Axenfeld or Rieger anomaly).



PIGMENTED CONGENITAL IRIS CYSTS

63
The most probable cause of a coloboma of the ciliary body in which the defect is limited to the ciliary region is a persistence of the mesoderm associated with the embryonic vascular system. As one would expect, vascularized connective tissue may lay in the floor of the coloboma.

Q: The ciliary body is made up of the _____, _____ and the _____.

A: Ciliary ring, ciliary process, ciliary muscle

64
Atypical coloboma of the choroid occurs at a location other than in line with the choroidal fissure. Several possible causes are: a defect in the ectoderm, such as an accessory cleft in the optic cup; a mesodermal defect; or as the result of an intrauterine inflammation. This is usually inherited as a simple recessive.

Q: What tissues may be involved in a typical coloboma?

A: Any tissues of the eyeball

65
Leber congenital amaurosis (also termed retinal aplasia) is a form of congenital blindness associated with congenital absence of outer retinal elements and extinguished electroretinography. The fundus picture may vary from normal in appearance, to salt-and-pepper retinopathy, to a picture similar to retinitis pigmentosa. Most certainly a heterogeneous group, Leber congenital amaurosis has often been seen in association with other abnormalities such as keratoconus or keratoglobus, posterior lenticonus, subluxated lens, cataract, macular coloboma, deafness, epilepsy, mental and motor retardation and dwarfism (Edwards, Price and Macdonald, Jr., Amer. J. Ophth., 72: 724, 1971). Most often inheritance is autosomal recessive but rare dominant appearing pedigrees exist (Sorsby and Williams, Brit. Med. J., 1: 293, 1960).

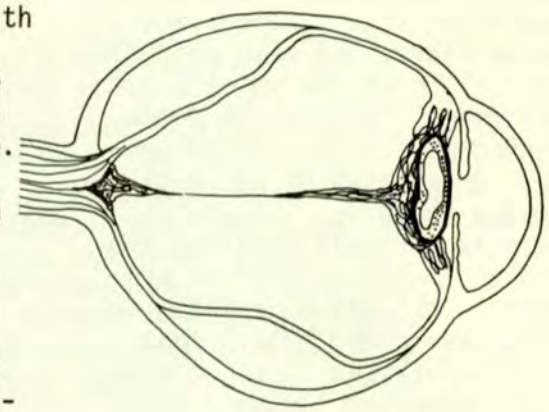
OCULODIGITAL SIGN

Q: A child blind since birth, with wandering nystagmus and oculodigital sign (rubs or pokes fingers into eyes to self-stimulate retina) may have _____. The most important test for this condition is _____.

A: Leber congenital amaurosis, electroretinography

66

Persistent hyperplastic primary vitreous (PHPV) is the term used to designate the condition in which the vascular tunics of the lens and part of the hyaloid system persist and undergo a hyperplastic response, filling the space posterior to the lens with fibrovascular tissue. Since the mass of tissue conforms in position to that of the primary vitreous, the latter is considered a major contributor to the reactive tissue. There appears to be two types of PHPV, an anterior form and a posterior form. In anterior PHPV the lens is often invaded and cataractous and the ciliary processes are drawn into the fibro-vascular mass--a finding of considerable diagnostic importance clinically. The anterior chamber is usually shallow and the chamber angle immature. Glaucoma, often with angle closure, is common. Retinal dysplasia usually is present. PHPV is often seen in colobomatous, microphthalmic or otherwise congenitally deranged eyes.



PERSISTENT HYPERPLASTIC

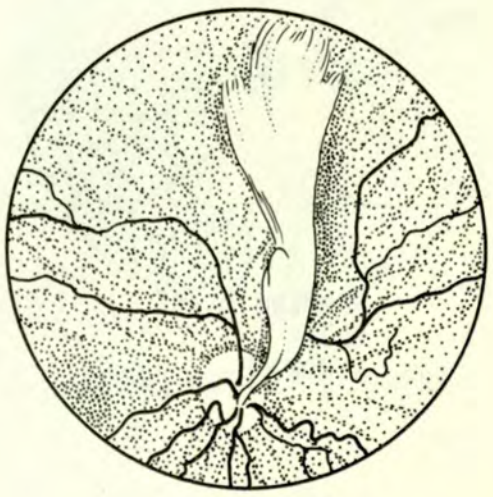
PRIMARY VITREOUS

Q: The best test to differentiate Leber congenital amaurosis from septo-optic dysplasia (or de Morsier syndrome) is _____.

A: Electroretinography

67

Posterior PHPV results from the failure to break down of posterior elements of the primary vitreous and associated branches of the hyaloid artery during the formation of the secondary vitreous, giving rise to a fold of the retina, often with a remnant of the hyaloid artery found in its free edge. This fold is called a falciform retinal fold, and it is usually unilateral. Ida Mann suggested that this anomaly was due to attachment and persistence of hyaloid vessels and primary vitreous to the inner rim of the optic cup. This adhesion, occurring after the 13 mm. stage, prevents the circumferential development of the secondary vitreous.



RETINAL FOLD

Q: Rieger or Axenfeld anomaly consists of _____, _____ and _____.

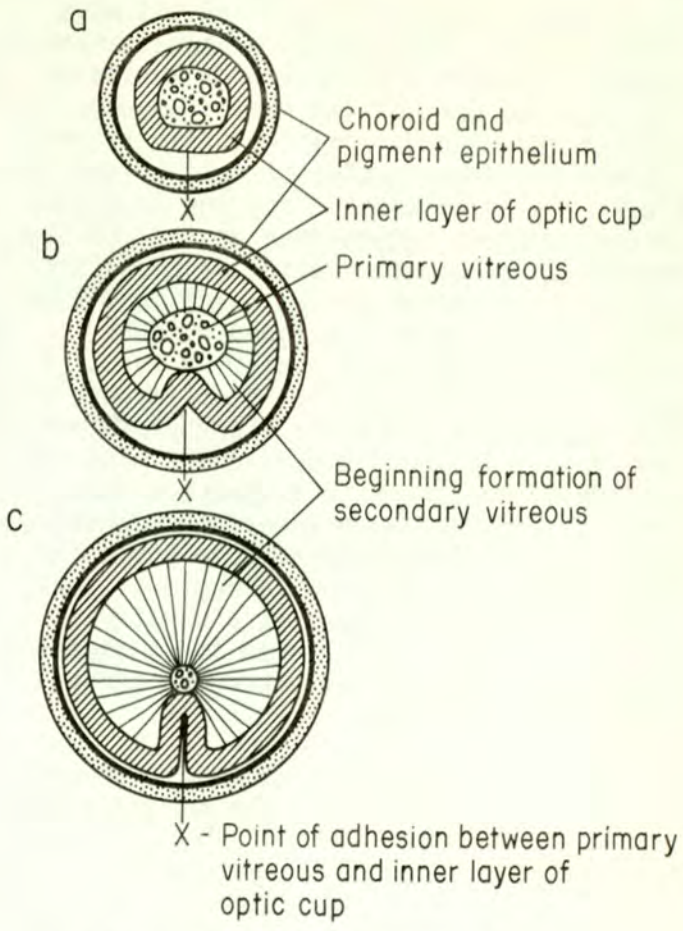
A: Iris hypoplasia, posterior embryotoxon, iridocorneal processes

68

Remnants of the primary vitreous, hyaloid system and/or Bergmeister's papilla may persist and proliferate at the optic nerve head producing the characteristic finding of a white fibroglial mass obscuring the origin of the vessels off the disc. This may be accompanied by a tent-like congenital detachment of the retina around the disc. Vision is usually markedly impaired and often strabismus will be present. This may be related to PHPV and indeed be the same entity referred to as morning glory syndrome (Joseph, Ivry and Oliver, Amer. J. Ophth., 73: 580, 1972).

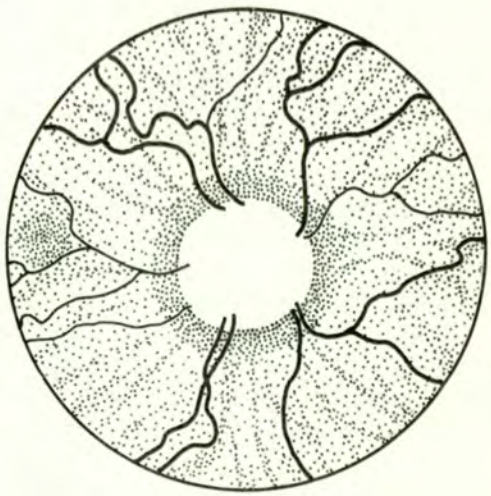
Q: Persistent hyperplastic primary vitreous of the posterior pole presents as an eye with _____, _____ and _____ at the disc.

A: Decreased vision since birth, squint, fibroglial mass



a. 13 MM b. 50 MM c. BIRTH

MORNING GLORY SYNDROME



69

In Part I, you learned of the importance of the expanding secondary vitreous and its role in stimulating the retinal pigment epithelial layer to expand. As you recall, the retina will grow independently of vitreous growth, producing retinal folds if the vitreous fails to do its part, whereas the growth of the retinal pigment epithelium is dependent upon the expansion of the secondary vitreous.

Q: Persistence of the primary vitreous of the posterior pole is often seen in microphthalmic globes, which, because of the independence of the growth of the retina, often have _____.

A: Retinal folds

70

Retinal dysplasia is caused by uncontrolled growth of the inner or outer neuroblastic layers of the developing retina resulting in finger-like projections of retinal cells into the vitreous cavity. Cross sections of the dysplastic retina characteristically show the projections as rosettes made up of cells derived from the inner layer of the optic cup. Attempts have been made to classify retinal dysplasia both clinically and histopathologically (Lahav, Albert and Wyand, Amer. J. Ophth., 75: 648, 1973; Silverstein, Osburn and Prendergast, Amer. J. Ophth., 72: 13, 1971). Rosettes may be environmentally produced as in a vitamin A deficiency or X-ray exposure. Retinal dysplasia is often seen in trisomy 13, Meckel syndrome (MacRae, Howard, Albert and Hsia, Arch. Ophth., 88: 106, 1972), Norrie disease, microphthalmia, and in association with colobomas.

Q: _____ results when the optic vesicle fails to develop.

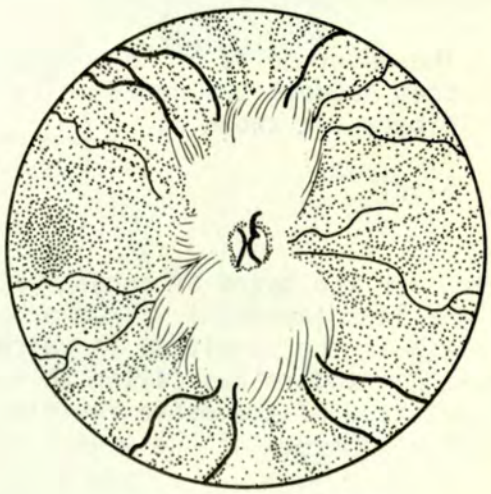
A: Anophthalmos

71

Medullation of the axons of the ganglion cells peripheral to the lamina cribrosa is fairly common and asymptomatic. Since medullation proceeds peripherally from the brain and reaches the lamina cribrosa only at birth, this anomaly develops after birth.

Q: Optic nerve fiber growth begins at the _____ and proceeds to the _____ while medullation of the optic nerve proceeds from the _____ to the _____.

A: Retina, brain, brain, eye



MEDULLATED NERVE FIBERS

72

The macula commonly varies in position. This is presumably due to post-natal environmental influences on growth rates of the various parts. Size and shape show variations on a cellular level.

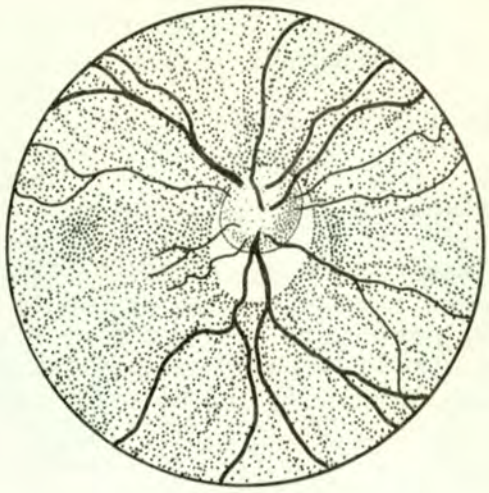
Q: The macula is thought to be hypoplastic in the condition known as _____.

A: Aniridia

73
Congenital crescent (conus) of the optic disc is a white semilunar crescent-shaped exposure of sclera which most commonly lies inferior to the optic disc. The defect seems to be due to a failure in the development of the posterior walls of the optic vesicle around the optic nerve. Tilting of the optic nerve as it enters the eye better explains this anomaly. Partial loss of the visual field (altitudinal defect or scotoma) may accompany the defect.

Q: An obliquity of the intrascleral path of the optic nerve may give rise to a(n) _____.

A: Congenital crescent

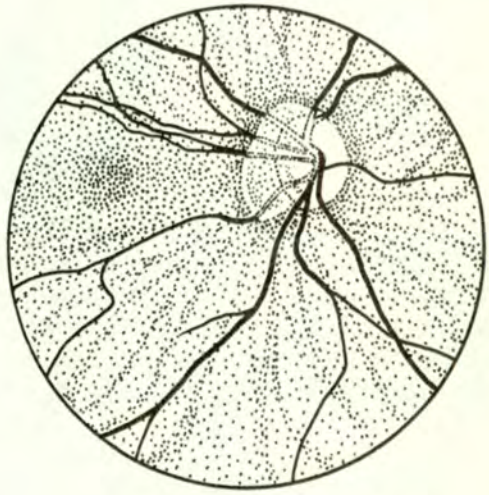


INFERIOR CONGENITAL CONUS

74
Gliotic pre-papillary veils occasionally persist as remnants of the hyaloid vessels with contribution of glial tissue from Bergmeister's papilla. These remnants are harmless, do not affect vision and do not progress or proliferate.

Q: The outer cells of the optic stalk that support the nerve cells and fibers are known as _____ cells.

A: Glial



PRE-PAPILLARY MEMBRANE

75
There are two types of congenital absence of the lens (aphakia). True or primary aphakia is the condition in which the surface ectoderm has failed to react to the stimulation of the optic vesicle, leaving a complete absence of the lens. It is very rare.

Q: Normally the optic vesicle stimulates the _____ to invaginate and form the _____.

A: Lens placode, lens vesicle

76
Apparent or secondary aphakia is characterized by a reabsorption of the lens subsequent to its development. Here, the lens is represented by only a wrinkled capsule which may be partially invaded and destroyed by vascular mesoderm. It is caused by teratogenic agents in the intrauterine environment and is more common that primary aphakia.

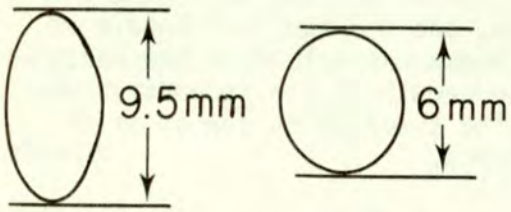
Q: The effect of a teratogenic agent will vary according to the _____ at which it acts upon the embryo.

A: Stage of development

77
Microspherophakia is the term used where the lens is unusually small and spherical in shape. Generally accepted as its cause is an arrest in the development of the lens during the 5th or 6th month when it is normally spherical in shape. It is usually bilateral and opacities are not associated with it. Although it may be sporadic (?recessive) or, more rarely, inherited as a dominant trait, microspherophakia is more commonly seen as part of the Weill-Marchesani syndrome. Spherophakia has been reported also in Marfan syndrome, homocystinuria and hyperlysinemia.

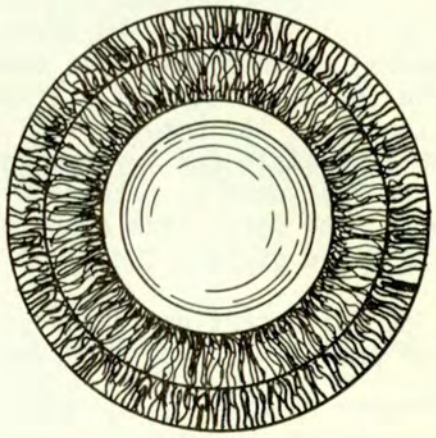
Q: The _____ lens fibers are responsible for the ultimate shape of the lens.

A: Secondary

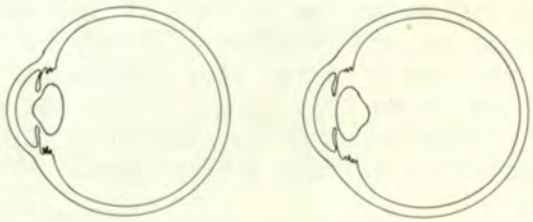


NORMAL LENS

MICROSPHERO-PHAKIA LENS



78
In the conditions called anterior or posterior lenticonus, the anterior or posterior surface of the lens protrudes forming a conical shape. There appears to be a weakness and consequent stretching of the capsule. A polar or subcapsular cataract may be present. Lenticonus occurs more commonly in males than in females and has been reported to occur in Alport syndrome. (Schatz, Amer. J. Ophth., 71:1236, 1971)



ANTERIOR LENTICONUS

POSTERIOR LENTICONUS

Q: Adhesions between the _____ and _____ might be expected to occur in anterior lenticonus.

A: Iris, lens

79
Absence of the ciliary body may be brought about by a defective closure of the anterior part of the choroidal fissure. A subsequent loss of the zonular fibers provides for an unequal pull on the lens capsule producing flattening of a notch on the affected side: a coloboma of the lens. This may also result from a persistence of the tunica vasculosa lentis, with pressure from these vessels causing defective formation of the iris, ciliary body and lens. Some cases are transmitted as an autosomal dominant trait.

Q: The zonular fibers extend from the _____ to the _____.

A: Ciliary body, lens

80
An association of coloboma of the lens with giant retinal tears and retinal detachment has been reported by Hovland et al., Arch. Ophth., 80: 325, 1968. This entity appears to be related to an abnormality of development of the tertiary vitreous occurring during the 3rd or 4th month. Normally the anterior part of the secondary vitreous at about the 48 mm. stage (10th week) insinuates itself between the anterior rim of the optic cup and the lens to form the marginal bundle of Druault (or "faisceau isthmique"). During the 3rd to 4th month the zonules, or the suspensory ligaments of the lens (or tertiary vitreous), form within this area and at the same time the marginal bundle begins to atrophy. If mesoderm persists between the optic cup and the lens, the zonules fail to develop, and the marginal bundle of Druault persists (or any combination of these events), then the lens will be flattened or notched with further growth of the secondary lens fibers. Any persistent adhesions producing traction on the anterior retina could explain the giant retinal tears.

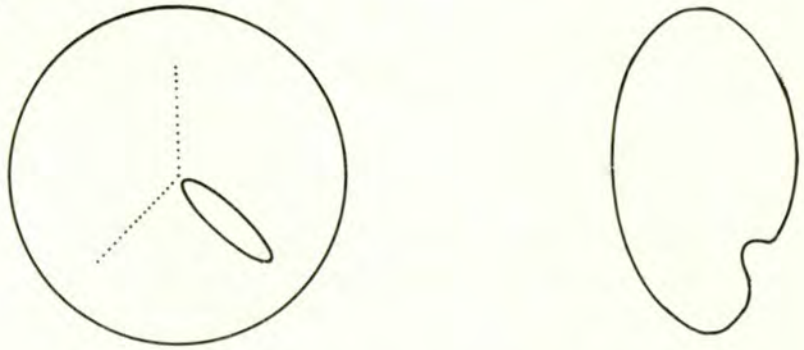
Q: Special attention to the peripheral aspect of the lens in examination of pediatric cases of retinal detachment is necessary to detect _____ of the _____.

A: Coloboma, lens

81
A depression on the surface of the lens is known as an umbilication. It may be due to a failure of a few lens fibers to attain full length so they do not reach the suture. This can occur on either the anterior or posterior surface of the lens.

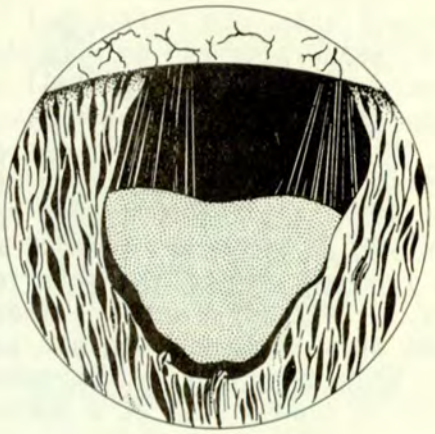
Q: Failure of the _____ lens fibers to reach their full length could cause an umbilication of the lens.

A: Secondary



UMBILICATION OF THE LENS

82
When a defect in the zonule occurs, the lens is apt to be asymmetrical, the lens being displaced in a direction away from the defective segment. Ectopia lentis is common and occurs as (1) an isolated phenomenon; (2) in association with a displaced pupil; and (3) in systemic syndromes along with mesodermal anomalies and skeletal defects (e.g., Marfan syndrome with arachnodactyly and Marchesani syndrome with microphakia and brachymorphia) or aminoacidurias (e.g., homocystinuria and hyperlysinemia). Hereditary tendency is either dominant as in Marfan syndrome or recessive as in homocystinuria and Marchesani syndrome.



LENS COLOBOMA ASSOCIATED WITH ABSENCE OF ZONULAR FIBERS

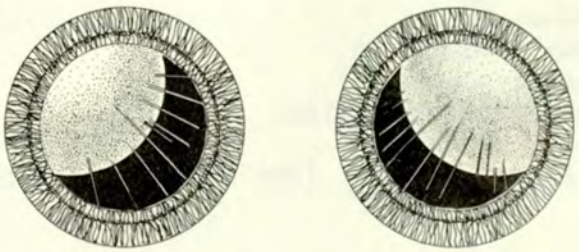
Q: Zonular fibers mark the posterior extent of the _____ chamber.

A: Posterior

83
The ectopic lenses in Marfan syndrome are usually dislocated upward (68%) but may be dislocated in any direction. The ectopic lens in homocystinuria is usually inferior and/or nasal in position. Glaucoma and retinal detachment are the two most difficult ocular complications of these disorders. An excellent review by Cross and Jensen (Amer. J. Ophth., 75: 405, 1973) covers the various features of these two disorders.

Q: Conditions which are associated with ectopia lentis include _____, _____, _____ and _____.

A: Marfan syndrome, Marchesani syndrome, megalocornea, aniridia, corectopia, homocystinuria, (hyperlysinemia--single report) (any order)



MARFAN SYNDROME

HOMOCYSTINURIA

84

Technically, any opacity of the crystalline lens is defined as a cataract. Since the lens grows continually throughout life, almost all cataracts can be considered developmental in origin. We will confine ourselves to those embryologically determined. In all cases, these are aberrations of development rather than arrests. Anterior embryonic cataracts are opacities that consist of a number of small white dots in front or behind the anterior Y-suture. It is believed that these opacities are ill-formed nuclear lens fibers. When hereditarily determined, the trait is transmitted as a dominant.

ANTERIOR EMBRYONIC CATARACTS

Q: The anterior Y-suture is formed by the meeting of the ends of the _____.

A: Secondary lens fibers

85

A sutural cataract is a deposition of a substance along the lines of the Y-shaped sutures of the embryonic lens. Both the anterior and posterior Y-shaped sutures may be affected and the condition is usually bilateral. They produce no symptoms and do not reduce visual acuity markedly. It is possible that sutural cataracts result from an excess amount of the cement substance which is normally present between the ends of the lens fibers in the sutures. Inheritance is usually autosomal dominant. In families showing X-linked inheritance, the hemizygous affected males have nuclear cataracts which may progress to maturity, whereas the heterozygous carrier females have only sutural opacities.

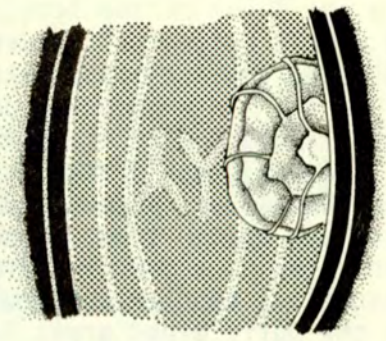
SUTURAL CATARACTS

Q: Continued growth of the _____ lens fibers causes obliteration of the lens vesicle.

A: Primary

86

Anterior polar cataracts, small opacities situated centrally at the anterior pole of the lens, are allegedly attributed to an abnormality of separation of the lens vesicle from surface ectoderm. However, the embryonic nucleus is invariably clear and most likely only secondary fibers are affected. Another theory suggests that the opacities are due to secondary changes in the lens epithelial cells of the lens capsule. Still another theory relates anterior polar cataracts to incomplete resolution of blood vessels and mesoderm present in front of the lens. This latter theory might explain the often associated finding of attachments of the anterior lens to persistent pupillary membrane remnants. Posterior polar cataracts are often associated with persistence of part of the hyaloid system and/or primary vitreous.



ANTERIOR POLAR CATARACT

Q: In Marfan syndrome the lens usually is dislocated _____; whereas in homocystinuria the lens is usually dislocated _____.

A: Upward (or superiorly), downward (or inferior-nasally)

87

Congenital pulverulent nuclear cataract is a lens opacity affecting only the embryonic nucleus. Tiny punctate whitish dots are scattered throughout the embryonic nucleus especially its more peripheral aspect. This cataract is inherited as an autosomal dominant trait.

Q: Primary lens fibers give rise to a lens which is _____ in shape.

A: Spherical

88

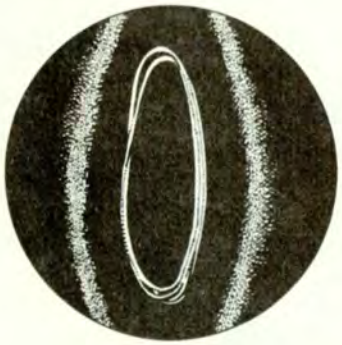
A lamellar or zonular cataract is a condition in which the opacity is limited to one layer of the lens. This form of cataract accounts for about 40% of all congenital cataracts. The cataract consists of hundreds of minute white dot-like opacities arranged in one or more concentric layers or zones. This occurs because the causitive agent produces opacification only during the period in which the lens fibers are actively growing. The influence of the agent may then cease and normal lens fibers are formed thereafter, although the causative factor may act again to produce another opaque zone. Zonular cataracts, when familial, are almost always inherited as a dominant trait. One form of congenital cataract, called congenital zonular pulverulent cataract, is believed to be closely linked to the Duffy blood group locus (Renwick and Lawler, Ann. Hum. Genet., 27: 67, 1963). Through recently detected linkage between the Duffy blood group locus and a heritable structural abnormality of chromosome 1, originally called Uncoiler 1 but now referred to as 1qh+, the locus for this form of cataract has been assigned to chromosome number 1. (Donahue, Bias, Renwidk and McKusick, Proc. Natl. Acad. Sci. U.S.A., 61: 949, 1968.)

Q: Secondary lens fibers are formed by _____ cells.

A: Cuboidal

ZONULAR CATARACT

FRONT



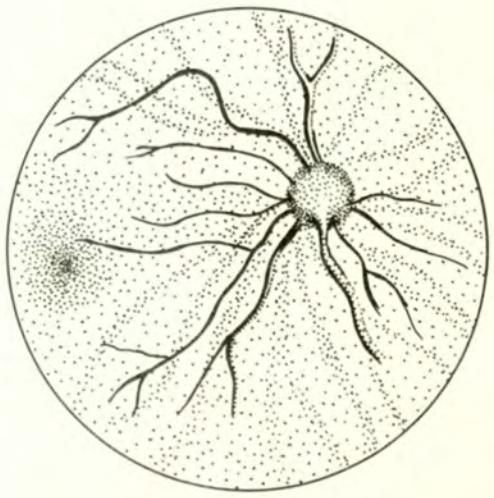
BIOMICROSCOPY

89

It is quite common for some portion of the otherwise transient vascular system to persist as either patent blood vessels or strands of tissue. This type of anomaly is considered as a failure to atrophy due to a temporary arrest during development. Such a factor may act in the 3rd month leaving a part of the vascular tunic of the lens, or during the 6th to 7th month when the hyaloid artery and pupillary membrane normally involute.

Q: If the hyaloid artery atrophies normally, the only remnant in the adult is the _____ (_____ canal).

A: Central canal of the vitreous (Clocquet's canal)



PERSISTENT HYALOID ARTERY

90

Although it rarely remains in its entirety, one of the most common developmental anomalies of the human eye is a persistence of part of the central hyaloid artery. When the nerve layer fibers turn the corner at the site of the future optic disc to grow into the optic stalk, they pinch off a cone shaped mass of ectodermal glial cells which forms the primitive epithelial papilla. This mass of glial cells contributes the proximal sheath of the intravitreal portion of the hyaloid artery. Complete atrophy of a previously large cone of glial cells may result in a large physiologic disc cup. Failure of the glial tissue surrounding the hyaloid artery to atrophy gives rise to a plug of neuroepithelial tissue on the optic disc known as Bergmeister's papilla.

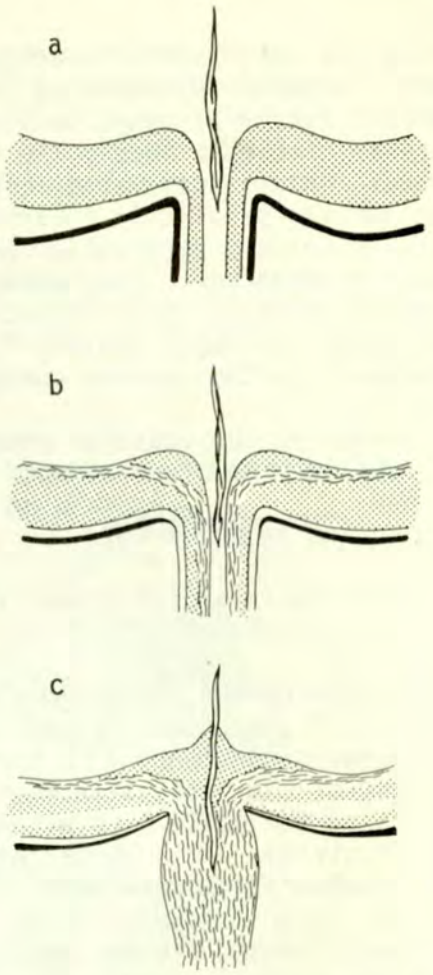
Q: Bergmeister's papilla is composed of tissue from the _____ germ layer.

A: Neural ectoderm

a. PRIMITIVE EPITHELIAL PAPILLA (P.E.P.)

b. NERVE FIBERS CUT OFF PART OF P.E.P.

c. BERGMEISTER'S PAPILLA LEFT AS REMNANT OF P.E.P.



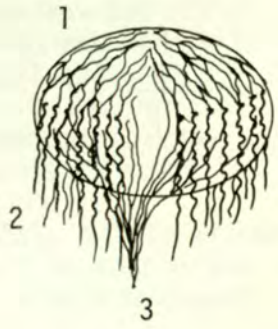
FORMATION OF BERGMEISTER'S PAPILLA (after Ida Mann)

91

The hyaloid system is, from the 40 to 60 mm. stage, at its greatest degree of development and from this point on, begins to atrophy and involute. The development and prominence of the tunica vasculosa lentis closely parallels that of the hyaloid system. At the 60 mm. stage the smallest peripheral branches of the vasa hyaloidea propria begin to involute, at first proximally. They attenuate, separate and contract in a characteristic corkscrew fashion, and are left hanging distally from the posterior aspect of the lens. By 8.5 months these vessels have almost completely atrophied and only occasionally persist after birth as fine strands known as muscae volitantes.

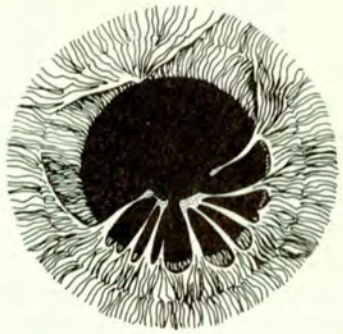
Q: The physiologic cup of the optic disc results from complete atrophy of the cone of glial cells known as the _____.

A: Primitive epithelial papilla



BEGINNING ATROPHY OF VASA HYALOIDEA PROPRIA (after Duke-Elder)
1 anterior vascular capsule.
2 vasa hyaloidea propria.
3 main trunk of hyaloid

92
During the 6th month of development the central arcades that make up the pupillary membrane partly atrophy, leaving the minor vascular circle to supply the iris. These arcades and the associated mesodermal membrane may persist in a variety of forms that are collectively called persistent pupillary membrane. They appear as non-pigmented strands of obliterated vessels that cross the pupil and may find secondary attachment to the lens or cornea.

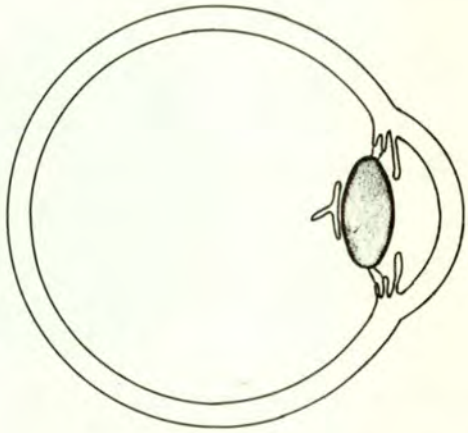


PERSISTENT PUPILLARY MEMBRANE

Q: Normally, the vascular arcades of the pupillary membrane atrophy leaving the _____ circle on the anterior surface of the iris.

A: Minor vascular (or lesser vascular)

93
During development the hyaloid artery ramifies in the posterior part of the tunica vasculosa lentis. A persisting tiny fragment of the fetal attachment commonly adheres to the adult lens without impairment of vision. This is called Mittendorf's dot. However, abnormal lens fiber development may occur secondary to an abnormally prominent remnant and may result in posterior polar cataract. If the mass contracts after birth, a tear in the lens capsule, if associated with a patent hyaloid vessel, may result leading to intralental hemorrhage and blindness.



Q: In the adult, the vessels which are contained within the optic nerve are the _____ and its vein.

A: Central artery of the retina

94
Random fragments of the hyaloid arterial system and small bits of retinal tissue from the region of the ora serrata are seen by ophthalmologists as causes of vitreous floaters. These are seen by patients as "spots before the eyes".

Q: Vitreous floaters may be caused by fragments of the _____ or _____.

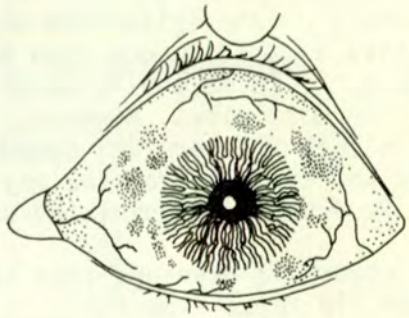
A: Hyaloid vessels, retina

95
Branching anomalies depend upon the level within the optic nerve at which the central vessels divide. Normally two large ones emerge, but anomalously several secondary vessels may occur. Occasionally, the inferior quadrant of the retina may be supplied by a superior vessel, either artery or vein. In addition, many types of crossing-over occur.

Q: The hyaloid artery originally gained entrance into the eye via the _____.

A: Choroidal fissure

96
Melanosis bulbi is characterized by greatly increased pigmentation of the uveal tract and scattered pigment throughout the sclera. It generally occurs in individuals who are otherwise heavily pigmented. In those cases in which a hereditary tendency exists, the most common mode of transmission is dominant (with relatively weak penetrance). The function of the eye is not impaired.



MELANOSIS BULBI

Q: Lens coloboma can be seen in _____, _____ and _____.

A: Ectopia lentis (e.g., Marfan syndrome), coloboma of the ciliary body, as an autosomal dominant trait, or in association with giant retinal tears with detachment (any three).

97
Oculo-cutaneous albinism involves the pigmentation of the entire body, and in the eye interferes with the mesodermal and ectodermal pigments. It is due to interference with the body's ability to produce melanin and in certain cases, there appears to be an insufficient amount of a specific enzyme, tyrosinase. Others appear to possess tyrosinase and are termed "tyrosinase-positive". Associated with decreased pigmentation is retarded growth of the choroid, macula, and iris. The individual has nystagmus and poor visual acuity. Oculo-cutaneous albinism is an autosomal recessive trait. A different form of albinism, limited to the eye, is ocular albinism which is an X-linked intermediate trait.

Q: In autosomal recessive transmission, two normal parents would need to be _____ to have an affected child.

A: Heterozygous

98
Simple heterochromia is a condition in which one eye is blue and the other is brown. It is considered to be an arrest in development of iris pigmentation and in some cases has been related to a birth injury of the cervical sympathetics on the side of the blue eye. In some families heterochromia iridis appears as a dominantly inherited trait.

Q: Eye color is determined by the (amount or character) _____ of pigment found in the _____ layer of the iris.

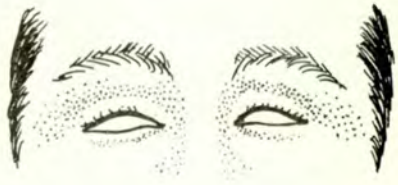
A: Amount, stromal

99
A complete failure of the lid folds characterizes cryptophthalmos (ablepharon). The epithelium which normally forms the cornea and conjunctiva is transformed into skin and is therefore continuous over the eye. It is a rare condition which may have many different causes. In most cases, however, there is a failure or slowing of growth in both the paraxial mesoderm and the maxillary processes. The lids and conjunctival sac may fail entirely to form. Cryptophthalmos is probably transmitted as a recessive.

Q: The upper lid develops from the _____ mesoderm while the lower lid forms from the _____ process.

A: Paraxial, maxillary

100
Microblepharon is a condition where the lids are shortened in their vertical measurements during development. The eyelids are, therefore, not quite long enough to close in sleep. This may result from a failure in growth.

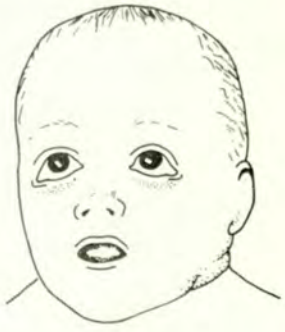


MICROBLEPHARON

Q: By the 9th week, the eyelids normally are completely _____. The eyelid adhesions begin to break down in the 6th to 7th month.

A: Fused

101
Euryblepharon is the condition in which there is congenital symmetrical enlargement horizontally of the palpebral fissures. Considerable racial and individual variation exists but the usual adult palpebral dimensions are 28-30 mm. by 12-14 mm. Patients with familial euryblepharon may have palpebral fissures 35 to 40 mm. in horizontal width (or length).



EURYBLEPHARON

Q: _____ is the condition where the eyelids are short in their vertical dimension; whereas _____ is the name applicable to excessively wide palpebral fissures.

A: Microblepharon, euryblepharon

102

Congenital blepharophimosis relates to a general diminution of palpebral fissure dimensions in both horizontal and vertical directions. An autosomal dominant trait, blepharophimosis is often associated with blepharoptosis and epicanthus inversus and may rarely be associated with other congenital anomalies.

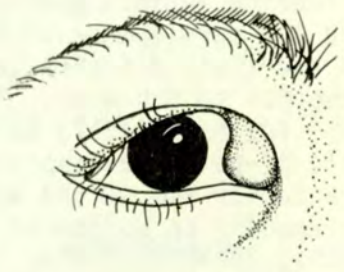
Q: A patient with bilateral ptosis and lid fissures measuring 8 mm. in length by 3 mm. in height has the condition _____ which is inherited as a(n) _____ trait.

A: Blepharophimosis (with ptosis), autosomal dominant

BLEPHAROPHIMOSIS

103

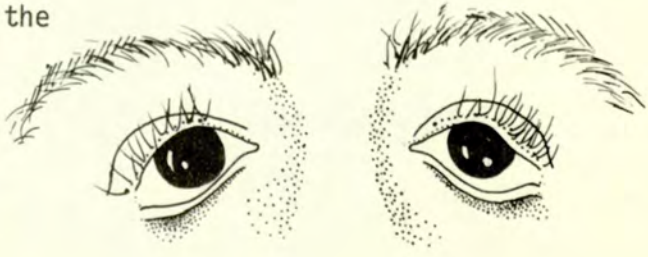
Notches of various sizes in the eyelids are called colobomas of the lids. According to Mann, the defect in the upper lid is usually between the inner and middle third of the lid, whereas in the lower lid, the defect is located between the middle and outer third of the lid. Milder forms may represent the result of failure of mesodermal folds to fuse completely during development. Other possible mechanisms are failure of primary adhesion of the developing eyelids (normally almost complete by 2nd month) or premature separation of the lids prior to the 5th to 7th month with lag or differential growth. Since lash, tarsal and marginal differentiation takes place while the lids are fused, this would explain the absence of these structures in the region of the defect. Palpebral colobomata are often associated with coloboma of uveal tract or microphthalmia.



UPPER LID COLOBOMA

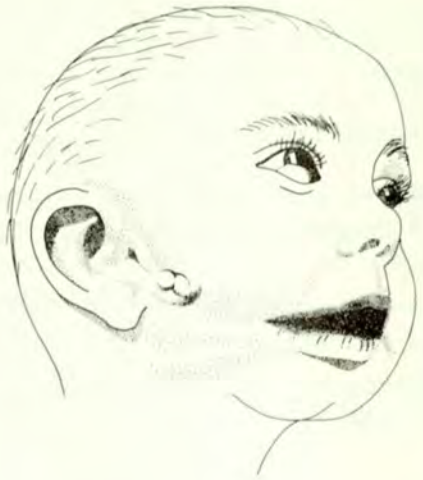
Q: Can a coloboma of the lid be called typical or atypical? Why?

A: No, not related in any way to the choroidal fissure



BILATERAL LOWER LID COLOBOMA

Epibulbar dermoids and/or subconjunctival lipodermoids, often bilateral and usually temporal, are manifestations of Goldenhar syndrome (or oculoauriculovertebral dysplasia). This clinical entity, which is sporadic and nonfamilial, is probably related to faulty development of the first and second branchial arches and the first branchial cleft. Colobomata of the upper eyelid often overlie the epibulbar tumor and the palpebral fissures may show a mild anti-mongoloid slant. Pre-auricular tags are constant and conduction deafness, other ear anomalies, facial asymmetry, macrostomia, micrognathia, and vertebral anomalies are often present. Anophthalmia, microphthalmia, microcornea, Duane syndrome and congenital cystic eye as well as iris atrophy, uveal colobomata, cataract and optic atrophy have been reported. Hemifacial microsomia, cleft palate, seizure disorder, congenital heart disease, and mental retardation may be seen as part of Goldenhar syndrome. The time of embryonic insult leading to this entity is most likely during the development of the branchial arches and their differentiation into face, ears and eyelids, i.e., from the 6th to 8th week. The vertebral anomalies arise during the 5th week. Ida Mann (1957) believed that the epibulbar tumors arise from pleuri-potential embryonic tissue located in the region between the anterior rim of the optic cup and the surface ectoderm. (For further reading on Goldenhar syndrome see Baum and Feingold, Amer. J. Ophth., 75: 250, 1973). Epibulbar dermoids have also been seen in median cleft face syndrome.



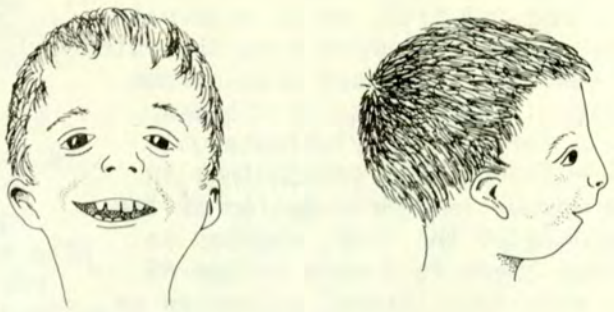
GOLDENHAR SYNDROME

Q: Anomalies of the ear, eye (epibulbar dermoids) and vertebrae are the major features of _____ syndrome.

A: Goldenhar (or oculoauriculovertebral dysplasia)

105

Differentiation should be made between Goldenhar syndrome and Treacher Collins syndrome (or mandibulofacial dysostosis). This latter syndrome also includes antimongoloid palpebral slant (often of large degree), colobomata of the lower outer third of the lower lid (present in 75% of cases), absent lower lacrimal puncta, hypoplasia of malar bones and zygomatic arches, prominent nose, abnormal pinna, pre-auricular skin tags, blind fistulas between ears and mouth, micrognathia and occasionally uveal coloboma. Colobomas of the upper lid, epibulbar dermoids, and vertebral anomalies are absent in Treacher Collins syndrome whereas they are prominent features in Goldenhar syndrome (Gorlin and Pindborg, 1964). Inheritance in Treacher Collins is autosomal dominant with high penetrance but variable expressivity, whereas the vast majority of patients with Goldenhar syndrome have been sporadic.



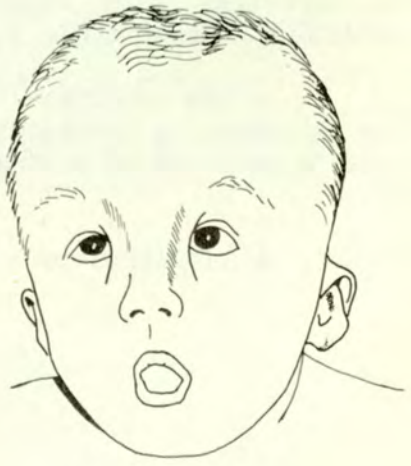
TREACHER COLLINS SYNDROME

Q: Colobomata usually involve the upper eyelids (rarely the lower) in _____ syndrome, whereas only lower eyelid colobomata are seen in _____ syndrome.

A: Goldenhar, Treacher Collins

106

Epicanthus is the condition in which a continuous fold of skin stretches along the side of the bridge of the nose partially hiding the inner canthus. The three known types are characterized on the basis of the origin of the skin fold on the upper end: 1) epicanthus superciliaris, 2) epicanthus palpebralis, 3) epicanthus tarsalis (see Duke-Elder, Vol. III, Part 2, p. 851-3). The condition usually occurs bilaterally and shows a strong hereditary tendence as a dominant trait.



EPICANTHAL FOLDS

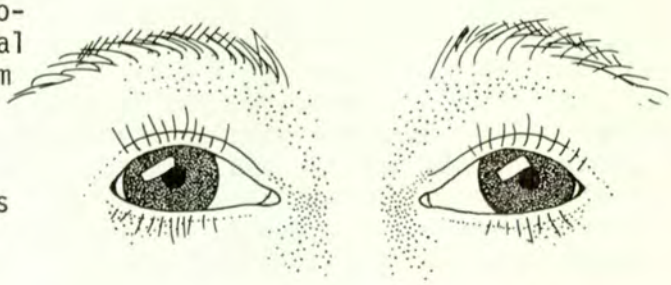
Q: The _____ germinal tissue forms the naso-lacrimal ducts.

A: Surface ectoderm

107

Internal ankyloblepharon is characterized by a union of the lids from the inner canthus outwards, while external ankyloblepharon is a union from the outer canthus inwards. They are true unions with connective and vascular tissues enclosed. Internal ankyloblepharon is differentiated from telecanthus in that the former is simply fusion of the nasal aspects of the lids, whereas in telecanthus there is a wide bridge of the nose with true lateral extension or displacement of the medial canthi. External ankyloblepharon similarly should not be confused with blepharophimosis. Both internal and external ankyloblepharon probably result from faulty or incomplete lid separation in the 6th or 7th month.

INTERNAL ANKYLOBLEPHARON



EXTERNAL ANKYLOBLEPHARON

Q: Normal separation of the eyelids is completed shortly before _____.

A: Birth

108

Internal ankyloblepharon plus lateral displacement of the lacrimal puncti are seen as part of the blepharo-naso-facial syndrome (Putterman, Pashayan, and Pruzansky, Amer. J. Ophth., 76: 825, 1973). Other features include lacrimal drainage obstruction, telecanthus, mask-like facies, bulky nose, torsion dystonia, and mental retardation. Inheritance is autosomal dominant.

Q: _____ is the condition in which the inner canthi position is laterally displaced; whereas _____ is the term used to describe an abnormal union of the palpebral fissures.

A: Telecanthus, ankyloblepharon

109
When there is an inability to raise the upper lid, congenital ptosis exists. It usually occurs alone, but occasionally (3.5%, according to Berke, Arch. Ophth., 41: 188, 1949) is associated with blepharophimosis or epicanthus. Two main causes are known: (1) congenital anomalies (aplasia, hypoplasia and abnormal insertions) of the levator palpebrae superioris (occasionally with associated hypoplasia of part of the superior rectus muscles), or (2) paralysis of the levator or levator and external eye muscles due to a lesion at the base of the brain. Isolated ptosis is usually transmitted as a dominant characteristic. When combined with epicanthus, males predominate those affected almost 2 to 1; however, male to male transmission exists even in these families, essentially precluding X-linked inheritance.

UNILATERAL PTOSIS OF RIGHT UPPER LID

Q: A drooping eyelid may be caused by a congenital anomaly of the _____ muscle or abnormal _____ of the levator or external muscles of the eye.

A: Levator palpebrae superioris, innervation

110
A number of apparently unconnected characteristics which are expressed concurrently to form a composite clinical picture is termed a syndrome. Some of these are due to the body's inability to synthesize a specific enzyme, e.g., the so-called inborn errors of metabolism. These often have manifestations in ocular structures.

Q: One form of oculo-cutaneous albinism is caused by an inability to form the enzyme _____ which hinders _____ production throughout the body.

A: Tyrosinase, melanin

111
The three cardinal manifestations of Van der Hoeve syndrome (osteogenesis imperfecta) are blue sclera, brittle bones, and deafness. Corneal thickness is decreased and keratoconus has been reported. This mesodermal disorder is usually sporadic but occasionally inherited as a recessive trait.

Q: Can blue sclera be normal at birth? Yes ( ) No ( )

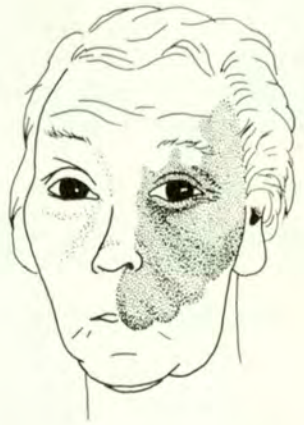
A: Yes

112
Marfan syndrome (arachnodactyly) is a mesodermal tissue disturbance which is widespread throughout the body. The urine contains abnormal amounts of hydroxyproline, suggesting a defect in the production of collagen. The zonular fibers are weakened and subluxation of the lenses occurs in about 80% of all patients with the syndrome. It is further characterized by flaccid musculature, relaxed joints, long slender bones, minimal subcutaneous fat, kyphoscoliosis, and sternal deformities. Cardiovascular complications (aortic dilatation, dissecting aneurysm and mitral regurgitation) may be life-threatening.

Q: Van der Hoeve syndrome is characterized by _____, _____ and _____.

A: Blue sclera, brittle bones, deafness

113
Sturge-Weber syndrome (encephalo-[oculo]-facial angiomatosis) is characterized by a capillary nevus that affects the skin of the face as well as may affect the mucosa of the lids, mouth and pharynx. The nevus usually covers a segment of the distribution of the trigeminal nerve but always involves the forehead and the upper eyelid (Duke-Elder, 1964). Almost invariably present is an ipsilateral leptomeningeal angioma which becomes progressively calcified with age. Although by no means invariable, ocular manifestations occur frequently, most commonly choroidal angioma but including dilated episcleral and retinal vessels. Congenital or late onset glaucoma occurs often, with greater frequency and severity on the same side as the nevus. This entity appears to result from maldevelopment at an early stage when the vascular system of the head is represented by a plexiform arrangement of vessels.



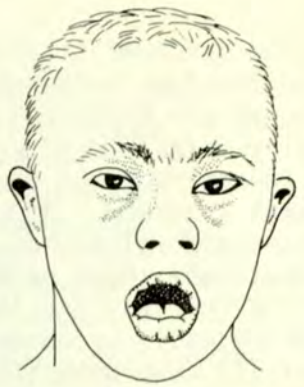
STURGE-WEBER SYNDROME

Q: The lenses are subluxed in Marfan syndrome because the zonular fibers are weakened due to a defect in _____production.

A: Collagen

114

Though there is no single diagnostic feature to Down syndrome (mongolism), there are certain features peculiar to the eye. The palpebral aperture is short, wide and set obliquely up and outward, which is different from that of Mongolian races who have long and narrow apertures. In Down syndrome the greatest vertical dimension of the palpebral fissures is at the middle of the upper lid, in comparison to the junction of the inner and middle third of the upper lid in normals. Frequently the epicanthal folds are exaggerated. The iris is covered with gold or white speckles known as Brushfield spots (seen in 85%). Often cataracts are present. Other ocular associations include myopia, strabismus, keratoconus, nystagmus and an increased number of vessels radiating off the disc (Williams, McCormick and Tischler, Arch. Ophth., 89:269, 1973). Down syndrome patients exhibit increased sensitivity to atropine, both systemically and topically. Down syndrome may be caused by two mechanisms of chromosomal aberrations, non-disjunction, producing trisomy of chromosome 21 or through unbalanced translocation, producing duplication of chromosome 21. (For details see Krill's Syllabus of Genetics or M. Goldberg, Genetic and Metabolic Eye Disease, 1974, p. 540.)



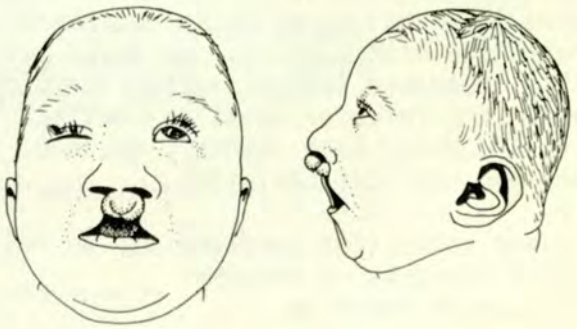
DOWN SYNDROME

Q: In Down syndrome caused by an unbalanced translocation between chromosomes No. 14 and No. 21, one of the parents may carry a balanced translocation involving part of _____ transferred onto _____.

A: Chromosome 21, chromosome 14

115

Of the three major trisomy syndromes, trisomy 13 has by far the most frequent and most severe eye abnormalities. Ocular abnormalities are nearly constant in this syndrome and include uveal colobomas (often containing cartilage histologically), optic nerve colobomas, microphthalmos, clinical anophthalmos, cyclopia, arhinencephaly or holoprosencephaly (with extreme hypotelorism), immature anterior chamber angles, sclerocornea, cataract, persistent hyperplastic primary vitreous, persistent tunica vasculosa lentis, congenital nonattachment of retina, falciform retinal fold, and retinal dysplasia.



TRISOMY 13 SYNDROME

Q: Brushfield spots are seen in approximately _____ percent of Down syndrome patients; whereas about _____ percent of normals show this finding.

A: 85%, 24%

116
Moebius syndrome is another congenital syndrome with wide variations in expression, although for the ophthalmologist the most important features are bilateral nuclear palsies of 6th and 7th cranial nerves, usually with lateral gaze palsy and esotropia. Duane retraction (or co-contraction) syndrome has been reported in association with Moebius syndrome. Atrophy of a portion of the tongue is often present and related to hypoplasia of the hypoglossal nuclei. Some studies have shown on histopathology normal facial nerve and its nucleus; others have shown either absence of facial muscles histopathologically or abnormal facial muscle activity on electromyography. About 1/3 have associated limb, facial or skeletal anomalies and autosomal dominant inheritance is suggested in certain familial cases.

Q: Moebius syndrome involves congenital nuclear _____ and _____ cranial nerve palsies often in association with other _____.

A: Facial, abducens, congenital anomalies

117
Duane retraction syndrome is a congenital incomitant form of strabismus where there exists limitation of duction (abduction +/or adduction) with retraction of the globe on movement opposite (adduction or abduction, respectively). Most likely a heterogeneous group of entities, Duane retraction syndrome has been explained by 1) mechanisms based on structurally abnormal muscles with fibrosis and by 2) mechanisms based on abnormal innervation, the most prevalent theory evoking hypoplasia of the 6th cranial nerve nucleus, with abnormal innervation of the lateral rectus. Electromyography has shown abnormal innervation in certain patients. The most usual finding is normal or slightly decreased lateral rectus activity in primary gaze with markedly decreased activity in abduction and usually increased lateral rectus activity in adduction. Often the superior and inferior recti co-contract in attempted adduction (Scott and Wong, Arch. Ophth., 87: 140, 1972), accounting for the often seen vertical deviation.

Q: Duane retraction syndrome may be related to abnormal _____ with fibrosis or abnormal _____ with misdirection allowing for co-contraction.

A: Ocular musculature, innervation

118
Duane retraction syndrome, especially where sporadic, may be associated with other congenital abnormalities, mostly facial anomalies, ear and hearing anomalies, and anomalies of the extremities and the skeleton. Although most cases of Duane syndrome appear to be sporadic, approximately 5-15% show autosomal dominant inheritance; however, of these familial cases, few have shown non-ocular congenital anomalies (Pfaffenbach, Cross and Kearns, Arch. Ophth., 88: 635, 1972). The constellation of anomalies in Duane syndrome probably occurs from the fourth to tenth week of gestation (Cross and Pfaffenbach, Amer. J. Ophth., 73:442, 1972).

Q: Duane retraction syndrome appears to be (a discrete single entity, a group of several heterogeneous entities) _____ and although mostly _____, certain families may show _____ inheritance.

A: Group of several heterogeneous entities, sporadic, autosomal dominant

119
Several syndromes include an association of cleft palate with hereditary vitreoretinal degeneration, specifically high myopia and retinal detachment (Knobloch and Layer, Amer. J. Ophth., 73: 517, 1972; Gorlin, SYNDROMES OF HEAD AND NECK, 1964). Often, as in the entity known as Stickler syndrome, patients also have bony dysplasias, maxillary hypoplasia, and/or joint defects. The palatoschisis (cleft palate) may be represented by only a submucous cleft or a bifid uvula. Inheritance of Stickler syndrome seemingly is autosomal dominant.

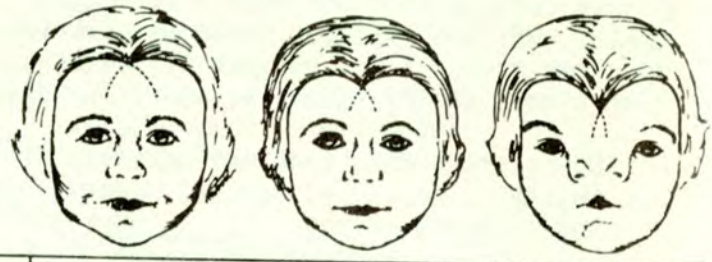
Q: The presence of palatoschisis in a child with either a personal or family history of retinal detachment is indication for ophthalmologic examination of siblings and of other family members for _____.

A: Vitreoretinal degeneration or retinal detachment

120
FACE DEVELOPMENT

It is suggested from the study of dysmorphology and comparative morphology that the optic vesicle somehow induces the formation of not only the eyebrows, eyelids, and eyelashes, but also a surrounding hairless area which becomes that side of the forehead and cheek. This hairless region, in combination with the other side, determines the configuration of the frontal hairline and the presence or absence of a Widow's peak, depending on the size of the periorbital field of hair-growth suppression and the intra-orbital distance (Smith and Cohen, Lancet, Vol. II, p. 1127, 1973).

WIDOW'S PEAK



PERIOCULAR FIELDS	NORMAL	DECREASED	NORMAL
INTEROCULAR DISTANCE	NORMAL	NORMAL	INCREASED

(from Smith and Cohen - Lancet)

Q: The _____ distance and the size of the periorbital _____ determine the height of the frontal hairline and the presence or absence of a Widow's peak.

A: Inter-orbital, hair-growth suppression

121
The significance of the presence of a Widow's peak is that it suggests either a smaller area of peri-orbital hair growth suppression or increased inter-orbital distance.

Q: The presence of a prominent Widow's peak should clue the examiner to check for the existence of _____ and if present, consider the many conditions associated with this physical finding.

A: Hypertelorism

Median cleft face syndrome or fronto-nasal dysplasia includes hypertelorism, telecanthus, and median clefts of palate, premaxilla, upper lip, and nose (bifid nose). Epibulbar dermoids have been reported and cranium bifidum occultum is often present. Frontal meningocoele or encephalocoele may occur and should not be confused with an intranasal polyp. Although almost always sporadic, a few families have been reported showing autosomal dominant inheritance. Cohen et al. (Birth Defects: Original Article Series, Vol. III, no. 7, p. 117, 1971) relate the disorder to failure of development of the nasal capsule with a filling in of the space by the primitive brain vesicles, arresting the normal forward migration of the orbits in their relatively hyperteloristic fetal position.

MEDIAN CLEFT FACE SYNDROME

DeMyer (Neurology, 17: 961, 1967) pointed out the fact that moderate to severe degrees of hypertelorism, when seen alone, are usually associated with mental retardation; whereas, ocular hypertelorism, when seen in the setting of median cleft face syndrome, even when the facial deformity is severe, is usually associated with normal or near normal intelligence. On the other hand, moderate to severe hypotelorism, when seen with median facial abnormalities, carries a much more grave prognosis as to forebrain maldevelopment; furthermore, the degree of retardation correlates with the severity of the hypotelorism.

Q: A mass present in the nose or nasopharynx in association with hypertelorism and/or median facial clefting may represent a(n) _____ and biopsy is (indicated, contra-indicated) _____.

A: Encephalocoele, contra-indicated

Norrie disease (or hereditary oculo-acoustic-cerebral degeneration) is an X-linked recessive disorder which presents as a newborn infant with congenital blindness and a retrolental mass or membrane. Often misdiagnosed as atypical retrolental fibroplasia (atypical because of full term pregnancy, normal birth weight, and no history of supplemental oxygen), Norrie disease is important to remember because, being X-linked, prognostic and genetic family counseling becomes paramount. The condition is bilateral and has been confused diagnostically with retinoblastoma, bilateral persistent hyperplastic primary vitreous and retinal dysplasia. Often the eyes appear externally normal for a few weeks (although demonstrable vision is difficult to assess in this age infant) but soon a white fibrovascular retrolental membrane is noted. The anterior chamber becomes shallow, cataracts develop, secondary glaucoma may occur, and eventually the eye softens and goes into phthisis bulbi. Hearing defects are often present and, although intelligence may be normal, varying degrees of mental retardation may be present.

Q: A mother who has had two sons with Norrie disease has what chance of passing the affected gene to her sons (i.e., statistically what percent of her sons should be affected)? What chances of passing the gene to her daughters? Will the daughters be affected?

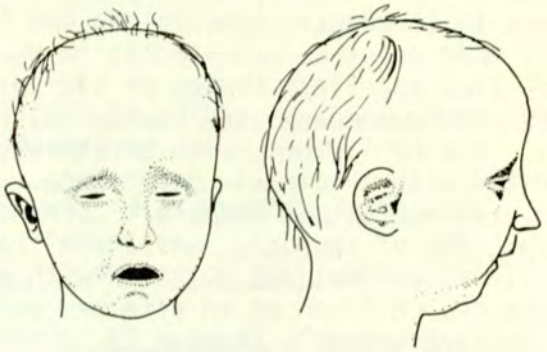
A: 50%, 50%, no (but they will be carriers)

Q: A man, blind since infancy from Norrie disease, will have what chance of passing the gene to his sons? To his daughters? Will the daughter be affected?

A: Nil, 100%, no (but they are obligate carriers because they have to have received their father's abnormal X chromosoms)

Hallermann-Streiff syndrome, called the dyscephalic syndrome by Francois, is an important entity for the ophthalmologist because of the constancy of the eye anomalies. The syndrome consists of:

1) Dyscephaly with bird-like face (beaked nose, hypoplastic mandible, and brachycephaly).
2) Dental abnormalities (missing or mis-shapen teeth, malocclusion).
3) Proportionate dwarfism.
4) Hypotrichosis (both general and localized, including eyelashes and eyebrows).
5) Cutaneous atrophy (especially of head and face, most marked on nose).
6) Bilateral microphthalmia (near constant).
7) Congenital cataracts (bilateral).



HALLERMANN-STREIFF SYNDROME

Differentiating this syndrome from others is that there are no ear anomalies, lid colobomas, muscle atrophy, premature arteriosclerosis, nail anomalies (or gross abnormalities of extremities) or mental retardation. Ocular findings include poor vision, nystagmus, strabismus, peripapillary choroidal atrophy, congenital retinal detachment of disc and posterior pole, hypoplasia of disc, blue sclera, glaucoma, clumping of pigment in macula and falciform retinal fold. The time of embryogenesis of the syndrome probably is from the 5th to 7th week. Since no affected persons have reproduced, a sporadic dominant trait cannot be ruled out. However, consanguinity has been reported in about 6% of cases and several members of the same sib-ship have been affected. Males and females are equally affected.

Q: Hypertelorism, with median facial clefting syndrome, is usually associated with (normal intelligence, mental retardation) _____.

A: normal intelligence

Deletion of a part of the long arm of chromosome 13, the 13q- syndrome, produces a characteristic malformation syndrome, which includes, in some, retinoblastoma, usually bilateral. The significance of this finding is at present not certain, but there appears to be genetic material on the long arm of chromosome 13 which, when deleted, predisposes to the development of retinoblastoma. (For excellent review of 13q- plus other chromosomal syndromes see Lewandowski and Yunis, Am. J. Dis. Child., 125: 515, 1975). Retinoblastoma, when bilateral, is autosomally dominantly inherited with incomplete penetrance. When unilateral and sporadic 80% of retinoblastoma cases are nongenetic (somatic mutation?); however, 20% of sporadic, unilateral retinoblastoma represent actually a new dominant mutation with a 50% chance of passing the gene to the children of an affected person. (For excellent review see "Retinoblastoma", Chapter 18, p. 447-461 by Mette Warburg in Goldberg, GENETIC AND METABOLIC EYE DISEASE, 1974.)

Q: Retinoblastoma, when bilateral, and 20% of the time when unilateral and sporadic, behaves for future offspring of an affected individual as a(n) _____ trait.

A: Autosomal dominant

Review Questions on Part II: Anomalies

1) A condition so far from the average that it cannot be considered within the range of variations is called a(n) _____.

2) Normal development of the eye requires that the _____ and _____ factors fall within normal limits.

3) Congenital anomalies are a subdivision of _____.

4) A(n) _____ is a chemical or physical agent acting on the fetus during _____ life to cause anomalies in development.

5) Name four mechanisms whereby embryological development departs from normal to produce congenital abnormalities.

6) The most important determinant in the character of a teratogen is the _____ at which it acts.

7) Name three classes of teratogenic factors.

8) The term _____ usually involves genes on the X chromosomes rather than on autosomes.

9) _____ describes a trait produced by a gene that must be homozygous to be expressed.

10) _____ refers to the frequency with which a gene produces a trait in the population of those known to have the gene, while _____ specifies the degree of manifestation of the trait when expressed.

11) The genetic constitution of an individual is its _____ and the _____ is its clinical appearance.

12) _____ can be clinically misclassified as anophthalmos.

13) If the optic vesicles fuse, _____ or _____ may result.

14) Congenital cystic eye results from a(n) _____.

15) A(n) _____ coloboma is one which occurs along the embryonic fissure, while those appearing elsewhere are _____.

16) A coloboma resulting from an improper closure of the embryonic cleft would be expected to involve the _____ area of the eye.

17) A failure of closure in the anterior part of the choroidal (embryonic) fissure would result in a disturbance of the _____, _____ and _____.

18) Congenital absence of the cornea, partial or complete, is associated with _____ in which case the skin covers the anterior surface of the eye.

19) In _____ only the cornea is enlarged, but in _____ the entire eye is enlarged.

20) Keratoconus occurs when the _____ of the cornea is greater than normal.

21) The most common congenital anomalies of the cornea are _____.

22) Up to the fourth month of fetal life, the _____ and the _____ have the same curvature.

23) A gene which does not show an effect in an individual of a family where that member should be affected is said to have _____.

24) In _____ the cornea is markedly steeper than normal, but in _____ it is extremely flat.

25) In _____ the length of the eyeball is greater than normal, while in _____ the light rays focus behind the retina.

26) The term used for multiple effects of a single gene, often in separate regions or tissues of the body, is _____.

27) _____ refers to a condition where there is decreased aqueous outflow leading to increased intraocular pressure. _____ is the distention of the entire eye as a result of this pressure.

28) A condition of absence of the iris is called _____.

29) Absence of the dilator iris muscle produces _____ while a condition of more than one pupil is called _____.

30) _____ is an absence of the iris and _____ is a condition where one pupil is smaller than the other.

31) An anomalous position of the lens is termed _____ and a misplaced pupil is called _____.

32) _____ involves a defect along the choroidal (embryonic) fissure while those occurring elsewhere are classified as _____.

33) Hypoplasia of the optic disc, hypopituitarism and agenesis of the septum pellucidum are the main features of _____.

34) _____ is the term used to describe abnormally widely-spaced orbits.

35) Telecanthus is the term used to describe abnormally wide _____ distance compared to _____ distance.

36) A congenital crescent (conus) occurring (position) _____ the optic disc may be caused by a defect in the closure of the embryonic fissure.

37) _____ is an absence of the lens and _____ is where the lens is unusually small and spherical in shape.

38) A considerable defect in the _____ can cause a displacement of the lens as in a condition of _____, or it can make a notch in the lens called a(n) _____.

39) A number of white dots in front or behind the anterior Y-shaped suture are classified as a(n) _____ cataract, while an opacity involving a deposition of a substance along the lines of the sutures is called a(n) _____ cataract.

40) A _____ cataract is a condition where the opacity is limited to one layer or area of the lens.

41) _____ of the fetal vascular system because of a(n) _____ in development causes many eye anomalies.

42) Bergmeister's papilla is a plug of _____ tissue on the _____.

43) If the central vascular arcades of the iris fail to completely atrophy, _____ will result.

44) _____ may be caused by fragments of the hyaloid artery or pieces of retina from the ora serrata.

45) _____ may be associated with retarded growth of the macula and choroid, nystagmus, poor visual acuity and an obvious _____ in pigmentation.

46) _____ may be due to increased pigmentation while _____ is due to decreased pigmentation.

47) A complete failure of the lid folds to form is a condition of _____.

48) Especially when associated with other congenital anomalies, sporadic aniridia presents a significant risk of _____.

49) _____ is a continuous fold of skin stretching from the bridge of the nose over the inner canthus.

50) When there is an inability to raise the upper lid, _____ exists.

51) An eye defect seen in a majority of the patients with Marfan's syndrome is _____.

52) Van der Hoeve syndrome is characterized by _____, _____ and _____.

53) The most important test in diagnosis of Leber congenital anaurosis is the _____.

54) A syndrome characterized by Brushfield spots, exaggerated epicanthal folds, and oblique, short, wide palpebral fissures, and other ocular and non-ocular anomalies, is known as _____. It is caused by _____.

55) In cases of melanosis the normal function of the eye is _____.

56) The three features of Rieger or Axenfeld anomaly are _____, _____ and _____.

Answers to Review Questions

If your answers do not agree with those listed below, refer to the section or frame listed in parentheses.

1) anomaly (refer to I-A)
2) environmental, genetic (I-B)
3) developmental anomalies (I-A)
4) teratogen, intrauterine (I-B)
5) Possible answers: developmental failure, arrested development, failures in fusion, failure to atrophy, failure of cell interaction, excessive cell death, changed rate of proliferation, impeded cell migration, or interference of morphogenic processes.

6) time or stage in development (II-B)
7) Possible answers: mechanical interference, ionizing radiation, hypoxia, presence or excess of metals, drugs, infectious agents (II-B)
8) sex-linked inheritance (II-C)
9) recessive (II-C)
10) penetrance, expression (II-C)
11) genotype, phenotype (II-C)
12) microphthalmos (Frame #4)
13) cyclopia, synophthalmos (#5 & #6)
14) failure of invagination of the optic vesicle (#17 & #18)
15) typical, atypical (#22)
16) inferior-medial (#22)
17) iris, ciliary body, zonular fibers (or choroid) (#28)
18) cryptophthalmos (#29)
19) megalocornea, buphthalmos (#33 & #47)
20) curvature (#39)
21) alterations in transparency or corneal opacities (#35)
22) cornea, sclera (or globe) (#37)
23) reduced penetrance (II-C)
24) keratoconus, cornea plana (#39 & #37)
25) axial myopia or nearsightedness, hyperopia or hypermetropia or farsightedness (#44 & #45)
26) pleiotropism (II-C)
27) congenital glaucoma, buphthalmos (#47)
28) aniridia (#49)
29) microcoria, polycoria (#52 & #54)
30) aniridia, anisocoria (#49 & #55)
31) ectopia lentis, corectopia (#82 & #56)
32) typical coloboma, atypical colobomas (#22)
33) septo-optic dysplasia or de Morsier syndrome (#9)
34) hypertelorism (#12)
35) inner canthal, interpupillary or interorbital (#14)
36) below or inferior to (#73)
37) congenital aphakia, microspherophakia (#75 & #77)
38) zonular fibers, ectopia lentis, coloboma of the lens (#79 & #82)
39) anterior embryonic, sutural (#84 & #85)
40) lamellar or zonular (#88)
41) persistence, failure to atrophy or arrest (I-C & #89)
42) neuroepithelial, optic disc (#90)
43) persistent pupillary membrane (#92)
44) vitreous floaters (#94)
45) albinism, decrease (#97)
46) melanosis bulbi, albinism (#96 & #97)
47) cryptophthalmos or ablepharon (#99, 29, 30, 31)
48) Wilm's tumor (#49)
49) epicanthus (#106)
50) ptosis (#109)
51) subluxed lenses or ectopia lentis (#112)
52) blue sclera, otosclerosis, brittle bones (#111)
53) electroretinogram (#65)
54) Down syndrome or mongolism, chromosomal aberrations (#114)
55) unimpaired (#96)
56) iris hypoplasia, iris processes bridging angle, and centrally displaced, prominent Schwalbe's line (any order)

INDEX OF PART II

Additional References and Suggested Reading

Arey, L. B. 1965 Developmental Anatomy. S. B. Saunders Co., Philadelphia.

Barber, A. 1955 Embryology of the Human Eye. C. V. Mosby Co., St. Louis.

Cogan, D. G. 1948 Neurology of the Ocular Muscles. C. C. Thomas, Springfield, Ill.

Corner, G. W. and G. K. Smelser. 1950 The Embryology of the Eye (a motion picture). Produced by Sturgis-Grant Productions, Inc. for the American Academy of Ophthalmology and Otolaryngology in cooperation with the Department of Embryology of the Carnegie Institution of Washington, Baltimore.

Davson, H. 1962 The Eye. Academic Press, New York.

De Coursey, E. and J. E. Ash. 1939 Atlas of Ophthalmic Pathology. The American Academy of Ophthalmology and Otolaryngology, Omaha, Nebraska.

Donaldson, D. D. 1966 Atlas of External Diseases of the Eye. C. V. Mosby Co., St. Louis.

Duke-Elder, S. 1963 Systems of Ophthalmology. Vol. III Normal and Abnormal Development. Part 2 Congenital Deformities. C. V. Mosby Co., St. Louis.

Duke-Elder, S. and C. Cook 1963 Systems of Ophthalmology. Vol. III Normal and Abnormal Development. Part I Embryology. C. V. Mosby Co., St. Louis.

Ford, F. R. 1966 Diseases of the nervous system in infancy, childhood, and adolescence. 5th ed., C. C. Thomas, Springfield, Ill.

Francois, J. 1961 Heredity in Ophthalmology. C. V. Mosby Co., St. Louis.

Geeraets, W. J. 1965 Ocular Syndromes. Lea and Febiger, Philadelphia, Pa.

Hamilton, W. J., J. D. Boyd and H. W. Mossman 1962 Human Embryology. Williams and Wilkins Co., Baltimore, Md.

Hogan, J. H. et al 1971 Histology of the Human Eye. W. B. Saunders Co. Philadelphia.

Keeney, A. H. 1951 Chronology of Ophthalmic Development. C. C. Thomas, Springfield, Ill.

Kestenbaum, A. 1963 Applied Anatomy of the Eye. Grune and Stratton, New York.

Kronfeld, P. C. 1943 The Human Eye in Anatomical Transparencies. Bausch and Lomb Press, Rochester, N.Y.

Last, R. J. and E. Wolf 1961 Anatomy of the Eye and Orbit. W. B. Saunders Co., Philadelphia, Pa.

Lopashov, G. V. 1963 Developmental Mechanisms of the Vertebrate Eye Rudiments. Pergamon Press, Oxford, N.Y.

Mann, Ida 1957 Developmental Abnormalities of the Eye. The University Press, Cambridge, England.

Mann, Ida 1964 The Development of the Human Eye. The University Press, Cambridge, England.

Polyak, S. L. 1957 The vertebrate Visual System. University of Chicago Press, Chicago.

Prince, J. H. 1956 Comparative Anatomy of the Eye. C. C. Thomas, Springfield, Ill.

Scobee, R. G. 1955 Rehabilitation of a Child's Eye. C. V. Mosby Co., St. Louis.

Smelser, G. K. 1961 The Structure of the Eye. International Congress of Anatomists. Academic Press, New York.

Streeter, G. L. 1942, 1945, 1948 Developmental horizons in human embryos. Carnegie Contributions to Embryology, Nos. 197, 199, 211.

Waardenburg, P. J., A. Franceschetti and D. Klein 1961 Genetics and Ophthalmology. C. C. Thomas, Springfield, Ill.

Walls, G. L. 1942 The Vertebrate Eye and Its Adaptive Radiation. Cranbrook Institute of Science, Bloomfield Hills, Mich.

Whitnall, S. E. 1932 The Anatomy of the Human Orbit and Accessory Organs of Vision. Oxford University Press, New York.

Addenda

O'Rahilly, R. 1966 The early development of the eye in staged human embryos. Carnegie Contributions to Embryology, no. 259.

Walsh, F. B. and W. F. Hoyt 1969 Clinical Neuro-Ophthalmology. Williams and Wilkins Co., Baltimore.

The Development of the Eye
____ Edition

TO THE READER

Your answers to these questions will help us in planning a revision of this book.

1. Did you complete this book? Part I ( ) Yes ( ) No
   Part II ( ) Yes ( ) No

2. If you did not complete this book would you mind telling us why?_____
   _____

3. Was the material ( ) over simplified ( ) too detailed ( ) not enough details ( ) about right?

4. Were the questions helpful? ( ) Yes ( ) No
   Remarks_____

5. If you completed this book did you like it? ( ) Yes ( ) No If you did not like this book would you mind telling us why?_____
   _____

6. Do you think that the material presented in this book was of value to you? ( ) Yes ( ) No

7. In comparison with other forms of reading material do you find this type of book for review ( ) more valuable ( ) equally valuable, or ( ) less valuable?_____
   _____

8. What changes would you suggest in a revision of this book? Make a list of the topics which should have been included in this manual.
   _____

9. Do you find that "hi-lighting" certain words and phrases helps the learning process?_____ When you are asked to label and color certain drawings, do you feel more actively involved?_____ Does this help?_____
   Other comments and suggestions_____

We will appreciate your criticism, suggestions and comments.
Please send this to: Dr. A. A. Pearson
Professor Emeritus of Anatomy
University of Oregon Medical School
Portland, Oregon 97201

Date_____ Graduate of school_____

Name_____ _____

Address_____ Position or status_____

_____ _____

The Development of the eye