**Quain's elements of anatomy.**

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# QUAIN'S ANATOMY

## VOL. I.

## EMBRYOLOGY

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# QUAIN'S ANATOMY

## EMBRYOLOGY

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# QUAIN'S
# ELEMENTS OF ANATOMY

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IN FOUR VOLUMES

VOL. I.

## EMBRYOLOGY

By T. H. BRYCE

ILLUSTRATED BY MORE THAN 300 ENGRAVINGS
MANY OF WHICH ARE COLOURED

ELEVENTH EDITION

LONGMANS, GREEN, AND CO.
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1908

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# PREFACE

THE present edition of 'Quain's Anatomy' will appear in four volumes, of which this one, containing the Embryology, is the first. The remaining volumes will comprise respectively General and Visceral Anatomy; the Nervous System and Sense Organs; and the Bones, Ligaments, Muscles, and Blood-vessels. Each volume will be complete in itself and will serve as a text-book for the particular subject or subjects with which it deals. Thus the first volume is intended to form a complete text-book of Human Embryology, the second a text-book of Histology and Visceral Anatomy, the third a text-book of Neurology, while the fourth will deal with the systems which are not included in the second and third volumes.

The work has been completely re-edited and brought up to date. The volume on Embryology, which was written for the previous edition by Professor Schäfer, has in the present edition been entrusted to Dr. Bryce, who has re-written it and has added a large number of illustrations. The advances in our knowledge of human embryology have necessitated considerable additions to the text, and this, combined with the profuseness of illustration, has resulted in some increase in bulk of the volume; but, in spite of the wealth of detail with which the subject is treated, this is by no means excessive. There has been some saving of space by the omission of the bibliographical list which in the former edition followed each subject. These lists, although at the time useful, are no longer necessary, since they are to be found in a very complete form in the compendious 'Handbuch der Entwickelungslehre,' by numerous authors, which has lately been published under the editorship of Professor O. Hertwig, as well as in the earlier 'Bibliography of Vertebrate Embryology,' by Professor Minot.

In the matter of illustrations the volume is indebted to the skill of Mr. A. Kirkpatrick Maxwell for the original drawings of figs. 116, 118, 119, 121, 122, 129, 130, and 136, as well as for some adaptations of figures from other authors. For the photographic illustrations of his preparations which are reproduced in figs. 74, 156, 157, 162, 163, 164, 176, 220, and 246, Dr. Bryce desires to signify his obligation to Dr. J. H. Teacher. All other original drawings and diagrams, both in black-and-white and in colour, and most of the adaptations, are from his own pencil. In addition to the original illustrations, Mr. Gustav Fischer of Jena has supplied *clichés* of a number of valuable figures, many of them from the well-known text-book of Professor Kollmann. Dr. Bryce further begs to acknowledge the obligation he is under to Professor J. Graham Kerr for reading the proof-sheets of Section I. The Index to this volume has been prepared by Miss Agnes Picken, M.A., M.B.Ch.B., Demonstrator of Anatomy in the Department for Women, University of Glasgow.

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even under high powers of the microscope, no signs of any finer structure; in other cases, especially after fixation, it exhibits a meshwork or reticular appearance, which has been variously interpreted as indicating a filar, a spongy, or an alveolar structure, but in view of the effects produced by most fixing reagents on colloid solutions, such interpretations must be received with caution.

The granules which are generally present in the cytoplasm may be either essential constituents of the protoplasm, or included non-protoplasmic bodies of various kinds. The granules of the former kind (*cytomicrosomes*) are very minute, and form apparently an important element in the active protoplasm. They have been called *mitochondria* by Benda, and have been shown, as we shall see, to play an important part in the sex-cells. The non-protoplasmic granules include such as pigment-granules, yolk-grains, and so on; but larger inclusions, such as fluid vacuoles, fat-drops, &c., also occur. All these may be collectively designated by the terms *deutoplasm* or *paraplasm*.

While we generally speak of the tissues as being composed of separate cells, we shall have occasion in the course of this work to refer to instances of tissues in which the so-called cells

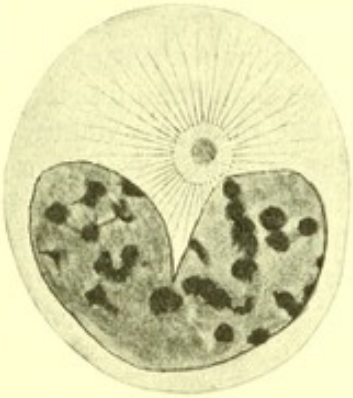


FIG. 1.—LEUCOCYTE (*Lepidosiren paradoxa*) SHOWING ATTRACTION-SPHERE. (T. H. Bryce.)

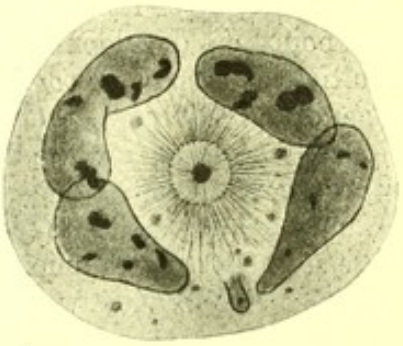


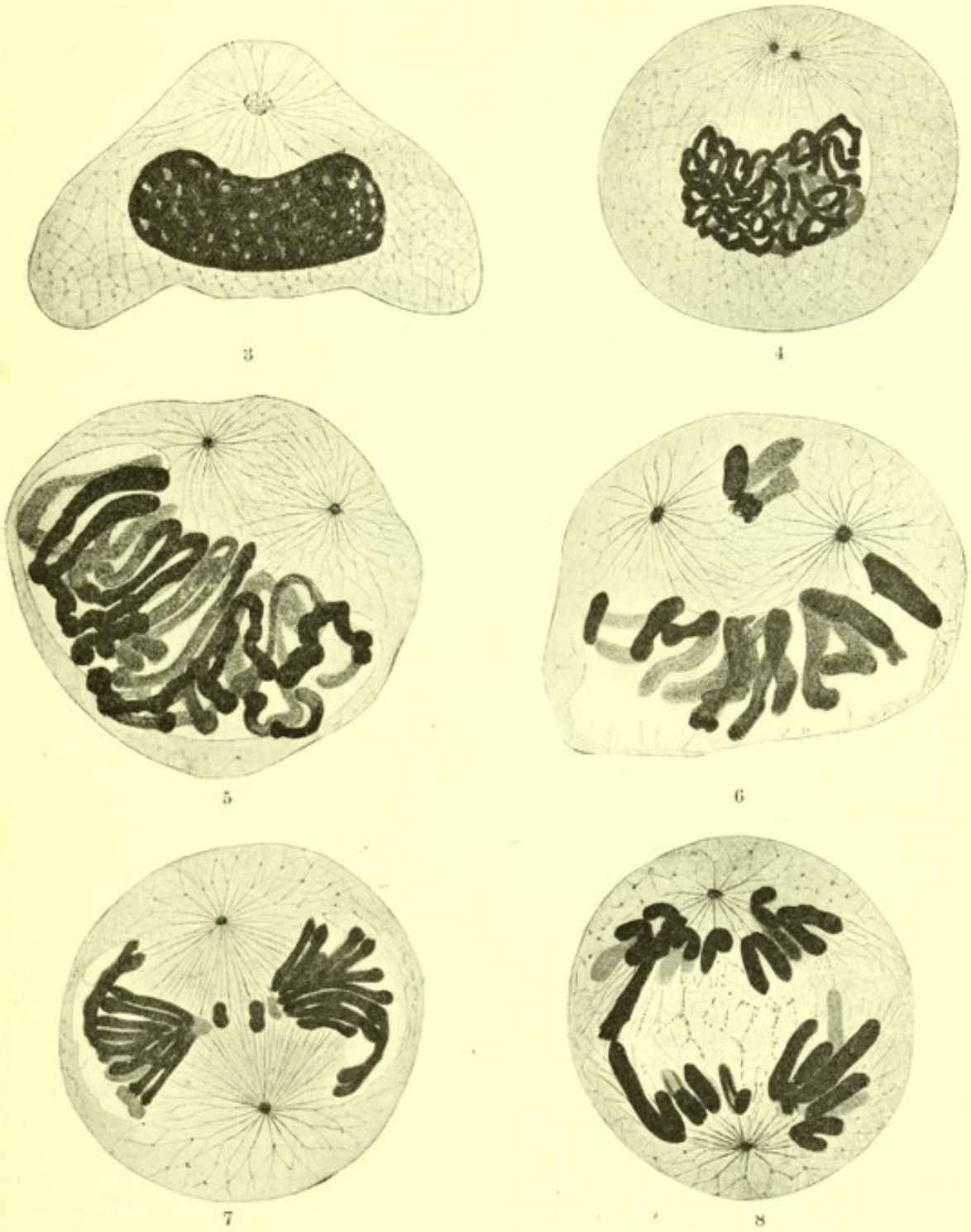
FIG. 2.—POLYMORPHONUCLEAR LEUCOCYTE OF LEPIDOSIREN, SHOWING LOBED NUCLEUS, ATTRACTION-SPHERE, AND SOME GRANULES. (T. H. Bryce.)

are joined together by protoplasmic strands. The tissue in such cases is really a multinucleated protoplasmic network. In other instances, owing to the division of the nuclei without cleavage of the protoplasm, a multinucleated mass or layer of protoplasm is produced. Any such multinucleated mass is termed a *syncytium*.

**Centrosome: central particle.**—In most cells there is generally to be demonstrated a point in the cytoplasm, as a rule close to the nucleus, where by suitable stains a single granule, a double granule, or a group of granules, may be made visible. These are surrounded by a clear structureless area, round which the protoplasm may be arranged in a radial fashion. When fully developed, as in wandering leucocytes (figs. 1 and 2), the whole arrangement is named the *attraction sphere*. The substance of the sphere is known as the *archoplasm* or *centroplasm*. The central area, containing the granule or granules, has been named the *centrosome* by Boveri. When it contains a single granule, the particle is called the *centriole*. In cells in which the granule is the only obvious feature, it may itself be termed the centrosome. A centrosome is absent in plant-cells, and it has been proved by Morgan and Wilson that focal points, having all the characters of centrosomes, may be produced in the protoplasm of the echinoderm-egg by treatment with chemical reagents.

**Nucleus.**—The nucleus in the vast majority of cells is a spheroidal or slightly ovoidal body; but it may be lobed as in leucocytes (figs. 1 and 2). It has a definite

membrane, and is made up of two parts of different chemical and physical characters, a formed substance with great affinity for certain dyes, and hence called *chromatin*, and a structureless more fluid substance, the *achromatin* or *karyoplasm*. The chromatin is generally in the form of a network, with thickenings at the nodal points; but often the nodes are the more prominent feature, and the network



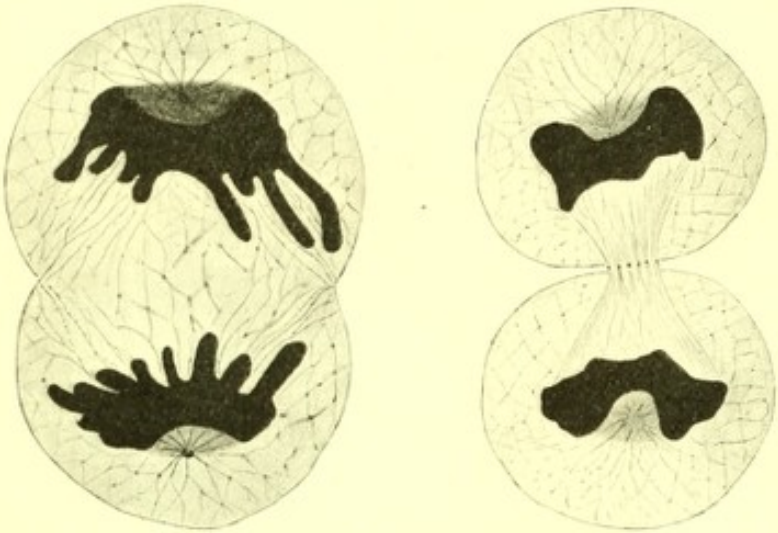

FIGS. 3 TO 8.—KARYOKINESIS IN RED BLOOD-CORPUSCLES OF LARVAL LEPIDOSIREN. (T. H. Bryce.)

forms only a mesh of fine threads between them. The thickenings are named *karyosomes*. The chromatin, which generally takes the form of solid filaments, but frequently also is seen in the form of granules in a non-staining basis (*linin*), has a special affinity for basic dyes, and is hence called *basichromatin*; but there are also granules in the filaments composed of a material which stains with acid dyes, hence

called *oxychromatin*. The karyoplasm occupies the meshes of the reticulum, and seems to be of the same nature as the fluid part of the cytoplasm. There are often, but not always, one or more rounded bodies staining somewhat differently from basichromatin, the *true nucleoli* or *plasmosomes*.

Cell-division.—While in a few cases it is believed that cells divide directly, by constriction of the nucleus and then of the cell-body (*amitosis*), the almost universal rule is that they divide by a complicated mechanism called *indirect division*, *mitosis*, or *karyokinesis*. The process is an elaborate device for the exact partition of the chromatin between the daughter-cells.

**Karyokinesis** (figs. 3 to 11).—The process of indirect cell-division does not present the same picture in every detail in all classes of cells, variations occurring according to the relative size of nucleus and cell-body; but, apart from minor variations, there is one type of mitosis which, in certain particulars, differs essentially from that seen in ordinary somatic cells. This, which is known as the *heterotypical* mitosis, is characteristic of the sex-cells, and will be dealt with later; but, in order that its character and significance may be more readily understood, a brief description of ordinary mitosis, as it occurs in somatic cells, will be here given.



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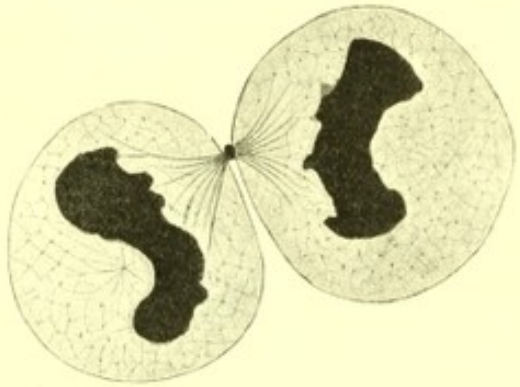

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Figs. 9 to 11.—Karyokinesis in red blood-corpuscles of larval Lepidosiren (*continued*). (T. H. Bryce.)

The process is initiated by the division of the centrosome (fig. 4). As the two centrosomes draw apart in a direction tangential to the nucleus, protoplasmic radiations become centred on them, and a spindle system of fibres is drawn out between them (fig. 5). The network of the nucleus meanwhile takes the form of an apparently continuous skein (fig. 4), which then arranges itself into loops directed towards the developing spindle system (fig. 5). The loops then break apart at the opposite pole of the nucleus, to form a series of V-shaped filaments or *chromosomes* (fig. 6). The nuclear membrane meanwhile disappears, the spindle system gradually takes up a position of equilibrium in the centre of the cell, and the chromosomes arrange themselves round the equator of the spindle with their apices applied to it (fig. 7). The chromosomes have in the meantime split longitudinally along their whole length, and now the two halves become separated from one another, the apices of the daughter-V's being drawn towards opposite spindle-poles (fig. 8). The

daughter-V's next get free from one another and pass to the apices of the spindle where they gather in groups round the poles (fig. 9). They then merge together again to form the reticulum of each resting daughter-nucleus (figs. 10 and 11).

As the final stages of nuclear division are being completed, the cell-body is constricted round the equator, and the constriction gradually deepens to divide the cell into two exactly equal parts. The spindle and polar radiations die away, the last remains of the system appearing as a strand of fibres gathered into the narrowing bridge between the two cells. This persists for a time as a bond of union between them even after the cytoplasm has completely divided (fig. 11).

For convenience of description and reference to the different pictures presented by the nucleus in different stages of karyokinesis, it has become customary to divide the continuous process into arbitrary phases. The preparatory stages up to the completed spindle are known as the *prophase*; the stage in which the split rods are being resolved (on the equator of the spindle) into the daughter-chromosomes as the *metaphase*; the stage of separation as the *anaphase*; and the stage of reconstruction as the *telophase*.

## HISTORY OF THE SEX-CELLS.

### STRUCTURE AND DEVELOPMENT OF THE SPERMATOZOON.

**Structure of the spermatozoon.**—The human spermatozoon (fig. 12) is a minute body possessed of a head and a long flagellum or tail. The *head* is conical when seen in profile, but being compressed in one diameter, it is broadly oval when seen in face view. At its pointed end it shows a somewhat different staining reaction from the remainder; this portion is known as the *cap*. The base of the tail shows a thicker section, usually termed the *middle piece*. It includes two parts, more distinctly separated from one another in some animals, the *neck* and the *connecting piece*.

The complete length of the spermatozoon is from 52 to 62 $\mu$, the head being responsible for 4 to 5 $\mu$, and the connecting piece for 6 $\mu$ of the total figure.

The pointed process of the head is sometimes called the *perforatorium*. It is prolonged in some animals into a hooked projection. The limit of the cap is marked by a distinct line on the head. The tail has an axial filament which is prolonged through the connecting piece. In this it is imbedded in a sheath derived from the cell-protoplasm, which is characterised by the presence of a remarkable *spiral filament*. At the junction of the head and neck, and again at the union of the neck with the connecting piece, there are certain darkly staining granules derived from the centrosomes of the cell from which the spermatozoon is developed. The tail filament is related to those which lie at the union of neck and connecting piece. In some animals the tail has connected with it a very delicate lateral membranous fold, which ceases a little distance short of the tip (*end piece*).

The picture of the spermatozoon is strikingly different from that of a typical cell, and when seen in active movement produced by the lashing of the motile flagellum, the theory of the early observers, to which it owes the name of *spermatozoon* (given to it by von Baer), seems not unnatural. Kölliker (1841) first showed its true nature, by proving that the head is derived from the nucleus of the cell from which the spermatozoon is formed. By recent work all the various parts have been traced back to the constituent elements of the testicular cell.

**Spermatogenesis** (fig. 13).—The subject of spermatogenesis will be treated of in the description of the testis; but some account of the process may here be given.

The spermatozoa are derived from the cells lining the testicular tubules, which are said to multiply by amitosis, with differentiation into elements possessing

distinctive nuclear characters—the *spermatogonia*. These divide rapidly for a time, then cease to multiply and give rise to a new generation of cells—the *spermatocytes*. In this generation a series of changes in the nucleus is effected which are of profound significance, and will be described later. Gradually enlarging, the spermatocytes divide into rather smaller elements, the *spermatocytes of the second order*, which in turn again divide to form the *spermatids*. It will thus be seen that from each spermatogonium, by two successive divisions, four equivalent spermatids are formed. Each member of this group of four becomes, by further changes, a spermatozoon. The spermatids lie near the lumen of the tubules, and become attached to certain remarkable elongated striated cells known as the *cells of Sertoli*, or *foot-cells*. The spermatids have meanwhile acquired flagella, and remain attached to the foot-cells in groups, becoming gradually converted into the young spermatozoa, which lie in groups with their tails gathered into the lumen of the tubule. When mature, the spermatozoa are set free in the tubule by losing their connexion with the foot-cells, which then shrink back to the wall of the tubule.

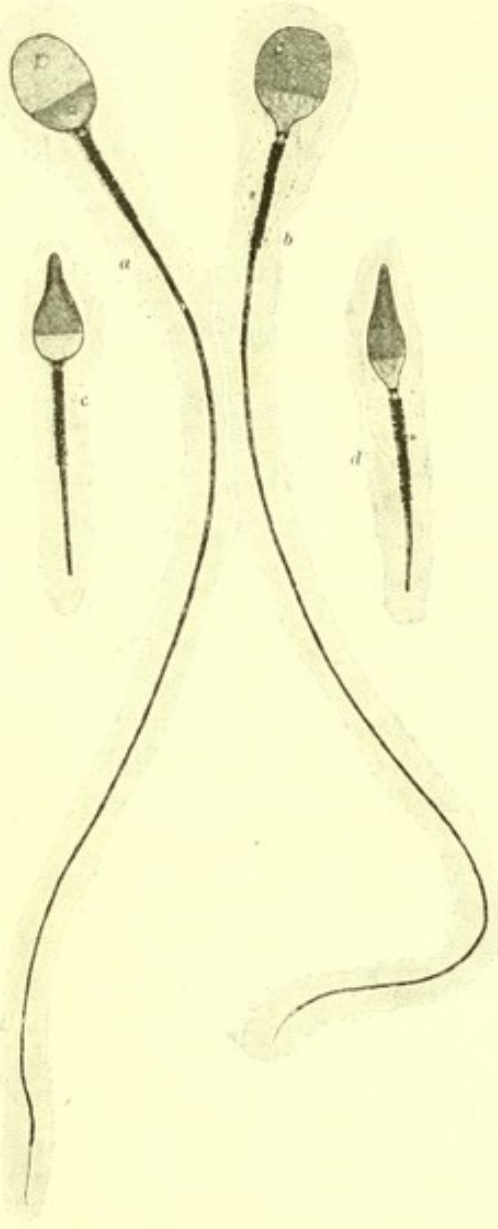



FIG. 12.—HUMAN SPERMATOZOA. (Broman.)
*a* and *b* represent spermatozoa in face (in different foci), *c* and *d* in profile view.

The process of metamorphosis of spermatid into spermatozoon is one of much complexity, by which the nucleus becomes the head, while the protoplasm is reduced to a rudiment in the middle piece. The mitochondria of the spermatid have been shown by Benda and Meves to give origin to the spiral filament. Of the two centrosomes of the spermatid, one remains as an independent body, while the other becomes related to the flagellum, and the attraction-sphere (*idiosome*) undergoes remarkable changes to form the cap.

The accompanying diagrams (fig. 14), founded on drawings and descriptions by Meves and by Moore and Walker,[1] will convey a general impression of the process of histogenesis leading to the evolution of the spermatozoon.

[1] Reports of Thompson-Yates and Johnstone Laboratories, University of Liverpool, No. VII. Part I. 1906. For earlier papers by Ballowitz, Bardeleben, Lenhossék, Benda, Meves, Moore, Ebner, Regaud Wilcox, and others, on mammalian and human spermatogenesis, see Hertwig, Handbuch der Entwickelungsgeschichte, Literature, i. 431 *seq*. In the matter of structure see also Retzius, Biolog. Untersuch., Neue Folge, x. 1902; Broman, Anat. Anzeiger. xxi.; Wederhake, *ibid*. xxvii.

## STRUCTURE AND DEVELOPMENT OF THE OVUM.

**Structure of the ovum.**—The mature human ovum ready for fertilisation and outside the Graafian follicle has not yet been observed. It is necessary, therefore, to begin with a stage prior to the formation of the polar bodies, and homologous with the spermatocyte in the male series—the stage of the *oocyte*.

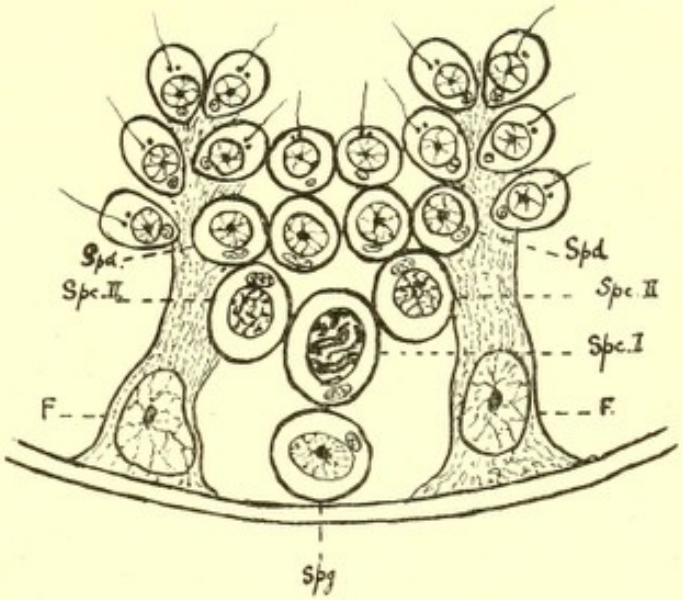



FIG. 13.—DIAGRAM OF SPERMATOGENESIS. (T. H. Bryce.)

*F*, two cells of Sertoli attached to wall of tubule; *Spg.*, a spermatogonium; *Spc. I.*, spermatocyte of the first order; *Spc. II.*, spermatocyte of the second order; *Spd.*, spermatids.

**The oocyte (ovarian ovum)** (fig. 15) resembles that of all other mammals (with the exception of monotremes) in its minute size. Immediately before the time of its discharge from the Graafian follicle of the ovary in which it has been formed, it is a small spherical vesicle measuring about ·22 to ·32 mm. in diameter, and is just visible as a clear speck to the naked eye. When it is examined with the microscope, in a fresh condition in the liquor folliculi, it is found to be invested by a comparatively thick, clear covering. This, when the centre of the ovum is exactly focussed, has the

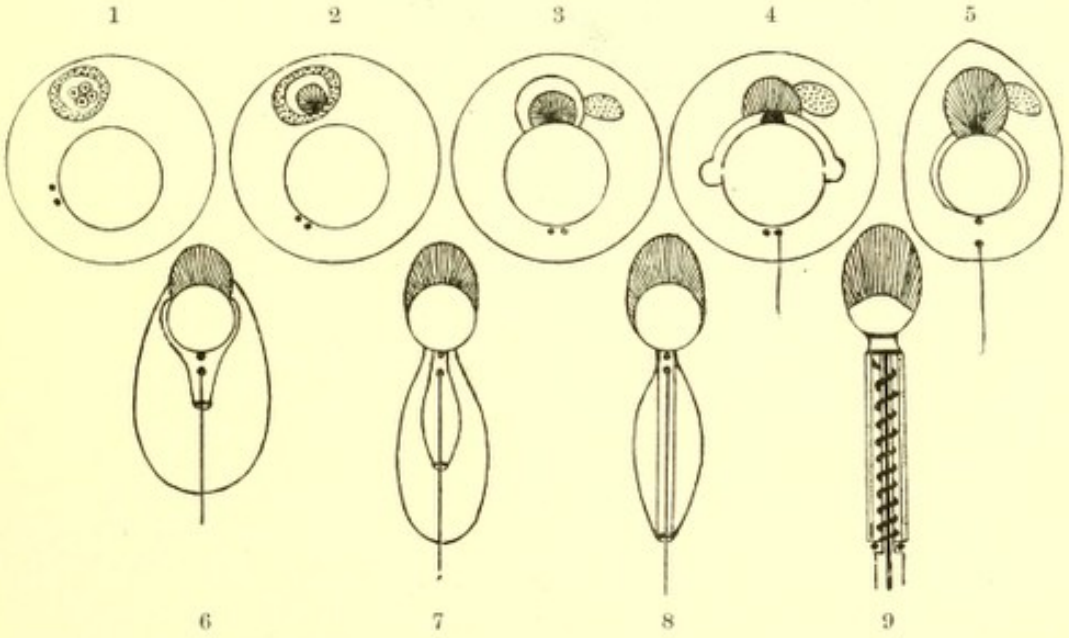



FIG. 14.—DIAGRAM OF THE DEVELOPMENT OF THE SPERMATID INTO THE SPERMATOZOON. (T. H. Bryce.)

The cell-body is represented in 1 by the outer circle; its gradual reduction and displacement till it forms the middle piece with its spiral filament in 9 is shown. The nucleus is represented by the inner circle; it forms the main part of the head. The modified attraction-sphere in 1 and 2 shows a central body and a vesicle (*archoplasmic vesicle*, Moore and Walker). The central body (shaded) forms the cap; the vesicle becomes the tail-sheath (Moore and Walker). The centrosomes are shown as dots; the growth from one of them of the tail-filament is seen.

appearance in optical section of a clear girdle or zone encircling the ovum (fig. 15), and was hence named *zona pellucida* by von Baer (1827). Under a

moderate power of the microscope a faint radial striation can generally be made out, but this is seen more distinctly in ova which have been fixed by reagents, and more especially in sections. On this account, and especially since a similar radially striated membrane forms a characteristic part of the investment of the ovum in many animals belonging to widely different classes, it is usual, in place of the name zona pellucida, which has been exclusively used to designate this investment in mammals, to employ the more general term *zona radiata* (Waldeyer, 1870), or to speak of it simply as the *striated membrane* of the ovum.

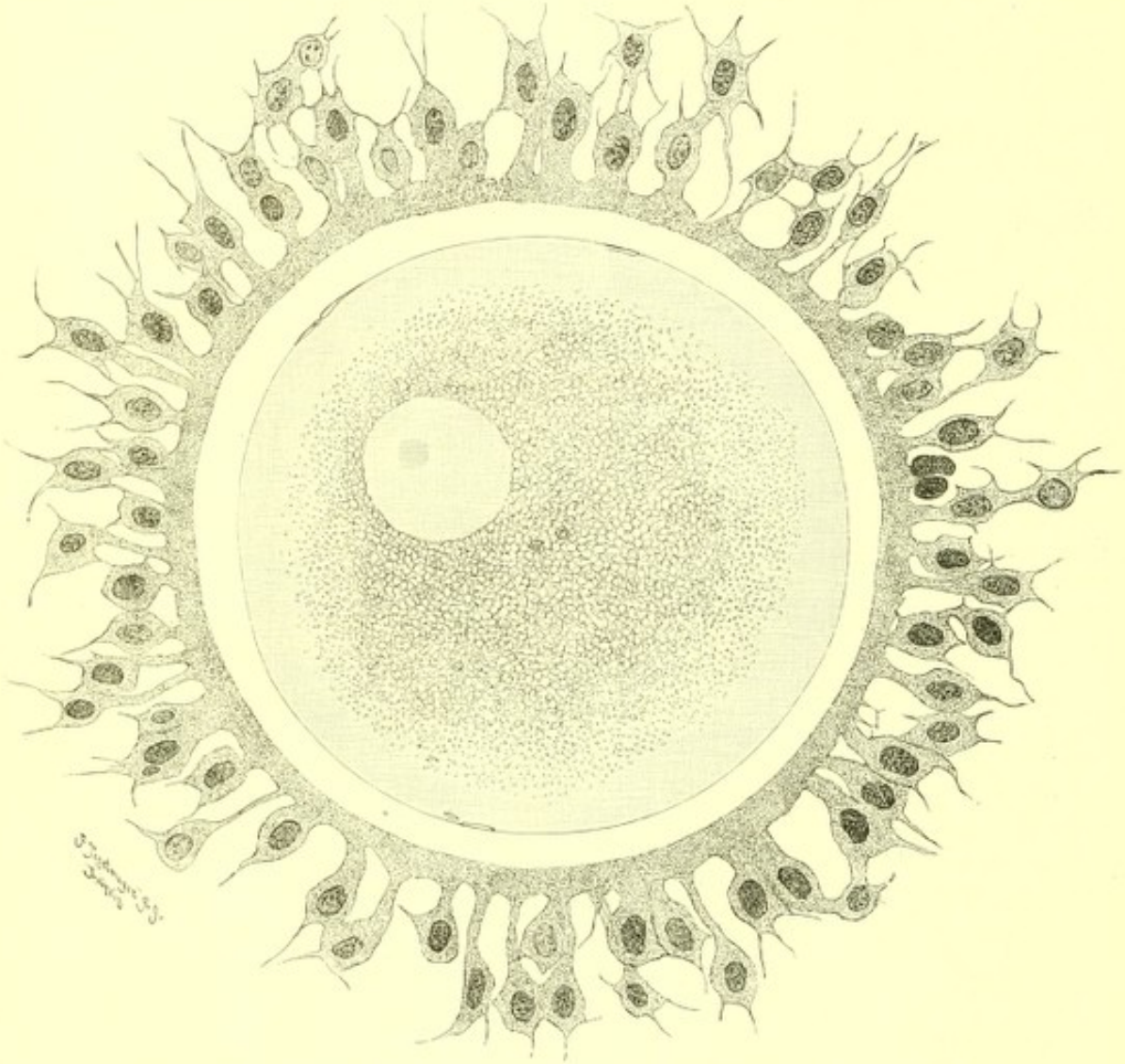


FIG. 15.—HUMAN OVUM EXAMINED FRESH IN THE LIQUOR FOLLICULI. (Waldeyer.)

The zona pellucida is seen as a thick clear girdle surrounded by the cells of the corona radiata. The egg itself shows a central granular deutoplasmic area and a peripheral clear layer, and encloses the germinal vesicle, in which is seen the germinal spot

The zona radiata of the mammalian ovum is sufficiently tough to prevent the escape of the contents of the ovum, even when subjected to a considerable amount of pressure. If, however, the pressure be excessive, the tunic splits, and the soft contents are extruded (fig. 16). It has, however, to be particularly noticed that part of the contents remain, at any rate in all but the riper oocytes, attached to the zona. The striæ are believed to be minute pores; and it has been shown by Flemming, Heape, Retzius, and Ebner, that they are occupied by processes of the cells of the *corona radiata*. This name is given

to an investment of several layers of epithelial cells derived from the *discus proligerus* of the Graafian follicle (fig. 15). In the ripening oocytes these follicular cells form a syncytial layer immediately applied to the zona. Within the zona a second membrane of great tenuity has been described by various authors (recently by Van der Stricht in the human ovum). but its existence has been denied by many, and it is supposed by some that the processes of the follicular cells are continued through the zona into the egg-protoplasm. The fact that when the zona is ruptured in young oocytes the contents do not separate from it is in favour of such connexion (Ebner). In young oocytes there does not seem to be any space round the protoplasm. The egg-protoplasm is filled with globules and granules of different sizes, but all possessing a high index of refraction. Compared with that of some lower mammals, the human ovum is distinguished by the ill-defined characters of its specially minute deutoplasmic bodies. When examined in the fresh condition the egg (fig. 15) is very transparent, the deutoplasm being massed towards the centre, while there is a clear or very finely granular layer round the periphery.

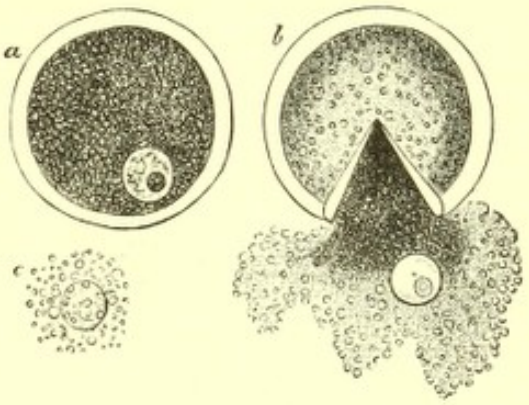



FIG. 16.—OVARIAN OVUM OF A MAMMIFER. (Allen Thomson.)

*a*, the entire ovum, viewed under pressure; the granular cells have been removed from the outer surface, the germinal vesicle is seen in the yolk-substance within; *b*, the external coat or zona, burst by increased pressure, the yolk-protoplasm and the germinal vesicle having escaped from within; *c*, germinal vesicle more freed from the yolk-substance. In all of them the macula is seen.

The deutoplasmic bodies in the egg-protoplasm are spoken of collectively as the *yolk*. There is great variety in the different orders of animals in respect of the amount of yolk stored in the egg. The term *alecithal* is used to denote an ovum such as that of the mammal, Amphioxus, and many echinoderms, in which the yolk-particles are absent, or very small in amount and uniformly distributed, while a heavily yolked egg in which the yolk is accumulated at one end is termed *telolecithal*. There are many different degrees of this condition (amphibians, fishes, reptiles, and birds). In the very exaggeratedly telolecithal egg of the bird the amount of yolk-substance is so vastly greater than that of the protoplasm itself that it is only in the neighbourhood of the nucleus (germinal vesicle) itself that the protoplasm can be distinctly recognised. This point is conveniently distinguished as the *animal pole*, as opposed to the *vegetative pole* marked by accumulation of yolk-material.

The amount and distribution of yolk is the main factor in determining the character of the egg-cleavage. It is related to the determination of the period when the organism will assume an independent existence. Thus in the bird the ovum contains necessarily all the nutriment required by the chick until it is sufficiently developed to emerge from the egg and obtain food independently. In the frog the yolk is sufficient for the early stages only and the tadpole is hatched in a very immature condition, while in Amphioxus and many invertebrates the organism is set free still earlier as a free-swimming ciliated blastula.

In the mammal the conditions are wholly different, and the small amount of nutritive material in the egg is obviously related to its retention in the uterus, from which it is able directly to derive its nutriment. It is probable that the alecithal condition of the mammalian egg is a secondary condition related to the introduction of uterine gestation.

Imbedded in the protoplasm, usually eccentrically[1], is a large spherical nucleus, which was termed by its discoverer, Purkinje, the *germinal vesicle*.[2] This, which is about 30 to 45 $\mu$ in diameter, has all the characters of the nucleus of a

[1] Bull. de l'Acad. Roy. de Médicine de Belgique (4th sér.), xix. 1905.

[2] Purkinje discovered the germinal vesicle in the bird's ovum in 1825; that of mammals was first noticed by Coste in 1833.

cell. It consists of a nuclear membrane enclosing a clear material or matrix, imbedded within which may sometimes be seen strands of karyoplasm; it always encloses one or more well-marked nucleoli (fig. 15). Frequently there is but one nucleolus, which is then large and prominent, and has received the name of *germinal spot* (*macula germinativa*, Wagner, 1835).

In the young oocyte (fig. 17) there is a body (*idiosome*) near the nucleus, corresponding to the attraction-sphere of other cells. It encloses a central granule, and is itself surrounded by a mass of fine granules (mitochondria). Van der Stricht identifies this body with the *yolk-nucleus* or *body of Balbiani*.[1] There are also other cell-inclusions to which various names have been given, but it is doubtful what significance they possess.

**Oogenesis.**—The earlier stages of oogenesis and the development of the Graafian follicle will be treated of under the head of the ovary. Here we shall begin with a stage in which the young egg-cell is already imbedded in the developing gland, and surrounded by a layer of follicular cells.

FIG. 17.—YOUNG OOCYTE SURROUNDED BY A SINGLE LAYER OF FOLLICULAR CELLS. (Van der Stricht.)

Showing attraction-sphere, centrosome, and mitochondria.

It will be recollected that the spermatozoa are derived from the spermatogonia lining the testicular tubules, and that the first phase is characterised by marked and comparatively rapid growth of the spermatocytes. The process begins at puberty and proceeds continuously throughout the greater part of the life of the individual. The young egg-cells or *oogonia*, on the other hand, have all become converted into *oocytes* by the time of birth. These undergo a very slow process of growth and ripening, and are discharged singly at periodic intervals during a relatively short period of reproductive activity.

As the oocyte grows the Graafian follicle is gradually enlarged. The follicular cells, at first laid down as a single layer (fig. 17), multiply to form a many-layered investment to the ovum. By the formation of fluid among them (fig. 18) the cells come to bound a cavity into which, from one part of the wall, a cellular mass projects surrounding the egg (the discus proligerus). The cells of the discus proligerus are arranged in an epithelial fashion round the ovum, and remain in intimate relationship to it during the process of ripening.

The oocyte is not at first provided with a zona pellucida, and the manner in which this develops has not yet been quite cleared up. Authorities differ as to whether it is formed by the follicular cells or is a true egg-membrane secreted by the ovum.

**Maturation of the oocyte; formation of the polar bodies.**—By the term 'maturation' is signified the series of changes which prepare the egg for fertilisation. During a very prolonged period of growth the deutoplasm becomes gradually accumulated in the protoplasm. The phenomena observed during this period have been recently described for the human ovum in great detail by Van der Stricht.[2] From this it would appear that the mitochondria, which are regarded as specific cytomicrosomes, are concerned in the elaboration of the yolk. They first collect round the idiosome, then become scattered, arrange themselves in chains (*chondriomites*), solid rods (*pseudo-chromosomes*), and irregular bodies; later they become arranged in double rows to form minute tubules, which extend

[1] See also Gurwitsch, Archiv f. mikr. Anat. lvi. 1900; and Winiwarter, Archives de Biologie, xvii. 1900.

[2] *Loc. cit.*

through the protoplasm as a sort of framework. These again disappear as the deutoplasm collects in the centre of the cell in the form of minute vacuoles with clear contents, fat-spheres, and minute highly refractile bodies (fig. 19).

When growth and storage of yolk-food are completed, the ovum is matured by the extrusion of the polar bodies. The maturation stages now to be described have not been seen in the human ovum, but observations on other mammals put it beyond question that the process occurs in essentially the same way as in lower forms. The phases leading up to maturation have been described by Heape[1] in the rabbit.

Prior to the beginning of the sexual season in that animal certain of the Graafian vesicles enlarge, and the growth of those near the surface causes them to project and form swellings on the surface of the ovary. The wall of the follicle and the tunic of the ovary is here much attenuated: so much so that in some of them, when ripe, the structure is sufficiently transparent to allow of the ovum

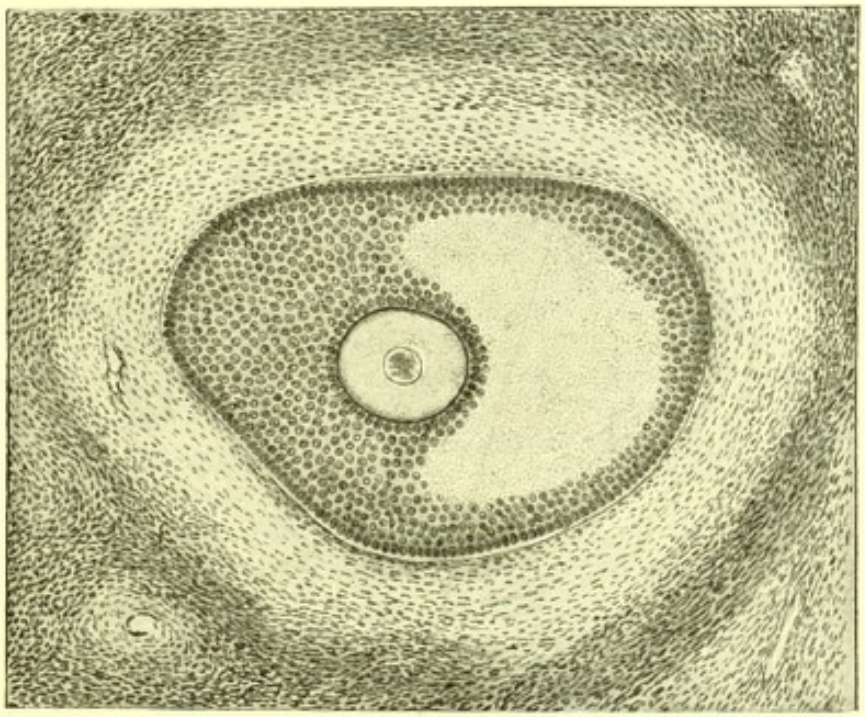


FIG. 18.—EARLY STAGE OF THE GRAAFIAN FOLLICLE, HUMAN. (Sellheim.)

The follicular epithelium has become many-layered, and a cavity has appeared among the follicular cells containing the liquor folliculi. The mass of cells which encloses the ovum is the discus proligerus.

being seen within the vesicle. During *proœstrum* (period preceding 'heat') the blood-vessels surrounding the follicle enlarge, and these, running in the thin wall which projects from the surface of the ovary, give the follicle the bright pink colour which is characteristic of it. When maturation sets in, the cells of the discus proligerus begin to withdraw from the ovum, and eventually remain attached to the zona only by very fine protoplasmic strands. At the same time the ovum withdraws from the zona, and a narrow perivitelline space appears.

The polar bodies are now thrown off (figs. 20 and 21). They are minute portions of the egg-substance budded off in quick succession from the same point on the surface into the perivitelline space. In this they persist for a time, but ultimately disappear. They were originally termed *polar bodies* or *directive corpuscles*, from the supposition that their presence determines the pole of the egg at which the first segmentation will take place should the ovum become fertilised. As a matter of fact, they occupy the pole which becomes afterwards the vegetative pole (Van

[1] Proc. Roy. Soc. B. vol. lxxvi. 1905.

der Stricht in the bat),[1] and it has now long been known that the process by which each polar body is formed is in reality a cell-division, in which the nucleus is *equally*, but the protoplasm very *unequally*, divided. They are thus minute cells, often called the pole-cells, and are regarded as abortive ova. In some cases the first polar body undergoes division; when this occurs, the typical group of four becomes formed. Such groups are of frequent occurrence in the production of the gametes, not only in the animal, but also in the vegetable kingdom. Only one of the four is, however, functional.

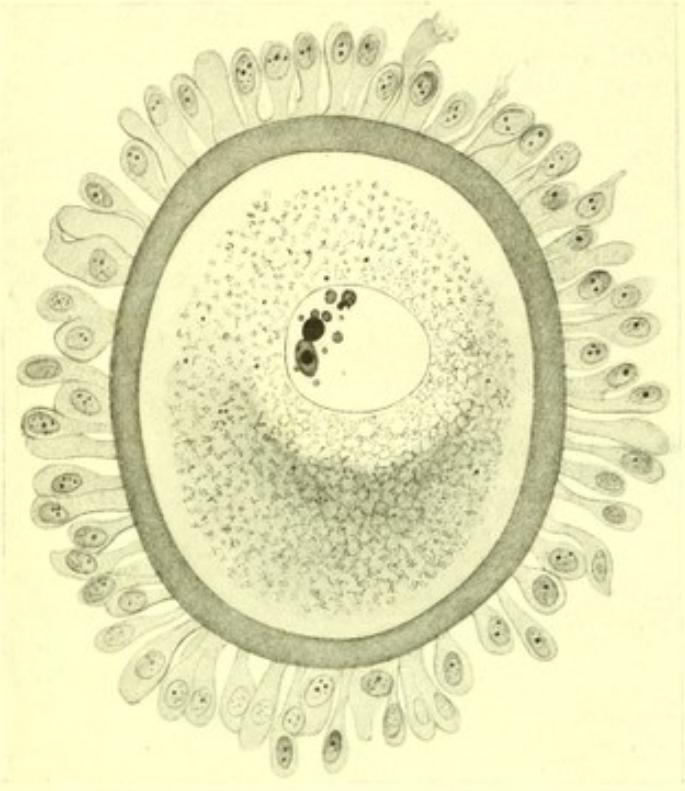


FIG. 19.—HUMAN OVUM AT END OF GROWTH-PERIOD. (Van der Stricht.)

Showing distribution of mitochondria in deutoplasmic zone, with vacuoles, fat-drops, yolk-granules, &c

The oocyte after the first division is called the *oocyte of the second order*; and when this again divides, and the second polar body is thrown off, the egg is said to be *mature*. The essential difference is that the large vesicular nucleus of the oocyte of the first order has been converted into a smaller nucleus, which retires to the centre of the egg, there to await the advent of the sperm-nucleus in fertilisation. It is to the egg at this final stage that, strictly speaking, the term *ovum* should be applied.

During the maturation of the ovum important nuclear phenomena present themselves, which are essentially similar to those which take place in the sperm-cells, as was first proved by Oscar Hertwig in his classical researches on *Ascaris megalocephala*, published in 1890. The full significance of these nuclear changes cannot, however, be made clear until the process of fertilisation is understood. The treatment of the history of the nucleus during maturation will therefore be deferred until that process has been studied.

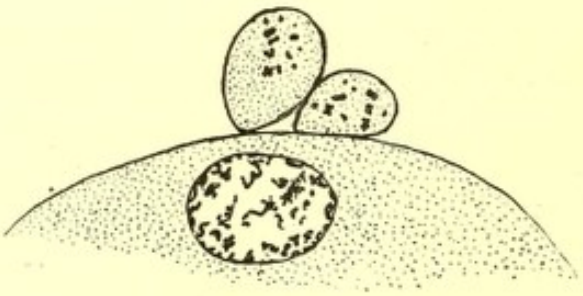


FIG. 20.—THE POLAR BODIES AND EGG-NUCLEUS; ECHINUS ESCULENTUS. (T. H. Bryce.)

Only a portion of the ovum is represented. × 1200 diameters.

In the process of spermatogenesis the centrosome, it will be recollected, persists and is related to the flagellum, but in the case of the egg it in many instances seems wholly to disappear during maturation. This has been made the basis of certain theories of fertilisation which will be alluded to later.

In the above account the case has been described in which maturation is completed before the egg leaves the ovary. In many animals the spermatozoon

[1] Anat. Anzeiger, Ergänzungsheft, xxvii. 1905.

enters the egg before the second polar body is extruded. The final phases of maturation then proceed concurrently with the initial phases of fertilisation.

While there is a general correspondence or homology between the different cell-generations in spermatogenesis and oogenesis (fig. 22), it must be noted at

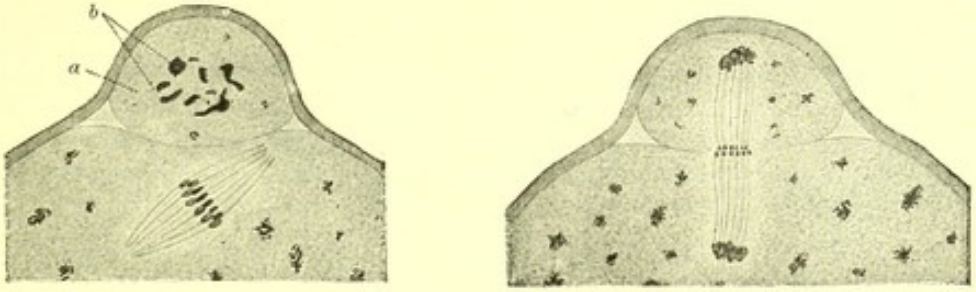



FIG. 21.—FORMATION OF SECOND POLAR BODY OF THE MOUSE. (Sobotta.)
I. First polar body (*a*) and its nucleus (*b*), with second polar spindle.
II. Second polar body, with remains of the spindle and cell-plate. × 1200 diameters

this point that there are two differences between the two series of cells. First, after the second division is over the egg undergoes no further modification, while the spermatid becomes converted, by a complicated process of cytohistogenesis, into the functional spermatozoon; secondly, all four spermatids become

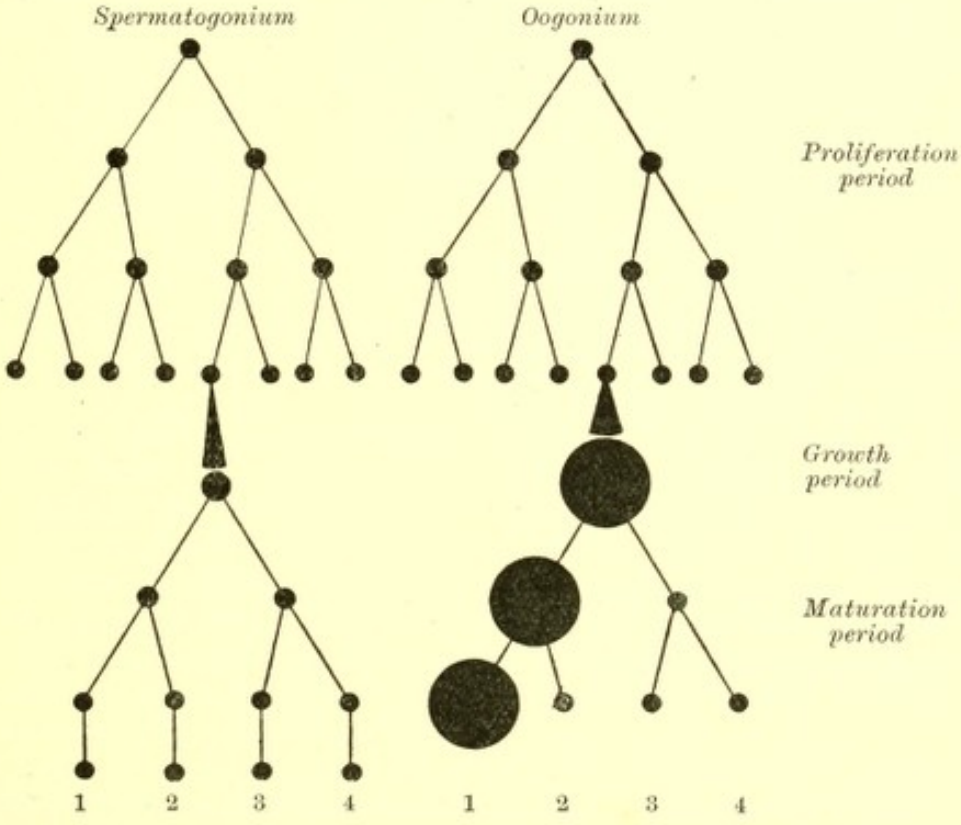



FIG. 22.—SCHEME OF SPERMATOGENESIS AND OOGENESIS. (After Boveri.)

spermatozoa, while only one of the products of division of the original oocyte becomes a functional ovum.

From the foregoing descriptions it will be clear that in the *dimorphism* of the sex-cells we have an instance, of a marked kind, of division of labour. In the most primitive forms among the protozoa conjugation of cellular individuals occurs, but they are indifferent and equivalent individuals; while, on the other hand, in many of the higher Protozoa new conditions of life are established, the sessile habit, for instance, which necessitates that one of the pair should have a degree of mobility. Thus we have micro- and macro-gametes. There are instances of colonial

forms, in which certain individuals of the colony become macro-, others micro-gametes (*e.g.* Volvox), and from this stage the step to the differentiation of dimorphic sex-cells is theoretically a simple one.

**Fertilisation.**—The ovum after its expulsion from the Graafian follicle is received upon the fimbriated end of the Fallopian tube. The fimbriæ are covered by a prolongation of the ciliated lining of the tube, and the action of the cilia serves to propel the minute ovum into and along the tube towards the uterus. In this passage it may, if impregnation has occurred, meet with the spermatozoa, and one of them may penetrate the zona pellucida to fertilise the ovum. It is possible in some instances for fertilisation to occur on the fimbriated extremity of the tube, or even in the Graafian follicle, and this may result in an extra-uterine pregnancy.

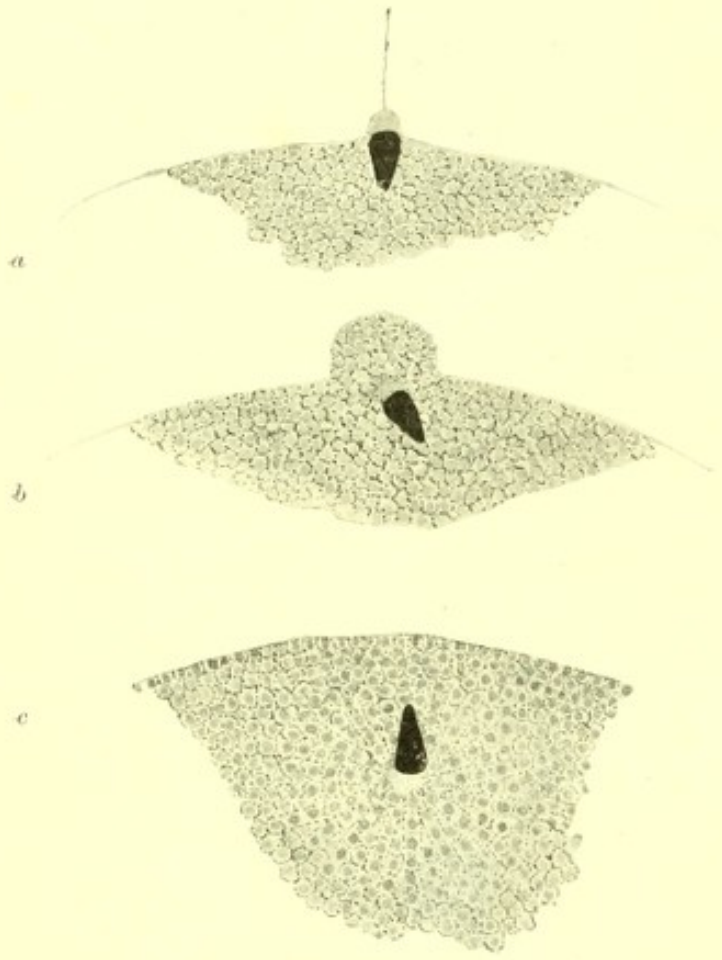



FIG. 23.—FERTILISATION IN ECHINUS ESCULENTUS; DRAWN FROM SECTIONS HIGHLY MAGNIFIED. (T. H. Bryce.)

*a*, entrance of spermatozoon; *b*, commencing rotation of sperm-head; *c*, completed rotation of sperm-head; commencing sperm-aster.

The details of the process of fertilisation have been observed in a few mammals, most clearly in the mouse by Sobotta. The process can be easily followed in the transparent egg of an echinoderm, and for this reason the phenomena as seen in the common sea-urchin will first be briefly described, and then a comparison will be made with the facts established for the egg of the mouse. This is the more convenient because the two cases represent two types of the process.

When the spermatozoon which is to effect the fertilisation of the echinoderm-egg touches its surface the protoplasm streams out at the point of contact, to form what is known as the entrance cone (fig. 23, *b*). As soon as the sperm-head is fixed, a membrane is thrown off from the egg. It may happen, however, that before this is effected several spermatozoa may have obtained an entrance, and *polyspermy* results. This is always followed by abnormal development. The spermatozoon, by the action of the flagellum, now bores its way into the egg until the whole head and the middle piece are imbedded in the protoplasm. The flagellum, no longer of service, is thrown off, and the sperm-head undergoes a rotation through 180° (fig. 23, *b*, *c*), until the middle piece is directed inwards. Radiations now appear in the protoplasm centred on the situation of the middle piece, which is no longer distinguishable, and the sperm-head commences a movement towards the centre of the egg. In living eggs the radiations are seen gradually to extend

through the whole cell-body, and meanwhile the conical sperm-head assumes a spheroidal form, and is converted into the *sperm-nucleus* (fig. 24, *a*). Several observers have described the existence of a minute granule in the centre of the radiation or *sperm-aster*, and it has been identified as the centrosome of the spermatozoon. As previously mentioned, it has been supposed that the centrosome disappears in the ovum during maturation. According to Boveri's theory of fertilisation, the sperm-centrosome supplies a new divisional centre, and plays the leading *rôle* in initiating cleavage of the egg. Wilson's[1] observations, however, on eggs which undergo parthenogenetic development as the result of treatment by chemical substances, make it doubtful whether we can interpret the phenomena in this way. His experiments prove that centrosomes may arise *de novo* in the egg-protoplasm, and therefore it is possible that the spermatozoon produces an effect on the egg-protoplasm such as to produce a centrosome, or physiological centre of activity, made manifest by the radiations of the aster.

As the result of this protoplasmic activity the sperm-nucleus now changes its position and moves toward a point not quite in the centre of the egg, while

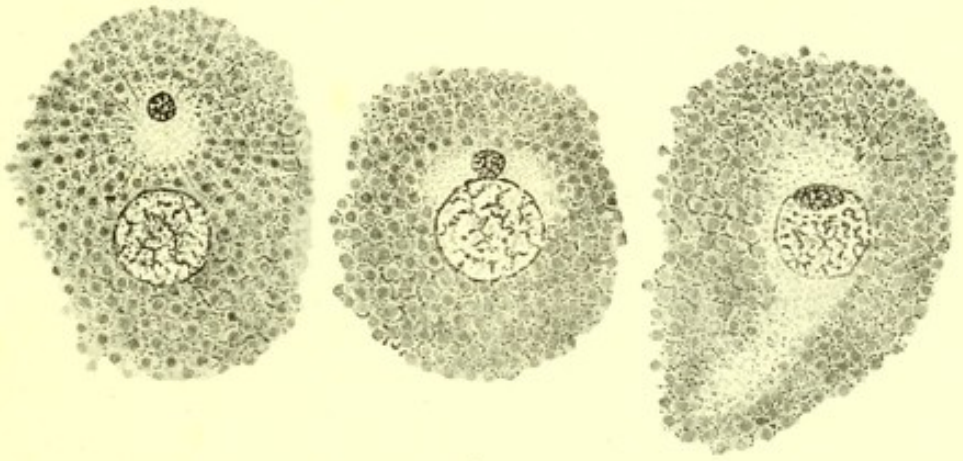



FIG. 24.—THREE STAGES IN THE CONJUGATION OF THE SPERM WITH THE GERM-NUCLEUS IN ECHINUS; DRAWN FROM SECTIONS. × 1200 D. (T. H. Bryce.

at the same time the germ-nucleus is also drawn to the same point. As the nuclei approach one another the aster comes into contact with the germ-nucleus, and the clear area at its centre spreads over the side of that body. The nuclei then conjugate (fig. 24, *b*, *c*), the aster becomes double, and the radiations die away during a pause in which the compound nucleus, or, as it is now called, the *segmentation-nucleus*, grows in size. The two asters then become related to the poles of the nucleus, the radiations reappear, and the first nuclear division of the egg is inaugurated. From the figures it will be clear that the nuclei conjugate while in the vesicular phase, with the chromatin in the form of a network.

The process in the mouse[2] (fig. 25) is essentially the same, but there are certain variations. The spermatozoon meets the egg in the second third of the oviduct, before the second pole-cell has been formed. Entrance is probably effected by the piercing of the zona, and not through one of the pores in the membrane. The tail seems to be cast off, and only the head and middle piece enter the egg; but in the bat the whole spermatozoon is figured by Van der Stricht as entering (fig. 26). A rotation of the head occurs, and it then becomes converted into a small vesicular nucleus, which is at first distinguished from the germ-nucleus by its smaller size.

[1] Archiv f. Entwickelungsmechanik, xii. 1901.

[2] See Sobotta, Arch. f. mikr. Anat. xlv. 1895. Cf. also Van der Stricht, Anat. Anzeiger, Ergänzungsheft, 1902, and Rubaschkin, Anat. Hefte, xix. 1905.

It expands, however, before conjugation takes place, and the two nuclei, now of equal size, lie side by side. In each the nuclear network is converted into a spireme thread, the membrane disappears, and the thread is divided into the chromosomes. The paternal and maternal chromosomes thus form separate groups, and these appear to remain distinct as the rods from each nucleus are gathered into the equatorial plate of the first segmentation-spindle. The mixture of the chromatin is probably not effected, therefore, until the first segmentation-

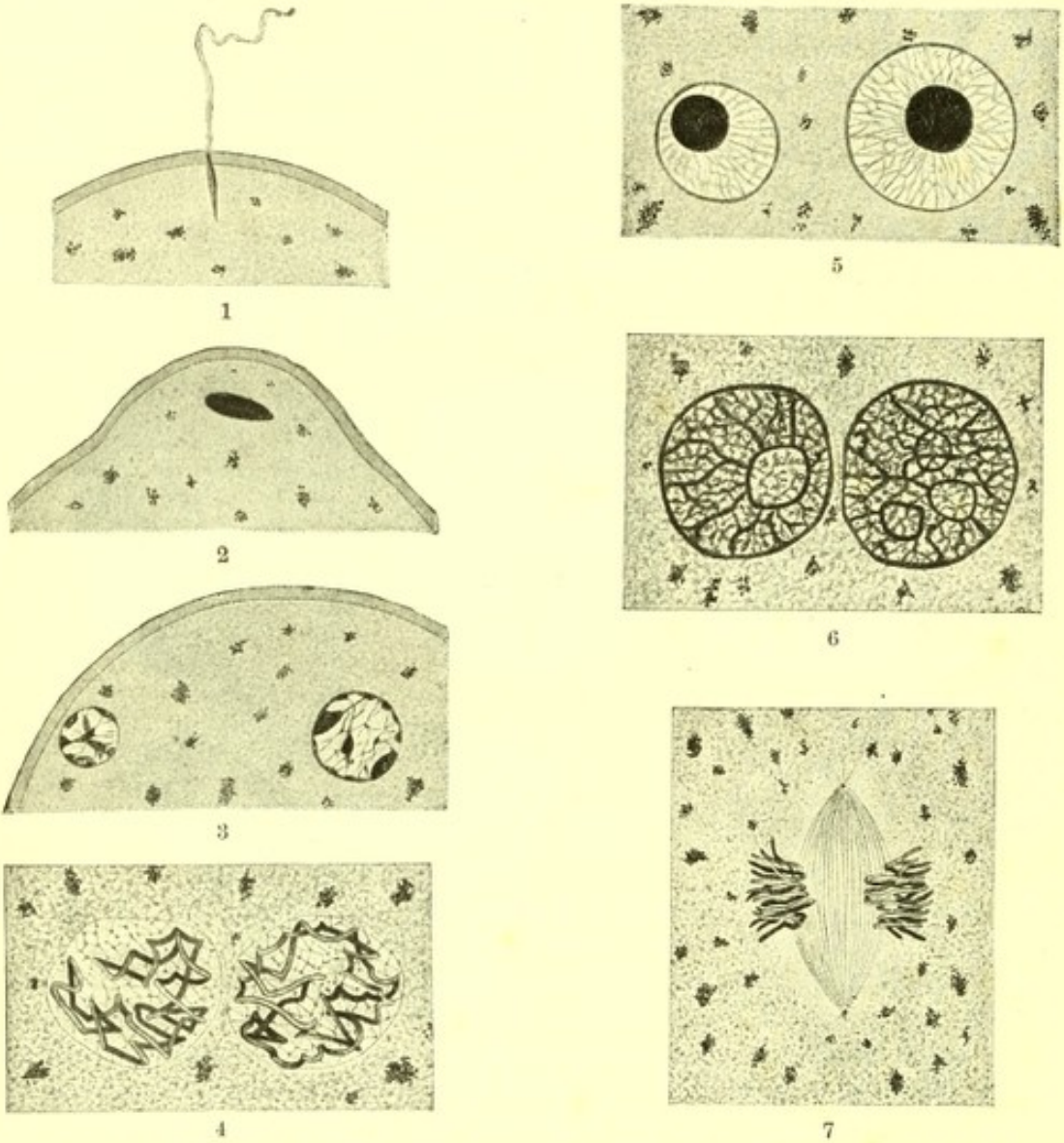



FIG. 25 (1–7).—STAGES IN THE FERTILISATION OF THE EGG OF THE MOUSE. (Sobotta.)

1, Entrance of spermatozoon; 2, rotation of sperm-head; 3, formation of sperm-nucleus, which lies to the left; the germ-nucleus lies to the right; 4, resolution of nuclei; 5, vesicular stage of nuclei; the smaller is the sperm-nucleus; 6, enlargement of sperm-nucleus and its approach to germ-nucleus; 7, first segmentation-spindle, with group of paternal chromosomes to left and of maternal to right.

division has begun; and it has been proved in Ascaris, which has only four chromosomes, that the rods are divided, after splitting, between the two first blastomeres in such a way that each receives an equal number of paternal and maternal chromosomes (fig. 27). This is a fact of capital importance, and plays a prominent part in modern theories of heredity.

If we analyse the phenomena of fertilisation we must recognise two factors: (1) The initiation of cell-division, and (2) the union of the nuclei. Though closely bound up with one another, these two factors are distinct and independent phenomena. Thus it has been demonstrated

by the brilliant experiments of Boveri, Delage, and others, that portions of sea-urchin eggs broken by shaking, or cut into fragments (merogony), which contain no part of the germ-nucleus, may, when fertilised by spermatozoa, divide, and ultimately form larvæ. The sperm nucleus is thus sufficient by itself for the segmentation of the egg, a centrosome being introduced or produced in the protoplasm. Again, it has been shown, first by Loeb and then by many others, that the eggs of echinoderms and other invertebrates may be made to segment and form larvæ by treatment, in various ways, with certain chemical substances, by shaking and so forth, without the influence of the spermatozoon. The egg-nucleus is thus sufficient in itself for segmentation and development of the egg when, by artificial means, a centrosome is produced in the protoplasm.[1]

Thus we reach the general conclusion that the union of the nuclei is not the *means* by which the developmental process is started, but nevertheless it is the essential factor in fertilisation —in short, it is the end and aim of the process. The union of the paternal and maternal chromatin (*amphimixis*) is the all-important fact, and for this reason, that (without denying to the protoplasm a certain influence) the chromatin of the nucleus is the material basis of the hereditary qualities handed on from one generation to another.

**Reduction of chromatin.**—It is sufficiently obvious that if there is a fusion of paternal and maternal chromatin in fertilisation at each generation the amount of chromatin would be doubled, on the assumption that the mass is constant in all the nuclei of each generation. The necessary reduction is effected during the maturation of the sexual cells.

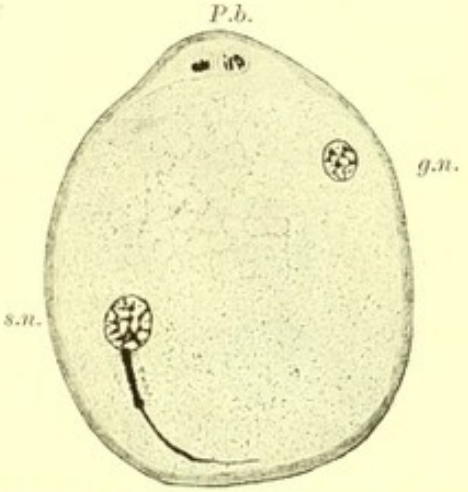



FIG. 26.—FERTILISATION; EGG OF BAT. (Van der Stricht.)

*S.n.*, sperm-nucleus; *g.n.*, germ-nucleus; *P.b.*, polar bodies.

Before entering on a description of the process of reduction, it is necessary to refer briefly to two related hypotheses as to the constitution of the nucleus.

It is now practically certain that the number of chromosomes is constant in each species, and that out of a resting nucleus the same number of chromosomes emerge as entered it at the end of the preceding division. It is believed by some that the chromosomes retain their identity in the resting nucleus, so that the chromosomes which emerge from it are the same as those which entered it.[2] As a corollary to this theory of the persistent identity of the chromosomes, there is a second hypothesis that the paternal and maternal chromosomes, equally distributed between the two first blastomeres (fig. 27), have a separate and persistent identity in all the cells of the soma, and consequently in the spermatogonia and oogonia.

**Nuclear phenomena during development of the sexual cells.**—The history of the sexual cells in respect of the nuclear changes may be divided into three phases—a pre-reduction, a reduction, and a post-reduction phase.[3] The pre-reduction phase includes all the cell-generations up to that of the spermatogonia and oogonia (fig. 22). During this period the nuclei behave in all respects like the nuclei of somatic cells, and possess the same number of chromosomes. The reduction phase involves the generations known as spermatocytes and oocytes of the first and second orders, and is characterised by two divisions differing in their characters from all other varieties of mitosis, during which the number of chromosomes is reduced to one-half of the somatic number. The first division is known as

[1] Further information as to the observations here referred to will be found in a review of the literature in the Quarterly Journal of Microscopical Science, xlvi. 1902, by T. H. Bryce.

[2] It appears to me that the facts of maturation of the ovum, as will be seen later, form an obstacle to the present unrestricted acceptance of the theory of the persistent identity of the chromosomes in its crude form, but that, notwithstanding, it is necessary to assume a segregation in the chromatin mass, which may, as it were, crystallise at each division into chromosomes of specific characters.—T. H. B.

[3] For these phases the terms *pre-meiotic*, *meiotic*, and *post-meiotic* are employed by Moore and Walker (derived from μειόω, to make smaller).

the *heterotypical*, the second as the *homotypical*, division. The post-reduction phase is represented in animal forms by the mature sex-cells, but in certain plants in which there is alternation of generations it includes all the cells of the sexual generation. The post-reduction phase comes to an end with the union of the nuclei of the sex-cells, and it is obvious that as each conjugating nucleus has only one-half the number of chromosomes possessed by the somatic cells, the somatic

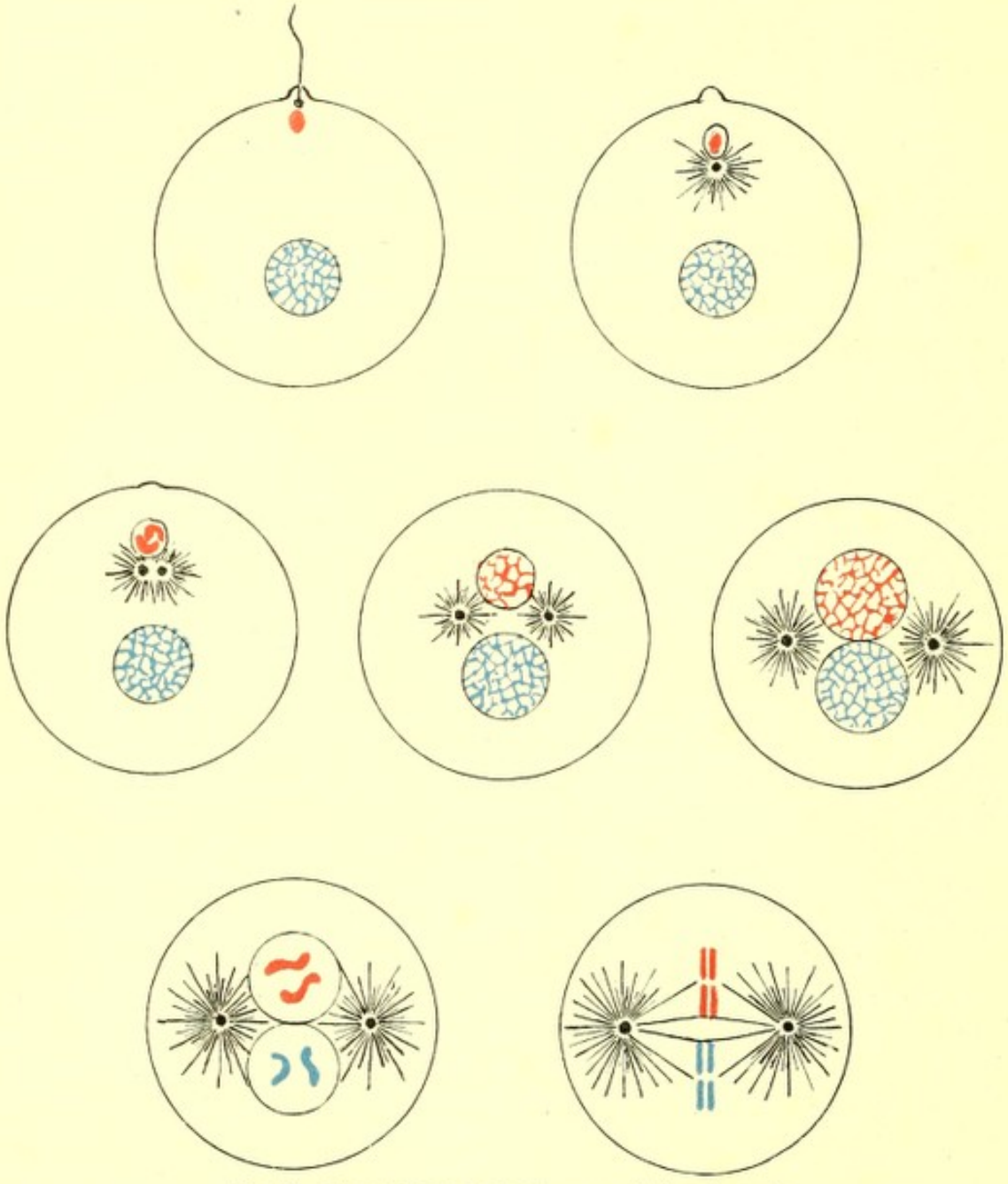


FIG. 27.—DIAGRAM OF FERTILISATION. (After Boveri.)
The number of chromosomes is four: paternal, red; maternal, blue.

number of chromatin-rods is restored in the segmentation-nucleus formed by the union of the sperm- with the germ-nucleus.

The phenomena are seen with greater clearness in the sperm-cells than in the germ-cells, as there are certain modifications of the process in the maturation of the ovum which will be alluded to later.

The prophase of the first or heterotypical division is very prolonged, and the chromatin undergoes changes too intricate to be followed in detail here. One

phase is especially important. During it the chromatin is gathered into a tangled skein at one side of the nucleus (fig. 28, B). This may be named the *synaptic phase* (synapsis of Moore; see p. 22). During this phase a reduction in the number of chromosomes takes place by a fusion of the somatic chromosomes in pairs. The manner of the fusion is disputed, some observers holding that the chromosomes unite end to end; others that they fuse along their whole length. The fused rods (now one-half the number characteristic of the somatic cells) go through elaborate changes, and ultimately form double rods (fig. 28, *a*—*e*), which take various forms (pseudotetrads, rings, &c.), according to the manner in which the rods are united together. In a very small number of cases (Ascaris) the prophase figures take the form of four isolated bodies or tetrads. Such cases fall into a special category, and will be treated separately.

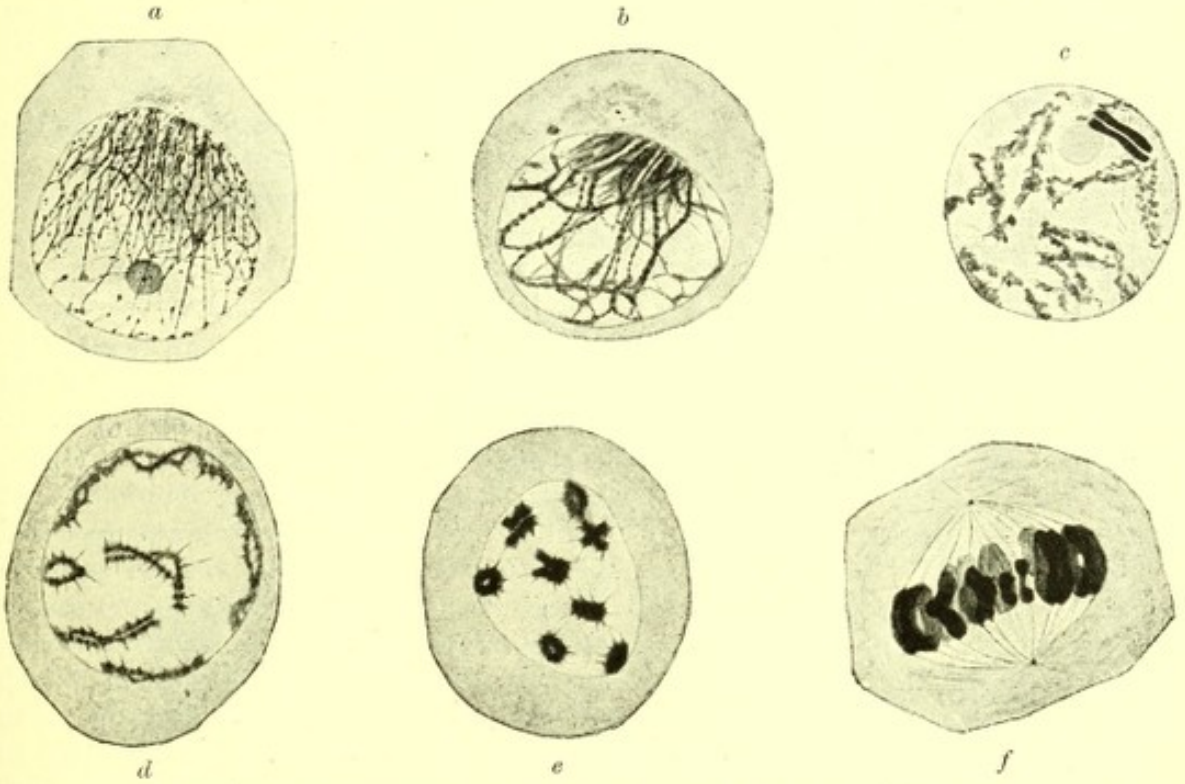



FIG. 28.—SOME STAGES IN SPERMATOGENESIS OF MYXINE. (Schreiner.)
*a* and *b*, synaptic phase; *c*, *d*, double thread stages; *e*, double chromosomes (rings and double rods); *f*, metaphase of heterotype.

These double-rod prophase figures ('gemini') are gathered on to the equator of the first maturation-spindle, and the resulting metaphase figures vary according to the manner in which they are attached to the threads of the spindle. They may be attached at their extremities, at their middle points, or nearer one end (fig. 29). It follows that when the two portions of the double rods are separated on the spindle, in the first case the chromosome will be a straight rod, in the second a V, in the third a V with unequal limbs (fig. 29, *b*). The result is the same in each case: the two portions of the double rod are separated, and as these portions represent not a longitudinally divided chromosome, but the two somatic chromosomes which have fused in the synaptic phase, whole chromosomes are separated and distributed on the spindle, instead of the halves of the longitudinally split chromosome, as in ordinary mitosis. A further complication of the heterotypical division is that a cleavage of the rods manifests itself as they pass to the poles of the spindle, and a double figure again results (figs. 29 *c*, 30 *b*). This cleavage is preparatory to the second or homotypical division, in which the elements are

separated without further splitting (fig. 30, *c*). In very many cases there is no reconstruction of the nucleus between the heterotype and the homotype division, but in others a partial reconstruction takes place, without however a loss of the identity of the halves of the double anaphase figures of the heterotype.

The case of *true tetrads* involves certain difficulties, but the explanation of their occurrence seems to be that the second, or anaphase cleavage, which is foreshadowed in the prophase in many forms, has been completed before the formation of the first spindle. There has been much diversity of opinion as to the character of the second cleavage, whether it is a longitudinal splitting or transverse breaking of the spireme-thread. If it be a longitudinal splitting of the elements of the 'synaptic gemini,' the case falls in with the scheme adopted.

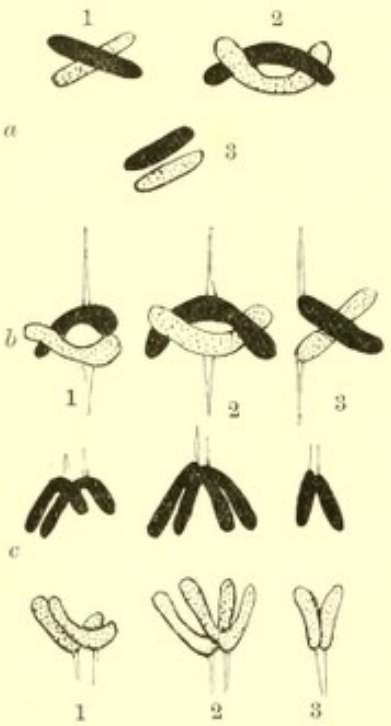



FIG. 29.—DIAGRAM REPRESENTING THE BEHAVIOUR OF THE DOUBLE CHROMOSOMES OF THE HETEROTYPICAL DIVISION. (After Grégoire.)

*a*, Three double chromosomes, variously arranged; *b*, the mode of attachment to the spindle of the three types—1, near the ends; 2, opposite the middle points; 3, at the ends; *c*, resulting double anaphase figures—1, tailed V's; 2, simple V's; 3, straight rods.

Difficult as the stages are to follow during maturation of the sperm-cells, they are still further complicated during the maturation of the egg, by the fact that an immensely long period of repose occurs between the early stages of the heterotypical prophase and the actual division of the nucleus, during which the nucleus assumes the vesicular form characteristic of the ripening oocyte (fig. 31). As the oocytes are all formed before birth, the beginning of the prophase must, in the human subject, be separated by many years from the actual division. The manner in which the chromosomes are re-formed out of the germinal vesicle when maturation sets in, is by no means cleared up. The chromatin-threads are, according to competent observers, completely lost sight of in the vesicle, and the chromatin gathered into nucleoli, which again give rise to chromosomes. This is a difficulty with which the theory of persistence of the chromosomes has to contend; but in any case double-rod figures appear, which pass into the metaphase (fig. 32) exactly as in spermatogenesis. In maturation of the egg in Echinus the double-rod figures (pseudotetrads) are attached to the spindle by their extremities. The figures, though minute, are simple, and are here reproduced as an example of the process (fig. 33).[1]

**Significance of the nuclear phenomena.**—It is impossible here to deal at length with the history of opinion on the interpretation and significance of the phenomena described above. In the last edition of this work two theories were briefly alluded to—the sex theory of Minot and the hypothesis of Weismann. Minot's theory, which applied to the ovum only, postulated that the cells were hermaphrodite, and supposed that in the extrusion of the polar bodies the male element was got rid of from the ovum, to be replaced again in fertilisation. This became untenable when the parallelism of the maturation processes in spermatogenesis and oogenesis was established, and it was proved that all four elements resulting from the division of the spermatocytes became functional spermatozoa, while only one of the products of the division of

[1] The following works may be consulted on this subject: Ed. B. Wilson, The Cell in Inheritance and Heredity, 1900; Winiwarter, Arch. de Biol. 1900; Korschelt and Heider, Lehrbuch d. vergleich. Entwickelungsgeschichte d. wirbellosen Tiere, Lieferung ii. 1903. Grégoire, La Cellule, xxii. 1905, gives a useful summary and bibliography to date of publication. Since then, among other papers, have appeared Farmer and Moore, Quart. Jour. Micro. Sc. xlviii.; J. E. Lane-Claypon, Proc. R. S. 1905; Janssens, La Cellule, xxii.; A. and K. E. Schreiner, Arch. de Biol. xxii., and Anat. Anzeiger, xxix.; Van der Stricht (bat), Compt. rend. de l'Assoc. des Anat., 8e Réunion, Bordeaux, 1906; Moore and Walker, The Meiotic Process in Mammalia, Rep. Cancer Research Lab., Univ. Liverpool, 1906.

the oocyte became a functional ovum. Weismann's theory, very briefly put, postulated a qualitative reduction of the hereditary substance, brought about by a transverse cleavage of the chromatin-rods, the halves of which were separated in the second division, the rods or *idants* by his hypothesis being organised into lower-grade groups of the ultimate particles of the hereditary substance (*ids* and *determinants*). During more than a decade of research to which this

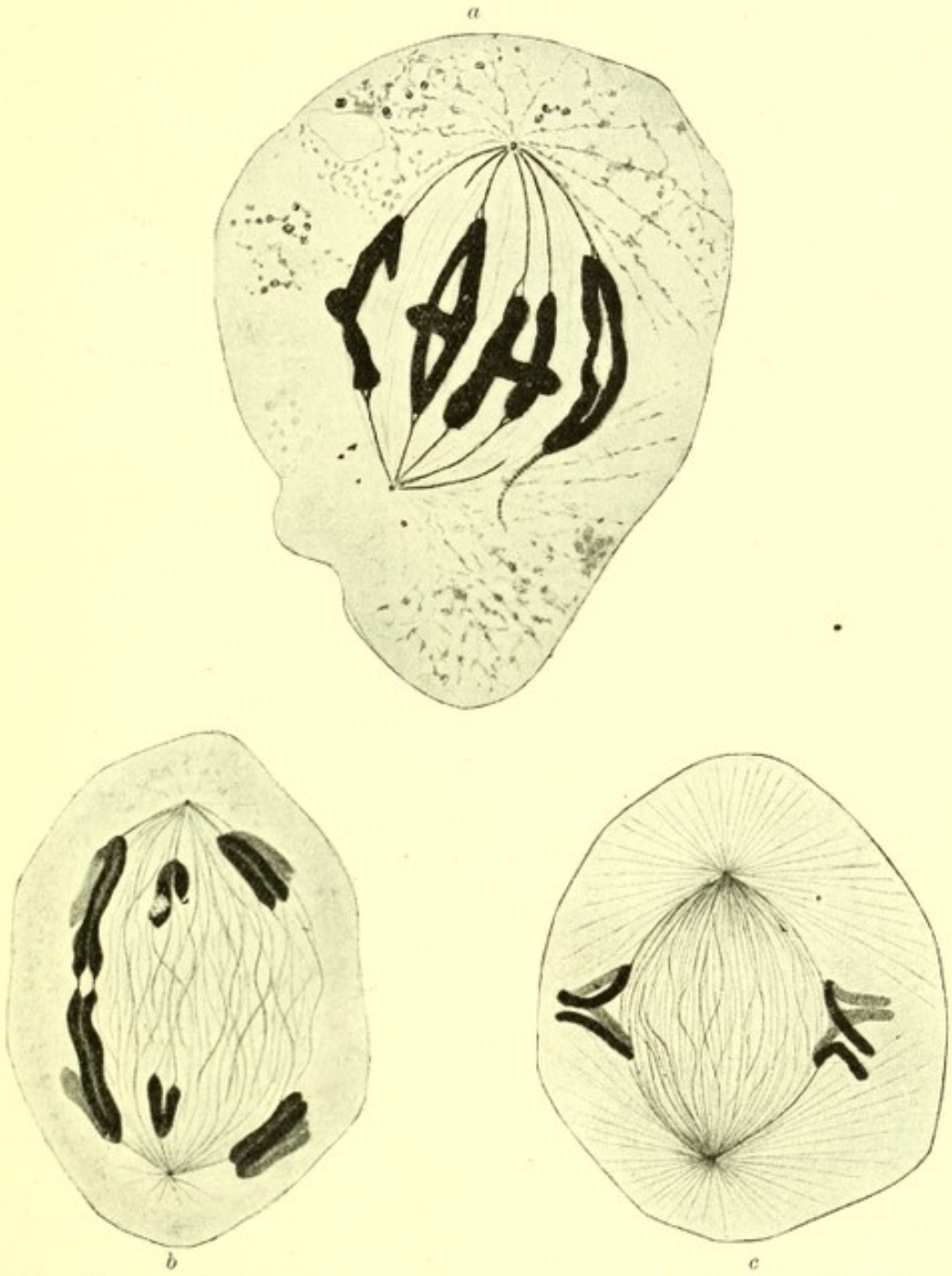



FIG. 30.—FIGURES ILLUSTRATING BEHAVIOUR OF CHROMOSOMES DURING MATURATION DIVISION.

*a*, Metaphase of heterotypical division, spermatocyte I. of Batrachoseps (Eisen); *b*, anaphase of heterotypical division in spermatocyte I. of Salamandra, showing secondary cleavage of chromosomes; *c*, metaphase of homotypical division, spermatocyte II. of Salamandra (Meves).

hypothesis gave rise, the evidence for and against its actual realisation in fact was pretty equally divided. The cases in which the two maturation chromosomal cleavages seemed both to be longitudinal, resulting therefore in an *equal* distribution of the chromatin-mass to the quaternary group of gametes, were supported by as cogent evidence as those in which the splitting was described to be once longitudinal and once transverse, as was necessary for the idea of an *unequal* distribution of the supposed hereditary substance. So great was the contradiction

among the results of the most eminent of observers that some writers gave expression to the opinion that the problem was a barren one; but within the last few years a new light has been thrown on it by the work of numerous observers. The ultimate result has emerged in the form of an interesting hypothesis which combines, in a fashion, the theories of Minot and Weismann.

In 1896 Moore described a phase in which the chromatin of the nucleus is clumped, which, as already mentioned, he named the *synapsis*. This proved to be a very general phenomenon in spermatogenesis, and although missed at first in oogenesis was shown by Winiwarter (1901) to occur at an extremely early stage in the history of the oocyte. The idea that the double-rod prophase heterotypical figures might arise from fusion of chromosomes was not quite a new one. It had been suggested by Korschelt, Wilcox, and Calkins, but it took a new form when by the observations of Winiwarter, Montgomery, Sutton, Farmer, and Moore, it was

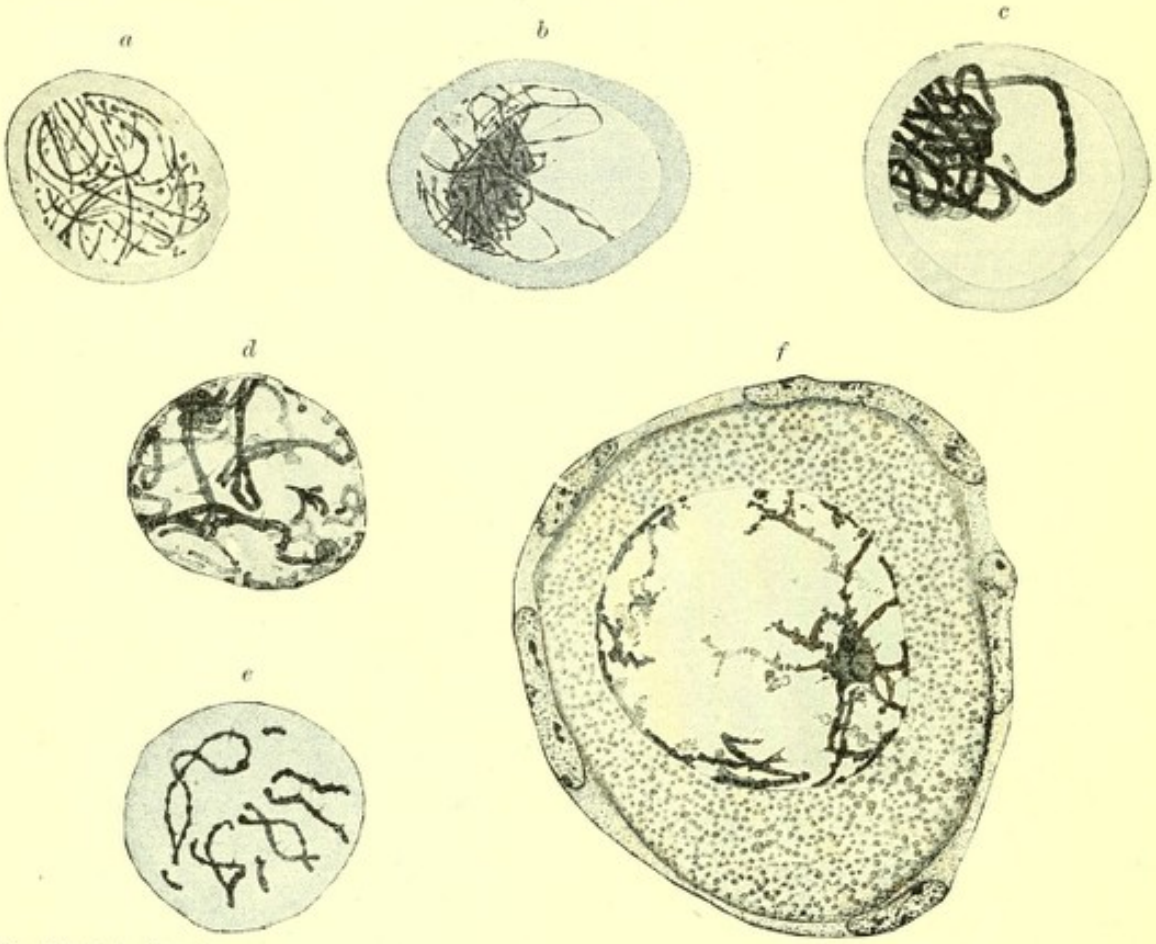



FIG. 31 (*a* to *f*).—SOME STAGES IN THE MATURATION OF THE EGG OF THE RABBIT. ×1700 diameters. (Winiwarter.)

*a*, nuclear network converted into delicate looping threads; *b*, synaptic stage (fine threads); *c*, synaptic stage (thick threads); *d*, nucleus now occupied by double filaments; *e*, double chromosomes; *f*, resting vesicular stage of nucleus in which the network is re-established.

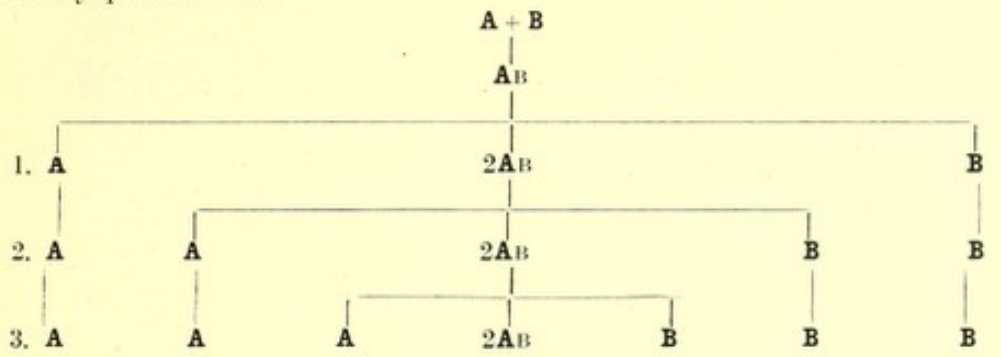
shown that in the synaptic phase the chromatin threads or loops fuse in pairs, thus producing reduction in the number of chromosomes. Sutton showed in 1902 that there is a certain order in the fusion, leading to the suggestion that the maternal and paternal chromosomes—present by hypothesis as persistent individuals in all the somatic nuclei resulting from the fusion in fertilisation of the male and female germ-nuclei—become fused in pairs. The double-rod prophase figure therefore represents not a longitudinally split chromosome, but two chromosomes, one paternal, the other maternal, and the first maturation division separates the paternal from the maternal.[1] It follows that of the four products of the two maturation divisions, two possess paternal and two maternal rods.

This new idea of reduction of hereditary qualities is different from that of Weismann, but equally well accounts for a redistribution of hereditary attributes (represented by the chromatin)

[1] In some forms it may be that the actual separation takes place in the second division; the result is the same.

during the maturation divisions. The theory is usually known as the chromosome theory of development and heredity.

It is further of interest that when the process as defined by this theory is analysed, it has suggestive relations to Mendel's 'law of heredity.' This law may be very briefly alluded to here because of its relation to the cytological data. It may be represented in terms of a single pair of hereditary qualities thus :




in which **A** and **B** represent single and distinctive qualities—one being dominant, the other recessive—of two individuals uniting in a cross, **AB**. In the cross one quality, **A**, alone manifests itself (the *dominant*); the other, **B**, is latent (the *recessive*), so that the offspring of the cross appears as pure **A**. In the next generation, no new cross in respect of these qualities being effected, the offspring appear in the proportion of *three* individuals with the **A** quality to *one* with the **B** quality. The **B** individuals now breed pure in all succeeding generations, and some **A** individuals do the same; but a second set of **A**'s are really **AB**'s, and they in the next generation split up again into pure **A**'s, **AB**'s (appearing as **A**'s) and pure **B**'s, and so on.

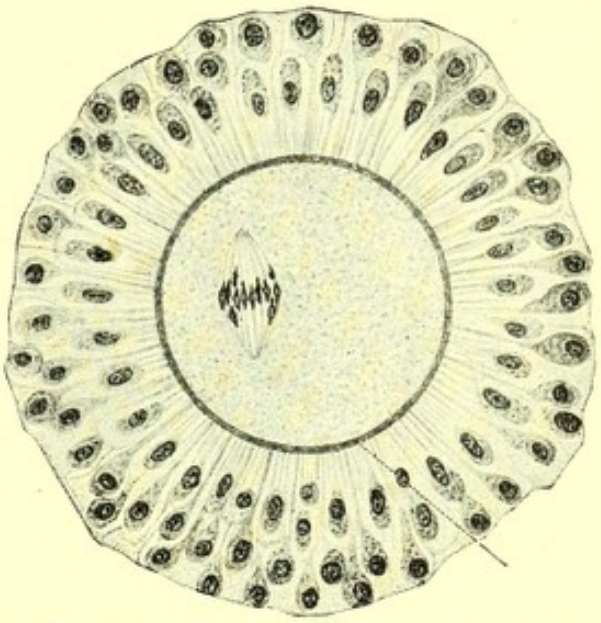


FIG. 32.—FIRST POLAR SPINDLE (METAPHASE OF HETEROTYPE), EGG OF MOUSE. (Sobotta.)

The theory involves as a corollary the purity of the gametes in respect of the qualities, and this purity would be attained by just such a process as is assumed by the chromosome theory to take place in maturation. Thus, if two **AB**'s cross, the gametes being pure in respect of the qualities will be either $\mathbf{A}^1$ or $\mathbf{B}^1$, $\mathbf{A}^2$ or $\mathbf{B}^2$. Four combinations are possible between these gametes—viz. $\mathbf{A}^1\mathbf{A}^2$, $\mathbf{A}^1\mathbf{B}^2$, $\mathbf{A}^2\mathbf{B}^1$, $\mathbf{B}^1\mathbf{B}^2$, giving rise to three classes of individuals, pure **A**'s, mixed **AB**'s, and pure **B**'s. The mixed individuals, however, always appear as **A**'s, that quality being dominant and **B** recessive, so that there are three **A**'s to one **B**, as expressed in the 'law.' In higher forms, all the individual gametes of the four groups are not functional, the three polar cells being abortive ova, so that the formula requires a slightly different statement. The ovum in respect of two qualities may be either **A** or **B**—

(1) **A** + **A**′ or **B**′ = **AA**′ or **B**′**A**; or
(2) **B** + **A**′ or **B**′ = **BA**′ or **BB**′.

In a sufficiently large progeny from a single pair the expectation would still be the same—viz. one pure **A**, two mixed **AB**'s appearing as **A**'s and one pure **B**.[1]

[1] For some interesting human cases see Bateson, Brit. Med. Journal, July 14, 1906. The reader must be referred for further information and for criticism of this theory, as well as for a statement of other doctrines of heredity, to special treatises on the subject. For the cytological data, see more especially Boveri, Ergebnisse über die Konstitution der chromatischen Kernsubstanz, Jena, 1903; Sutton, 'Chromosomes in Heredity,' Biol. Bull., April 1903. For a statement of Mendel's law, see Bateson, Mendel's Principles of Heredity, &c. (Cambridge University Press, 1902). The literature is fully reviewed in Schwalbe's Jahresberichte of recent years. For a criticism from the cytological side, a paper by R. Fick, Arch. Anat. und Physiol. Anat. Abt. 1905, may be mentioned.

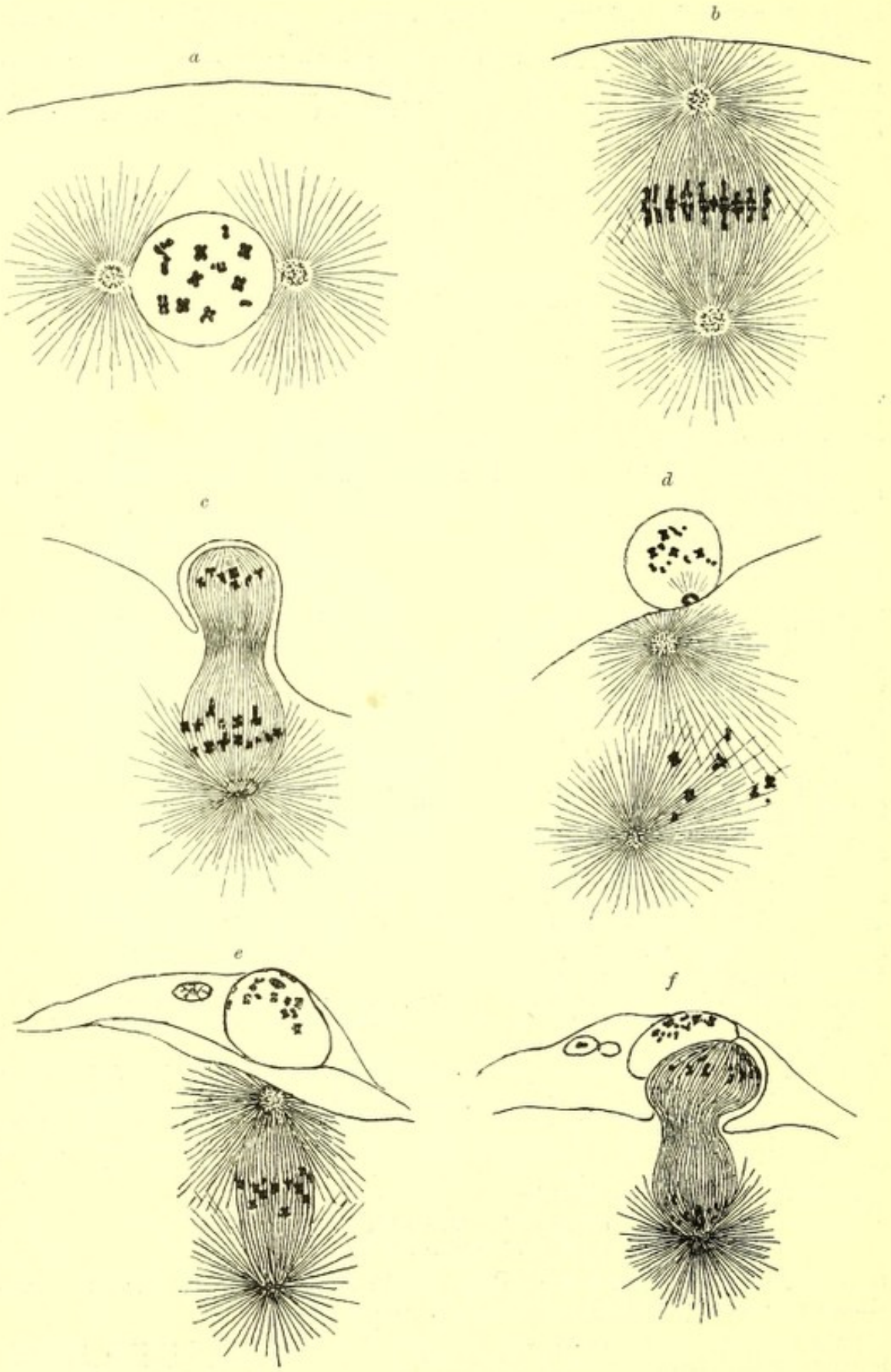



FIG. 33.—STAGES OF MATURATION, EGG OF ECHINUS ESCULENTUS. ×1200 diameters. (T. H. Bryce.)

*a*, Prophase of heterotype: double chromosomes; *b*, metaphase of heterotype: separation of chromosomes I. and their commencing secondary cleavage; *c*, anaphase of heterotype: completion of secondary cleavage: extrusion of first polar body; *d*, prophase of homotype: chromosomes pass unchanged into second polar spindle; *e*, metaphase of homotype; *f*, anaphase of homotype: separation of chromosomes II.: extrusion of second polar body.

# HISTORY OF THE SOMA.

## FORMATION OF THE BLASTODERM AND EMBRYONIC AXIS.

### SEGMENTATION OF THE OVUM.

Immediately after the sperm- and germ-nuclei have conjugated, the egg divides into two segments or *blastomeres* (fig. 34). The division of the cell-body is preceded, as in ordinary cell-division, by the mitotic cleavage of the nucleus, and, as previously stated, each daughter-nucleus receives an equal complement of paternal and maternal chromosomes. Each blastomere now divides to form a group of four segments, which again cleave into eight, and the process of binary division continues until a mass of small nucleated segments is formed, called the mulberry mass or *morula* (fig. 34). This is enclosed by the zona radiata, and is little, if at all, larger than the single ovum which it replaces within the zona. The segmentation of the mammalian egg is complete or *holoblastic* (see p. 27),

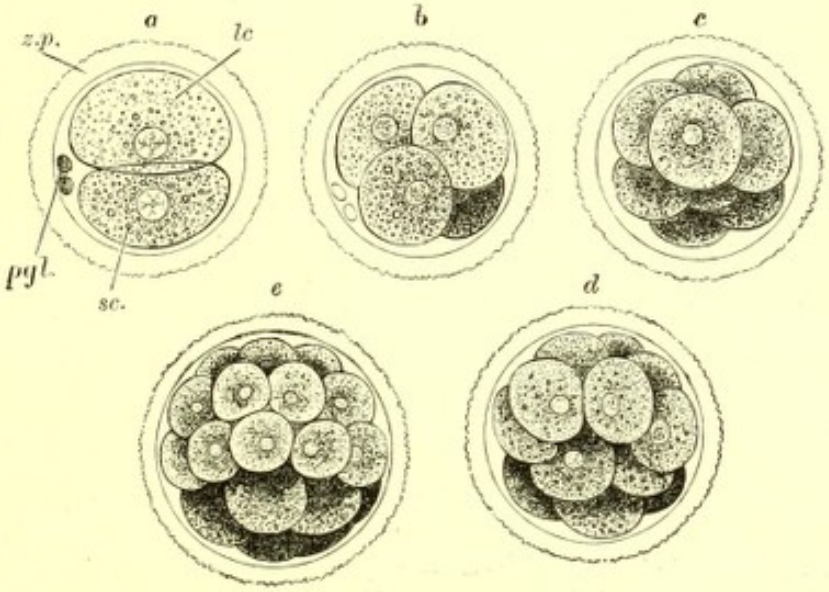



FIG. 34.—FIRST STAGES OF SEGMENTATION OF A MAMMALIAN OVUM: SEMI-DIAGRAMMATIC.
(Drawn by Allen Thomson after E. Van Beneden's description.)

*z.p.*, zona pellucida; *pgl.*, polar globules; *a*, division into two segments; *lc*, larger and clearer segment; *sc.*, smaller, more granular segment; *b*, stage of four segments; *c*, eight segments; *d*, *e*, succeeding stages of segmentation showing the more rapid division of the clearer segments and the enclosure of the darker segments by them.

but is neither quite equal nor quite regular. Some of the cells divide more rapidly than others, so that groups with an odd number of segments occur, such as 3, 6, 12 or 7, 9, 10; and when the morula stage is reached there is a definite grouping of the segments, the centre of the sphere being occupied by larger, more granular, cells, surrounded by a layer of smaller, clearer elements. It is not certain at what stage the distinction between the two categories of cells is established, though some believe that it is effected at the first cleavage; but it is clear (even though the evidence for a definite *epibolic* process is incomplete) that certain of the cells divide more rapidly, take a superficial position, and come to cover and enclose the remainder.

The cleavage of the human ovum has not been observed, and only one stage has so far been seen in any of the lower Primates (fig. 35). It is a four-cell stage found in an oviduct of *Macacus nemestrinus* given to Selenka by Hubrecht.[1] The blastomeres are of nearly equal size, two

[1] Selenka, Studien über Entwickelungsgeschichte der Tiere, Heft x., Wiesbaden; Kreidel, 1903, p. 331.

being somewhat oval, two nearly spherical. The observation shows that in the other Primates, and therefore practically certainly also in man, segmentation takes place in the oviduct, and after the same fashion as in the lower mammals. It will be observed that there is no zona radiata represented. In most mammals the zona persists during the earlier phases of development, and it is difficult to account for its absence in this and other cases. It is doubtful whether it is to be ascribed to the preservatives used, or to a normal precocious solution of the membrane.

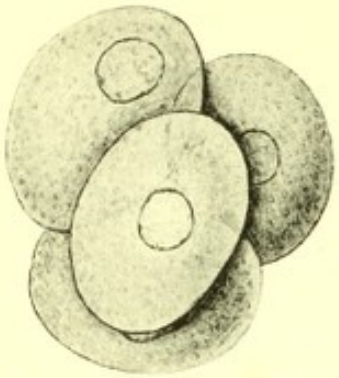
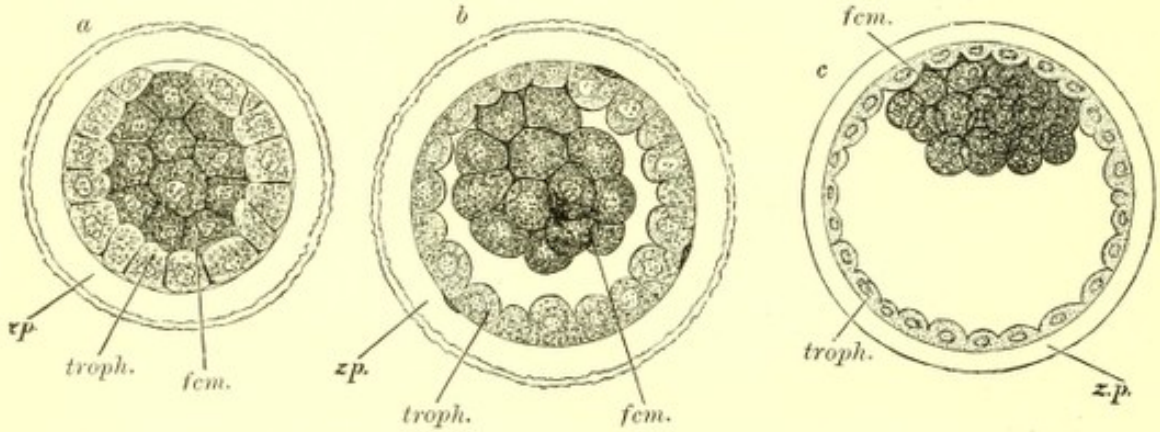


FIG. 35.—SEGMENTING EGG OF MACACUS NEMESTRINUS. (After Selenka.) × 400 diameters.

Fluid now appears between the peripheral layer and the central mass, and separates them everywhere except at one point (fig. 36, *b*). As the fluid accumulates, the morula is converted into a vesicle (fig. 36, *c*), the walls of which are formed of a single layer of small clear cells, except at the point where the central mass is attached and projects into the cavity (figs. 36, *c*, *d*, and 37). The outer layer takes no part in the building up of the embryo, but is concerned solely with the establishment of relations between the ovum and the uterine mucosa. It has been termed by Hubrecht the *trophoblast*. The inner mass provides the material out of which embryo, yolk-sac, and in man and apes almost certainly also the amnion, are formed,



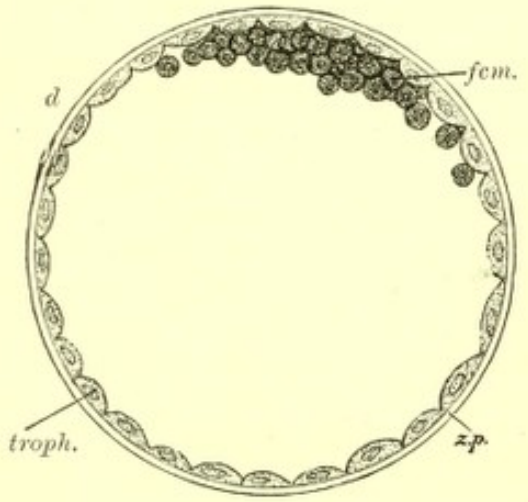




FIG. 36.—SECTIONS OF THE OVUM OF THE RABBIT DURING THE LATER STAGES OF SEGMENTATION, SHOWING THE FORMATION OF THE BLASTOCYST. (E. Van Beneden.)

*a*, Section showing the enclosure of darker cells, *fcm.*, by clearer cells, *troph.*: the enclosure is usually complete; *b*, more advanced stage in which fluid is beginning to accumulate between the inner and outer cells; *c*, the fluid has much increased, so that a large space separates inner from outer cells except at one part; *d*, blastocyst, its wall formed of a layer of flattened cells (trophoblast), with a patch of dark granular cells (formative cell-mass) adhering to it at one part; *z.p.*, zona pellucida.

and may be termed the *formative* or *embryonic cell-mass*. At this stage the ovum has usually been termed the *blastodermic vesicle*, but as the actual blastoderm is not yet formed it is better to call it the *blastocyst*.

When the whole ovum is involved in segmentation the egg is termed *holoblastic*. This variety of cleavage occurs in all eggs which are either *alecithal* (see p. 9) or *moderately telolecithal*, though in the latter the division is very unequal, as, for instance, in the common frog. In exaggeratedly telolecithal eggs like those of some fishes, birds, reptiles, and monotremes among mammals, the cleavage is confined to the animal or protoplasmic pole, and they are then said to be *meroblastic*. In all holoblastic eggs, except in the case of the mammal, the whole ovum is utilised for the formation of the embryo; while in meroblastic eggs only a small portion forms the embryo, the remainder becoming the yolk-sac and the egg-membranes. The egg of the placental mammals is holoblastic, yet the later stages correspond with those of meroblastic ova; hence it is a commonly accepted opinion among embryologists that the mammalian ancestry had large yolk-laden eggs. This opinion is strengthened by the fact that the most primitive mammals—the *Monotremata*—have eggs like those of reptiles. We are therefore justified in believing that in the descent of the mammalia the yolk was lost when the egg came to be retained in the uterus and established nutritive relations with the maternal tissues, but that it has retained in some respects its ancestral mode of development. It must be added, however, that, while this is the view of most embryologists, others (*e.g.* Hubrecht) maintain the opinion that the mammalian ovum inherits its mode of development from ancestors with telolecithal holoblastic eggs, like those of the present-day amphibian forms.

## FORMATION OF THE GERMINAL LAYERS.

The youngest known human ovum (fig. 93, p. 65) is already considerably advanced beyond the stage of the blastocyst. The resemblance between the early stages in man, apes, and monkeys is very close. In certain particulars they differ from the early stages of any other mammalian form except *Tarsius spectrum*.

This creature has been commonly placed among the lemurs, but Hubrecht has shown from embryological evidence that it is more closely related to the apes and to man, and he has proposed to limit the order Primates so as to include only man, the apes and monkeys, and Tarsius. These form embryologically a group by themselves among the mammals, and it is now possible, thanks to the work of Selenka and of Keibel on the apes, and of Hubrecht on Tarsius, to combine the data for the lower Primates with the data collected for man first by His and Graf v. Spee, then by Keibel, Kollman, Peters, Eternod, Mall, Minot, and others, so as to obtain a fairly complete, if in some points still hypothetical, picture of the early history of the primate ovum.

The earliest phases have been observed only in *Tarsius*,[1] but from later resemblances there are cogent reasons for believing that, except in one or two particulars, these phases may be taken as representing what actually takes place in the development of the human ovum.

**Formation of the entoderm.**—We shall begin with the stage of the *blastocyst*, represented in fig. 37. The trophoblast forms a continuous layer over the inner or formative cell-mass, which projects as a rounded knob into the cavity of the vesicle. Compared with the blastocyst of the lower Amniota, this mass of cells is as it were projected (invaginated) into the interior of the vesicle instead of being spread out on the surface (fig. 38).

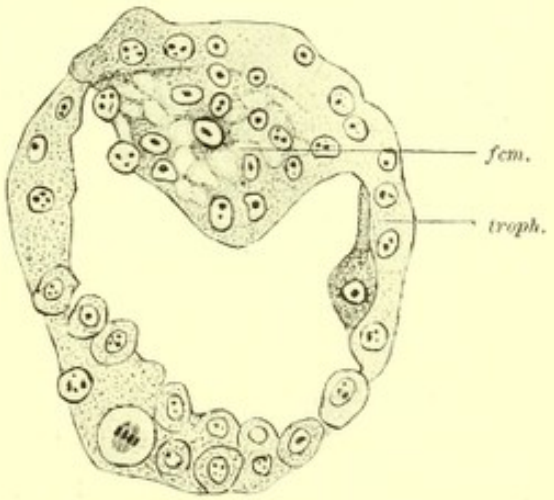



FIG. 37.—BLASTOCYST OF TARSIUS SPECTRUM. (After Hubrecht.)
*fcm.*, formative cell-mass; *troph.*, trophoblast.

From the inner face of the inner cell-mass a layer of cells becomes split off, which is generally called the *primitive* or *yolk entoderm* (*lécithophore* of Van Beneden) (fig. 39, A). Contrary to what happens in most lower mammals, this entoderm

[1] A. A. W. Hubrecht, 'Furchung und Keimblattbildung bei Tarsius spectrum,' Verhandelingen der Koninklijke Akademie van Wetenschappen te Amsterdam, viii. 1902.

does not grow out round the wall of the vesicle closely applied to the ectoderm (see fig. 41), but speedily forms a small closed sac, the *entodermic* or future *yolk-sac* (fig. 39, *b* and *c*), separated by a space from the trophoblastic wall

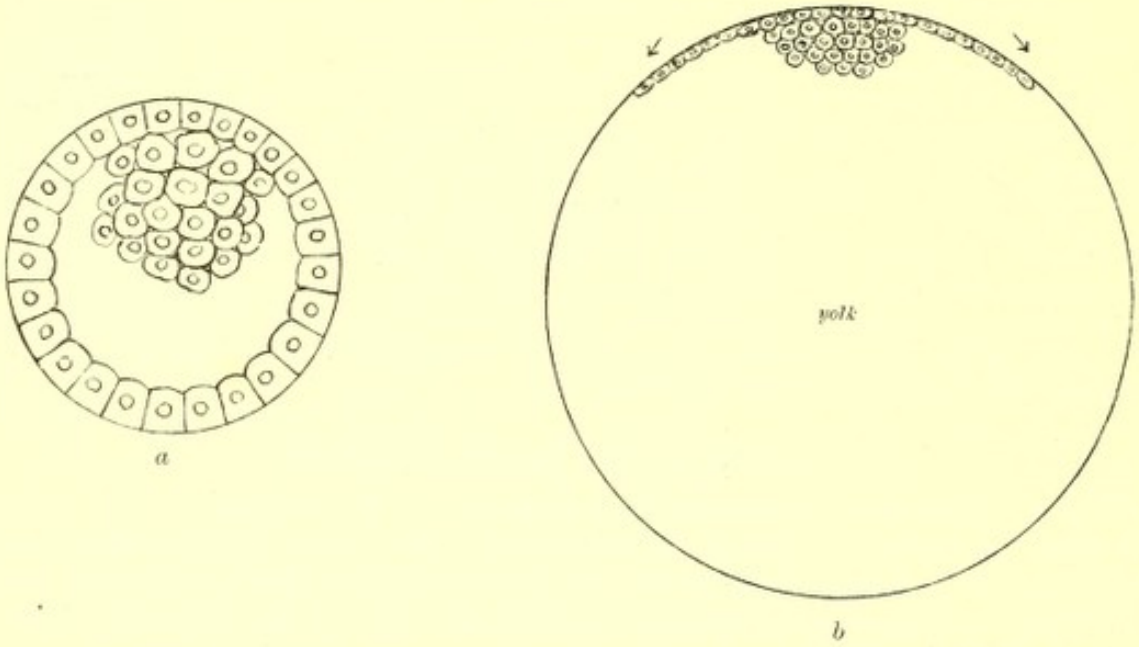



FIG. 38.—DIAGRAM TO SHOW THE DIFFERENCE BETWEEN THE BLASTOCYST (BLASTULA) OF A PLACENTAL MAMMAL *a*, AND THAT OF ONE OF THE LOWER AMNIOTA *b*. (After Semon.)

In *a*, the wall of the blastocyst is complete from the first, and the formative cell-mass projects into its interior; in *b*, the wall is completed only at a much later stage by the growth of the ectoderm over the yolk, and the formative cells spread out on the surface.

of the blastocyst. This peculiarity is clearly secondary, and is due to the precocious and extensive expansion of the trophoblast shell, while the formative cell-mass lags behind in development. The entoderm layer, which clings to the

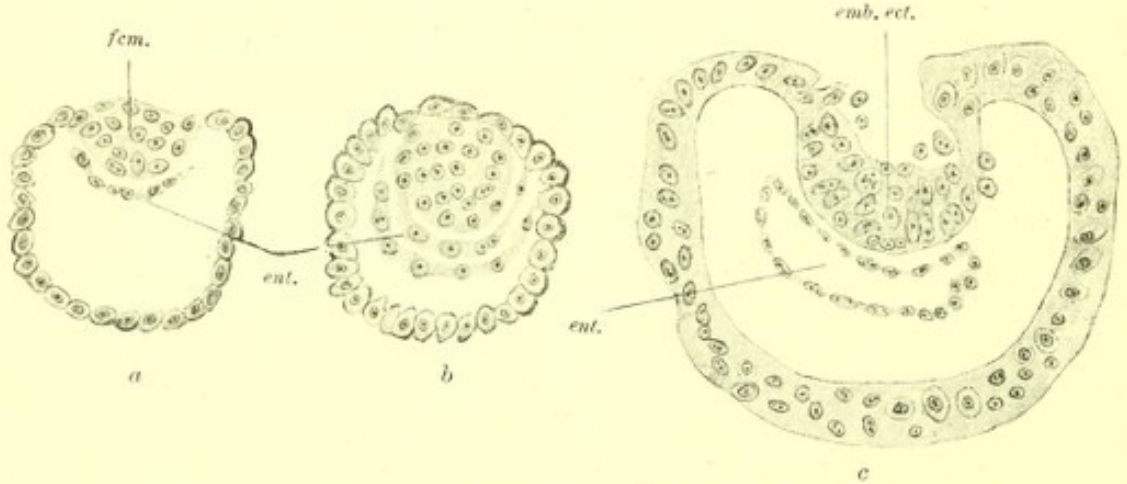



FIG. 39.—EARLY STAGES IN THE FORMATION OF THE GERMINAL LAYERS IN TARSIUS SPECTRUM. (After Hubrecht.)

*fcm.*, formative cell-mass; *ent.*, entoderm; *emb. ect.*, embryonic ectoderm.

embryonal cell-mass, is composed, as in many lower mammalian forms, of larger more loosely arranged cells, while the free portion is formed of more flattened elements.

It is not quite clear how the layer of entoderm cells becomes converted into a sac. There are three possibilities: 1. The cell-layer grows meridionally in all directions, finally to close in

ventrally. This would correspond to the extension round the wall of the blastocyst that occurs in lower mammals. 2. The layer bends round in front and grows backwards to close at the posterior end. 3. The cavity is formed by a splitting among the budded-off entoderm cells so that they are separated into two lamellæ. None of Hubrecht's figures of this stage directly favour this last possibility, but it has been suggested that the yolk-sac in the human ovum may be formed out of a solid mass of cells in this way.

**Formation of the embryonic ectoderm: bilaminar blastoderm.**—Though the primitive entoderm is already formed, the stage of a bilaminar blastoderm is not yet reached. The formative cell-mass is still a rounded knob, continuous with, but to be distinguished from, the trophoblast. In the next phase a splitting takes place among the cells, so as to form a cavity (*amnio-embryonic cavity*, fig. 40) in the heart of the knob. The cells forming the floor of the cavity arrange themselves in a columnar manner, and form a plate, which is the *embryonic ectoderm*. This plate is at first necessarily concave owing to the invagination of the formative cell-mass. The fate of the cells forming the roof of the cavity differs in Tarsius and the higher Primates. In Tarsius, as the plate increases in size it becomes flattened out; the primitive invagination (inward projection) is undone, and the embryonic ectoderm comes to lie free on the surface of the blastocyst by the disappearance, due to retraction or otherwise, of the cells forming the roof of the amnio-embryonic cavity. At a considerably later period of development, when the embryo has been laid down, the cavity is as it were again

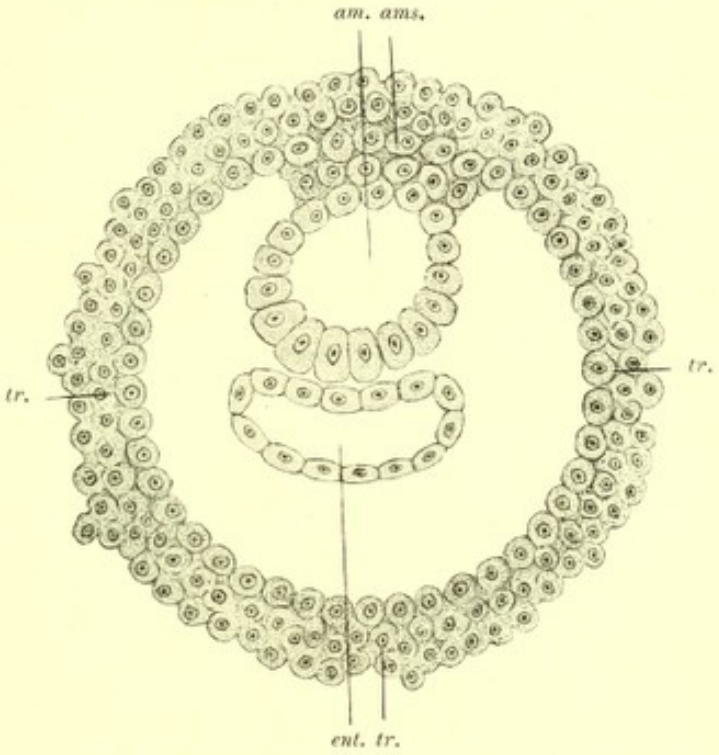



FIG. 40.—HYPOTHETICAL STAGE OF HUMAN BLASTOCYST (T. H. Bryce.)

*tr.*, trophoblast; *am.*, amnio-embryonic cavity; *ams.*, amnion-stalk; *ent.*, entoderm.

FIG. 41.—SECTION OF PART OF THE BLASTODERMIC VESICLE OF THE RABBIT AT SIX DAYS. (From E. Van Beneden.)

*a*, trophoblast (Rauber's layer); *b*, formative ectoderm; *c*, entoderm.

restored by the formation of folds which meet over the embryo and form the definitive amnion, as will be explained later.

In man and the apes this early stage is as yet unknown; but the later phases are most adequately explained by assuming that the roof of the cavity persists, that the primary invagination is not at this stage undone, and that the formative ectoderm never comes to lie free on the surface of the blastocyst. The cavity in the formative cell-mass thus becomes the definitive amniotic cavity, which is

closed from the first. Its floor becomes the embryonic ectoderm, its roof the amniotic ectoderm, and this is attached to the trophoblast by a short stalk, which may be termed the *amnion-stalk*. Fig. 40, which represents an attempt to visualise this hypothetical stage of the human ovum, will make these statements clear; but for a full understanding of the points at issue, a comprehension of the phenomenon known as *entypy of the germinal area* is necessary.

It must be stated here that the view adopted in the text has not the assent of all embryologists. It is clear that the early blastoderm is invaginated in the human ovum, but is the invagination primary as described above, or is it secondary? It is held by some that, owing to the complete imbedding of the ovum in the decidua, the embryonic ectoderm, at first on the surface of the blastocyst, is very early closed in by precocious amnion folds. As a further result, the growth of the blastoderm causes it to be inverted into the cavity of the vesicle, and the stage imagined in fig. 40 would be reached by the fusion of the folds over the embryonic area to form what has been named the amnion-stalk. Certain observations of Selenka on Hylobates embryos, and of Mall on abnormal human ova, support this view, which has also been advocated by Keibel. The view adopted in the text is that of Van Beneden, Selenka, Hubrecht, and others,

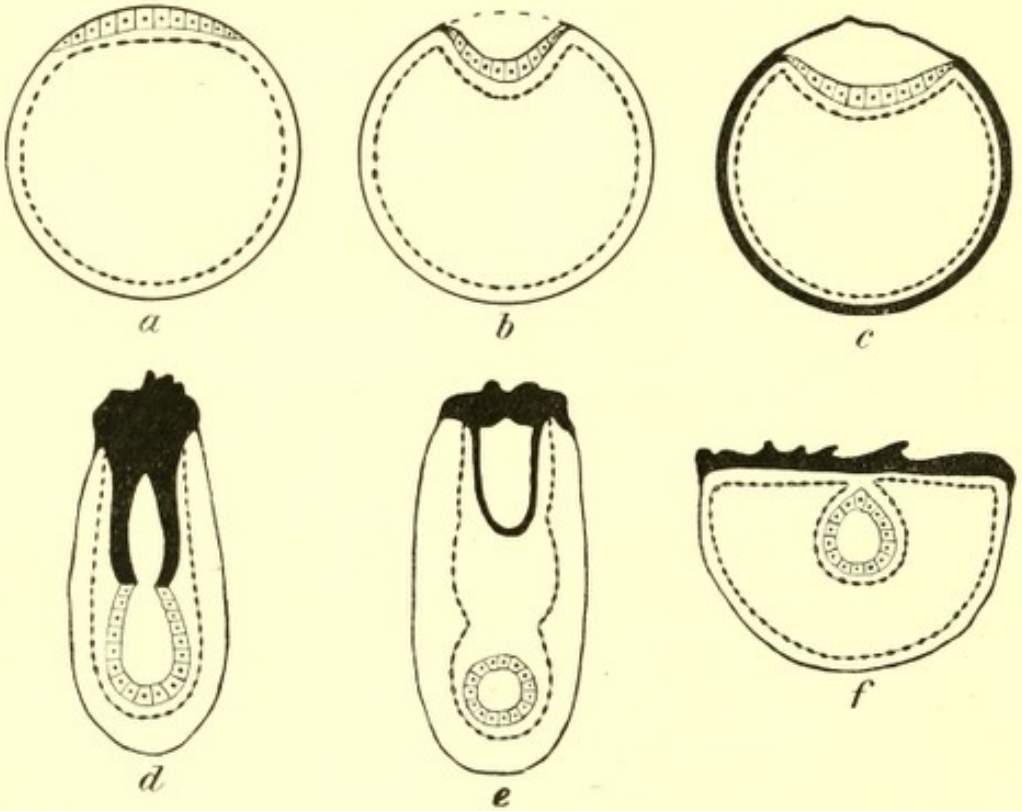



FIG. 42.—DIAGRAMS TO ILLUSTRATE ENTYPY OF THE GERMINAL AREA. (T. H. Bryce.)

Blastodermic vesicle: *a*, of rabbit; *b*, of mole; *c*, of bat; *d*, of mouse or rat; *e*, of guinea-pig; *f*, of kalong.

Trophoblast represented by continuous black lines or masses; entoderm by interrupted lines; embryonic ectoderm by epithelial cells.

and it differs from the first only in holding that from the circumstances of the complete imbedding of the ovum the embryo-amnio-genetic ectoderm is invaginated at a still earlier stage, the blastocyst wall being folded over the formative ectoderm even before it is differentiated into embryonic ectoderm.

**Entypy of the germinal area.**—In the rabbit ovum at this stage the trophoblast is reduced to a thin sheet of flattened cells, against which the cells of the formative cell-mass spread themselves out at an early stage (fig. 36, *d*, p. 26). After the formation of the entoderm, the cells between that layer and the trophoblast form a plate of columnar cells, the embryonic ectoderm (fig. 41, *a*), which is flat from the first, and directly applied to the covering layer of trophoblast (here

called *Rauber's layer*). No amnio-embryonic cavity appears between them. Soon Rauber's layer disappears, and the embryonic ectoderm lies free on the upper pole of the blastocyst. In some mammals, such as the mole, pig, and Tupaja, the germinal area is for a short time distinctly inverted, as in Tarsius ; but the phases resulting in the opening out of the blastoderm on to the surface are even more distinctly seen than in that animal. In the mole, for instance (fig. 42, *b*), the cavity which hollows out the heart of the formative cell-mass is larger and deeper, and is roofed in by the trophoblast for a time. The embryonic ectoderm is at first markedly concave, but this is very soon rectified by the straightening of the plate ; and the roof of the cavity disappearing, a phase is reached exactly like that described for the rabbit after the disappearance of Rauber's layer.

In another and considerable series of mammals, the inversion persists rather longer, and the cavity never opens out on the surface of the blastocyst, but remains roofed in by the trophoblast layer. This condition was named by Selenka 'entypy of the germinal area.'

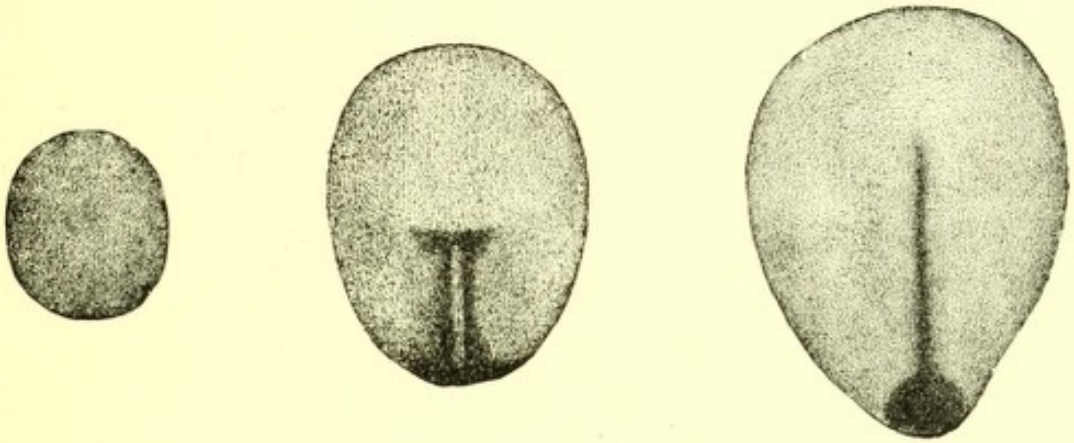


FIG. 43.—EMBRYONIC AREA OF MOLE IMMEDIATELY PRIOR TO APPEARANCE OF PRIMITIVE STREAK AND FORMED OF TWO LAYERS ONLY.

FIG. 44.—EMBRYONIC AREA OF MOLE, SHOWING THE PRIMITIVE STREAK AND GROOVE ENDING POSTERIORLY IN A CRESCENTIC THICKENING.

The area is bilaminar in front, trilaminar in the posterior half.

FIG. 45.—A SOMEWHAT LATER STAGE IN WHICH THE PRIMITIVE STREAK REACHES TWO-THIRDS OF THE LENGTH OF THE EMBRYONIC AREA, AND ENDS BEHIND IN A KNOB OR THICKENING.

(Figs. 43, 44, and 45 are copied from Heape. They are magnified 49 diameters.)

There are a number of variations in the manner in which the condition manifests itself.

(A) In some of the bats (fig. 42, *c*) and in the hedgehog the cavity remains roofed in by trophoblast, and persists as the amniotic cavity, the walls of the definitive amnion being formed not by the folds as in the other group, but by upgrowth of cells on the inner surface of the covering trophoblastic layer.

(B) In mice and rats (fig. 42, *d*) the trophoblast over the formative cell-mass becomes greatly thickened and invaginated into the interior of the blastocyte, necessarily pushing the mass before it. A cavity appears in this mass of trophoblast (false amniotic cavity), which becomes continuous with the primitive amnio-embryonic cavity. The whole blastocyst becoming tubular, the germinal layers appear reversed, the entoderm being external to the ectoderm. In the further course of development this persistent inversion of the germinal area is rectified by the tardy straightening of the blastoderm and opening out of the amniotic cavity.

(C) In the guinea-pig (fig. 42, *e*) the blastocyst is drawn out into a tubular shape just as in rats and mice, and the formative cell-mass is inverted in the same fashion into its cavity. The placental thickening of the trophoblast is not, however, invaginated to the same degree as the formative cell-mass, so that direct connexion between them is lost. Accordingly, when the amnio-embryonic cavity is formed, its roof is independent of the trophoblast ; it never opens into the cavity in the interior of the trophoblast plug (false amniotic cavity), and it becomes the definitive amnion.

(D) In the kalong (an East Indian bat, *Pteropus edulis*) (fig. 42, *f*) the condition is much the same as in the guinea-pig, but the blastocyst remains rounded; there is no invagination of the trophoblast; no false amnionic cavity; and there is not much greater inversion of the layers than occurs in the bats.

In apes and man (fig. 40) some such condition as in Pteropus in all probability exists; but there is this difference, that, owing to the great expansion of the trophoblast-shell and to the tardy formation of the entoderm, there is from the first a space between the trophoblastic wall of the blastocyst and the entodermic sac.

**Formation of the trilaminar blastoderm: mesoderm and embryonic axis.**—The mode of the formation of the middle layer in the Primates varies in certain important particulars from that generally regarded as typical. It will be convenient to give first a brief general description of the mode of formation of the mesoderm in one of the lower mammals—*e.g.* the mole or rabbit.

The germinal area, at the stage now reached, is a circular disc on the upper pole of the blastocyst (fig. 43). By unequal growth the disc becomes oval, and at its smaller end a linear shading appears which is produced by a keel-like thickening

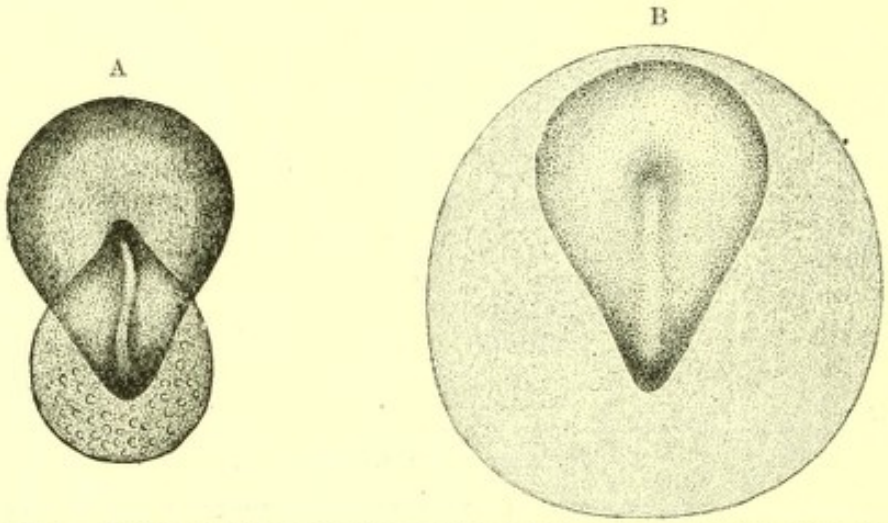



FIG. 46, A AND B.—VIEWS OF THE EMBRYONIC AREA OF THE RABBIT, SHOWING TWO STAGES IN THE EXTENSION OF THE MESODERM. (Kölliker.)

In A the mesoderm extends on either side of the primitive streak over the posterior part of the embryonic area, and also behind the primitive streak beyond the limits of that area.

In B the mesoderm extends over a circular area which surrounds the embryonic area. The embryonic area is also trilaminar, except in the middle line in front of the primitive streak.

of the ectoderm, known as the *primitive streak* (figs. 44 and 45). The first part of the streak to appear is a knob-like thickening which forms its head (*Hensen's knot*). From the primitive streak cells are budded off into the space between ectoderm and entoderm. They form a loosely arranged layer of branched elements named the *mesoderm*. The ectodermic thickening, at first separate from the entoderm, quickly fuses with it, so that all three layers are continuous in the primitive streak. By constant proliferation the mesoderm spreads round the wall of the blastocyst until finally it entirely surrounds it. It will be noticed that at first the extension is mainly backwards in a continuous sheet behind the germinal area (fig. 46). This portion of the layer takes no part in the formation of the embryo, but is concerned in the laying down of the peripheral mesoderm of the future vascular area. Within the germinal area the sheet is divided into two lateral wings, separated by the primitive streak from which they spring (fig. 58, p. 40; fig. 66, p. 44; and fig. 47). As the mesoderm continues to spread, the embryo begins to take form in front of the primitive streak, and the lateral wings of the mesoderm are found extending forwards on each side of a

plate of cells which is the rudiment of the notochord (fig. 66, V. p. 44). In front of the embryonal axis, in most lower mammals, there is an area named the *pro-amnion*, into which the mesoderm does not spread until a later period, and where therefore the blastoderm is formed merely of ectoderm and entoderm.

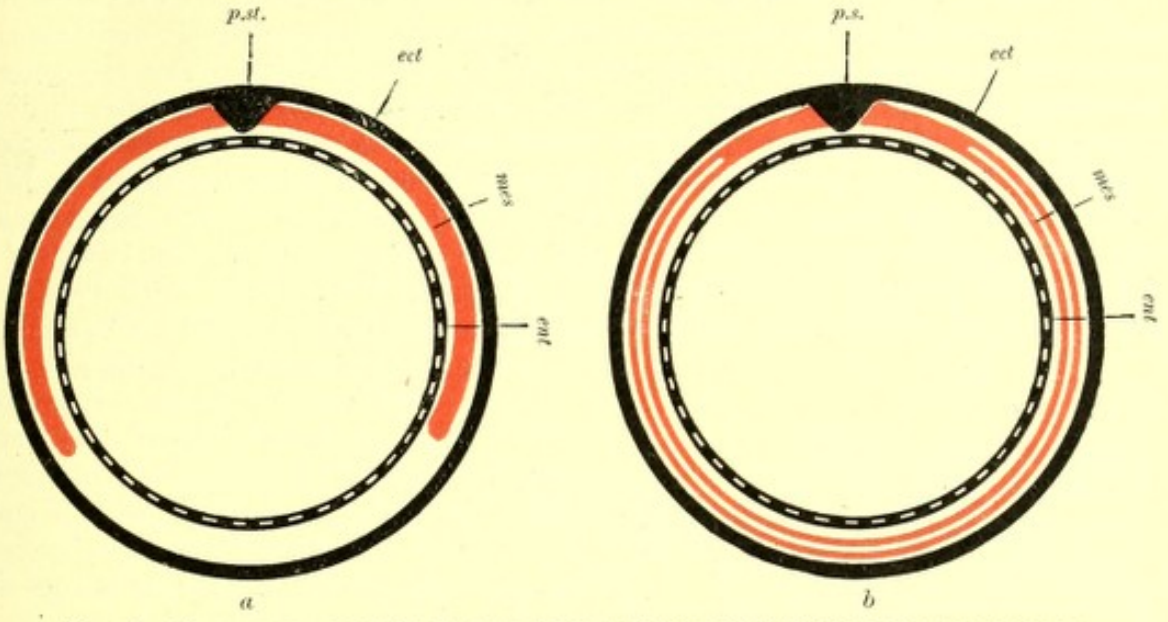



FIG. 47.—DIAGRAM TO ILLUSTRATE THE SPREAD OF THE MESODERM FROM THE PRIMITIVE STREAK, *p.st.*, IN A TYPICAL LOWER MAMMAL. (T. H. Bryce.)

In *a* the mesoderm has not yet spread round the entodermic sac, and is undivided; in *b* it has completely surrounded the blastocyst and is divided into somatopleuric and splanchnopleuric layers. *ect*, *mes*, *ent*, ectoderm, mesoderm, entoderm.

The mesoderm sheet now splits on either side into two lamellæ—parietal and visceral (fig. 47). The parietal layer adheres to the ectoderm, and forms with it the *somatopleure*; the visceral becomes associated with the entoderm, and with it

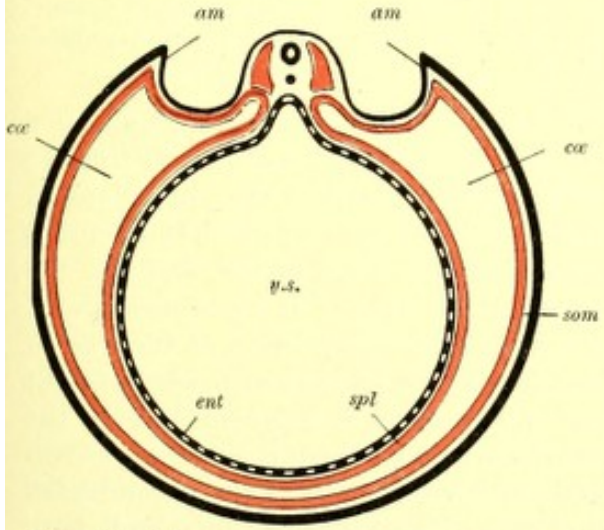



FIG. 48.—DIAGRAM TO ILLUSTRATE A STAGE IN THE DEVELOPMENT OF THE MESODERM LATER THAN IN FIG. 47 *b*, AND THE FORMATION OF THE AMNION, IN A TYPICAL LOWER MAMMAL. (T. H. Bryce.)

*am*, *am*, amnion folds; *cœ*, cœlom; *som*, somatopleure; *spl*, splanchnopleure; *ent*, entoderm of yolk-sac, *y.s.*

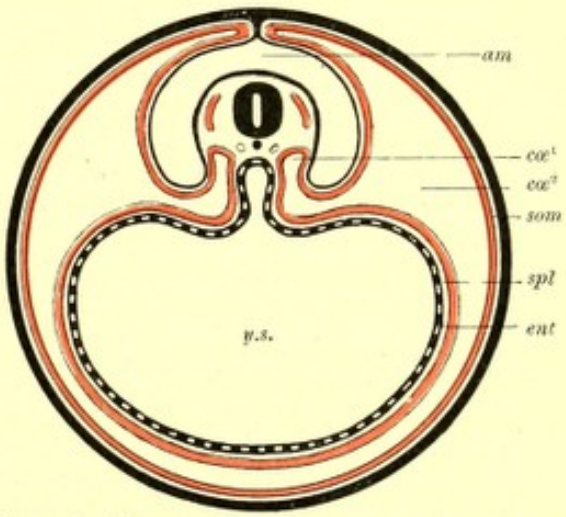



FIG. 49.—DIAGRAM TO SHOW A LATER STAGE IN DEVELOPMENT OF THE AMNION AND YOLK-SAC THAN IN FIG. 48. (T. H. Bryce.)

*am*, amnion, now closed; *cœ*$^1$, intra-embryonic cœlom; *cœ*$^2$, extra-embryonic cœlom; *som*, somatopleure; *spl*, splanchnopleure; *ent*, entoderm of yolk-sac, *y.s.*

constitutes the *splanchnopleure*. The splitting first takes place in the embryonic area, and spreads outwards until in certain forms it completely separates the blastocyst wall from the entodermic vesicle, now called the *yolk-sac*. The space

between the layers is named the *cœlom*. As the embryo takes form, it sinks down, as it were, into the blastocyst, and a fold of the somatopleure comes to overlap it all round. The edges of the fold ultimately meet over the embryo and enclose the cavity of the *amnion* (figs. 48 and 49).

The special feature about the formation of the middle layer in the Primates [1] is that the whole extra-embryonic mesoderm is formed, at a relatively early stage, before the primitive streak has appeared on the germinal disc. The precocious mesoderm consists in part of cells budded off from the posterior edge of the germinal area, which spread round the wall of the blastocyst and over the yolk-sac (figs. 50 to 53). The tissue formed is a loosely arranged layer concerned in the formation of the lining of the trophoblast and covering of the entodermic sac, and from the earliest period it forms a thick stalk of connexion (*Haftstiel ; embryophore*) between embryonic area and trophoblast. This stalk becomes vascularised at an early date, independently of the allantois, and constitutes at this stage a formation peculiar to the Primates. In respect of its fate it may be considered as corresponding to the mesoderm which extends from the posterior end of the primitive streak behind the germinal disc in a typical lower mammal.[2]

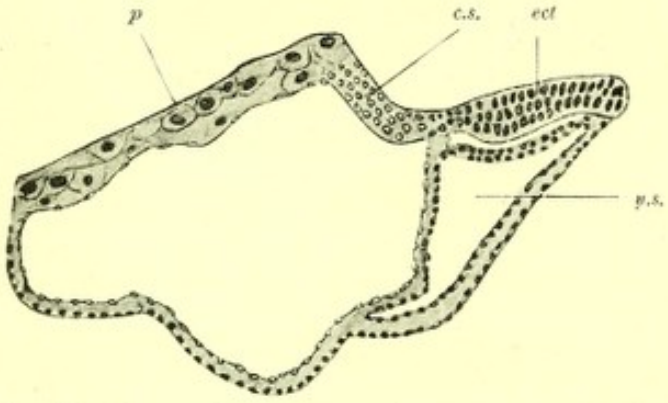



FIG. 50.—SECTION (DIAGRAMMATIC) OF EARLY EMBRYO OF TARSIUS SPECTRUM. (After Hubrecht.)

*ect*, embryonic ectoderm; *y.s.*, yolk-sac; *c.s.*, connecting stalk; *p*, thickened trophoblast = ectoplacenta.

The blastocyst is not completely imbedded in the uterine mucosa, and only a portion of the trophoblast therefore takes part in the formation of the placenta. The 'ventral' mesoderm covers only the posterior surface of the yolk-sac.

The actual origin of this early mesoderm is unknown in man. In Tarsius it is derived from the ectoderm (Hubrecht). In *Semnopithecus nasicus* Selenka considers it to be of entodermic origin, but as it comes from the same region of the disc as in Tarsius, it is possible that an earlier stage would exhibit appearances susceptible of a similar interpretation to that of Hubrecht.

While in all the Primates a connecting stalk is a distinctive feature of the early stages, there are some differences between the conditions in Tarsius and those in apes and man, determined by the manner in which the ovum is imbedded, and by the mode of formation of the amnion (cf. figs. 50, 52, and 53). In Tarsius the ovum is not completely imbedded in the uterine mucous membrane, and the amnio-embryonic cavity is early opened out ; only a portion of the wall of the blastocyst is thickened to form the placenta, and the mesoderm passes straight back from the hinder end of the embryonic plate to it, and covers, at first, the posterior wall of the yolk-sac only. Owing to the maintenance of the primary inversion in the higher Primates, on the other hand, the mesoderm is, in them, conducted to the blastocyst-wall by the 'amnion stalk' (figs. 52 and 53). It surrounds both yolk-sac and amnion, so that the embryonic rudiment with its two cavities hangs from the wall of the vesicle completely imbedded in the early mesoderm. The

[1] The origin of the mesoderm in the primate blastoderm has been studied in detail only in Tarsius by Hubrecht. The following account is mainly founded on his description.

[2] The early mesoderm arising from the hinder border of the germinal area in Tarsius is named by Hubrecht the *ventral mesoblast*, because of the theoretical relationship he believes it to bear to the mesoderm of the ventral lip of the blastopore in the Amphibia. He uses the term 'mesoblast' in preference to 'mesoderm,' as he does not place the middle layer complex on the same morphological plane as the ectoderm and entoderm. Rückert (Hertwig's Handbuch, i. Part II.) has, on similar grounds, adopted the term *ventral* mesoderm to signify the peripheral mesoderm, which appears first, and springs from the hinder end of the primitive streak in the lower mammals and Amniota generally.

extra-embryonic cœlom is also occupied by delicate strands of the same tissue stretching between the yolk-sac and wall of the blastocyst. These constitute what has been named the *magma reticulare*.

While this loose mesoderm is developing, the entoderm, forming the roof of the entodermic sac, becomes in Tarsius thickened into a many-celled plate (fig. 51). This plate is produced by proliferation from the entoderm (Hubrecht), and is continuous at the margins of the disc with the yolk-sac mesoderm, in the formation of which it seems to share. It is therefore a second source of mesoderm-cells, quite independent of the earlier one. It is named by Hubrecht the *protochordal plate*, but it will be here referred to as the *primitive entodermic plate*, to avoid any theoretical implication.

In Selenka's figure of a blastoderm of *Semnopithecus nasicus* (fig. 54) the mesoderm is represented at this stage as extending forwards into the disc from its hinder end. It would therefore seem to be derived from the same source as the mesoderm of the connecting stalk, which, however, as already said, he refers to the entoderm. In Peters' and in Graf v. Spee's early human ova a similar layer is seen (fig. 55).

From this description it will be gathered that the ectoderm and entoderm are everywhere separated in the Primates by a middle layer before there is any sign of a primitive streak. Although different from the conventional account of the origin of the mesoderm, there is no doubt that the facts are as stated. Their theoretical significance will be dealt with in a later paragraph.

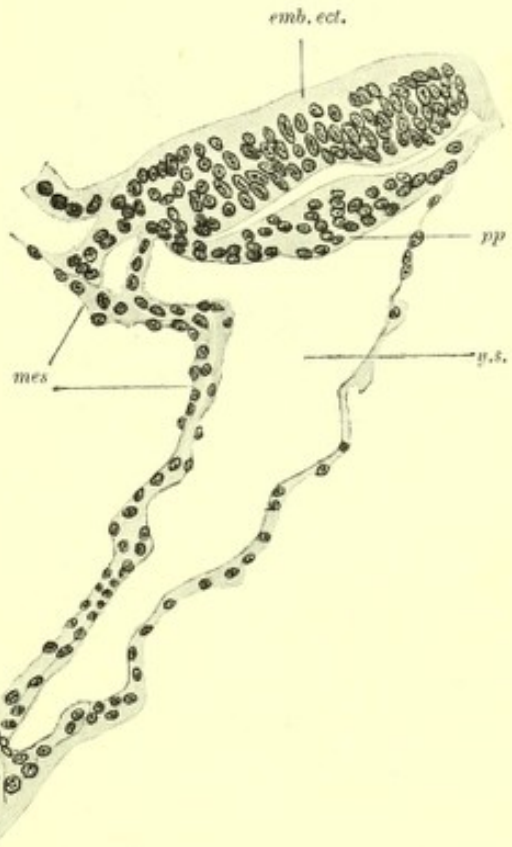



FIG. 51.—MEDIAN LONGITUDINAL SECTION THROUGH THE EMBRYONIC PLATE AND YOLK-SAC OF TARSIUS AT THE SAME STAGE AS IN FIG. 50, MORE HIGHLY MAGNIFIED. (After Hubrecht.)

*emb. ect.*, embryonic ectoderm; *pp*, primitive entodermic plate; *y.s.*, yolk-sac; *mes*, ventral mesoderm.

Up to the stage now reached, only that part of the three-layered blastoderm which we may call the *head-plate*, because it will form the extreme head end of the embryo, is laid down, and we have next to describe a series of stages by which the embryonic axis, forming the trunk, is developed. As in the typical case described above, the germinal disc enlarges (fig. 56), and Hensen's knot (*protochordal knot*, Hubrecht) appears as a thickening of the ectoderm. This thickening extends inwards and forwards between the two primary layers (fig. 57), and is continuous with the thickened entodermal plate in front. It then becomes fused with the entoderm on its under aspect. The primitive streak next appears as an extension backwards of the ectodermic thickening. Sections of the primitive streak show that from its sides, as well as from Hensen's knot, wing-like masses of mesoderm extend laterally between ectoderm and entoderm (fig. 58). They are formed from cells budded off from the streak, and from this period onwards the new mesoderm of that part of the blastoderm which lies between the head-plate in front and the connecting stalk behind, and which gradually increases in length as the embryonal axis is laid down, may be considered as arising from this source.

Hubrecht describes in Tarsius a tract of middle-layer cells springing from the entoderm over a ring-shaped area, continuous in front with the primitive middle-

layer cells of the head-plate and passing behind on to the wall of the yolk-sac. The ring is closed behind when the hind-gut becomes cut off from the yolk-sac. It is apparently directly related to the development of the blood-vessels. A similar ring

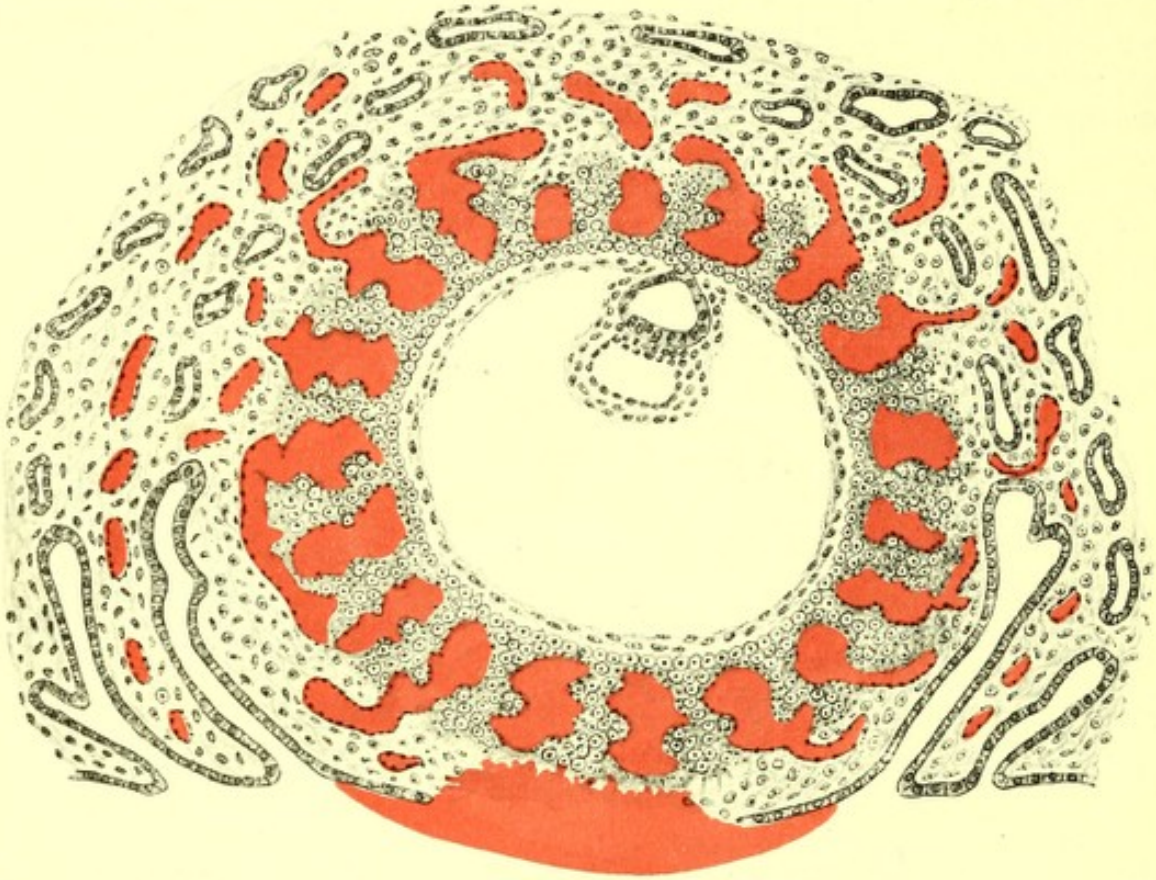


FIG. 52.—HYPOTHETICAL STAGE OF THE HUMAN OVUM IMBEDDED IN THE DECIDUA, SOMEWHAT YOUNGER THAN PETERS' OVUM. THE TROPHOBLAST IS GREATLY THICKENED, AND LINED WITH MESODERM, WHICH SURROUNDS ALSO THE EMBRYONIC RUDIMENT, WITH ITS YOLK-SAC AND AMNIO-EMBRYONIC CAVITY. (T. H. Bryce.)

The embryonic rudiment is proportionally on too large a scale.

was described by the same observer in the shrew, and by Bonnet in the sheep, but it has not been found in other mammals.

The primitive streak (although this feature is not marked in any of Hubrecht's figures of Tarsius) becomes deeply indented by a furrow called the *primitive groove*, and it is to be observed

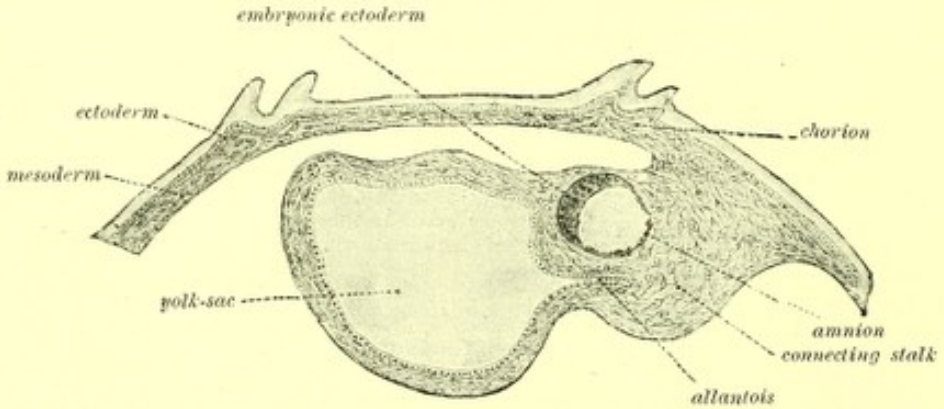



FIG. 53.—MEDIAN LONGITUDINAL SECTION OF AN EARLY HUMAN OVUM 0·4 MM. IN LENGTH. (After Graf v. Spee, from Kollmann's Entwickelungsgeschichte). × 27 diameters.

that in Graf v. Spee's embryo of 2 mm. (fig. 59), the mesoderm-sheets are represented as partially subdivided into two lamellæ, one connected with the ectoderm, the other with the entoderm. This feature, also seen in a number of lower forms, has been interpreted by Hertwig as a vestige of an original development of the mesoderm by cœlomic pouches (see p. 46).

The growth of the blastoderm at first chiefly affects the region behind Hensen's knot. The primitive streak elongates and occupies the pointed end of the oval disc which is now generally called the *embryonic shield* (fig. 56, *b* and *c*).

The next phase is characterised by a shifting of the maximum growth-activity to the part of the shield in front of Hensen's knot, and the embryonic axis begins to be laid down from *before backwards*, either by proliferation of the cells at the anterior end of the primitive streak, as some think, or by gradual conversion of the growing streak into the axis, as is indicated by experiments on the developing blastoderm.[1] As the portion of the shield in front of the streak increases in length, the mass of cells extending from Hensen's knot (*protochordal process*), already described, is necessarily lengthened into a column of cells (figs. 60, 61). It becomes, however, at the same time flattened out into a plate; and as it is fused

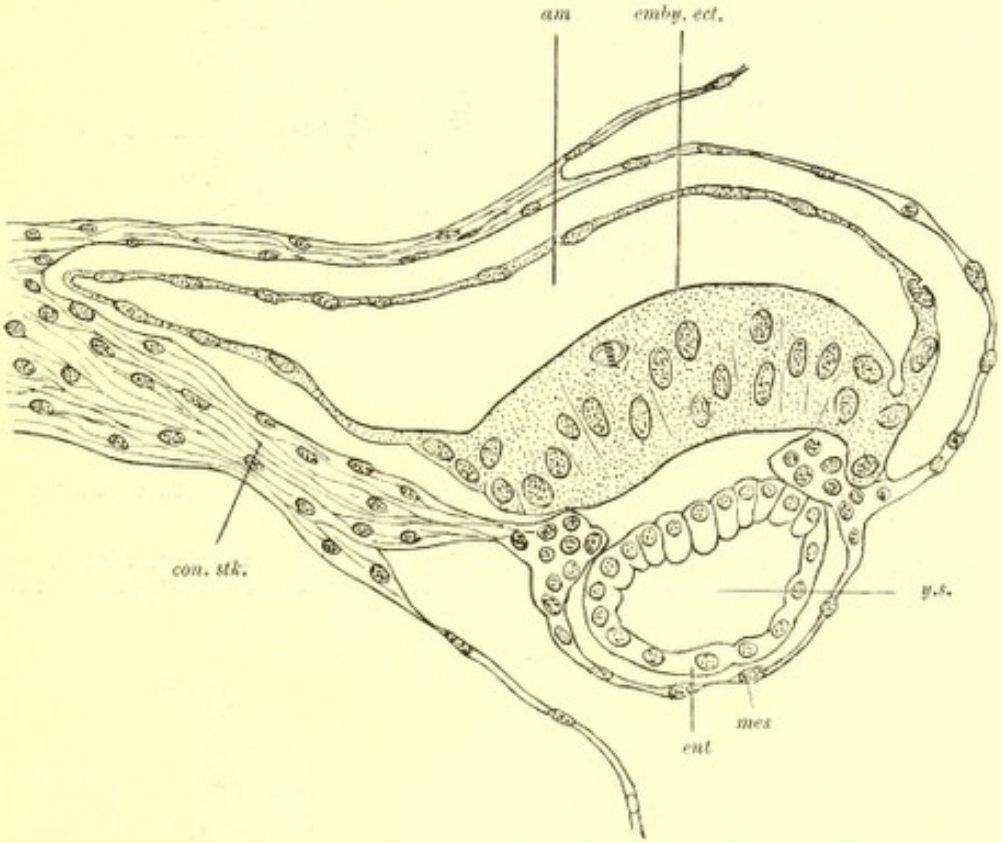



FIG. 54.—SECTION OF AN EARLY EMBRYO OF SEMNOPITHECUS NASICUS. (After Selenka.)

*am*, amnion; *emby. ect.*, embryonic ectoderm; *y.s.*, yolk-sac; *ent*, entoderm; *mes*, mesoderm covering yolk-sac and extending between embryonic ectoderm and entoderm; *con. stk.*, connecting-stalk mesoderm.

with the primitive entoderm on its under aspect, the result of this flattening and opening out is, that it comes to roof-in the cavity under the shield along the middle line. This plate is named the *notochord-plate*,[2] and is recognisable in some cases as a shading in front of the streak in surface views of the blastoderm (fig. 63). A section of the shield (fig. 64) shows that the plate is continuous on each side with the general entoderm, and, where plate and entoderm join, also with wings of mesoderm which spread outwards between ectoderm and entoderm. In front the plate passes into the thickened primitive entodermic plate, and behind into the mass of cells at the head end of the primitive streak, out of

[1] See Assheton, Proc. Roy. Soc. 1896, also Anat. Anzeiger, xxvii.; Kopsch, Verhl. d. fünfte internat. zool. Kongress, Berlin, 1901, and Internat. Monatschr. f. Anat. und Phys. xix.; Peebles, Archiv f. Entwickelungsmech. vii.

[2] It has been also termed the *archenteric plate* (*Urdarmplatte*, Bonnet), for reasons which will be given later on.

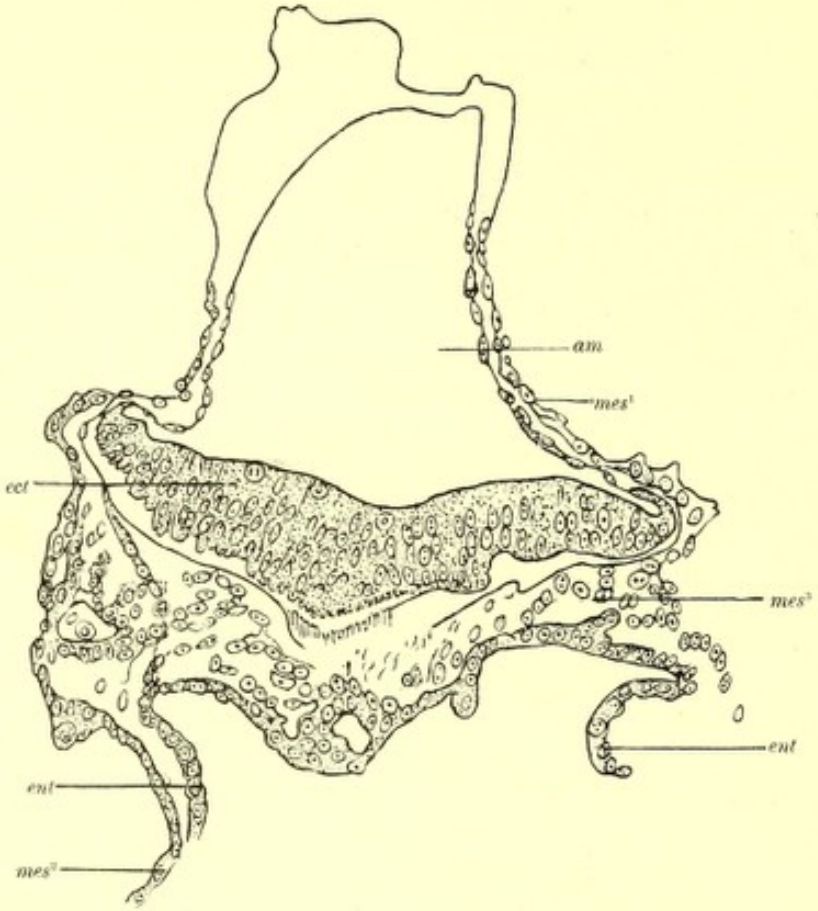



FIG. 55.—TRANSVERSE SECTION THROUGH AN EARLY HUMAN EMBRYO OF 0·4 MM. (Graf v. Spee; cf. fig. 53.)

*am*, amnion; *mes*¹, mesoderm of amnion; *ect*, embryonic ectoderm; *ent*, entoderm; *mes*², mesoderm of yolk-sac; *mes*⁻, scattered cells between ectoderm and entoderm of germinal disc.

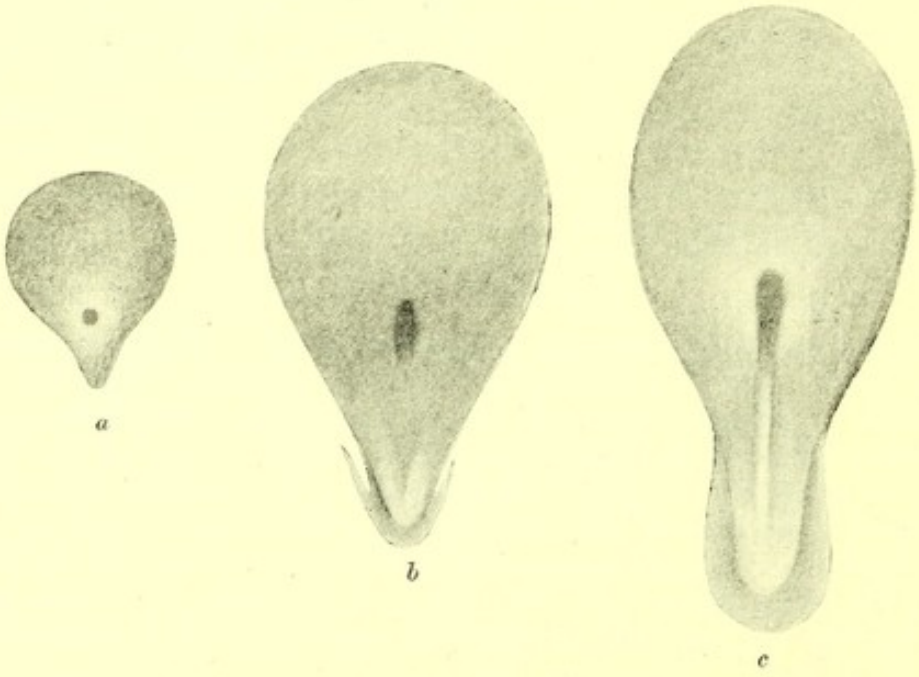



FIG. 56.—SURFACE VIEWS OF GERMINAL DISC OF TARSIUS SPECTRUM AT THREE SUCCESSIVE STAGES. (After Hubrecht.)

In *a* the dark spot represents Hensen's knot (protochordal knot, Hubrecht). As the pointed end of the disc extends backwards, the thickening known as the primitive streak develops on it, *c*.

which it is continually being added to. The wings of mesoderm springing from the sides of the notochord-plate are of course continuous with those arising from the sides of the primitive streak.[1] As the axis extends, the streak mesoderm may be conceived as continually becoming converted into axial mesoderm.

Through this thickened head of the streak a fissure has meanwhile appeared, which becomes converted into a short canal directed obliquely forwards, and opening into the cavity of the yolk-sac (figs. 61, 62, 63, 65). It is called the *notochordal* or *neurenteric canal*. In apes (figs. 62 and 63) the canal is considerably wider than in Tarsius, and it is a very prominent feature in early human embryos (figs. 65, 72). In some lower mammals—the rabbit, for instance—the canal does not break through at any stage, although it is well seen in others—for example, in the mole (fig. 64). In the higher Primates the canal is present at a very early stage—considerably earlier than in Tarsius ; and it may also be mentioned here that the primitive streak seems to be comparatively short in all the Primates (figs. 62, 63, 65). The canal tunnels through the mass of cells in which the

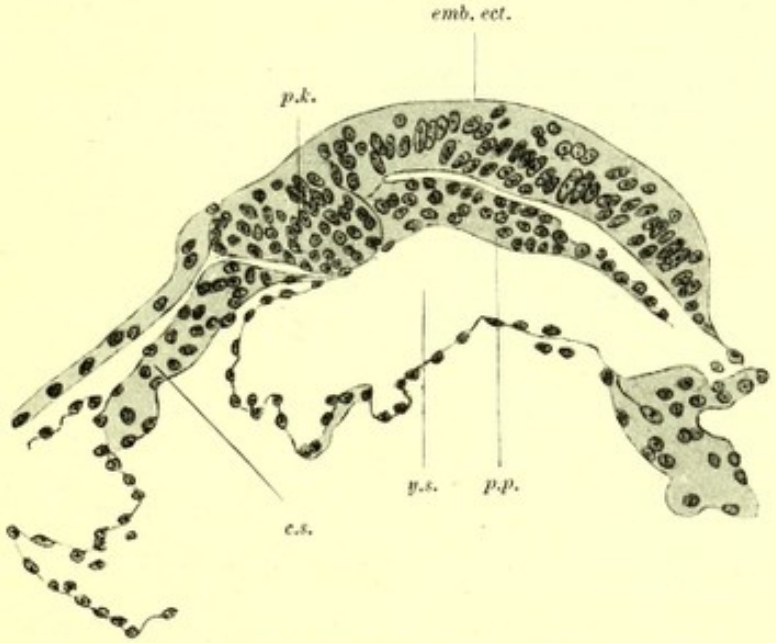



FIG. 57.—MEDIAN LONGITUDINAL SECTION THROUGH A BLASTODERM OF TARSIUS AT A STAGE ABOUT THE SAME AS REPRESENTED IN FIG. 56, *a*. (After Hubrecht.)

*p.k.*, Hensen's (protochordal) knot ; *emb. ect.*, embryonic ectoderm ; *y.s.*, yolk-sac ; *pp*, primitive entodermic (protochordal) plate : *c.s.*, ventral mesoderm (connecting stalk).

notochord-plate ends, and it has been given the name 'notochordal canal' because of its relations to that plate and the notochord which is formed from it. The term 'neurenteric canal' signifies properly only the persisting posterior portion of the notochordal canal, this name being given because it corresponds, when the neural groove is formed, to the neurenteric canal of lower vertebrates. It has been already explained that at an earlier stage the protochordal process becomes fused with the entoderm on its under aspect, and that the column of cells arising from the process opens out into a plate, and thus comes to roof-in the cavity under the shield along the middle line. The final result of this process, therefore, is the same as it would have been had the notochordal canal tunnelled the whole length of the protochordal column of cells, and had then broken through into the cavity of the yolk-sac

[1] Hubrecht leaves it open whether these lateral sheets are formed in part or in whole from the protochordal process. Bonnet, in the dog, represents the facts as described in the text. The point is important theoretically, but not from a mere descriptive point of view.

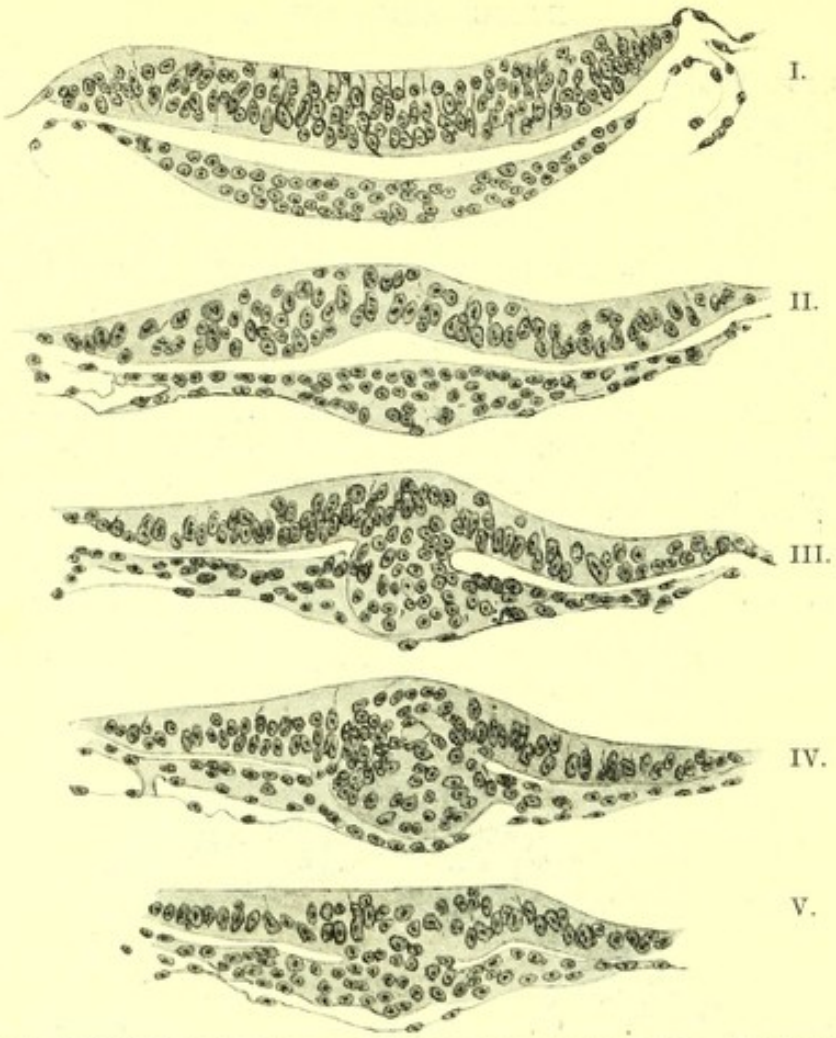



FIG. 58.—SERIES OF TRANSVERSE SECTIONS THROUGH THE GERMINAL DISC OF TARSIUS AT A STAGE SOMEWHAT EARLIER THAN THE DISC REPRESENTED IN FIG. 56, *b*. (After Hubrecht.)

Section I. passes through the blastoderm in front of Hensen's (protochordal) knot, and shows only the ectoderm and primitive entodermal plate. Section II. cuts the head end of the protochordal process where it is continuous with the primitive entodermic plate. Sections III. and IV. pass through Hensen's knot, which is seen in V. tapering away into the primitive streak. In III., IV., and V. the mesoderm-sheets are seen springing from the keel-like thickening of the ectoderm, which in III. and IV. is observed to be continuous into the entoderm.

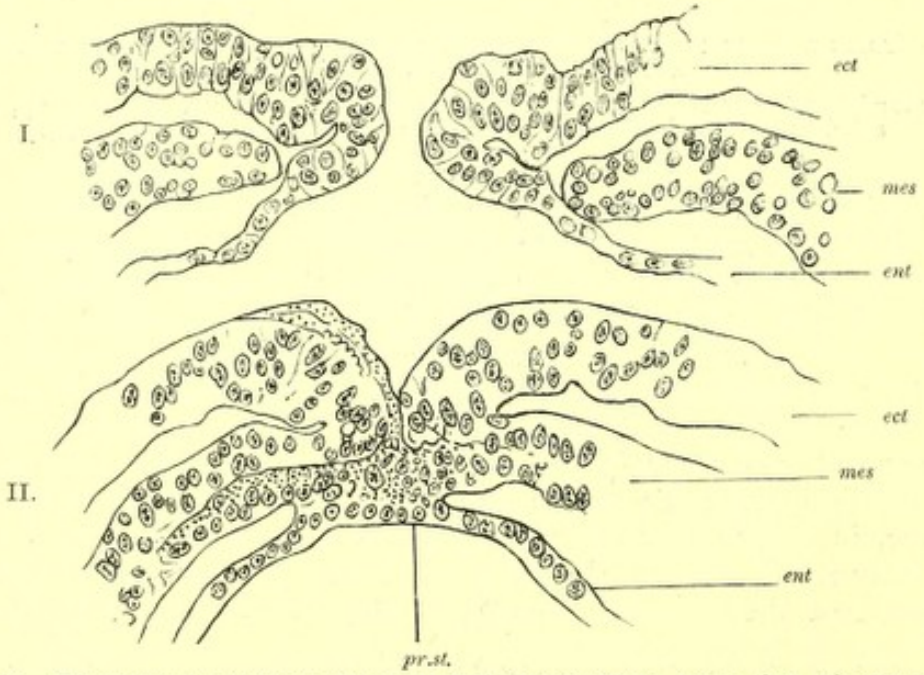



FIG. 59.—TRANSVERSE SECTIONS THROUGH THE NEURENTERIC CANAL (NO I.) AND PRIMITIVE STREAK (NO. II.) OF A HUMAN EMBRYO OF 2 MM. (FIG. 72, P. 49). (After Graf v. Spee.)

*ect*, ectoderm; *mes*, mesoderm; *ent*, entoderm; *pr. st.*, primitive streak. The mesoderm-sheet springing from the streak show two lamellæ.

by the splitting apart of its floor. Such a process actually takes place in reptiles, and in an abbreviated fashion in the bats among mammals (figs. 67 and 68, p. 45).

Looking back to the complicated series of changes described above, we may divide the period of the appearance of the mesoderm into two stages. In the first the mesoderm of the

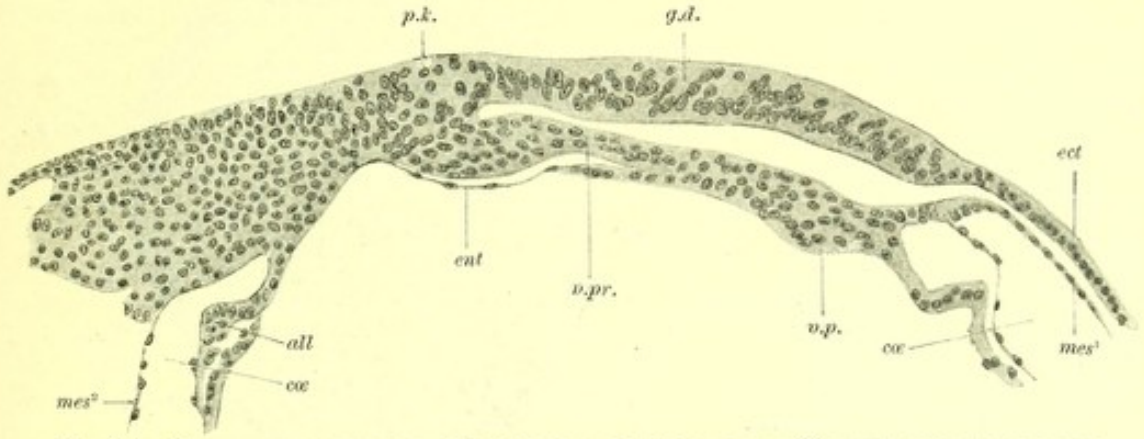



FIG. 60.—MEDIAN LONGITUDINAL SECTION OF A BLASTODERM OF TARSIUS SOMEWHAT LATER THAN THAT SHOWN IN FIG. 57. (After Hubrecht.)

*p.k.*, Hensen's (protochordal) knot continued backwards into the thickening of the primitive streak; *g.d.*, germinal disc; *ect*, ectoderm of somatopleure; *mes*¹, mesoderm of ditto; *cœ*, cœlom; *p.p.*, primitive entodermic (protochordal) plate, continuous with *p.pr.*, protochordal process; *ent*, entoderm; *all*, rudiment of allantoic diverticulum; *mes*², mesoderm of splanchnopleure.

connecting stalk (yolk-sac and amnion) and the head-plate is laid down. It is a continuous and unpaired sheet, and is at no time segmented. In the second phase the primitive streak appears, and the mesoderm now springs from its sides as bilateral sheets; the embryonic axis is differentiated out of the proliferating streak-tissue, the notochordal process and plate take form, and from the sides of the plate the mesoderm continues to be thrown off as the dorsal segmented mesoderm of the embryonic body.

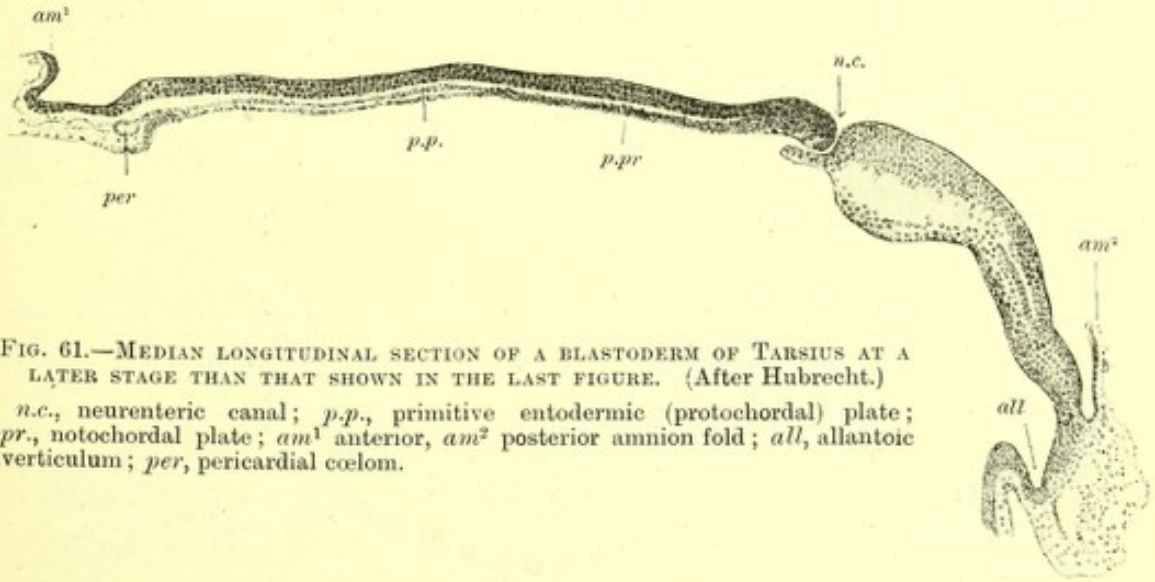



FIG. 61.—MEDIAN LONGITUDINAL SECTION OF A BLASTODERM OF TARSIUS AT A LATER STAGE THAN THAT SHOWN IN THE LAST FIGURE. (After Hubrecht.)

*n.c.*, neurenteric canal; *p.p.*, primitive entodermic (protochordal) plate; *p.pr.*, notochordal plate; *am*¹ anterior, *am*² posterior amnion fold; *all*, allantoic diverticulum; *per*, pericardial cœlom.

At the period now reached the blastoderm has the appearance presented in fig. 63. Sections demonstrate that the mesoderm everywhere forms a continuous layer. Within the shield it is still undivided, but outside the shield it spreads as two lamellæ from the edge of the disc, the *somatopleuric* lamella surrounding the amnion and lining the wall of the blastocyst, and the *splanchnopleuric* enveloping the yolk-sac.

**The gastrula theory and the mammalian ovum.**—It is impossible here to deal at length with the gastrula theory, because the evidence can only be satisfactorily presented by extensive comparative treatment. A short statement must therefore suffice.

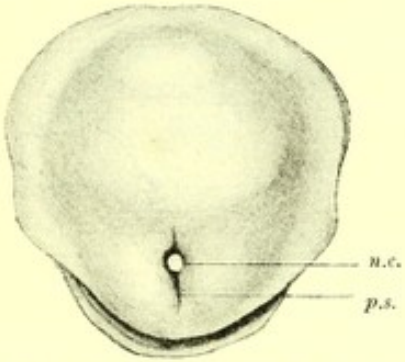



FIG. 62.—SURFACE VIEW OF A BLASTODERM OF CERCOCEBUS CYNOMOLGUS. (After Selenka.)

*n.c.*, neurenteric canal; *p.s.*, primitive streak.

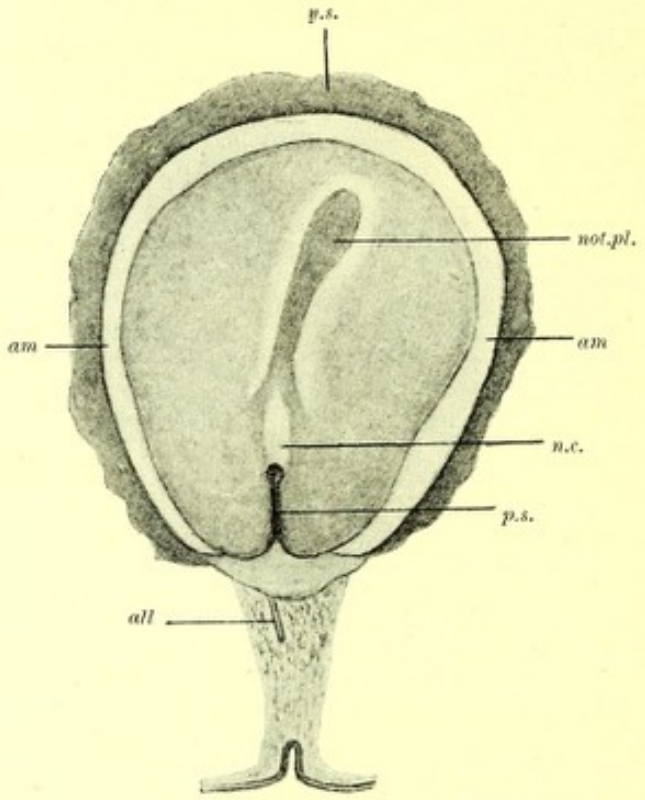



FIG. 63.—SURFACE VIEW OF A BLASTODERM OF HYLOBATES CONCOLOR. (After Selenka.)

The amnion has been opened to expose the germinal disc.

*am*, cut edge of amnion; *y.s.*, yolk-sac; *not.pl.*, notochord-plate; *n.c.*, neurenteric canal; *p.s.*, primitive streak; *all*, allantoic diverticulum in connecting stalk.

It will be observed that in the mammal the two primary layers of the blastoderm, at least their principal part, are formed by a separation into two strata of the cells of the inner granular mass, which occupies the interior of the ovum after segmentation. The bilaminar condition

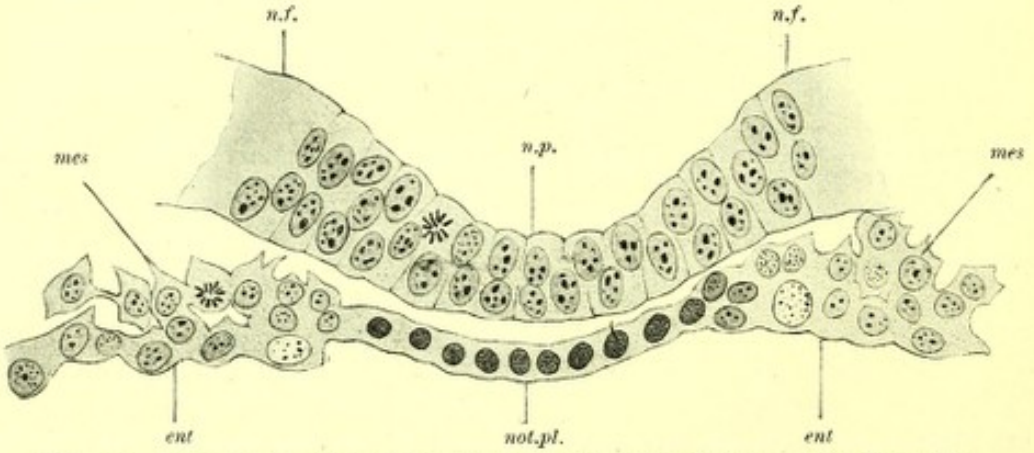



FIG. 64.—TRANSVERSE SECTION THROUGH BLASTODERM OF DOG. (After Bonnet.)

*n.p.*, neural plate; *n.f.* neural folds; *not.pl.*, notochordal plate; *ent*, entoderm; *mes*, mesoderm.

may therefore be said to result from a process of delamination in an originally simple mass or stratum. But in Amphioxus amongst vertebrates, and in many invertebrates with holoblastic (alecithal) ova, the bilaminar blastoderm is produced not by delamination, but by

the invagination of one pole of an originally simple hollow sphere—the *blastula*—the invaginated portion becoming the primitive entoderm and the remaining part of the wall of the vesicle forming the primitive ectoderm (fig. 69). This condition, which was discovered by Kowalewsky, is known as the *gastrula stage*, and it is regarded by many embryologists, following Haeckel, as typical of the mode of formation of the bilaminar blastoderm throughout the animal kingdom. The aperture by which the cavity of the gastrula, whether formed by delamination or invagination, communicates for a time with the exterior has been termed the *blastopore* (Lankester).

There are not wanting observations in mammals pointing to the existence in the bilaminar blastoderm of a blastoporic aperture. Thus in the mole Heape figures an aperture just before the primitive streak appears (fig. 70). Similar figures have been published, though for rather earlier stages, by Selenka in the opossum, by Hubrecht in the shrew and hedgehog, by Keibel in the rabbit, and by Bonnet in the dog; while in Tarsius the narrow slit in fig. 57, p. 39, may have the same significance (Hubrecht). In other mammals, however, no such aperture has

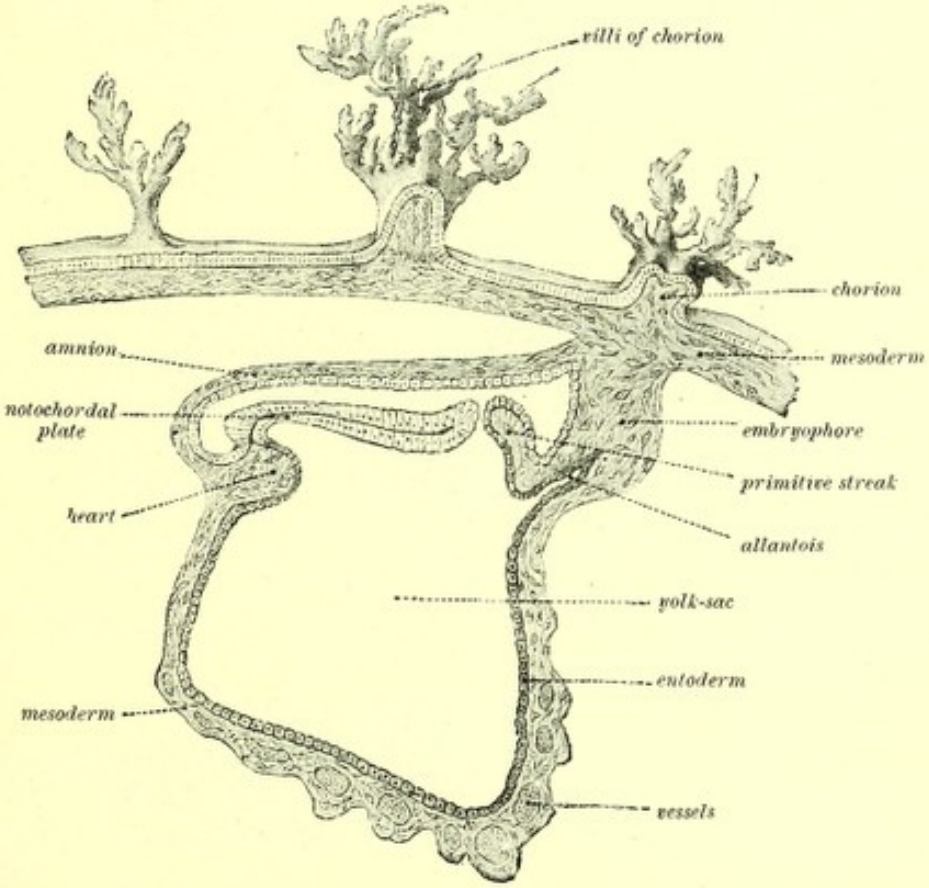



FIG. 65.—MEDIAN LONGITUDINAL SECTION OF THE HUMAN OVUM REPRESENTED IN FIG. 72, P. 49. (After Graf v. Spee, from Kollmann.)

The wide and vertical neurenteric canal is seen opening from the amniotic cavity into the yolk-sac.

been seen at this stage, and the opening in all cases has only a transitory existence. It is doubtful how far it corresponds to the blastopore of a gastrula derived from a holoblastic ovum, the whole of which is utilised for the formation of the embryo.

The accumulation of yolk in the egg profoundly modifies the process of gastrulation. Thus in the amphibian holoblastic egg, owing to the character of the segmentation, a considerable proportion of the yolk-laden entomeres are already within the blastula, and the invagination phenomena by which the so-called gastrula is completed, represent a second phase of gastrulation concerned in the formation of a dorsal plate which forms the dorsal wall of the trunk with the notochord and segmented mesoderm. During the development of the plate the gastrula cavity (*archenteron*) is formed by a partial invagination, and the breaking through of the space so produced into the cavity of the blastula. The archenteron is slit-like, because the gastrula is almost entirely filled by the entomeres (segmented yolk). In the lower Amniota the animal pole of the telolecithal egg alone segments. The germinal disc in its early phases represents a small portion of the blastula-wall, which is not theoretically completed till long afterwards, when the blastoderm has grown

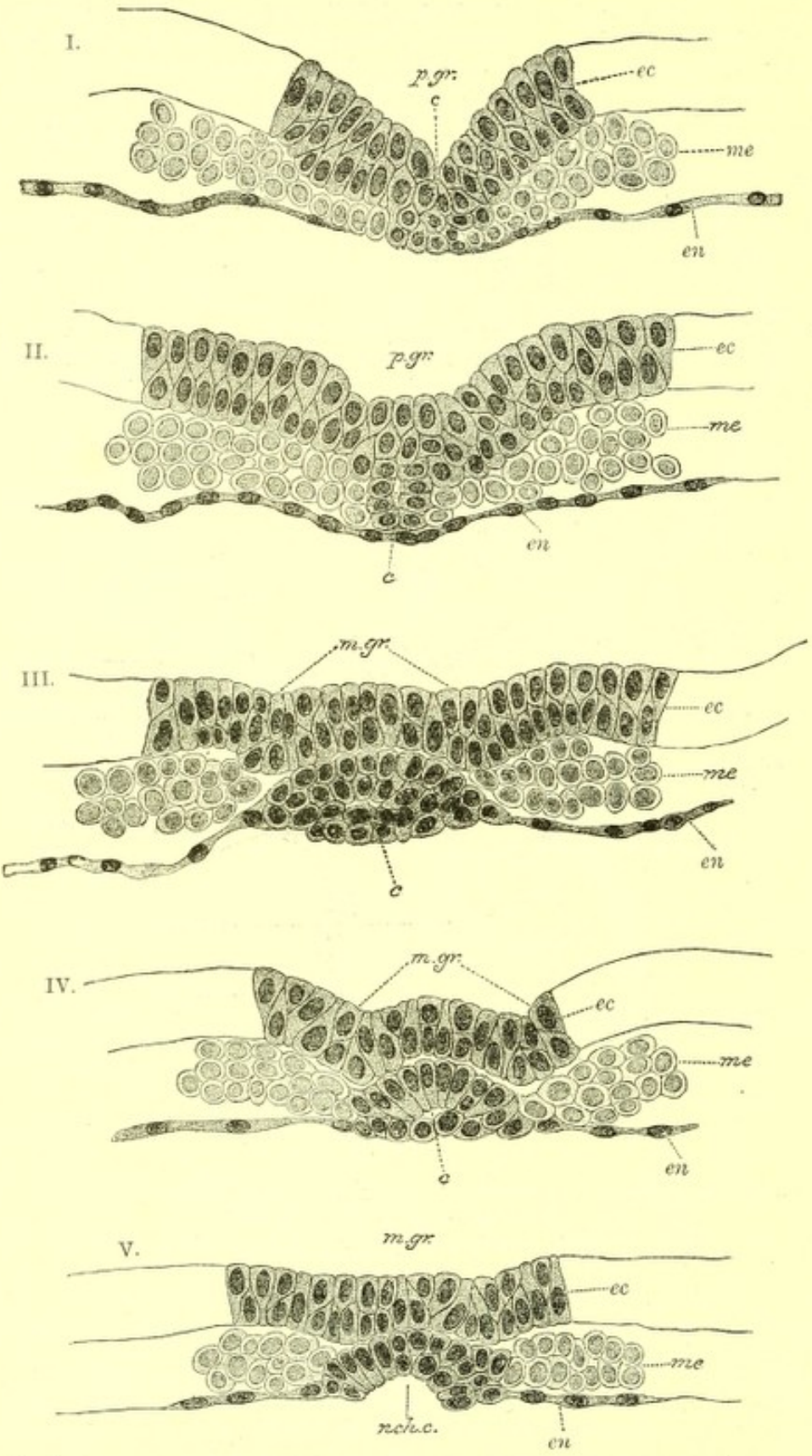



FIG. 66.—A SERIES OF TRANSVERSE SECTIONS THROUGH THE NEURENTERIC CANAL OF A MOLE EMBRYO. (Heape.)

The dorsal opening is shown in I., continued into the primitive groove; the canal passes thence through the head end of the primitive streak (II.) into the thickened posterior end of the notochord-plate (III.), along which it extends for some distance (IV.), and eventually opens ventrally in a median groove (V.).

*ec*, *me*, *en*, ectoderm, mesoderm, entoderm; *p.gr.* (in I. and II.), primitive groove; *c*, neurenteric canal; *m.gr.* (in III., IV., and V.), medullary groove.

over the yolk. The entoderm is produced by delamination (first stage of gastrulation). It is from the first entirely within the theoretical blastula, which is completely filled, as it were, by the entomeres and the great mass of unsegmented yolk. Owing to the profoundly altered conditions, the second phase of gastrulation is further modified and abbreviated, as will be explained presently.

In the Mammalia the egg is holoblastic, but the blastocyst does not represent a blastula like that of Amphioxus, but is rather like the theoretical blastula of one of the lower Amniota, empty of yolk and with one portion of its wall invaginated. The entoderm is formed by delamination, but when the embryonic ectoderm-plate is differentiated a circular blastopore such as is seen in none of the lower Amniota in some cases breaks through.

Now, analysing the early appearances in the primate blastoderm in terms of the gastrula theory and in the light of the above interpretations, the posterior edge of the germinal area

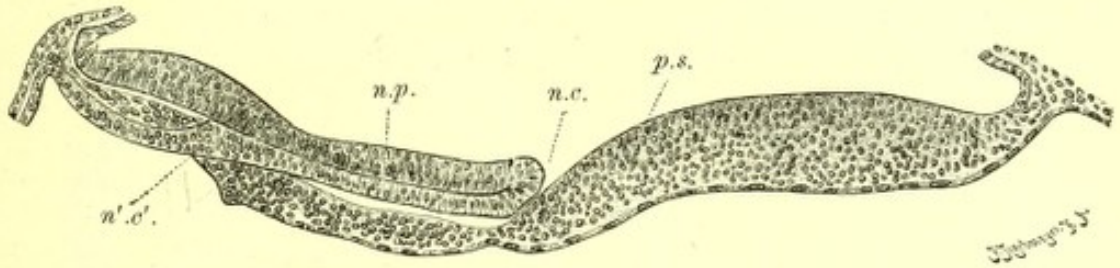



FIG. 67.—MEDIAN LONGITUDINAL SECTION OF A BLASTODERM OF VESPERTILIO MURINUS, SHOWING THE NOTOCHORDAL CANAL BEFORE ITS OPENING. (Van Beneden.)

*n.c.*, posterior opening of notochord-canal; *n'.c'.*, its anterior opening; *p.s.*, primitive streak; *n.p.*, notochord-plate.

from which the mesoderm first springs would represent the ventral lip of the blastopore, and Hensen's knot its dorsal lip. Hensen's knot, however, signifies the commencement of active changes in the dorsal lip which are concerned in the formation of the embryonic axis, and before these are initiated a continuous layer of unpaired, and always unsegmented mesoderm is laid down from the lips of the blastopore, which has no part in the embryo except at its extreme head end. The formation of the primitive streak, during which the posterior border of the disc or ventral lip is carried away from Hensen's knot by the growth of the pointed posterior end of the shield, would signify the drawing out of the gastrula-mouth into a lineal aperture of which the lips are fused. The second phase of gastrulation is now entered on, during which a true invagination, but of a modified character, appears to occur. It is associated with the backward growth of the dorsal lip and the laying down of the dorsal plate (embryonic axis)

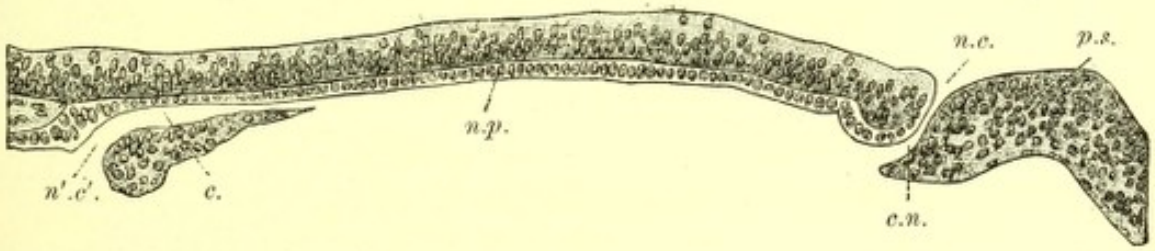



FIG. 68.—MEDIAN LONGITUDINAL SECTION OF A BLASTODERM OF VESPERTILIO MURINUS, SHOWING THE NOTOCHORDAL CANAL AFTER THE BREAKING THROUGH OF ITS FLOOR. (Van Beneden.)

*c.n.*, neurenteric canal; *c*, anterior persisting portion of the notochordal canal; , other letters as in fig. 67.

in front of it, and the re-establishment of the blastopore in the formation of the notochordal canal.

In the Reptilia processes are observed which throw a light on the much more modified phases in mammals, and can again be linked on to the processes seen in those amphibian eggs which are heavily yolked. On the posterior border of the germinal area a thickening appears called the *primitive plate*. On this a slight pocket appears, marking a spot where ectoderm and entoderm are indistinguishable. The appearances are suggestive of proliferation of cells to form the entoderm, but there is no true invagination. Later (second phase of gastrulation), at the anterior end of the primitive plate the pocket deepens to form a true invagination, which, as the dorsal lip increases in length to form the dorsal plate, becomes extended into a canal. The floor of the canal fuses with the primitive or yolk entoderm, and then breaks through, so

that the cavity under the developing dorsal plate (embryonic axis) is roofed-in by the upper wall of the canal and opens behind on to the surface of the primitive plate by the mouth of the original invagination or blastopore. In some Reptilia this invaginated canal is wide, in others narrow; but it clearly corresponds to the solid protochordal process of mammals which is tunnelled in its later stages, and in most forms only at its posterior end, by the notochordal canal, which opens on the surface as the blastopore. It is a common experience in embryology to find a developmental process modified, in the sense that a hollow rudiment is replaced by a solid rudiment which is afterwards hollowed out.

The space under the embryonal axis, formed in the manner described, may be taken, still following this conception, as representing the dorsal part of the archenteron of Amphioxus

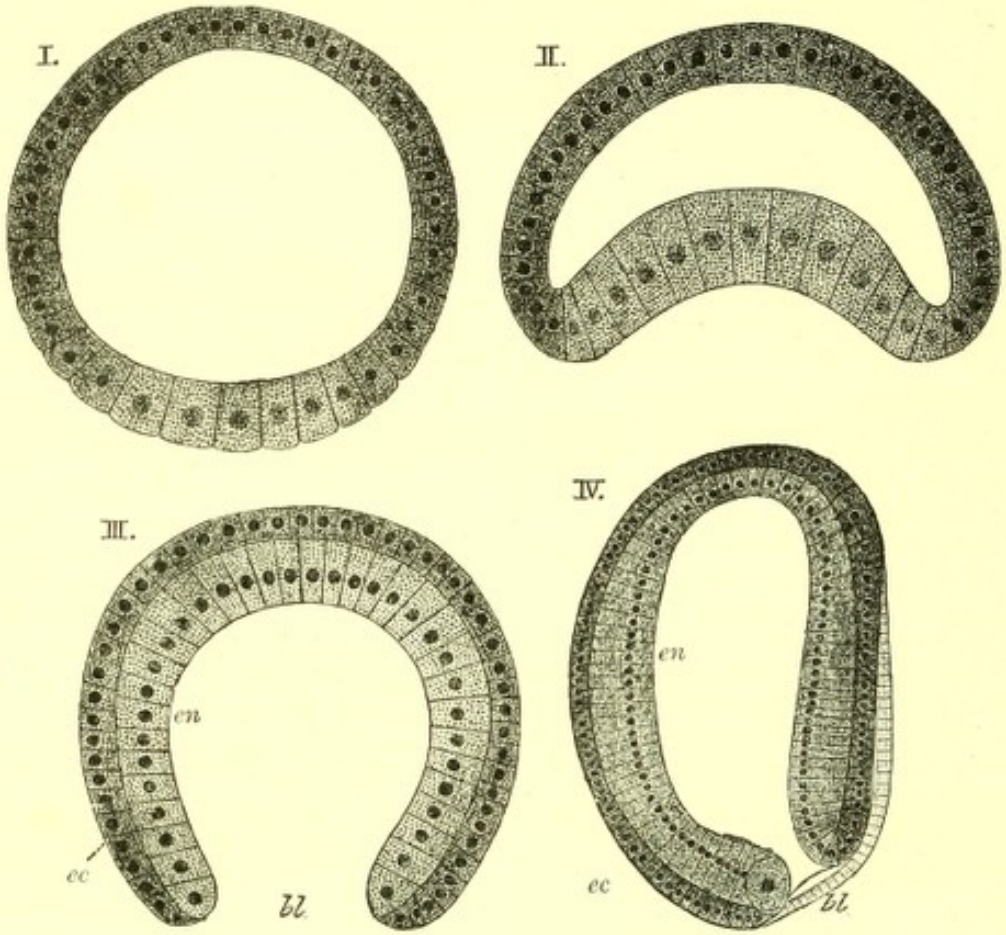



FIG. 69.—FOUR STAGES IN THE DEVELOPMENT OF AMPHIOXUS, ILLUSTRATING THE FORMATION OF THE GASTRULA. (Hatschek.)

I. Spherical blastoderm; the cells at the lower pole are larger than the others, and filled with granules.

II. Invagination of the lower pole producing a cupping of the vesicle.

III. Completion of the invagination; the blastoderm is now bilaminar, and forms a cup with narrowed mouth, the blastopore, *bl*, and a double wall of ectoderm, *ec*, and entoderm, *en*.

IV. The ovum is now elongated; the cavity of the gastrula forms a primitive alimentary canal, the orifice of which is the blastopore, which is directed dorsally. Extending from this along the dorsal surface (right in the figure) a shallow groove is seen in optical section: this is the rudiment of the nervous system.

(fig. 71); and just as in that form, the entoderm of the roof gives origin to the notochord, while the axial mesoderm arises from its lateral diverticula (cœlomic pouches).

Van Beneden has shown that the floor of the notochordal canal persists for a time in the bat; but in the Primates, and most other mammals, there is nothing to indicate the true nature of the developmental phases, the whole series of phenomena being repeated in a still more abbreviated form. Eternod [1] has, however, observed in the early human blastoderm the occurrence of scattered cells adhering to its under aspect, or to the lip of the neurenteric canal, which he regards as traces of the floor of the archenteric sac or canal.

[1] Anat. Anzeiger, xvi.; Compt. rend. de l'Assoc. des Anat., 7e réunion, Geneva, 1905; *ibid.* 8e Réunion, 1906; Bibliograph. Anat. xv.

The question here arises, What is the fate of the primitive streak ? Is it converted into the embryonal axis as it increases in length, or is the growth of the embryo effected by a continuous proliferation from a growth-centre at the head end of the streak ? Experimental data seem to show that the portion of the blastoderm in front of the streak gives rise to the extreme head end of the embryo, that the anterior end of the streak forms the rest of the head, while the remainder is converted into the trunk, the growth-centre being placed near its posterior end, and forming ultimately the knob of undifferentiated blastema which gives rise to the tail.

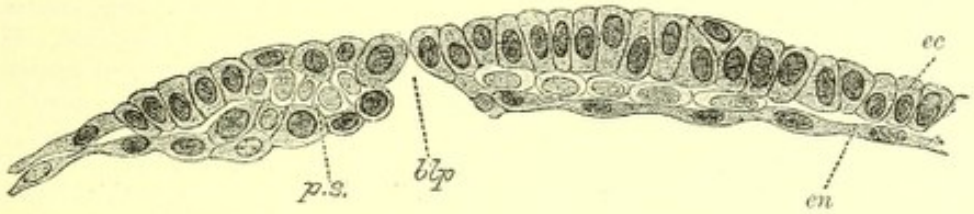



FIG. 70.—LONGITUDINAL SECTION THROUGH THE MIDDLE LINE OF PART OF AN EMBRYONIC AREA (MOLE) IN WHICH THE PRIMITIVE STREAK HAS BEGUN TO FORM. (Heape.)

The blastoderm is perforated in front of the (short) primitive streak (? blastopore, *blp*) ; a few mesoderm-cells are seen anterior to the perforation; *ec*, ectoderm; *en*, entoderm; *p.s.*, primitive streak.

Starting from these premises, and accepting the assumption that the streak represents the gastrula-mouth drawn out, the axial increase from before backwards has been interpreted as signifying the fusion of the lips of the blastopore postulated by the *concrescence* theories of His, Minot, and Oscar Hertwig. According to this conception, the bilateral symmetry of the vertebrate has been brought about by the elongation of the radial gastrula into a cylinder, and the fusion along the dorsal aspect of the lips of the gastrula-mouth. The fusion takes place from before backwards, and is manifested by the apparent backward growth of the dorsal lip of the blastopore, as the embryonal axis is laid down in front of it. This process results in the closing-in

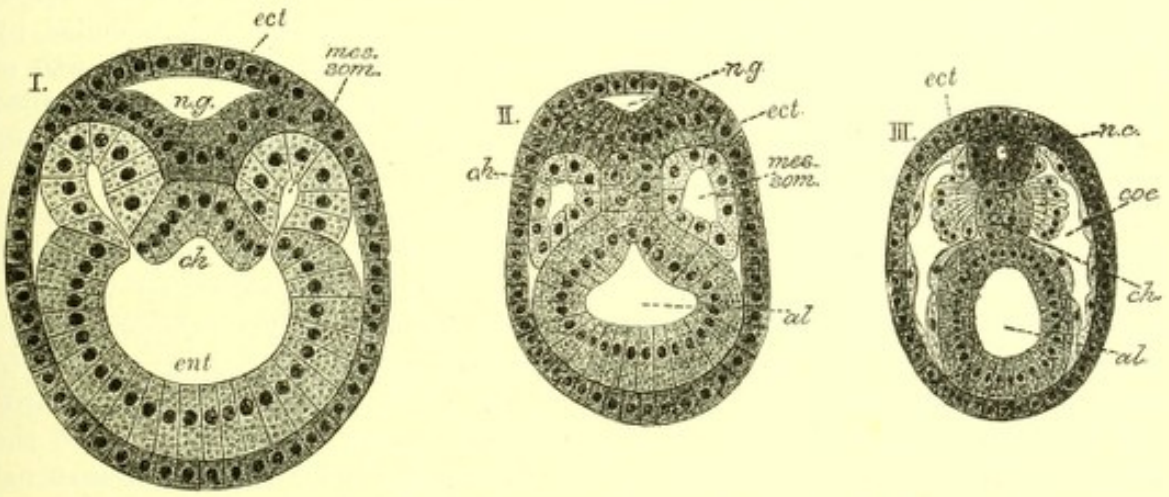



FIG. 71.—SECTIONS ACROSS AN AMPHIOXUS EMBRYO. (Hatschek.)

*n.g.*, neural groove ; *n.c.*, neural canal ; *ch*, rudiment of notochord ; *mes. som.*, mesodermic somite. In I. its cavity is in free communication with the alimentary cavity ; *ect*, ectoderm ; *ent*, entoderm ; *al*, alimentary cavity. In III. the cavity of the somite has extended on either side of the alimentary canal and forms a cœlom, or body-cavity (*cœ*).

of the archenteron, the roof of which forms the dorsal aspect or axis of the embryo, with the notochord and segmented mesoderm.

A considerable tide of opinion has in recent years set in in favour of a somewhat modified conception of gastrulation. Keibel and Hubrecht[1] in 1888 independently worked out the conception of gastrulation in two phases; Hubrecht in 1902 named these two stages *kephalogenesis* and *notogenesis*. The primary gastrula, formed in all Craniota by delamination, has a radial symmetry and forms the fore-part of the head. The second stage of ontogeny, embracing the

[1] See Hubrecht and Keibel, Quart. Jour. Micro. Sc. xlix. 1905.

formation of the primitive streak and of the notochord, although involving invagination phenomena, is not to be reckoned as part of the gastrulation process, but represents a phylogenetic stage by which a radial cœlenterate form was converted into a proto-vertebrate by the elongation of the gastrula and the formation of a dorsal plate which became the notochord. The primitive streak is thus not the gastrula-mouth of ontogeny, but represents the *protostoma* of an Actinia-like form, as suggested by Sedgwick and Van Beneden.

Assheton's[1] theory also involves the acceptance of two ontogenetic phases: a first (which may be exemplified by the earliest phases in Tarsius) resulting in the formation of the forepart of the head, and a second represented by the formation of trunk and tail. The idea is that the lips of the circular blastopore grow actively so as to produce a cylindrical gastrula. The dorsal lip, however, grows more actively in vertebrates, and produces the back and ultimately the tail or post-anal part of the axis. The anus represents the blastopore, while the mouth is a new opening (like the gill-slits) into the alimentary canal. Such a process is greatly modified, of course, in the Amniota, whether those with mesoblastic eggs or mammals, and the ventral lip of the gastrula is greatly masked by the presence of the yolk-sac. According to this conception, the primitive streak is only a phase in the development of the embryonic axis out of the growing blastema of the blastopore-lip, or secondary 'growth-centre.'[2]

## EARLY CHANGES IN THE BLASTODERM, RESULTING IN THE FORMATION OF THE EMBRYO.

### FORMATION OF THE NEURAL CANAL, NOTOCHORD, AND MESODERMIC SEGMENTS.

**Neural canal.**—While the embryonic axis is developing, as described above, a shallow groove appears on its surface in front of the primitive streak (fig. 72). This elongates with the axis, and encloses, behind, the anterior end of the streak with its neurenteric passage. Anteriorly and laterally it is bounded by a fold of the ectoderm, the groove indeed being produced by the upgrowth of the limiting folds (figs. 73 and 76). The thickened ectoderm of the groove is called the *neural plate*, because the central nervous system is formed from it, and the bounding folds are termed the *neural folds*.

By the continued upgrowth of the neural folds (fig. 73) the neural groove is converted into a deep furrow, and ultimately, by their fusion in the mid-axial line, into a closed canal (fig. 82, p. 57). The neural plate is then separated from the surface-ectoderm, and the closed canal becomes isolated as the rudiment of the cerebrospinal axis. The closure of the canal appears in the human embryo to begin in the region of the future trunk of the embryo, and proceeds forwards and backwards. The point where the final closure occurs in front is called the *anterior neuropore*. When the neural canal closes posteriorly, the neurenteric canal comes to lie in its floor, but it is obliterated at an early stage by the fusion of its lips and soon completely disappears. The anterior end of the neural canal extends beyond the notochord, and becomes enlarged to form the anterior of three primary cerebral vesicles round which the brain is formed.

At the point where the lips of the neural folds meet, a mass of ectoderm-cells forms a thickening known as the *neural crest*, from which, by a series of changes afterwards to be described, the nerve-ganglia are formed.

**Notochord.**—It will be recollected that in last section we considered the development of a plate of cells which we named the notochord-plate. We

[1] Anat. Anzeiger, xxvii. 1905.

[2] The literature of the germinal layers in mammals and man up to 1902 will be found fully given in Hertwig, i. Part I. pp. 81 and 949. For a critical review of the earlier literature, see Born in Merkel and Bonnet's Ergebnisse d. Anat. u. Entwickelungsgesch. i. 1891; and of the later literature, Keibel in the same publication, x. 1901.

saw that, in the early stages, it lies under the neural groove (fig. 64), is directly continuous on each side with the primitive entoderm, and at the points where it joins with that layer also with the lateral sheets of mesoderm. By a process of differentiation from before backwards, *pari passu* with the axial growth, the plate now loses its connexion with the mesoderm-plates, although it continues to pass directly into the lateral entoderm (fig. 76, III.). It next becomes converted into a rounded rod of cells, at first continuous with, then detached from, an underlying layer of entoderm. The mechanism of this process is probably the doubling up of the notochordal plate and the fusion of the lips of the groove thus formed in the mid-axial line, just as in the case of the neural canal. The rod of cells thus formed is the *notochord* (figs. 81 and 82). The anterior end of the notochord does not reach to the anterior end of the embryo, but terminates in a recurved point against the wall of the *hypophysis cerebri* (epithelial part of the pituitary body) in the situation of the future body of the sphenoid bone, and close to the dorsal attachment of the bucco-pharyngeal membrane (see Development of the Mouth). It will be seen, therefore, that a portion of the neural canal is *prechordal*.

It would seem from the data given for Tarsius by Hubrecht, and also for the dog by Bonnet, that the anterior or head end of the notochord is formed by differentiation directly out of the primitive entodermic plate (fig. 78, p. 54) (*protochordal plate*, Hubrecht; *Ergänzungsplatte*, Bonnet).

The notochord is essentially an embryonic structure in mammals, although it does not completely disappear, for traces of it are to be found throughout life in the middle of the intervertebral discs. When fully developed it is a cylindrical rod composed of clear epithelium-like cells, enclosed within a special sheath of homogeneous substance. These cells, although they may become considerably enlarged and vacuolated, undergo no marked histogenetic change and take no part in the formation of any tissue of the adult.

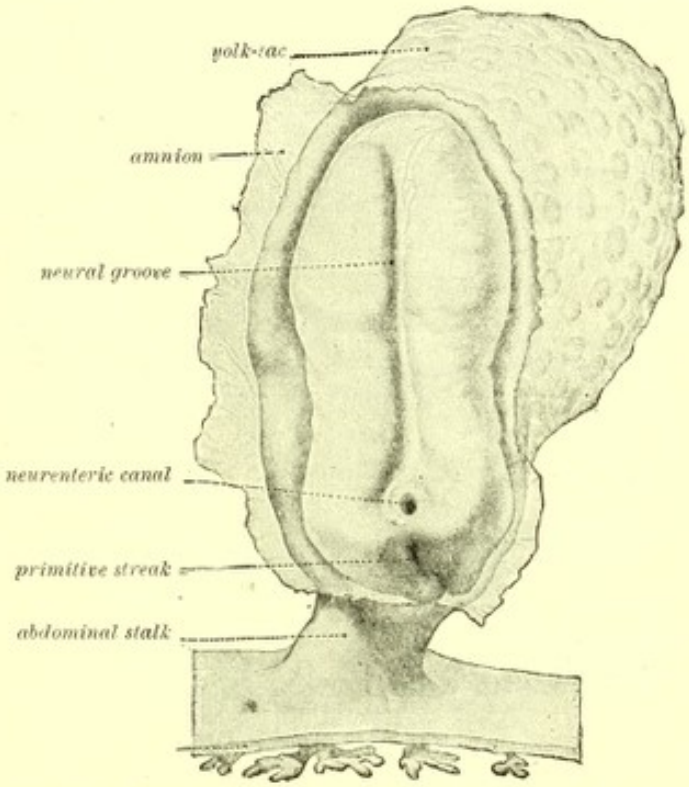



FIG. 72.—SURFACE VIEW OF EARLY HUMAN EMBRYO, 2 MM. IN LENGTH. (After Graf v. Spee, from Kollmann's Entwickelungsgeschichte.) × 30 diameters.

The amnion is opened, and on the blastoderm are seen the primitive streak, the dorsal opening of the neurenteric canal, and the neural groove.

**Later history of the mesoderm: formation of the mesodermic or primitive segments and of the cœlom.**—At the time when the neural groove is beginning to appear (figs. 73 and 76) a solid sheet of mesoderm extends outwards from the notochordal plate between ectoderm and entoderm, to be continuous outside the embryonic shield with the two layers of the extra-embryonic mesoderm. As the neural folds rise, the central portions of these sheets expand to occupy the spaces, triangular in section (fig. 73), which the folds enclose. These longitudinal thickenings gradually thin off laterally into what is known as the *lateral mesoderm* (fig. 73). They give origin to the voluntary muscular tissue of the body, and form what may be termed the *paraxial*, as distinguished from the *lateral mesoderm*. These paraxial thickenings now become cut up—by the occurrence at regular intervals,

transversely across the mass, of a process of thinning—into a linear series of small cubical masses (fig. 74), the *mesodermic* or *primitive segments.*[1] The first pair of these segments appears a short distance in front of Hensen's knot (fig. 75), in what will ultimately become the junction of the head and trunk of the embryo. They are produced in succession from before backwards, being gradually added as the embryonal axis increases in length, until the full number (thirty-five or more for the human embryo) is laid down. It has been shown in lower forms that the earliest segment to appear is not the most anterior

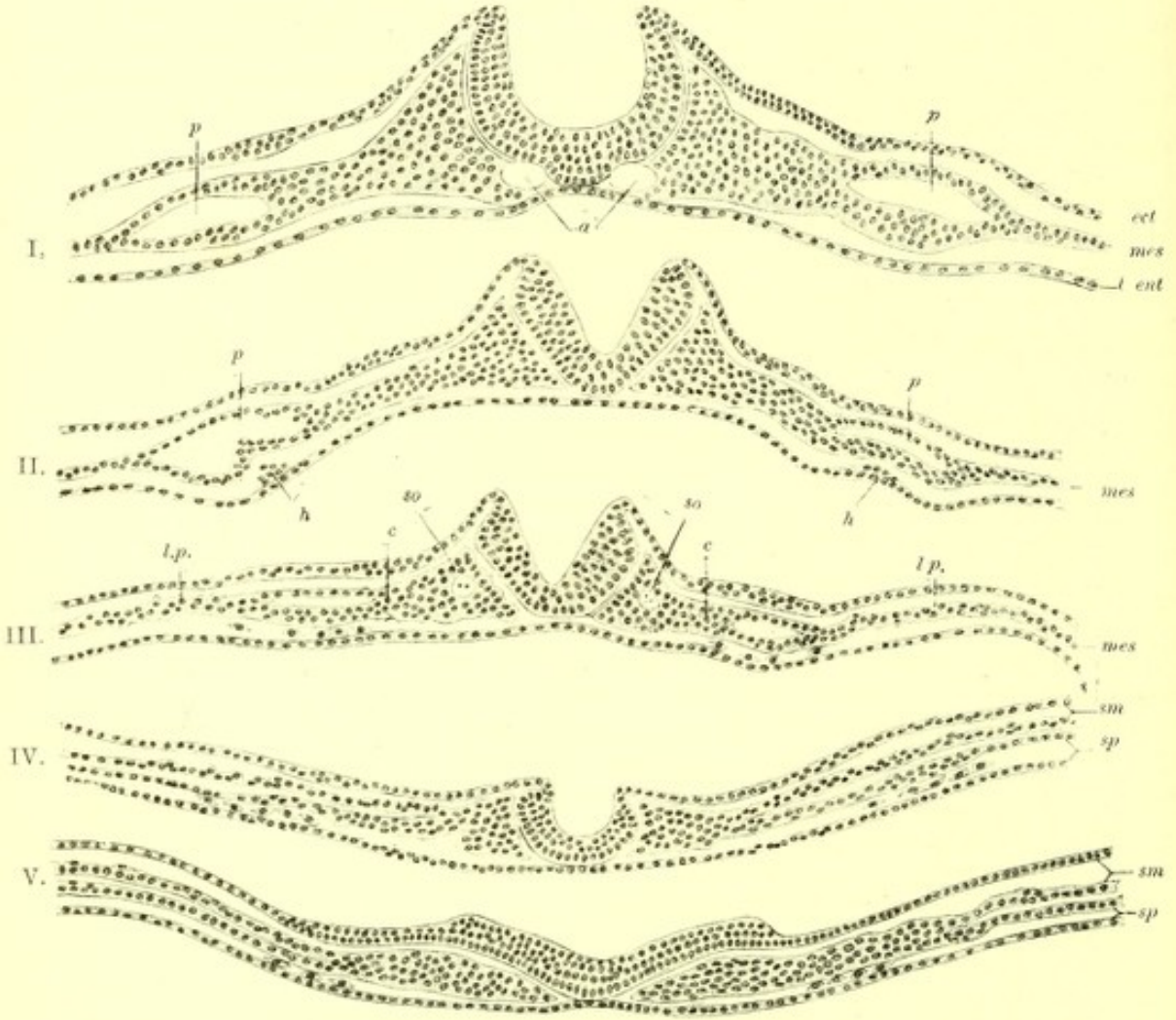



FIG. 73.—A SERIES OF TRANSVERSE SECTIONS THROUGH AN EMBRYO OF THE DOG. (After Bonnet.)
Section I. is the most anterior. In V. the neural plate is spread out nearly flat.
The series shows the uprising of the neural folds to form the neural canal.

*ect*, ectoderm; *ent*, entoderm; *mes*, mesoderm; *so*, segment; *c*, intermediate cell-mass; *l.p.*, lateral plate still undivided in I., II., and III.: in IV. and V. split into somatopleuric (*sm*) and splanchnopleuric (*sp*) lamellæ; *p*, pericardium; *h*, *h*, rudiments of endothelial heart-tubes. In III., IV., and V. the scattered cells represented between the entoderm and splanchnic layer of mesoderm are the vasoformative cells which give origin in front, according to Bonnet, to the heart-tubes (*h*); (*a*) aortæ.

of the series, as a number of *head-segments* develop from behind forwards in front of that first differentiating. In the human embryo there are probably three such.

The most anterior segment, in higher vertebrates, lies some distance behind the head end of the notochord in the future occipital region, and there is no trace of segmentation in front of this point.[2] As the segments are being cut out of the

[1] Formerly known as 'protovertebræ.' The term 'somite' is also frequently employed to designate them.

[2] In Petromyzon and Selachians the mesoderm is segmented at least as far forwards as the notochord extends; the segments in front of the occipital region undergo retrogressive changes, and disappear at an early stage.

paraxial mesoderm, each remains attached to the undivided lateral plate by a continuous tract called the *intermediate mesoderm* or *intermediate cell-mass* (fig. 73, III. *c*). According to Felix, this continuous tract is formed by the fusion, at a very early stage, of the stalks of the segments. As the excretory ducts are afterwards laid down in this tissue, it corresponds to those portions of the hollow primitive segments which are named the *nephrotomes* in the Anamnia.

A cleavage has meanwhile taken place in the lateral mesoderm, dividing it into a *parietal* and a *visceral* plate. The parietal plate is associated with the ectoderm to form the *somatopleure*, and the visceral plate with the entoderm to form the

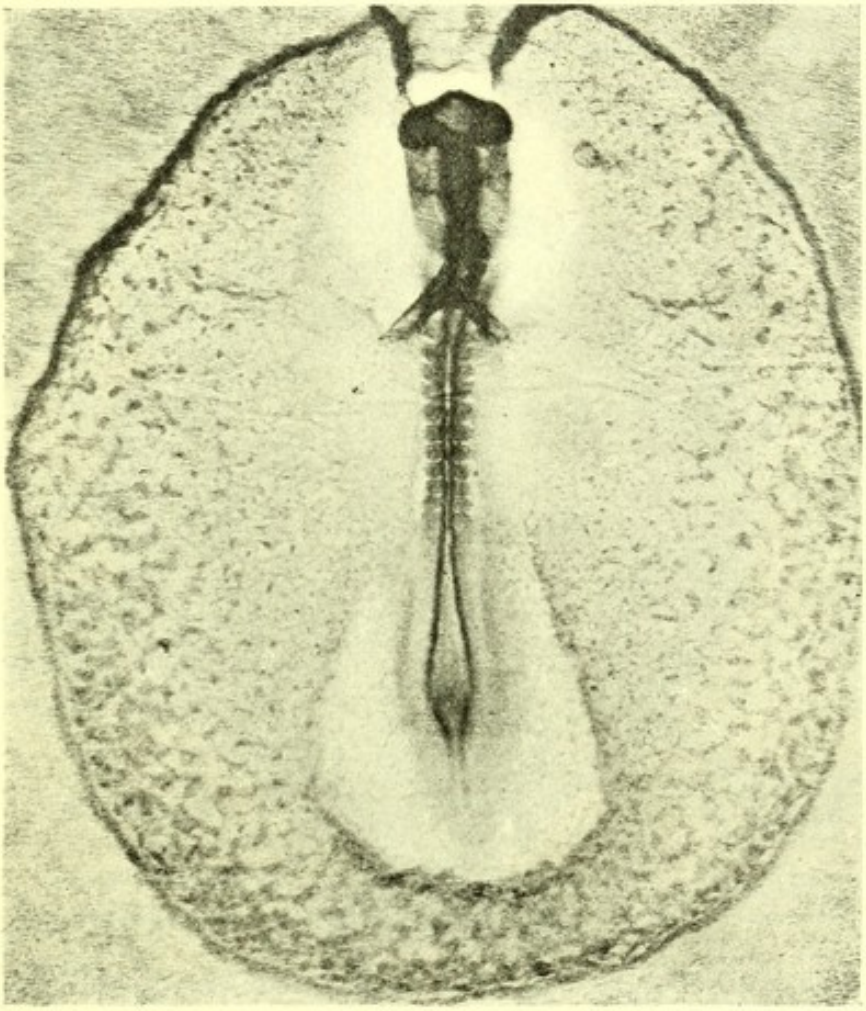


FIG. 74.—PHOTOGRAPH OF A CHICKEN EMBRYO. × 20 diameters. (T. H. Bryce.)

The mesodermic segments, eleven in number at this stage, are seen as small cubical masses on each side of the axis of the embryo. The eleventh is still continuous with the unsegmented axial mesoderm, which in turn passes behind into the primitive-streak mesoderm. The neural folds have not united, and they embrace posteriorly the head of the primitive streak. The optic vesicles are prominent lateral projections from the fore-brain; the mid-brain vesicle is visible behind the fore-brain, but that of the hind-brain is hidden by the tubular heart, which receives posteriorly the two vitelline veins from the vascular area.

*splanchnopleure*. The space between the layers becomes the *intra-embryonic cœlom* (*body-cavity*), and it follows that when the cleavage reaches the borders of the shield the intra-embryonic will become continuous with the extra-embryonic cœlom, and the relations of the layers will be established which are reached at a much earlier stage in lower mammals (fig. 77 ; cf. fig. 49, p. 33).

The segments now also show a small cavity in their interior, round which the cells arrange themselves in an epithelial fashion. The cavity represents a part of the cœlomic cleft, which in lower vertebrates is continuous with the general cœlom.

The cleavage first makes its appearance at the anterior end of the axis in the region where the heart-tubes will be formed. Thence it extends backwards, and at the same time forwards round the head end of the axis, so that the lateral cœlomic spaces are continuous with one another in front, by a pericephalic cleft which afterwards becomes the pericardium.

The relations of the layers immediately in front of and behind the axis must finally be referred to. In the axial line the notochord passes in front into the head-plate. If this be followed forwards (fig. 78), it will be seen that it is continued into a portion of the blastoderm between the head end of the axis and the pericephalic cœlom, into which the mesoderm has not extended (or from which it has disappeared). The ectoderm and entoderm are therefore here in contact, and form a membrane known as the *buccopharyngeal membrane*, which later becomes perforated to form the mouth-opening. The region of the blastoderm between the buccopharyngeal membrane and the edge of the shield corresponds to the 'pro-

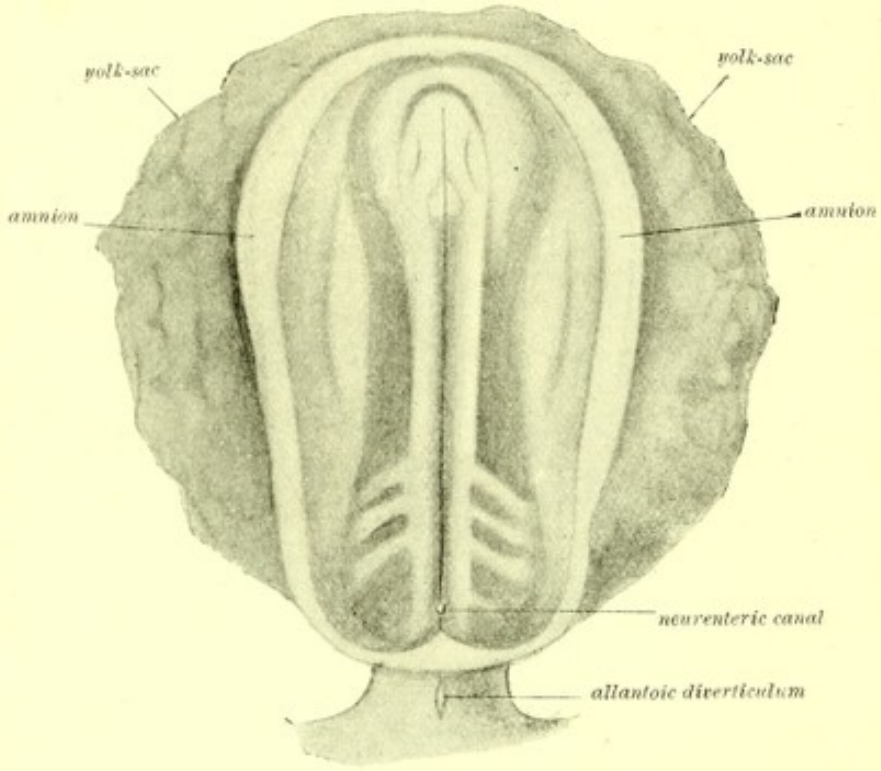


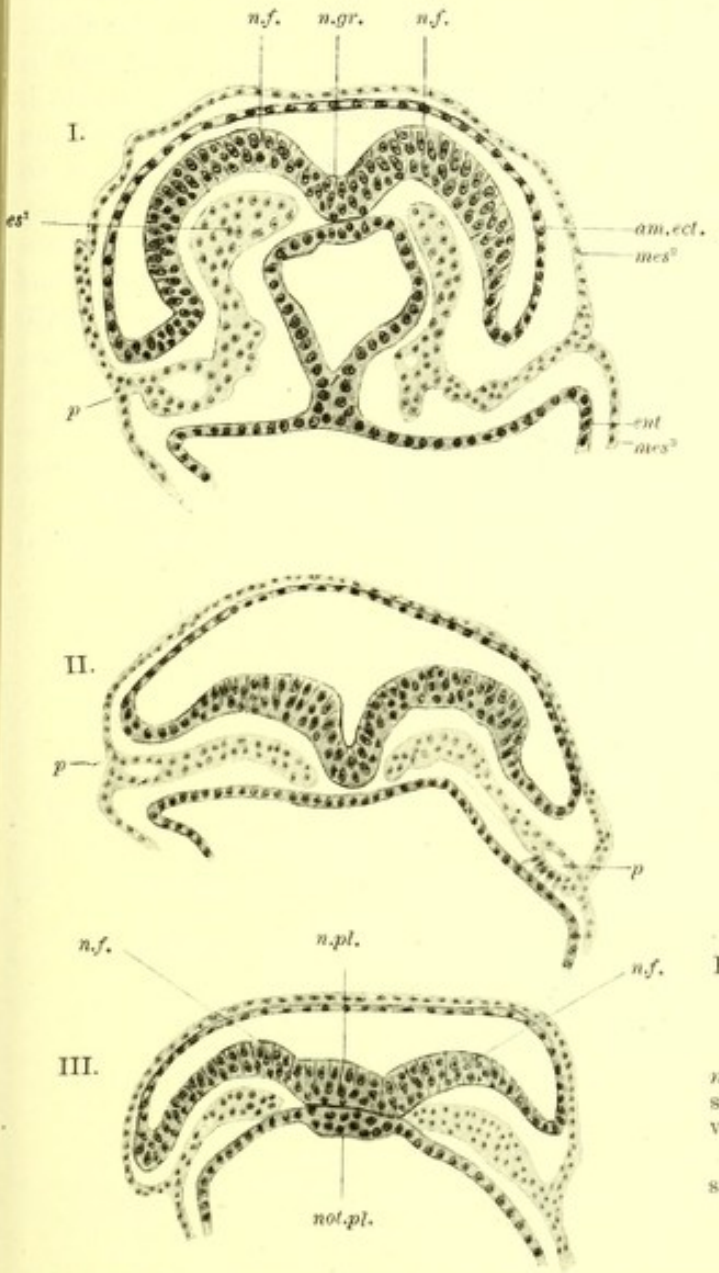

FIG. 75.—SURFACE VIEW OF A BLASTODERM OF CERCOPITHECUS CYNOMOLGUS. (After Selenka.)

The amnion has been opened. The first three segments are visible in front of the neurenteric canal on each side of the neural groove, which is still open.

amnion' of lower mammals; but in the human embryo the ectoderm and entoderm are, from the first, here separated by mesoderm. This is not split, however, so that the pericephalic is separated from the extra-embryonic cœlom by a bridge of tissue. Again, at the posterior end of the axis, behind the growing point or tail-knob, the primitive streak becomes detached from the lateral mesodermic sheets and resolved into an ectodermal and an entodermal lamella, which together form the *cloacal membrane*. This is afterwards perforated to form the urogenital and anal apertures.

**Separation of the embryo: history of the yolk-sac and allantois.**—As the embryo increases in length, there is a certain increment also in the breadth of the embryonic shield; and although the yolk-sac has much increased in size, the embryo soon begins to expand in all directions beyond the limits of the mouth of the sac. A folding-in round the margin of the shield, along the line where amniotic and embryonic ectoderm meet, consequently takes place. The anterior

fold first appears (fig. 79), and as a result of the forward growth of the front end of the axis a diverticulum of the yolk-sac is formed. This becomes in part the pharynx, but the *fore-gut*, as the diverticulum is called, is gradually lengthened by the deepening of the fold and the coming together of the splanchnopleuric folds, which are nipped in from each side (fig. 76, I.). In consequence of the formation of the anterior fold, the buccopharyngeal membrane becomes bent in under the



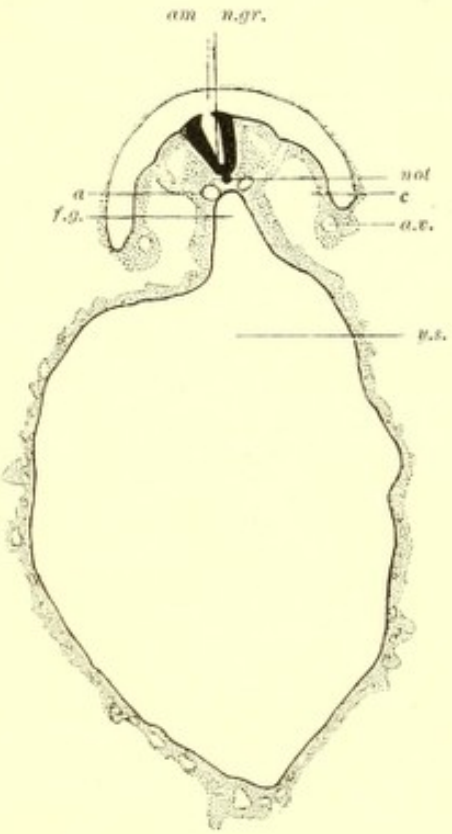




FIG. 77.—TRANSVERSE SECTION THROUGH A HUMAN EMBRYO OF 2·4 MM. (T. H. Bryce.)

*am*, amnion; *n.gr.*, neural groove; *not*, notochord; *f.g.*, fore-gut; *y.s.*, yolk-sac; *a*, aorta of right side; *a.v.*, allantoic vein of left side; *c*, cœlom.

Vessels are seen covering the whole surface of the yolk-sac.

FIG. 76.—TRANSVERSE SECTIONS OF THE HUMAN EMBRYO OF 2 MM. REPRESENTED IN FIG. 72. (After Graf v. Spee.)

In I., which is most anterior, the fore-gut is separated off from the yolk-sac.

*n.gr.*, neural groove; *n.f.*, neural folds; *n.pl.* (in III.), neural plate; *mes*¹, intra-embryonic mesoderm still undivided: the commencing intra-embryonic cœlom shows as a space (*p*)—in I. to the left, and in II. on both sides; it becomes the pericardium; *am.ect.*, amniotic ectoderm; *mes*², amniotic mesoderm; *ent*, entoderm of yolk-sac; *mes*³, mesoderm of yolk-sac; *not.pl.* (in III.), notochordal plate.

head of the embryo and, reversed in position, now forms the still closed anterior end of the fore-gut. Further, the pericephalic portion of the cœlom, also reversed in position, comes to lie below the fore-gut, while the bridge of mesoderm separating it from the extra-embryonic cœlom, and originally at the edge of the shield, now forms the anterior lip of the primitive umbilical opening, and

constitutes what is known as the *septum transversum*. The folding-in at the tail end of the embryo takes place rather later, and is complicated by the presence of the connecting stalk. In the earliest known human embryos (fig. 79) there is a pocket between the posterior end of the axis and the upper aspect of the stalk. As the embryo increases in length this deepens, the stalk is displaced forwards, and the primitive streak is bent in to form, as the anal membrane, the floor of a diverticulum named the *hind-gut*. In front of the attachment of the stalk the yolk-sac is further folded in and the hind-gut is gradually elongated. Up to this stage the name connecting stalk has been applied to the cord of mesoderm uniting the embryonic rudiment with the chorion. When the tail-fold is produced, it is bent round to the ventral

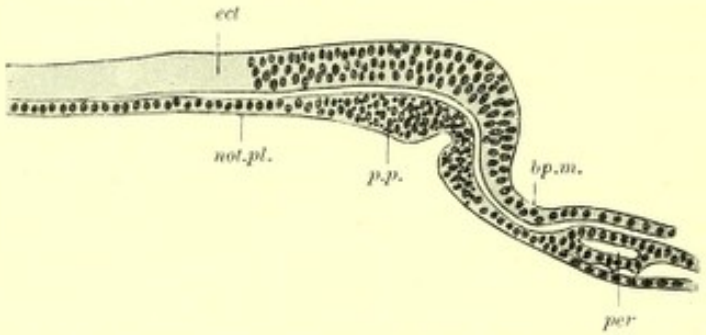



FIG. 78.—MESIAL LONGITUDINAL SECTION THROUGH THE HEAD END OF THE GERMINAL DISC OF THE DOG BEFORE THE FORMATION OF THE HEAD-FOLD. (After Bonnet.)

*ect*, ectoderm of shield; *not.pl.*, notochordal plate; *p.p.*, primitive entodermal plate (*Ergänzungsplatte*, Bonnet); *bp.m.*, buccopharyngeal membrane; *per*, pericephalic portion of pericardial cœlom.

The notochordal plate (archenteric plate, Bonnet) passes directly into the primitive entodermal plate (*Ergänzungsplatte*, Bonnet).

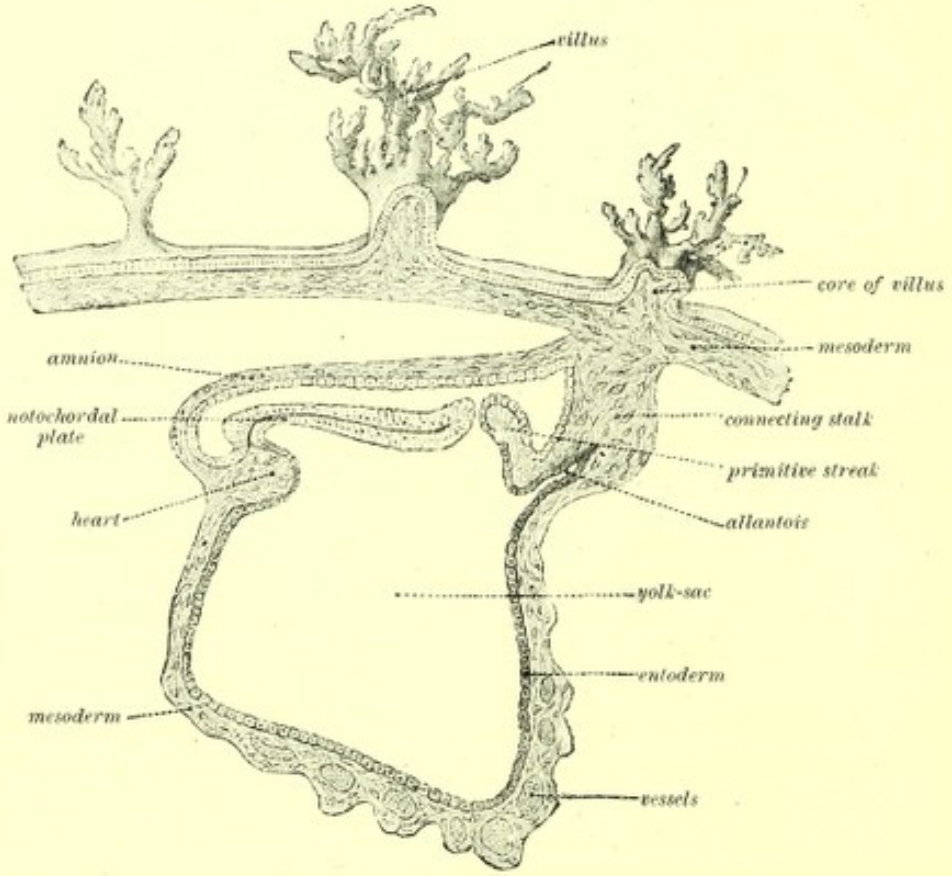



FIG. 79.—MEDIAN LONGITUDINAL SECTION OF AN EMBRYO OF 2 MM. (*see* FIG. 72). (Graf v. Spee.)

aspect of the body of the embryo, and may henceforward be appropriately named the *abdominal stalk* (*Bauchstiel*, His).

Between the hind-gut and the fore-gut there is at first a wide opening into the yolk-sac (fig. 92), which is gradually reduced to a narrow aperture, and the stalk

thus formed is drawn out into a long tubular passage, the *vitelline duct*, which widens distally into a rounded vesicle called the *umbilical vesicle*.

**Allantois.**—In all the Primates the vesicular allantois of lower forms is represented merely by a narrow tubular passage imbedded in the mesoderm of the connecting stalk. It appears as a recess of the posterior wall of the yolk-sac at a very early stage, before the formation of the hind-gut (figs. 53, 60, 61, 79). This recess is drawn out into a tube as the connecting stalk increases in length.

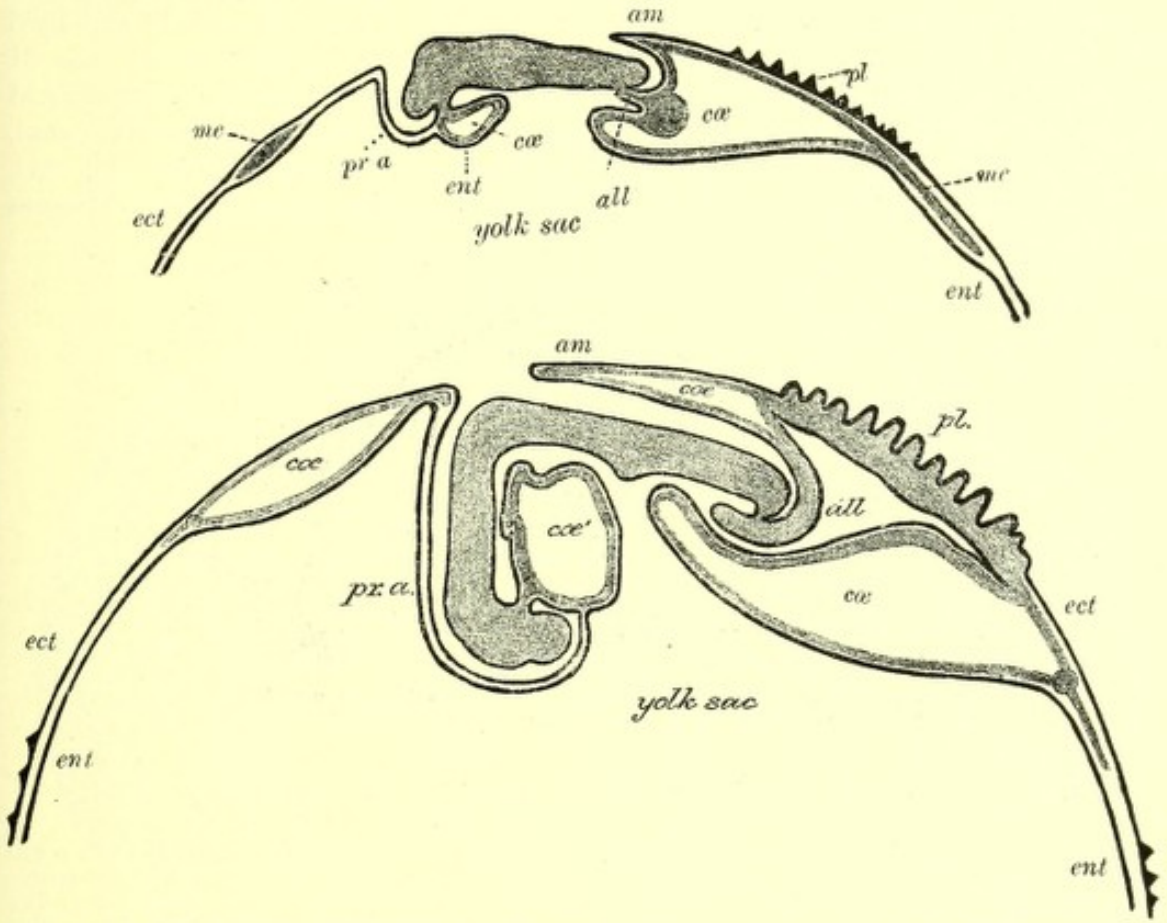



FIG. 80.—DIAGRAMMATIC LONGITUDINAL SECTIONS THROUGH THE EMBRYO OF THE RABBIT. THE SECTIONS SHOW THE MANNER IN WHICH THE PRO-AMNION IS FORMED BY A DIPPING DOWN OF THE HEAD AND ANTERIOR PART OF THE BODY INTO A DEPRESSION OF THE BLASTODERM, WHICH AT THIS PART IS FORMED OF ECTODERM AND ENTODERM ONLY. THE DIAGRAMS ALSO ILLUSTRATE THE MODE OF FORMATION OF THE ALLANTOIS AND OF THE TAIL-FOLD OF THE AMNION IN THIS ANIMAL. (Van Beneden and Julin.)

*ect*, ectoderm; *ent*, entoderm; *me*, mesoderm; *cœ*, parts of the cœlom; *cœ'*, pericardial cœlom, the heart not being represented; *pr.a.*, pro-amnion; *pl*, seat of formation of the placenta; *all*, allantois; *am*, amnion.

When the stalk is displaced to the ventral aspect, and the umbilical cord is formed, the passage persists for a time in the cord, while its intra-embryonic portion becomes the *urachus*.

In lower mammals the entodermic diverticulum varies much in the degree of its development. In the ungulates and carnivores it forms a large vesicle; in most rodents (fig. 80) it is less extensive, being confined to the placental site; in the guinea-pig it is reduced to a tubular passage in the body-wall and the stalk is a solid cord of mesoderm; but in all below Primates the diverticulum, with its covering layer of mesoderm, projects free into the extra-embryonic cœlom before it comes into contact with the chorion. In the Primates the embryonic shield is connected from the first with the chorion by the mesodermic connecting stalk, and the allantois never projects free into the cœlom. The chorion is thus vascularised directly and not through the agency of the allantois. This close attachment of the

embryo to the chorion by the short abdominal stalk is accompanied by a certain retardation of the development of the hind end of the embryo.

**Early stages in the development of the muscles and of the connective tissue and blood-vessels: mesenchyme.**—It will be recollected that the mesodermic segments were traced to a stage in which each shows a central lumen round which the cells are arranged in an epithelial fashion (fig. 82). In some cases the cavity is occupied by branching cells budded off from the ventral wall. In transverse section each segment is oval in shape, and now the lower part of the inner and ventral walls becomes resolved into a mass of loosely arranged cells, wedge-shaped in section, which encroaches on the cavity (*sclerotome*) (figs. 81 and 82). These cells, along with those in the cavity of the segment, divide actively and wander inwards, to invest the notochord (fig. 83) and ultimately the neural canal, in a continuous sheet of loose syncytial tissue known as *mesenchyme*[1] (fig. 84). It constitutes the blastema out of which the axial connective and skeletal tissues are formed.

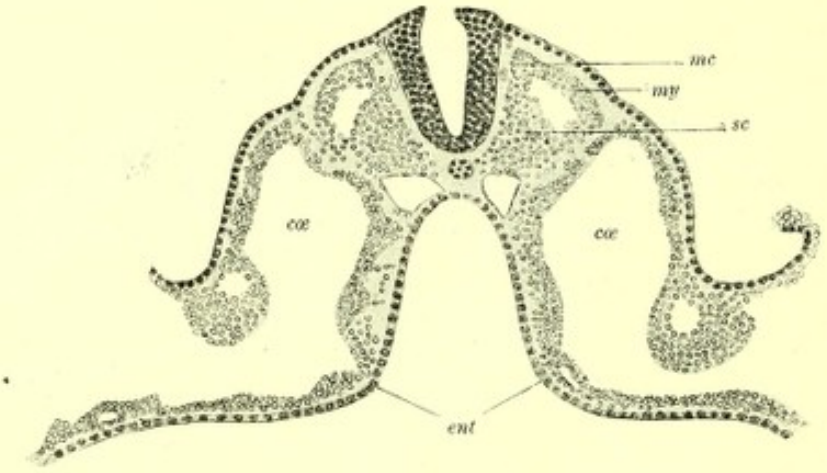



FIG. 81.—TRANSVERSE SECTION OF THE HUMAN EMBRYO OF 2·4 MM. (*see* FIG. 77), MORE HIGHLY MAGNIFIED. (T. H. Bryce.)

*ent*, entoderm of yolk-sac: the lines indicate the points of the splanchnopleuric layers which will come together to cut off the gut from the cavity of the yolk-sac; *my*, outer wall of mesodermic segment; *mc*, part of its wall which gives rise to the muscle-plate; *sc*, sclerotome; *cœ*, cœlom. The other structures as lettered in fig. 77. The amnion, having been torn, is not completed in this figure.

While the sclerotomes are becoming differentiated, the cavity of the segment is reduced to a narrow slit bounded by an outer and an inner lamella derived respectively from the outer and inner wall of the segment (fig. 84). The cells of the inner lamella elongate, become arranged longitudinally, and are ultimately (third week) converted into muscle-cells. Hence this lamella is named the *muscle-plate* (*myotome*). It is the rudiment of the voluntary musculature of the body. The outer lamella of the segment retains its epithelial arrangement for a time; according to Maurer, it becomes entirely resolved later into a layer of subcutaneous mesenchyme.

Balfour originally described both inner and outer lamellæ as becoming differentiated into muscle, and in some forms this certainly seems to be the case—*e.g.* Lepidosiren (Graham Kerr[2]) and pig (Bardeen[3]). As regards the human embryo, Kollmann (1891) described the outer wall as yielding muscle at least in part, but Bardeen and Lewis state[4] that the whole outer lamella becomes muscular tissue.

[1] For definition of this term, see p. 58.
[2] Rep. Brit. Assoc. 1902.
[3] Johns Hopkins Hospital Reports ix.
[4] Amer. Journ. of Anat. i.

Each primitive segment is thus differentiated into *myotome* and *sclerotome*, while its ventral part, concerned in the formation of the excretory ducts, may be termed the *nephrotome*. The myotomes retain their segmental disposition, but the sclerotomes have really no separate identity, being at once fused into a continuous axial sheet of mesenchyme. The primitive segments are not, however, the only source of the embryonic connective tissue. The parietal and visceral plates of mesoderm become likewise resolved into the mesenchyme of the body-wall and gut-wall respectively, with the exception of the cells lining the cœlom, which become the endothelial lining of the body-cavities (*mesothelium*).

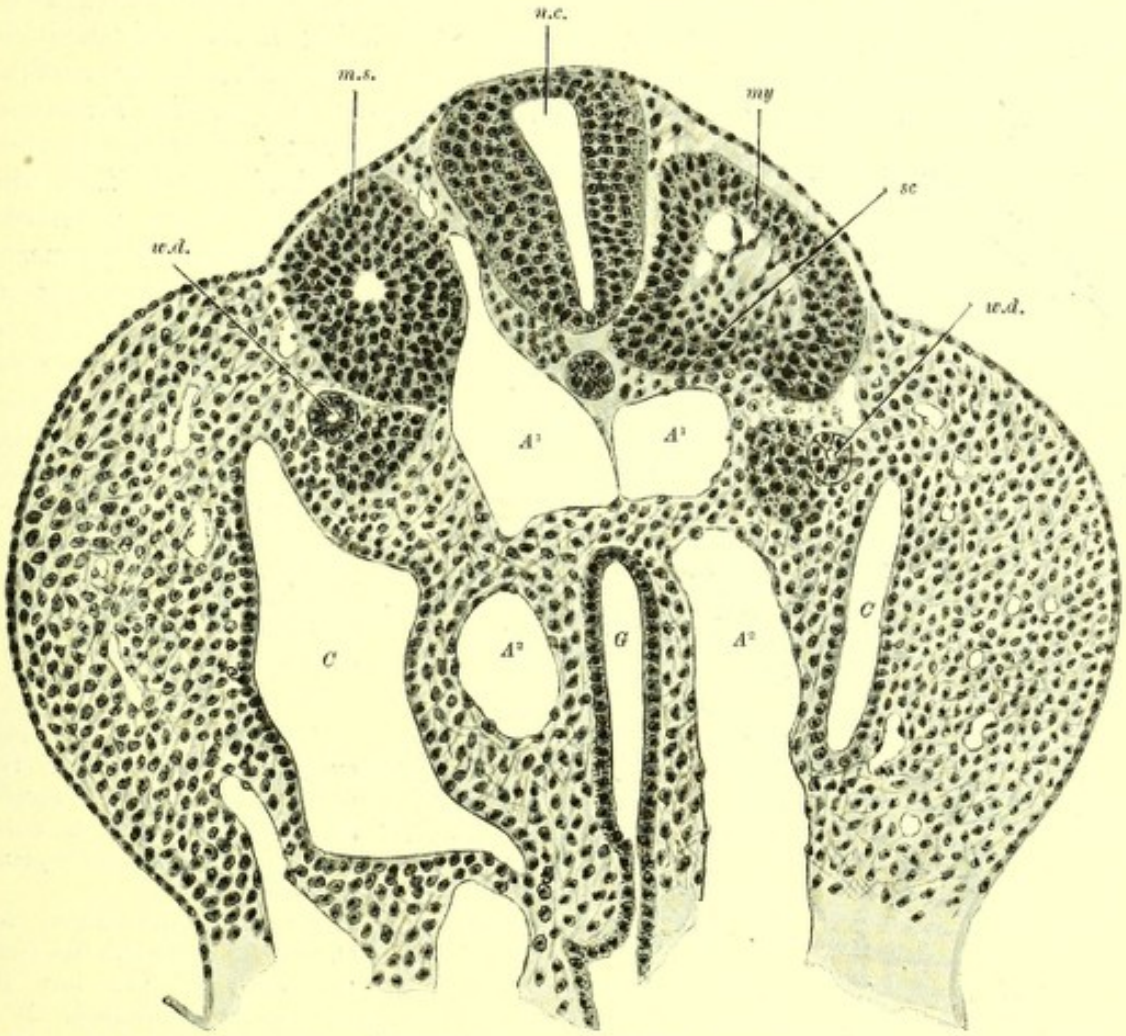



FIG. 82.—TRANSVERSE SECTION THROUGH THE TRUNK AND HIND-LIMB BUDS OF A RABBIT EMBRYO OF THE TENTH DAY. THE LINE OF SECTION IS SLIGHTLY OBLIQUE. (T. H. Bryce.)

*n.c.*, neural canal; *m.s.*, mesodermic segment; *sc*, ventral wall of segment becoming resolved to form sclerotome; *my*, outer wall of segment; *w.d.*, *w.d.*, Wolffian ducts; on the inner aspect of each a cord of nephrogenetic tissue; $A^1$, $A^1$, the two primitive aortæ cut close to where they separate into the allantoic arteries, $A^2$, $A^2$; *C*, cœlom; *G*, gut.

We have already seen that the mesoderm remains unsegmented in the region of the head. Moreover, there is here no distinction between paraxial and lateral mesoderm, and no splitting to form cœlomic spaces. The whole unsegmented mesoderm becomes resolved into a continuous mesenchyme which surrounds the cerebral vesicles and the head end of the notochord.

In lower vertebrates certain cœlomic cavities appear in the head which are concerned in the formation of the muscles of the eyes, and of the branchial region. They correspond to the preoccipital head-segments already alluded to, and are

considered by some as equivalent to trunk-segments. They will be referred to again in a subsequent section.

**Mesenchyme.**—The term *mesenchyme* is here employed to denote that part of the middle layer which is the blastema of the connective tissues. Its use involves the recognition of two orders of mesoderm. First, mesoderm in the stricter sense of the term (*mesothelium*)—*i.e.* that which we have termed the dorsal or segmented mesoderm in earlier sections. It is laid down in a coherent layer, in which the cœlom is formed by a process of splitting. It may be considered as typically developed from cœlomic pouches of the archenteron (see p. 46), although in general, owing to the accumulation of yolk in the egg and the secondary modifications resulting therefrom, the rudiment is solid and secondarily excavated. It gives origin to the skeletal muscles, the endothelial lining of the body-cavities, the epithelium of the excretory ducts, the germinal epithelium, and the cortical portion of the suprarenal body. Second, mesenchyme, a syncytial formation formed of cells budded off individually from the epithelial layers, or formed by resolution of the mesoderm into a loose mass of anastomosing cells. From it are developed the several forms of connective tissue, the unstriped muscular tissue, perhaps even striped muscles, and also possibly the blood and blood-vessels, though in respect of the blood there is much difference of opinion.

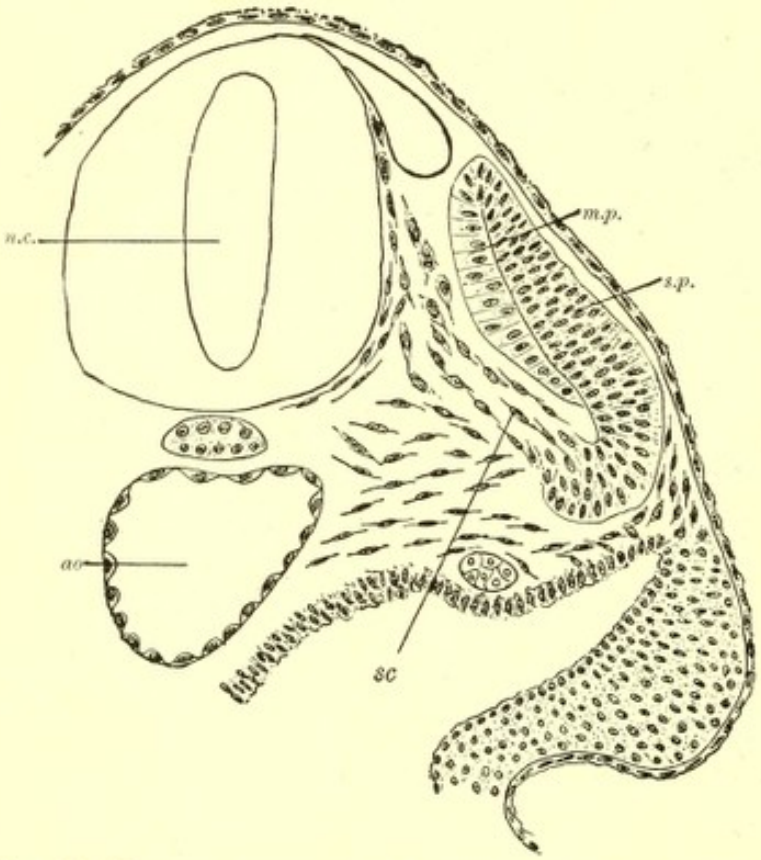



FIG. 83.—TRANSVERSE SECTION OF A HUMAN EMBRYO OF THE THIRD WEEK TO SHOW DIFFERENTIATION OF MESODERMIC SEGMENT. (Kollmann.)

*n.c.*, neural canal; *ao*, aorta; *m.p.*, muscle-plate; *s.p.*, skin-plate; *sc*, sclerotome.

The mesenchyme occupies everywhere the intervals between the epithelial layers, and forms a complex on quite a different morphological plane from them.

Originally introduced by O. and R. Hertwig,[1] the term 'mesenchyme' has lost its more strict significance. It is now known to arise from several sites, and though in general a derivative of the mesoderm, it is said to arise in some cases directly from the entoderm. The circular band of 'mesoblast,' for instance, described (after Hubrecht) in the section on the early formation of the middle layer (footnote, p. 34) as arising from the entoderm in Tarsius and concerned in the formation of the blood-vessels is a case in point. Further, some authors (Kastchenko, Goronowitsch, Sewertzoff, Klaatsch, Julia Platt, Lundborg, Koltzoff) have described tracts of connective tissue arising from the ectoderm. But this has not gone uncontradicted; and in general it seems proper to hold that the mesenchyme is essentially and primarily of mesodermic origin; although, included in the complex, and indistinguishable in their undifferentiated state from the cells derived from this source, there are possibly other portions of different parentage. Thus among the cells of mesodermic origin many authors have described cells which they believe come from the ectoderm or entoderm. Maurer, for

[1] Die Cölomtheorie, Jena, 1881; and Studien z. Blättertheorie, 1883.

instance, and others are of opinion that the leucocytes found in the wall of the gut are derived from the entodermic epithelium; while, again, there is some reason to believe that ectoderm-cells may wander from the neural crest, and even from the neural canal along the primitive ventral nerve-roots, and spread to quite distant parts within the mesoderm.

In connexion with the first appearance of individual cells between the layers, it may here be mentioned that, according to the observations of Szily,[1] the epithelia are all connected together by protoplasmic threads which are spun out as they draw apart in the course of development. The spaces between the epithelial layers are not vacant, as they appear to be in sections treated by ordinary methods, but are occupied by a delicate protoplasmic reticulum, which forms a basis on which the wandering mesenchyme-cells arrange themselves into a syncytium.

The **blood** and **blood-vessels** first appear in the wall of the yolk-sac. In the lower mammals a vascular area is developed (fig. 85), as in the Sauropsida,

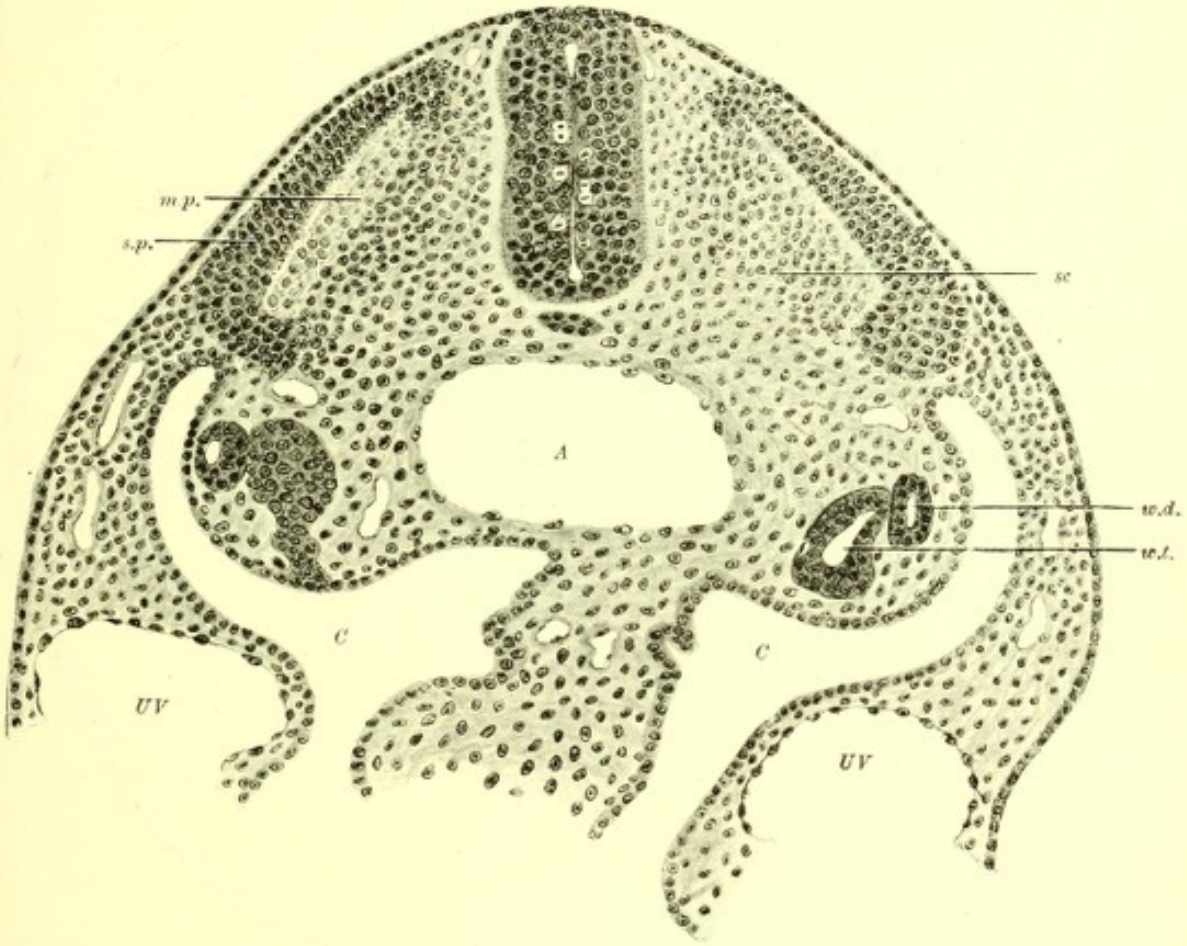



FIG. 84.—TRANSVERSE SECTION THROUGH THE TRUNK OF A RABBIT EMBRYO OF THE ELEVENTH DAY. (T. H. Bryce.)

*m.p.*, muscle-plate; *s.p.*, skin-plate; *sc*, sclerotome; *w.d.*, Wolffian duct; *w.t.*, Wolffian tubule. The ridge in which the duct and tubule lie is the Wolffian ridge. To the left the section has cut the wall of a Woffian tubule where it is connected by a cellular strand with the cœlomic epithelium. *A*, aorta; *C*, cœlom; *UV*, *UV*, umbilical veins.

but in the Primates the earliest vessels appear on the under aspect of the sac (fig. 79) and gradually extend over its upper pole, until the whole sphere is covered by a vascular network. Further, in Primates there is no terminal sinus. These are regarded as secondary modifications due to the small size of the yolk-sac.

The first indication of blood and blood-vessels is the appearance of irregular projections on the surface of the vesicle due to the formation of the *blood-islands of Pander* between the entoderm and mesoderm. The blood-islands are groups of rounded nucleated corpuscles closely packed together: indeed the cell outlines are

[1] Anat. Anzeiger, xxiv. 1903.

not clearly distinguishable. The peripheral layer of cells becomes the endothelium of the vessel-wall, while the central mass is resolved into the primitive nucleated blood-corpuscles. The islands are united together by cellular processes which, becoming hollow, produce a continuous network of vessels.

From the third week onwards until the liver is developed, it appears from the descriptions of Graf v. Spee that the wall of the yolk-sac becomes converted into a tissue resembling liver-tissue in its simplest form. Saccular dilatations of the entodermic lining of the vesicle are produced, and from the walls of these dilatations solid masses of cells are budded off. Among

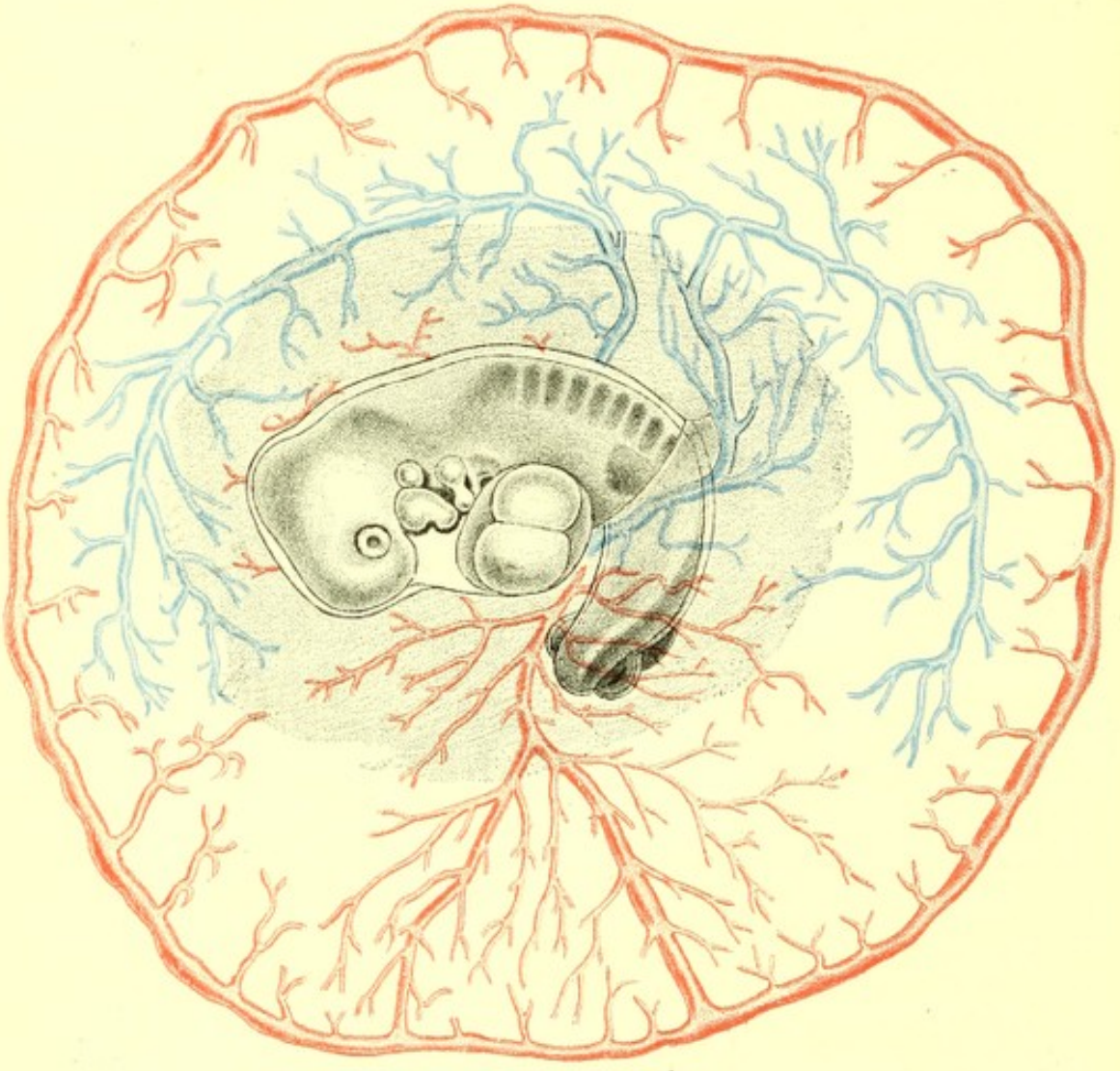


FIG. 85.—VASCULAR AREA OF THE RABBIT OF ELEVEN DAYS. (v. Beneden and Julin.)

The arteries are represented red, the veins blue; the capillaries are not shown. The terminal sinus is seen to be arterial.

the cells are seen 'giant' elements, derived possibly from the epithelial cells, and within these are smaller cells closely resembling young nucleated blood-corpuscles.

Once formed, the blood-vessels on the yolk-sac are in direct continuity with vessels which develop in the connecting stalk, and through them with the vessels of the chorion. In this respect the conditions in the Primates again differ from those prevailing in the lower mammals. Thus Selenka has shown that in *Hylobates rafflesi* the vessels on the under aspect of the yolk-sac communicate with the vessels of the chorion by a pair of vessels surrounding the allantoic tube, before there are any vessels in the embryo itself. This arrangement seems to be present in the human embryo also, for a similar vascular loop was described by Eternod in his young embryo, and named by him the *sinus ensiforme*.

**Early stages in the development of heart and embryonic vessels.**—The first embryonic blood-vessels are laid down in the splanchnopleure, and the earliest channels to appear are two short tubes on each side of the head end of the embryonic axis. These form the double rudiment of the heart.

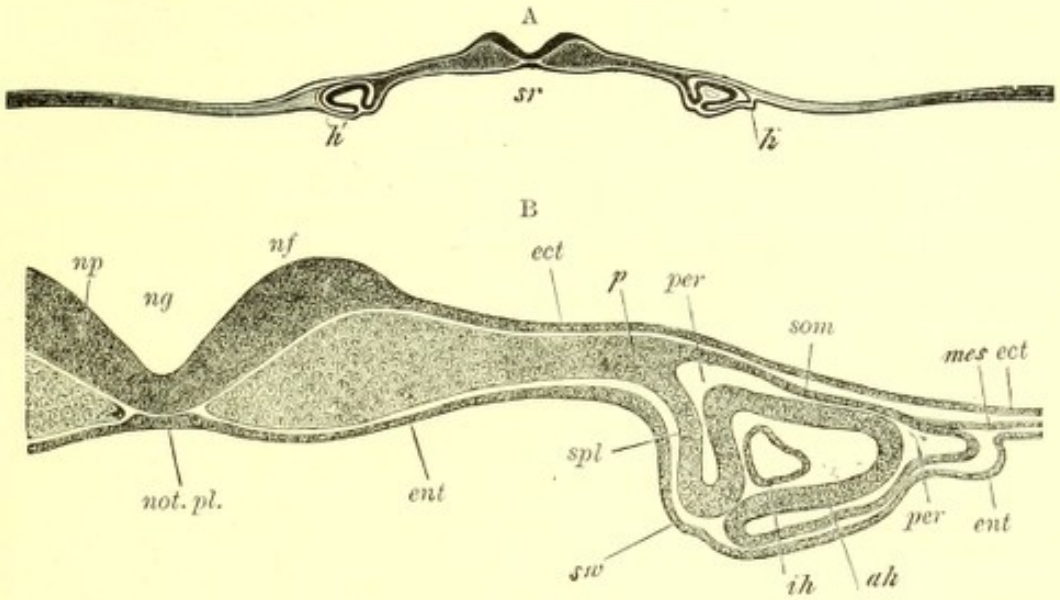



FIG. 86.—A. TRANSVERSE SECTION THROUGH THE HEAD OF AN EMBRYO RABBIT OF EIGHT DAYS AND FOURTEEN HOURS, WITH A PART OF THE PERIPHERAL BLASTODERM. $\frac{45}{1}$. (Kölliker.)

*h*, *h*, rudiments of the heart; *sr*, pharyngeal groove, with notochord-plate.

B. PART OF THE SAME MORE HIGHLY MAGNIFIED. $\frac{152}{1}$. (Kölliker.)

*n.p.*, neural plate (of hind-brain); *n.g.*, neural groove; *n.f.*, neural fold; *ect*, ectoderm; *ent*, entoderm; *mes*, mesoderm; *p*, paraxial mesoderm; *som*, somatopleure; *spl*, splanchnopleure; *per*, pericardial cœlom; *ah*, fold of splanchnopleure which will form wall of heart; *ih*, endothelial tube of heart; *sw*, wall of fore-gut; *not.pl.*, notochord-plate.

Various views are held as to the origin of the vessels in the embryo. One is that they grow into the embryo from the vascular area, by a budding of the endothelial walls of the vessels first laid down there (His); another, that the whole closed vascular system is produced by extension of two primary endothelial sacs, the heart-tubes (Rabl); a third, that they arise *in situ*. The third theory is on the whole most consonant with the appearances seen in mammalian

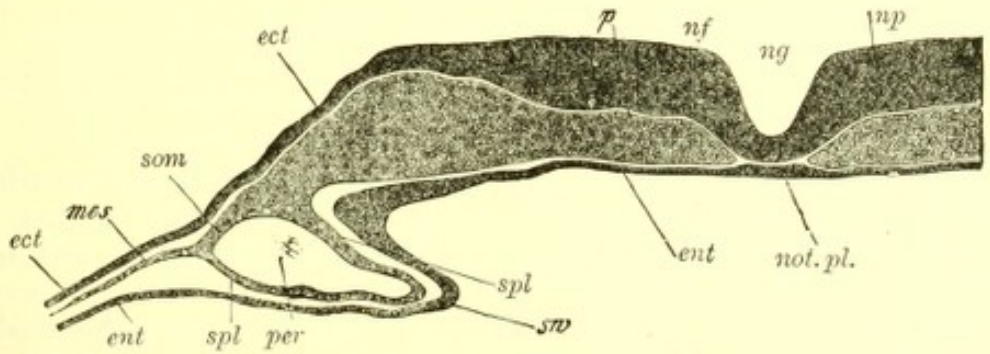



FIG. 87.—SECTION FROM THE SAME EMBRYO FARTHER FORWARD THAN THAT SHOWN IN THE PRECEDING FIGURE. (Kölliker.)

Lettering as in fig. 86.

embryos, but varying accounts are given of the actual mode of origin of the channels and the source of the vaso-formative cells. According to one interpretation, the channels are spaces in the mesenchyme which become converted into vessels by the transformation of the surrounding cells into an endothelium; and these spaces have been looked on hypothetically as the remains

of the interval between the germ-layers (Ziegler). According to another account, the vessels appear first as cords or strings of cells which arrange themselves round a lumen, and form the endothelium of the vessel wall (Rückert). The vessels in terms of both these interpretations are intercellular spaces; but according to still other observers, the extension of the channels is brought about by the formation of spaces within the vaso-formative cells, which are converted into vessels by being linked up together.

The vaso-formative cells are most generally regarded as mesodermic in origin; but they are considered by some as being derived independently from the entoderm, forming thus an entodermic, as distinguished from the mesodermic mesenchyme.

In Tarsius, it will be recollected, a ring-shaped thickening of the entoderm was mentioned as giving rise to a band of middle-layer cells related to the formation of the vessels. According to Hubrecht's account, therefore, the vascular mesenchyme arises direct from the entoderm. It may be noted that the disposition of the ring closely corresponds with the primitive vessels of the early human embryo as described by Eternod.

In the absence of detail for the early phases of the primate heart, the stages in the rabbit-embryo may be taken as a type for the development of the parts.

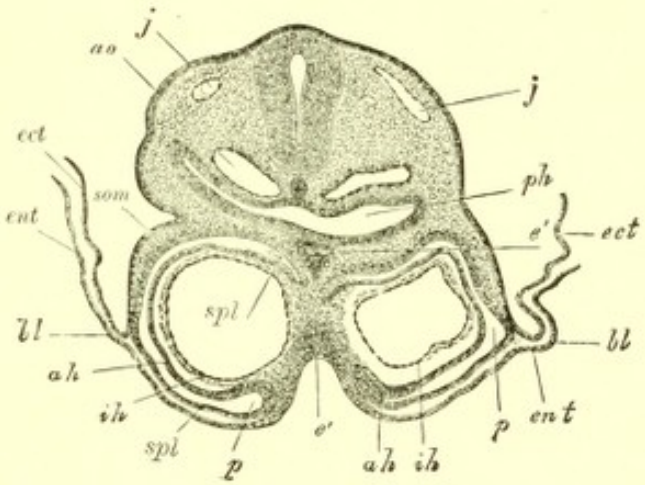



FIG. 88.—TRANSVERSE SECTION THROUGH THE REGION OF THE HEART IN A RABBIT EMBRYO OF NINE DAYS, SHOWING THE COMMENCING FUSION OF THE TWO TUBES. $\frac{80}{1}$. (Kölliker.)

*j*, *j*, jugular veins; *ao*, aortæ; *ph*, pharynx; *som*, somatopleure of body-wall; *bl*, bilaminar portion of blastoderm forming pro-amnion; *ect*, *ent*, its two layers (ectoderm and entoderm); *p*, pericardium; *spl*, splanchnopleure; *ah*, outer wall of heart; *ih*, endothelial lining of heart; *e'*, septum between the two heart-tubes.

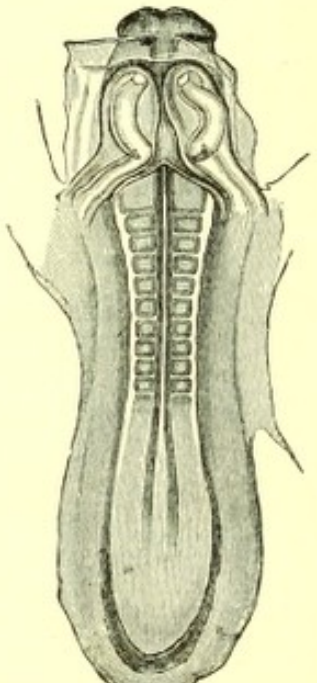


FIG. 89.—EMBRYO RABBIT OF EIGHT DAYS AND EIGHTEEN HOURS, WITH NINE PROTOVERTEBRÆ; VENTRAL ASPECT. $\frac{25}{1}$. (Kölliker.)

The heart is still a double tube.

At an early period, before the splanchnopleuric folds have begun to fold in to form the fore-gut, it will be seen (fig. 86) that the pericardial portion of the cœlom is occupied by a fold of the splanchnic mesoderm. This fold becomes subsequently closed-in to form the muscular wall of the heart. It encloses a second tube composed of flattened cells, which becomes the endothelial lining of the heart. Authorities differ as to the origin of these cells, some deriving them from the mesoderm, while others trace them direct from the entoderm, either in the form of an evagination or as a solid cord of cells. When the splanchnopleuric folds bend in to form the floor of the fore-gut, the two tubes are brought together (fig. 88) below the pharynx. They at first lie side by side, but soon fuse into a single median tube by the absorption of the dividing septum. The heart-tube remains attached to the gut by a mesentery, the *mesocardium posterius* (fig. 90).

In the earliest stage described for the human embryo (thirteenth day) the heart-tubes are still separate from one another. We owe to Eternod [1] a description, arrived at by reconstruction from sections, of the vessels of an embryo of the thirteenth day, when the channels are still in the course of formation in the mesenchyme. The heart-tubes are simply dilated portions of a continuous sinus-like vessel which surrounds the mouth of the yolk-sac and ends in a common stem in the abdominal stalk, which is in turn distributed to the chorion (fig. 91). The two tubes are united for a short distance under the fore-gut into a single vessel, which is the rudiment of the aortic bulb. From this two vessels sweep back on each side of the notochord, which is still in the stage of the notochordal plate: these are the primitive aortæ, and the loops between the ventral bulb and the dorsal aorta are the first or primitive aortic arches.[2] Behind, the aortæ, sweeping past the neurenteric canal, bend round the caudal end of the embryonic axis into the abdominal stalk, and pass in this to the chorion. Where the abdominal stalk becomes continuous with the yolk-sac the sinus-like vessel is joined by a vascular loop from the back and under side of the yolk-sac (sinus ensiforme), but the vitelline veins proper, which afterwards convey the blood from the vitelline circulation to the heart, have not yet been laid down.

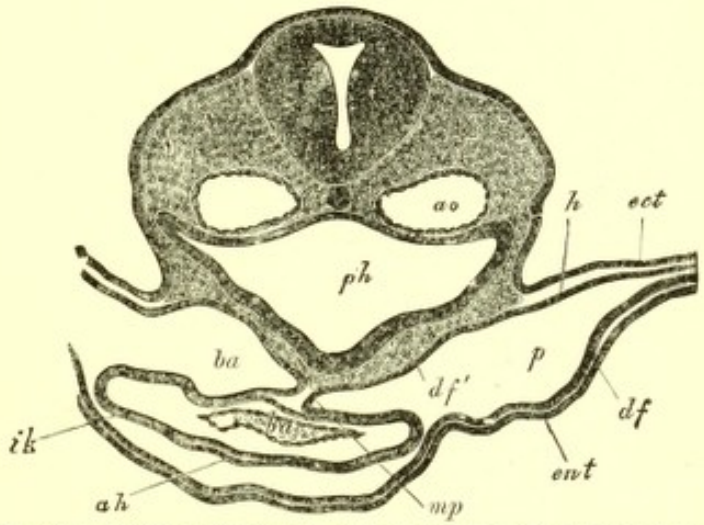



FIG. 90.—SECTION THROUGH THE REGION OF THE HEART IN A RABBIT EMBRYO OF TEN DAYS, AFTER THE TWO TUBES HAVE UNITED INTO A SINGLE MEDIAN ORGAN. (Kölliker.)

*ao*, descending aortæ; *ba*, bulbus aortæ; *ah*, its external wall; *ik*, its endothelial lining; *mp*, mesocardium posterius, uniting the heart to the ventral wall of the pharynx, *ph*, and here separating the pleuropericardial cœlom, *p*, into two halves, which are, however, united on the ventral side of the heart; *ent*, entoderm of yolk-sac; *df*, its mesoderm; *df'*, mesoderm of pharynx; *h*, mesoderm of somatopleure; *ect*, ectoderm.

It would thus seem that there is a circulation set up between embryo and chorion at a very early stage, before even the yolk circulation is established. This is to be correlated with the vestigial condition of the yolk-sac, and is another instance of the remarkable series of variations from the ordinary type which the development of the primate embryo exhibits.

In the next stage of which we have complete detail, a human embryo of fifteen days (His' embryo Lg., fig. 92), and for the lower Primates an embryo of *Cercocebus cynomolgus* described by Selenka, the yolk circulation is fully established, and the course of the vessels has become so modified as to conform to the condition described for the lower mammals with a large yolk-sac and a vascular area.

The heart is now a single tube, and shows a subdivision into an auricular, a ventricular, and a bulbar part. It receives three veins on each side, which join a transverse vessel placed in the septum transversum, named the *sinus venosus*.

The three pairs of veins are the *vitelline*, running in the splanchnopleure from the yolk-sac; the *allantoic*, running in the edges of the somatopleure and

[1] Anat. Anzeiger, xv. 1899.

[2] It may be mentioned that even at this very early stage, according to Eternod's descriptions, there are indications of the rudiments of two, perhaps three, connecting vessels on each side representing future aortic arches.

connected behind with the common stem of the earlier stage in the body-stalk, and bringing blood from the chorion; and the *ducts of Cuvier*, formed by the junction of two veins from the body of the embryo (*anterior* and *posterior cardinal*). The ducts of Cuvier and allantoic veins effect a junction before they reach the sinus venosus.

The aortic bulb passes into two ventral vessels, which join with the dorsal aortæ by two arches. The dorsal aortæ in turn sweep back on each side of the

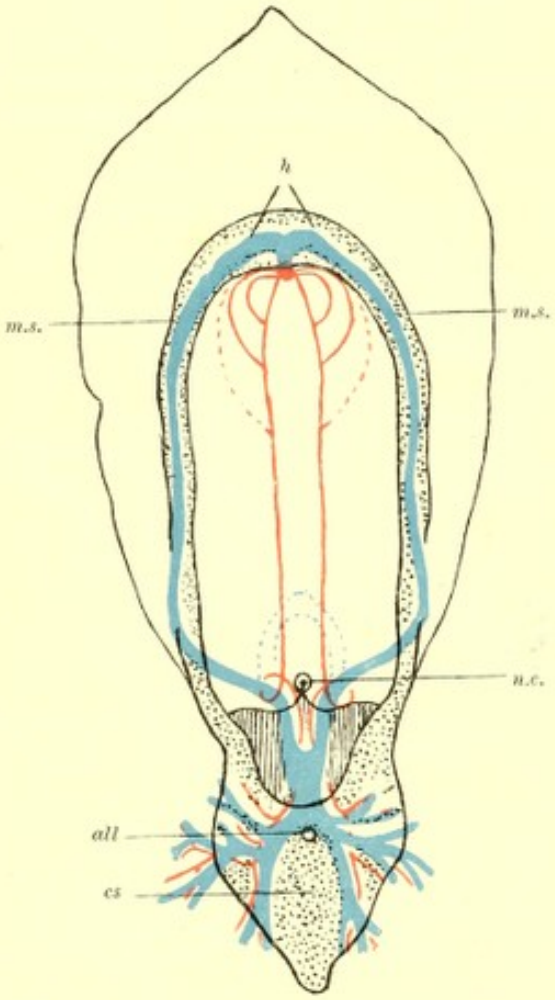



Fig. 91.—Diagram of the vascular channels in a human embryo of the second week. (After Eternod.)

The position of the vessels will be understood if the diagram be compared with the surface view of the blastoderm at this stage given in fig. 72 (p. 49). The afferent channels (including the two heart-tubes) are coloured blue; the efferent (aortæ) red. *m.s.*, *m.s.*, marginal sinus (primitive umbilical veins: the anterior dilated portions of the veins are the primitive heart-tubes, *h*); *cs*, section of abdominal stalk enclosing *all*, allantoic diverticulum, a single venous, and two arterial channels; *n.c.*, neurenteric canal. The dotted blue lines indicate the position on the back of the yolk-sac, and therefore not seen from this view, of the sinus ensiforme.

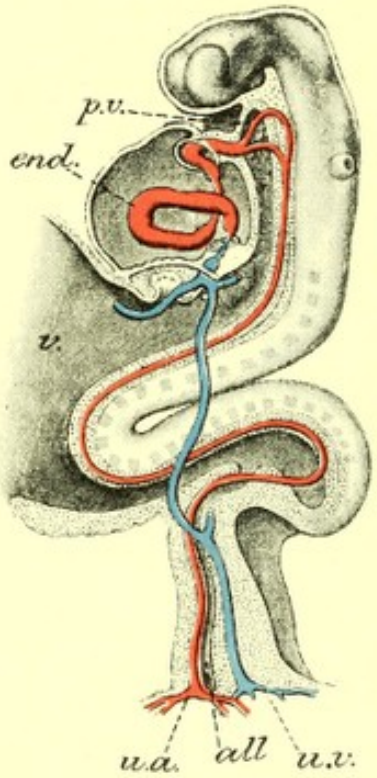



Fig. 92.—Profile view of a human embryo of about fifteen days, with the alimentary canal in longitudinal section. (His.)

*p.v.*, primitive velum; *end*, endothelial tube of heart; *v*, yolk-sac; *u.a.*, umbilical (allantoic) artery; *u.v.*, umbilical vein; *all*, allantoic diverticulum.

notochord, giving branches (vitelline arteries) to the yolk-sac; they terminate by bending round the tail end of the embryo into the body-stalk, within which they are carried to the chorion.

The further changes in the heart and vessels will be treated of in the second part of this volume. It will suffice, at this stage, to have shown that in Primates the embryonic vessels are connected from the earliest period with the chorion, and that by the end of the second week the circulation between that membrane and the embryo is fully established.

## DEVELOPMENT OF THE FŒTAL MEMBRANES AND PLACENTA; IMBEDDING OF THE OVUM.

Having determined the manner in which the principal organs of the body make their appearance, we must now study in somewhat greater detail than we have yet done the history of the chorion and amnion, in order to ascertain how the *placenta*, or organ which nourishes the fœtus, and the *membranes* which protect it during its sojourn in the uterus, are developed. It will be necessary, however, first to describe how the ovum is imbedded in the uterine mucous membrane, and the changes that take place in that membrane during pregnancy.

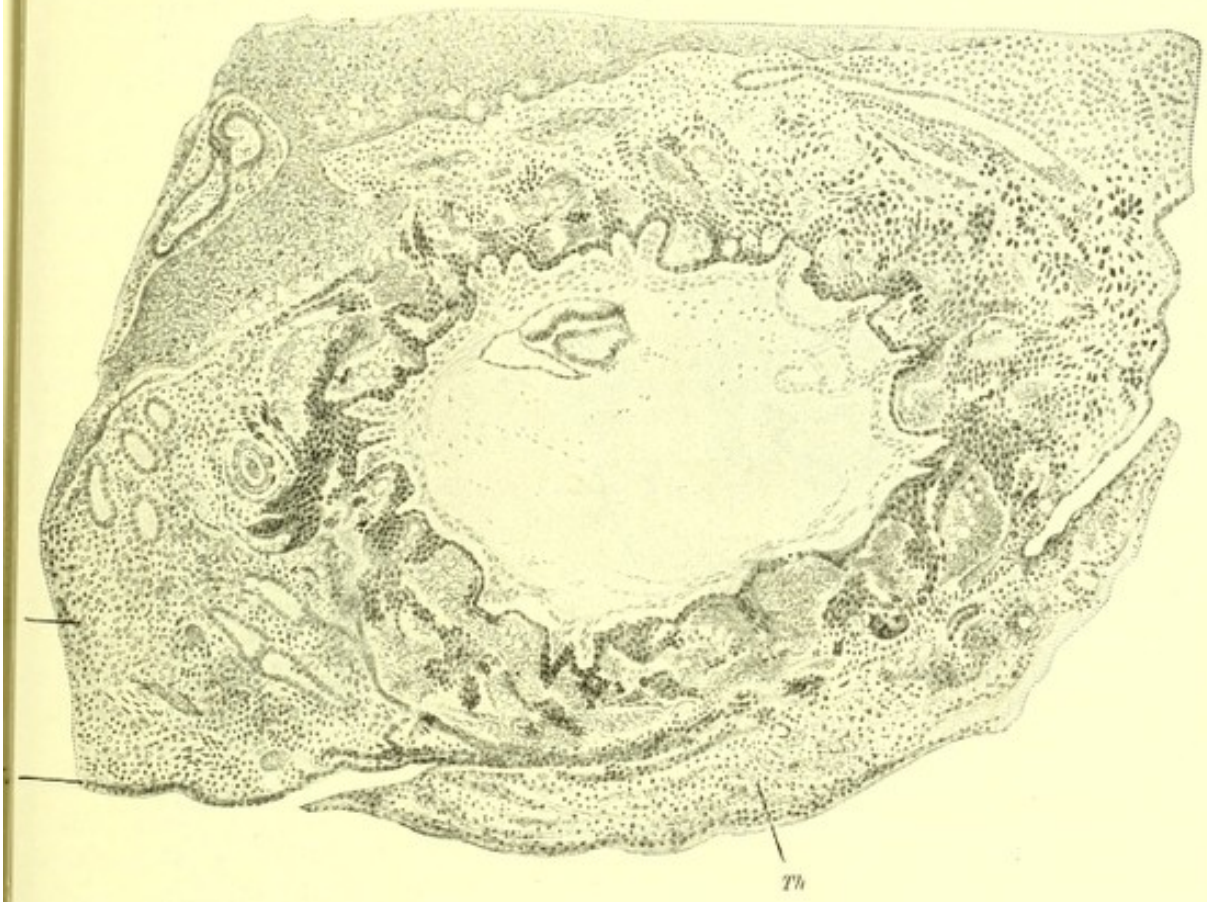



FIG. 93.—SECTION THROUGH AN OVUM OF THE FIRST WEEK.
(Reduced from Peters; from Hertwig's Handbuch.)

The section passes through the embryonic rudiment. *Th*, thrombus closing an opening on the surface of the uterine epithelium, *U.E.*; *D*, decidua. The very irregular strands of trophoblast are distinguished by their darker tint.

**Imbedding of the ovum.**—The earliest known human ova are already completely imbedded in the uterine mucous membrane. The site of implantation in man is normally the posterior wall of the uterus near the fundus. Peters' and Leopold's ova lay in this position; their situation was not marked by any projection of the mucous membrane beyond the general level of the swollen surface. The blastocyst in Peters' case (fig. 93) was oval in shape. The wall was relatively thick and already intimately related to the mucous membrane (*decidua*). Over the ovum there was an area, one millimetre in diameter, where the uterine epithelium was absent, and here there was a soft thrombus (*Th*), which had a narrow stalk occupying the hole in the epithelium, and a broad head spreading out like a mushroom over the edges of the opening. The uterine glands in the neighbourhood of the blastocyst took a somewhat concentric course round

it, as if pushed aside by the growing ovum, and there was absolutely no indication that any gland-mouths opened into the cavity in the mucous membrane, nor were there any traces of uterine epithelium lining it. These facts, which have been recently confirmed in the ovum described by Leopold, clearly indicate that the ovum is at a very early stage cut off from the general cavity of the uterus,

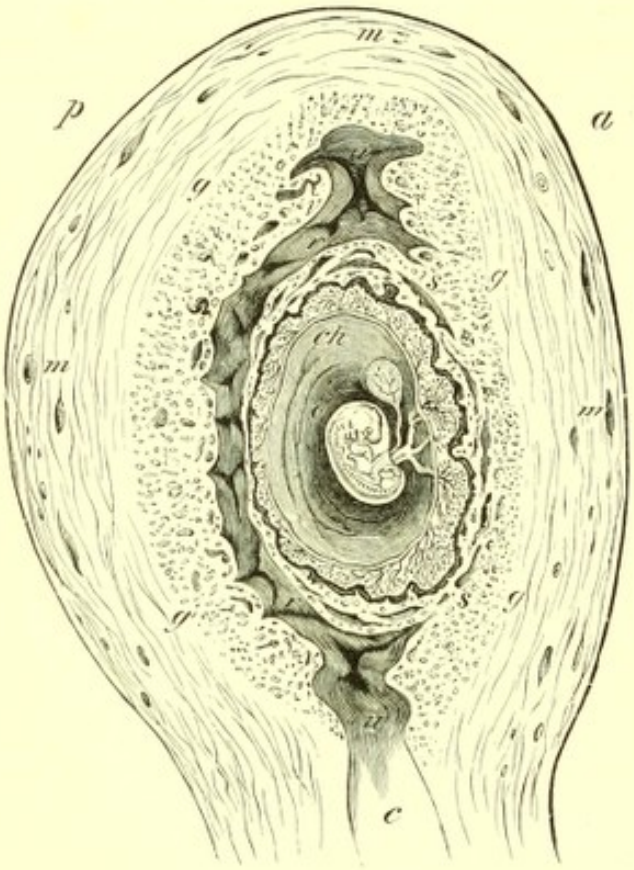



FIG. 94.—ANTERO-POSTERIOR SECTION OF THE GRAVID UTERUS AND OVUM OF FIVE WEEKS: DIAGRAMMATIC. (Allen Thomson.)

*a*, anterior, *p*, posterior uterine wall; *m*, muscular substance; *u*, placed in the cavity of the uterus; *g*, the glandular layer of the decidua vera; *r*, the decidua capsularis; *s*, decidua basalis; *c*, cervix uteri; *ch*, chorion with its villi, which are more highly developed on the placental side; *e*, the embryo enclosed in the amnion, with the allantoic vessels passing along a short allantoic stalk into the placenta, and the umbilical vesicle lying free in the space between amnion and chorion.

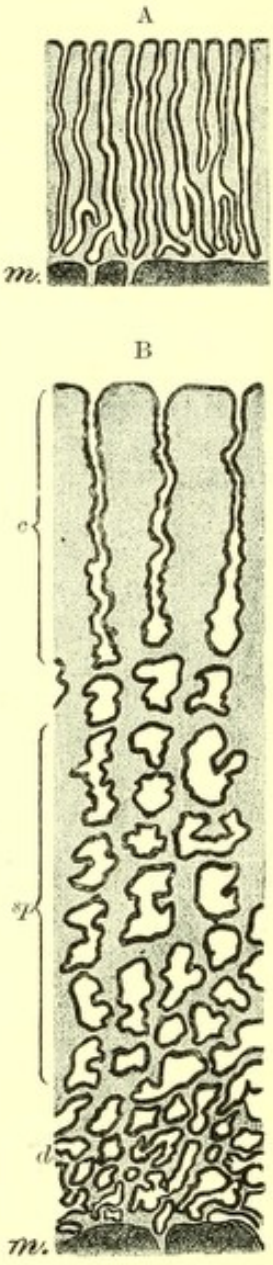



FIG. 95.—DIAGRAMMATIC SECTIONS OF THE UTERINE MUCOUS MEMBRANE, SHOWING THE CHANGES WHICH THE GLANDS UNDERGO WITH THE SUPERVENTION OF PREGNANCY. (From Kundrat and Engelmann.)

A. Diagram of the glands of the non-pregnant uterus; *m*, muscular layer. B. Condition of the glands at the beginning of pregnancy; *c*, compact layer near free surface of decidua; the glands are here somewhat enlarged but not very tortuous, and the mucous membrane is rendered compact by hypertrophy of the interglandular tissue; *sp*, spongy layer, containing the middle portion of the glands greatly enlarged and tortuous, producing a spongy condition in the mucous membrane; *d*, deepest portion of the glands, elongated and tortuous, but not much enlarged.

not, however, as used to be supposed, by an upgrowth round it of the mucous membrane, but in some different fashion. For a parallel we must look to those cases among the lower mammals in which the blastocyst remains very small, and becomes very early surrounded by decidual tissue. Such cases occur among the *Insectivora*—*e.g.* the hedgehog—and also among the *Cheiroptera*; but the nearest

analogy is to be found in those mammals in which there is so-called 'inversion of the germinal layers,' the *Muridæ* (mice and rats) and *Cavia* (guinea-pig) among the rodents. In some way the early nesting of the ovum in the decidua is related to the inversion of the layers, and both phenomena are probably to be correlated with the very minute size of the blastocyst.

The idea that the imbedding occurs by 'circumvallation' being given up, there remain two possibilities—either (*a*) that the minute ovum is received into a crypt of the mucous membrane, or (*b*) that it, in virtue of a biochemical action of the trophoblastic ectoderm, absorbs the epithelium, and eats its way into the connective tissue of the mucous membrane. If the first alternative be adopted, we must conceive the process to take place as it does in the mouse.[1] In this animal the small blastocyst is received into a recess of the uterine cavity. The epithelium lining this cavity becomes flattened and then disappears, so that the trophoblast and decidua become closely related. The ectoplacenta blocks the aperture between the decidual cavity and the lumen of the uterus, and the cavity later becomes obliterated at the site of implantation, by the disappearance of its epithelium and fusion of the exposed decidual walls. The gland-tubes disappear as the mucous membrane becomes converted into decidua, and new capillaries are freely produced, especially in the neighbourhood of the ectoplacenta, where the maternal part of the placenta is formed.[2]

If the second alternative be adopted, then we have to conceive the process as described by Graf v. Spee[3] for the guinea-pig. In that case the ovum reaches the uterus in the morula or early blastocyst stage, and destroys the epithelium at the point of contact with it. It becomes imbedded by a process of degeneration of the connective tissue, which ultimately forms a sort of granulation-tissue capsule around it.

The evidence afforded by Peters', Leopold's, and other early ova is strongly in favour of the view that the ovum actually absorbs the uterine tissue before it, and therefore becomes implanted by the absorptive activities of its ectodermic covering. In either case, at a very early stage the blastocyst lies surrounded on all sides by mucous membrane without any trace of an epithelial layer.

**Changes in the uterus during pregnancy.**—The mucous membrane of the pregnant uterus is known as the *decidua*. For convenience of description, the parts of the mucous membrane immediately enclosing the ovum, and that lining the general cavity of the uterus, have received distinctive names. Thus the layer of membrane around the ovum is known as the *decidua capsularis* (*reflexa*); the part next the uterine wall where the placenta is afterwards formed is the *decidua basalis* (*serotina*); while the membrane lining the cavity of the uterus is termed *decidua vera* (fig. 94).

With the subsequent growth and consequent expansion of the ovum the enclosing decidua capsularis expands also *pari passu*, encroaching more and more upon the cavity of the uterus and coming into contact everywhere with the decidua vera. Eventually it blends entirely with the decidua vera, so that the two layers are indistinguishable and the cavity of the uterus is obliterated (except at the cervix uteri).

The ovum is received into the uterus when the mucous membrane is in the premenstrual phase, and in the earliest pregnancies described (Peters' and Leopold's cases) the mucosa has all the characters of the menstrual decidua (fig. 96). It is

[1] See G. Burckhard, Archiv mikr. Anat. lvii.

[2] Disse (Sitzungsber. Ges. Beförd. gesammt. Naturwiss., Marburg 1905) has shown that in mice and rats there occur large giant-cells in the developing decidua, which have a phagocytic action, and excavate it for the growing ovum. See also Disse, Ergebnisse der Anat. und Entwick. xv. 1905.

[3] Zeitschr. Anat. u. Anthropol. iii.

very soft and markedly œdematous. The glands are enlarged and the blood-vessels much dilated. There is considerable effusion of blood from ruptured vessels; the blood occupying spaces in the loose connective tissue, and even the interior of gland-tubes, which show desquamation of their epithelium and breaking down of their walls.

The decidua undergoes further structural changes during the early months of pregnancy, some of these changes being common to all three parts of the membrane, whilst others are special to that part (d. basalis) which enters into the construction of the placenta. The following is a brief account of these changes.

**Decidua vera.**—With the supervention of pregnancy the mucous membrane lining the uterus becomes thickened and the tubular glands become both dilated and greatly elongated. This thickening of the membrane and enlargement of the glands goes on during the early months of pregnancy until, between the second and third months, the decidua vera reaches its maximum thickness of more than a quarter of an inch. Its glands have further undergone so considerable an elongation that they now no longer pass nearly straight through the membrane, but run in a tortuous manner from the inner surface to the vascular layer, so that a vertical

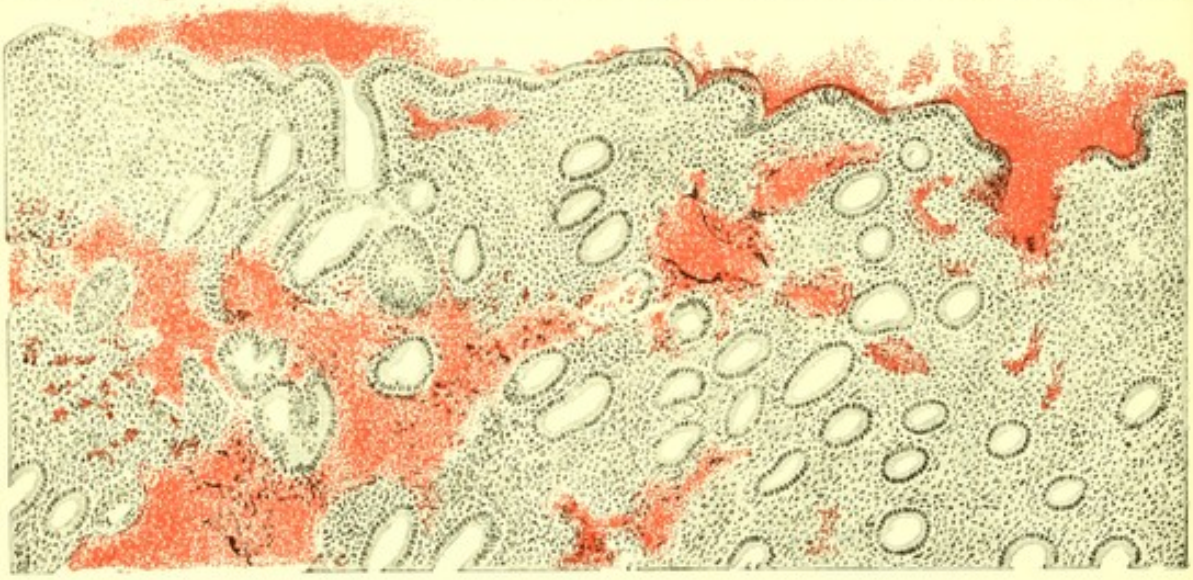


Fig. 96.—Section of uterine mucous membrane during menstruation (Sellheim).

section of the membrane exhibits them cut quite as often obliquely or transversely as longitudinally. They are also generally dilated, but the dilatation is by far most marked at the mouths of the glands, which come thus to have a funnel-like shape, and in the deeper part of the membrane, where the dilatations look in sections like a series of cavities, lined by cubical or flattened epithelium and separated from one another by a relatively small amount of interglandular substance. This gives a spongy appearance to the part in question, and it has been accordingly termed the *stratum spongiosum* of the decidua (fig. 95, *sp*). The deepest part of the glands—that, namely, which is in contact with, and is imbedded in the superficial portion of the muscular coat—does not share in this dilatation, and its epithelium also retains the columnar character. The part of each gland between the funnel-shaped mouth and the dilatations above described also becomes enlarged, but not to so great an extent, the hypertrophy of the mucous membrane being here chiefly confined to the interglandular tissue, which becomes filled with large epithelium-like cells (*decidual cells* of Friedländer) and with numerous and large capillary blood-vessels. This layer of the decidua has been termed the *stratum compactum* in contradistinction to the stratum spongiosum external to it (fig. 95, *c*).

By the sixth week degenerative changes show themselves. The glandular epithelium in the stratum spongiosum begins to be shed in places; and, soon after, the surface epithelium is thrown off, until in the fourth month all traces of it have disappeared.

After the fourth month, by which time the great increase in size of the chorionic vesicle with its contained embryo has brought the decidua capsularis into close contact with the decidua vera, the latter begins to undergo an atrophic process, the result to all appearance of the compression and distension to which it is thus subjected. Its tissue becomes thinner and less vascular, and both the funnel-shaped mouths of the glands and those parts of the glands which run through the stratum compactum become gradually obliterated, so that eventually hardly any trace remains. In the stratum spongiosum the spaces which have resulted from the dilatation of the gland-tubes lose their lining epithelium, and become flattened out conformably to the surface, so that they now appear as a layer of compressed lacunæ, separated by thin fibrous trabeculæ.

**Decidua capsularis (reflexa).**—It has already been shown that the decidua capsularis is not formed, as used to be supposed, by an upgrowth of folds round the ovum, but is originally that part of the mucous membrane in which the ovum has excavated a cavity for its lodgment. As the ovum imbeds itself in the stratum compactum alone, it follows that the decidua capsularis represents only the superficial part of the mucous membrane, and therefore has not a stratum spongiosum properly so called. Over the ovum there is at first an area in which there is little or no decidual tissue, the capsule being completed by a fibrinous lamella formed by the organisation of the blood-clot at the point of entrance. This constitutes *Reichert's scar*, which used to be considered as the point of fusion of the folds of the reflexa. The inner aspect of the capsularis is irregular; it is not covered with epithelium, nor do any gland-mouths open into the decidual cavity.

The decidua capsularis resembles at first in every essential respect that portion of the excavation which lies next the uterine wall and which becomes the decidua basalis. The inter-relations between the mucous membrane and the villi are at first similar all round the ovum. As the growing ovum expands, however, the decidua capsularis and the villi imbedded in it degenerate (fig. 97). A gradual process of atrophy supervenes until the membrane is reduced to a thin fibrinous or hyaline lamella in which all traces of glands and vessels have disappeared. By the third month the capsularis has nearly everywhere come into contact with the decidua vera so as to obliterate the cavity of the uterus. In the advanced months of pregnancy it wholly disappears, so that the chorion comes to lie directly against the decidua vera. The degenerative process at work in the membrane does not seem to be a fatty degeneration, as long held, but a coagulation necrosis.

**Decidua basalis (serotina).**—The decidua basalis is that portion of the mucous membrane which intervenes between the blastocyst and the uterine wall, opposite the original point of entrance of the ovum (fig. 93). The deeper portions of the gland-tubes proper to it become much dilated, the final result being the formation of a spongy layer, with irregular clefts flattened out conformably to the surface, and from which the epithelium has entirely disappeared. At the same time all the parts of the glands which are superficial to this layer suffer complete atrophy, the only portions which remain nearly unaltered being the deepest parts of the tubes, which are partly imbedded in the muscular coat of the uterus, and retain their epithelium. After separation of the placenta from the uterine wall at parturition, the uterine mucous membrane, with its epithelium and glands, becomes renewed from this deepest portion of the decidua basalis. The blood-capillaries become much dilated into sinus-like vessels, and the interglandular tissue becomes crowded with decidual cells, derived, as in the decidua vera, from the

connective-tissue cells by a process of enlargement, and also by multiplication of the elements. The decidua is also invaded by fœtal tissue, as will be explained later.

Before proceeding to the description of the development of the placenta, it will be convenient to consider first the later history of the amnion and chorion.

**Amnion.**—As we have seen in an earlier section, there is good reason for believing that in man, apes, and monkeys the amnion is closed from the beginning.

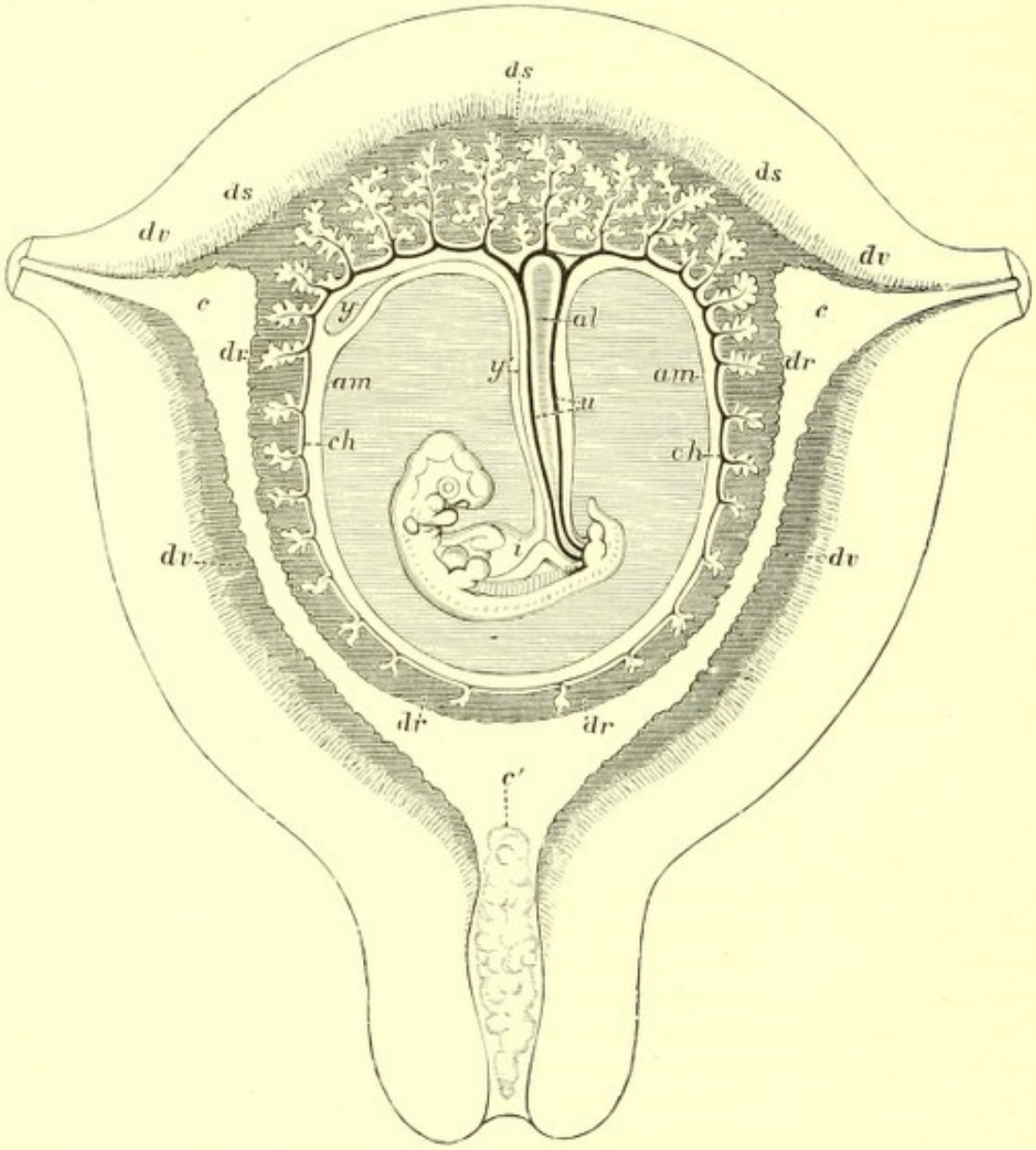



FIG. 97.—DIAGRAMMATIC SECTION OF THE PREGNANT HUMAN UTERUS AT THE SEVENTH OR EIGHTH WEEK. (Allen Thomson.)

*c*, *c*, openings of Fallopian tubes into the cavity of the uterus; *c'*, cervix, filled by a plug of mucus: the letters *c* and *c'* are placed within the original cavity of the uterus; *dv*, decidua vera; *dr*, decidua capsularis; *ds*, decidua basalis; *ch*, chorion with its villi growing into the decidua capsularis and d. serotina: in the former the villi are becoming atrophied (chorion læve); *u*, umbilical cord, the dotted lines indicate blood-vessels within it; *al*, allantois; *y*, yolk-sac (umbilical vesicle); *y'*, its stalk, passing in the umbilical cord and connected with the intestine of the embryo, *i*; *am*, amnion.

In all the earliest known normal embryos it forms a thin membrane over the embryonic shield, consisting of an inner layer of flattened ectoderm-cells and an outer layer of mesoderm. At first, as will be noticed in a later section, it closely invests the embryo, but at the beginning of the second month it is distended into a sac of considerable dimensions containing an albuminous fluid—the *liquor amnii*—in which

the embryo floats. During the second month (fig. 97) it comes to fill the cavity of the chorion, and the extra-embryonic cœlom is obliterated. As the umbilical cord elongates, the amnion forms a tubular sheath round it, enclosing the vessels, along with the allantoic and vitelline ducts, which are imbedded in mucous connective tissue. From the cord it is reflected over the surface of the placenta on to the chorion, with which it is intimately united to form what are known as the fœtal membranes. Between the amnion and chorion of the placenta lies the umbilical vesicle.

The flattened ectodermic cells of the amnion become cubical during pregnancy, and at full time the membrane consists of an epithelial layer, and a lamella of fibrous tissue. The epithelium has the form of a very regular layer of cubical

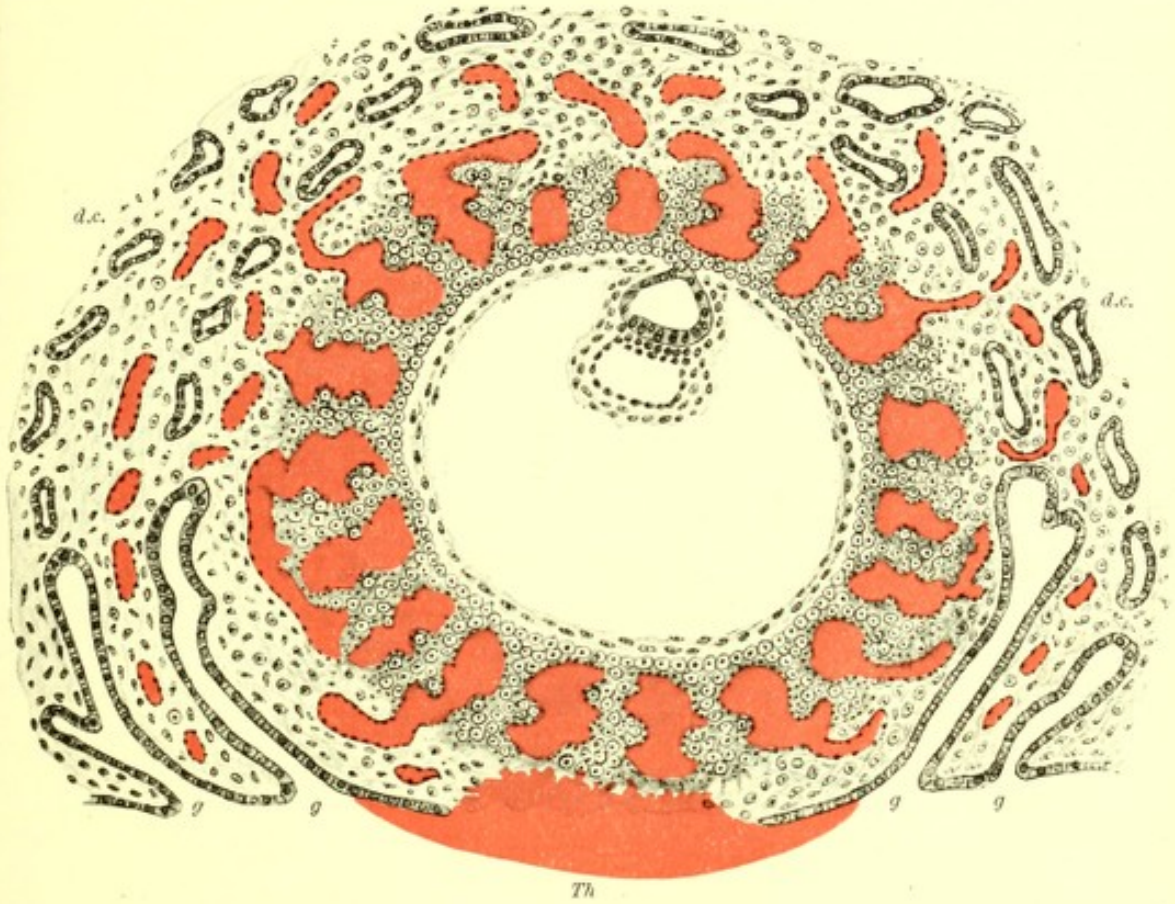



FIG. 98.—DIAGRAM OF A HUMAN OVUM AT A (HYPOTHETICAL) STAGE SOMEWHAT YOUNGER THAN PETERS' OVUM; IMBEDDED IN THE DECIDUA. (T. H. Bryce.)

*Th*, blood-clot at point of entrance; *g*, *g*, glands opening on the surface of the mucous membrane; *d.c.*, decidua capsularis. The trophoblast partly cellular, partly plasmodial, is seen invading the decidua, and opening up the dilated capillaries. The extravasated blood occupies the spaces or blood-lacunæ between the strands of trophoblast. The gland-tubules in the decidua take a concentric course round the ovum.

cells joined by distinct cell-bridges. The liquor amnii varies in amount at different periods of gestation; it is relatively most abundant about the fifth or sixth month. In the later months of pregnancy it contains urea, which is probably excreted by the kidneys of the fœtus.

**Chorion.**—We have already seen in an earlier section that the formative cell-mass, from which entoderm, as well as embryonic and amniotic ectoderm, are formed, is completely surrounded in the primate ovum by a layer of cells which has been named the *trophoblast*. In the youngest known ova the trophoblast shows a very irregular outer surface (figs. 93 and 98) consisting of cellular strands separated by spaces containing maternal blood. Round the wall of the vesicle

the mesoderm is seen sending out buds which indent the trophoblast. By the outward growth of these the epithelial strands acquire a mesodermic core, as will be afterwards more fully explained; vessels develop in the mesoderm, and the result is that the whole surface of the chorion becomes occupied by vascular projections or *villi*, enclosing fœtal vessels and bathed by the maternal blood. At first equally distributed, the villi in the region of the decidua basalis become larger, longer, and more branched, while those related to the decidua capsularis remain relatively smaller and ultimately disappear by atrophy. The part of the chorion in which the villi persist is known as the *chorion frondosum*. The remainder is termed the *chorion læve* (fig. 97). In the third month the chorion frondosum forms the fœtal part of the definitive placenta, while the chorion læve, after the disappearance of the decidua capsularis, comes in contact with the decidua vera,

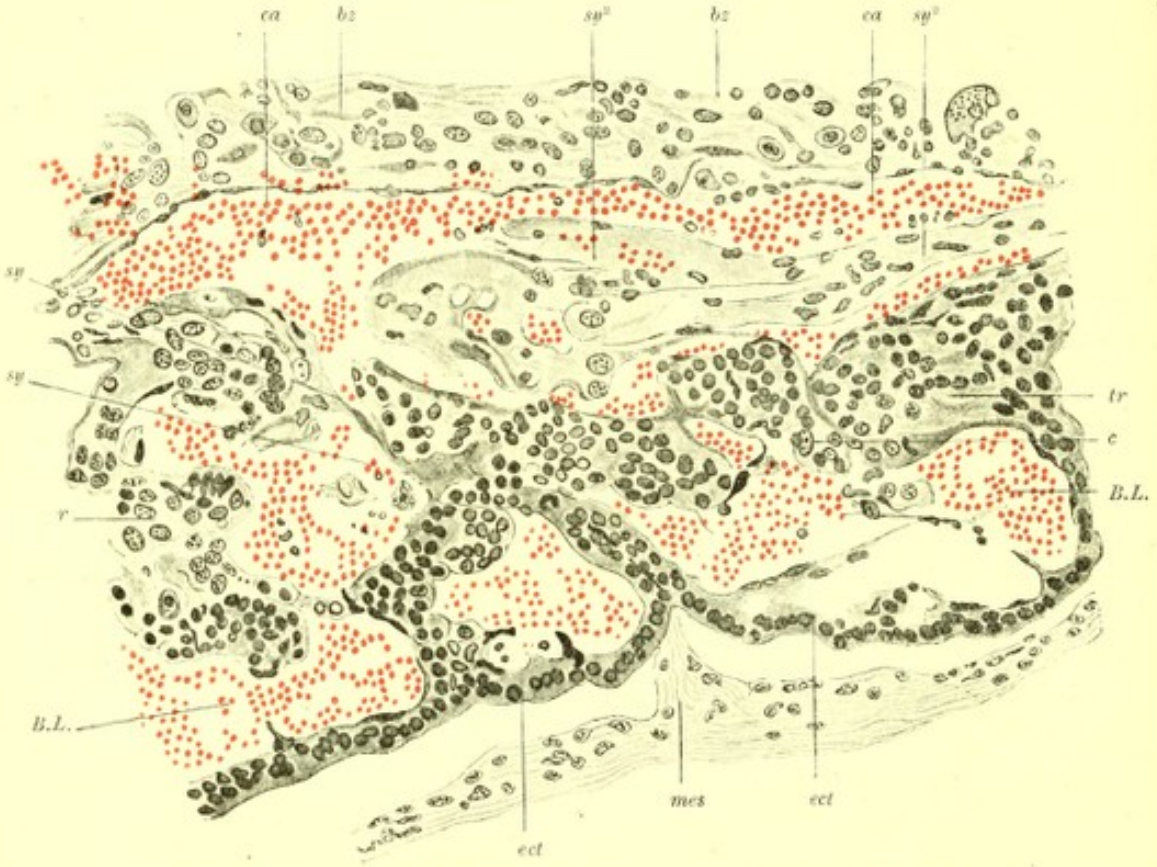



FIG. 99.—PORTION OF THE TROPHOBLAST OF PETERS' OVUM. (After Peters.)

*ect*, *ect*, chorionic ectoderm; *mes*, mesoderm budding out to form a villus core; *B.L.*, *B.L.*, blood-lacunæ lined with a thin layer of syncytium; *tr*, *tr*, cellular layer of trophoblast; *sy*, *sy*, syncytium; $sy^2$, $sy^2$, mass of syncytium invading the lumen of a maternal blood-capillary, *ca*, *ca*; *bz*, boundary-zone between trophoblast and decidua; *c*, trophoblast-cell showing alteration of nucleus.

and along with the amnion, as already stated, forms the double membrane lining the uterine cavity.

Having now sketched the history of the decidua and of the chorion, we are in a position to study in greater detail the changes which lead to the formation of the placenta.

**Placenta.**—We have to distinguish two phases of placentation in the human subject, a primary and a secondary. In the first phase, the whole chorion is covered by vascular villi, similarly related to the decidua and the maternal blood, and the placenta is therefore said to be *diffuse*. In the second stage, after the atrophy of the villi of the chorion læve, the placenta is a discoidal plate formed from one part only of the chorion (*i.e.* chorion frondosum), intimately united with the decidua basalis.

In recent years several early ova [1] imbedded in the mucous membrane have been studied by modern histological methods, and the facts elicited have considerably modified the older views as to the structure of the placenta, and the interrelations of uterine and fœtal tissues in it.

In the earliest known stage, the ovum, as already stated, lies imbedded in the stratum compactum of the mucosa. There is good reason for believing that it has eaten its way into the mucous membrane by the activities of its trophoblastic covering. In Peters' ovum (figs. 93 and 98) and the still earlier ovum of Leopold, the trophoblast is composed of irregular cellular strands attached by their outer ends to the decidua. In the interspaces between these are lacunæ filled with maternal blood. The trophoblast is bounded on the fœtal side by a fairly regular epithelial layer (fig. 99, *ect*), which is lined by mesoderm. It is indented at intervals by the processes of that layer, which become the cores of the future villi. The blood-lacunæ reach down to this inner layer. They are everywhere lined by a nucleated protoplasmic lamella in which there are no traces of cell-outlines. This is known as the *placental plasmodium* or *syncytium*. The plasmodium where it lines the blood-lacunæ is reduced to a thin endothelium-like layer, but where the decidua and trophoblast merge it spreads out into masses, which are seen invading the decidua and pushing their way into the capillaries. The stratum compactum is beginning to be crowded with decidual cells, the existing capillaries are enormously enlarged, and there is evidence of the formation of new blood-channels. Immediately round the ovum there is a zone in which the decidual changes are taking place more actively; it contains many large decidual cells, leucocytes and extravasated red blood-corpuscles, besides multinucleated elements of which it is difficult to affirm whether they are fœtal or maternal derivatives (fig. 99). Some certainly, probably all, are of trophoblastic origin. In this zone the capillaries are dilated and sinus-like, and open directly into the blood-lacunæ. Masses of syncytium are seen in the interior of capillaries, and many sections show capillaries which are lined on the decidual side by endothelium, and on the side of the ovum by syncytium (fig. 99, *syˀ*). That the vessels are being opened up, and the endothelium destroyed by the trophoblast, is clearly indicated by these appearances, as well as by the occurrence of masses of broken-down endothelial cells.

We do not know by direct observation how this stage is reached in the case of the human ovum, but recent work on the comparative histology of the placenta leaves no room for reasonable doubt on the main point—viz. that cellular strands, syncytial masses, and syncytial lining of the blood-lacunæ are all equally derivatives of the chorionic ectoderm.

**Origin of the placental syncytium.**—The view here adopted that the syncytium is merely the surface-layer of the chorionic epithelium is now very generally accepted, but there are some other interpretations of the appearances which may be briefly alluded to.

1. It has been derived by some from the maternal epithelium either of the surface or of the glands of the mucosa. If the newer views as to the imbedding of the ovum be correct, such a derivation is very improbable; but it is finally excluded by the fact that the villi of a chorionic vesicle, which has become imbedded in the ovary owing to fertilisation of the ovum having occurred while it was yet in the Graafian follicle, are provided with a well developed plasmodial layer. Fig. 100 is a drawing of a villus branch from such a case, and if compared with fig. 104, p. 76, which is a drawing of a villus from an early uterine pregnancy, it will be seen that the mesodermic core is covered, in both, by identical layers cellular and syncytial.[2]

[1] See H. Peters, Ueber die Einbettung des menschlichen Eies, &c. Deuticke, Leipzig und Wien, 1899; Siegenbeck van Heukelom, Arch. f. Anat. 1898; Marchand, Arch. Gynäkol. 1904: Anat. Anzeiger (Ergänzungsheft), xxi.: Anat. Hefte, H. 67, xxi.; Rossi Doria, Arch. Gynäkol. lxxvi.; Beneke, Deut. med. Wochenschr. Jahrg. xxx. 1904: Monatschr. f. Geburtsh. u. Gynäkol. xix.; Graf v. Spee, Verhandl. deutsch. Ges. Gynäkol. xi. 1905; Leopold, Arbeit. a. d. k. Frauenklinik, Dresden, iv.; H. Happe, Anat. Hefte, xxxii.; Keibel, Anat. Anz. (Ergänzungsheft), xxx. 1907; Frassi, Arch. f. mikr. Anat. lxx. 1907.

[2] Ovarian pregnancies are very rare. I am indebted to Dr. Munro Kerr for the opportunity of examining the sections (prepared by Dr. J. H. Teacher) of an ovary, fixed immediately after removal

2. The outer covering of the villi has been regarded as derived from the decidual tissue, or from the endothelium of the maternal capillaries. The idea is that there occurs a blending or interlocking of fœtal (chorionic) and maternal (decidual) tissue, so that the villi become clothed with a layer of decidual tissue (subchorionic membrane, Turner), or that the endothelium of the dilated capillaries persists as the lining of the blood-spaces (Waldeyer). Such an interpretation is difficult to disprove directly, but it is inconsistent with the newer views regarding the nature and the activities of the trophoblast. Recent research has provided nearly conclusive evidence for the simpler reading of the facts, advanced more especially by Hubrecht and Van Beneden for lower mammals, and for the human subject by Peters, Leopold, Minot, Webster, Hart and Gulland, and others, in terms of which the whole placenta, except a thin layer of decidua on its uterine surface, is derived from the chorion—that, in short, it is a great sponge-like mass of fœtal tissue filled with maternal blood.

If we proceed, then, upon the assumption that the cellular strands (*cytoblast*, Van Beneden) and the syncytium (*plasmodiblast*, Van Beneden) are both derivatives

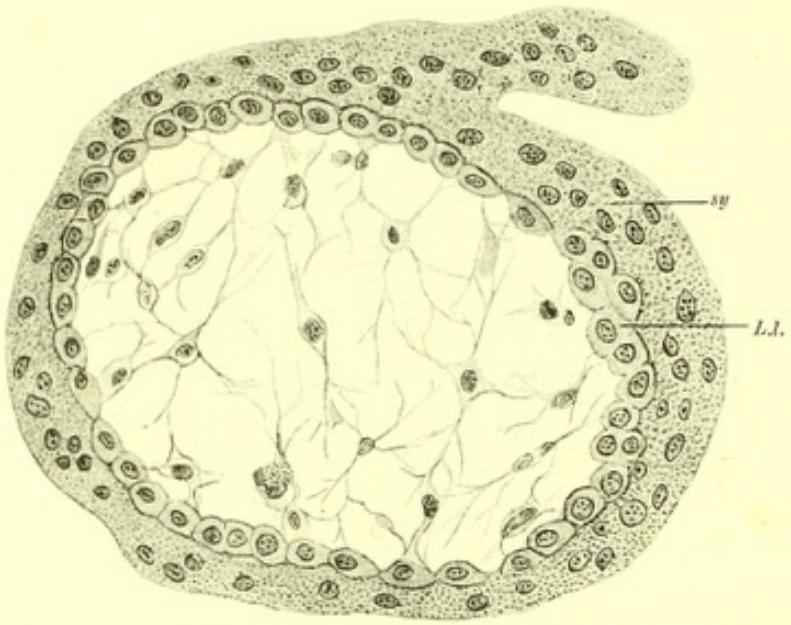



Fig. 100.—Section of a villus from a case of ovarian pregnancy. (T. H. Bryce.)
*sy*, syncytium; *L.l.*, Langhans' layer.

of the chorionic epithelium, the appearances described in Peters' and Leopold's ova may be explained as follows: At a very early stage, before there is any differentiation of the embryonic ectoderm, the trophoblast proliferates actively, and its surface becomes irregular by the outgrowth of epithelial buds. As these extend into the decidua the maternal tissue is absorbed before them.[2] The capillaries are opened up by the destruction of their endothelial walls, and the maternal blood is thus extravasated into the spaces between the strands of the trophoblast. These spaces now necessarily form a system of intercommunicating blood-lacunæ (fig. 98).

by operation, in which a blastocyst lay imbedded partly in the ovarian stroma and partly in a mass of fibrin and extravasated blood. The evidence of the sections is conclusive in favour of the fœtal origin of both cellular and syncytial layers.—T. H. B.

[1] The trophoblast-cells are supposed to act like phagocytes, and the maternal tissue to serve as pabulum for the growing ovum. It was on account of the assumed physiological activity of the chorionic epithelium that Hubrecht gave it the name of 'trophoblast'—*i.e.* 'trophic epiblast.' Here, and elsewhere in this work, the term 'trophoblast' is used in Hubrecht's original sense, to signify that part of the ectoderm which does not share in the formation of the embryo, but constitutes the wall of the blastocyst. Minot has introduced the word *trophoderm* for the proliferated chorionic ectoderm, or mantle, which is concerned in the implantation of the egg. The term is not used in this work, because trophoblast has the priority, and also because in some particulars the processes involved are here interpreted rather differently than by Minot (Trans. Amer. Gynec. Soc. 1904).

The chorionic epithelium, whether by reason of its active proliferation or otherwise, becomes, in its superficial lamella, converted into a continuous plasmodial mass, while the cells in the central portions of the epithelial strands remain isolated from one another by distinct cell-boundaries. Peters in his original memoir suggested that the conversion of the surface-layer of the epithelium into syncytium was due to the action of the maternal blood on it; but it is more probable that the differentiation into two lamellæ takes place much earlier (*cf.* fig. 40, p. 29), as Van Beneden has demonstrated for the placenta of the bat.

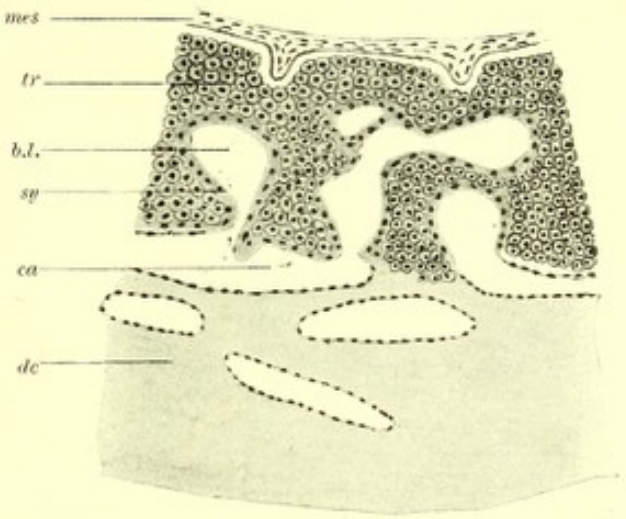



FIG. 101.—DIAGRAM TO ILLUSTRATE THE FIRST PHASE OF THE PLACENTA. (After Peters.)

*mes*, mesoderm; *tr*, trophoblast; *b.l.*, blood-lacuna; *sy*, syncytium; *ca*, maternal capillary; *dc*, decidua.

The further changes leading to the formation of the placenta will be readily understood by reference to the diagrams given in figs. 101 to 103. The trophoblast-strands become invaded by processes from the mesoderm (fig. 103), and are thus converted into the primary villi. The villus-stems are at first simple and attached at their outer ends to the decidua (figs. 101 and 102), but they soon become drawn out and greatly branched (figs. 102 and 103). As the mesoderm extends into the epithelial strands, to form the cores of the villi, it is necessarily covered by both cellular and plasmodial layers. The cellular layer becomes reduced, as the villi develop, to a single layer of cells, except at their attached ends, and the

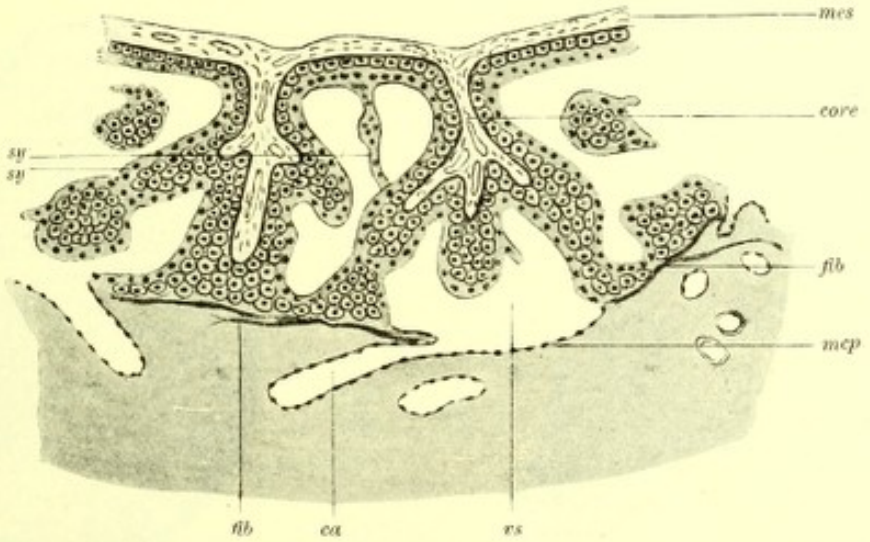



FIG. 102.—DIAGRAM TO ILLUSTRATE THE SECOND PHASE OF THE PLACENTA. (After Peters.)

The mesodermic core has now invaded the strands of the trophoblast, and is beginning to branch. *mes*, mesoderm; *core*, core of villus; *sy*, syncytium; *mcp*, endothelium of maternal capillary, *ca*; *vs*, intervillous space; *fib*, fibrinous material deposited at junction of trophoblast with decidua.

stems and branches now show the structure seen in fig. 104. In the mesodermic core capillaries are seen containing nucleated blood-corpuscles from the embryo, carried thither by the allantoic vessels in the abdominal stalk. The core is covered by a double membrane, a cellular (*Langhans' layer*) and a syncytial.

Meanwhile, as the villi become drawn out and branched, the original intercommunicating blood-lacunæ become expanded into the *intervillous space*, in which the maternal blood slowly circulates and bathes the villi. The placenta at first

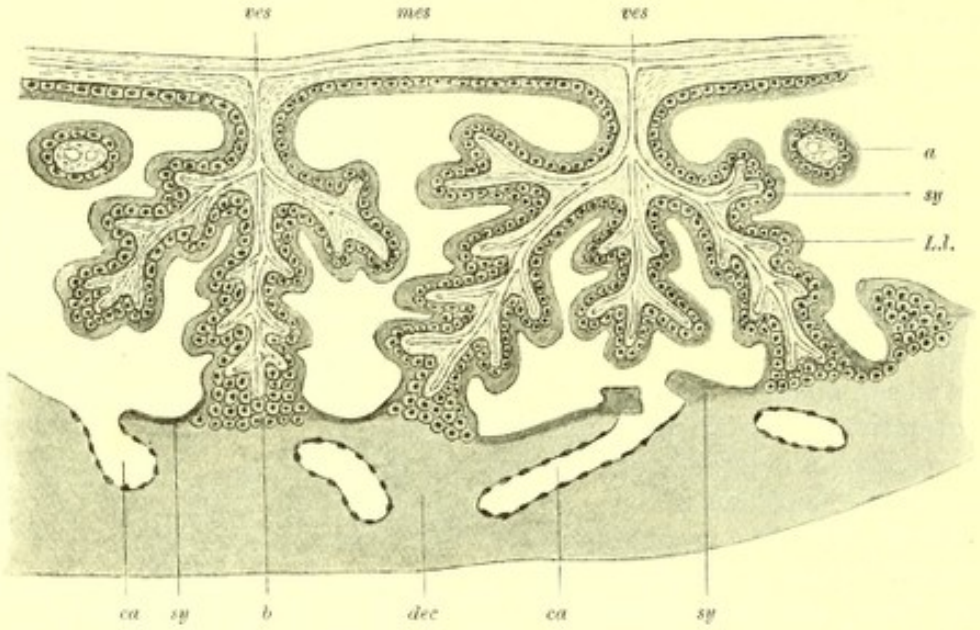



FIG. 103.—DIAGRAM TO ILLUSTRATE THE THIRD PHASE OF THE PLACENTA. (T. H. Bryce.)

The mesodermic processes have further branched, and are now everywhere covered by a single layer of cells (Langhans' layer) and a lamella of syncytium. At *b*, where a villus is attached, the cellular layer retains its primitive arrangement; *mes*, mesoderm; *ves*, *ves*, vessels going to villi; *sy*, syncytium; *L.l.*, Langhans' layer; *a*, cross-section of a villus; *dec*, decidua; *ca*, maternal capillary.

extends over the whole chorion, but when the villi of the chorion læve degenerate it becomes confined to the chorion frondosum. Here the villi become continually more branched, and new villi are formed, until the complicated sponge-work

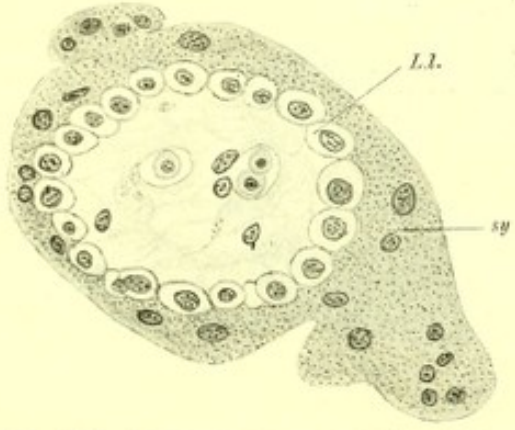



FIG. 104.—SECTION OF A VILLUS FROM AN OVUM OF THE THIRD WEEK. (T. H. Bryce.)

*sy*, syncytium; *L.l.*, Langhans' layer.

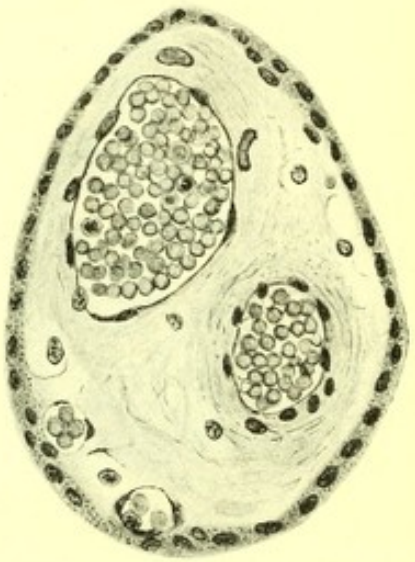


FIG. 105.—SECTION OF A VILLUS FROM A PLACENTA AT THE SEVENTH MONTH. (T. H. Bryce.)

of the discoidal placenta is fully developed. In the later months of pregnancy the Langhans layer on the villi disappears, and the fœtal capillaries are separated from the maternal blood by the connective tissue of the villus and a thin lamella of syncytium only (fig. 105).

The changes which occur in the decidua basalis have been already (p. 69) alluded to. It becomes invaded by masses of syncytium, which penetrate it even to the muscular layer, and it gradually undergoes a process of degeneration until it is reduced to a thin layer. This lamella may even be incomplete, for the villi are sometimes found in direct contact with the muscular tissue. The final term of the degeneration is the development of a fibrinous layer which serves to mark off the fœtal and maternal tissues. A similar degeneration affects the ends of the villi, and in the later months this extends to the villi themselves, so that in many parts the cellular elements have in great part disappeared, as will immediately be noticed in the description of the full-time placenta.

**The shed placenta.** — At full time the placenta is a discoidal plate measuring from 16 to 21 cm. in diameter and 3 to 4 cm. in thickness, but in shape and dimensions it is subject to considerable variations. It is thickest in the centre, and thins away at the margin where it is continuous with the chorion and portions of the decidua.

The surface which has been detached from the uterus shows a number of irregular areas (cotyledons) separated by shallow fissures. The detachment generally takes place through the remains of the decidua basalis, so that a thin layer of decidual tissue covers the ends of the villi. The fœtal surface is covered by the amnion, and under it are seen the vessels radiating outwards from the umbilical cord before they dip into the substance of the organ. The cord is usually attached near the centre. It conveys two arteries to the placenta. They branch freely but irregularly, and extend outwards in the connective tissue of the chorion to reach the villi in a series of terrace-like steps, spreading out horizontally and dipping in vertically several times. They end in the villi in capillary loops (fig. 106), from which the blood is gathered into veins which, closely following the arteries, finally unite to form the single umbilical vein round which the arteries coil spirally.

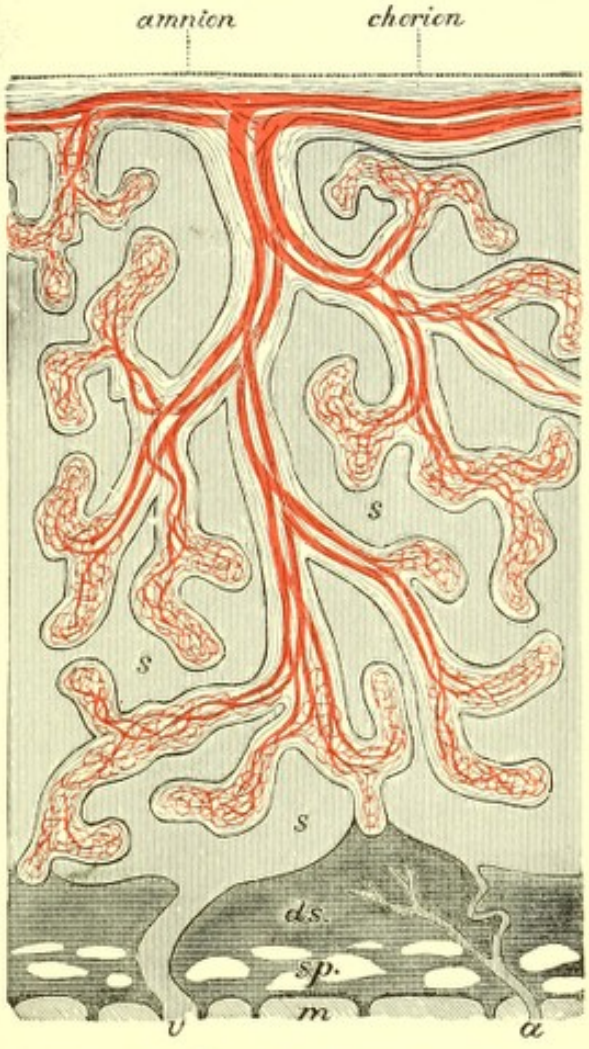



Fig. 106.—Diagram of the placenta. (E. A. Schäfer.)

*s*, placental sinus; *d.s.* decidua basalis; *sp*, spongy layer; *m*, muscularis; *a*, *v*, uterine artery and vein opening into placental sinus.

A section across the placenta (fig. 107) shows that the mass of the organ between the amniotic and chorionic membranes on the fœtal side, and the thin covering of decidua on the uterine side, is made up of immense numbers of arborescent villi, hanging free in a great space filled with maternal blood. Here and there the root of a villus is seen springing from the chorion, while the larger stems and finer branches are seen cut in every direction. A certain number of the villi are attached to the decidua, but the greater number hang free into the intervillous space. Projecting into the placenta from the decidua there are certain

connective-tissue processes, or septa, to which villi are attached, as well as to the general decidual surface. These to some extent divide up the placenta into

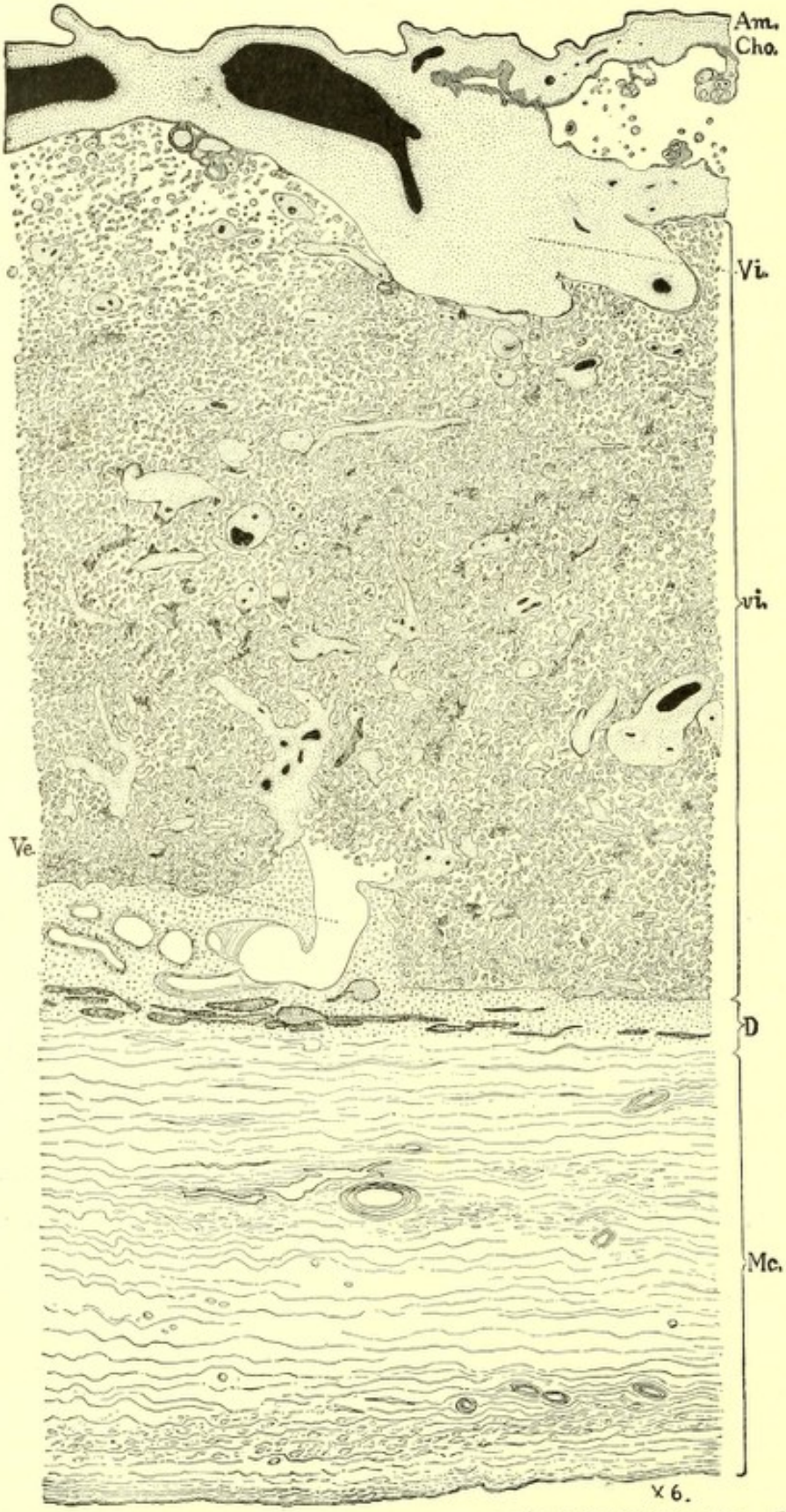



FIG. 107.—SECTION THROUGH A NORMAL PLACENTA OF SEVEN MONTHS IN SITU. (Minot.)

*Am*, amnion; *Cho*, chorion; *Vi*, root of a villus; *vi*, sections of the ramifications of villi in the intervillous space: the larger blood-vessels within them are represented black; *D*, deep layer of the decidua, showing flattened remnants of enlarged glands in spongy stratum; *Ve*, uterine vessel opening out of placental sinus; *Mc*, muscular wall of uterus.

loculi. The villi are clothed by a thin layer of continuous protoplasm in which nuclei are regularly arranged (figs. 105 and 108), and many of them have a layer of fibrinous material under this syncytium. In the outer part of the placenta the syncytial layer has in large measure disappeared, to be replaced by a thick mass of fibrin, and many of the stems have undergone complete fibrinous degeneration (fig. 108). A dense layer of the same substance also occupies the outer part of the remnant of the decidua basalis adhering to the placenta. The blood enters the intervillous space by afferent vessels in the decidua

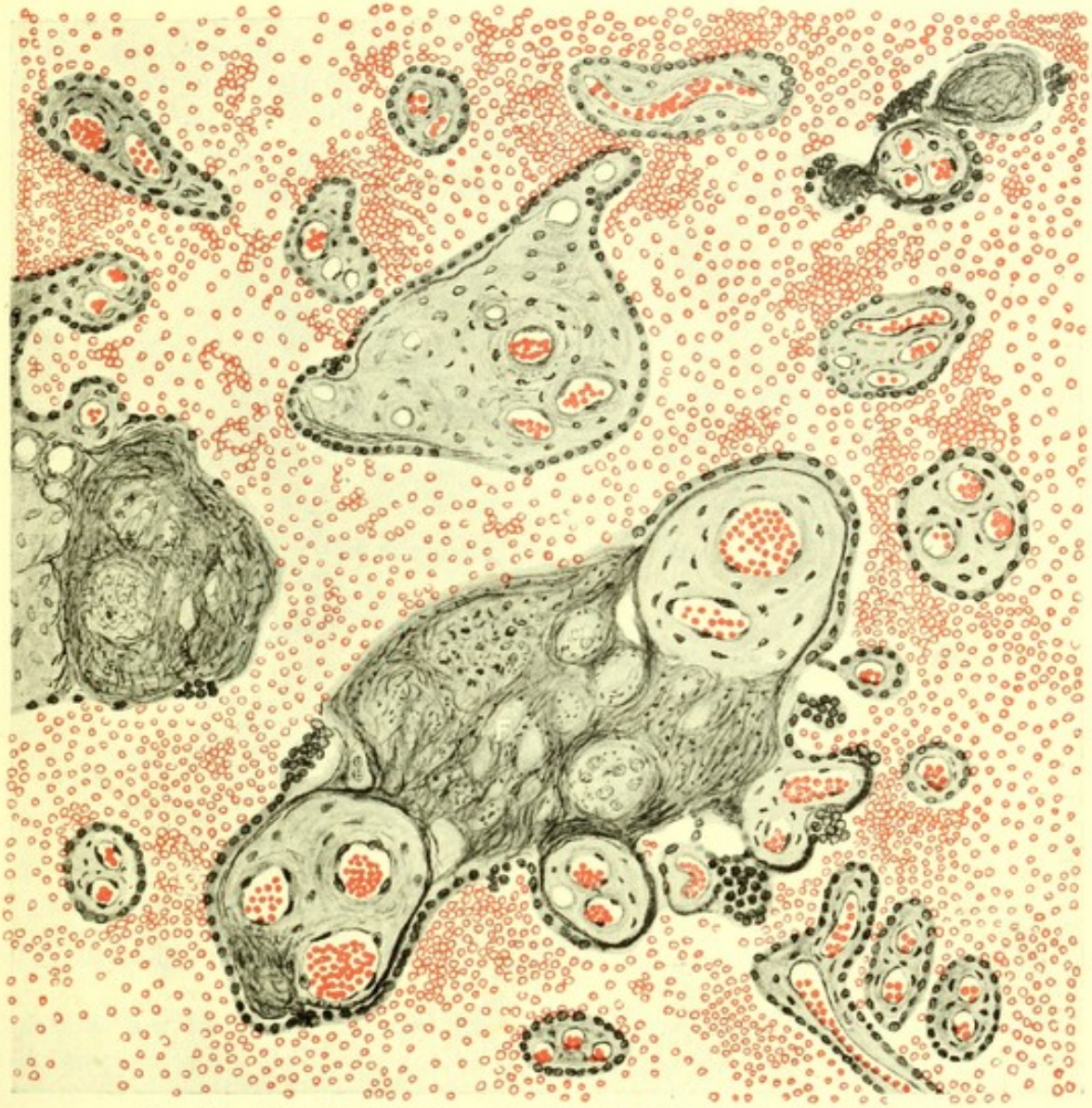


FIG. 108.—SECTION THROUGH A PLACENTA AT FULL TIME. (T. H. Bryce.)

The intervillous space is represented filled with maternal blood. The fœtal capillaries were injected by stripping back the umbilical cord before it was tied, and the corpuscles are represented solid to distinguish them from the maternal. Notice the layer of syncytium on the villi; under it, in many villi, there is a layer of fibrinous material represented by a continuous line; *F* is a large villus which has undergone fibrinous degeneration. (From a preparation by Dr. J. H. Teacher.)

connected with small arteries which pursue a spiral course, and are hence called the 'curling arteries,' while it leaves it by efferent vessels connected with the veins in the deep part of the remnant of the decidua basalis.[1]

[1] For the literature of the placenta, see Strahl in Hertwig's Handbuch, i. Teil I., II. p. 356; also for some later papers, Kollmann's Handatlas, 1907, appendix, p. 35. See also J. Clarence Webster, Human Placentation, Chicago, 1901; and for comparative data, Arthur Robinson (Hunterian Lectures), Jour. of Anat. and Phys. vol. xxxviii.

## GENERAL HISTORY OF THE DEVELOPMENT OF THE HUMAN EMBRYO.

**Estimation of age.**—In estimating the age of embryos prematurely expelled from the uterus, we must, in the absence of data as to the early stages, have recourse to a conventional rule. The rule generally adopted is that formulated by His. It reckons the duration of pregnancy from the first day of the first omitted period, the cessation of the menses being the earliest positive sign of impregnation.[1]

**First month.**—The ova of Leopold, of Peters, of Beneke, and one of those described by Graf v. Spee, must, according to His' rule, be reckoned to belong to the first few days of pregnancy. Leopold's ovum is probably the youngest yet discovered, but the relations were somewhat disturbed by intense congestion of the decidua, and no embryonic rudiment was identified.

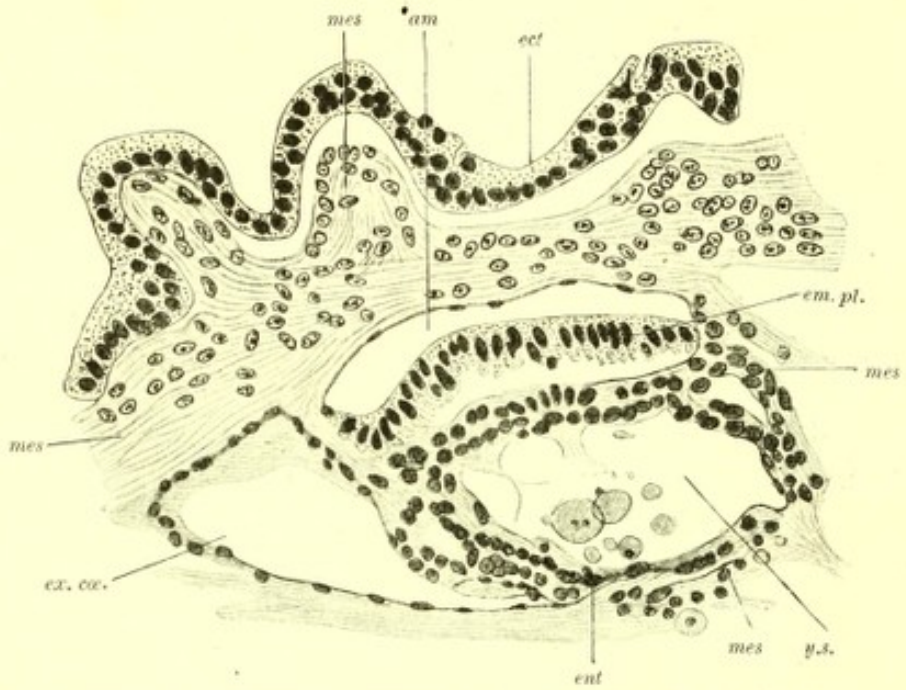



FIG. 109.—SECTION OF EMBRYONIC RUDIMENT IN PETERS' OVUM (FIRST WEEK). (After Peters.)
*ect*, ectoderm of chorion; *mes*, mesoderm; *am*, amnion; *em.pl.*, embryonic plate; *y.s.*, yolk-sac; *ent*, entoderm; *ex.ce*, portion of extra-embryonic cœlom limited by a strand of the magma reticulare.

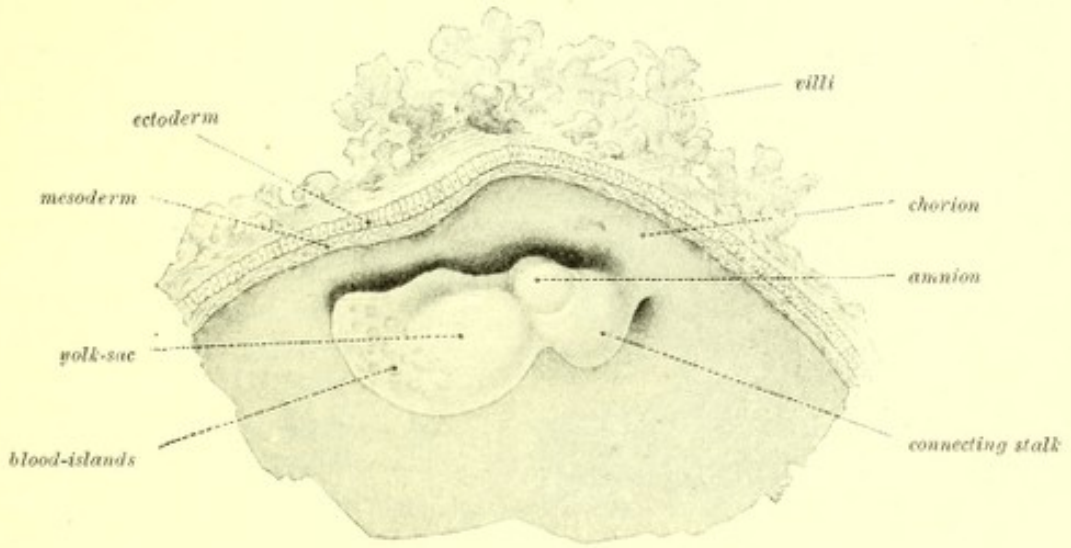
We therefore begin with Peters' ovum. In this the cavity of the chorionic vesicle measures 1·6, ·8, and ·9 mm. in its three diameters. It is entirely surrounded by very irregular trophoblast-strands, and the mesoderm is beginning to extend into these strands to form the primitive villi. The embryonic rudiment (fig. 109) is still a single layer of ectoderm, to which is attached a small yolk-sac, while it is covered by a closed amnionic sac. The yolk-sac and amnion are contained within, and attached to the completely closed chorion, by mesoderm which is already separated into visceral and parietal layers. The extra-embryonic cœlom thus formed is relatively very large, and is intersected by strands of fibrillæ known as the *magma reticulare*.

The next stage may be illustrated by Spee's embryo *v H* (fig. 110), belonging to the beginning of the second week. The chorionic vesicle measures

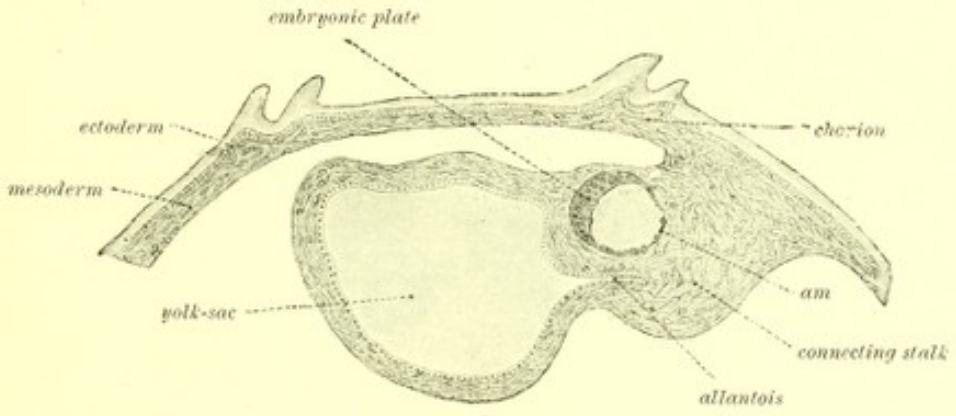
[1] Mall gives a useful formula for estimating the age of human embryos up to 100 mm. in length: $\sqrt{100 \times \text{length in mm.}}$ = age in days. In fœtuses measuring from 100 to 220 mm. the vertex-breech millimetre length is approximately equal to the age in days.

7 mm. by 5·5 mm., and is entirely covered by villi.[1] The embryonic rudiment projects from the chorion in an oblique direction, and is attached by a broad mesodermic stalk. The yolk-sac is larger than in the earlier stage, being 1·083 mm. in diameter; the embryonic shield is oval, has indications of a primitive streak, and is somewhat concave, the embryonic ectoderm being directly continuous with the flattened ectoderm of the small closed amnionic sac. The connecting stalk contains a short diverticulum of the yolk-sac, the rudiment of the allantois.

By the end of the second week the chorionic vesicle measures about 8·5 mm. by 6·5 mm., and is entirely covered by villi in all the specimens described. In Spee's




A




B

FIG. 110 A.—EMBRYO OF 0·4 MM. (LETTERED *vH*) BELONGING TO SECOND WEEK, SHOWING ITS POSITION AND ATTACHMENT TO INNER ASPECT OF CHORION.

FIG. 110 B. THE SAME IN MESIAL LONGITUDINAL SECTION. (After Graf v. Spee, from Kollmann.)

*am*, amnion.

embryo *Gle* (fig. 111) the embryonic shield measures 1·54 mm. The embryo is separated by a slight constriction from the yolk-sac, and shows a short primitive groove, a large neurenteric canal, and a shallow neural groove. The yolk-sac is covered by projections caused by the development of blood-islands, and distinct vessels are formed on its lower segment. The connecting stalk has narrowed down relatively, and, compared with the embryo *v H*, it would appear that in the laying down of the embryonic axis in front of the primitive streak a change in the relative position of parts has taken place, the yolk-sac coming to lie below the shield and

[1] The ovum described by Reichert and one described by Mall of about the same age, or rather older, had merely a circle of villi round the equator, the poles being bare.

the connecting stalk at the posterior end. The fore-gut is beginning to be formed, and the allantoic diverticulum is a distinct tubular passage. The heart, as already described, is represented by two lateral vessels which unite together in front of the neural groove.

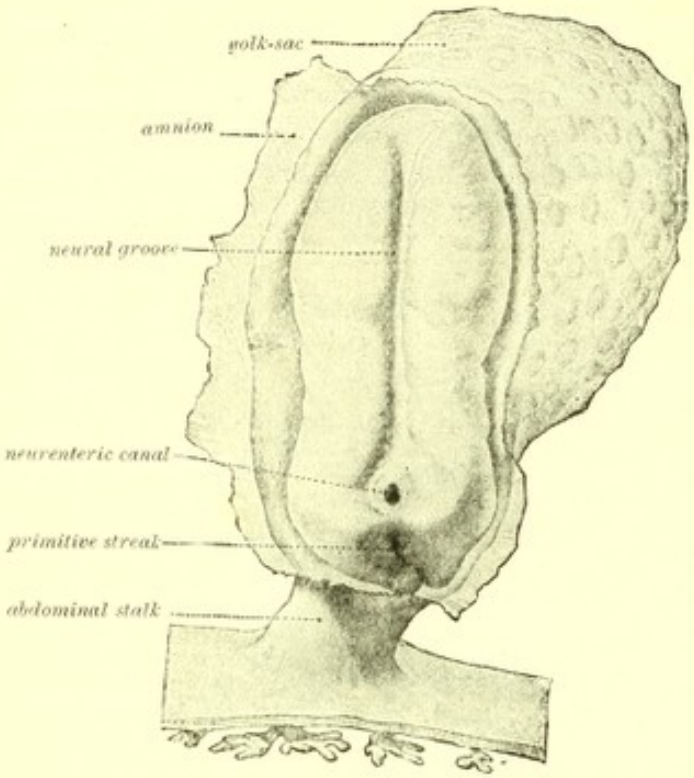



FIG. 111.—EMBRYO OF 2 MM. (LETTERED *Gle*) ABOUT THIRTEEN DAYS OLD. (After Graf v. Spee, from Kollmann.)

His' embryos *E* and *S R* (fig. 112), estimated to be about thirteen days, and Eternod's embryo present the same characters.

Kollmann's embryo (fig. 113), estimated as fourteen days old, is farther advanced. It measures 2·4 mm. in length, and is separated both in front and behind from the yolk-sac. The neural groove is closed behind, but open in front, where the cerebral vesicles form a conspicuous feature. There are fourteen mesodermic segments, and the heart is now a single coiled tube. The embryonic axis is slightly concave.

By the thirteenth day, as illustrated by His' embryo lettered *Lg* (fig. 114), the chorionic vesicle has enlarged to 15 mm. by 12·5 mm., and the villi are numerous and branched. (In this particular case they were absent from patches at the poles.) The amnion closely surrounds the embryo, which in most specimens shows a remarkable dorsiflexion. This flexure may possibly be a normal[1] though passing feature, as it is seen also in some of the lower primate embryos of the same stage of development. The yolk-sac is spherical and about 2 mm. in diameter. The fore-gut and hind-gut are formed, but the cavity of the sac has still a wide mouth. The neural groove is closed, and the fore-brain is bent downward to form the cranial flexure; the optic vesicles project from the sides of the fore-brain; the ear-vesicles are seen as distinct pits above the branchial region, which is marked by two

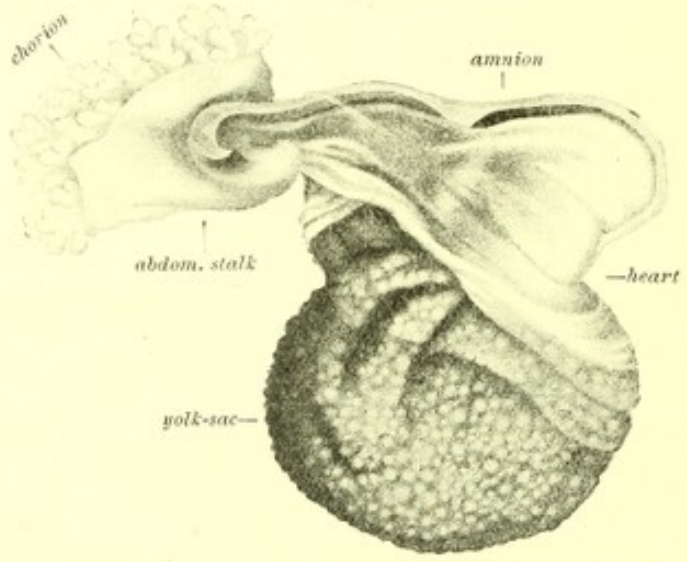



FIG. 112.—EMBRYO OF 2·2 MM. (LETTERED *SR*) TWELVE TO FIFTEEN DAYS OLD. (His.)

[1] An embryo of 2·5 mm., and estimated as about fifteen days old, studied and modelled by Dr. Peter Thompson, does not show this dorsiflexion (Jour. Anat. and Phys. xli. April 1907).

slit-like external branchial pouches. The heart is a very prominent structure lying immediately below the branchial region. About thirty-five pairs of segments can be counted, and the tail forms a prominent rounded projection, from the under aspect of which a short thick abdominal stalk connects the embryo with the chorion, and contains the allantoic diverticulum and allantoic vessels. The

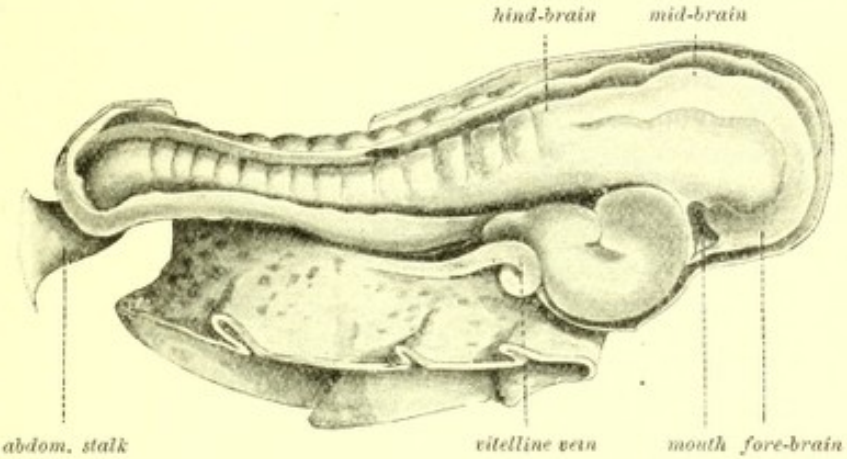



FIG. 113.—EMBRYO OF 2·4 MM. ABOUT FOURTEEN DAYS OLD. (Kollmann.)

stomodœum is a recess between the under aspect of the fore-brain and pericardial region, and is separated by the buccopharyngeal membrane from the fore-gut.

Coste's embryo is of about the same age as the one just described.

By the end of the third week a stage is reached represented by His' embryo lettered *Lr* (fig. 115). The embryo is almost completely cut off from the yolk-sac, the mouth of which is narrowed into the yolk-stalk. The embryo measures in a straight line between its most projecting anterior and posterior ends 4·2 mm. The head end is bent on the trunk in the neck region, forming the cervical flexure. The dorsiflexion of the body is no longer seen, and the tail is bent in towards the ventral aspect. The abdominal stalk, which is now lengthened out somewhat, passes back to the chorion on the right side of the tail.

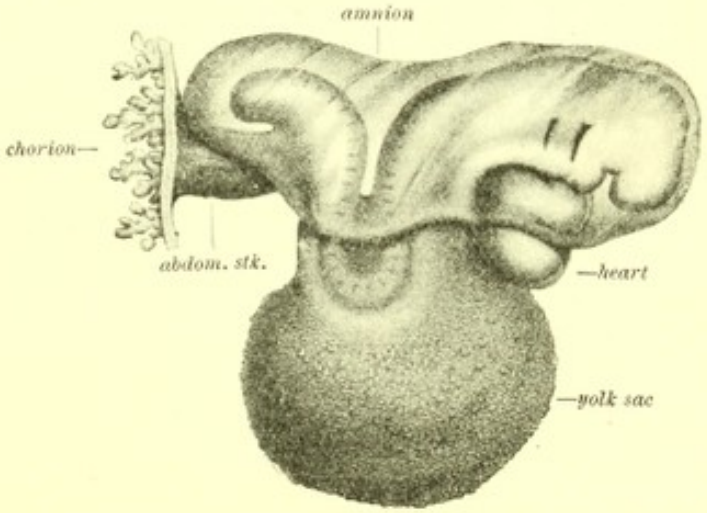



FIG. 114.—EMBRYO OF 2·15 MM. (LETTERED *Lq*) ABOUT FIFTEEN DAYS OLD. (His.)

The olfactory pit is beginning to show on each side of the fore-brain; the optic vesicles are prominent swellings, but the lens pit is not yet developed; the auditory pits are closed, and the branchial region, triangular in shape, shows four branchial depressions. The ridges bounding the branchial clefts are now named the mandibular, the hyoid, and the (three) branchial arches. The mandibular arch bounds the stomodœum behind, the hyoid lies between the first and second branchial clefts, the branchial arches bound the remaining fissures. The hyoid arch is the largest of the series. The heart, which now lies rather farther back than before, shows distinct constrictions separating off its several parts. The

mesodermic segments are distinct, and ventral to them on each side is a longitudinal ridge called the Wolffian ridge. This ridge is more prominent at two points, opposite the posterior end of the heart and allantoic stalk; the small swellings thus produced are the earliest signs of the limb-buds.

The general features of a fœtation at the *end of the first month* are well illustrated in fig. 116. The chorionic vesicle is laid open. It is still very large relatively to the contained embryo. The yolk-sac is a rounded vesicle attached to the embryo by a stout pedicle, and, owing to the flexion of the embryo, the abdominal stalk and vitelline stalk come to be applied to one another. The embryo is closely invested by the amnion, and is markedly bent on itself. This bending is best seen about the twenty-third day, when head and tail touch or even overlap one another. The greatest diameter of the embryo by the end of the fourth week is about 7·5 mm., so that, allowing for the flexion, it has obviously much increased in size. The cervical flexure is very marked.

Fig. 119 represents an enlarged view of an embryo at this stage. On the side of the head are seen the olfactory pits, above them are the optic vesicles; the lens-rudiments have the form of shallow open pits. The auditory vesicles are prominent rounded swellings, opposite the hyoid arches. The mouth is now a wide cavity bounded in front (fig. 123) by a broad field intervening between the olfactory pits called the *fronto-nasal process*, behind by the *mandibular arches*, and on each side by lateral processes named the *maxillary processes*, which project forwards between the optic vesicles and mandibular arches. The mandibular and hyoid arches are each beginning to show swellings separated by constrictions, and the hinder branchial arches are hidden from view, being overlapped by the anterior arches. This telescoping of the arches produces a recess between the branchial region and trunk, known as the *precervical sinus*.

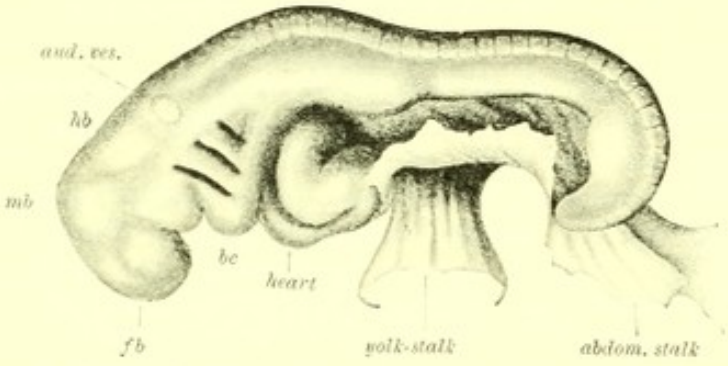



FIG. 115.—EMBRYO OF 4·2 MM. (LETTERED *Lr*) EIGHTEEN TO TWENTY-ONE DAYS OLD. (His.)

*aud. ves.*, auditory vesicle; *bc*, stomodœum; *fb*, fore-brain; *mb*, mid-brain; *hb*, hind-brain.

The mesodermic segments are very prominent objects; they are thirty-five in number. In the early part of the fourth week the paired swellings on the Wolffian ridges become more prominent, and by the end of the week are seen as distinct buds, the rudiments of the limbs. The heart is relatively very large, and, with the developing liver behind and slightly above it, forms the prominent rounded swelling represented in the figure.

It will thus be seen that by the end of the first month all the organs have been laid down, and the embryo closely resembles any other mammalian embryo at a corresponding stage—as, for instance, the rabbit embryo at the end of the eleventh day. During the course of the second month, however, changes take place, which confer distinctively human features on the embryo.

**Second month.**—During the first month the chorionic vesicle is, as we have seen, relatively very large compared with the embryo and its amnion, and the villi are uniformly distributed. By the end of the second month the distinction between chorion frondosum and chorion læve is established, and the amnion has become greatly enlarged, so as to come in contact with the chorion and obliterate

the extra-embryonic cœlom. With the enlargement of the amnion the vitelline and abdominal stalks are bound up together in a tubular prolongation of the membrane to form the umbilical cord. At the end of the month the cord is about 10 mm. in length, and still contains at its attachment the primary coils of the small intestine. The embryo enlarges greatly, but not so rapidly as during the first month. The back is straightened and the head uplifted, and in consequence the

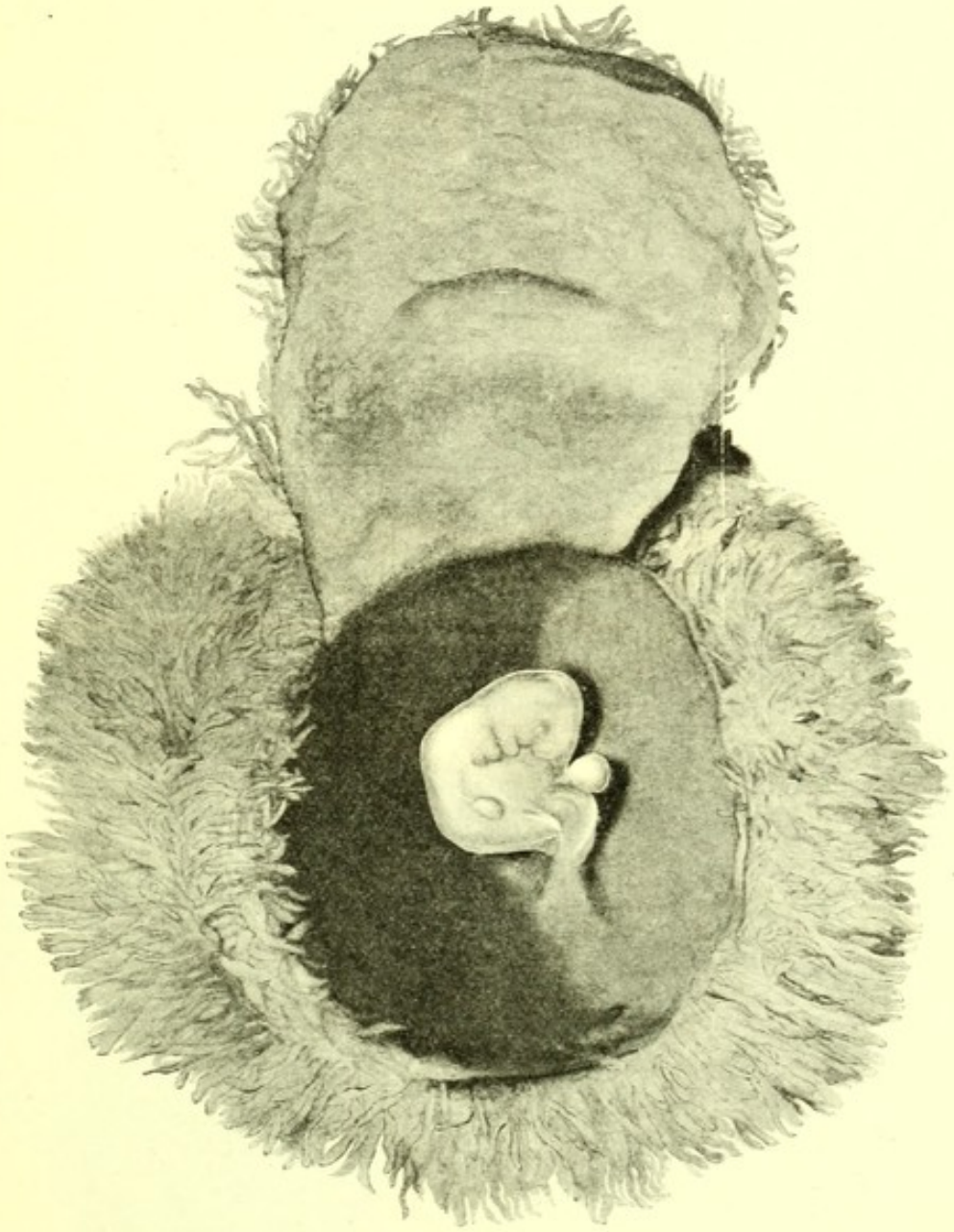


FIG. 116.—CHORIONIC VESICLE AT THE END OF THE FIRST MONTH. Magnified.
(From a preparation by Dr. J. H. Teacher.)

The vesicle has been opened; the embryo, closely invested by the amnion, is seen attached by the abdominal stalk to the chorion.

extreme curvature is to some degree undone. The tissues become condensed and opaque, so that the internal organs can no longer be made out. The head remains relatively very large, being at the end of the month nearly as large as the body of the embryo.

At the end of the fifth week the embryo measures, from neck to breech, about 12 mm., at the end of the sixth week about 17 mm., at the end of the seventh week about 20 mm., and at the end of the second month about 30 mm.

(measured from vertex to breech). The chief changes, as far as outward form is concerned, are the formation of the face and external ear, and the development of the limbs.

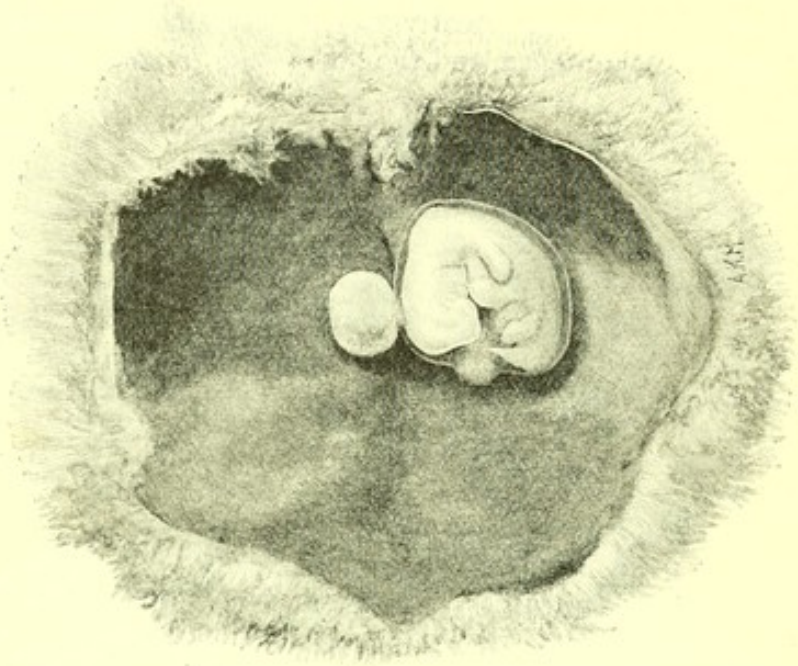


FIG. 117.—CHORIONIC VESICLE, EMBRYO, AND YOLK-SAC AT THE BEGINNING OF THE SECOND MONTH.
(By permission, from a preparation in the Hunterian Museum, University of Glasgow.)

*Face.*—In the latter part of the fourth week the olfactory pits have narrowed down to form grooves running backwards in the roof of the stomodœum. The

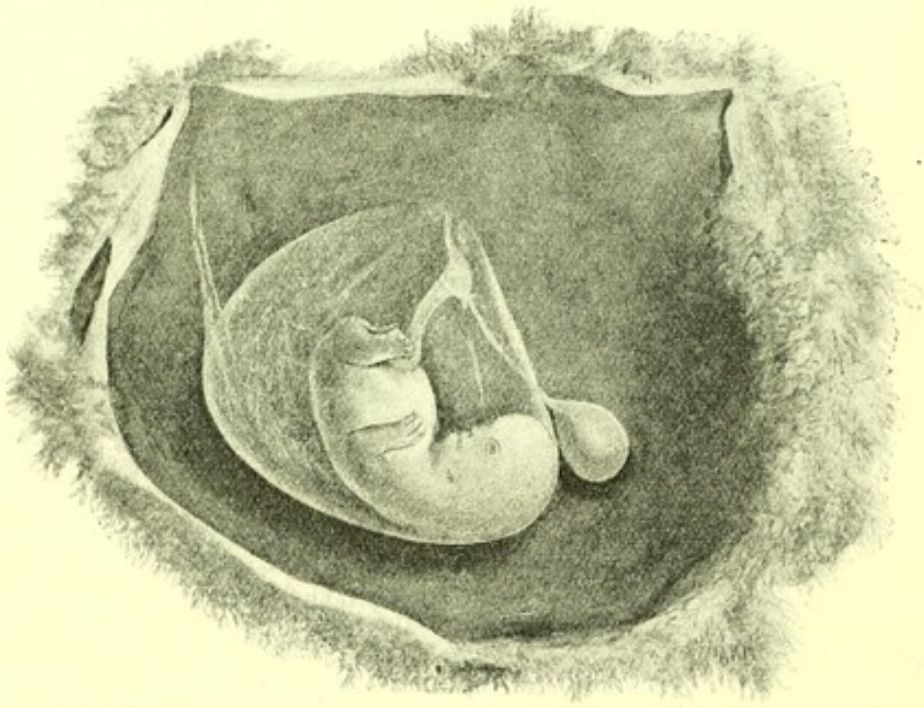


FIG. 118.—CHORIONIC VESICLE, EMBRYO IN ITS AMNION, AND YOLK-SAC TOWARDS THE END OF THE SECOND MONTH.
(By permission, from a preparation in the Hunterian Museum, University of Glasgow.)

margins of these grooves become raised into swellings, which superficially form what are known as the *lateral* and *mesial nasal processes* (processus globulares) (figs. 123,

124). Between the mesial processes there is a depressed area on the frontonasal process. In the fifth week an angular projection appears on this area, which

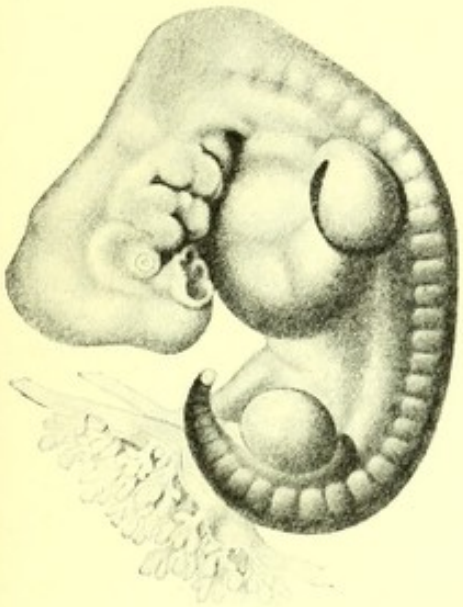


FIG. 119.—EMBRYO OF 7·5 MM. (LETTERED *A*) TWENTY-SEVEN TO THIRTY DAYS OLD. (His.)

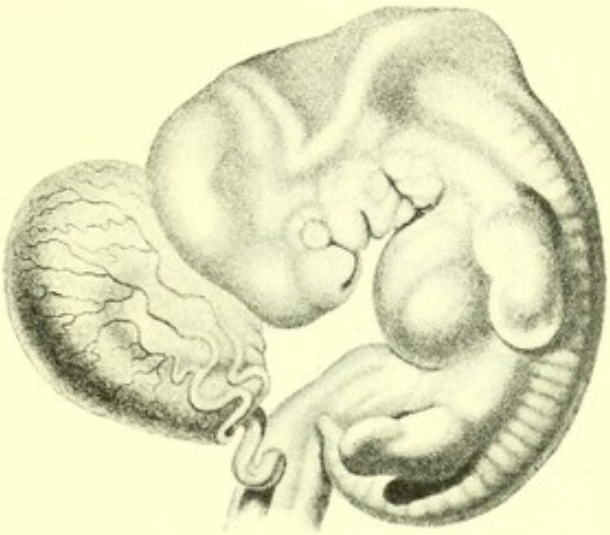


FIG. 120.—EMBRYO OF 9·1 MM., THIRTY-ONE TO THIRTY-FOUR DAYS OLD. (His.)

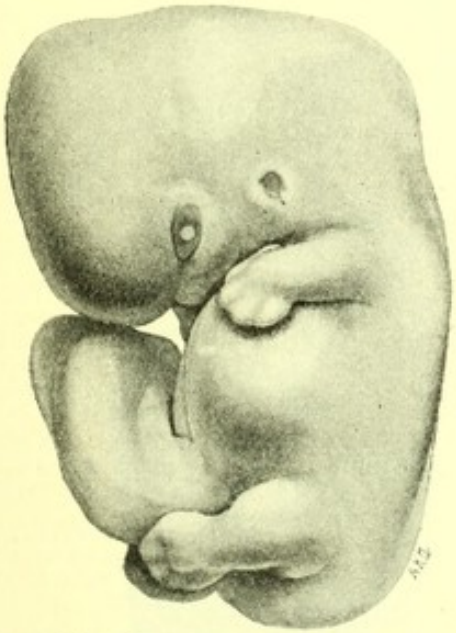


FIG. 121.—EMBRYO OF 15·5 MM. (NECK-BREECH LENGTH) ABOUT THE BEGINNING OF THE SIXTH WEEK. (T. H. Bryce.)

This embryo was obtained in a uterus removed for a large fibroid tumour by Dr. Oliphant, Glasgow, and fixed *in situ* with sublimate solution immediately after the operation. It may be considered perfectly normal.

FIG. 122.—EMBRYO OF 30 MM. ABOUT THE BEGINNING OF THE THIRD MONTH OR RATHER EARLIER. (T. H. Bryce.)

(This embryo was fixed *in situ*.)

afterwards forms the tip of the nose, while the area above it later forms the bridge. The mesial processes enlarge, and the maxillary processes grow forwards to meet their outwardly curving ends. The mouth is thus reduced to a narrow slit.

During the sixth week the maxillary processes fuse with the lateral nasal and mesial nasal processes to form the cheeks, the lateral parts of the upper lip (fig. 125),

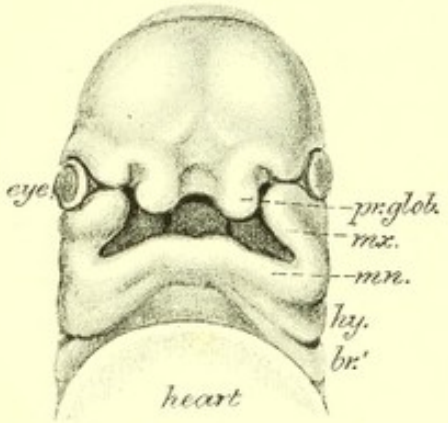



FIG. 123.—HEAD OF AN EMBRYO ABOUT TWENTY-NINE DAYS OLD, FROM BEFORE. (His.)

*pr.glob.*, globular extremity of the mesial nasal process; *mx*, maxilla; *mn*, mandible; *hy*, hyoid arch; *br'*, first branchial arch.

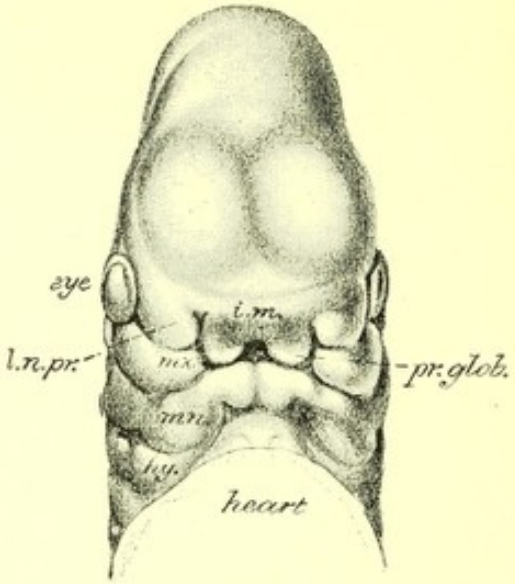



FIG. 124.—HEAD OF AN EMBRYO ABOUT THIRTY-FOUR DAYS OLD. (His.)

*i.m.*, placed on the frontal-nasal process and just above its intermediate depressed part; *l.n.pr.*, lateral nasal process; *m.n.pr.*, mesial nasal process; *pr.glob.*, as in the previous figure.

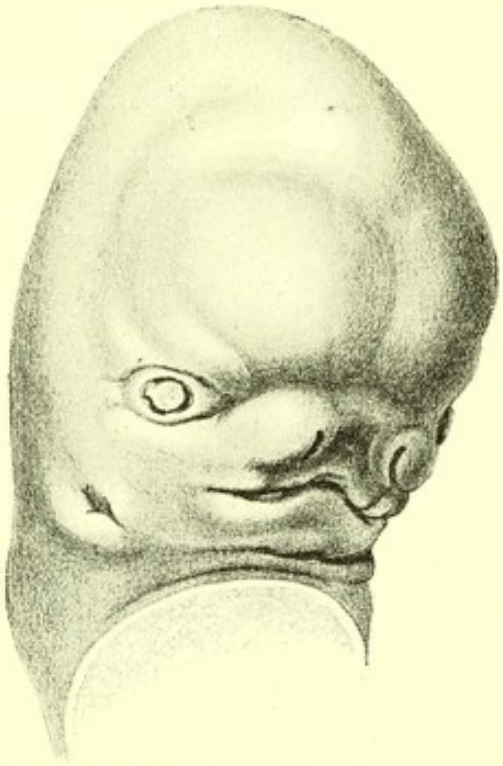


FIG. 125.—HEAD OF AN EMBRYO OF ABOUT SEVEN WEEKS. (His.)

The external nasal processes have united with the maxillary and globular processes to shut off the olfactory pit from the orifice of the mouth.

FIG. 126.—HEAD OF AN EMBRYO AT THE END OF THE SECOND MONTH, WITH THE PARTS OF THE NOSE AND MOUTH BEGINNING TO ASSUME THEIR PERMANENT RELATIONSHIPS. (His.)

and the alæ of the nose; while by the end of the second month the mesial nasal processes fuse with one another to form the mesial part of the upper lip and the

columna nasi (fig. 126). The nose is, however, still broad and flat, while the nostrils remain far apart and look forwards. It is only later that the bridge of the nose is developed, and the nostrils come to be directed downwards. During the second month an epithelial plug develops in each nostril, which occludes the passage for a time. This condition, first described by Kölliker, has recently been further investigated by Retzius.[1] There is no doubt that such a plug exists in the fœtus figured in fig. 122 (see Development of the Nose).

The mandibular processes are at first separated by a flat area, but in the sixth week they fuse together, and a mesial projection is developed which is the rudi-

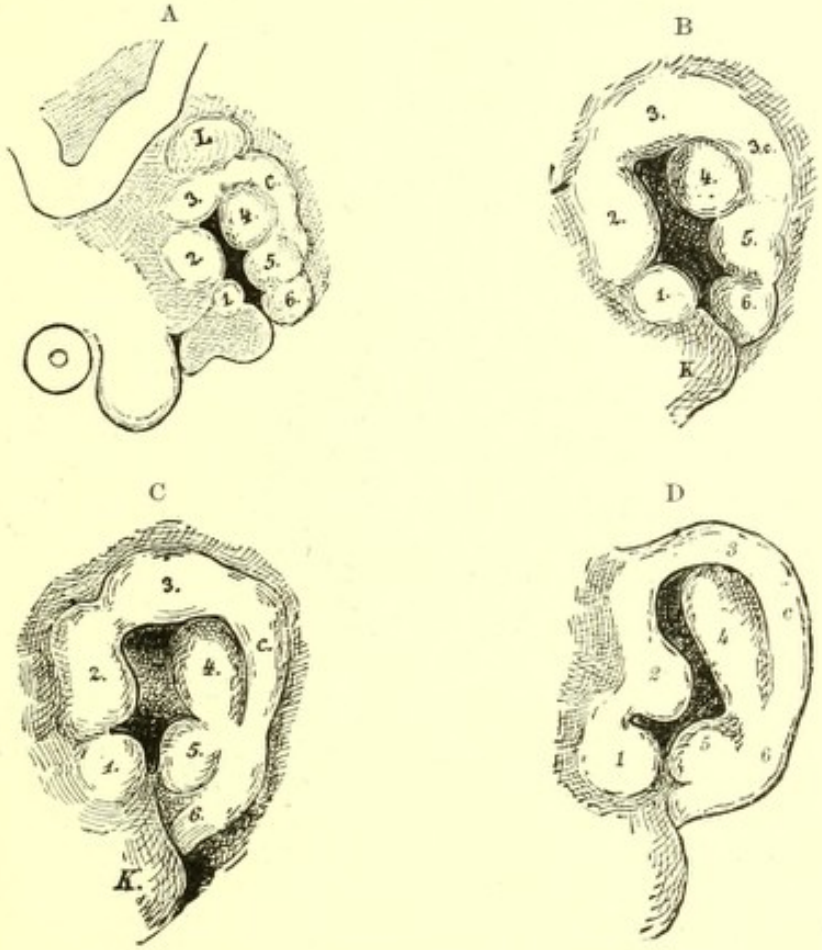



FIG. 127.—SKETCHES SHOWING THE DEVELOPMENT OF THE PARTS OF THE EXTERNAL EAR FROM PROMINENCES UPON THE MANDIBULAR AND HYOID ARCHES. (His.) Variously magnified.

A, embryo at the end of the first month; B, embryo of thirty-five days; C, embryo of thirty-eight days; D, embryo at the end of the second month.

1, tuberculum tragicum; 2, tuberculum anterius helicis; 3, tuberculum intermedium helicis; 3c and *c*, cauda helicis; 4, tuberculum antihelicis; 5, tuberculum antitragicum; 6, tuberculum lobulare; L, in A, auditory vesicle; K, lower jaw.

ment of the chin. The lips appear as folds of skin in the sixth week, and by the end of the eighth week have considerably advanced in development, but the red margins do not appear till the third month. The eyelids are developed during the same period as the lips, also as folds of skin. The *lacrymal groove* between the eye and stomodœum is covered over by the fusion of the maxillary and lateral nasal processes. During the second month the branchial arches are telescoped within the hyoid arch, so that the hyomandibular cleft is alone seen on the surface, and by the end of the month the sinus prccervicalis is obliterated.

*Ear.*—Round the hyomandibular cleft small swellings or tubercles appear, which are named after the different portions of the adult pinna to which they

[1] Biolog. Untersuchungen, 1904.

give rise, while the cleft itself becomes the concha and part of the external auditory meatus. By the end of the month the auricle is so far developed that the adult parts can be readily recognised. The transformations may be readily understood from the study of the accompanying series of sketches copied from His, which show these parts in gradually advancing stages in the human embryo (fig. 127).

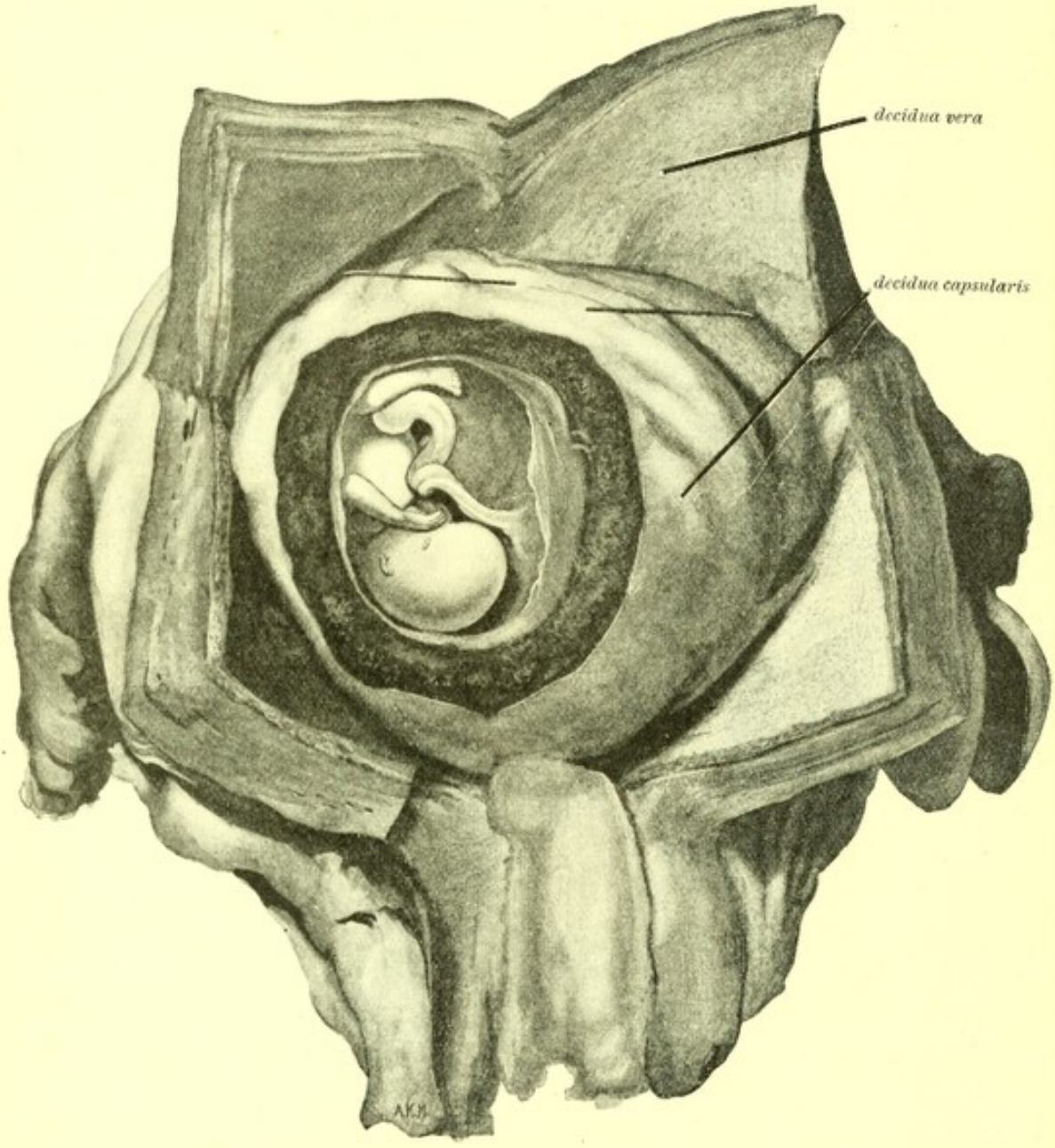



FIG 128.—PREGNANT UTERUS AT THE BEGINNING OF THE THIRD MONTH.

The uterus has been opened up; a window has been made in the decidua capsularis, and also in the amnion, to show the fœtus *in situ*. A large plug of mucus occupies the canal of the cervix. The bristles indicate the openings of the Fallopian tubes. The cut edge of the decidua capsularis shows the villi of the chorion læve. (From a preparation by Dr. J. H. Teacher.)

*Limbs.*—In the fifth week the limb-buds considerably enlarge, and show a subdivision into two, then into three, segments (fig. 121). The terminal segment which forms the hand or foot is broadened out and differentiated into a thicker basal, and a thinner marginal portion. At the base of the thin marginal segment the rudiments of the fingers and toes appear as small tubercles, which soon reach the free margin. During the sixth week the limbs increase in size, the elbow and

knee form prominent angles, and a certain rotation takes place so that the elbow comes to be directed backwards and the knee forwards (fig. 122). The hind-limb is at first smaller than the fore-limb, and is not so advanced in development. Thus the fingers project from the free margin of the hand during the sixth week, while

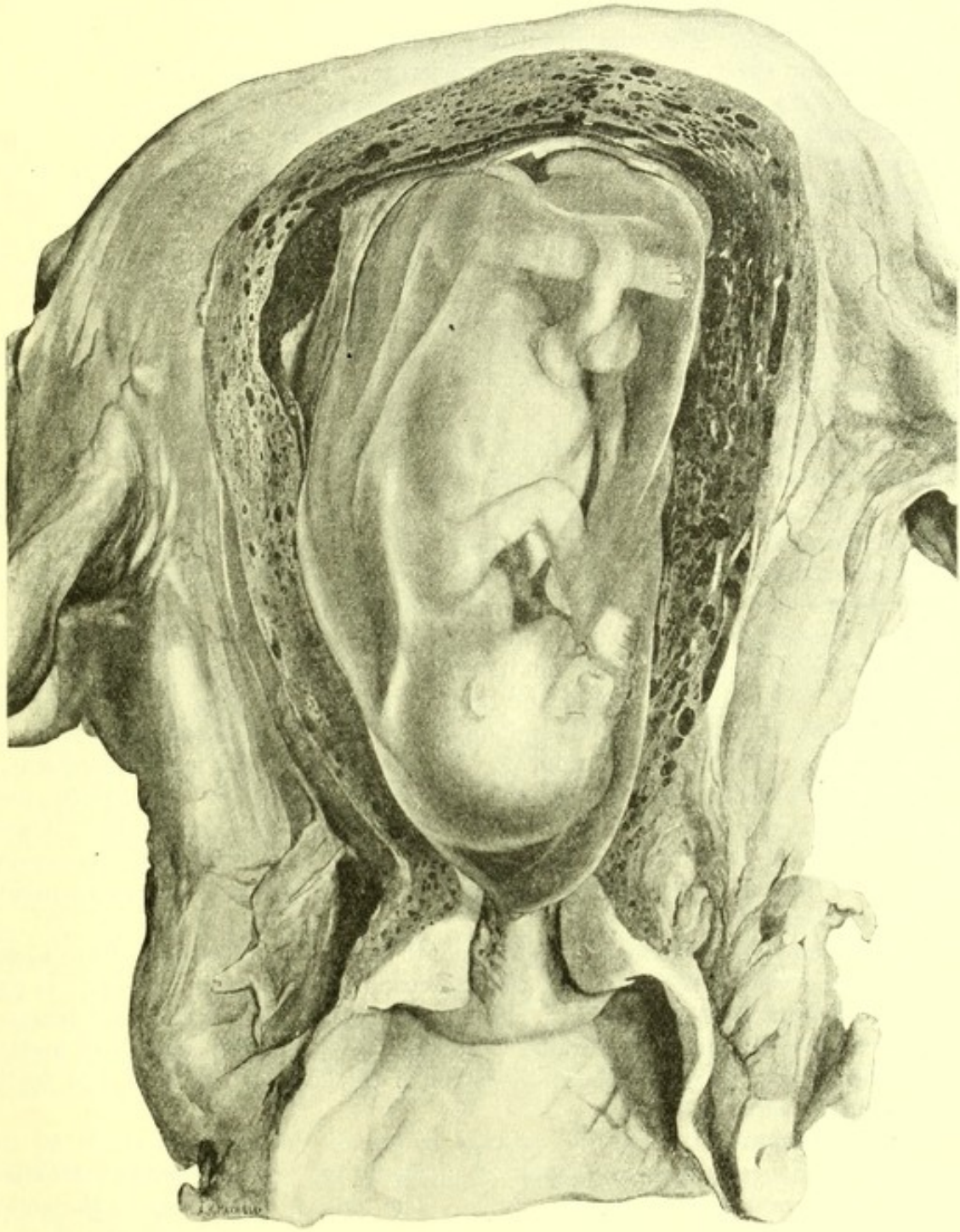


FIG. 129.—PREGNANT UTERUS OF THE FOURTH MONTH.

The anterior wall of the uterus has been removed to show the fœtus in the amnion. (By permission, from a preparation in the Hunterian Museum, University of Glasgow.)

the toes do not reach the free border till the seventh week ; the foot is still in the same plane with the leg. By the end of the eighth week the limbs extend beyond the body, but the legs are still smaller than the arms. The thumb projects at an angle different from the other fingers. The ankle-flexure now begins to show, but the limbs are so rotated that the soles of the feet look towards one another.

The tail, which began to disappear in the sixth week, is still distinct at the end of the second month, but reduced to a minute tubercle. The human characters are all established, and the embryo may now be spoken of as the *fœtus*.

**Third month.**—Fig. 128 shows the general relations of fœtus and uterus at the beginning of the third month. The decidua capsularis is not yet fused with the decidua vera. It is still a thickish layer intimately associated with the villi of the chorion læve. The amnion fills the whole chorionic vesicle. The umbilical cord is a short, stout, and now twisted structure. The fœtus by the end of the month measures about 7 cm. from vertex to coccyx. All its parts have nearly assumed their relative proportions, though the head is still large. The eyelids and lips are closed, and the auricle folded. The nails have appeared on fingers and toes, and the external genital organs are apparent. The vitelline loop of the intestine is now withdrawn into the body-cavity.

**Fourth month** (fig. 129).—During the fourth month the fœtus increases to 12 cm. or 13 cm. in length from vertex to coccyx. The muscles are now so far developed as to give rise to movements of the limbs and body.

The skin becomes firmer, and is rose-coloured. Short colourless hairs appear on the head, and finer downy hairs over the rest of the body. The chin is a more prominent feature, the arms and legs are of nearly equal length, the umbilicus is situated close above the pubes, and the sex characters are fully established.

**Fifth month.**—By the end of the fifth month the fœtus measures about 20 cm. from vertex to coccyx, and 25 cm. to 27 cm. if the legs be included in the measurement. Its weight is now about half a kilogramme. The skin shows patches of sebaceous matter, and the hair is better developed. The legs are longer than the arms, and the umbilicus lies farther forwards.

**Sixth month.**—At the end of the month the length of the fœtus from vertex to heels is 30 cm. to 32 cm.; it has doubled its weight, which is now about one kilogramme. The skin is wrinkled and dull red in colour. Sebaceous matter has increased, especially in the axillæ and groins. The hair is darker and stronger, and the eyebrows and eyelashes appear. The umbilicus is still farther forwards.

**Seventh month.**—The length of the fœtus at the end of the month, from vertex to heels, is about 35 or 36 cm.; it weighs about 1½ kilogrammes. Owing to the deposit of subcutaneous fat, the body has become plumper; the eyelids re-open, and the hair is now plentiful on the head. The fœtus, if born at this period, is capable of surviving.

**Eighth month.**—During the eighth month the fœtus increases to 40 to 45 cm. in length from vertex to heels, but the increase in bulk is more marked; it now weighs from 2 to 2½ kilogrammes. The skin loses the dull red tint, and becomes of a bright flesh-colour. Its surface is covered all over with sebaceous matter, now known as the *vernix caseosa*; the layer is thickest on the head and in the axillæ and groins.

**Ninth month.**—At birth the average length of the fœtus is about 50 cm. from vertex to heels, that is, about 20 inches; the average weight is about 3 to 3½ kilogrammes, or 6½ to 7½ pounds. The skin is paler than in the eighth month, the body is more plump and rounded; the hair is long and abundant on the head, but the downy hair (lanugo) on the body has begun to disappear. The umbilicus now occupies the centre of the body.[1]

[1] For literature other and later than His's Anatomie menschlichen Embryonen, Leipzig, 1885, and Archiv Anat. u. Phys. Anat. Abt., 1892, see Keibel in Hertwig's Handbuch, I. Teil i., ii. 174; and general literature list, I. Teil i. 83; P. Michaelis, Arch. Gynäkol. lxxviii.; Retzius, Biol. Untersuchungen, N.F. xi., Stockholm, 1904. Kollmann (Handatlas Appendix, p. 37) gives a full list of papers. In addition are the following: Gage, Amer. Jour. Anat. iv.; Bremner, Amer. Jour. Anat. v.; Bonnot and Seevers, Anat. Anzeiger, xxix.; P. Thompson, Jour. Anat. Phys. xli.; Ingalls, Arch. mikr. Anat. lxx.

## Section II.

# DEVELOPMENT OF THE ORGANS OF THE BODY.

**Classification.**—The organs of the body are generally classified according to the germinal layer from which their primary or *specific elements* are derived, but the middle layer enters into the construction of all organs inasmuch as their connective-tissue framework, sheathing or covering membranes, and blood-vessels are derived therefrom. From the histological point of view such a classification is of importance, because the tissues springing from the several layers show a certain specific character, both in their history and structural features. This is especially true of the epithelia derived from the two primary layers, and it holds also, though less rigidly, for the derivatives of the dorsal, gastral, or epithelial mesoderm. The second order of mesoderm—the so-called mesenchyme—is, however, a blastema of more heterogeneous characters.

With these reservations, the following classification will form the general basis of the descriptive account of organogeny. From the **ectoderm** are derived the epidermis and dermal appendages (hair and nails); the epithelium of the sebaceous and sweat glands as well as of the mammary gland; of the mouth (in part); of the anal canal (in part); of the nasal passages as well as of the glands and cavities opening thereinto; the glandular part of the pituitary body; the enamel of the teeth; the whole central and peripheral nervous system; the epithelium of the sense-organs; the sympathetic-chromophil system, and medulla of the suprarenal body. From the **entoderm** are derived the epithelium of the alimentary canal and all the glands connected therewith; of the Eustachian tube and tympanum; of the larynx, trachea, bronchi, and pulmonary alveoli; of the thyroid and thymus; of the urinary bladder and of part of the urethra. From the **epithelial mesoderm** are derived the voluntary muscles; the epithelium of the Wolffian and Müllerian ducts, and of the excretory tubules both of Wolffian body and kidney; the epithelial lining of the body-cavity; the cortex of the suprarenal body; the genital cords of ovary and testis (and perhaps the germ-cells). From the **mesenchyme** are derived the connective tissues, the involuntary muscular tissue, the spleen, hæmolymph and lymphatic glands, the endothelial lining of the heart, blood and lymph vessels, the red blood-corpuscles, and perhaps the lymph-corpuscles.

## DEVELOPMENT OF THE SKIN, CUTANEOUS GLANDS, ETC.

In the section dealing with the formation of the embryo on the blastoderm, it has already been noted that the ectoderm is early differentiated into a thickened axial plate, the neural plate, and thinner lateral portions. When the neural canal has become closed and the embryo is separated from the yolk-sac, the surface ectoderm forms a continuous layer which gives rise to the epidermis. The ectoderm at first consists of an epithelial layer of more or less columnar cells; but in the stage represented in fig. 81, p. 56, it has taken the form of a thin lamella of apparently continuous granular protoplasm with a single layer of nuclei regularly and closely disposed. By the end of the first or beginning of

the second month this layer has resolved itself into two lamellæ—a deeper of polyhedral cells, and a superficial of flattened cells, the rudiment of the *stratum corneum* of the skin. As development proceeds, both of these layers increase in thickness, and several cellular strata are laid down. By the fifth month the surface cells begin to be shed, and form with the secretion of the sebaceous glands the cheesy layer on the skin of the fœtus known as the *vernix caseosa*. Meantime, the underlying mesenchyme has differentiated into a connective-tissue layer which becomes the corium or true skin, and projections from this develop into the vascular papillæ. The epithelium of the glands is formed from the deeper layer of the primitive epidermis. Solid processes grow inwards from this into the mesenchyme; in these a lumen is developed later. The sweat-glands open on to the surface, but the sebaceous glands are formed in connexion with primitive ingrowths of the epidermis, which give rise to the hairs and their root-sheaths. The surrounding mesenchyme gives rise to the connective-tissue elements of the glands, the sheaths, and papillæ of the hairs, and also to the muscular tissue of the *arrectores pilæ* muscles and muscular tissue of the sweat-glands.[1]

The primitive downy hair of the fœtus is known as the *lanugo*. It is partly shed in the later months of pregnancy, and is replaced after birth by permanent hair.

## DEVELOPMENT OF THE NERVOUS SYSTEM.[2]

As has been already described, the whole of the central nervous system takes origin from the thickened walls of a dorsally situated axial groove, subsequently converted into a canal, which runs forwards in front of the primitive streak. The anterior end of this canal becomes enlarged and converted by constrictions into three vesicles, around which the several parts of the brain are formed. These enlargements are known as the primary cerebral vesicles. The rest of the neural canal remains of nearly uniform diameter; its walls become converted into the substance of the spinal cord, while the cavity itself becomes eventually the central canal of the cord. The walls of the neural groove are of course composed of ectoderm, and it therefore follows that the whole structure of the central nervous system is laid down in that layer, and consists in the main of more or less modified ectodermic elements, except where mesodermic tissues subsequently penetrate into it, conveying blood-vessels into its substance. The same is in all probability true for all the nerves of the body, cranial and spinal.

**Histogenesis of nervous tissue and peripheral nerves.**—Before entering on a description of the phases through which the neural canal passes as the brain and spinal cord take form, it will be convenient to give a general account of the changes by which the ectoderm of the wall of the canal is converted into nervous tissue. The changes are in essence the same in all parts of the tube, and in all vertebrates.

The neural plate consists at first of a layer of columnar epithelium. The divisional planes between the cells are rather ill-defined. The outer ends of the elements are composed of granular protoplasm, the inner ends are finely striated. The nuclei are in several ranges, placed at different levels; the innermost are almost without exception in one phase or another of karyokinesis (fig. 130). Proliferation is thus taking place on the free surface (afterwards the inner surface of the closed neural canal), and through all successive phases this zone of dividing nuclei persists until a certain stage of development is reached. It is therefore

[1] Some authorities derive the muscular tissue of the sweat-glands from the ectoderm.

[2] The literature concerning the morphogenesis of the central nervous system in the Primates will be found in Ziehen's article in Hertwig's Handbuch II. Part III. p. 386 *seq.*; that concerning histogenesis, *ibid.* p. 434 *seq.* For the literature of the development of the peripheral nervous system see Neumayer, *ibid.* p. 621 *seq.* References to more recent papers mentioned in the text are given in the footnotes.

spoken of as the *germinal zone*. The second stage is characterised by a disappearance of cell-outlines, so that the wall of the canal appears formed of continuous protoplasmic columns. These then break up (third stage) into a mesh-work

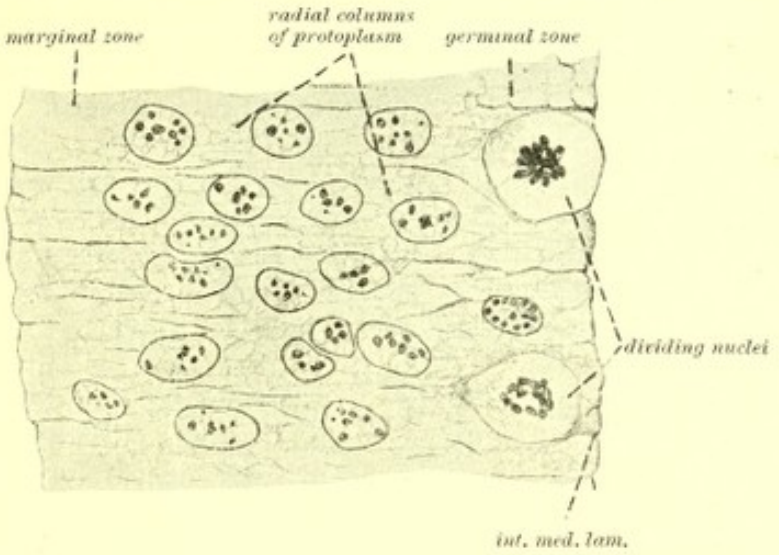



FIG. 130.—SECTION OF THE WALL OF THE NEURAL CANAL FROM AN EMBRYO PIG, JUST AFTER THE CLOSURE OF THE NEURAL GROOVE. (Hardesty).

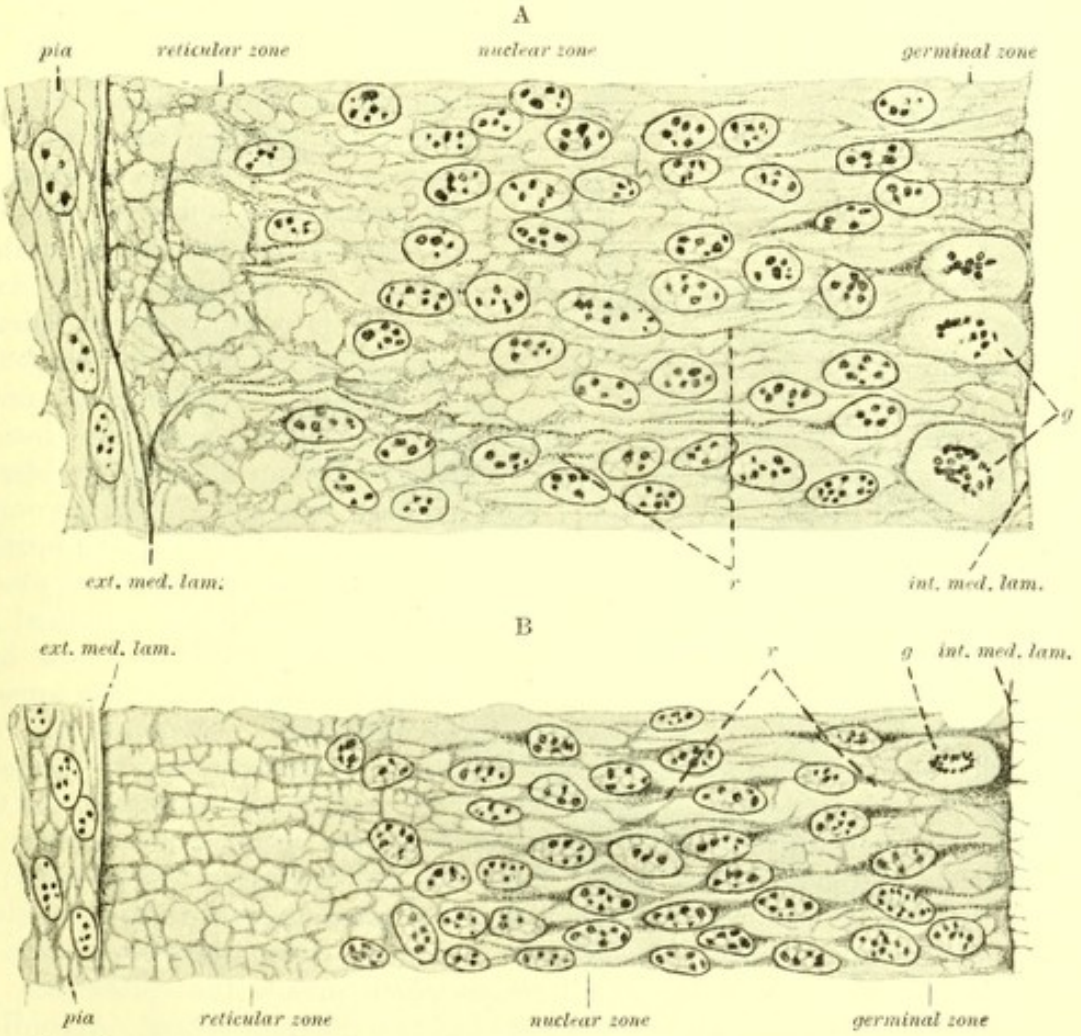



FIG. 131.—SECTIONS OF THE WALL OF THE NEURAL CANAL OF THE PIG AT LATER STAGES THAN THAT SHOWN IN FIG. 130. (Hardesty).

A, from an embryo of 7 mm.; B, from an embryo of 10 mm.; *g*, dividing nuclei in germinal zone; *r*, filaments of myelospongium.

(His [1]), in which the trabeculæ have, in a general way, a radiating disposition, and the oval nuclei, which are distributed throughout the whole thickness of the wall, have a vertical direction (fig. 131A). On both the inner and outer surfaces the trabeculæ fuse to form a limiting membrane (*membrana limitans interna* and *externa*). The nuclei now become densely crowded in the central part of the thickening wall of the tube, and on the outer aspect a layer appears in which there are no nuclei. It is crossed by delicate, radially disposed, protoplasmic strands, which break up into a system of anastomosing threads. The original epithelium has thus been converted into a protoplasmic framework (*myelospongium*), which has a columnar and radial disposition and shows three layers : (1) An inner *germinal zone* ; (2) a middle nuclear *mantle zone* ; and (3) an outer nuclear-free *reticular* or *boundary zone*. The columns of the framework are not separate, long-drawn-out epithelial cells, but the radial trabeculæ of a continuous syncytial network, which are more accentuated than the side branches (Hardesty [2]). In the germinal zone the dividing nuclei are separated by delicately striated columns of protoplasm which broaden out and fuse into the internal limiting membrane (fig. 131B). This appearance is due to the persistence in this inner layer of the second stage of the epithelium, when the cell-outlines have disappeared and it consists of columns of protoplasm. The inner zone is afterwards, when the nuclei have ceased to divide, resolved into the ependymal lining of the canal, and each ependymal cell is continued, through the thickness of the wall of the tube, into a fibre which represents a radial strand of the myelospongium (fig. 132). During the transformation of the neural epithelium into the myelospongium nuclear proliferation has been very active, and the crowded nuclei in the mantle zone (during the third stage) are obviously the products of the divisions in the germinal zone. Among them there can now be detected certain nuclei which appear to belong to pear-shaped cells with long tapering processes. These are the future nerve-cells, and were named by His *neuroblasts* in contradistinction to the cells of the framework which he termed *spongioblasts*. It is generally admitted, the existence of two categories of cells in the early stages being allowed, that both spongioblasts and neuroblasts spring from the multiplying ectoderm-cells ; and further it is believed that the neuroglia-elements of later stages are also of ectodermic origin, though mesodermic elements—*i.e.* common connective-tissue cells—are necessarily introduced with the blood-vessels which invade the epithelium. The appearances described have been interpreted in two different senses. According to the interpretation hitherto almost universally accepted and due to His, each neuroblast has a separate and isolated protoplasmic body from which a single

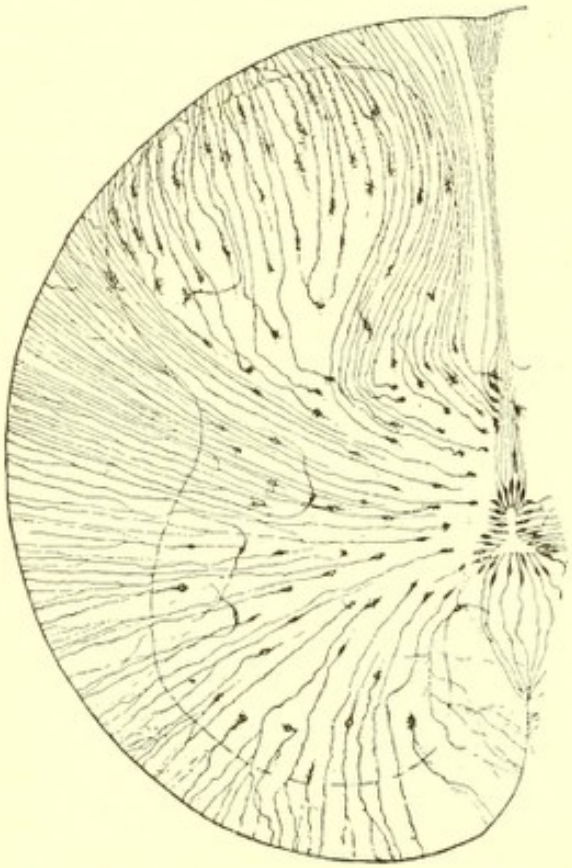


FIG. 132.—SECTION OF THE SPINAL CORD TO SHOW THE ARRANGEMENT OF THE EPENDYMAL AND GLIAL FIBRES OF THE DEVELOPING CORD. (Lenhossék.)

[1] Die Entwickelung des menschlichen Gehirns während der ersten Monate ; Leipzig, 1904.
[2] Amer. Jour. of Anat. ii. 1904.

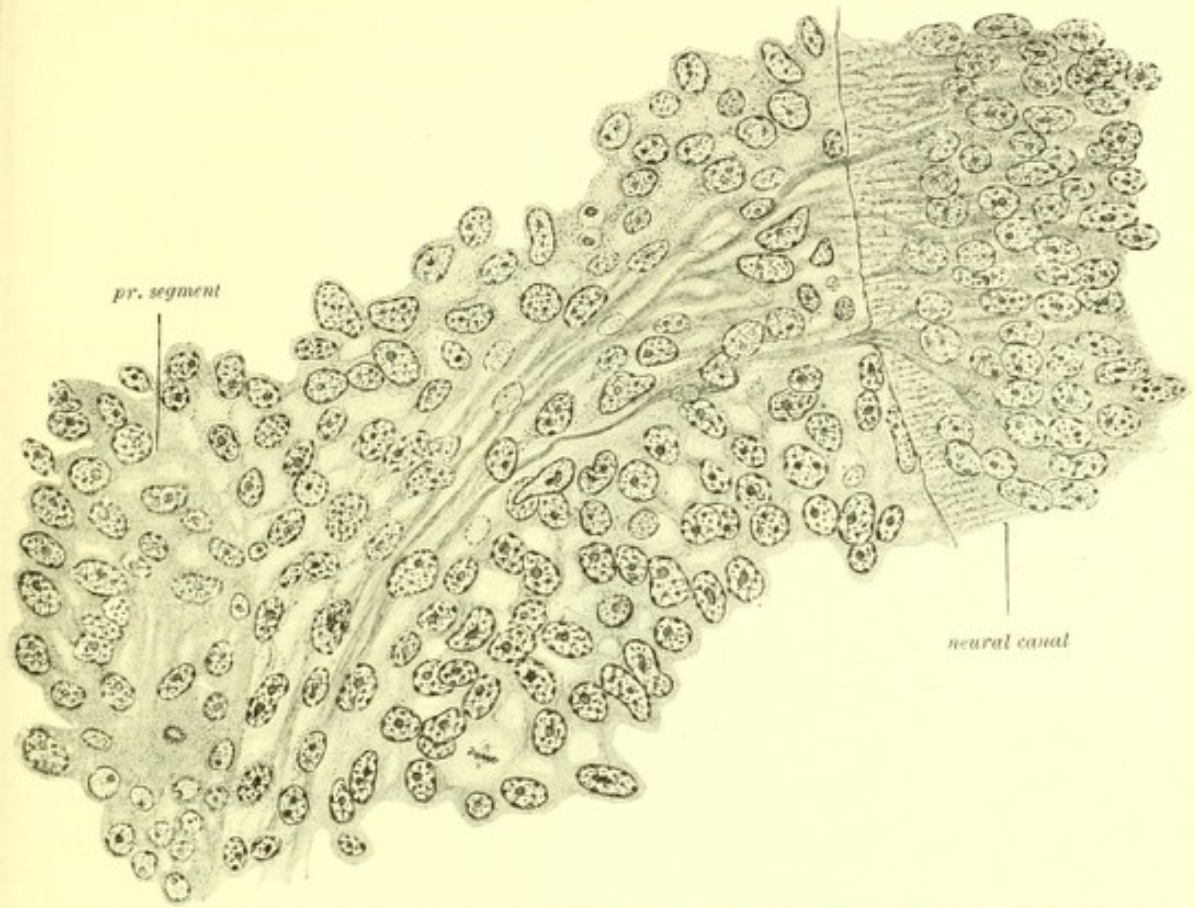



FIG. 133.—VENTRAL ROOT OF A SPINAL NERVE WITH THE SURROUNDING MESENCHYME IN A RABBIT-EMBRYO OF THE ELEVENTH DAY. (T. H. Bryce.)

FIG. 134.—PRIMITIVE SPINAL NERVE-TRUNK IN AN EMBRYO OF LEPIDOSIREN PARADOXA. (Graham Kerr.)

*np.*, wall of neural canal; *n.t.*, nerve-trunk; *mes*, mesenchyme-cell; *pr.s.*, primitive sheath; *my*, myotome. The white bodies are yolk-grains.

protoplasmic process grows to become the axis-cylinder process of the future nerve-cell, and by further extension a nerve-fibre. The dendritic processes are secondary outgrowths which, according to the manner of their branching, confer distinctive characters on the several varieties of nerve-cells. The neuroblasts occupy the spaces of the myelospongium, and the nerve-fibre processes thread its interstices. The spongioblasts form supporting elements merely. According to another interpretation, founded on the conception of nerve-tissue put forward by Apathy and Bethe, and advocated by Held,[1] the neuroblasts are cells of the syncytium in which neurofibrillæ are differentiated. These form a plexus in the cell-body, surround the nucleus and extend first, as a chief bundle (pear-shaped stage), through one of the cell-bridges and along a definite path through the syncytial framework to form the axis-cylinder process, and later into the other cell-bridges to form the dendrites. While this interpretation differs from the first in so far as that the nerve-fibres are regarded as neurofibrillar tracts in the substance of the myelospongium, not free processes threading its meshes, the two theories agree in respect that the nerve-fibre is represented as an active outgrowth from the nerve-cell. On this point Held's view differs from that of Apathy, who conceives the conducting fibrillæ as being laid down *in situ* along a protoplasmic path provided by cells ('nerve-cells') united into a syncytium.

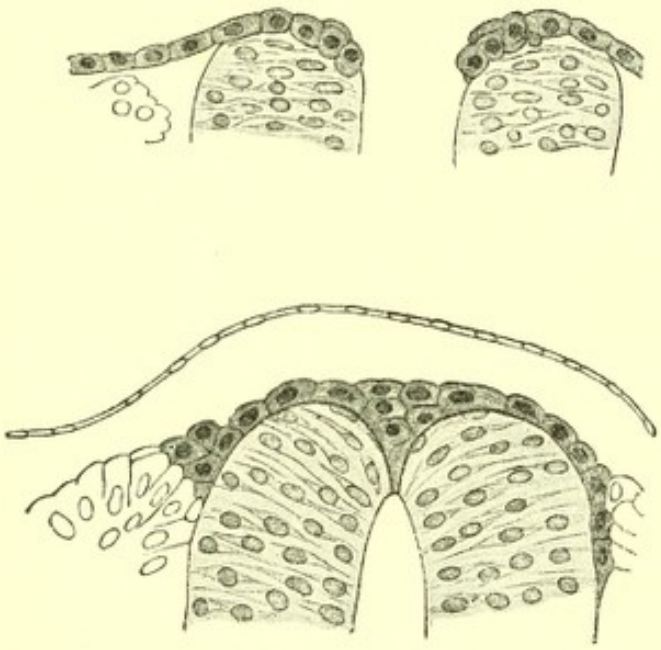


FIG. 135.—TWO STAGES IN THE DEVELOPMENT OF THE NEURAL CREST IN THE HUMAN EMBRYO. (Lenhossék.)

**Origin of the nerve-roots.**—The *motor nerve-roots* appear before the sensory. In mammalian embryos, when first detected, the rudiments of the motor nerves appear as bundles of extremely delicate protoplasmic fibrillæ extending among the mesenchyme-cells from the wall of the neural tube, within which the bundles can be traced backwards through the commencing reticular framework to neuroblasts in the mantle zone (fig. 133). Followed outwards, they pass towards the myotome (fig. 134). In the case of the spinal nerves each motor root is joined by a contingent of fibrillæ from the spinal ganglion, and the mixed nerve so formed is seen extending into the Wolffian ridge along the mesial aspect of the growing muscle-rudiment.

The *sensory roots* are developed from primitive ganglia which arise from the neural crest. This is formed of cells derived from the ectoderm at the angles of the neural folds (fig. 135). From the sides of the crest cells are budded off into the space between neural canal, myotome, and surface ectoderm, and are there collected into paired groups, which are the rudiments of the spinal and cranial nerve-ganglia. In the trunk these are segmentally disposed. It is possible that only a certain proportion of the cells are so utilised, for there is reason to believe that some of them wander farther afield. Each ganglion is at first connected with the side of the neural tube by a

[1] Anat. Anzeiger, Ergänzungsheft, xxix. 1906; and Anat. Anzeiger, xxx. 1907.

cord of ectoderm-cells. Differentiation next occurs in the ganglion exactly as it does in the neural tube, and bundles of fibres appear among the cells. These extend through the cellular strand (fig. 136) and enter the wall of the neural tube, where they form a special bundle in the reticular zone (see p. 101). From the opposite end of the ganglion, bundles of fibres extend peripherally and join the fibres of the ventral root to form the mixed nerve-trunk. The picture presented by a preparation of a developing spinal ganglion stained by the Golgi method shows that the bundles of fibres are proximal and distal processes of bipolar neuroblasts, or, as Held believes, bundles of neurofibrillæ extending proximally and distally from the ganglion-cells through a syncytium into which the primitive ganglion has been resolved. The mixed nerve-trunks are at first composed of rather loosely arranged fibrils, but soon they appear as tracts of compactly arranged bundles of fibres which, traced outwards, divide up, and finally have the appearance of ending freely as single fibres, on which a terminal enlargement is shown by the Golgi method of staining. This terminal enlargement is highly characteristic of developing nerve-fibres.

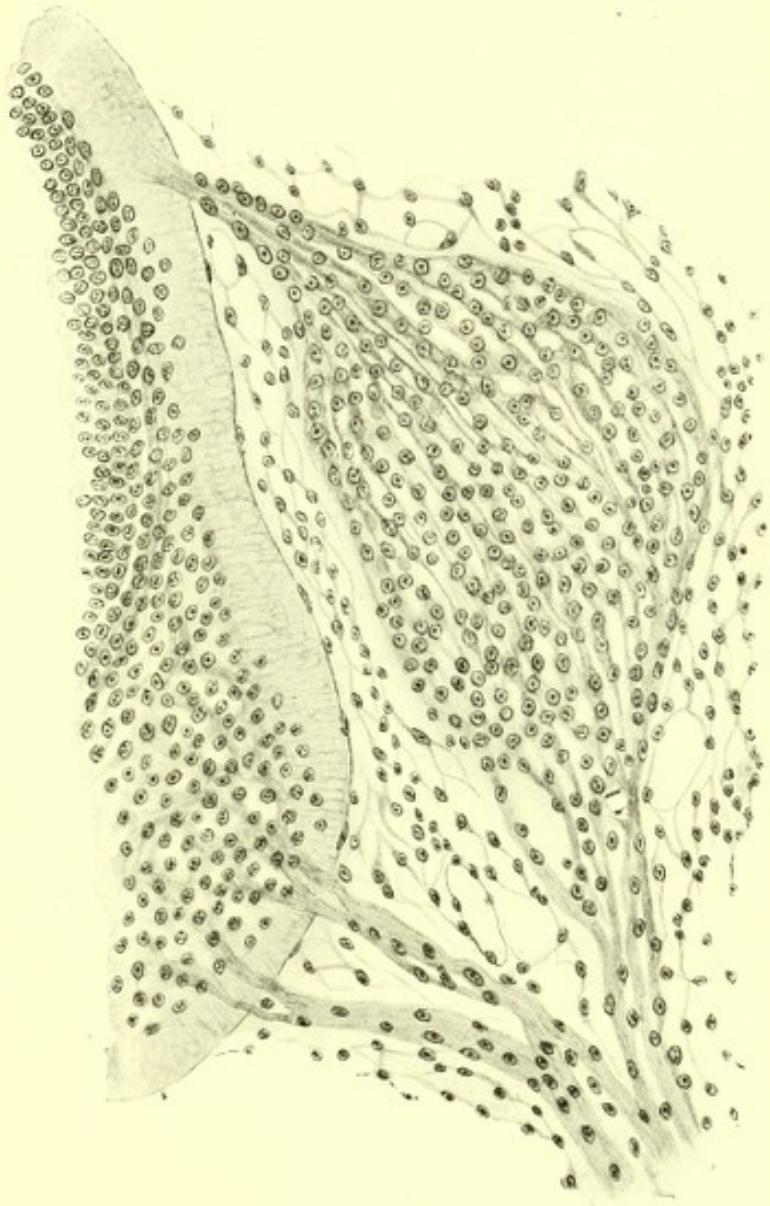


FIG. 136.—SPINAL GANGLION AND ANTERIOR NERVE-ROOT IN A RABBIT-EMBRYO OF THE TWELFTH DAY. (T. H. Bryce.)

The developing nerve-paths are studded with nuclei. It is generally agreed that these represent the nuclei of the future sheath of Schwann, but opinion is divided as to their origin.

It is not possible here to give more than the briefest notice of the main hypotheses which have been advanced regarding the mode of formation and growth of nerve-fibres. They may be represented in tabular form thus:

I. *Outgrowth theory* (Bidder, Kupffer, His, Cajal, Kölliker, Lenhossék).—Each nerve-fibre is the process of a nerve-cell (neuroblast) which by *free terminal growth* seeks out its proper end-organ and comes *secondarily* into relation with it. In the case of the bipolar neuroblasts there is growth in two directions.

II. *Cell-chain theory* (Balfour, Marshall, Dohrn, van Wijhe).—Each nerve is the product of a chain of medullary ectoderm-cells, which extends by proliferation and establishes a *secondary nexus* between central and end organ.

III. *Syncytial nucleated network theory* (O. Schultze).—There is a *primary nexus* between central and end organ in the form of a network of anastomosing cells, which becomes differentiated nto nerve-fibres. Apathy's conception of a plexus of '*nerve*'-cells in which neurofibrillæ are deposited to join up '*ganglion*'-cell and end-organ is closely akin to this.

IV. *Outgrowth with early union theory* (Hertwigs).—The end organ is brought very early nto connexion with the central organ by a protoplasmic process which is differentiated into a nerve and pulled out as the organs draw apart.

V. *Primitive-nerve theory* (Baer, Hensen, Sedgwick).—There is a *primary nexus* between central and end organ in the form of protoplasmic strands which become fibrillar, and are drawn out into nerve-fibres as the organs draw apart.

VI. *Primitive nexus and outgrowth theory* (Held).—There is a primitive protoplasmic nexus between central and end organ, along which neurofibrillæ grow from the nerve-cell outwards.

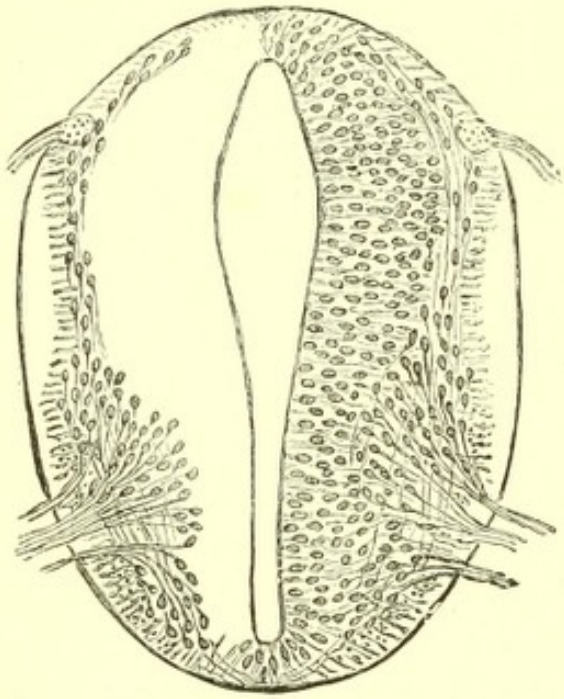


FIG. 137.—SECTION OF SPINAL CORD OF FOUR-WEEKS HUMAN EMBRYO. (His.)

The dorsal roots are continued within the cord into a small longitudinal bundle which is the rudiment of the dorsal white column. The anterior roots are formed by the convergence of the processes of the neuroblasts. The latter, along with the elongated cells of the myelospongium, compose the grey matter. The external layer of the cord is traversed by radiating fibres which are the outer ends of the spongioblasts. The ventral commissure is beginning to appear.

In the first stage of the nerve the path is non-nuclear, being furnished by Szily's inter-epithelial network (see p. 59); in the second stage it is nucleated, being provided by the cellular (mesenchymic) syncytium.

The sheath of Schwann is variously interpreted. According to theories III. and IV., the nuclei of the sheath are those of the cells entering into the formation of the nerve-fibre, while the remaining hypotheses refer them to a secondary investment either of mesenchyme, or of ectoderm cells derived from the ganglion-crest, or from the neural tube along the motor root. It has been stated above that the fibrous stage of the dorsal roots of the ganglia is preceded by a cellular stage, and the same is true of the peripheral branches of certain purely sensory nerves (A. F. Dixon[1] and others). When the fibrous stage is established these cells envelop the nerve-fibres. It would appear probable from this that the sheath of Schwann has an ectodermic origin in sensory nerves; and that the same is true of the motor nerve-fibres is pointed to by Harrison's experiments in which the motor nerves were found to develop without a cellular sheath in tadpoles from which the neural crest had been removed by operation (the dorsal roots remaining of course undeveloped). This derivation of the sheath-cells from the neural-crest ectoderm has suggested that the peripheral extension of the nerves may be associated with a continuous proliferation of indifferent cells which may become ganglion-cells in the sympathetic, or sheath-cells, in the nerve-trunks (Kohn). On the other hand, the evidence is strong in some cases that the mesenchyme-cells furnish a nutritive sheath to the developing nerve (figs. 133, 134), and it seems not impossible that the nuclei in and around the nerve-path may be derived from both sources.

The outgrowth-theory of His has been very generally accepted by anatomists and physiologists as the embryological basis of the *Neurone-theory*, and it has obtained its chief support from the Golgi method of staining, as applied more especially by Ramon y Cajal. But, as will be obvious from the above statement of the various views which are prevalent on this subject, His' theory is by no means universally admitted. The work of Held seems to show that, while

[1] Trans. Roy. Dublin Soc. vi. (Series II.), 1896.

the main principle underlying the theory may be maintained, the divergent results of different observers in matters of detail cannot yet be brought into line in any general hypothesis.

## MORPHOGENESIS OF THE SPINAL CORD AND BRAIN.

**SPINAL CORD.**—By the end of the first month the neural canal in the region of the trunk shows, instead of the primitive rounded cavity, a narrow cleft-like lumen, which widens somewhat at its dorsal end (fig. 137). This change is

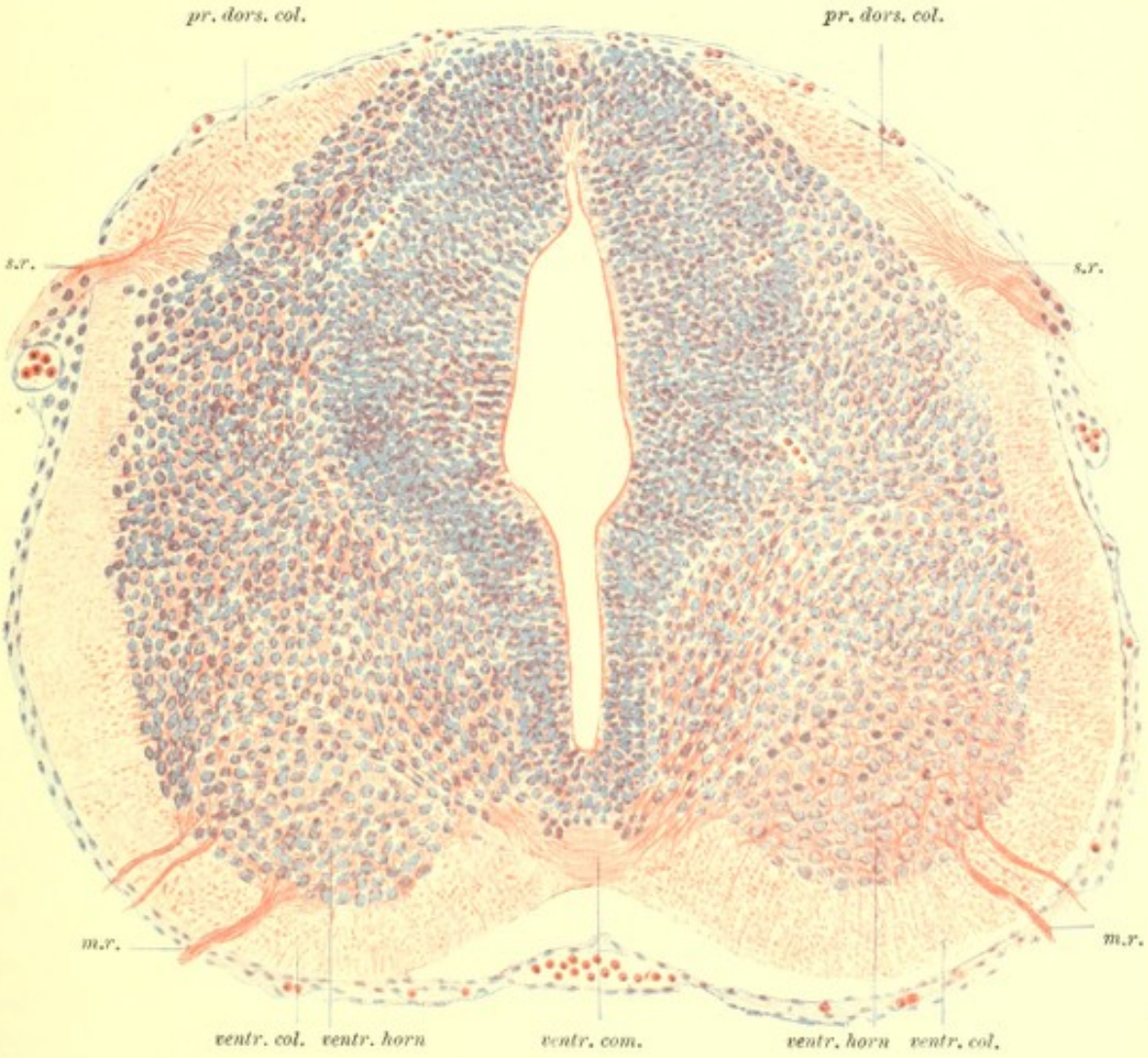



FIG. 138.—SPINAL CORD OF A HUMAN EMBRYO OF 15·5 MM. (T. H. Bryce.)

*ventr. com.*, ventral commissure; *ventr. col.*, ventral column: *ventr. horn*, primitive ventral horn; *pr. dors. col.*, primitive dorsal column; *m.r.* motor, *s.r.* sensory root.

due to thickening of the lateral walls, which shows the three zones already described—inner *ependymal*, middle *mantle*, and outer *reticular*; while the roof and floor are represented merely by the ependymal lamella. The mantle zone shows large numbers of neuroblasts whose nerve-fibre paths tend towards the ventro-lateral aspect and leave the cord as the ventral nerve-roots. By the end of the fifth week (fig. 138) the lumen shows a dorsal and ventral narrowing and a mesial expansion, indicating a later demarcation of the lateral walls into dorsal or *alar*, and ventral or *basal* plates. The ependymal roof projects beyond the general surface as a convex swelling, and on each side of this is a portion of the

reticular zone, which is connected with the dorsal nerve-roots, and is known as the primitive dorsal column. Ventrally the mantle zone is much expanded, and forms the rudiment of the ventral horn of the grey crescent on each side; while over this the reticular zone is thickened, and projects as the primitive ventral column. The rudiment of the ventral horn is in the fifth week (fig. 138) sharply marked off from the rest of the mantle zone by the character of its rounded and less deeply staining nuclei. The ventral root-fibres can be seen emerging from the ventro-lateral aspect. Between the horn and the central canal the fibre-paths all tend towards the ventral commissure. Between the dorsal and ventral expansion is a recessed area in which the boundary zone is very thin. In succeeding stages this

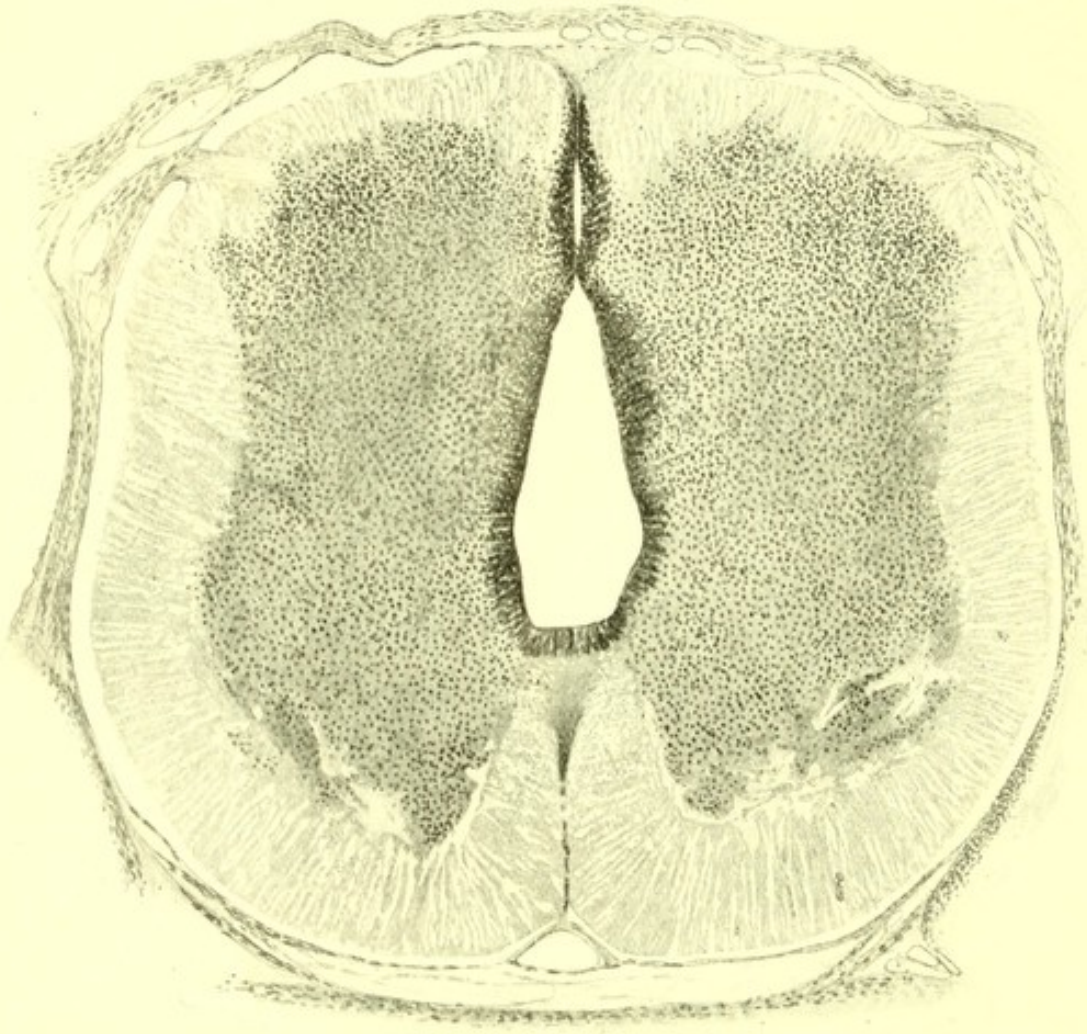


Fig. 139.—Section of the spinal cord of a human embryo of 30 mm. (T. H. Bryce.)

is gradually filled up, until the ventral projection reaches the dorsal root, and the continuous ventro-lateral column is laid down. The mantle zone of this region becomes the dorsal horn of the grey crescent. It is at first separated from its fellow by the now slit-like dorsal portion of the lumen, but it later becomes isolated as the dorsal septum is laid down.

The *anterior* or *ventral median fissure* is at first a shallow recess between the projecting primitive ventral columns. As these grow in dimensions the lips of the fissure close in to form a narrow cleft, which encloses a process of pia mater developed from the mesenchyme surrounding the cord. At the bottom of the fissure the *anterior* or *ventral commissure* is laid down by the extension of nerve-fibres across the middle line.

The so-called *posterior* or *dorsal median fissure* appears first in the sixth week as a distinct infolding of the dorsal plate towards the lumen. At this time the primitive dorsal columns are still separated by the projection of the plate on the dorsal aspect of the cord. In the succeeding weeks the upper part of the primitive canal appears to be obliterated, and only the ventral portion persists as the definitive central canal of the cord. The apparent closure of the lumen is associated with great expansion of the primary dorsal columns (future *tracts of Burdach*) and the formation of new mesial columns (future *tracts of Goll*) (fig. 139). As these columns increase in size, the dorsal horns of the grey crescents are isolated and clothed on their mesial aspects by white substance. Meanwhile the walls of the dorsal part of the central canal become apposed, and the ependymal cells become obliquely arranged, the obliquity of their direction increasing as the dorsal wall is approached. From this a mesial fibrillar septum extends to the free surface. These appearances suggest that the canal is not obliterated by a simple fusion of its walls, but, on the other hand, they cannot be explained wholly by the growth of the posterior columns and posterior horns with persistence of the primary canal and extension of the primary infolding of the dorsal plate. Both factors probably share in the process.

The end part of the central canal is expanded into what has been termed the *terminal ventricle*. It forms the dilated part of the central canal in the conus medullaris.

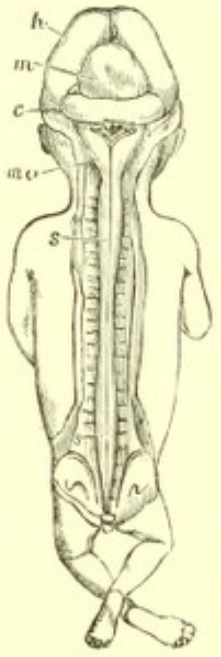



FIG. 140.—BRAIN AND SPINAL CORD EXPOSED FROM BEHIND IN A FŒTUS OF THREE MONTHS. (From Kölliker.)

*h*, the hemispheres; *m*, the mesencephalic vesicle or corpora quadrigemina; *c*, the cerebellum; below this are the medulla oblongata, *mo*, and fourth ventricle, with remains of the membrana obturatoria. The spinal cord, *s*, extends to the lower end of the sacral canal, and shows brachial and crural enlargements.

In the sixth week the lateral walls show a distinct separation into *alar* and *basal laminæ*. With the former the afferent nerve-fibres become connected; while from the latter the efferent fibres take origin (His).

The characteristic cylindrical form of the cord is only attained with the development of the lateral columns. The cervical and lumbar enlargements are manifest at the end of the third month (fig. 140).

Up to the fourth month, the cord and the vertebral canal increase in length *pari passu*, but the vertebral column then begins to grow more rapidly than the cord, so that by the time of birth the coccygeal end of the cord is opposite the third lumbar vertebra, while in the adult its limit is the lower end of the first lumbar. Along with this relative shifting of the cord and its containing tube the lower nerve-roots lose their regular rectangular course, and become oblique. They alone, with the *filum terminale*, occupy the lower end of the neural canal, where they form the *cauda equina*.

The nerve-fibres of the white columns are at first entirely non-medullated, and the white substance has a greyish transparent appearance. The medullary sheath is not formed simultaneously in all parts, but appears at different times in different

[1] In the figures published by His of the developing spinal cord, certain other folds of the wall are represented. Wilson (Jour. of Anat. and Phys. vol. xl.) has recently again drawn attention to these folds. He suggests that they have morphological significance, and may possibly indicate a triple division of the neural tube. It is doubtful, however, how far such folds or furrows are to be regarded as normal. The appearance of the basal plate (see fig. 138) seems to be correlated with the earlier differentiation of the motor region of the mantle zone. In a well-fixed embryo of 15·5 mm. (obtained at an operation), and in one of 21 mm. I cannot satisfy myself that there are any irregularities of the wall of the canal such as are seen in His' figures.—T. H. B.

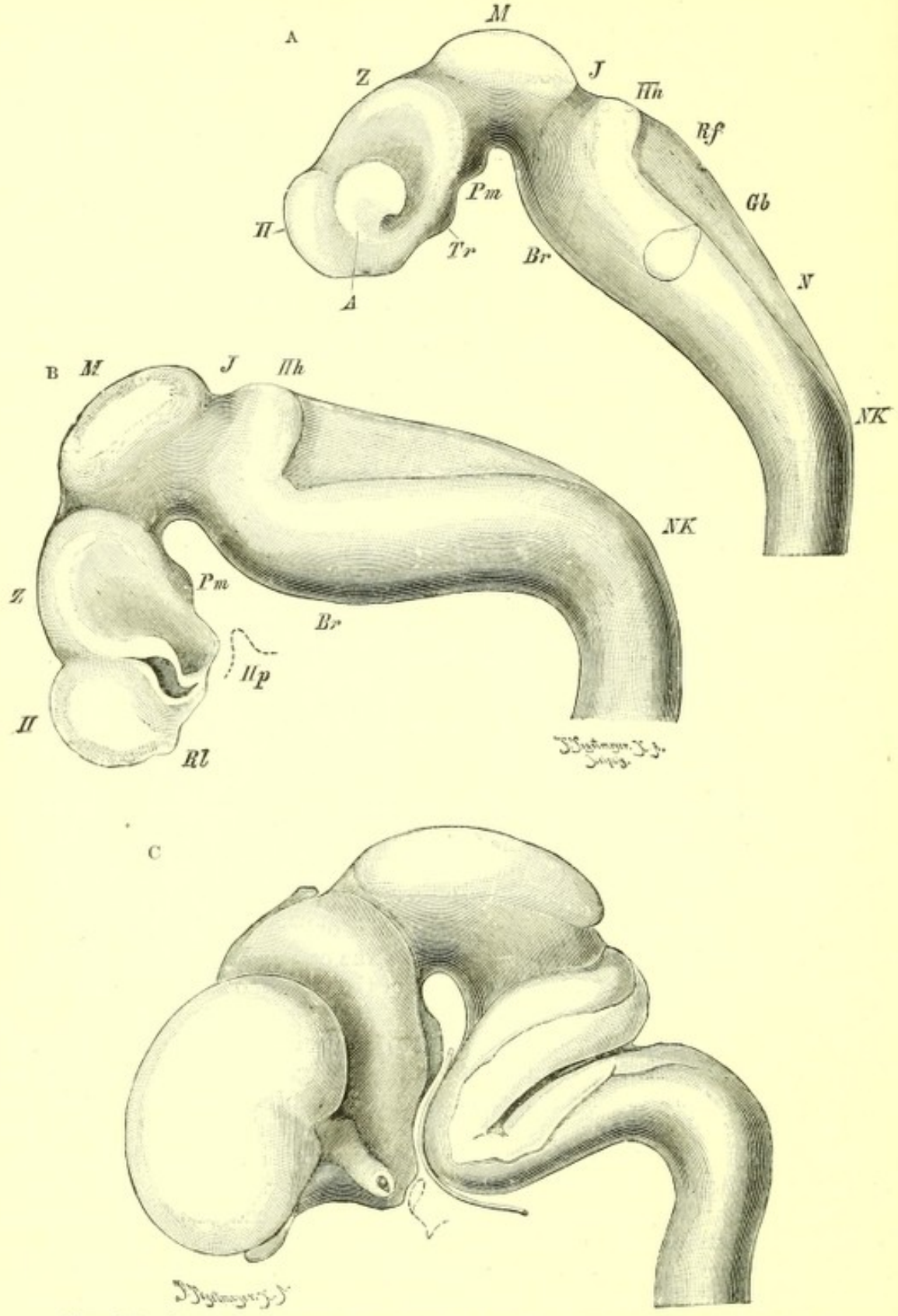



FIG. 141.—PROFILE VIEWS OF THE BRAIN OF HUMAN EMBRYOS AT SUCCESSIVE STAGES, RECONSTRUCTED FROM SECTIONS. (His.)

A. Brain of an embryo of about fifteen days (the embryo itself is shown in fig. 115) magnified 35 diameters.

B. Brain of an embryo about three and a-half weeks old. The optic vesicle has been cut away.

C. Brain of an embryo about seven and a-half weeks old. The optic stalk is cut through.

*A*, optic vesicle; *H*, vesicle of cerebral hemisphere; *Z*, diencephalon; *M*, mid-brain; *J*, isthmus between mid- and hind-brain; *Hh*, cerebellum; *N*, rhombic brain; *Gb*, otic vesicle; *Rf*, fourth ventricle; *Nk*, neck-curvature; *Br*, pons-curvature; *Pm*, mamillary process; *Tr*, infundibulum; *Hp* (in B), outline of hypophysis-fold of buccal ectoderm; *Rl*, olfactory lobe. In C the basilar artery is represented along its whole course.

columns corresponding with the tracts of conduction; the last of these tracts to become medullated are the pyramidal tracts.

FIG. 142.—SECTIONS ACROSS THE REGION OF THE CALAMUS SCRIPTORIUS OF THE BRAIN REPRESENTED IN FIG. 141, A. (His.)

A, region of the glosso-pharyngeal ganglion. B, region of the auditory facial ganglion.

The membranes are formed from the mesenchyme of the sclerotomes, which extends over and under the cord and becomes enclosed along with that structure within the developing vertebral canal. The septa of connective tissue which are

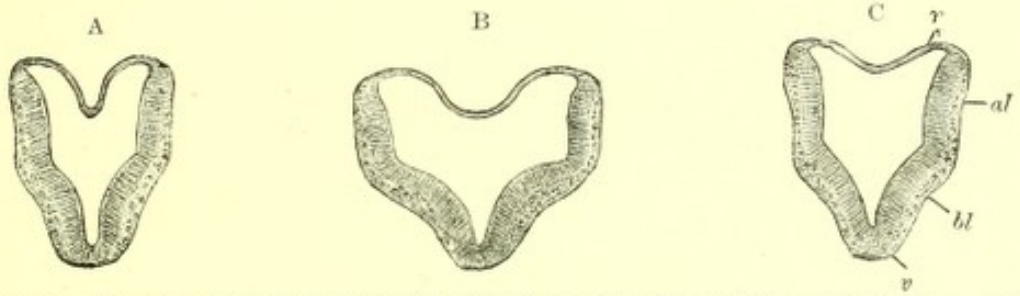



FIG. 143.—SECTIONS ACROSS THE FOURTH VENTRICLE OF A SOMEWHAT OLDER EMBRYO. (His.)

A, section taken through the lower part. B, across the widest part (trigeminus region).
C, through upper part (cerebellar region).
*r*, roof of neural canal; *al*, alar lamina; *bl*, basal lamina; *v*, ventral border.

seen penetrating into the substance of the cord from the pia mater grow in from this mesenchyme, carrying blood-vessels amongst the nervous elements.

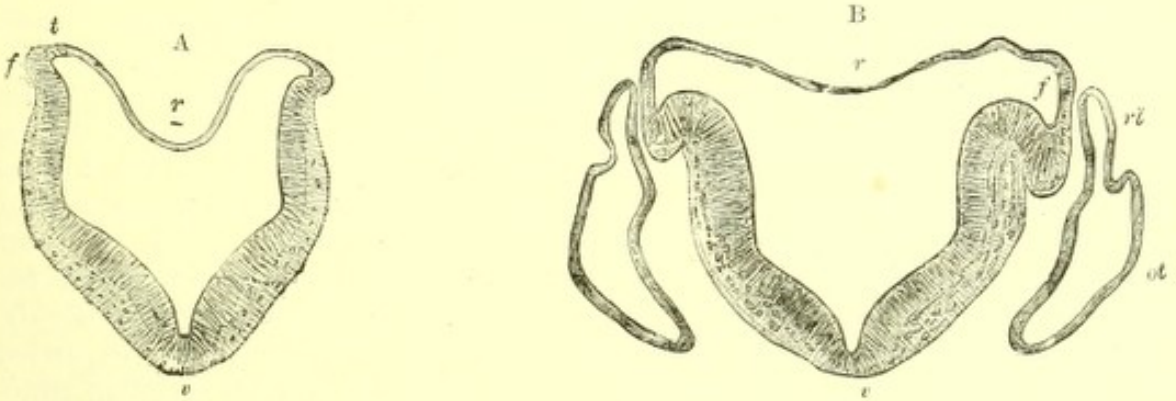



FIG. 144.—SECTIONS ACROSS THE LOWER HALF OF THE RHOMBENCEPHALON OF A STILL OLDER EMBRYO, SHOWING GRADUAL OPENING OUT OF THE NEURAL CANAL AND THE COMMENCING FOLDING OVER OF THE ALAR LAMINA (at *f*).

*v*, ventral border; *t*, tænia; *ot*, otic vesicle; *r.l.*, recessus labyrinthi.
In the succeeding stage (not here represented) the angle at *v* has almost disappeared, the fold *f* (*rhombic lip*) has extended over the alar lamina, and the two thickened halves are in the same horizontal plane, covered by a greatly expanded and thinned-out roof.

**BRAIN.**—The cephalic part of the neural tube closes rather later than the spinal part. In some mammals (pig; Keibel) the medullary laminæ close only after organogenesis has proceeded to some extent, and after the cephalic flexure has

begun to be developed. This is probably the case in the human embryo also. The optic vesicles are formed in the pig as pits on the spread-out neural laminæ, and in the human embryo they are seen as hollow outgrowths from the fore-brain before the laminæ have united. In an embryo at the beginning of the third week (embryo of 3·1 mm.) the brain-tube shows an anterior and posterior dilatation connected by a narrower portion which corresponds to a sharp flexure (*cephalic flexure*) which has bent the anterior on the posterior segment. The hinder and larger dilatation is named the *hind-brain* (*rhombencephalon*), the anterior the *fore-brain* (*prosencephalon*), while the intermediate portion is termed the *mid-brain* (*mesencephalon*). The terminal wall of the fore-brain as shown in His' model is not yet completely closed, a foramen being left called the *neuropore*. From the fore-brain the optic vesicles project as wide-open diverticula connected now by narrower portions, the optic stalks.

During the third and fourth weeks, as the primitive brain increases in length and the embryo becomes more folded, two other bends appear. The first of these occurs at the junction of the brain and spinal cord, and is due to the head being bent down on the trunk (fig. 141A). It is called the *cervical flexure*, and its concavity is necessarily ventral like that of the primary head bend (fig. 141B). The second flexure involves the rhombic brain, and is not determined by the curving of the embryonal axis. It is produced by a doubling of the hind-brain on itself. Its concavity is directed dorsally, and the point of the bend corresponds to the position of the future pons; it is hence called the *pontine flexure* (fig. 141C). While these bends are forming, the fore-brain, by the increase of the cephalic flexure, is folded back below the parts of the tube originally behind it, so that its ventral aspect becomes closely applied to the ventral surface of the rhombic brain, and the space between them is reduced to a narrow cleft filled with the mesenchymatous investment of the primitive brain. In this tissue the dorsum sellæ is afterwards formed. Owing to this increase in the cephalic flexure the mid-brain comes to be the most anterior part of the brain-tube, and is for some time a very prominent feature, although later it loses in prominence by the greater development of cerebrum and cerebellum. As morphogenesis proceeds, the walls of the brain-tube, thus sinuously curved, become thickened and expanded in certain regions to form the several parts of the adult organ, while in other situations they remain mere ependymal lamellæ, which, becoming inflected into the interior of the primitive vesicles and carrying vascular mesenchyme between their layers, form the epithelium of the *choroid plexuses*. Instead of tracing the development of the brain as a whole from stage to stage, it will be more convenient to describe separately, through all the phases, the several parts derived from each primary division of the tube.

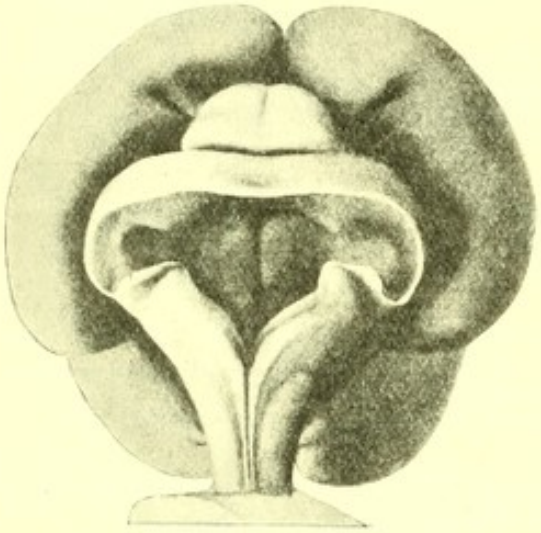


FIG. 145.—MODEL OF THE BRAIN OF A HUMAN EMBRYO OF 53 MM. (ELEVENTH WEEK) FROM BEHIND, TO SHOW THE FOURTH VENTRICLE, RESTIFORM BODIES, AND CEREBELLUM. (His.)

**Rhombic brain (rhombencephalon).**—The hind-brain in its early stages has the very characteristic feature that the ependymal roof-plate is greatly thinned and expanded. At first full and convex, this membranous lamella has a triangular

shape when viewed from the surface. Its apex corresponds to the cervical flexure ; its base is marked off by a thickened band, which afterwards develops into the cerebellum. The hind-brain is broadest at the level of this transverse thickened band ; in front it is connected with the mesencephalon by a thinner portion called the *isthmus* (His) ; behind it gradually tapers to its junction with the spinal cord at the cervical flexure.

In early stages, as shown for the human embryo by Broman and by Peter Thompson,[1] the rhombic brain shows slight constrictions marking off a series of segments or *neuromeres*, seven in number.

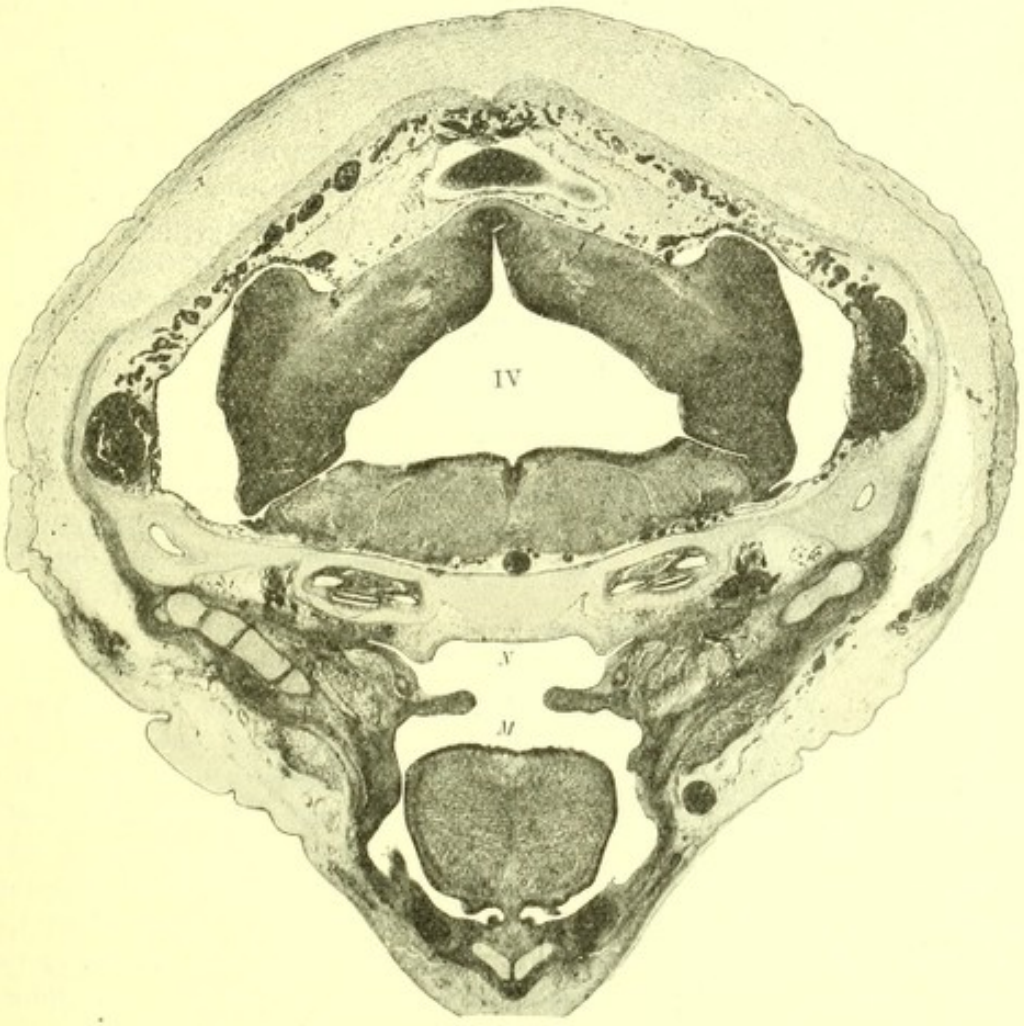



FIG. 146.—SECTION OF THE HEAD OF A HUMAN EMBRYO OF 30 MM. (BEGINNING OF THIRD MONTH). Photograph. (T. H. Bryce.)

IV, cavity of rhombencephalon or fourth ventricle; in the roof of the ventricle the paired cerebellar plate; the lateral enlargements are the rhombic lips cut where they pass into the cerebellar plate. *N* is placed in the naso-pharynx still continuous between the two palatal folds with the buccal cavity (*M*). The Eustachian tubes are seen opening into the naso-pharynx on each side; above them in the cranial base are the auditory labyrinths; in the floor of the mouth is the tongue. Below the tongue are seen the distal ends of Meckel's cartilages; above on each side their proximal ends.

*Pari passu* with the development of the pontine flexure the lateral walls of the hind-brain are opened out, and the epithelial roof becomes greatly expanded (figs. 142, 143, 144). This seems to be the mechanical effect of the forces causing the ventral folding ; the behaviour of the tube has been compared to that of a split indiarubber tube which is bent on itself. The thickened lateral walls are divided, just as in the spinal portion of the neural canal, by lateral grooves into

[1] Jour. Anat. and Phys. xli.

alar and basal laminæ. When the tube is opened up these become laid out horizontally, and form the mesial and lateral portions of the floor of the fourth ventricle. The lateral grooves bounding the alar and basal laminæ are represented by the superior and inferior fovea of the adult brain; the basal lamina becomes the trigonum hypoglossi and eminentia teres, and the alar lamina the ala cinerea, the tuberculum acusticum, and locus cœruleus.[1] The apex of the fourth ventricle reaches at first to the cervical bend—*i.e.* the beginning of the spinal cord. The closed part of the medulla oblongata is a later formation produced by the neural laminæ closing in again (His), presumably owing to the great development of the ganglionic masses in the alar laminæ which form the clavate and cuneate nuclei. The obex is the remains of the ependymal roof of this portion of the hind-brain.

At a stage when the alar laminæ still stand vertically their dorsal borders become recurved and form what are known as the *rhombic lips* (fig. 144B). The two folds of the lips fuse with one another, and form marginal swellings which run in front into the cerebellar lamina. They become ultimately the *restiform bodies* (third month), and share in the formation of the cerebellum (fig. 145). At an early stage the afferent fibres of the vagus and glossopharyngeal nerves which have grown in from the corresponding ganglia form a conspicuous bundle (*funiculus solitarius*) on the surface just ventral to the rhombic lip. It represents the primary dorsal column of the cord in this region. In each rhombic lip a mass of neuroblasts develops which corresponds to the dorsal horn in the cord, and from this mass the cuneate nucleus and substance of Rolando are developed. In the mantle zone of the alar and basal laminæ, close to the inner aspect, definite groups of neuroblasts constitute the nuclei of the cerebral nerves; but more superficially there are large numbers of scattered neuroblasts, which persist as the nerve-cells of the formatio reticularis. Again, close to the middle line on each side, but separated from it by a lamella of the reticular zone, a large group of neuroblasts forms the rudiment of the *corpus dentatum* of the *olive*.

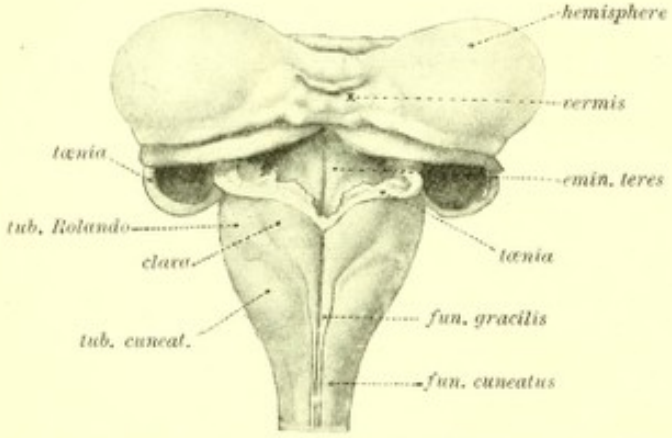



FIG. 147.—CEREBELLUM, MEDULLA OBLONGATA, AND FOURTH VENTRICLE IN A FŒTUS OF THE FIFTH MONTH. (From Kollmann's Entwickelungsgeschichte.)

The reticular formation of the medulla oblongata is produced by a great expansion of the reticular zone associated with the development of the nerve-paths connected with the neuroblasts of the rhombic lips and olivary nuclei; the mesial raphe, like the ventral commissure of the cord, is partly formed by these fibres crossing the middle line. As the reticular formation is gradually added to, the funiculus solitarius becomes deeply buried. Its position in the adult indicates the original surface of the embryonic medulla oblongata. The last formations to appear are the *pyramids* as expansions of the reticular structure mesial to the olivary nuclei. As they develop, they displace the olives laterally, while at the same time the ventral median fissure is formed as a recess between them.

[1] According to Wilson (Jour. of Anat. and Phys. vol. xl.), the alar lamina is represented by the area postrema of Retzius only, and the subdivision of the floor of the fourth ventricle described in the text is not the primary one, which is triple, as in some lower forms.

The upper part of the hind-brain, so far as its ventral area is concerned, undergoes changes essentially similar to those described for the lower part. The mass of transverse fibres forming the *pons* is very late in appearing.

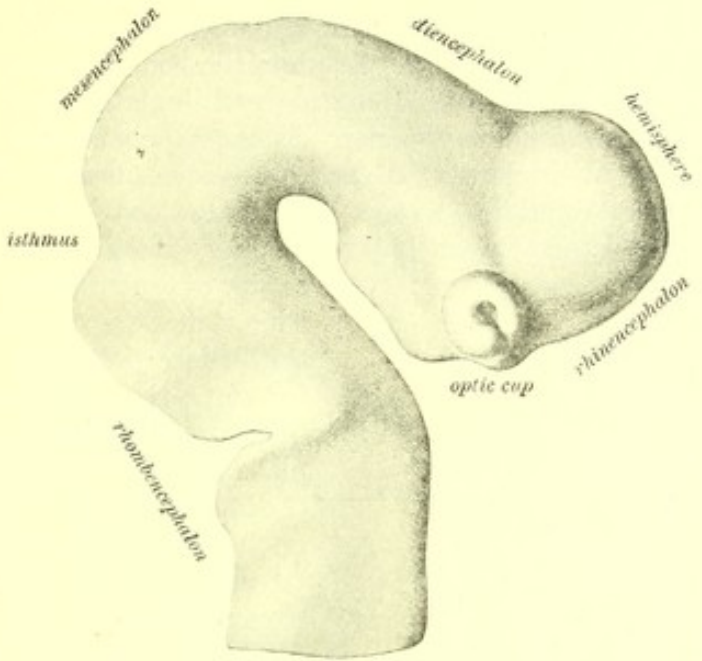



FIG. 148.—MODEL OF THE BRAIN OF A HUMAN EMBRYO OF 6·9 MM. (FOURTH WEEK) LATERAL ASPECT. (His.)

**Cerebellum.**—We have already seen that over the rhombic brain the ependymal roof-plate is much thinned and expanded. It is reduced to a simple

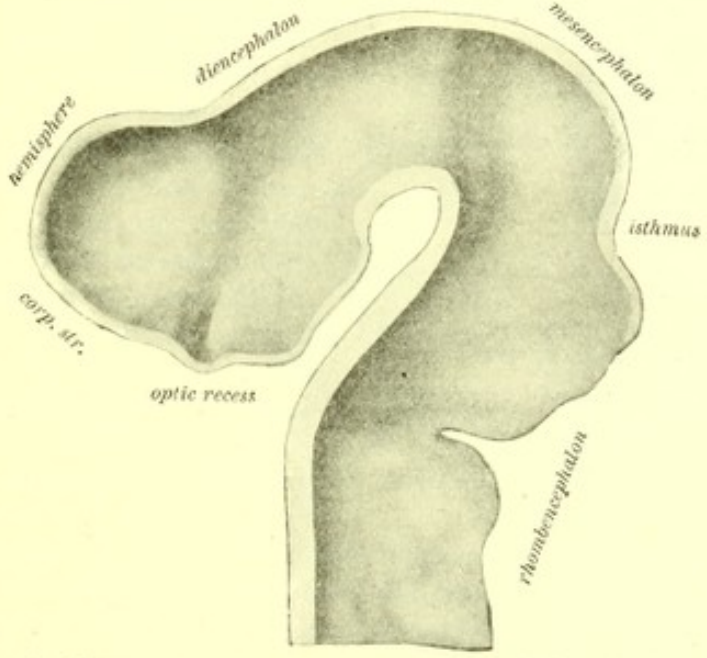



FIG. 149.—SAME MODEL AS THAT SHOWN IN FIG. 148; MESIAL ASPECT.

The mouth of the hemisphere vesicle, the future foramen of Monro, is bounded below by the corpus striatum and behind by a fold separating the pallium from the lateral wall of the diencephalon which becomes the thalamus. The niche above the optic recess where the corpus striatum is continuous with the thalamus is the stalk of the primitive hemisphere-vesicle.

epithelial layer, except along the line of attachment to the rhombic lip, where it retains some nervous tissue and forms the *ligula*. Opposite the pontine flexure it forms a fold which projects into the cavity of the vesicle, and becomes much

plicated (fig. 151). Between the plaits of the membrane vessels are formed in the included mesenchymatous tissue, and thus is produced the choroid plexus of the fourth ventricle (*plica choroidea inferior*). If we follow the ependymal lamella forwards we find it to be continuous with the cerebellar band already mentioned. Just below this it retains its more primitive characters, and forms the *inferior medullary velum*. In the region of the isthmus the roof-plate forms similarly the *superior medullary velum* (valve of Vieussens), while laterally it is thickened to produce the *superior cerebellar peduncles*. The cerebellar band proper becomes enormously increased in thickness to form the cerebellum. The thickening of the roof-plate is at first bilateral, so that two plates are laid down, joined by a thin intermediate band, and separated by a cleft which communicates with the cavity of the rhombic vesicle (fig. 146). This cleft is afterwards obliterated by the fusion of its lips, but a part may for some time persist as a small cerebellar ventricle (Blake). The central plate forms the central lobe or vermis; the lateral lobes or hemispheres appear later as rounded enlargements of its lateral portions. During the earlier stages the cerebellum has a smooth surface, but by the end of the third month it begins to be folded owing to the increase of its surface area (fig. 147). Fissures appear which separate certain definite areas or primitive lobes from one another. The first partition involves the lateral and posterior borders, which are cut off by lateral fissures (*floccular fissures*) to form the *flocculus* and *paraflocculus*. The floccular fissures meet on the vermis, and mark off an area which becomes the *nodule*. A deep fissure (*fissura prima* of Stroud) also appears on the vermis which separates the future *culmen* and *clivus monticuli*, and extends on to the hemispheres. Later two other fissures mark off the *pyramid* from the *tuber valvulæ* (*sulcus prepyramidalis*; *fissura secunda*, Elliot Smith) on the one side and the *uvula* on the other. These four fissures constitute the main dividing furrows of the vermis, but during the fourth and fifth months various furrows appear on the hemispheres which further subdivide its surface. The morphology of the fissures and lobes of the cerebellum will be considered in the volume of this work devoted to Neurology, but it may be here stated that the great horizontal fissure is of late appearance, and is not of morphological importance, being produced merely by the great growth of the hemispheres in the region of the lobus clivi and the lobus pyramis, which is so special a feature in the human embryo (Bradley).[1]

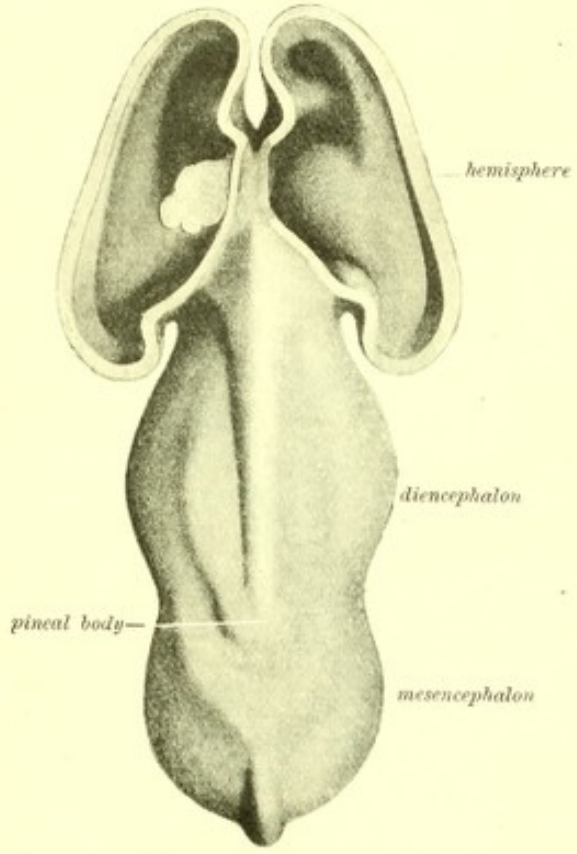



FIG. 150.—MODEL OF THE BRAIN OF A HUMAN EMBRYO OF 13·6 MM. VIEWED FROM ABOVE. (His.)

The hemisphere-vesicles are laid open; in the left the choroid plexus has been left in position, in the right it has been removed to show the corpus striatum. For description, see text.

[1] For the literature of the cerebellum, see Hertwig's Handbuch, *loc. cit.* and Bradley, Journ. of Anat. and Phys., vol. xxxviii.; on the mammalian hind-brain, see also the same author, Journ. of Anat. and Phys. vol. xli.

The **mid-brain** (**mesencephalon**) is marked off from the isthmus by the crossing of the trochlear roots, while in front, in early stages, it is separated from the fore-brain merely by a slight fold in the roof-plate which extends on to the lateral wall (figs. 148, 149). The cavity is at first relatively large, and owing to the expansion of the roof it is prolonged backwards over the isthmus (fig. 151). This diverticulum is ultimately obliterated and the lumen of the vesicle is reduced to a narrow passage—the *aqueductus cerebri* (*aqueduct of Sylvius*). The roof-plate shows at first a mesial ridge (fig. 150), which in later stages disappears except at its posterior extremity where it persists as the *frænum* of the valve of Vieussens. It then becomes thickened on each side to form two lateral swellings, subsequently divided again by a transverse groove into the *corpora quadrigemina*. The ventral portion of the vesicle forms the *pedunculi* (*crura*) *cerebri*, of which the *tegmentum*

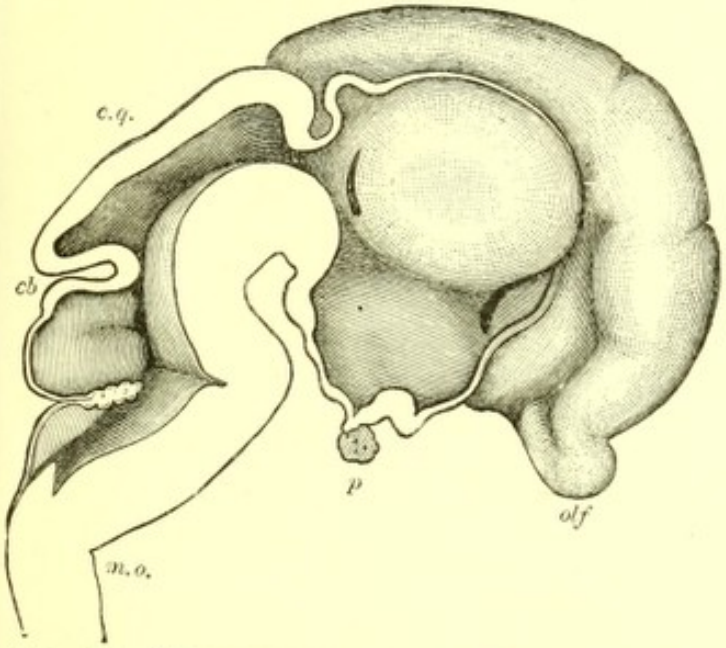



FIG. 151.—MEDIAN SECTION THROUGH THE BRAIN OF A TWO AND A-HALF MONTHS FŒTUS. (His.) Magnified 5 diameters.

The mesial surface of the left cerebral hemisphere is seen in the upper and right-hand part of the figure; the large cavity of the third ventricle is bounded above and in front by a thin lamina; below is seen the infundibulum and pituitary body. Filling the upper part of the cavity is the thalamus opticus; in front and below this is the slit-like foramen of Monro. Behind the thalamus is seen another slit-like opening which leads into the still hollow external geniculate body.

*olf*, olfactory lobe; *p*, pituitary body; *c.q.*, corpora quadrigemina; *cb*, cerebellum; *m o.*, medulla oblongata.

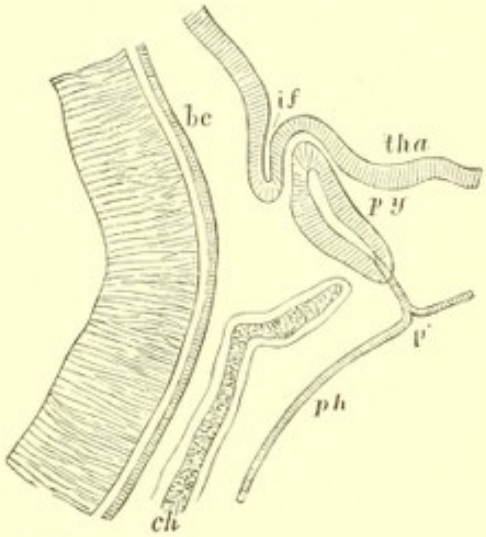



FIG. 152.—MEDIAN SAGITTAL SECTION OF THE INFUNDIBULUM AND PITUITARY DIVERTICULUM IN A RABBIT-EMBRYO, AFTER THE OPENING OF THE FAUCES. (From Mihalkovics.)

*bc*, basis cranii with basilar artery; *if*, infundibulum; *tha*, floor of thalamencephalon; *py*, pituitary diverticulum, now closed; *p'*, stalk of original communication with the mouth; *ph*, pharynx; *ch*, notochord in the spheno-occipital part of the cranial basis.

is first laid down, while the *crusta* is, like the other portions of the pyramid tract, a later formation.

The **fore-brain** (**prosencephalon**) undergoes a much more complicated series of changes, which result in the formation of the *thalami*, the *geniculate bodies*, the *pineal body and its peduncles*, the *optic nerves*, *chiasma*, *tracts*, and *retina*, *tuber cinereum* and *cerebral part of the pituitary body*, the *corpora mamillaria*, and the *cerebral hemispheres*.

The remarkable feature in the development of the human brain is the enormous expansion of the hemispheres till they dominate all the other portions of the brain, overlapping as they grow the part of the fore-brain from which they spring, then the mid-brain, and ultimately also the hind-brain.

At a very early stage, as has already been mentioned, the optic vesicles are developed as hollow diverticula from the fore-brain. The mouths of the diverti-

cula are gradually closed, and the vesicles remain attached by the optic stalks. The history of the vesicles will be considered in the chapter on the development of

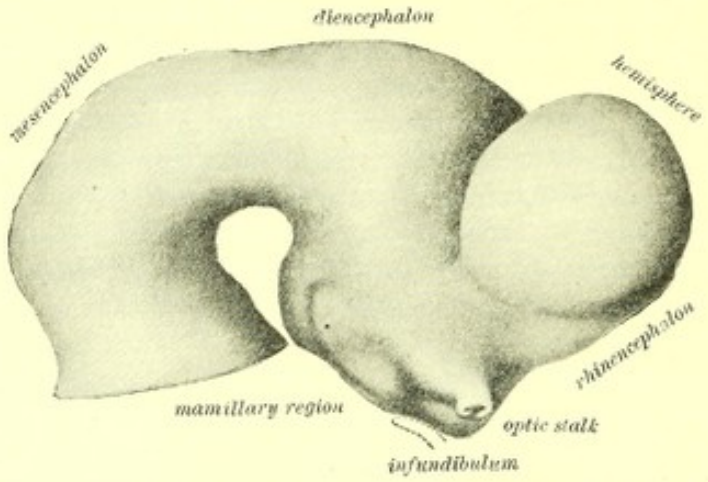



FIG. 153.—MODEL OF THE BRAIN OF A HUMAN EMBRYO OF 10·2 MM. (FIFTH WEEK). (His.)

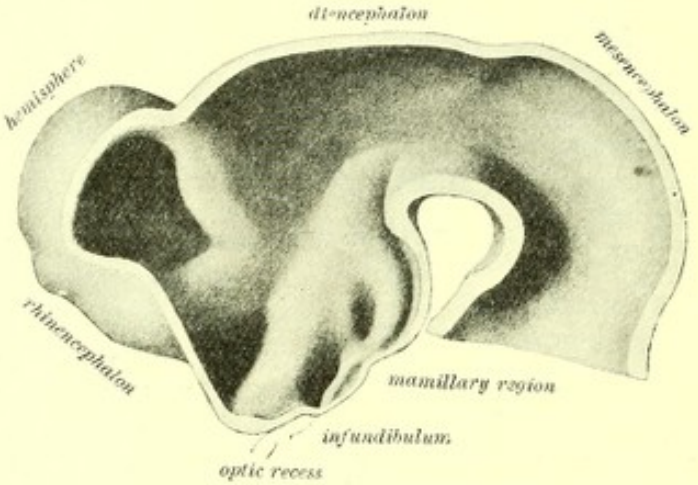



FIG. 154.—THE SAME MODEL AS IN FIG. 153 FROM THE MESIAL ASPECT.

The large opening into the hemisphere-vesicle is the foramen of Monro. On the wall of the diencephalon the sulcus of Monro is seen separating the thalamus (dark-shaded area) from the hypothalamus (lighter-shaded area).

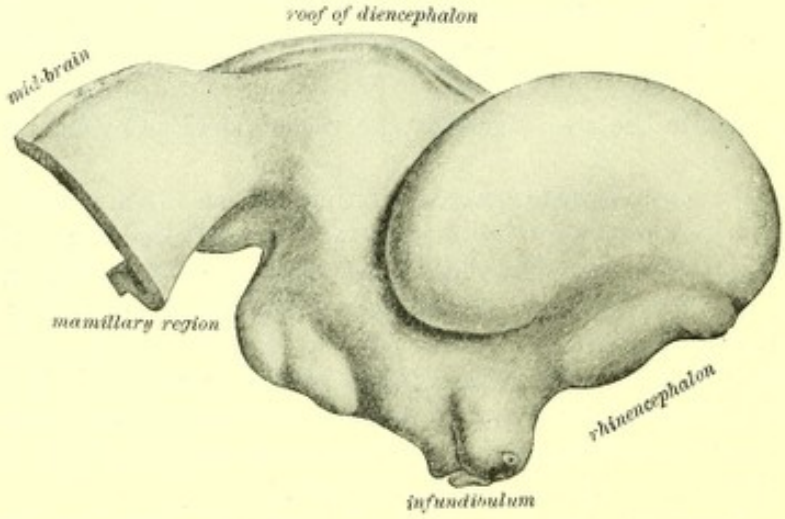



FIG. 155.—MODEL OF THE BRAIN OF A HUMAN EMBRYO OF 13·6 MM. (BEGINNING OF SIXTH WEEK) FROM THE SIDE. (His.)

the eye ; but it must here be noticed that between the mouths of the two vesicles there extends across the floor of the fore-brain a well-marked recess, which is known as the *optic recess* (fig. 149). In the posterior fold of this, the optic commissure is afterwards formed, and it is an important landmark during the development of the parts.

At first the fore-brain shows the typical regions of the rest of the neural tube—viz. a thin ependymal roof-plate, a floor-plate of the same constitution, and in the thick lateral walls a basal and alar lamina separated by a furrow (*sulcus of Monro*). The thalami are formed from the so-called alar laminæ, as are also the cerebral hemispheres, while the basal laminæ give rise to the hypothalami, the tuber cinereum, infundibulum, and mamillary bodies. It is doubtful whether this subdivision has the same morphological value as in the rest of the tube.

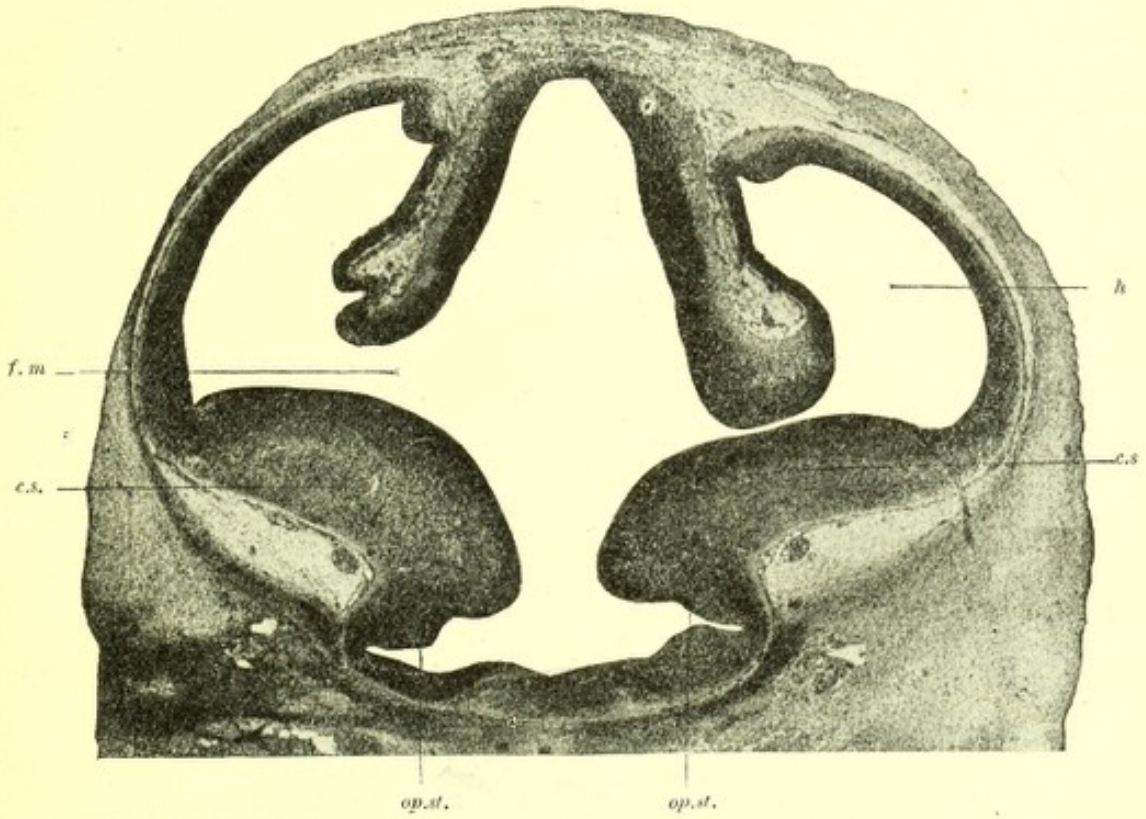



FIG. 156.—SECTION OF THE FORE-BRAIN OF A HUMAN EMBRYO AT THE END OF THE FIFTH OR BEGINNING OF THE SIXTH WEEK. Photograph. (T. H. Bryce.)

*h*, hemisphere-vesicle ; *f.m.*, foramen of Monro ; *c.s.*, *c.s.*, corpora striata ; *op.st.*, *op.st.*, proximal ends of optic stalks.

By the thickening of the lateral walls to form the thalami, the cavity of the vesicle of the fore-brain is reduced to a narrow vertical cleft—the third ventricle of the adult brain. The thalami ultimately come in contact with one another, and are joined by a grey lamina known as the *intermediate mass* or *middle commissure*. The ependymal roof at first shows a longitudinal convexity. As seen in His' model of the brain of a sixth week embryo (fig. 150), the roof broadens out in front where it reaches on each side the margin of the foramen of Monro, while behind, it runs into a mesial swelling, which is the rudiment of the *pineal body* or *epiphysis*. Extending forwards from the sides of this, two curved ridges represent the peduncles of the pineal body. Outside these, again, are two broader bands connected behind with a semilunar ridge on the roof of the mid-brain ; they become the brachia of the superior corpora quadrigemina. In front of the pineal body, and between the peduncular ridges, the roof becomes reduced to a simple epithelial layer which covers later the under aspect of the velum interpositum (tela choroidea of the

third ventricle). The pineal body is at first a simple diverticulum of the cavity of the fore-brain.[1] Its ependymal lining becomes thrown into folds, and the cavity is ultimately obliterated. The stalk remains patent, and forms the pineal recess. It is at first directed upwards; but as the hemisphere grows backwards the gland is thrown over on to the corpora quadrigemina, and the stalk assumes the curvature seen in the adult brain. The prominent rounded swellings seen on the sides of the fore-brain (fig. 150) are the rudiments of the *lateral geniculate bodies*. A section (fig. 164, p. 120) shows that the external prominences correspond to diverticula of the cavity of the vesicle. The area on each side, between the geniculate prominence, the superior brachium, and pineal peduncular ridge is the *habenular region*. When the hemisphere grows back over the thalamus (see below), the geniculate

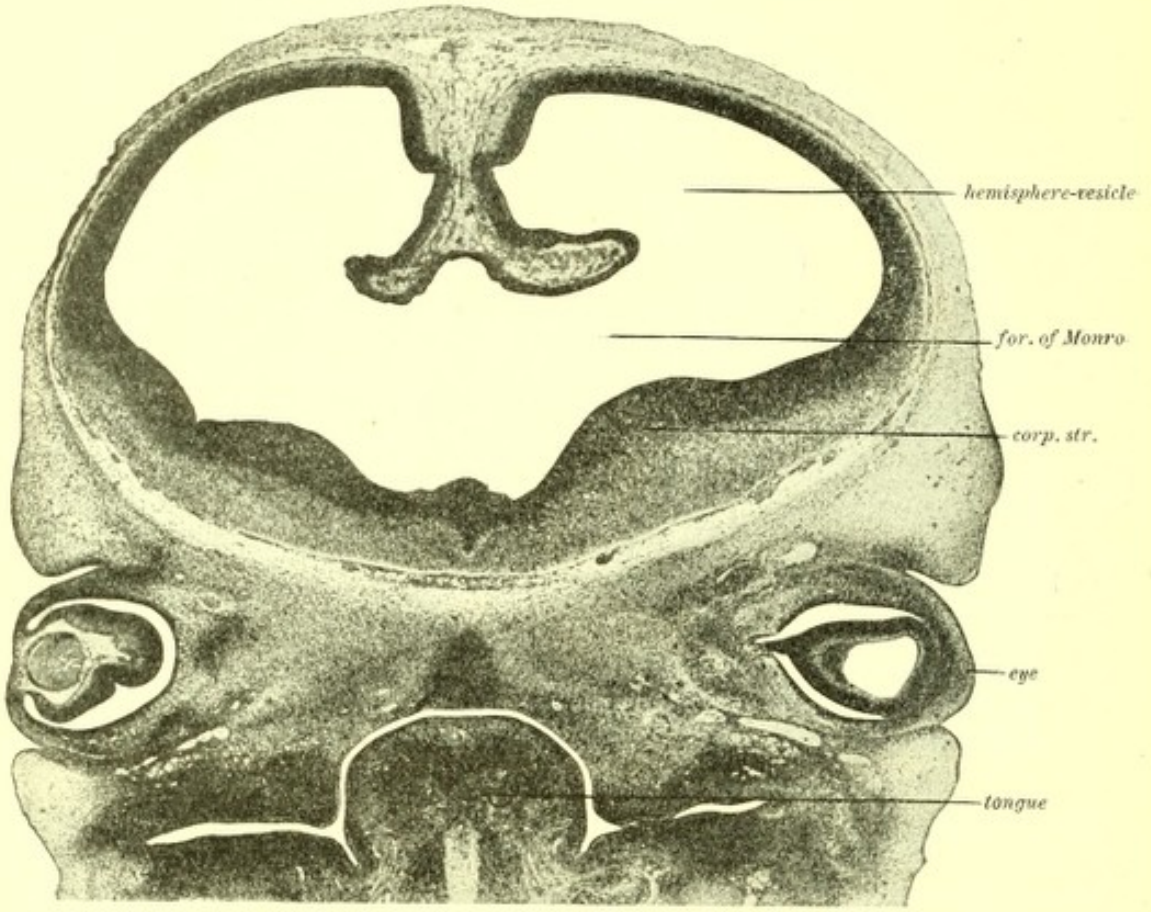



FIG. 157.—SECTION OF THE CEREBRAL HEMISPHERES FURTHER FORWARDS THAN THE SECTION GIVEN IN FIG. 156. Photograph. (T. H. Bryce.)

The section should be compared with the model represented in fig. 150. The mesenchyme in the great longitudinal fissure between the hemispheres is the primitive falx cerebri; the choroidal fold is in process of formation. On the left of the figure he corpus striatum is divided by a furrow into two limbs (see floor of right hemisphere in fig. 150)

angle is displaced backwards to its definitive position, and the habenular area forms the *trigonum habenulæ* and the *pulvinar*. The grey matter in the habenular area becomes the *ganglion habenulæ*, and the two areas are early connected by a commissure across the roof in front of the epiphysis. When the stalk of that body is folded back, the crossing fibres are found in the dorsal lamella of its peduncle. This *habenular commissure* must not be confused with the *posterior commissure* which forms at the junction of mid- and fore-brain below and behind the posterior, afterwards the ventral, lamella of the pineal stalk. The *mesial geniculate bodies*

[1] In lower vertebrates the pineal diverticulum is bilateral, but only that of the left side develops into the pineal gland (Cameron).

develop in the same manner as the lateral, showing at first as internal diverticula and outer prominences on the sides of the fore-brain. In the displacements resulting from the backward growth of the hemisphere they become pushed back so as to be seen on the surface of the mid-brain.

The floor of the fore-brain early shows a deep depression behind the optic recess, which becomes the infundibulum, and gives origin to the cerebral lobe of the *pituitary body*. This is at first an open diverticulum (fig. 152), but later it becomes cut off from the cavity by the obliteration of the lumen of the stalk. The vesicle thus formed comes into intimate relation with the epithelial portion of the body, to the posterior aspect of which it is applied, the two becoming bound together by vascular connective tissue. The epithelial portion is formed as a diverticulum of buccal ectoderm from the roof of the stomodœum. The diverticulum extends backwards as a flattened cleft (fig. 176, p. 134) which divides into two horns embracing the infundibulum. Towards the end of the second month

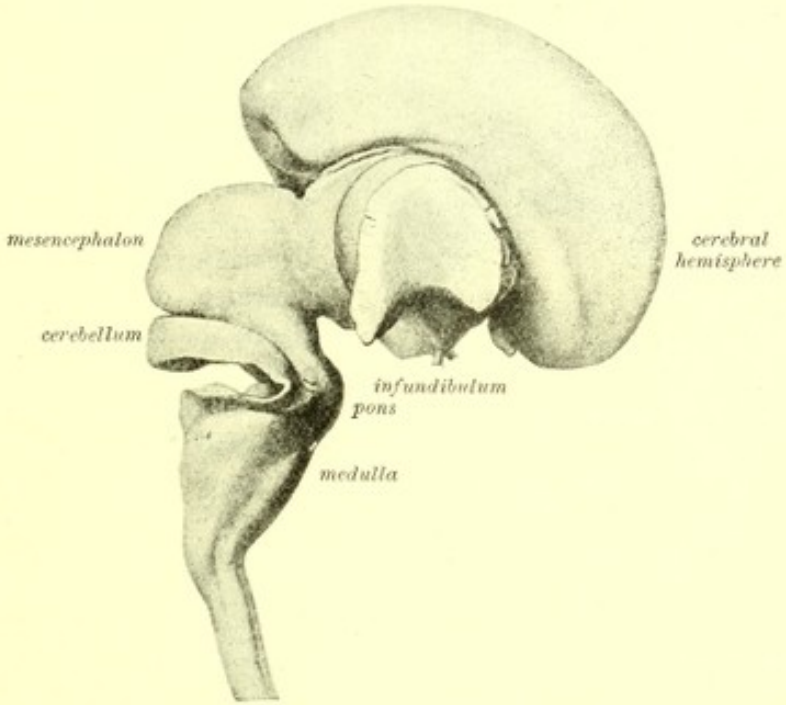



FIG. 158.—MODEL OF THE BRAIN OF A FŒTUS OF 53 MM. (ELEVENTH WEEK). (His.)

The right hemisphere has been cut away to show the mesial surface of the left hemisphere; the corpus striatum is seen arching round the stalk of the hemisphere.

the walls become folded and epithelial sprouts grow to form a small mass of tubules, the lumen of which is afterwards obliterated. The stalk is separated from the buccal epithelium and becomes absorbed.

The *mamillary bodies* are developed from a mesial recess of the floor of the fore-brain between the infundibulum and the anterior basal angle of the floor of the mid-brain.

**Cerebral hemispheres.**—The cerebral-hemisphere rudiments first appear as shallow bays in the fore-part of the alar laminæ (fig. 149). In the roof and anterior wall of the tube the walls of the bays run directly into one another, so that the two rudiments appear as a single anterior swelling of the fore-brain (fig. 148).

This, with the fore-part of the anterior extremity of the basal part of the fore-brain, is often termed the *telencephalon*, while the remainder is called the *diencephalon*. Opinions differ as to whether the hemispheres are to be looked on as separate lateral diverticula, or as two lobes of a single rudiment.

The hemispheres in an embryo of the fourth week (fig. 148) still form a single rounded swelling, but the position of the future separation is marked by a longitudinal ridge, which, however, does not reach the lower and anterior portion. Here an area on each hemisphere is clearly marked off by a slight lateral furrow as the rudiment of the *rhinencephalon*. When the hemisphere is looked at from within, it will be observed that two areas can be distinguished—an upper rounded, the rudiment of the *pallium*,[1] and a lower triangular, the rudiment of the *corpus striatum*. On the latter are seen three ridges running on to the mesial aspect of the rhinencephalic area. The mouth of the vesicle (the future *foramen of Monro*) has the following lips, which it is important to distinguish: (1) *pallio-thalamic*, where pallial and thalamic walls join one another; (2) *strio-thalamic*, where corpus striatum and thalamus are continuous; (3) *strio-hypothalamic*, where corpus striatum and hypothalamus meet; and (4) *lamina terminalis*, where rhinencephalon is continuous with rhinencephalon, and pallium with pallium.

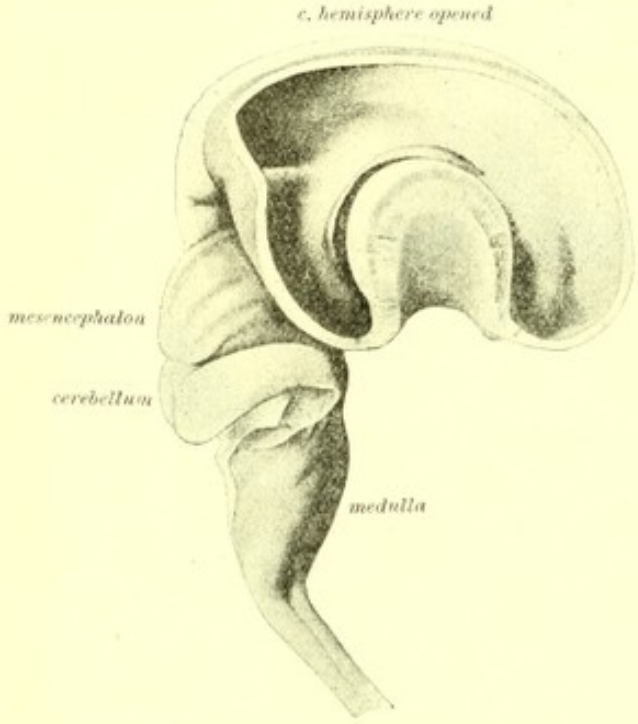



FIG. 159.—ANOTHER MODEL OF THE SAME BRAIN AS SHOWN IN FIG. 158. (His.)

The right hemisphere has been opened up to show the cavity of the vesicle and the inner aspect of its mesial wall. The inward projecting fold round the stalk is the hippocampus; the angular fold in the posterior lobe is the calcar avis.

In the early part of the fifth week the hemispheres begin to expand (figs. 153, 154). Their expansion takes place, like that of a growing soap-bubble, in every direction from the stationary mouth (foramen of Monro). The lamina terminalis thus comes to lie at the bottom of a fissure between the two hemispheres which is occupied by a lamella of mesenchyme, the common rudiment of the mesial pia and the falx cerebri; the pallio-thalamic border is at the same time converted into an angular arched fold which lies at the bottom of a cleft between the posterior part of the expanding vesicle and the thalamus.

The rhinencephalon is now marked off very distinctly from the pallium by a lateral furrow (*external rhinal fissure*). The pallial vesicle soon becomes bean-shaped (fig. 155), the hilum being represented by a depression above the rhinencephalon. This depression becomes the fossa of Sylvius, and corresponds to the stalk of the hemisphere—*i.e.* the point of union of corpus striatum and thalamus. The hemisphere-vesicle, anchored as it were to the two ends of the rhinencephalon, and expanding in all directions, becomes folded round the stalk. Its cavity is consequently horseshoe-shaped, and the horns of the semilune represent the future *frontal* and *temporal horns* of the lateral ventricle. There is no posterior horn as yet. It is developed later, when the vesicle has still further expanded backwards to form the occipital lobe.

[1] The terms *rhinencephalon* and *pallium* are used in a limited and ontogenetic sense. The division is in a measure arbitrary, as we shall see that a part of the pallium in this sense (limbic lobe) becomes closely related to the rhinencephalon, forming with it the 'rhinencephalon' of Elliot-Smith's definition. Ontogenetically, however, the above subdivision of the hemisphere-rudiment into rhinencephalon, pallium, and corpus striatum is not only justified by fact, but necessary in description.

The rhinencephalon at this stage is quite uncovered by the pallium and separated from it by the external rhinal fissure (fig. 155). It extends back to the extremity of

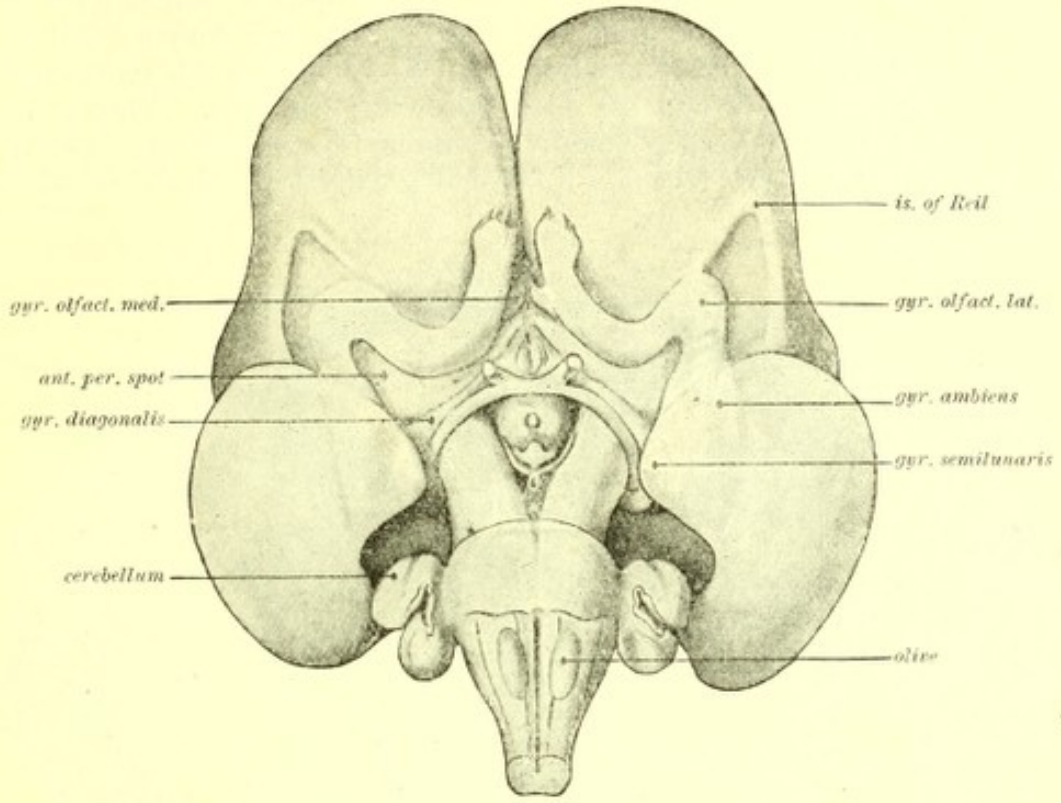



FIG. 160.—BRAIN OF A FŒTUS AT THE BEGINNING OF THE FOURTH MONTH, FROM BELOW. (From Kollmann.)

The gyrus olfactorius lateralis, gyrus ambiens, and gyrus semilunaris together form the lobus pyriformis.

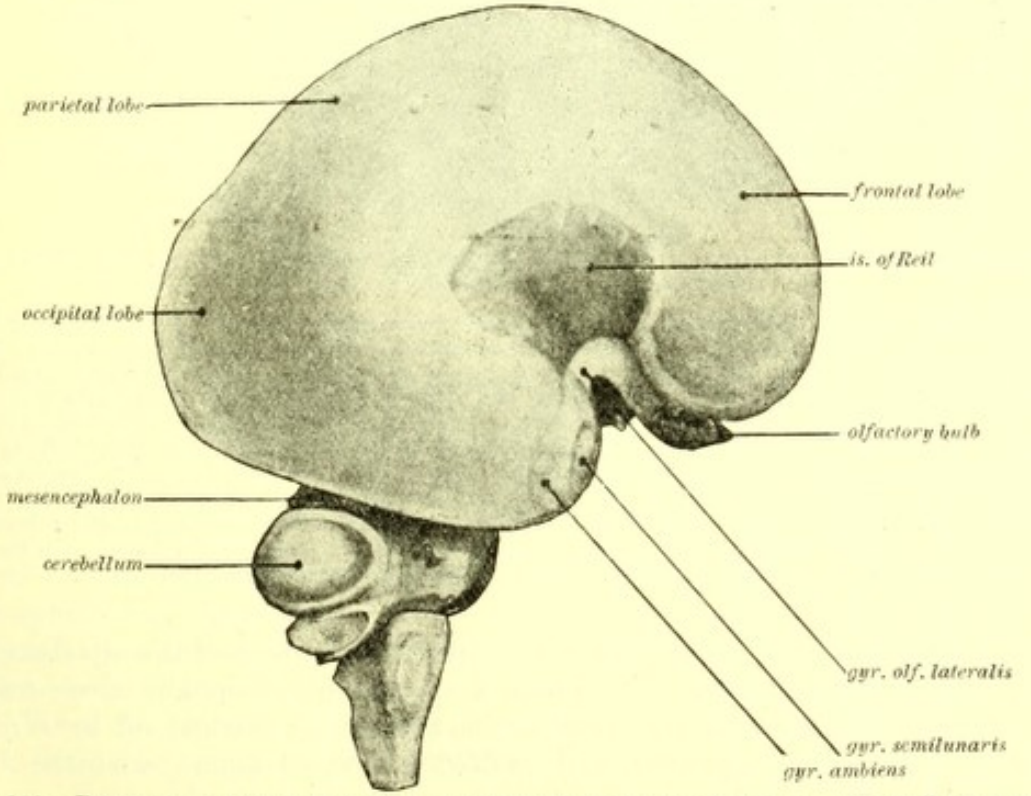



FIG. 161.—BRAIN OF A FŒTUS AT THE BEGINNING OF THE FOURTH MONTH. (From Kollmann.)

the temporal horn; but as the temporal pole grows downwards and forwards, its posterior extremity becomes covered over, and ultimately reversed in position,

thus giving rise to the *uncus*. Meanwhile the formation begins to be separated into its several parts. The anterior extremity becomes cut off from the frontal lobe, as a hollow stalk which communicates with the tip of the frontal horn of the cavity. This separated stalk forms the *olfactory bulb and tract* as well as the *trigone*. The remainder of the formation is not so isolated, and is represented by the *anterior perforated spot* and the *lobus pyriformis* (fig. 160). This is a well-marked swelling during the earlier months, extending from the olfactory tract to the inner aspect of the temporal lobe, but it becomes greatly reduced, and is ultimately

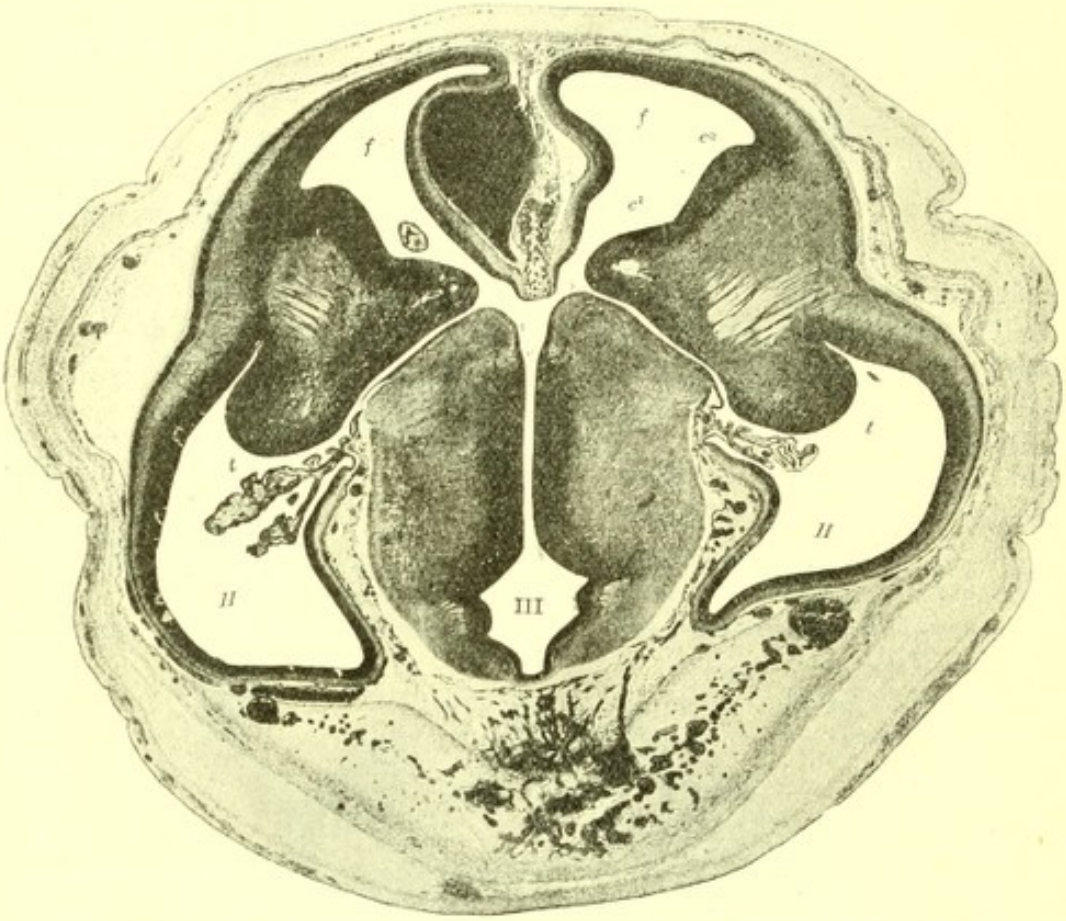



FIG. 162.—CORONAL SECTION OF THE BRAIN OF A HUMAN EMBRYO OF 30 MM. (BEGINNING OF THIRD MONTH). Photograph. (T. H. Bryce.)

The section cuts the thalami, cerebral hemispheres, and corpora striata. *H*, *H*, posterior lobes of hemisphere; *f*, *f*, frontal lobes. III is placed in the habenular region of the third ventricle; in front of this the cavity is slit-like, and bounded by the bodies of the thalami. Each thalamus terminates in a blunt-pointed end, the future anterior tubercle; the anterior portion of the outer surface is oblique, and separated from the overlapping corpus striatum by a fissure, in which the tænia semicircularis is afterwards developed. The infrachoroideal ependymal lamella (see especially on right side of figure) of the mesial hemisphere-wall is continued over this surface and fused with it. The corpus striatum being arched, is cut in two places, head ($c^1$, $c^2$) and tail ($t$); between these, the commencing internal capsule is seen. The head-end of the corpus striatum shows two crura, a mesial ($c^1$) and a lateral ($c^2$). The longitudinal fissure between the frontal lobes is distorted by a large hæmorrhage. On the left of the figure the mesial wall shows a fold, which is the upper end of the fissura prima.

represented only by the uncus and the so-called lateral root of the olfactory tract. On the mesial aspect of the hemisphere a special rhinencephalic area—*trapezoid plate* or *field* (His), *area paraterminalis* (Elliot-Smith) is marked off by a distinct fissure in front (*fissura prima*), and limited by the lamina terminalis behind (fig. 164). Its fate will be considered later.

On the mesial wall of the pallium the formation of the *choroidal fissure* has already taken place. The vesicle-wall, where it passes over on to the thalamus-wall, remains ependymal, and is folded into the cavity as a double layer enclosing

vascular pial tissue. Thus a *plica choroidea* is produced (fig. 150), which becomes so extensive as nearly to fill the interior of the vesicle. The choroidal fissure begins at the angle where the lamina terminalis and pallio-thalamic border of the foramen of Monro meet. It is at first short and nearly straight, but gradually extends round the hemisphere-stalk to the tip of the temporal horn. It is to be observed that below the fissure there is an ependymal lamella (*infrachoroideal membrane*) which becomes fused with the thalamus (see below).

It will be convenient at this stage to take the **development of the corpus striatum**. As we have already seen, it lies in the floor of the hemisphere-vesicle (figs. 156, 157); it is directly continuous, below and behind the primitive

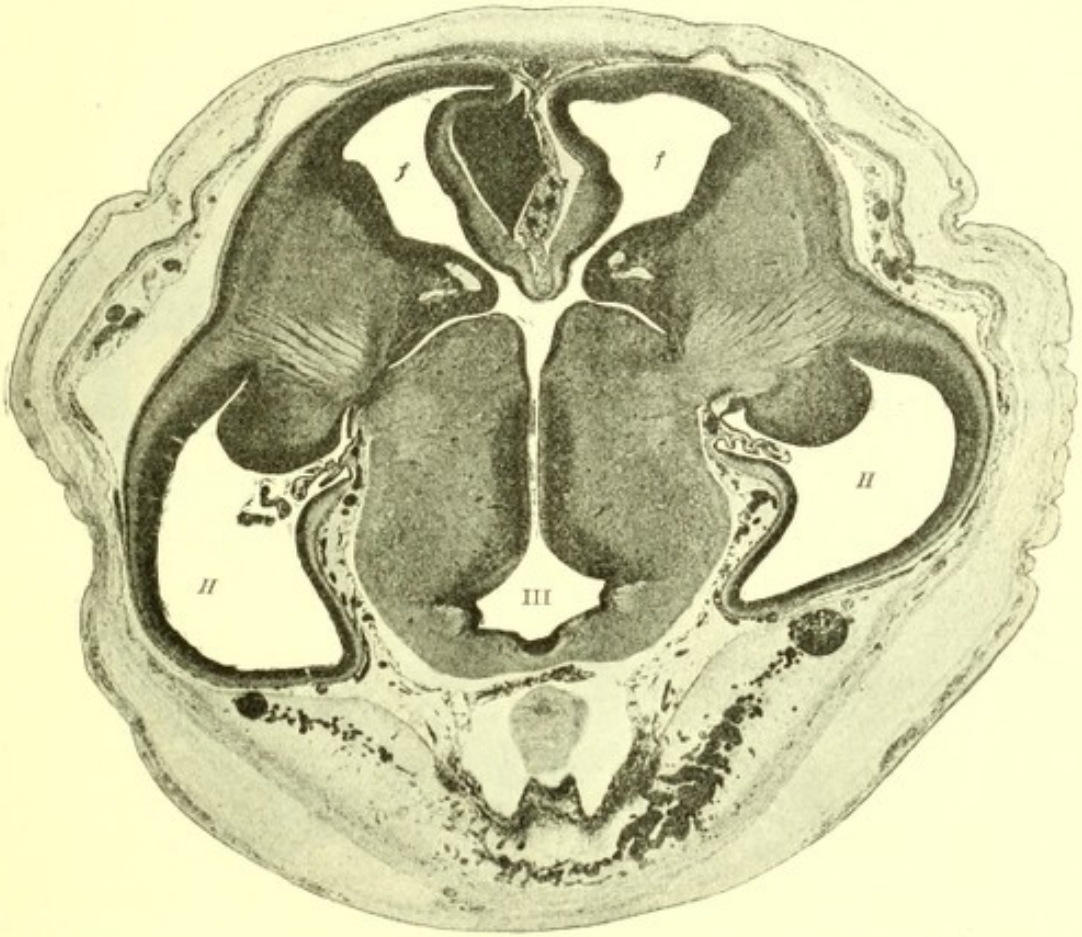



FIG. 163.—SECTION THROUGH THE SAME BRAIN AS SHOWN IN FIG. 162, SEVERAL SECTIONS NEARER THE BASE. (T. H. Bryce.)

The same general description as given under fig. 162 will apply here, but it will be noted that the fissure between the thalamus and corpus striatum is now interrupted by the large primary thalamus-bundle. This marks the stalk of the hemisphere, round which the corpus striatum arches; as the stalk enlarges, the fissure (also, of course, arched) is gradually obliterated, and is only represented in the adult brain by the furrow between caudate nucleus and thalamus, in which the tænia semicircularis lies. The hollow on the surface of the hemisphere opposite the stalk is the fossa of Sylvius.

foramen of Monro, with the thalamus, and is connected in front with the rhinencephalon by three roots. The middle of these fuses with the internal fold corresponding to the fissura prima (fig. 164) in the floor of the vesicle and cuts off a pocket of the frontal horn which is continuous with the cavity of the olfactory stalk. When the lumen of the stalk is obliterated this pocket disappears. The cleft behind this seems in part obliterated in its basal portion, but persists above as the space between the caudate nucleus and septum pellucidum in the adult brain. The body of the corpus striatum grows backwards *pari passu* with the development of the temporal horn of the vesicle, and its *tail* is thus produced (fig. 150). As the hemisphere-rudiment becomes more and more

arched the corpus striatum becomes highly bowed, surrounding the hemisphere-stalk and extending from the rhinencephalon in front (future locus perforatus anticus) to the extremity of the temporal horn (fig. 158). As the body is prolonged backwards into the tail it overlaps the thalamus, but is necessarily separated from it by the cleft between thalamus and hemisphere (see fig. 150). This cleft is obliterated from below, as thalamus and corpus striatum enlarge, by a fusion of the two bodies, associated with the fusion of the ependymal infrachoroidal lamella of the mesial hemisphere-wall with the

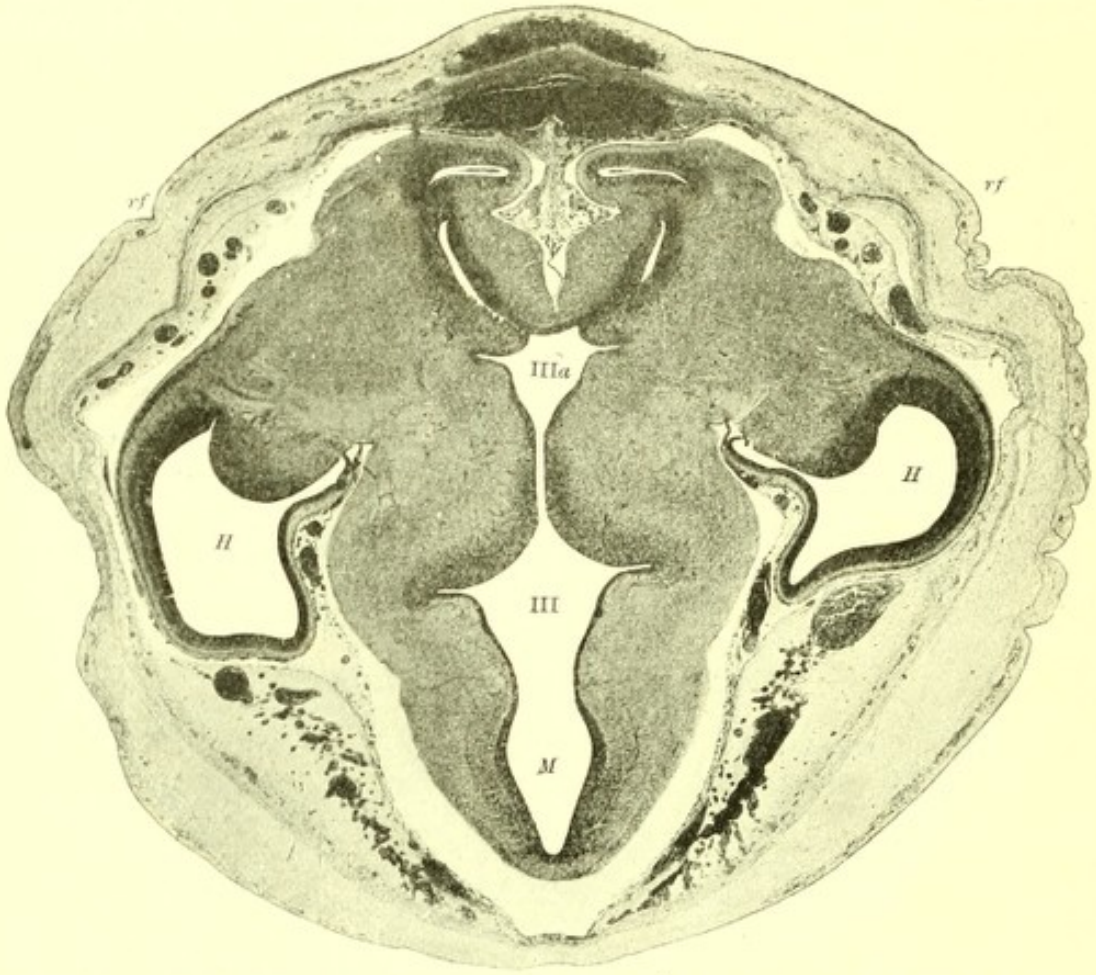



FIG. 164.—SECTION THROUGH THE SAME BRAIN AS IN FIGS. 162 AND 163, MUCH NEARER THE BASE. (T. H. Bryce.)

The section now cuts the mid-brain *M*. The diverticula on each side of III, placed in the cavity of the third ventricle, are the rudiments of the geniculate bodies; *H*, *H*, the temporal horns of the hemisphere-vesicles with the tail of the corpus striatum. The notch on the outer surface of each hemisphere opposite *rf* is the sulcus marking off the rhinencephalon on the lateral aspect of the brain; III*a* is placed in the fore and basal part of the third ventricle. Immediately in front (above in the figure) of III*a* is the lamina terminalis, here thickened. In front of the lamina terminalis are two triangular fields (trapezoid areas), separated by a narrow cleft occupied by a delicate prolongation of the primitive falx. In front of this the falx is much broadened out, and angular projections from it occupy the fissuræ primæ. The cavity of the hemisphere-vesicle is at this level interrupted by the union of the projection corresponding to the fissura prima with the lateral crus of the corpus striatum (see figs. 162, 163). The anterior pocket is the mouth of the cavity in the olfactory stalk.

outer side of the thalamus (fig. 162). The hemisphere-stalk is thus greatly enlarged, and in the tissue between the thalamus and corpus striatum the *internal capsule* takes form—first, by the formation of the thalamus bundle connecting that body with the hemisphere (fig. 163); and later by the addition of the pyramid-fibres connected with the crus cerebri.

It may here be pointed out that while the outer reticular zone in the spinal cord becomes the white covering, this zone remains quite a thin layer on the hemisphere, and the white matter is

laid down between the mantle zone and the ependymal zone by the development of the fibre-paths connecting the thalamus with the hemisphere, and later by the addition of the pyramid-fibres.

The cleft between corpus striatum and thalamus persists for a time as a groove in which the *stria terminalis* or *tænia semicircularis* is formed. During the formation of the internal capsule the *lenticular nucleus* and *claustrum* take shape as isolated portions of the striate body.

The *velum interpositum* (*tela choroidea ventriculi tertii*) arises from the vascular connective tissue within the longitudinal fissure. This grows in between the ependymal lamellæ of the choroidal fissures to form the choroid plexuses of the lateral ventricles. It also of course covers the optic thalami, and lies upon the ependymal roof of the primitive fore-brain, which it inflects into that cavity to form the choroid plexus of the third ventricle. The ependymal covering of each lateral choroidal plexus is derived from the mesial wall of the hemisphere, while the

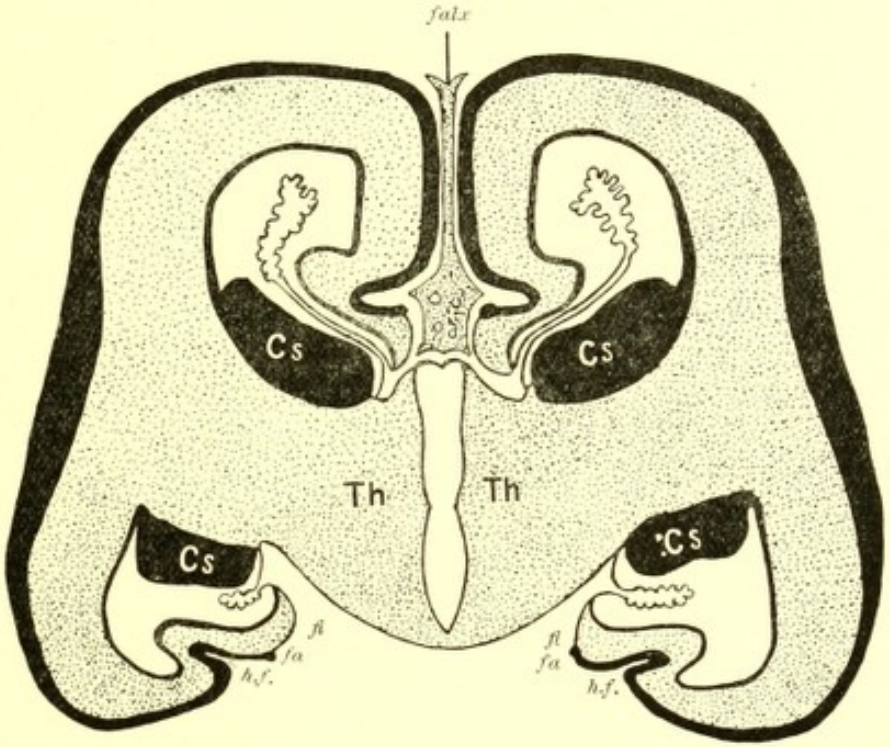



FIG. 165.—DIAGRAM OF A TRANSVERSE SECTION OF THE BRAIN TO SHOW THE RELATIONS AND FATE OF THE MARGIN OF THE MESIAL WALL OF THE HEMISPHERE. (After His.)

*Th*, thalamus; *Cs*, corpus striatum. The mesial wall is infolded, and the sunk grey cortex ends in a thickened seam, leaving a free edge of white matter. In the temporal horn the parts are labelled *hf*, hippocampal fissure; *fa*, marginal grey seam; *fi*, edge of white substance.

infrachoroidal lamella is prolonged over, and becomes adherent to, the thalamus (*lamina affixa*) as far as the stria terminalis, which represents the line of union of hemisphere-wall and thalamus-wall. In this way the anterior part of the thalamus comes to lie in the floor of the lateral ventricle.

**The hippocampal formation and the commissures.**—If a section of the mesial wall of the hemisphere be examined in the brain of an embryo at the beginning of the third month, it will be found that the cortical ganglionic layer which is forming over the pallial surface ceases before it reaches the choroidal fissure, in which, as we have seen, the ependymal layer is alone present. The reticular layer which in the hemisphere develops between the mantle and the ependymal layers, therefore, comes here to the surface (fig. 165). From frontal lobe to temporal horn the margin of the pallium thus consists of a zone in which the cortical grey layer is present, and a zone in which

it is absent, and this thins away by a margin (*tænia*) into the ependymal layer. This portion of the hemisphere becomes much complicated by the development of the fornix commissure and the corpus callosum. To make the matter clear, we shall first imagine it developed without either fornix commissure or corpus callosum.

The margin of the hemisphere becomes folded early in the third month, to form a fissure arching from the foramen of Monro to the temporal horn, parallel with the choroidal fissure. The inflected area is continuous in front with the trapezoid area (area paraterminalis). The fissure is a 'complete' one, and has an elevation within the vesicle corresponding to it. The thickened marginal seam of the grey matter sunk in the fissure, lies at the lip of the choroidal fissure, and the edge of the white matter is rolled inwards towards the ventricle, as it thins away into the ependymal layer covering the choroid plexus (fig. 165). The projection into the ventricle becomes the *hippocampus*, the marginal grey seam the *fascia dentata*, and the white lip the *fimbria*. The primitive hippocampal formation thus constituted extends from the front of the foramen of Monro to the temporal horn arching round parallel with the choroidal fissure. It is continuous in front with the trapezoid plate (area paraterminalis) and behind with the uncus.

This marginal area of the cerebral cortex is of great morphological importance. In lower forms, with a largely developed olfactory sense, it forms a prominent part of the brain, while the rest of the hemisphere is relatively little expanded. In man it remains a diminutive element, while the remainder of the cortex becomes enormously developed. Elliot-Smith, seeing that it is in all probability related to the sense of smell, has included it in his 'rhinencephalon,' while to the rest of the pallium he gives the name *neopallium*. On ontogenetic grounds it seems better to limit the term 'rhinencephalon' to that very distinct and early isolated part of the hemisphere-rudiment to which the term has been applied in the foregoing account. The later formed hippocampal formation is a part of the pallium in the sense defined in the note on page 116. In respect that it is intimately related to the olfactory apparatus it might perhaps be termed *rhinopallium* to distinguish it from the *neopallium*.

The primitive hippocampal formation becomes profoundly affected by the development of the commissures, hippocampal and neopallial (*corpus callosum*). These are developed in intimate relationship with the lamina terminalis, which, as we have seen, from the first connects rhinencephalon with rhinencephalon and pallium with pallium. The lamina terminalis becomes thickened; but opinion is divided as to the manner in which this is effected. Some regard the increase as due to interstitial growth, others believe that the opposed mesial surfaces of the hemispheres become fused to form the plate in which the commissures appear. The appearances seen in sections such as are here reproduced (fig. 164) are on the whole in favour of the latter view. Immediately in front of the ependymal lamina terminalis the faces of the trapezoid plates have fused to all appearance for a certain distance. In the band of tissue thus produced the anterior commissure first appears. It connects the corpora striata and temporal lobes. Both hippocampal commissure and corpus callosum develop in the upper part of the thickened lamina terminalis. The hippocampal fibres appear first, and the callosal later. They are indistinguishable to begin with, but the callosal soon accumulate on the dorsal aspect of the hippocampal, and form a short plate arching forwards over the cleft between the two trapezoid plates (areæ paraterminales). The cleft open below is now the *cavum septi*—the future fifth ventricle—and the two trapezoid plates will become the two leaves of the *septum pellucidum*.

Once laid down, the corpus callosum becomes elongated; there are two divergent interpretations of the process. According to one view, the growth is interstitial. The body is said to grow forwards and backwards, and is raised and separated from the hippocampal commissure. As the original union between the

two is at the posterior end of the corpus callosum, the hippocampal commissure (or, in other words, the upper part of the lamina terminalis) is stretched and

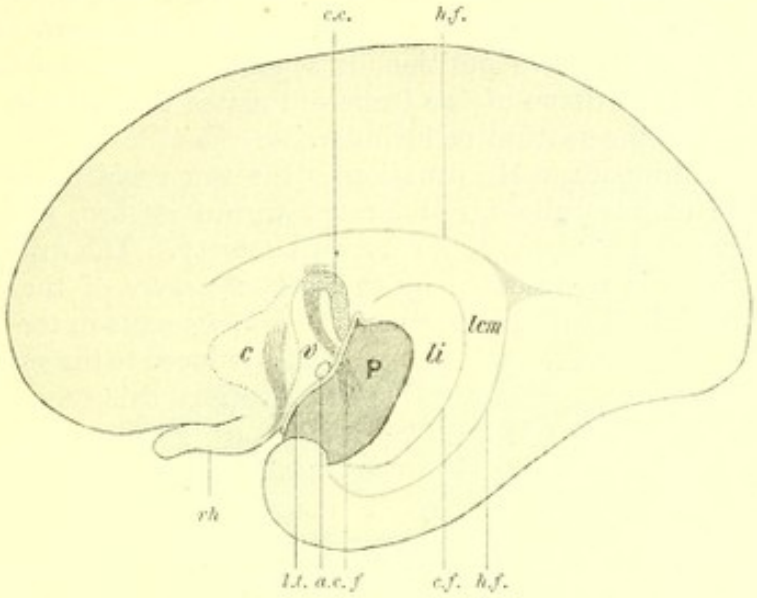



FIG. 166.—GRAPHIC RECONSTRUCTION OF THE MESIAL HEMISPHERE-WALL OF A FŒTUS 5·6 MM. LONG. (After His.)

*P*, stalk of hemisphere; *c*, *v*, anterior and posterior parts of trapezoid area (area paraterminalis); *l.i.*, lamina infrachoroidea of mesial hemisphere-wall below, *c.f.*, choroidal fissure; *lcm*, limbus of mesial hemisphere-wall below, *h.f.*, hippocampal fissure; *c.c*, corpus callosum; *l.t.*, lamina terminalis; *a.c.*, anterior commissure; *f*, commencing column (anterior pillar) of fornix; *rh*, olfactory stalk.

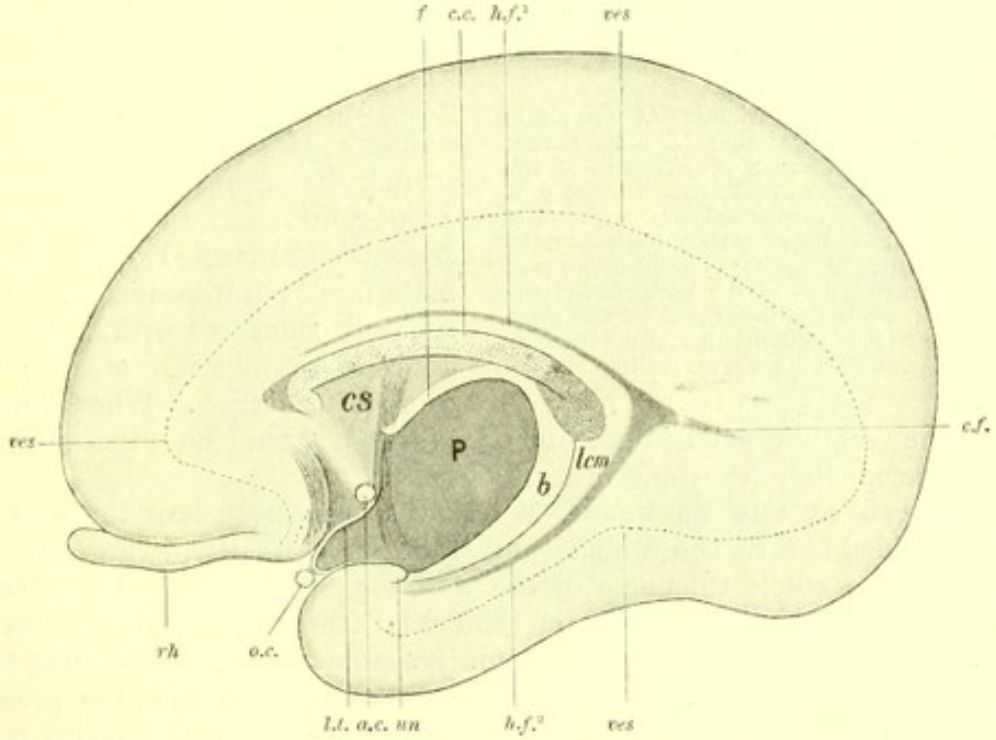



FIG. 167.—GRAPHIC RECONSTRUCTION OF THE MESIAL HEMISPHERE-WALL OF A FŒTUS OF 8·3 CM. LONG. (After His.)

*P*, stalk of hemisphere; *c.s.*, cavum septi; *b*, fimbria, continuous with *f*, fornix; *lcm*, limbus; *c.c.*, corpus callosum; *h.f.*¹, callosal fissure; *h.f.*², hippocampal fissure; *c.f.*, calcarine fissure; *un*, uncus; *a.c.*, anterior commissure; *l.t.*, lamina terminalis; *o.c.*, optic commissure; *rh*, olfactory stalk; *ves*, outline of cavity of hemisphere.

drawn into a horizontal position forming the *psalterium* or *lyra*, while the area paraterminalis is also drawn out to form the apical portion of the septum pellucidum (Elliot-Smith and others). According to the other view, the increase in length is

brought about by the free medullary edges of the margins of the hemispheres coming together, and by the growth of fibres across the bridge so produced (His and others). This takes place *pari passu* with the expansion of the pallium, and owing especially to expansion of the frontal lobes the hippocampal commissure, which remains small and retains its primitive position, is separated from the fore-part of the corpus callosum, and the tissue of the trapezoid plates is stretched between them to form the leaves of the septum pellucidum.

The fate of the hippocampal formation is the same whichever interpretation be adopted. The corpus callosum is formed within its arc, and causes by its growth a stretching and atrophy of its forward moiety. The *hippocampal fissure* of the temporal horn is represented by the *callosal fissure* of the mesial surface. The grey cortex sunk in the fissure becomes the *hippocampus* in the temporal horn, but is reduced to the *gyrus cinguli* above the corpus callosum. The marginal seam of grey matter becomes the *fascia dentata* below, the *indusium* above; while the *nervi Lancisii* are fibres arising from this wasted part of the hippocampal formation, just as the fornix-fibres spring from the hippocampus. The free edge of the white matter becomes the fimbria, the posterior pillar (crus), and body of the fornix. The anterior pillar (columna fornicis) is formed by a strand of fibres early formed in the wall of the hemisphere and connected with the thalamus of its own side (fig. 166). The so-called *peduncle of the corpus callosum* is a strand (*fasciculus præcommissuralis*, Elliot-Smith, or *gyrus subcallosus*, Zuckerkandl) formed on the trapezoid plate (area paraterminalis). It is intimately connected with, indeed is the anterior termination of, the hippocampal formation. When formed it closes-in the septum pellucidum, and separates it from the other derivatives of the rhinencephalon below and in front of it.

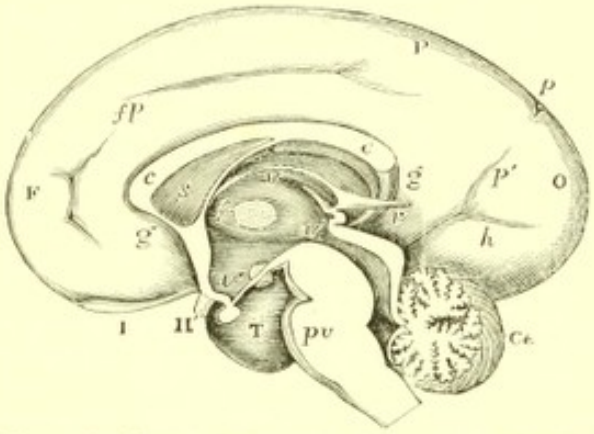



FIG. 168.—VIEW OF THE INNER SURFACE OF THE RIGHT HALF OF THE FŒTAL BRAIN OF ABOUT SIX MONTHS. (Reichert.)

*F*, frontal lobe; *P*, parietal; *O*, occipital; *T*, temporal; *I*, olfactory bulb; *II*, optic nerve; *fp*, calloso-marginal fissure; *p*, *p'*, parts of the parieto-occipital fissure; *h*, calcarine fissure; *g*, *g*, gyrus fornicatus; *c*, *c*, corpus callosum; *s*, septum pellucidum; *f*, placed between the middle commissure and the foramen of Monro; *v*, in the upper part of the third ventricle; *v'*, in the back part of the third ventricle; *v''*, in the lower part of the third ventricle above the infundibulum; *r*, recessus pinealis; *p.v.*, pons Varolii; *Ce*, cerebellum.

**Formation of the fissures.**—We have already seen how the wall of the vesicle is infolded to form the *choroidal* and *hippocampal* fissures. These are, in that they involve the whole thickness of the wall, *complete fissures*. Two other such fissures are produced—the *calcarine* on the mesial aspect of the hinder part of the vesicle, and the central portion of the definitive *collateral*. Corresponding to these fissures, the *calcar avis* (fig. 159) and *collateral eminence* are found as projections into the ventricle. From among the other fissures the fissure of Sylvius must be placed in a category by itself. It is formed by the uprising of the edges of the fossa of Sylvius until with the increasing expansion of the free portion of the pallium they meet over the grey area on the surface of the hemisphere-stalk. This becomes the *island of Reil*, and the meeting lips are named the *opercula*. The frontal operculum is last formed (Cunningham), and owing to the development of a triangular field upon it, the two small anterior limbs of the fissure of Sylvius are produced. The remaining sulci, which begin to appear in the sixth month, are merely folds produced during the progress of differentiation of the grey covering of the

hemispheres. They follow a definite pattern determined by differentiation of areas in the grey matter, which by their own growth, as well as by pressure on adjoining areas, produce the folding of the cortex. The subject will be fully treated of in the descriptive account of the brain (*see* Neurology).

## PERIPHERAL NERVOUS SYSTEM.

**Spinal nerves.**—In the human embryo of the third week the rudiments of the spinal ganglia are connected together by a continuous dorsal band, which extends

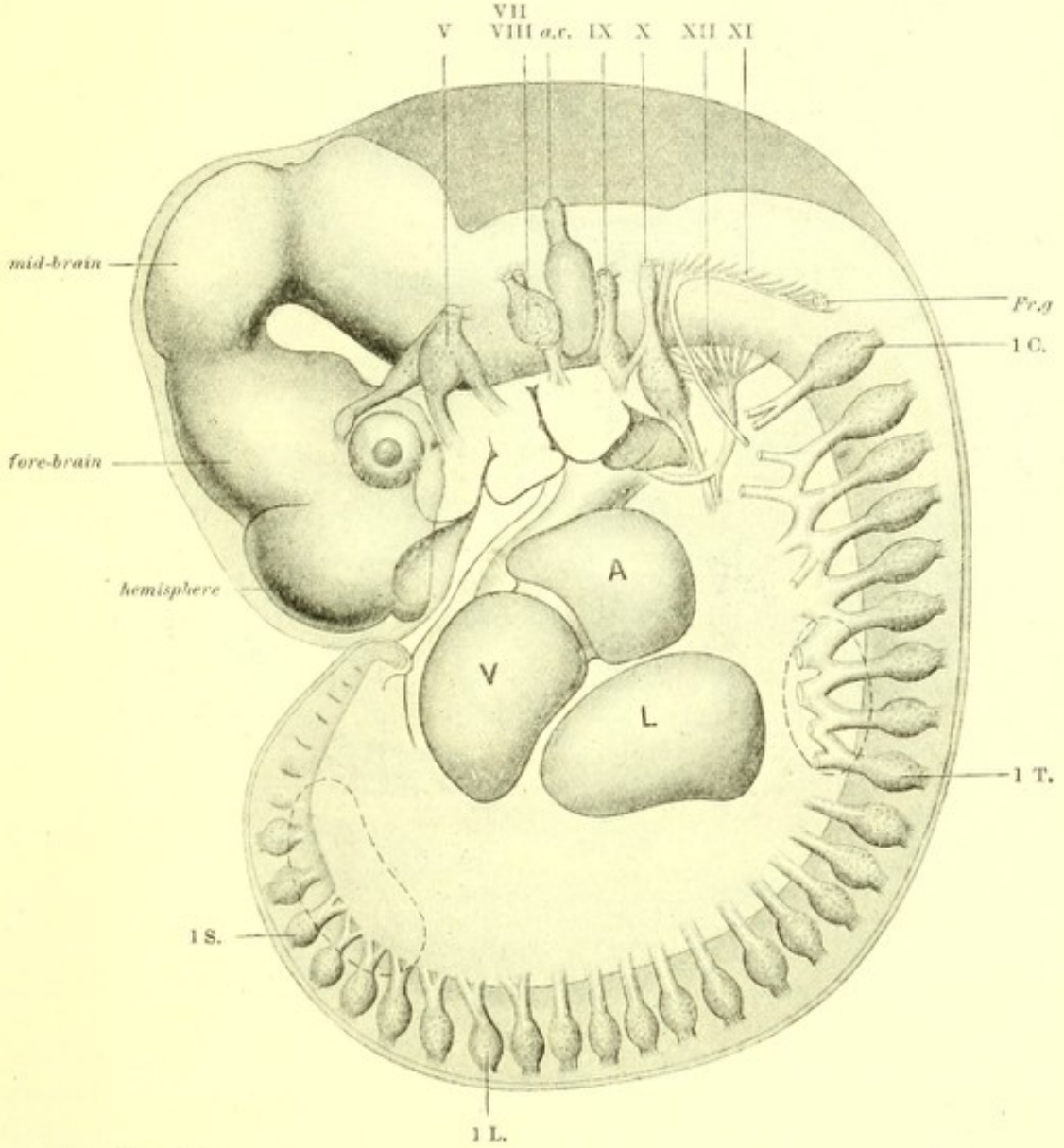



FIG. 169.—RECONSTRUCTION OF THE SPINAL AND CEREBRAL NERVES OF A HUMAN EMBRYO 6·9 MM. LONG. (After His.)

*V*, ventricle; *A*, auricle of heart; *L*, liver; *a.v.*, auditory vesicle; *Fr.g.* Froriep's ganglion. The Roman numerals indicate the cerebral nerves. 1 C., first cervical; 1 T., first thoracic; 1 L., first lumbar; 1 S. first sacral nerve.

from the auditory vesicle along the neural tube to its extreme tip (Streeter).[1] Though there are no signs as yet of dorsal roots, the ventral roots are present, and the ventral ends of the ganglia end diffusely among them as they pass out towards the myotomes (Streeter). The ganglion-crest becomes interrupted in the

[1] Amer. Jour. of Anat. iv. 1905.

fifth week between the ganglia, and the dorsal roots are by that time completed. Meantime the spinal nerve-roots have been formed by the union of fibres from the ganglia with the motor root-fibres. During the fourth week, at a time when the limb-buds are still small and undivided, the segmental nerves begin to be connected by anastomosis (fig. 169). The connecting filaments between the nerve-roots from the fourth cervical to the first thoracic, and again from the second lumbar to the second sacral, constitute the future limb-plexuses (fig. 173). Each segmental

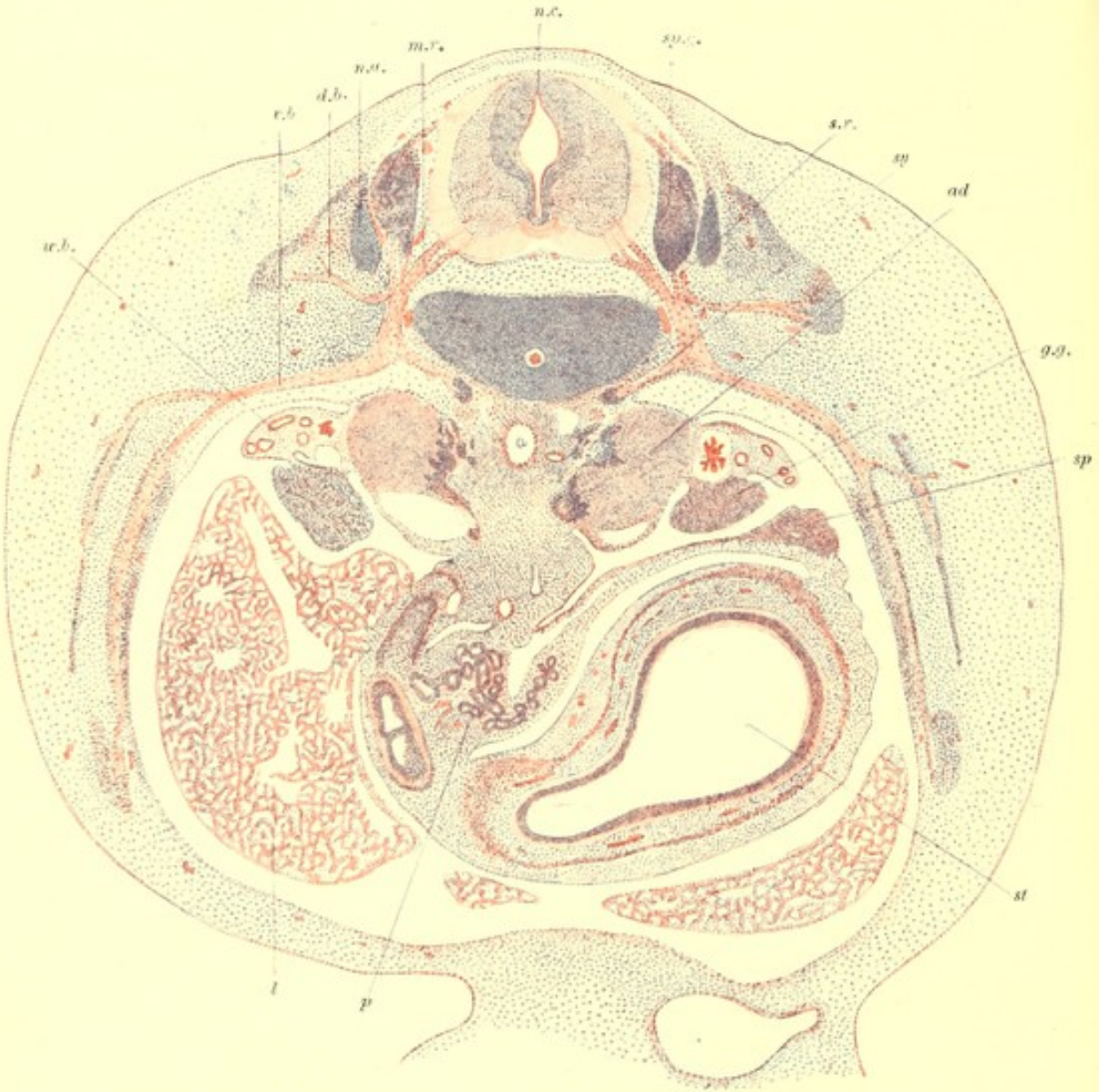



FIG. 170.—TRANSVERSE SECTION OF A HUMAN EMBRYO AT THE END OF THE FIFTH OR BEGINNING OF THE SIXTH WEEK. (T. H. Bryce.)

*n.c.*, neural canal; *n.a.*, neural arch; *sp.g.*, spinal ganglion; *s.r.*, sensory root; *m.r.*, motor root of spinal nerve; *d.b.*, dorsal branch; *v.b.*, ventral branch; *sy*, visceral branch of spinal nerve, with sympathetic ganglion; *st*, stomach; *sp*, spleen; *ad*, adrenal; *g.g.*, genital gland; *w.b.*, Wolffian body; *p*, pancreas; *l*, liver; *a*, aorta.

nerve early gives off a dorsal branch which passes through the myotome, and a ventral branch which passes along the inner side of its extended ventral part. From this a short visceral branch passes to the rudiment of the sympathetic ganglion (fig. 170). The ventral nerve extends quickly into the neighbourhood of the Wolffian ridge, and thence much more slowly round the body-wall. All the limb-nerves as they extend into the growing limb-bud divide into primary dorsal and ventral branches.

**Cerebral nerves.**—Exclusive of the olfactory and optic, which must be included in a different category from the others, and will be treated of with the sense-organs to which they belong, the cerebral nerves divide themselves into a group of pure motor nerves, the hypoglossus, abducens, trochlearis, and oculo-motorius, and a group of mixed sensory and motor nerves, the vagus and accessorius (vagus complex), the glossopharyngeus, the acousticus, facialis, and trigeminus.

The motor roots in both groups spring from the basal lamina of the neural tube, but the nuclei of origin appear in two series, a *mesial* and a *lateral*. The distinction is well marked as far forwards as the isthmus, but in that portion of the tube and in the mesencephalon the separation into two distinct ranges disappears to a considerable extent. The *mesial* column, which is a continuation upwards of the ventral nerve column of the cord, gives origin in the region behind the auditory

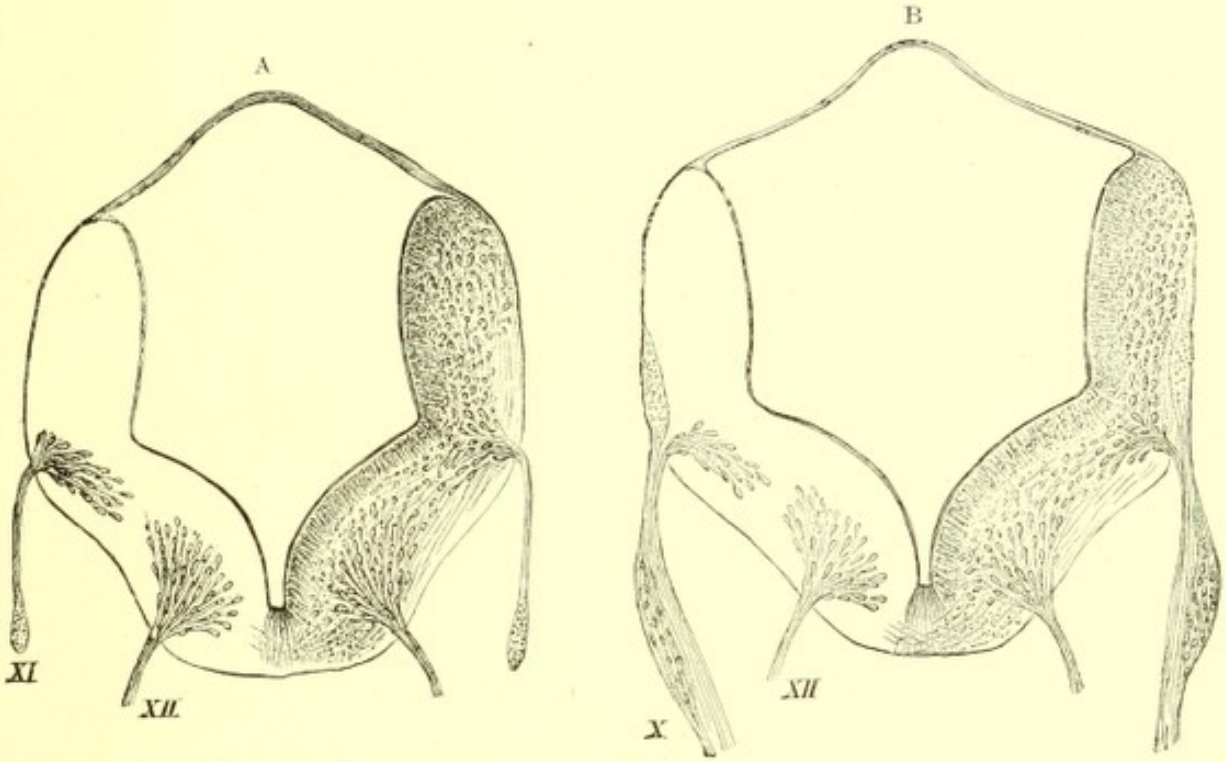



FIG. 171, A and B.—SECTIONS ACROSS THE HIND-BRAIN OF A HUMAN EMBRYO 10 MM. LONG. (His.) $\frac{4}{1}$.

In A, the origin of the spinal accessory and hypoglossal nerves is shown, the fibres of both arising from groups of neuroblasts in the basal lamina of the neural tube. In B, one of the roots of the hypoglossal is still seen and in addition the root of the vagus nerve. This is represented as in part arising, like that of the spinal accessory in A, from a group of neuroblasts in the basal lamina and in parts continuous with a bundle of longitudinally coursing fibres placed at the periphery of the alar lamina, and corresponding in situation to the commencing dorsal white columns shown in fig. 137.

vesicle to the *hypoglossal* nerve (fig. 171). Its roots are in series with those of the ventral roots of the cervical nerves, and it is to be regarded as representing several (three or four) segmental—*i.e.* trunk or spinal—nerves fused into one stem. This idea is strengthened by the fact that a ganglion-rudiment (Froriep's ganglion), typical but rudimentary, is occasionally present in connexion with one or more of the roots. These hypoglossal nerves are connected with the occipital myotomes, and are *occipito-spinal nerves* in Fürbringer's sense—*i.e.* nerves properly belonging to a part of the trunk which has become included in the hinder part of the head. In the pre-otic region the *abducens* springs from the mesial column (fig. 172), and its roots are in the same series as those of the hypoglossal. It is regarded therefore by nearly all observers as the ventral (somatic) root of a segmental nerve. The *trochlearis* and *oculo-motorius*, however, have been variously interpreted, some observers regarding them as ventral mesial, others as lateral, motor roots; they

have also been interpreted as being dorsal nerves. Fürbringer (1902) puts the trochlear in an intermediate position, but regards it as most resembling a lateral motor root. His (1904) regarded both it and the oculo-motor as nerves springing from a region in which the distinction between the columns is less sharp than elsewhere; he was not therefore inclined to lay special stress on the point. The oculo-motor he held to be certainly a mesial (ventral horn) nerve.

The *lateral* column includes the nuclei of the motor roots of the vagus and spinal accessory, glossopharyngeal, facial, and trigeminal. The fibres supply the visceral musculature.

The **sensory** roots are developed from ganglia which arise from a forward continuation of the common ganglion-crest, but they show no regular segmental

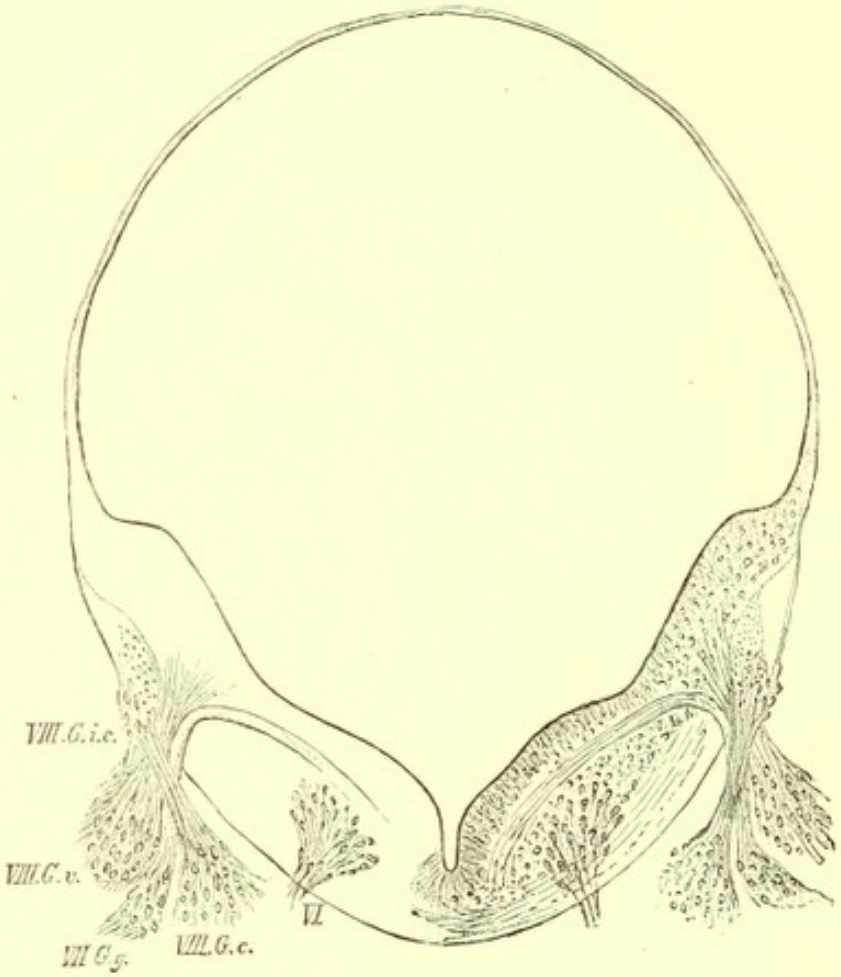



FIG. 172.—SECTION FROM THE SAME EMBRYO AT THE EXIT OF THE FACIAL NERVE. (His.)
(Several sections have been combined to form this figure.)

*VI.*, fibres of sixth nerve taking origin from group of neuroblasts in basal lamina; *VII.G.g.*, ganglion geniculi of the facial; *VIII.G.i.c.*, intracranial ganglion of auditory; *VIII.G.v.*, ganglion vestibuli; *VIII.G.c.*, ganglion cochleæ.

disposition. Moreover, unlike the spinal nerve-ganglia, they come into transient relation to thickened patches of the surface epithelium (*placodes*) which are placed above the gill-arches and have been interpreted in two ways. According to one view (van Wijhe, Beard, Froriep, and others), the placodes represent branchial sense-organs which have been lost in phylogeny, and they take no share in the formation of the cranial nerves. They occur in Selachians in two series, a *lateral* and an *epibranchial*. According to a second opinion (Kupffer, Goronowitsch, Julia Platt, Koltzoff, and others), these placodes are not rudimentary sense-organs, but thickenings from which cells are budded off to share in the formation of the definitive nerve-ganglia.

Thus in Petromyzon Koltzoff describes the segmental ganglia as originating from a mesial rudiment derived from the ganglion-crest, and from two peripheral ectodermic rudiments derived from the lateral and epibranchial placodes. In the region of the head these join to form the permanent ganglia; in the region of the trunk the surface placodes do not join with the central ganglion-rudiments, but remain separate and form the lateral-line organs.

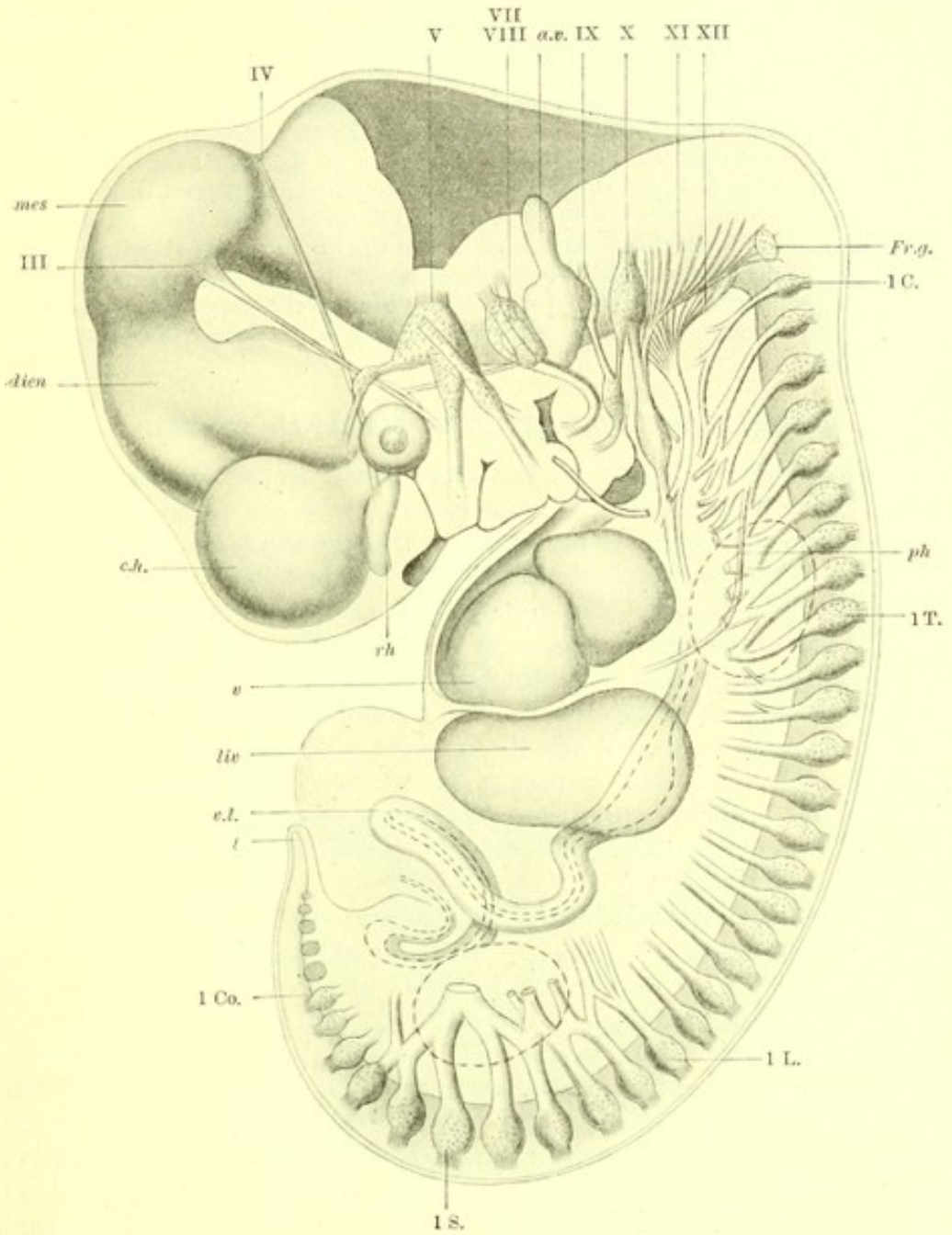



FIG. 173.—RECONSTRUCTION OF THE NERVOUS SYSTEM OF A HUMAN EMBRYO OF 10·2 MM. (After His.)

*v*, ventricle of heart; *liv*, liver; *v.l.*, vitelline loop of intestine; *t*, tail; *rh*, rhinencephalon; *c.h.*, cerebral hemisphere; *dien*, diencephalon; *mes*, mesencephalon; *a.v.*, auditory vesicle; *Fr.g.*, Froriep's ganglion; *ph*, phrenic nerve. The Roman numerals indicate the nerves. The sixth cerebral nerve is not labelled, but is seen passing forwards to the eye under the mandibular and maxillary branches of the fifth nerve.

In embryos of the third week the rhombic brain, as has already been indicated, shows a subdivision by slight folds into a series of divisions which have been termed *neuromeres* on the supposition that they represent a definite segmentation of the neural axis. In the pig Bradley finds the same number as Thompson in the human embryo—viz. seven—and states that the cerebellum lies opposite the first and the auditory vesicle opposite the third segment, while the trigeminal ganglia are related to the second, the acoustico-facial to the fourth, the glosso-pharyngeal to the sixth, and the vagus to the seventh. Broman describes in addition an eighth

neuromere in front of the cerebellum with which the fourth nerve is connected, and an indistinct ninth at the end of the series.

The lateral motor roots have been interpreted as representing in the cerebral nerves the *splanchnic efferent* fibres which in the cord leave the axis by the ventral root, and are not therefore separated from the *somatic efferent* fibres. They may be, on the other hand, represented by fibres which Lenhossék and Ramon y Cajal have shown to arise in the ventral horn of the embryonic cord (chick) and to run out in the dorsal roots. The cell column from which the lateral roots spring may represent the lateral horn column of the cord.

The accessory is (see below) ontogenetically a part of the vagus, wholly therefore a cerebral nerve. From his studies of the occipital nerves Streeter concludes that 'in all higher vertebrates, accompanying the conversion of certain gill-muscles into the trapezius and sternomastoid, the cranial elements (*i.e.* vagus complex) make a caudal invasion of the spinal cord.' The result of this invasion, added to the inclusion in the skull of the occipito-spinal segments, is a blurring of the line of demarcation between the nerves of spinal and those of cranial type, which is distinct in spite of the inclusion of the occipito-spinal segments in the skull in lower vertebrates.[1]

Numerous attempts have been made to bring the nerves of the head into a segmental scheme, and to homologise the cerebral with the spinal nerves. None of these are quite convincing, and there is still great uncertainty as to what interpretation should be put on the serial characters of the branchial region.

## DEVELOPMENT OF INDIVIDUAL CEREBRAL NERVES.

The **hypoglossal**[2] appears in the third week as a number of rootlets arranged in three or four segmental groups in series with the cervical motor roots, and connected with the occipital myotomes. During the fourth week they fuse into one trunk as they pass towards the floor of the primitive mouth. Owing to the bend in the neural tube, the hypoglossal and upper cervical nerves are brought close together 'like the spokes of a wheel' (Streeter) and grow side by side into a mass of tissue out of which the tongue and hyoid muscles are developed. They are bound more or less together by the developing sheaths, and connexions are established between them. When the muscles take form and draw apart the nerves are separated out into a plexus in which is foreshadowed the adult arrangement of the branches supplying this group of muscles.

A ganglion (*Froriep's ganglion*) is occasionally found in connexion with one of the roots (figs. 169 and 173).

The **vagus complex** includes the **vagus** and **spinal accessory**, which develop practically as a single structure. The ganglion-crest from which the vagus ganglion is developed is a continuation forwards of the spinal ganglion-crest as seen in embryos of the third week. It extends from the first and second cervical to the auditory vesicle (fig. 175), where it is interrupted, the gap representing the separation of the vagus from the glossopharyngeal. The motor fibres appear first; they form a strand which runs mesial to the crest as low as the third or fourth cervical segment, and are connected with the lateral-horn region of the neural tube. This strand is the primary accessory trunk; in front of its emerging roots and in line with them are a few scattered bundles at the head of the crest. The ganglion of the vagus early shows a duplicity—*ganglion of the trunk* and *ganglion of the root*. These separated masses have usually been described as due to a subdivision of the neural-crest ganglion; but Streeter supplies evidence which seems to indicate that the ganglion of the trunk (*g. nodosum*) may be developed separately. It is related to an ectodermal patch (epibranchial placode) above the gill-arches. The two ganglia are at first separated by a cellular tract, which is afterwards converted into a fibrous trunk. The ganglion-crest now (by the third week) becomes broken up into separate clumps by the laying down of fibre-paths. The most anterior of these form the definitive *ganglion of the root*; the remainder (three or

[1] *Loc. cit.*, p. 111.

[2] The summary of the development of the occipital nerves is mainly founded on Streeter's paper (*loc. cit.*).

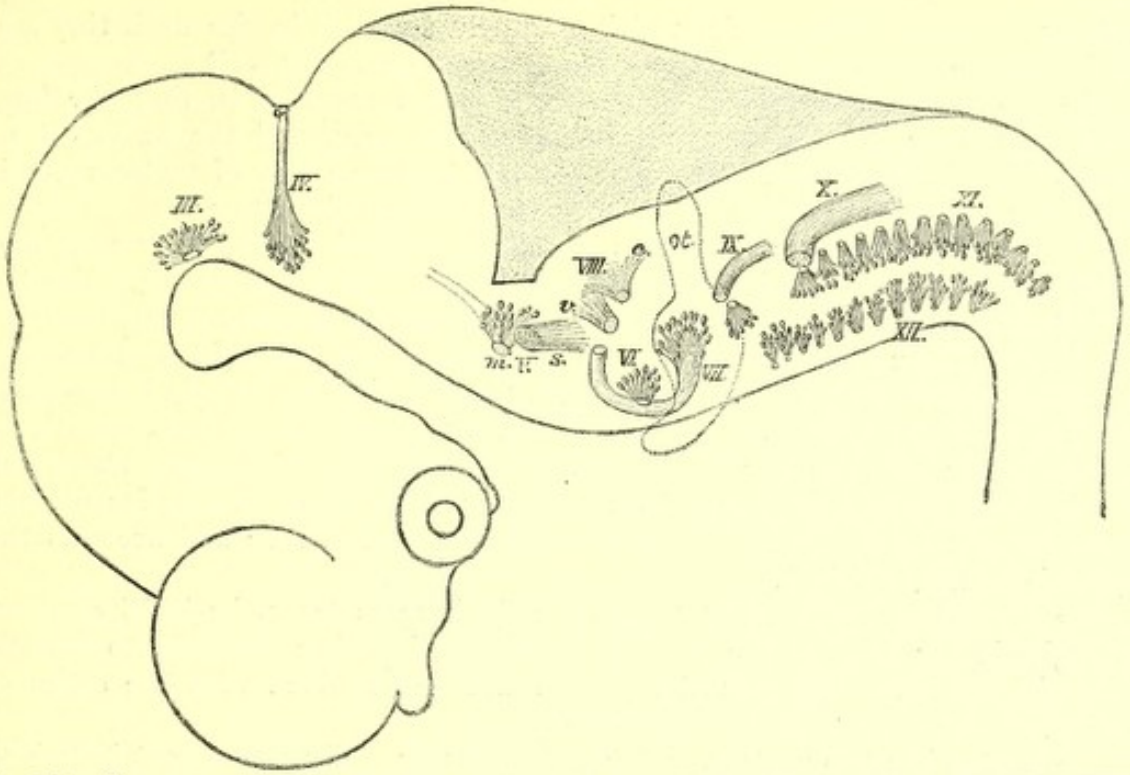



FIG. 174.—DIAGRAM SHOWING THE CENTRIPETAL AND CENTRIFUGAL ROOTS OF THE CEREBRAL NERVES OF THE SAME EMBRYO AS SHOWN IN FIG. 173. (His.)

The places of exit of the nerves are marked by dotted circles or ovals. The efferent nerves (*III*, *IV*, *mV*, *VI*, *VII*, part of *IX*, *XI*, and *XII*) are seen to arise within the nerve-centre from groups of neuroblasts; the afferent fibres (*V.s*, *VIII*, *v* and *c*, most of *IX*. and *X*) pass a certain distance inwards, and for the most part also caudalwards in the nerve-centre, and there end. The ganglion-rudiments from which they have grown are not shown here. They are represented in the preceding figure.

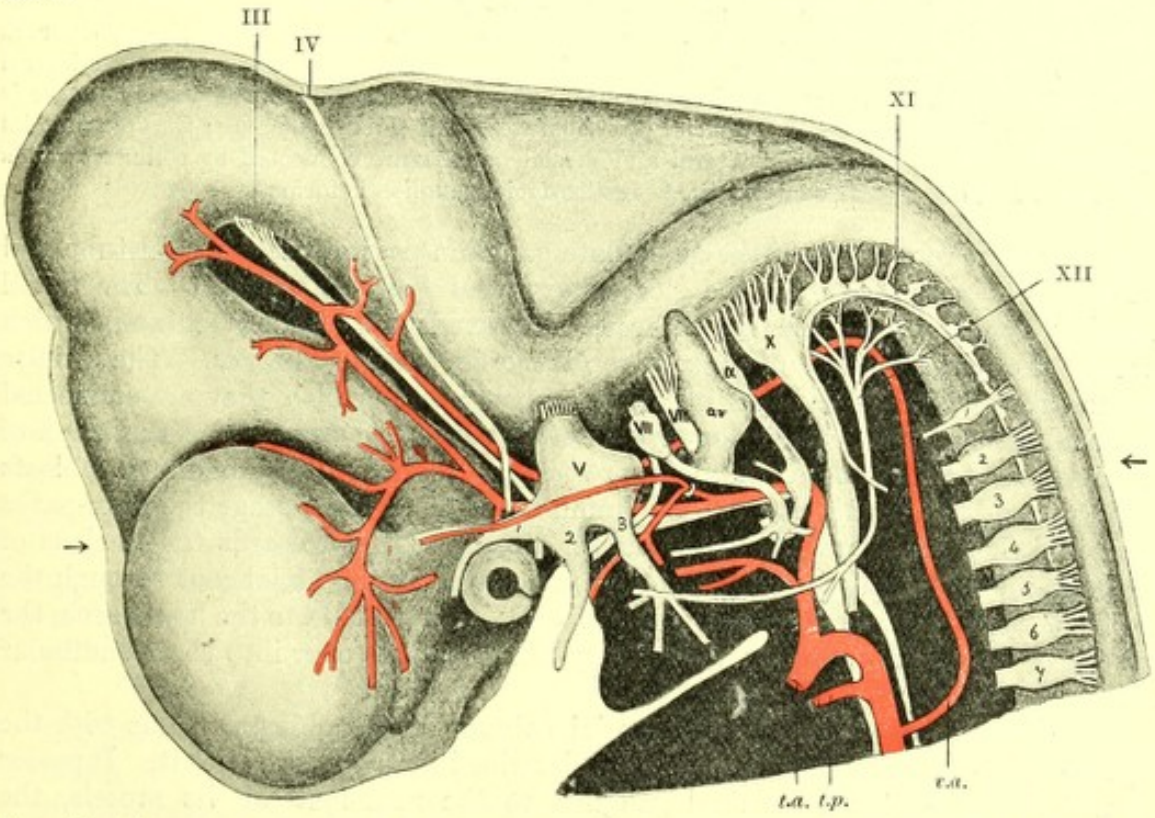



FIG. 175.—DIAGRAM REPRESENTING THE DISTRIBUTION OF THE CEREBRAL NERVES AND VESSELS OF THE HEAD IN AN EMBRYO ABOUT THE FIFTH WEEK; FOUNDED ON RECONSTRUCTIONS BY TANDLER, STREETER, AND MALL. (T. H. Bryce.)

III to XII, cerebral nerves; the sixth is not labelled: it is seen passing forwards below V 3, the mandibular branch of the fifth. 1 to 7, ganglia of the first seven spinal nerves; *a.v.*, auditory vesicle; *t.a.*, truncus aortæ; *t.p.*, truncus pulmonalis; *v.a.*, vertebral artery.

four) are accessory root-ganglia, which gradually diminish in size until they are found as mere rudiments in the root of the accessory nerve (fig. 173).

The result of the differentiation of the vagus complex is, that the fore-part or vagus division, becomes predominantly sensory, and the back-part or accessory division predominantly motor (Streeter). The series of motor roots is continuous, and both divisions are at first mixed motor and sensory.

The **glossopharyngeal** develops in a fashion identical with the vagus, and in the human embryo it arises independently of it. The *petrous ganglion*, like the vagal trunk-ganglion, is associated with an ectodermic thickening (epibranchial placode) above the third branchial arch. Though in the case of both vagus and glossopharyngeal the part of the ganglion connected with the placode has possibly an independent origin, Streeter does not describe any appearances which positively prove an origin from the placode, as has been described in lower vertebrates. The main bundle of fibres from the petrous ganglion runs in the third arch forming the lingual branch, while a second bundle runs into the second arch and becomes the tympanic branch (fig. 175).

The **acoustic** nerve arises from a ganglionic mass (*acoustico-facial complex*) which lies just in front of the auditory vesicle and is early separated into acoustic and facial portions. The acoustic portion will be described with the organ of hearing.

The **facial** has two roots, a motor and a sensory. The *sensory* root is derived from a ganglion distinguished by its larger cells, which is separated off from the common acoustico-facial ganglion and is named *geniculate*. It is directly continuous with an epidermic thickening over the hyo-mandibular cleft (embryo of twenty third day : Futamura [1]).

The acoustico-facial is generally considered a complex nerve connected with the hyoid arch Giglio-Tos, founding on observations in a seventeenth-day embryo, argues for the independence of the two nerves in the earliest phases. According to his description, each of the two nerves has a median proganglion derived from the neural crest and two peripheral proganglia, a lateral and an epibranchial, with corresponding placodes. The lateral placode of the acoustic nerve is the auditory epithelium, that of the facial is a separate and distinct thickening ; the epibranchial proganglia are continuous. The lateral and mesial ganglia are connected by cellular strands (pronerves), and out of this complex the acoustico-facial ganglion is formed.

The central root-fibres of the geniculate ganglion pass into the neural tube and end in series with those of the glossopharyngeal (*pars intermedia*). The distal branches appear about the fourth week as strands (A. Francis Dixon) which become the *great superficial petrosal* and *chorda tympani* nerves. They unite secondarily with the branches of the fifth nerve with which they are connected in the adult, and are well developed before the peripheral branches of the trunk of the facial can be recognised. The *motor root* springs from a group of neuroblasts in the antero-lateral part of the basal lamina, and at an early stage the fibre-paths connected therewith show a general mesial direction (His) towards the nucleus of the sixth nerve, foreshadowing the devious course of the facial root through the floor of the fourth ventricle. The motor fibres are distributed to the hyoid arch, the muscles of which they supply ; the sensory branches pass over into the mandibular arch.

The **abducens** arises from the mesial column of neuroblasts in line with the hypoglossal roots. No ganglion has been described in connexion with it. It passes forward mesial to the trigeminal ganglion to the rudiment of its muscle, the external rectus of the eye.

The **trigeminal** nerve has a motor and sensory rudiment. The chief *motor* nucleus appears as a group of neuroblasts which forms a keel-like projection of

[1] Anatomische Hefte, xxx. 1906.

the wall of the neural tube opposite the ganglion, and immediately to the mesial side of its entering dorsal root (fig. 174). The group of cells therefore belongs to the lateral column. The descending root appears later, and is derived from a mass of neuroblasts lying in close relationship to the oculo-motor and trochlear nuclei in the floor of the mid-brain. The *sensory* root arises from a large ganglion, a derivative (in part at least) of the ganglion-crest (see below). It is situated opposite the pontine flexure, and in the fourth week has become connected by a single dorsal root with the neural tube, while peripherally it is already provided with three primary branches—ophthalmic, maxillary, and mandibular (figs. 173, 175). The ganglion in an early phase is said by Giglio-Tos to be connected with the surface ectoderm (placode). The ganglion becomes the Gasserian ganglion. The various *subsidiary ganglia* (ciliary, Meckel's, otic, and sub-maxillary) arise like sympathetic ganglia (see below) in connection with the several branches of the nerve.

In some lower forms the trigeminal shows traces of a composite character, and it has hence been suggested that it represents the union of more than one segmental nerve. In a human embryo of the seventeenth day Giglio-Tos has described a complicated origin for the Gasserian ganglion. He believes, in the first place, that the rudiment is primarily connected with the mesencephalon, and that the nerve becomes displaced backwards. He recognises three neura 'proganglia,' three epibranchial 'proganglia' connected with surface placodes, and three 'pronerves'—*i.e.* cellular strands between the neural and lateral ganglia. This complex mass fuses into the single ganglion generally described as the rudiment of the dorsal root.

From the foregoing account it will be seen that ectodermic placodes have been described in connexion with all the cerebral nerve-ganglia in the human embryo; it must be left an open question, however, whether the ganglia which are related to these placodes have not an origin from the surface ectoderm.

The **trochlearis** springs from a tract of neuroblasts situated in the isthmus. They occupy both the mesial and lateral portions of the basal lamina (His, 1904). The fibres take a dorsal course in the reticular zone to the roof of the isthmus (future valve of Vieussens), where they cross and, again emerging, pass round the wall of the mid-brain to their muscle (superior oblique of the eye).

The trochlearis presents the special and puzzling peculiarities—first, that though a ventral nerve it emerges from the dorsal aspect of the neural tube; and second, that it crosses with its fellow to form a dorsal commissure. These facts have not received a satisfying ontogenetic explanation.[1]

The **oculomotorius** springs from a ventral and mesial tract of neuroblasts in the mesencephalon, and is generally pronounced a mesial or somatic nerve. The root passes off from the ventral aspect of the neural tube just in the cephalic bend, and passes backwards in its course to the rudiment of the ocular muscles, which it supplies.

It has no ganglion-rudiment, but in some forms the nerve-path is beset with nuclei, which have been regarded as such, and the ciliary ganglion has been sometimes considered as arising by an aggregation of the outwandering elements on this nerve instead of from the Gasserian ganglion of the fifth.

## DEVELOPMENT OF THE SYMPATHETIC SYSTEM

The problem of the origin of the sympathetic is only a part of the larger one of the origin of the peripheral nerves. There are two chief views regarding the source of the ganglion-cells. According to the one (Remak, Kölliker, Paterson), they are mesodermic; according to the other (Balfour, His Sr., His Jr., and many others), they are ectodermic in origin. The first view is based (Paterson) on the independent appearance in birds and mammals of an unsegmented strand of mesoderm

[1] For a general discussion of the question, see Fürbringer, 'Morphologische Streitfragen,' Morphologisches Jahrbuch, xxx., 1902.

into which, or through which, the visceral branches of the spinal nerves grow. The nerve-fibres are said to become connected with the cells, and certain of these persist to form the ganglia, while those of the intervening portion undergo changes resulting in the formation of the commissural cords. This view has found little

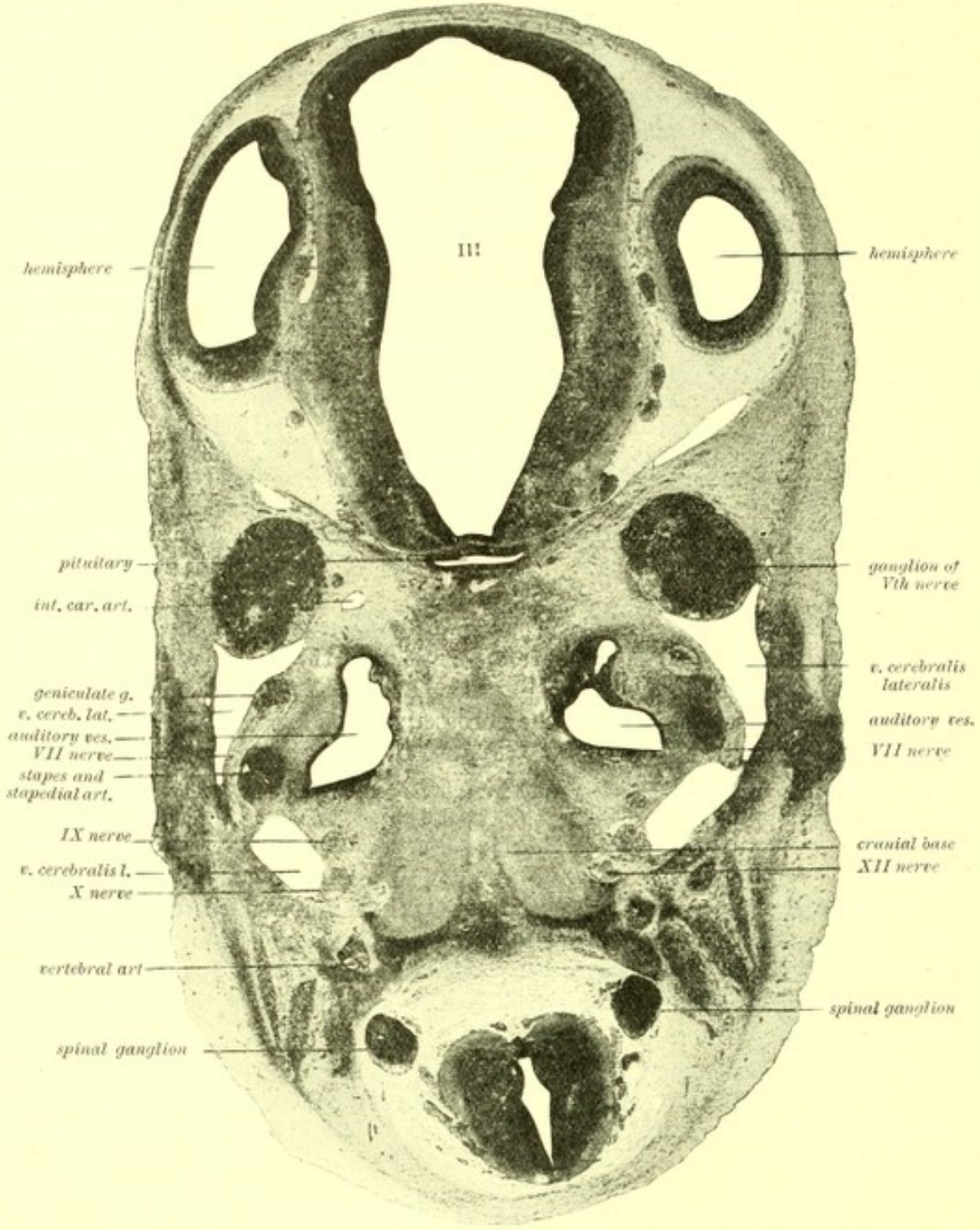



FIG. 176.—SECTION OF THE HEAD OF A HUMAN EMBRYO OF 15·5 MM. Photograph. (T. H. Bryce.)

The section will be readily understood if the structures be traced along the line between the two arrows in fig. 175, p. 131. III, cavity of diencephalon.

favour; and even though the cells may seem to arise *in situ*, our present knowledge of the composition of the mesenchyme does not warrant our pronouncing all elements in it necessarily mesodermic. The second view is presented in several forms. One account, based more especially on Selachian material, describes the

ganglia as formed from outgrowths of the spinal nerve-roots (Balfour), the cells of the outgrowths being identical with those which give origin to the nerve-trunks, and becoming differentiated *in situ* into ganglion-cells. Another account regards the sympathetic simply as detached parts of the spinal ganglia, the errant ganglia thus produced remaining attached to the spinal nerve by the ramus communicans, and becoming secondarily connected together to form the gangliated chain. His showed that in the human embryo the visceral branches of the spinal nerves appear before the ganglia. He accordingly modified the interpretation in the sense that the elements which form the sympathetic ganglia are not formed nerve-cells, but indifferent cells which, arising in the spinal ganglia, wander passively or actively along the previously formed nerve-paths to become aggregated into groups or primitive ganglia, where their transformation into nerve-cells is completed. A third interpretation goes one step further, and describes the growth of the sympathetic as a part merely of a general extension in the developing nerve-paths of indifferent ectoderm cells, which undergo their differentiation into nerve-cells, sheath-cells, or chromophil-cells only when they reach their peripheral situation (Kohn [1]) (see p. 100).

None of these interpretations of the appearances seen are easily capable of objective proof, but the weight of evidence is decidedly in favour of the purely ectodermic origin of the sympathetic, and of the discrete spread of indifferent cells.

The sympathetic first appears in the form of groups of cells closely applied to the ventral branches of the spinal nerves. Each of these soon becomes a cellular cord which is the rudiment of the *ramus communicans*. The ramus communicans next becomes fibrillar, and the ganglion is produced by proliferation of a terminal group of cells (fig. 170). The primitive ganglia are secondarily connected by cellular strands into a continuous cord, which becomes segmented later by the conversion of the intervening strands into nerve-fibres. There is little doubt that the whole system of plexuses and ganglia is formed by extension due either to proliferation or to wandering of the cells from the primary chain. In the neck the cord is closely related to the vagus, and the branches of the two are bound up in a common plexus for the supply of the heart and lungs. The superior cervical ganglion is said to be derived from the ganglion nodosum of the vagus, and perhaps also the ganglion of the glossopharyngeal (His, Jr.). The abdominal sympathetic consists at quite early stages of many groups of cells round the aorta, and many scattered groups which extend into the mesentery, through which the cells reach the stomach and intestine. The cells form a single layer in the wall of the stomach, afterwards separated into the two plexuses by the formation of the muscular coats (His, Jr.).

*Chromophil, chromaffin, or phäochrome bodies.*—It has within recent years been shown that, more especially in the region of the abdominal sympathetic, but also along the whole extent of the sympathetic cord, groups of cells are formed from the primary indifferent sympathetic cells, which have the special property of staining yellow brown with the salts of chromic acid. This chromophil system is represented in the adult by the medulla of the suprarenal body, and perhaps also by the carotid and coccygeal glands. Such chromophil bodies, first discovered in the human embryo in 1901 by Zuckerkandl, are seen grouped more especially between the kidneys and suprarenal bodies, extending downwards along the ureters into the pelvis. They consist of groups of large clear cells with very lightly staining nuclei (fig. 257, p. 204), and contrast strongly with the groups of densely arranged smaller and deeply staining cells traversed by nerve-fibres which are the rudiments of the sympathetic ganglia. It is more especially to the researches of Kohn that the recognition of the system in the human subject is due. It appears certain that the cells are sympathetic in origin ; they occur not only in masses, but in scattered groups in the ganglia. The histogenesis is conceived briefly

[1] Kohn, Arch. f. mikr. Anat. lxx. 1907.

as follows: The primary sympathetic cells are indifferent (ectodermic) elements which become differentiated into two families of cells through a stage named in one case the *sympathoblast*, and in the other *phäochromoblast* (Pol[1]), which become respectively sympathetic nerve-cells and chromophil or phäochrome cells. The significance of these researches in connexion with the adrenal will be alluded to later.

## DEVELOPMENT OF THE EYE.[2]

The eyes begin to develop as a pair of hollow protrusions from the primitive fore-brain, named the *optic vesicles*. In some mammals the protrusions appear before the neural canal is closed in by the fusion of the medullary folds; in the pig, for instance, as shown by Keibel, they show as shallow pits on the medullary folds while these are still spread out flat. The appearances presented by the very early human embryo drawn in fig. 177, show that this may occur in the human subject also. The optic vesicle is continuous on its outer side with the surface ectoderm of the side of the head; and as this point of attachment does not move so much during the formation of the cranial flexure as does the attachment to the brain-tube, it follows that the vesicle becomes obliquely placed (His),

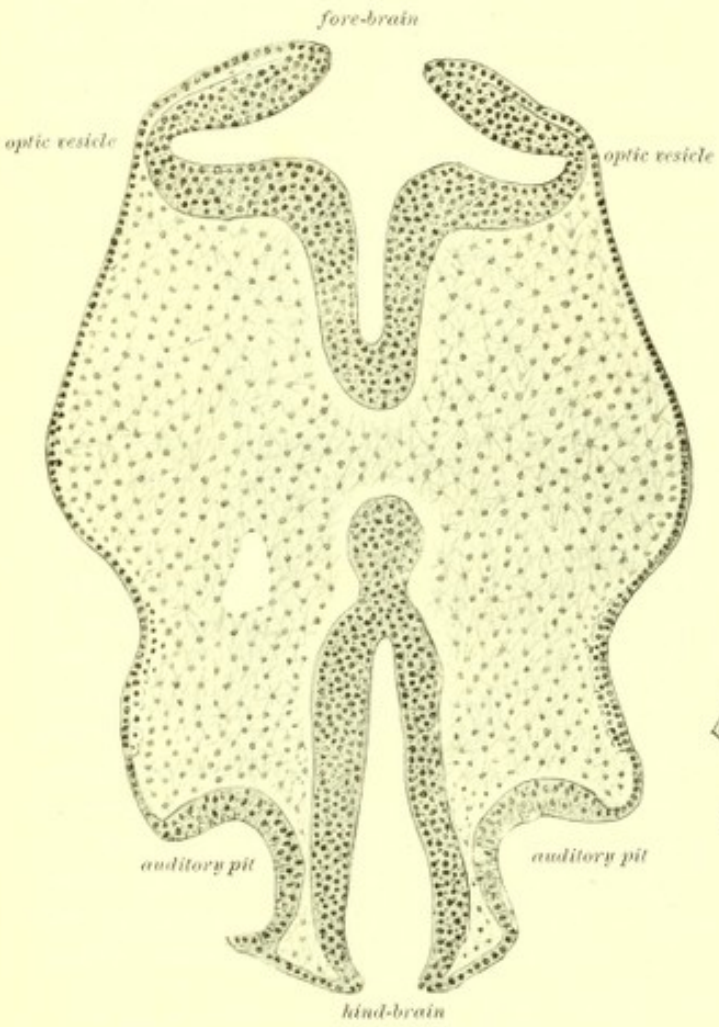



FIG. 177.—TRANSVERSE SECTION OF THE HEAD OF A HUMAN EMBRYO OF 2·4 MM., SHOWING THE OPTIC VESICLES AND AUDITORY PITS. (T. H. Bryce.)

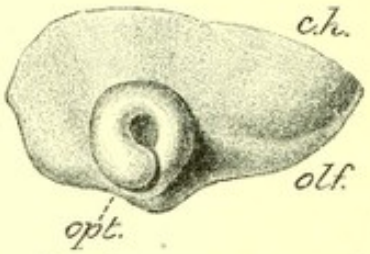



FIG. 178.—SIDE VIEW OF ANTERIOR PART OF BRAIN OF A HUMAN EMBRYO OF THE FOURTH WEEK, SHOWING THE PRIMARY OPTIC VESICLE FOLDED AND CUPPED. (His.)

*c.h.*, cerebral hemisphere (part of); *olf.*, olfactory lobe; *opt.*, optic cup.

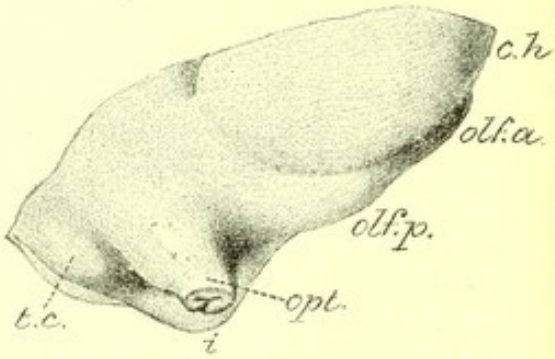



FIG. 179.—SIDE VIEW OF THE SAME PART OF THE BRAIN IN A STILL MORE ADVANCED EMBRYO, THE EYE HAVING BEEN CUT AWAY. (His.)

*opt.*, cut end of optic stalk, showing the manner in which it is folded: *i*, infundibulum; *olf.p.*, posterior part of olfactory lobe; *olf.a.*, anterior part of the same; *c.h.*, cerebral hemisphere; *t.c.*, tuber cinereum.

[1] In Hertwig's Handbuch der vergleich. Entwickelungslehre III. Th., for which see references to recent literature.

[2] For literature, see Froriep, Hertwig's Handbuch II. Th. i. and ii. p. 261 *seq.* More recent references in footnotes.

with its surface attachment dorsal and caudal, and its central end or stalk ventral and cranial. The surface ectoderm now becomes thickened and pitted-in so as to form a cup-shaped depression (fig. 180), which subsequently becomes converted into a vesicle by the closure of its mouth. This is the rudiment of the lens, and *pari passu* with its formation the optic vesicle becomes doubled up to form the *optic cup*. The cavity of the cup is occupied at first by the lens vesicle, but later it becomes opened out to form the cavity of the eyeball or vitreous chamber, while

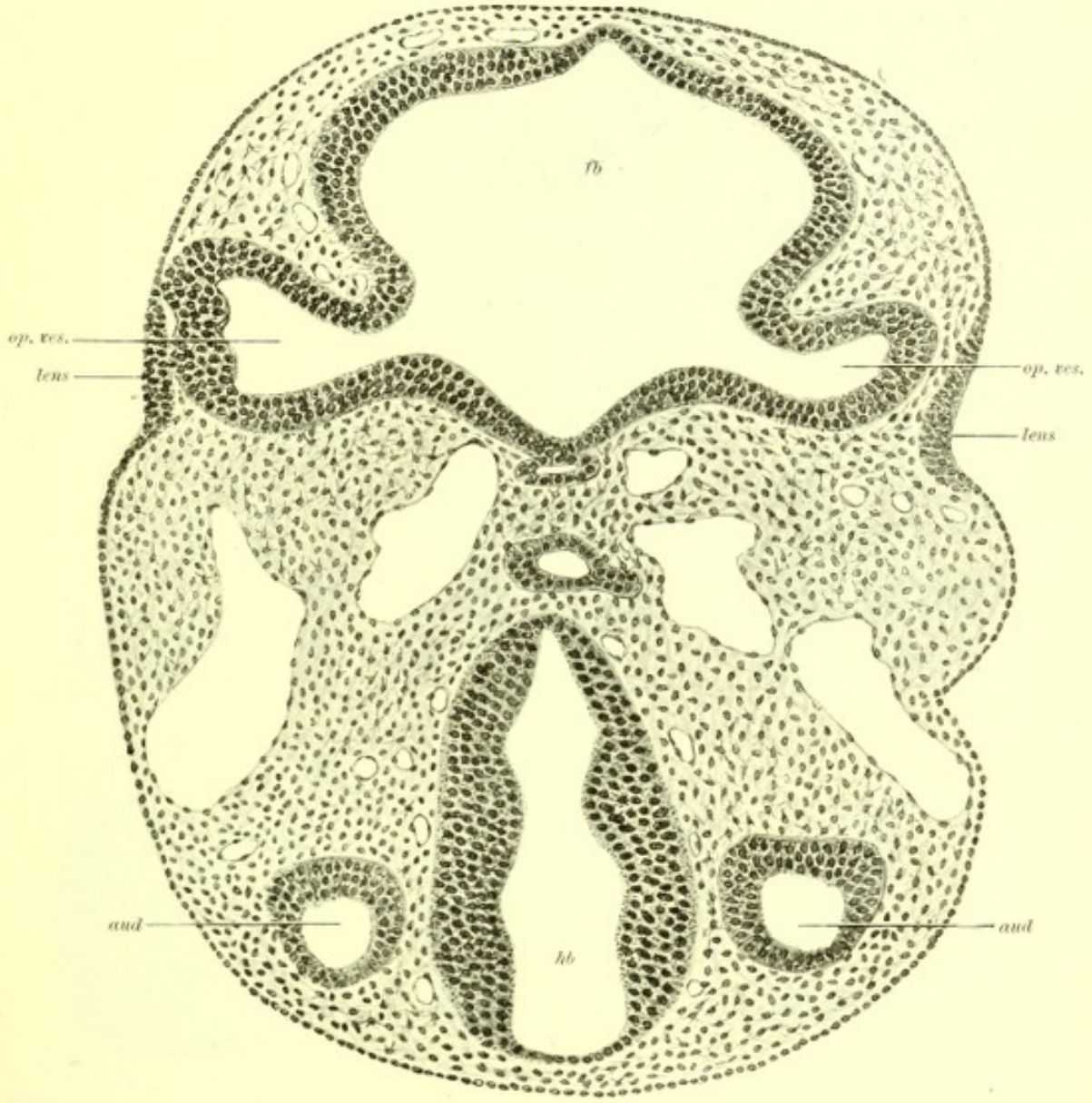



FIG. 180.—TRANSVERSE SECTION HEAD OF A RABBIT-EMBRYO OF THE ELEVENTH DAY. (T. H. Bryce.)

*fb*, fore-brain; *hb*, hind-brain; *op.ves.*, optic vesicles; *lens*, lens-plaque; *aud.*, auditory vesicles.

the original cavity of the optic vesicle is almost entirely obliterated, appearing merely as a cleft between the outer and inner walls of the cup.

**Development of the lens.**—The rudiment of the lens is a disc-shaped ectodermal plaque situated on the side of the head opposite the upper and outer aspect of the optic vesicle (fig. 178). The plaque is at first closely applied to the outer wall of the vesicle, but when this begins to be invaginated they draw apart somewhat, remaining connected, however, by protoplasmic strands (fig. 183). This syncytial connexion is in all probability maintained during the formation and

opening out of the optic cup—a point the significance of which will appear later. In the few cases in which an open lens-pit has been described in the human embryo it is figured as a thick-walled, cup-shaped, then flask-shaped depression, the lips of which come together to form a vesicle which is connected for a time with the surface ectoderm by an epithelial stalk, but afterwards becomes completely separated from it. The inner wall of the vesicle at an early stage

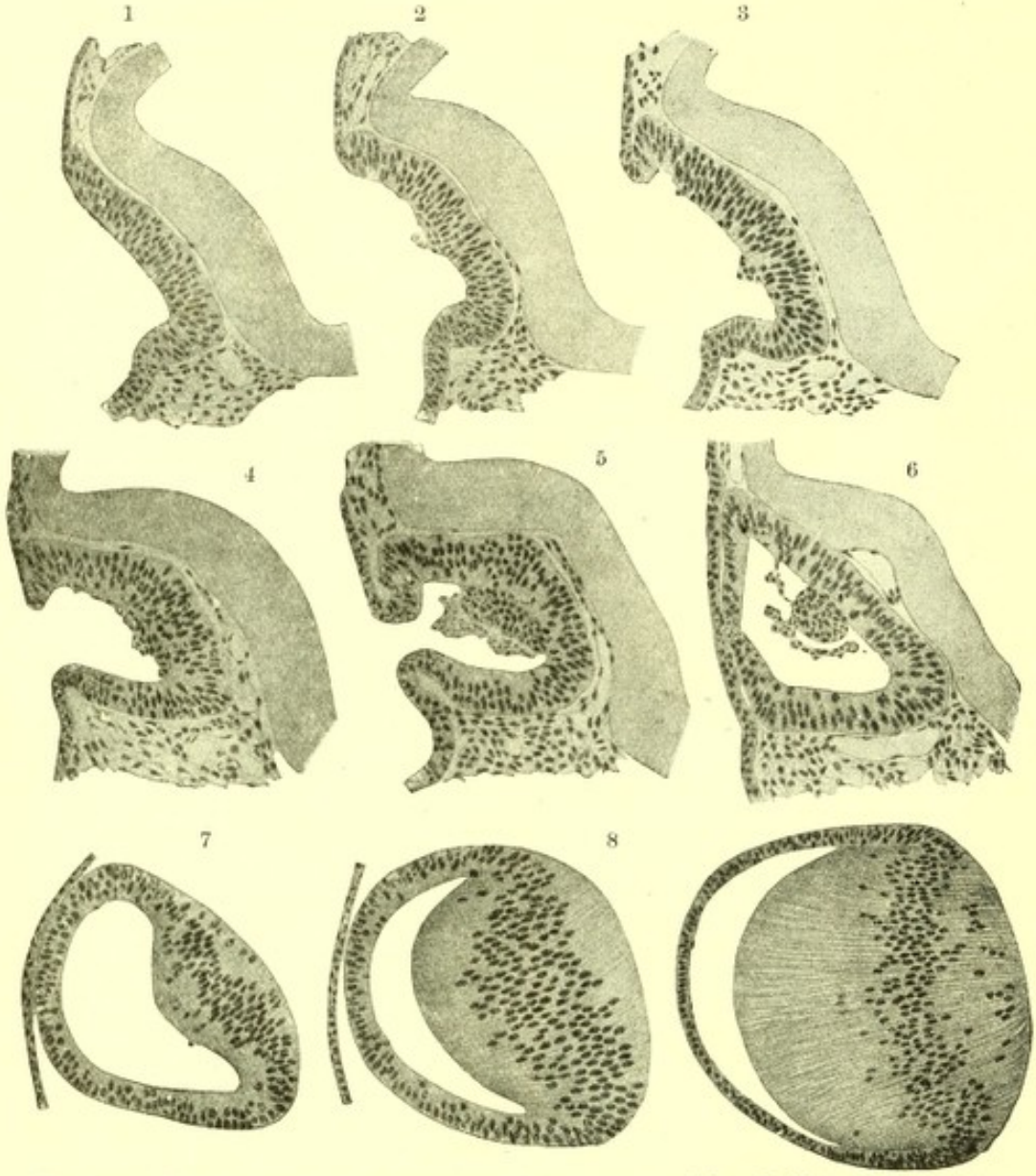



FIG. 181.—DEVELOPMENT OF THE LENS IN THE RABBIT. (After Rabl, from Hertwig's Handbuch der Entwickelungslehre.)

Nos. 1 to 8 × 130 diameters: No. 9 × 91 diameters. The stages 1 to 5 embryos from the middle of the eleventh to the middle of the twelfth day. No. 6 an embryo at the end of the twelfth day.

increases in thickness and encroaches on the cavity, while the outer remains a thin lamella (fig. 181).

In the rabbit embryo the lens-pit does not coincide with the centre of the lens-plaque; therefore in cross-section it is triangular, not hemispherical. The vesicle consequently is also triangular in section, and it is rather the upper and inner wall which becomes thickened by the elongation of its cells. The lens in its early stages thus appears in cross-sections of the embryo to be obliquely placed in the optic cup (fig. 181). It may also be mentioned, though the significance of the fact is unknown, that in the rabbit, and also in man (Rabl), the vesicle contains a mass of epithelial cells, which undergo degenerative changes and ultimately disappear.

The thin anterior layer remains throughout life as a simple layer of cubical cells, and forms the so-called lens-epithelium ; but the cells of the posterior layer grow forwards into the cavity of the lens-vesicle as the lens-fibres : the central fibres are the longest and straight (fig. 182), while the rest are slightly curved with their concavity towards the equator. The fibres become gradually shorter towards the circumference, where they pass through gradually shortening

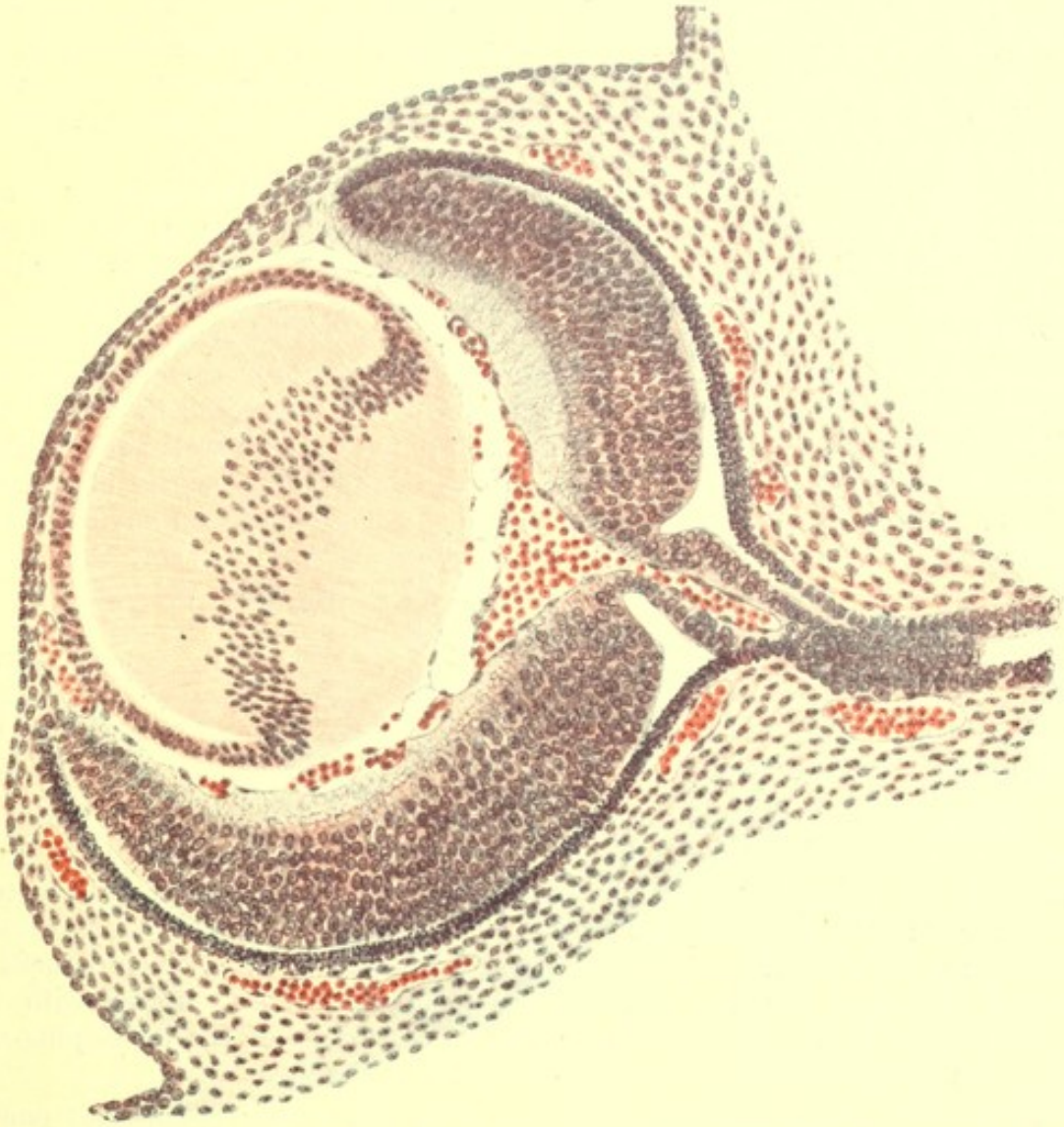


FIG. 182.—SECTION OF THE DEVELOPING EYE OF A RABBIT-EMBRYO OF THE THIRTEENTH DAY. (T. H. Bryce.)

The section passes through the optic stalk, and cuts the groove in which the central artery of the retina passes into the interior of the optic cup. The cavity of the lens-vesicle is not yet obliterated ; its anterior wall is formed of a layer of cubical cells ; its posterior wall, greatly thickened, is becoming converted into the lens-fibres. The cavity of the optic cup is almost filled by the lens. On the surface of the retinal layer of the cup is seen a protoplasmic nuclear-free zone which is the primitive vitreous. It has shrunk away from the lens, and thereby shows very clearly the vascular layer of mesenchyme on the posterior aspect of that body. The vessels are seen entering the optic cup through the choroidal fissure of the optic stalk, and also through the space between the lens and the mouth of the cup.

columnar cells (*transitional zone*) into continuity with the anterior epithelium. By the growth of these fibres the cavity of the lens-vesicle becomes obliterated.

In this manner the central part of the lens is developed, and it consists in the main of fibres which pass in an antero-posterior direction. The remainder of the lens is formed of fibres which are so disposed as to curve round its margin and over the ends of the first formed fibres ; they are, moreover, deposited in

successive layers and in three (or more) separate sections, so that their ends abut against one another in front and behind along tri-radiate (or multi-radiate) lines, such as may be seen in the macerated lens. These later deposited fibres are all formed at the equator (at the transitional zone), where cell-multiplication chiefly takes place, and they grow hence meridionally backwards over the ends of the already developed antero-posteriorly disposed fibres of the central part of the lens.

**Development of the optic cup.**—The doubling-in of the optic vesicle is a gradual process of involution, and from the first the invaginated outer wall is thicker than the inner (fig. 182). The thinner outer layer of the completed cup early shows a deposit of pigment, and becomes the hexagonal pigmented epithelium of the retina, while the thicker inner layer is converted by a complicated series of changes into the retina.

The optic vesicle at first opens into the cavity of the fore-brain by a wide aperture. As the vesicle enlarges the lips of this gradually close in, and the stalk becomes elongated into a hollow cord. The upper wall of this tube is thinner than the lower. When the optic cup is formed the thin upper wall of the stalk is continued into the outer layer, while the thick lower wall is continued into the thick retinal layer of the cup. This is due to the character of the invagination of the optic vesicle. It is not a simple in-pushing of the outer wall by the growing lens-vesicle, for the folding is not confined to the part of the wall against which the lens lies, but also implicates the ventral wall and commencement of the stalk (fig. 178). A cleft is thus left below the lens which is continued some distance along the stalk as a fold of its thick lower wall (fig. 179). The cleft and groove soon become closed in, but before this is effected vessels enter the hollow of the cup (fig. 182), the fate of which will be discussed later.

The line of closure of the lips of the cleft remains apparent for some time owing to the fact that when pigment develops in the wall of the cup this so-called *choroidal fissure* remains unpigmented for a time. The malformation known as *coloboma iridis* is attributed to a persistence of this fissure or unpigmented tract.

**Development of the retina.**—The thickened inner layer of the optic cup early shows a distinction into a thicker posterior portion, the *pars optica*, and a thinner anterior portion the *pars cæca*. The line of demarcation becomes marked by a thickened lip known as the *ora serrata*. The *pars cæca* becomes further divided into the *pars ciliaris retinæ* where the inner layer remains as a single lamella of columnar cells, and the *pars iridis* where it becomes closely united with the pigmented outer layer, and spread over the inner surface of the developing iris, to form the thickly pigmented epithelium known as the *uvea*.

The *pars optica* undergoes histological changes which are, in their essential and primary features precisely similar to those already described for the general neural epithelium. It is at first a single layer of high columnar epithelium with closely set nuclei at different levels. The germinal zone is necessarily on the outer convex side of the lamella, that having been the original inner surface. As the nuclei multiply a nuclear-free (or nearly free) zone is formed on the concave aspect, which corresponds to the reticular zone of the general neural epithelium. Sustentacular or primitive glial elements are laid down and persist as the *fibres of Müller*, and an outer and inner medullary lamina appear. The multiplying nuclei become arranged in zones separated by narrow reticular bands. This is the expression of the grouping of the neuroblasts into radiating cell-complexes, or, interpreted by the syncytial theory, of the arrangement of the neural syncytium into radiating multinuclear fibrillar paths. The nerve-fibre layer is formed as elsewhere from the marginal reticular zone. The rods and cones appear first in the axis of the globe as rounded refractile bodies projecting from the external medullary lamina into the cleft between the two layers. They are produced progressively from the central point of the retina to the periphery. Graham Kerr [1] finds in *Lepidosiren paradoxa*, in which the cells are of great size, that in the elements destined to become visual cells a vesicle appears which contains apparently a fatty substance. As this enlarges the cell bulges the external medullary

[1] Quart. Jour. Micro. Sci. xlvi.; see also Cameron, Jour. Anat. and Phys. xxxix.

lamina before it, so that a part projects into the space between the layers of the optic cup. From this a protoplasmic process is developed, which, elongating, becomes transversely striated and converted into the cuticular rod.

The **optic stalk** is, as we have already seen, hollow. Its lower wall is thicker than its upper and is invaginated by the choroidal fissure at its ocular end. The fissure soon closes, and the artery, entering the optic cup within the stalk, is enclosed. The ventricular cavity is obliterated by the middle of the second month, but the epithelial cells retain for some time longer their radial disposition. This soon becomes lost, and the stalk becomes converted into a glial network in

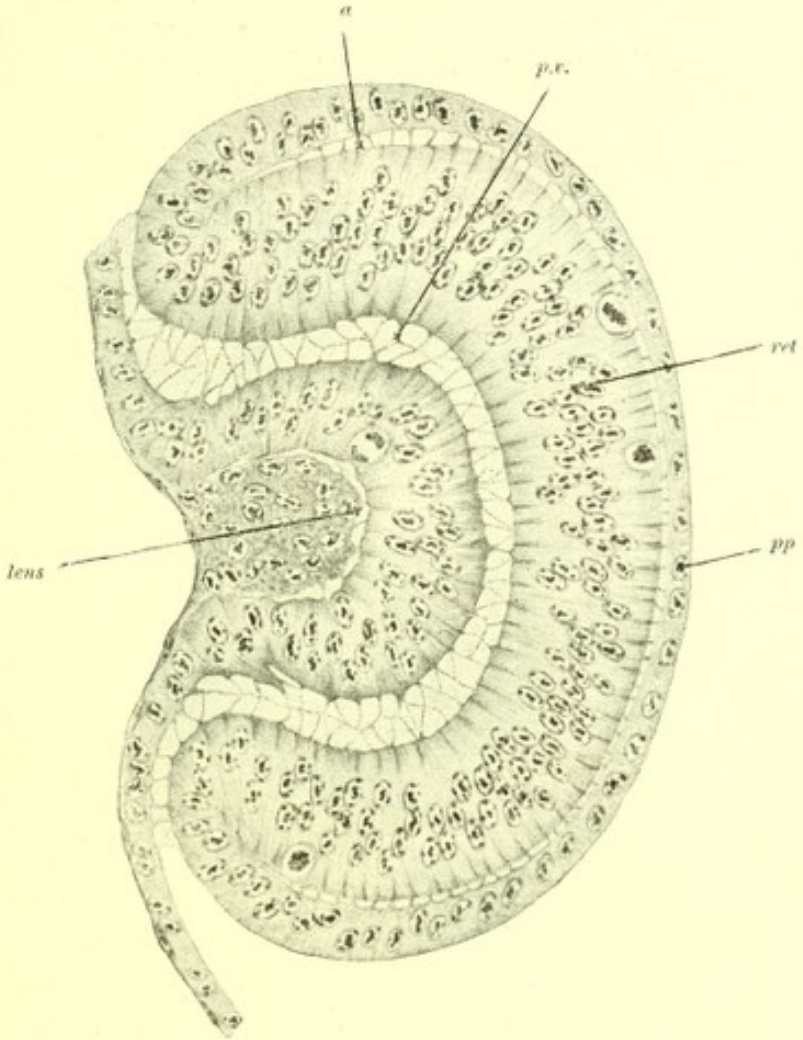



FIG. 183.—SECTION OF THE DEVELOPING EYE OF TROUT. (Szily.)

*lens*, lens-vesicle not yet closed; *ret*, inner layer, *pp*, outer layer of optic cup; *p.v.*, primitive vitreous; *a*, protoplasmic connexions between the cells of the outer and inner walls of the optic cup.

which the nerve-fibres appear at the end of the second month (His). The nerve-fibres begin in the retina and grow along the stalk towards the brain, extending into its thickened invaginated lower wall. The point where this is continuous with the retina at the centre of the optic cup becomes the optic disc. The optic chiasma is formed by fibres crossing in the posterior boundary of the optic recess, and the optic tract is a new formation by which the eye is secondarily connected with the optic thalamus and mid-brain.

**Development of the vitreous body and lens capsule.**[1]—The formed elements of the *vitreous body* and the *zonule of Zinn* are to be regarded as a special

[1] The following account is founded on the observations of Tornatola, Rabl, Addario, Van Pée, Lenhossék, Kölliker, and Szily. My own observations, on which the actual description is based, have been made on rabbit material.—T. H. B.

development of the syncytial system of nuclear-free protoplasmic threads which Szily has shown exist between all epithelial formations as they draw apart in the course of development. In most situations, as has already been indicated, this system is the basis of the mesenchymatous syncytial network when the free cells have wandered into it, but in the case of the vitreous it remains largely cell-free. The *lens capsule* belongs primarily to the same category, but in mammals, in which alone a *rete vasculosum lentis* is developed, mesoderm cells and blood-vessels enter into its formation.

We have already mentioned the existence of primary protoplasmic connexions between the lens and the future retinal epithelium (fig. 183). When the lens-pit closes in, similar connexions are formed between the outer wall of the vesicle and the surface epithelium. When the retinal layer draws away from the lens, and the

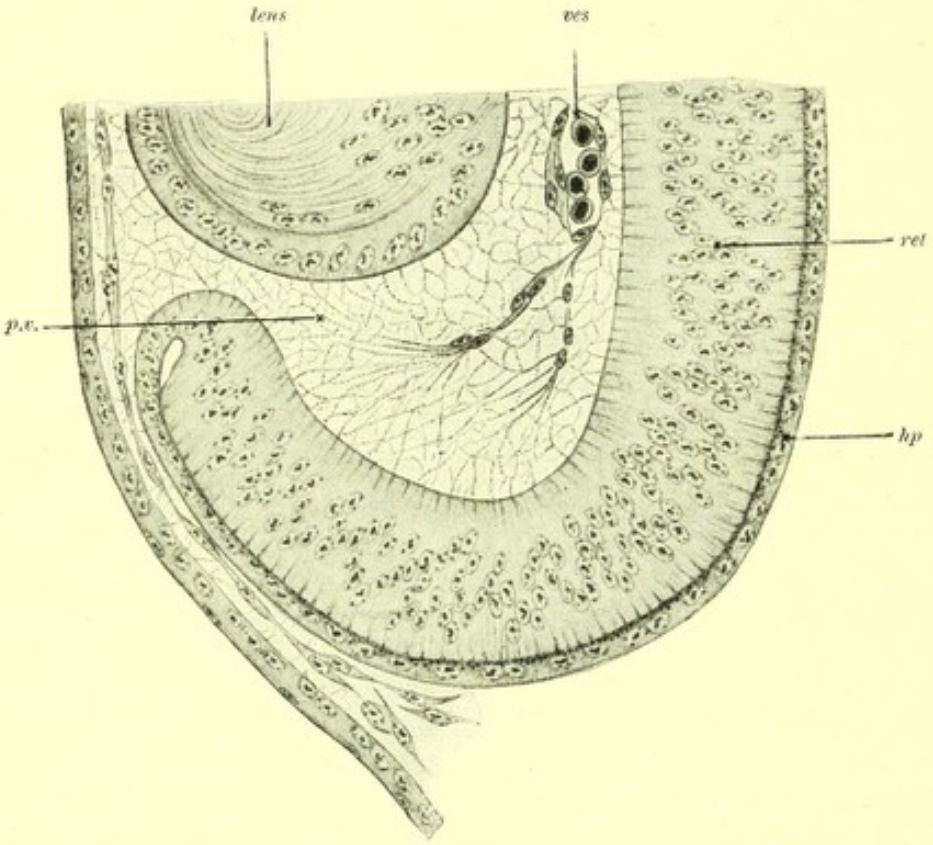



FIG. 184.—SECTION OF THE DEVELOPING EYE OF TROUT. (Szily.)

*lens*, lens; *ret*, retina; *hp*, outer layer of optic cup; *p.v.*, primitive vitreous; *ves*, blood-vessel. Mesenchyme-cells are seen passing into the space between the surface-ectoderm, the optic cup, and lens.

lens from the surface epithelium, these protoplasmic threads are drawn out into a mesh-work which fills the optic cup and surrounds the lens-vesicle (fig. 184). The mesenchyme surrounding the cup does not at first extend beyond its mouth, but in mammals mesenchyme-cells soon extend round the lens and form a layer on the back of that body, so that here the primitive syncytial meshwork is replaced by a lamella of typical mesenchyme. In this vessels appear, and these are supplied by a vascular loop which extends into the cup through the choroidal fissure. It ramifies among the vitreous threads, and later becomes the central artery of the retina and its hyaloid branch. As the optic cup expands this mesenchymatous lamella clings close to the lens (fig. 182), and the space behind it is seen to be filled with protoplasmic strands connected with every part of the retinal epithelium (Rabl, Kölliker, and others). The connexion of the fibrillæ with the pars optica is lost, but in the ciliary region the attachment persists, and the

fibrils from the ciliary epithelium form the greater part of the formed portion of the vitreous, the so-called hyaloid membrane, and zonule of Zinn.

The syncytial meshwork in front of the lens has a different fate. It becomes invaded by large numbers of mesenchyme-cells, and is converted into a thick cellular plate between the lens and the surface epithelium. At this stage a delicate refractile membrane appears round the lens, formed apparently from the meshwork, and this, together with the mesenchymatous layer behind the lens, and a delicate lamella of mesenchyme in front of it—separated off at a later stage from the anterior mass of mesoderm—becomes the lens-capsule.

The membrane thus defined becomes the *tunica vasculosa* of the later stages of fœtal development. The portion behind the equator of the lens is supplied by the *hyaloid artery*, and the part in front of the equator by the *anterior ciliary arteries*. Shortly before birth the vessels disappear: the hyaloid artery is obliterated, but its track in the vitreous persists as the canal of Stilling. The fore-part of the capsule is named the *pupillary membrane*.[1]

**Development of the protective and vascular coats; the iris and aqueous chamber.**—The optic cup is surrounded by a specially vascular mass of mesenchyme, and, as we have seen, this extends into the space between the lens and the surface epithelium. It here forms a thick cellular layer, which is the rudiment in great part of the *cornea*, while the surface ectoderm over it forms the corneal epithelium. The cornea is at first identical in structure with the primitive sclerotic, with which it is, of course, continuous. Later it undergoes histological changes which cause it to become transparent. The mesenchyme surrounding the optic cup becomes differentiated into two layers—an outer more condensed stratum which forms the *sclerotic* coat, and an inner, looser stratum, enclosing many vessels, which becomes the *choroid* coat. This is thickened near the margin of the cup to form the *ciliary body*, and its surface becomes radially folded over the thickening to give rise to the *ciliary processes*. On its outer side the *ciliary muscle* is laid down.

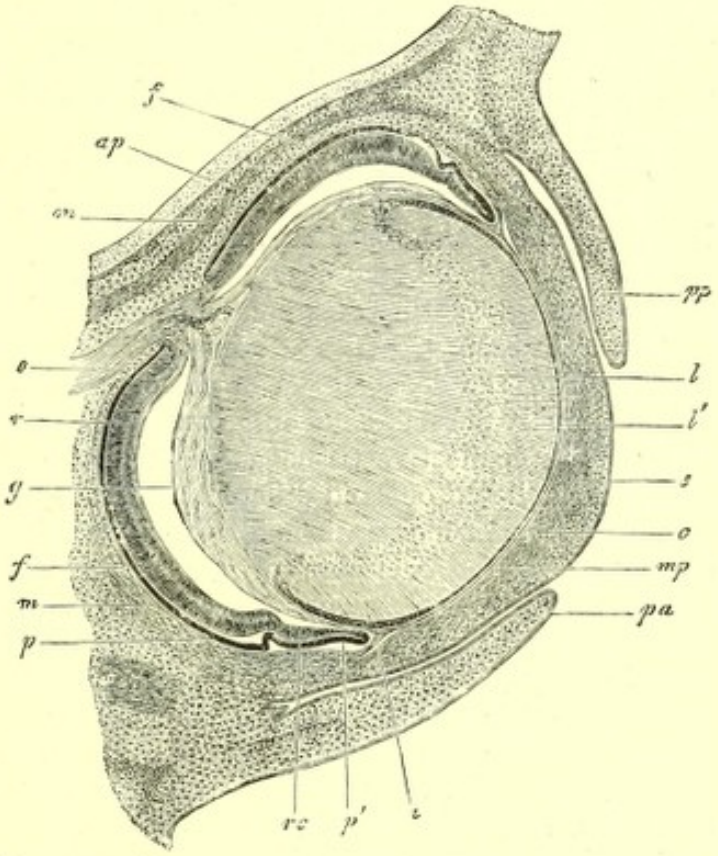



FIG. 185.—HORIZONTAL SECTION THROUGH THE EYE OF AN EMBRYO-RABBIT OF EIGHTEEN DAYS. $\frac{30}{1}$ (Kölliker.)

*o*, optic nerve; *p*, hexagonal pigment-layer; *r*, retina; *rc*, ciliary part of the retina; *p'*, fore-part of the optic cup (rudiment of the iris-pigment); *g*, vitreous, shrunk away from the retina, except where the vessels from the arteria centralis retinæ enter it; *i*, iris; *mp*, membrana pupillaris; *c*, cornea with epithelium *e*; *pp*, *pa*, palpebræ; *l*, lens; *l'*, lens-epithelium; *f*, sclerotic; *m*, recti muscles. The formation of the aqueous chamber is just beginning, and is seen as a cleft in front of the iris on each side.

The **aqueous chamber** is formed by a separation of the mass of mesenchyme between lens and surface into two lamellæ—a thick anterior layer which becomes

[1] For an exhaustive account of the development of the arteries of the mammalian eye, see Fuchs: Anat. Hefte xxviii. 1905.

the cornea, as above described, and a posterior which gives rise to the iris and the mesenchyme of the pupillary membrane (fig. 185). The separation begins just in front of the ciliary region. Here the posterior lamella is composed of loosely arranged mesenchyme, applied to the pars iridis of the optic cup. It gives origin to the stroma of the iris. The cleavage proceeds from the periphery over the front of the lens, but here only an excessively thin lamella is separated off, in which the vessels of the pupillary membrane develop. It is at first directly continuous with the iris (fig. 185), but when the vessels disappear it is dissociated from that structure, and if any trace of it remains it appears to be incorporated with the lens-capsule.

**Accessory structures.**—The **eyelids** make their appearance as folds of integument, subsequently to the formation of the eyeball. About the third month of fœtal life the two folds, one forming the upper and the other the lower lid, meet and unite by a growth together of the epithelium at the margins of the folds, so as to cut off the conjunctival sac from the exterior. Shortly before birth they again become disunited.

A third fold (of the conjunctiva) appears at the inner canthus, and in many vertebrates develops into a well-marked third eyelid, the *membrana nictitans*. In man it remains rudimentary, forming the *plica semilunaris*.

The glands, hairs, and other structures belonging to the eyelids are developed in the same way as the corresponding structures in the rest of the integument.

The **lacrymal gland** is developed in the third month as a number of outgrowths from the deeper layer of the epithelium, at the upper and outer part of the conjunctival sac. The outgrowths are at first solid, and branch into the surrounding connective tissue as in the case of racemose glands, subsequently becoming hollowed out and differentiated into ducts and acini.

The **lacrymal canals** and **ducts** were formerly described as being directly developed by the enclosure of the fissure which separates the lateral nasal process from the maxillary process (see Development of Face, p. 86), and which passes in the early embryo from the eye to the upper part of the naso-buccal cavity (lacrymal fissure). But it has been shown, chiefly by the researches of Born, that in most animals the canal is at first formed as a thickening of the rete mucosum of the epidermis, which sinks into the corium along the line of that fissure. The thickening subsequently becomes separated from the rest of the epidermis, and hollowed out to form an epithelial tube, which leads from the conjunctiva into the nasal cavity.

The bifurcation of the duct where it opens on the conjunctiva was formerly believed to be produced (Ewetsky) by a broadening out of the epithelial cord at the inner canthus, and its subsequent separation into two parts by an ingrowth of connective tissue in its middle, the two parts developing into the upper and lower lacrymal canals. It has been shown, however, (Matys, Fleischer, and Ask [1]), that, although the epithelial cord remains a long time in continuity with the conjunctiva, both the lacrymal canaliculi and nasal duct are produced by proliferation of the epithelial blastema in the connective tissue, and come secondarily and simultaneously into contact with conjunctival and nasal epithelium respectively. The lumen appears first in the inferior canaliculus, and then at different points in the cord. The upper canal lags behind the lower in development: it opens at first into the conjunctiva close to the inner canthus; while the lower canal opens considerably further out along the edge of the lid. Space is thus left in the lower lid, between the punctum lacrymale and the inner canthus, for the development of Meibomian follicles. As the lower canaliculus enlarges, these are compressed, and therefore atrophy, and the tissue in which they lie becomes the caruncula lacrymalis.

[1] Matys, Zeitschr. f. Augenheilk. xiv; Fleischer, Archiv f. Ophthal. lxii.; Ask, Anat. Anzeiger, xxx. 1907.

## DEVELOPMENT OF THE EAR.[1]

The essential part of the ear—viz. the epithelial lining of the labyrinth—is developed in much the same way as the crystalline lens, as an invagination of the external ectoderm, which at first appears as a pit of thickened epithelium (*auditory pit*, fig. 177), but is gradually converted by a growing together of the margins of the pit into a hollow island of ectoderm, the *auditory* or *otic vesicle* (fig. 180). This process occurs somewhat after the formation of the eye has begun, and at quite a different part of the head—viz. on either side of the hind-brain just over the upper end of the first post-oral visceral cleft. The vesicle comes at first into close contact with the hind-brain, except where the ganglionic rudiment of the auditory nerve projects between them, but it subsequently becomes entirely surrounded by mesoderm, which separates it from both the neural and external ectoderm.

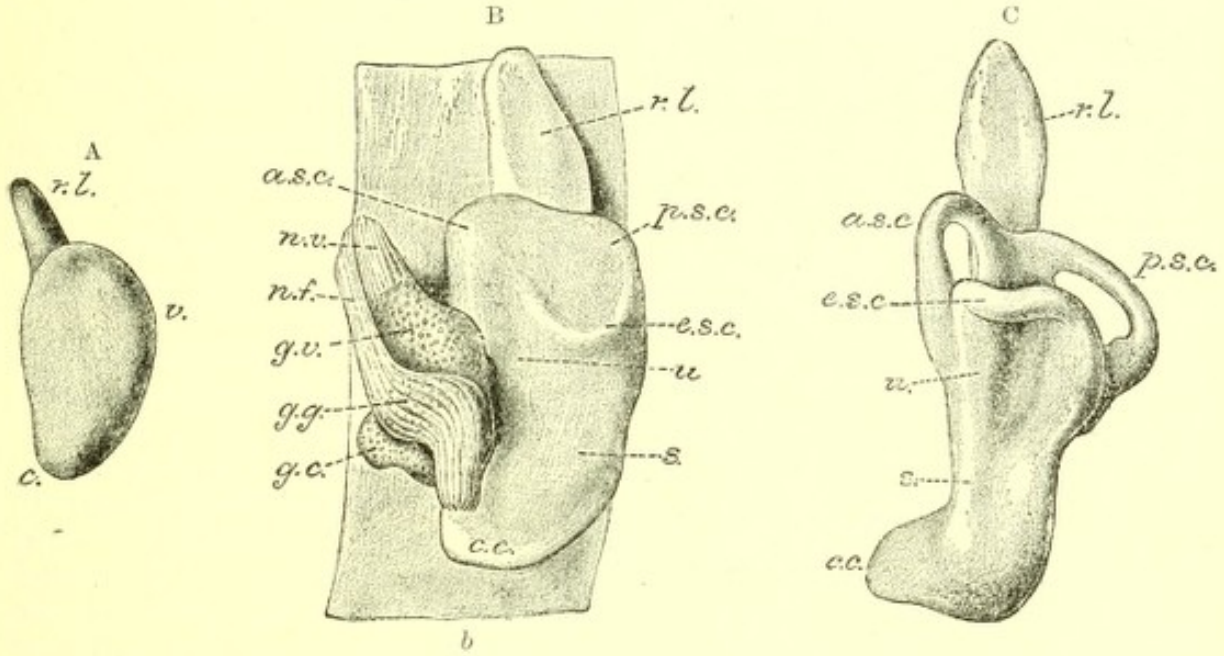



FIG. 186.—STAGES IN THE DEVELOPMENT OF THE MEMBRANOUS LABYRINTH. (W. His, Jr.)

A. Left labyrinth of a human embryo of about four weeks, viewed from the outer side. *v*, vestibular part; *c*, cochlear part; *r.l.*, recessus labyrinthi (aqueductus vestibuli).

B. Left labyrinth with parts of the facial and auditory nerves of a human embryo of about four and a-half weeks. *b*, surface of the hind-brain; *u*, utricular; *s*, saccular part of labyrinth; *a.s.c.*, *p.s.c.*, *e.s.c.*, rudimentary folds representing the two vertical and the horizontal semicircular canals; *r.l.*, upper part of recessus labyrinthi becoming enlarged into the endolymphic saccule; *c.c.*, rudiment of cochlea; *n.v.*, vestibular branch of auditory nerve; *g.v.*, vestibular ganglion (ganglion of Scarpa); *g.c.*, cochlear ganglion; *n.f.*, facial nerve, with geniculate ganglion, *g.g.*

C. Left labyrinth of a human embryo of about five weeks, viewed from without and below. Lettering as before. The horizontal canal is still only a fold. The ampullæ are beginning to be visible on the two vertical canals.

The otic vesicle is at first flask-shaped, with the somewhat elongated mouth of the flask directed externally towards the original point of connexion with the exterior. In elasmobranch fishes this passage is never closed, but remains throughout life in the form of a small duct-like tube which passes up through the cranial wall and opens on the epidermis. In other vertebrates the opening to the exterior becomes closed, and what remains of the original mouth, or canal of connexion with the exterior, is visible as a distinct but small process from the

[1] For literature see Krause, Hertwig II. Th. i. and ii. p. 133 *seq.* Reference to more recent papers in footnotes.

upper and inner angle of the vesicle, and is known as the *recess of the labyrinth* (fig. 186, *r.l.*). Eventually it develops into a long epithelial tube, which passes

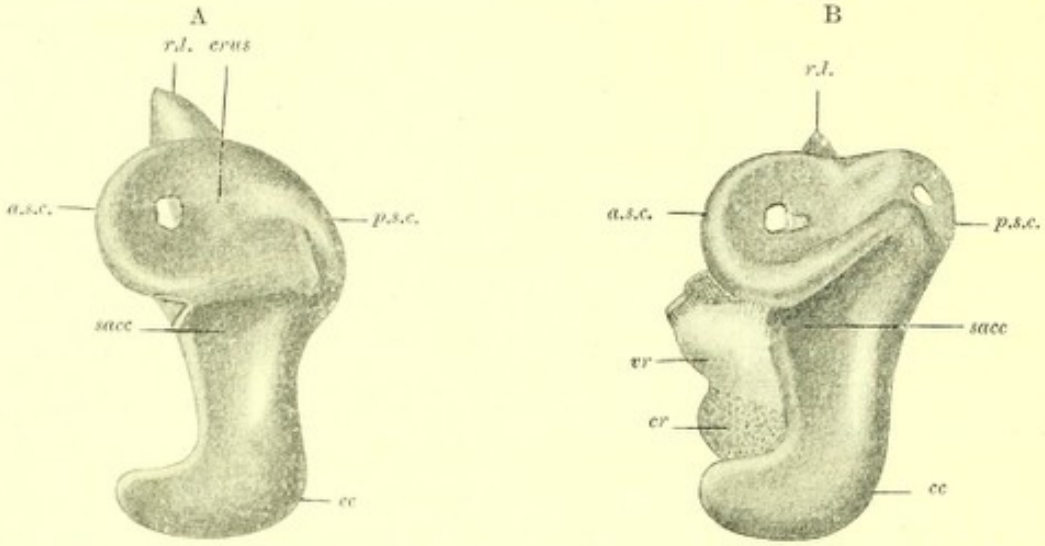



FIG. 187.—MODELS OF THE MEMBRANOUS LABYRINTH: A OF A HUMAN EMBRYO OF 11 MM., AND B OF AN EMBRYO OF 13 MM. (After Streeter.)

*sacc*, saccule; *cc*, cochlea; *r.l.*, recessus labyrinthi; *a.s.c.* superior, *p.s.c.* posterior semicircular canal. The future lateral semicircular canal is represented by the fold projecting outwards above *sacc*; *vr* vestibular, *cr* cochlear division of auditory nerve.

through the petrous bone, with an expanded end lying within the skull underneath the dura mater. This tube and its expanded termination form respectively the *endolymph canal* and *endolymph saccule* (fig. 189).

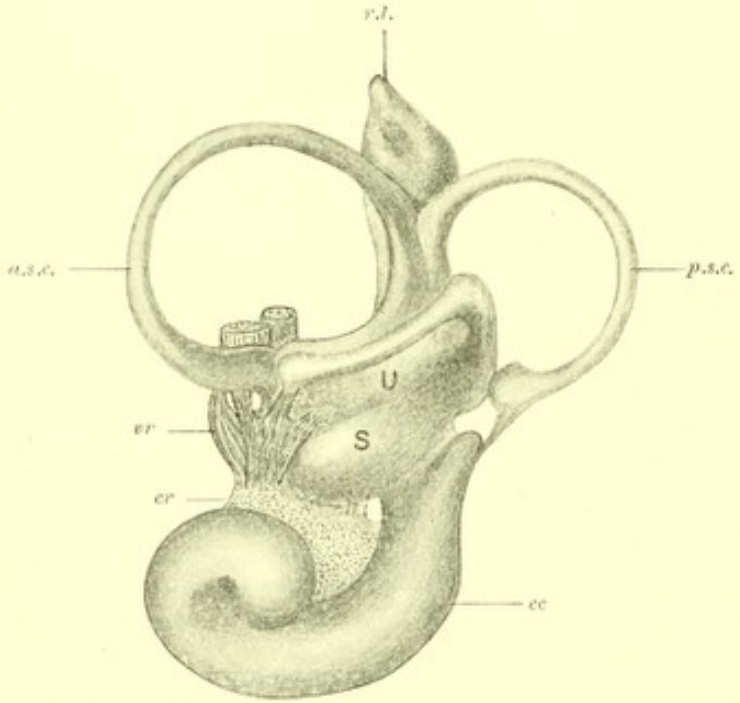



FIG. 188.—MODEL OF THE MEMBRANOUS LABYRINTH OF A HUMAN EMBRYO OF 20 MM. (After Streeter.)

U, utricle; S, saccule; *cc*, cochlea; *r.l.* recessus labyrinthi; *a.s.c.* superior, *p.s.c.* posterior semicircular canal; *vr* vestibular, *cr* cochlear division of auditory nerve.

In the meantime the auditory vesicle becomes elongated and begins to be irregular. It shows a larger triangular swelling in its dorsal part to which the endolymph canal is attached, and a smaller flattened sac which is the rudiment of the epithelial canal of the cochlea. At the junction between the two moieties a bulging, described by Denis and named *atrium* by Streeter,[1] constitutes the rudiment of the utricle and saccule. The dorsal or *vestibular* pouch soon shows a vertical and a little later a horizontal fold (fig. 186); the former is the rudiment of the two vertical (anterior and posterior) semicircular canals and their common opening (*crus*), the latter the rudiment of the horizontal (external) canal. The folds which give rise to the canals are flattened semicircular hollow protrusions from the wall of the vesicle. The layers of the folds next

[1] Amer. Journ. of Anat. vi. 1907.

come together and coalesce, except near the circumference of the semicircle, which now forms a tube connected at its ends with the vesicle. Subsequently, by absorption of the coalesced lamellæ, the tube is converted into a free loop. One of the ends becomes dilated into an ampulla and connected with a branch of the auditory nerve. In consequence of the manner in which the two vertical canals arise from the upper vertical fold they are at first in a line with one another, but as they take form they come by differential growth to be

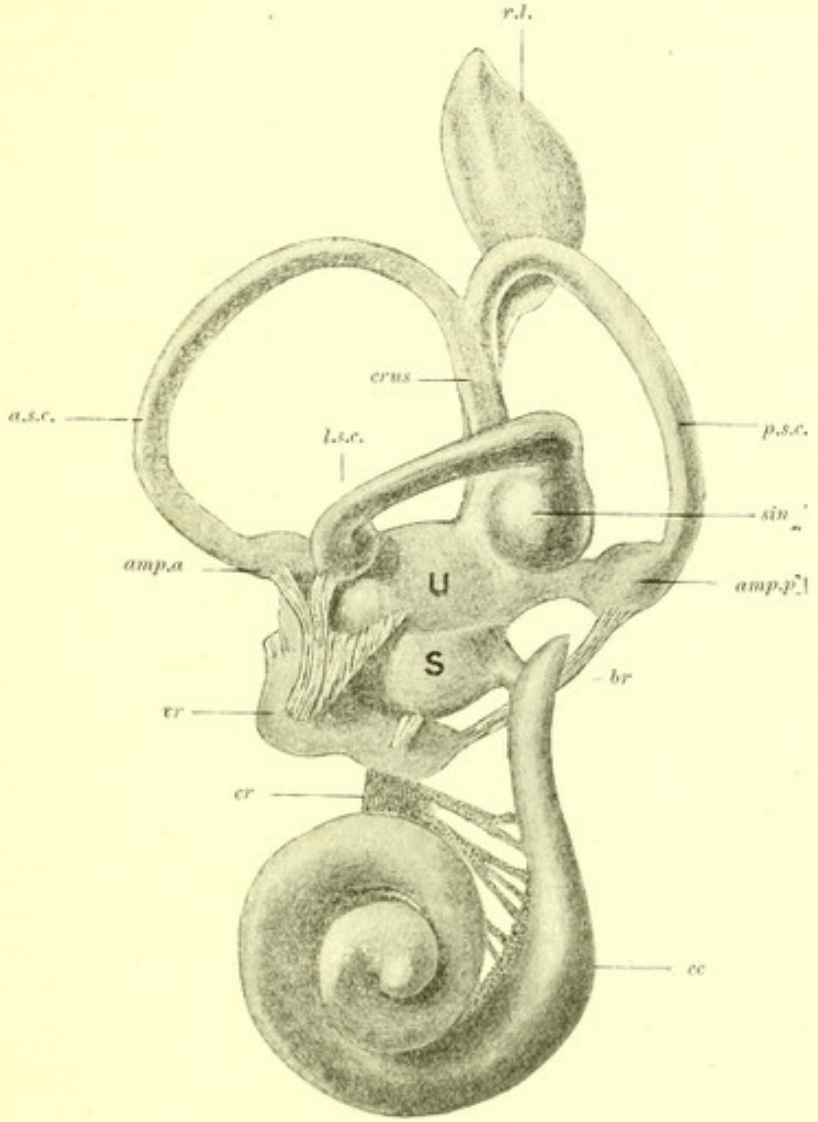



FIG. 189.—MODEL OF THE MEMBRANOUS LABYRINTH OF A HUMAN EMBRYO OF 30 MM. (After Streeter.)

U, utricle; S, saccule; *cc*, cochlea; *r.l.*, recessus labyrinthi (aqueductus vestibuli); *crus*, common opening of superior and posterior semicircular canals; *sin*, sinus utriculi lateralis; *a.s.c.* superior semicircular canal: *amp.a*, its ampulla; *p.s.c.*, posterior semicircular canal: *amp.p*, its ampulla; *l.s.c.* horizontal semicircular canal; *vr*, vestibular division; *cr*, cochlear division of auditory nerve; *br*, branch from vestibular division of nerve to ampulla of the posterior semicircular canal.

placed at right-angles to one another, the ampullary end of the superior retaining its original position. While the semicircular canals are forming, the ventral cochlear portion begins to grow out and become curved on itself, while the atrium becomes subdivided by a fold into an upper and posterior chamber connected with the semicircular canals, the *utricle*, and a ventral and anterior connected with the cochlea, the *saccule*. This fold extends into the attachment of the recess of the labyrinth and separates it longitudinally for a short distance into two tubes, one of which opens into the utricle and the other

into the saccule, forming the only permanent means of communication between them. Another fold, or constriction, appears presently, somewhat lower down and converts the connexion between the saccule and the cochlea into the narrow duct of Hensen (*canalis re-uniens*).

In the meantime the cochlea-rudiment at the ventral end of the now labyrinthine vesicle becomes elongated into a tube, which, as it grows, becomes coiled upon itself in such a manner as to produce the spiral structure of this part of the auditory organ (figs. 188, 189). This coiling, however, only occurs in mammals; in birds, the cochlea is a short straight blind tube.

All these parts of the labyrinth are, when first formed, simple epithelial tubes surrounded by and imbedded in embryonic connective tissue. As development proceeds, and the skull begins to form, a cartilaginous capsule becomes developed around the several parts of the labyrinth, and this at length becomes ossified. The cartilaginous capsule does not closely invest the epithelial structures; they are immediately surrounded by embryonic connective tissue, which forms an internal periosteal lining to the capsule and a special covering to the epithelial tube. These two connective-tissue membranes are everywhere separated from one another by gelatinous connective tissue, composed of semi-fluid ground substance and branching corpuscles, except along one border, where they are in continuity. But in the cochlea the gelatinous tissue is above and below the epithelial tube, the place of the modiolus being occupied by embryonic tissue which is not gelatinous, and is connected with that lining the capsule by similar non-gelatinous tissue separating the turns of the cochlea from one another, and also running in the position of the future spiral lamina.

The bone, which is formed by ossification of the cartilaginous capsule, is of a spongy nature, but it becomes coated internally by layers of compact bone deposited by the periosteal lining. The modiolus and septa of the cochlea, as well as the osseous spiral lamina, are formed wholly in connective tissue without any preformation in cartilage.

The perilymphatic spaces throughout the whole labyrinth are produced by a gradual vacuolation and disappearance of the gelatinous tissue which surrounds the membranous labyrinth. In the cochlea this conversion into perilymph begins in the proximal turn of the spiral and extends hence towards the distal end. It is only with the development of these perilymph-spaces (scalæ) that the cochlear tube, which was previously oval in section, acquires the characteristic triangular section which we see in the fully formed organ.

The cells which form the wall of the epithelial tube become variously modified in different parts of the labyrinth to produce the characteristic structures which there occur—viz. the hair-cells, the rods of Corti, the sustentacular cells of Deiters, and the epithelium lining the labyrinth. The membrana tectoria appears as a cuticular deposit over the columnar cells which are becoming developed into the organ of Corti.

The **auditory nerve** arises from a ganglionic mass which is early divided into an acoustic and a facial portion (geniculate ganglion) (fig. 186). The acoustic ganglion lies on the front edge of the auditory vesicle with its lower end turning on to its mesial aspect (figs. 186, 187). It consists (in embryos of 7 mm., twenty-sixth day) of an upper and a lower part. The central root of the ganglion springs from the upper part, and each division has its own peripheral branches. According to Streeter's researches, the lower part is not the cochlear ganglion as described by W. His, Jr. The *ganglion spirale* develops from the ventral border of the pars inferior, becomes coiled with the cochlea, isolated from the rest of the common ganglion, and connected secondarily with the neural tube by a separate nerve-root, the cochlear root. Thus the pars superior and pars inferior together constitute the *vestibular ganglion*. From its upper portion are derived the nerves to the utricle and to the ampullæ of the superior and lateral canals, while from the lower portion come the nerves to the saccule and ampulla of the posterior semicircular canal (fig. 189).

The primary ganglion is closely applied to the auditory vesicle, and the peripheral nerves are very short. The secondary ganglia become included in the capsule as this develops round the labyrinth.

## ACCESSORY PARTS OF THE ORGAN OF HEARING: MIDDLE EAR AND EXTERNAL AUDITORY MEATUS.

The **middle ear** and the **Eustachian tube** are derived from the first branchial pouch of the pharynx; the **auricular fossa** and the **external meatus** from the first branchial cleft; the former are therefore entodermic, the latter ectodermic derivatives.[1]

The bottom of the ectodermic cleft, which is shallow above and deeper below, comes into contact for a time with the entoderm of the corresponding pharyngeal pouch and its dorsal prolongation. The original depression persists as the fossa of the auricle (concha and upper auricular fossa), while the different folds of that structure are produced by a series of elevations which appear on the prominent

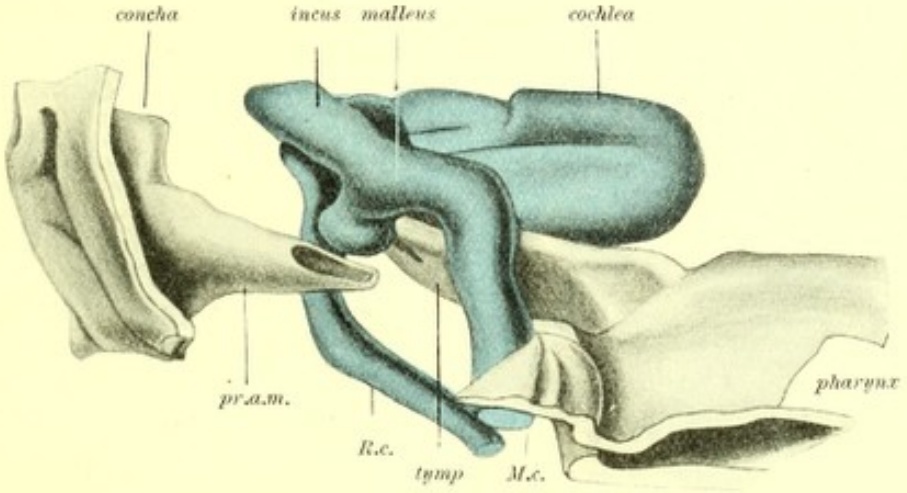



FIG. 190.—RECONSTRUCTION OF THE TYMPANUM, PRIMITIVE EXTERNAL AUDITORY MEATUS, COCHLEA, AND OSSICLES OF A HUMAN EMBRYO 24 MM. LONG, FROM THE FRONT. (After Hammar.)

The tympanic cleft (*tymp.*) is seen extending from the pharynx; at its outer end is a notch bounded by two recesses of the tympanic cavity, of which only the anterior is seen; opposite the notch is the handle of the malleus. Meckel's cartilage (*M.c.*) and Reichert's cartilage (*R.c.*) are cut across at their lower ends: the former is directly continuous with the rudiments of the malleus and incus. *pr.a.m.*, primitive external meatus. The spoon-shaped inward part of this is the meatal plate.

lips of the fissure (see Section I. p. 88). The external auditory meatus is in part produced from an inward tubular prolongation of the lower and deeper part of the cleft, and in part from a solid epithelial plate which grows obliquely from it inwards and downwards, below the fissure representing the tympanic cavity (fig. 190). The cartilaginous portion of the meatus and also a small part of the roof of the osseous meatus, which have a typical skin-lining, are derived from the tubular invagination; the deep portion of the osseous meatus is produced by the shedding of the central cells of the epithelial plate. The lumen thus produced lies obliquely like the solid plate, and its upper and inner wall forms ultimately the ectodermic covering of the tympanic membrane.

The primitive tympanic cavity is derived from the dorsal prolongation of the first visceral pouch. This and its lateral expansion are at first in contact with the ectoderm, but the epithelial layers are soon separated again by mesenchyme. The extremity of the dorsal prolongation is to be recognised at this stage, and through

[1] The following account is based on the very detailed descriptions given by J. August Hammar (Upsala), Archiv. f. mikr. Anat. lix. 1902.

all later stages, as a pocket named the *anterior tympanic recess*. From this, in a forward direction, a shallow groove extends along the roof of the pharynx, and another furrow runs backwards to the dorsal pocket of the second visceral pouch. This furrow is divided into two portions, a short, sharply descending section and a shallow horizontal posterior prolongation. At the junction of these two a second pocket develops which is named the *posterior tympanic recess*. By the expansion of the pouch and the deepening of these furrows the primitive tympanum is laid down as a wing-like diverticulum from the pharynx, which extends in a horizontal and then in a dorsal direction. In shape it is a narrow cleft, the inner wall being rendered salient by the growing cochlea. In the mesenchyme on its outer side the cartilages of Meckel and of Reichert are laid down. The upper end of the former passes over the two recesses above named and expands to form the rudiments of the malleus and incus. From the malleus a process extends downwards and inwards which is the rudiment of its handle (fig. 190). This causes a projection into

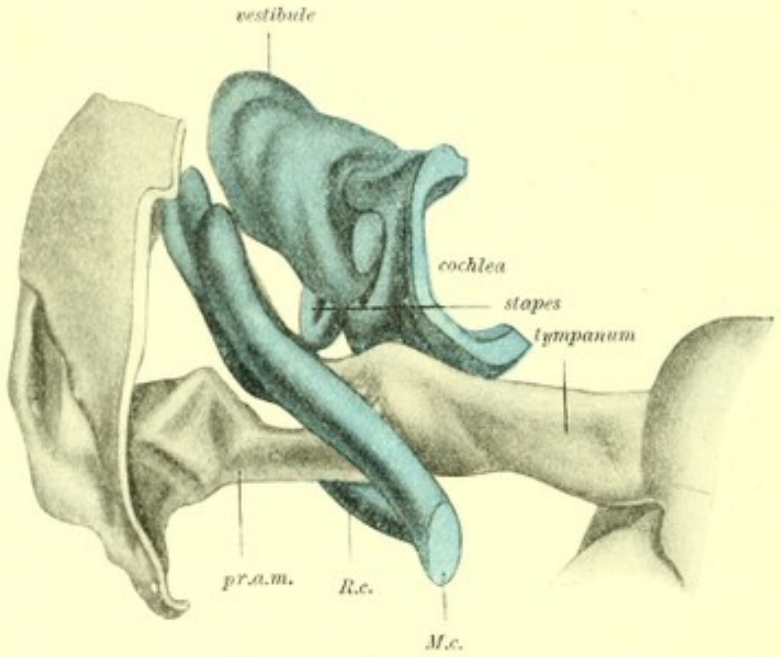



FIG. 191.—RECONSTRUCTION OF THE AUDITORY CAPSULE, THE TYMPANUM, AUDITORY OSSICLES, AND EXTERNAL AUDITORY MEATUS OF A HUMAN EMBRYO 24·4 MM. LONG, FROM THE FRONT. (After Hammar.)

*M.c.* cartilage of Meckel (the proximal end of Meckel's cartilage shows two points, the malleus and incus respectively); *R.c.*, cartilage of Reichert; *pr.a.m.*, the line points to the junction of the outer portion developed as a pit from the surface and the inner portion developed from the meatal plate.

the outer wall of the tympanum between the anterior and posterior tympanic recesses. The primitive tympanum is cut off from the pharynx from behind forwards until it opens only by a short tubal portion. At this stage the cut-off tubo-tympanic cleft is directed nearly horizontally outwards. Its outer end, with the two recesses, is obliquely placed, and overlaps the inner end of the meatal plate above described, a layer of mesenchyme—in which the handle of the malleus lies—intervening between them. This layer of mesenchyme gives rise to the membrana propria of the *drum*, and the epithelium to its inner mucous covering. The handle of the malleus lies between the two tympanic recesses. In later stages the tubo-tympanic cleft comes to lie more and more antero-posteriorly as the cranial base pushes forwards, and the short tubal portion becomes elongated, until the adult position and relationships are attained. During the later months of pregnancy the lining membrane of the tympanum becomes greatly thickened and gelatinous, so that the epithelial lamellæ are brought together and the lumen

obliterated. The cavity is again established after birth; it is believed that this is due, in part at any rate, to the establishment of respiration. By the expansion of the cavity in various directions its several recesses are formed, and the ossicles and the chorda tympani nerve, which, as we have seen, lie at first in the mesenchyme external to and above the primitive tympanum, come to be enclosed in folds of the mucous membrane within the fully developed cavity.

## DEVELOPMENT OF THE NOSE.[1]

The olfactory organ appears towards the end of the third week as an area of thickened ectoderm on either side of the fore-brain. By the upgrowth of its margins the area soon becomes depressed below the surface, and the so-called *olfactory pit* is produced. The depression is at first pyriform in shape, the smaller end running towards the stomodœum (fig. 192). The mouth of the pit next becomes constricted by the thickening and drawing-in of its lips; but at its pointed

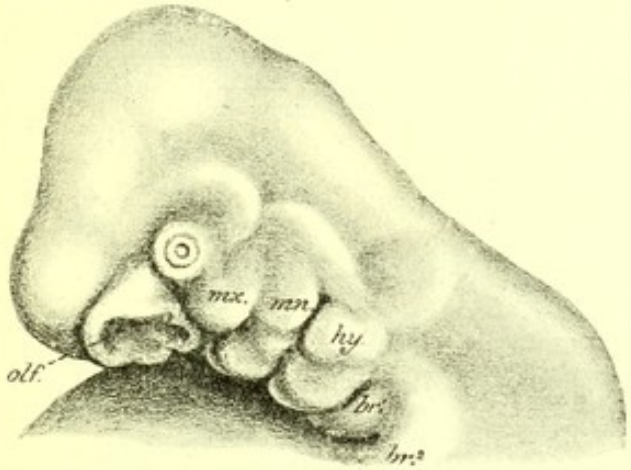



FIG. 192.—PROFILE VIEW OF THE HEAD OF A HUMAN EMBRYO OF NEARLY FOUR WEEKS. (His.)

*olf*, olfactory depression passing posteriorly into a deep pit, the rudiment of Jacobson's organ; *mx*, maxillary process; *mn*, mandibular arch; *hy*, hyoidean arch; $br^1$, $br^2$, first and second branchial arches.

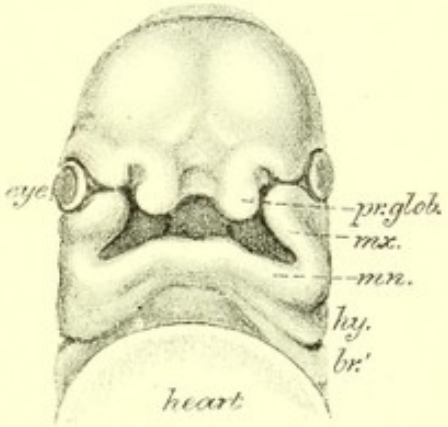



FIG. 193.—HEAD OF AN EMBRYO ABOUT TWENTY-NINE DAYS OLD, FROM BEFORE. (His.)

*pr.glob.*, globular extremity of the mesial nasal process. The other letters as in fig. 192.

(stomodœal) end the circumference is interrupted, the raised margin ending mesially and laterally in the *mesial* and *lateral nasal processes* (fig. 193). Between these the pit is continued as a groove or furrow on to the roof of the stomodœum. We have already seen (p. 88) that the lateral nasal processes form the alæ nasi, and unite with the maxillary processes, which in turn form the cheeks and outer parts of the upper lip; also that the mesial nasal processes (*processus globulares*) unite with one another to form the central part of the upper lip and philtrum, and then unite with the maxillary processes to complete the lip. If now the under aspect of the processes in their first phases be examined, it will be seen that they extend backwards in the roof of the embryonic mouth, being separated by the groove already referred to (fig. 194 B). The groove is not, however, an open fissure communicating with the olfactory pit, but is filled by a raphe of ectoderm produced by the fusion of the opposing surfaces of the several processes. It is not clear whether in man the epithelial raphe is a primary formation—an epithelial band between the mesial and lateral nasal processes (Hochstetter)—or is secondarily

[1] For literature, see Karl Peter, Hertwig H. Th. i. and ii. p. 78 *seq.* Later references in footnotes.

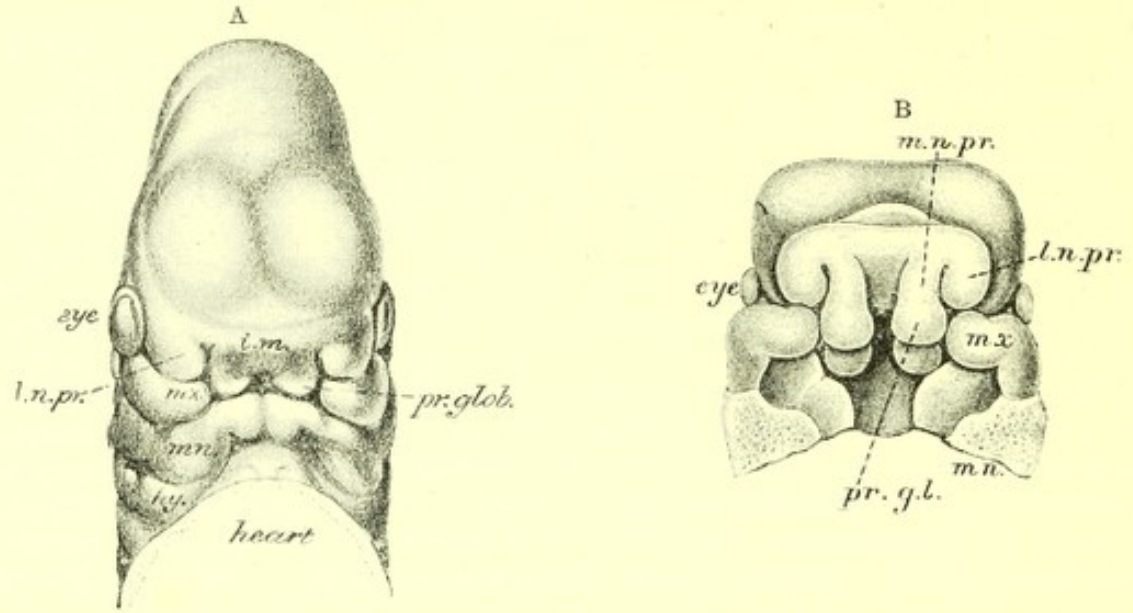



FIG. 194.—A, HEAD OF AN EMBRYO ABOUT THIRTY-FOUR DAYS OLD, FROM BELOW. B, THE ROOF OF THE PRIMITIVE MOUTH OF THE SAME EMBRYO AFTER REMOVAL OF THE MANDIBLE. (His.)

*i.m.*, placed on the fronto-nasal process, and just above its intermediate depressed part; *l.n.pr.*, lateral nasal process; *m.n.pr.*, mesial nasal process; other letters as in fig. 192. The nasal laminæ of the processus globulares and the palatine projections of the maxillary processes are seen in B.

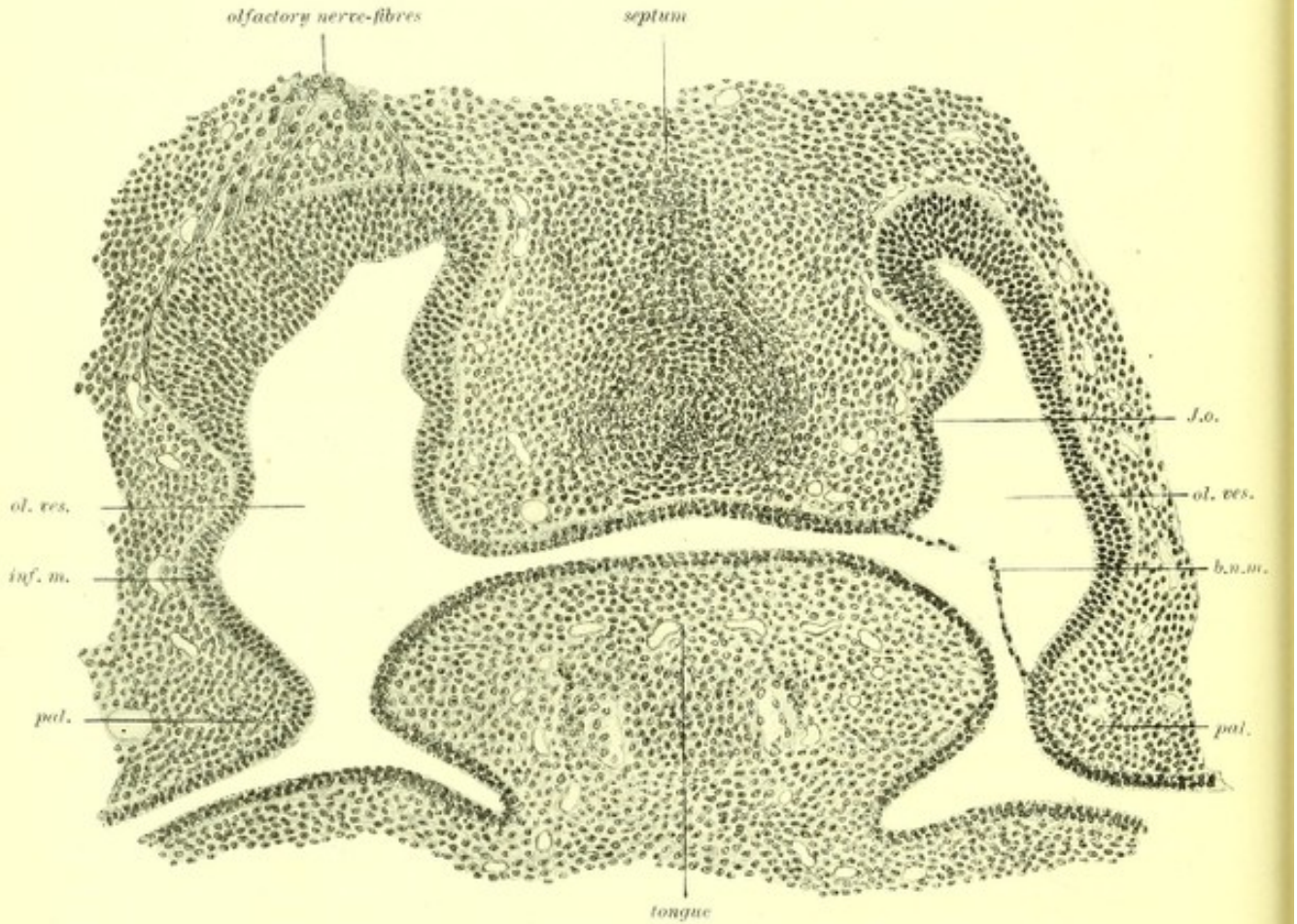



FIG. 195.—SECTION THROUGH THE OLFACTORY VESICLES IN A HUMAN EMBRYO OF 15·5 MM. (T. H. Bryce.)

*ol.ves.*, olfactory vesicle: on the right the vesicle is still separated from the mouth by the buccо-nasal membrane, *b.n.m.*: on the left this membrane has disappeared, and the section passes through the primitive choana; *J.o.*, groove which will become Jacobson's organ; *inf.m.*, groove which will become the inferior meatus; *pal.*, palatal folds.

produced by the walls of the groove being caught between the growing lateral nasal and maxillary processes (Lewis).

The mesial nasal process now becomes united with the lateral nasal and maxillary processes by the extension of mesenchyme between them, and the epithelial raphe

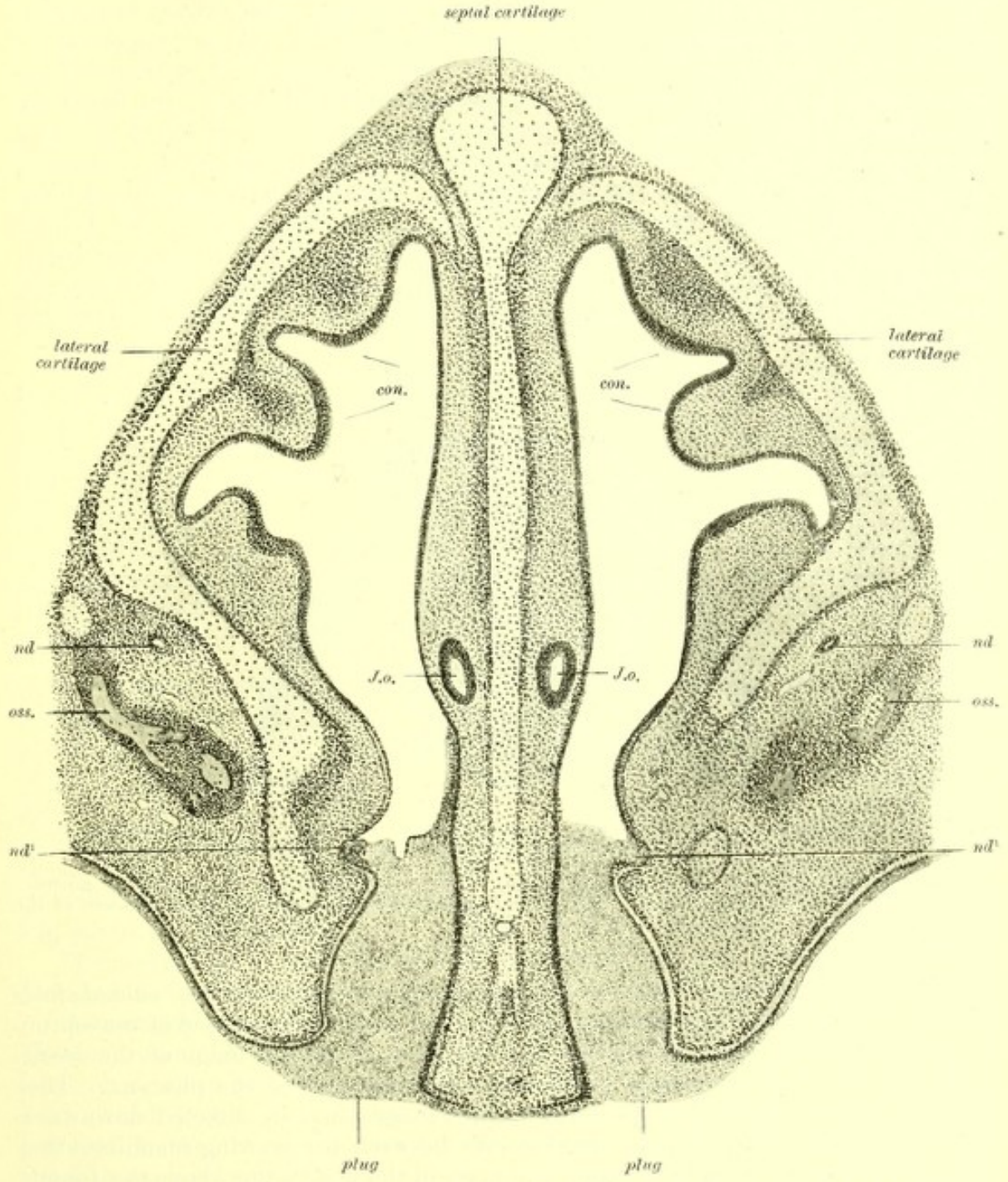



FIG. 196.—HORIZONTAL SECTION OF THE NASAL FOSSÆ OF A HUMAN EMBRYO OF 30 MM (T. H. Bryce.)

*J.o.*, Jacobson's organ; *con.*, conchæ; *nd*, lacrymal ducts; *nd*¹, their openings into the nasal fossæ; *oss.*, commencing ossification in maxilla.

is interrupted. It persists behind, however, and forms a thin membrane (*bucco-nasal membrane*), which breaks through later, so that a passage is established between the hitherto blind nasal sac and the stomodœum (fig. 195). The two openings thus produced are the primitive posterior nares (*choanæ*). The united

nasal and maxillary processes in the roof of the stomodœum constitute the primitive palate, while the two mesial nasal processes which have meantime fused together, form a broad primitive septum (intermaxillary process) (fig. 194 B). The primitive choanæ do not correspond in position to the permanent posterior nares, which are placed much farther back, and are established only in the third month, when the permanent palate has been developed. The nasal sacs extend backwards as the face takes shape and the interocular septum is produced, appearing as narrow clefts in the roof of the primitive mouth. Each is surrounded by mesenchyme in which a cartilaginous nasal capsule is laid down. On the outer side—that is in the lateral nasal process—the cartilage takes the form of a curved plate (fig. 196), connected behind with the trabecular region of the base of the skull, and ending below in a free margin. The two lateral cartilages join mesially with a septal cartilage (fig. 196), which has developed in the fronto-nasal process as a forward projection of the trabecular region of the base of the skull. The septal, like the lateral cartilage, ends below in a free edge, so that the capsule is open below. The floor of the fossæ is completed by the

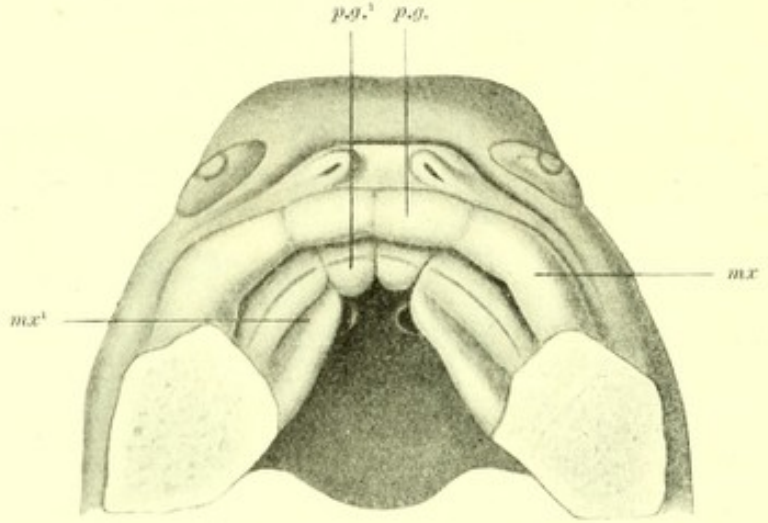



FIG. 197.—THE ROOF OF THE MOUTH OF A HUMAN EMBRYO ABOUT TWO AND A-HALF MONTHS OLD, SHOWING THE DEVELOPMENT OF THE PALATE. (After His.)

*p g.*, processus globularis; *p.g.*¹, palatal process of processus globularis; *mx*, maxillary process; *mx*¹, palatal fold of maxillary process. Close to the angle between this and the palatal process of the processus globularis, on each side, the primitive choanæ.

growth from the lower part of the maxillary processes of the *palatal folds* (fig. 197), which unite with one another and then with the lower end of the septum to form the palate. The palatal folds extend from the line of union of the mesial nasal and maxillary processes backwards on to the wall of the pharynx. They are at first below the level of the dorsum of the tongue, and are directed downwards and inwards (fig. 195). As the tongue sinks between the growing mandibles they are rotated into a horizontal position and meet in the middle line above the tongue. The posterior parts of the folds, however, maintain their original direction (Pölzl).[1]

We have already seen that the mesial nasal processes, which unite superficially to form the central part of the upper lip and the philtrum, extend backwards in the roof of the stomodœum, and there unite to form the intermaxillary process (fig. 197). This projects farthest back in the middle line, and has two oblique lateral borders,

[1] For suggested explanations of this change of position of the palatal folds, see the following papers: His, W., Abhand. math.-phys. Kl. Sächs. Ges. Wiss. 1901; Pölzl, Anna, Anat. Hefte, xxvii. 1904; Schorr, Anat. Anzeiger, xxx. 1907. See also Göppert, Morph. Jahrb. xxxi. 1903, and Anat. Anzeiger, xxiii. 1903, on the more general question as to the origin of the secondary palate.

with which the palatal folds meet to complete the palate in front. Between them openings persist for a time—the *ducts of Stenson*, which correspond to the permanent passages from the mouth to the nose in lower mammals. Though obliterated during embryonic life in man, the ducts are represented by strands of tissue occupying the foramina of the same name in the bony palate.

The hard palate is formed by the extension of bony plates into the membranous folds. Posteriorly these are absent, and muscular tissue extends into the folds, giving rise to the soft palate and uvula. The palato-pharyngeal folds represent the posterior ends of the palatal folds which do not in this region unite with one another. The turbinate processes appear in the second month, long before the palate is completed, as projections from the outer wall composed of a basis of mesenchyme covered by thickened epithelium (fig. 196). In these projections cartilaginous plates are laid down, connected with the nasal capsule, which, growing inwards and becoming curved, form the rudiments of the various conchæ. The accessory sinuses are produced by outgrowths from the originally simple furrows separating the primitive turbinate processes.

The mechanism by which the processes and furrows are formed is variously interpreted. In the first place, it may be definitely stated that the projections are not due to an inpushing of the wall by the cartilaginous strands which become the conchæ. The folds are present before cartilage is formed within them (fig. 196). There are two other explanations. The projections may be either free ingrowing folds of the mucous membrane (Killian, Mihalkovics, and others) or they may be elevations left by excavations of the furrows in the outer wall (Legal, Schönemann). According to Schönemann, epithelial ridges grow out in the position of the future furrows, and these are excavated into epithelial pockets. From this point of view, the complexities of the nasal fossæ are due to the operation of a single process, the early furrows being produced in the same fashion as the later sinuses. Both factors may be at work simultaneously (Glas).[1]

The **organ of Jacobson,** though represented by a vestige merely in the adult human being, is a well-marked structure in the embryo. It appears as a deep pocket at the stomodœal end of the olfactory pit, and afterwards, when the mouth of the pit is closed in, as a pocket on the lateral aspect of the mesial nasal process (fig. 195). Later, it has the form of a narrow duct, oval in section, running longitudinally in the substance of the septum (fig. 196) and opening anteriorly near the upper orifice of Stenson's duct. When the septal cartilage becomes formed, a special curved plate of cartilage is developed which partially encloses the organ and persists in the adult.

The nostrils are closed for a time by an epithelial plug (fig. 196), the permanent passages being established by a shedding of the central cells in the epithelial mass.

**Olfactory nerve.**—What was formerly described by anatomists as the olfactory nerve is in reality, as we have already seen, a portion of the cerebral hemisphere cut off to form a hollow stalk, which afterwards (in man) becomes a solid strand, just as does the optic stalk. The distal end of the olfactory stalk lies close to the developing olfactory pit, and the two become connected during the fifth week by nerve-fibres. During the fourth week the lining of the olfactory pit undergoes histogenetic changes comparable to those seen in the wall of the neural tube. According to His, a group of cells becomes detached from the epithelium, and constitutes a ganglion resembling a spinal ganglion. The cells become bipolar, and their processes, establishing a connexion on the one hand with the olfactory epithelium, and on the other with the brain, form the olfactory nerve-fibres. According to Disse (for the bird), the nerve-fibre-producing elements remain in the epithelium and themselves become the olfactory cells, which are thus directly connected with the brain by single central processes. This view of the

[1] Glas Anat. Hefte, B. xxv. 1904.

development of the olfactory nerves is in much closer accordance with what is known of the structure of the olfactory epithelium and of the olfactory bulb in the adult animal.

The olfactory nerve-fibres are seen at a very early stage running between the brain and the olfactory pit. They are at first connected (Mihalkovics) with every part of the epithelium derived from the ectoderm of the pit ; but it is only in the upper part of the fossæ that the permanent connexion by nerve-fibres with the olfactory lobe persists. In the lower parts of the fossæ the epithelium remains thinner, loses its nerve-connexions, and becomes ciliated, the fossæ assuming the *rôle* merely of respiratory passages.

## DEVELOPMENT OF THE ALIMENTARY CANAL.[1]

The early stages in the development of the alimentary canal have already been described in treating of the formation of the embryo (p. 52 *seq.*). We resume here at a phase reached during the third week, in which the primitive tract has assumed the condition of a tube, formed by the folding-in of the splanchnopleure, and consisting of an anterior section (*fore-gut*), a posterior section (*hind-gut*), and a middle section (*mid-gut*), continuous with the cavity of the umbilical vesicle (*yolk-sac*). The fore-gut is still closed in front by the *buccopharyngeal membrane* ; while the hind-gut is separated from the surface by the primitive cloacal membrane, formed from the persistent part of the primitive streak. From the hind-gut, further, the allantoic diverticulum extends as a narrow tube into the body-stalk. We must now consider the development of the organs derived from the several sections of the primitive alimentary canal ; but it will be convenient to consider in the first instance the formation of the buccal cavity.

### DEVELOPMENT OF THE MOUTH.

We have already seen (p. 52) that at a very early stage, while the blastoderm is still a flattened plate, there is an area between the head end of the axis and the cross portion of the cœlom, in which the ectoderm and entoderm are applied to one another without any intervention of mesoderm. This has been named the *buccopharyngeal membrane*. When the head-fold is developed and the fore-gut formed, the membrane is necessarily bent in below the head end of the embryo. It forms the floor of a wide and shallow fossa, bounded in front by the down-bent fore-brain, and behind by the pericardium, and constitutes a septum between this fossa, which is the stomodœum, and the fore-gut (fig. 198). This stage is reached by the twelfth day, but during the third week the depression is converted into an actual chamber by the forward growth of the fore-brain and by the development of the prominences which ultimately form the face. These prominences are the fronto-nasal which overlaps the depression above and in front, the mandibular arches which bound it behind, and the maxillary processes which close it in on each side. By the end of the third week (in embryos of 3·2 mm., His), the buccopharyngeal membrane becomes broken through so as to establish a communication between the stomodœum and fore-gut (fig. 199) ; but before this opening is effected, a pocket is developed immediately in front of the septum, which extends upwards in the angle between the fore-brain and hind-brain formed by the cephalic flexure. This recess (Rathke's pocket) comes presently into connexion with a projection from the floor of the fore-brain, and forms with it the pituitary body (see p. 115). The remains of the

[1] For literature of the alimentary tract and its gland, see to date of its publication, Maurer, Hertwig, Handbuch der Entwickelungslehre II. Th. pp. 241, *seq.*; of the respiratory tract *ib.* p. 105 *seq.*; of the mouth *ib.* p. 35 ; of the tongue, *ib.* p. 53.

septum seem to persist for a short time, and separate the *pocket of Rathke*, which is of course ectodermic in origin, from an entodermic pouch called *Seessel's pocket*, developed from the blind anterior end of the fore-gut.[1]

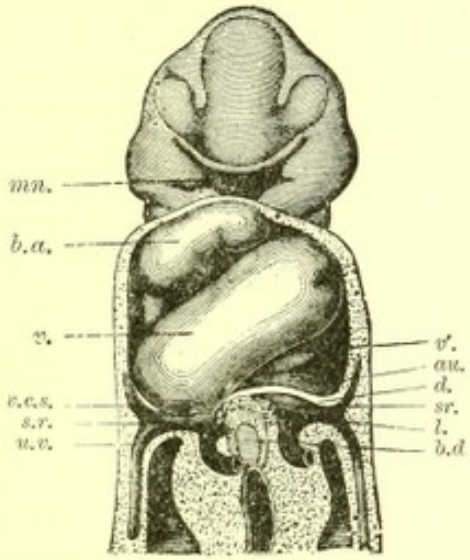



FIG. 198.—FRONTAL VIEW OF THE UPPER PART OF A HUMAN EMBRYO OF ABOUT FIFTEEN DAYS, RECONSTRUCTED FROM SERIAL SECTIONS. (His.) $\frac{40}{1}$.

The pericardium is opened to show the heart; between this and the fore-brain is seen the primitive buccal cavity.

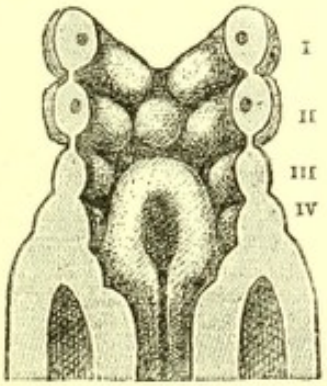



FIG. 200.—FLOOR OF THE PHARYNX OF AN EMBRYO ABOUT FIFTEEN DAYS OLD, AS SEEN FROM WITHIN. (His.) $\frac{50}{1}$.

The first or mandibular pair of arches join in the middle line; the second arches are separated by a rounded prominence (tuberculum impar). Behind (below) this is the forked prominence (furcula) bounding a median groove which will become the laryngeal orifice. In the sections of each of the first two arches the included artery is seen. The Roman numerals are opposite the corresponding arches.

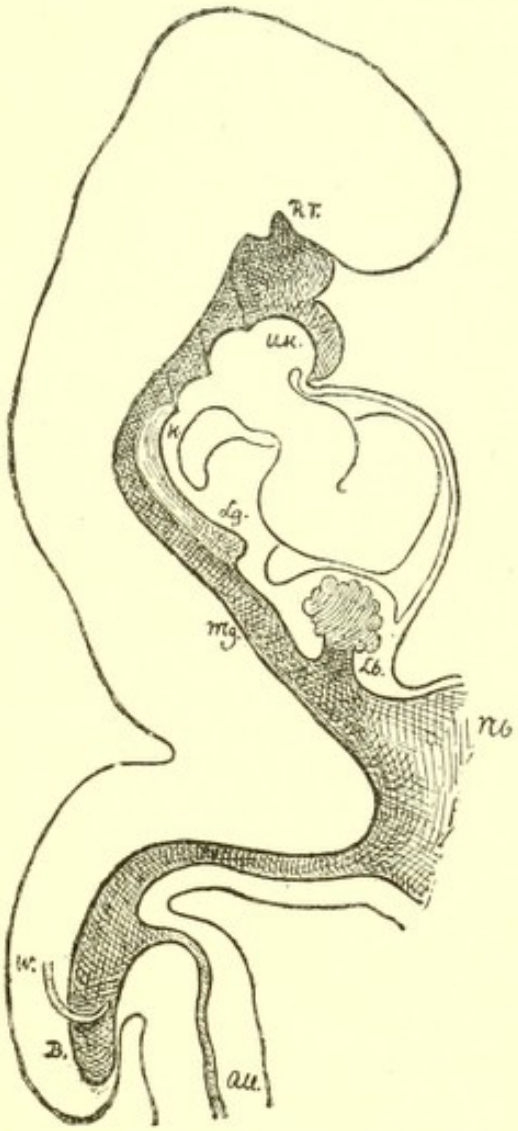



FIG. 199.—SKETCH OF A LONGITUDINAL SECTION THROUGH THE ALIMENTARY CANAL OF A HUMAN EMBRYO, SOON AFTER THE DISAPPEARANCE OF THE PRIMITIVE VELUM. (His.) $\frac{40}{1}$.

The alimentary canal is shaded throughout. *uk*, section of mandibular arch; *RT*, hypophysis, behind it the remains of the pharyngeal septum; *Lg*, commencing lung, the future orifice of the larynx being opposite *K*; *Mg*, stomach; *Lb*, liver; *Nb*, yolk-stalk; *W*, Wolffian duct; *B*, blind portion of hind-gut; *all*, allantois.

The remains of this septum have been termed the *primitive velum*, but the septum has nothing whatever to do with the formation of the permanent velum palati, or with the isthmus of the fauces. The plane of the septum forms in fact an angle with the plane of the future isthmus

[1] Zimmermann (Archiv. f. mikr. Anat. liii.) has described in a human embryo of four weeks two small vesicles in this region which he regarded as derivations of the pocket of Seessel, and as possible representatives of the *præoral gut* (v. Kupffer) of lower forms. See also Nusbaum, Anat. Anzeiger, xii. and Bonnet, Anat. Hefte, xvi.

faucium, so that the primitive mouth or stomodœum does not by any means correspond with the permanent mouth. In fact, the floor of the mouth, including the tongue, is developed *behind* the septum, and therefore in connexion with the fore-gut rather than with the stomodœum; whereas the uppermost part of the pharynx, including the choanæ, is *in front of* the septum, and therefore belongs to the stomodœum.

After the several prominences have united with one another, as described on p. 86, to form the face, the primitive mouth is converted into a transversely disposed cleft, and is divided by the development of the palate into an upper nasal and a lower buccal portion (see p. 154). On the margins of the processus globulares and maxillary processes where they form the upper, and also on the mandibular arches where they form the lower border of the mouth, shallow grooves running parallel to their outer edges appear. These are due to the presence of ingrowths of the epithelium (Kollman), which are divided by a shedding of the central cells into two lamellæ. The fissures thus produced gradually deepen and separate off the lips from the edges of the developing jaws on which the dental ridges are being developed. The *vestibulum oris* is produced by an extension of the clefts between the cheeks and the alveolar edges of the jaws. The cheeks themselves are formed by a union of the primitive lips as the buccal opening is gradually constricted.

## PHARYNX.

The anterior extremity of the fore-gut becomes dilated to form the pharynx. Its cavity is greatly flattened dorso-ventrally, but considerably expanded laterally. On the whole, it is funnel-shaped, and is bent on itself owing to the cephalic and cervical flexures. The cavity soon becomes irregular, due to the development of the *visceral pouches* and certain other evaginations. Four visceral pouches are present by the fifteenth day (fig. 200), and between them the branchial arches show as rounded ridges in the interior of the pharynx. All the pouches have ventral prolongations on to the ventral wall of the pharynx, and all except the fourth have also dorsal pockets. The ventral prolongation of the first pouch reaches farthest towards the mid-ventral line, joining the groove round the *tuberculum impar* (see below). The remaining pouches do not reach the floor of the pharynx. Each visceral pouch corresponds to an ectodermic visceral cleft. The external cleft and internal pouch are at first separated by mesenchyme; but later this disappears, and the ectoderm and entoderm come together on the lateral aspect of the pharynx to form a thin septum between them. It is this septum which is broken through in gill-breathing animals to form the gill-cleft, but it is probable that the pharynx does not communicate with the exterior at any stage in mammals.

The branchial arches in the fish develop gill-filaments containing capillary loops connecting the afferent and efferent branches of the aortic arches. No such filaments are developed in the higher vertebrates, and it might be expected that, with the loss of gill-respiration the gill-pouches would also have disappeared. They are retained to provide the cellular rudiments of certain important organs which arise from the epithelium of the gill-pouches in all vertebrates (Maurer).

Owing to the great expansion of the mandibular and hyoid arches, the funnel-shape of the pharynx becomes more pronounced as it narrows behind into the œsophagus, and the hinder pouches take a nearly horizontal direction owing to the manner in which the hinder arches are telescoped within the hyoid arch (fig. 201). At first neither the branchial arches nor the visceral pouches reach the mid-ventral line, so that the floor of the cavity is a flat plate overlying the developing heart. On this flat surface a depression appears opposite the third and fourth arches, which is the rudiment of the respiratory passages. This is bounded in front by a transverse ridge joining the ventral ends of the third arches, and on each side by lateral ridges,

the whole forming a forked elevation called by His the *furcula* (fig. 200). In front of the *furcula* a rounded swelling is developed in the angular space between the ventral ends of the first and second arches named the *tuberculum impar* (His).

**Development of the tongue.**—It is on the flat floor of the pharynx thus defined that the tongue takes form. According to His' account, the tuberculum impar enlarges, projects forward on the oral surface of the mandibular arch, and forms the body of the organ. It appears, however, from the extensive comparative

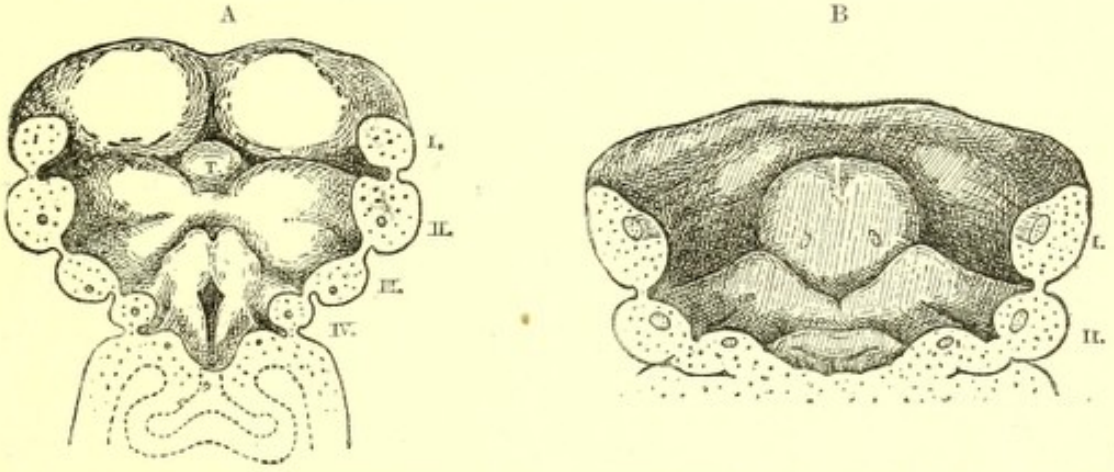



FIG. 201.—SIMILAR VIEWS IN OLDER EMBRYOS OF THE SAME PARTS AS IN FIG. 200. (His.) A, $\frac{18}{1}$; B, $\frac{16}{1}$. *T*, tuberculum impar.

researches of Kallius, confirmed in the case of the human embryo by Hammar,[1] that the greater part of the body of the tongue is really formed, as Born, indeed, showed for the pig in 1883, from two lateral swellings which rise from the floor of the mouth and surround the tuberculum impar. According to Hammar, the tuberculum impar forms in the human tongue only a small portion in front of the foramen cæcum, but Kallius holds that it gives rise to the central part of the organ. The lateral tongue-ridges are marked off externally by grooves which deepen, as development proceeds, into the alveolo-lingual sulci. The root of the organ is formed from a transverse ridge which develops between the ventral ends of the second arches (Born, Hammar). From this ridge two swellings grow forwards to embrace, as with the limbs of a V, the tuberculum impar (fig. 201). At the apex of the V, and between its limbs, a deep recess marks the rudiment of the mesial thyroid. The line of union between this (*copular*) part of the tongue and the body is marked in the adult by the *sulcus terminalis* of His, and the depression is represented by the *foramen cæcum* (fig. 202). The root of the tongue is at first continuous with the ridge which lies between the ends of the third arches and in front of the primitive glottis. Later a fold develops on this ridge, which is the rudiment of the *epiglottis*.

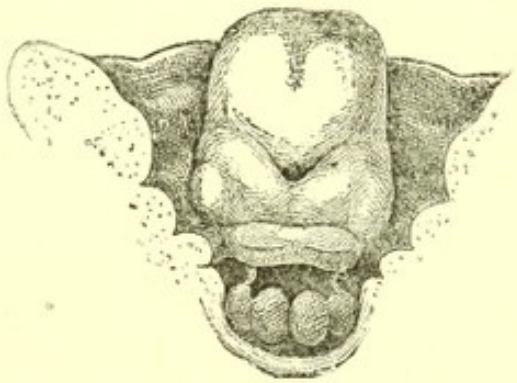


FIG. 202.—SIMILAR VIEW IN A CONSIDERABLY OLDER EMBRYO, BUT LESS MAGNIFIED. (His.)

[1] See Hammar, Arch. f. mikr. Anat. lxi. 1902; C. Rabl, Die Entwickelung des Gesichtes, Heft i. 1902; Kallius, Anat. Anzeiger (Ergänzungsheft), xxiii. 1903.

In front of the sulcus terminalis the circumvallate papillæ begin to show about the beginning of the third month (Gräberg). Their position is marked by a pair of ridges diverging in front, but meeting in the middle line behind. On these ridges circular epithelial thickenings appear which grow inwards and cut, as it were, the papilla out of the mucous membrane. A fissure next appears in the ingrowing wall of epithelium, produced by the shedding of the central cells, which becomes the trench round the papilla, while the marginal thickening on the surface into which the stratum proprium extends becomes the vallum. The fungiform papillæ appear about the beginning of the third month and the filiform a trifle later, both as projections of the connective tissue, over which the epithelium is thickened. The epithelial plaque in the case of the filiform papillæ is afterwards broken up by the irregular thickening of the epithelium over them.

The visceral pouches of the pharynx begin to disappear towards the end of the first month. The dorsal portions of the first pair become the tubo-tympanic

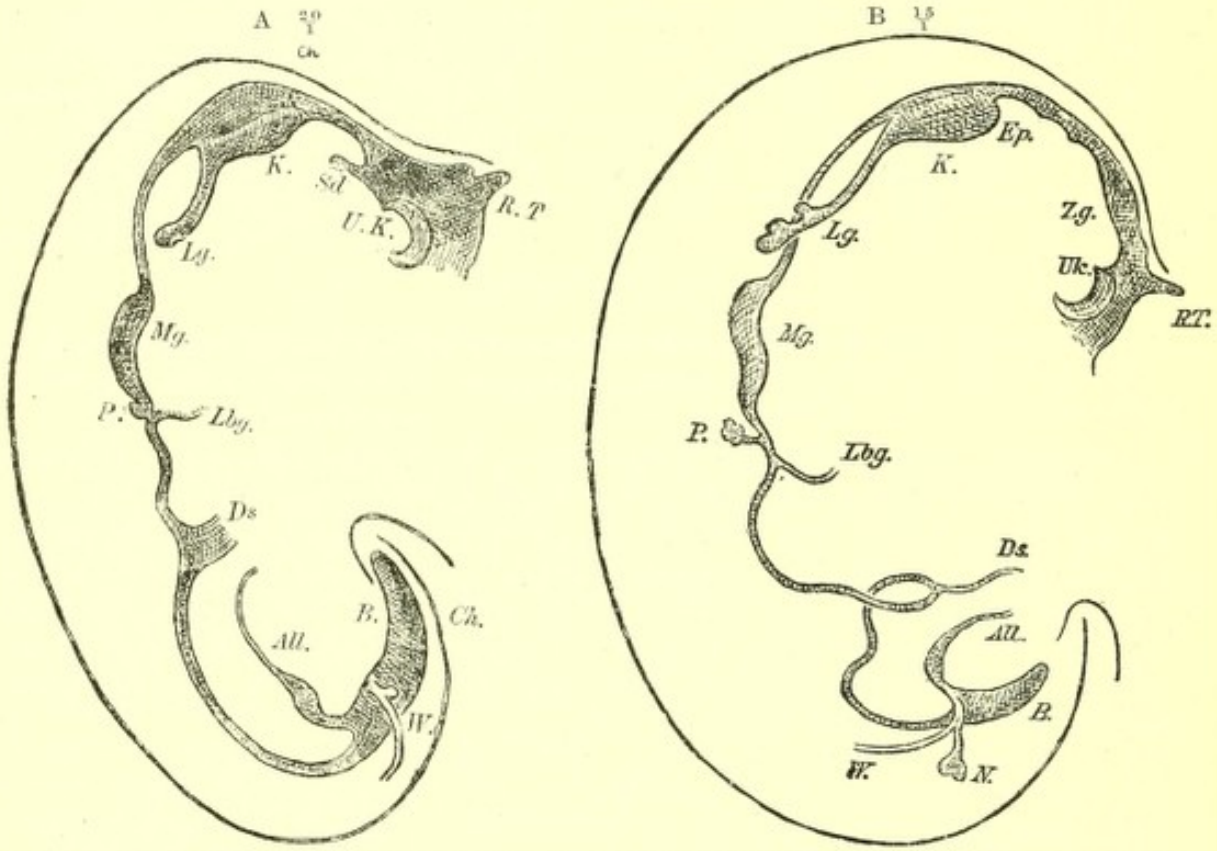



FIG. 203.—PROFILE SKETCHES OF TWO STAGES IN THE DEVELOPMENT OF THE ALIMENTARY CANAL IN THE HUMAN EMBRYO. (His.)

*Ch.*, notochord; *Sd* (in A), median rudiment of thyroid; *U.K.*, section of mandibular arch; *R.T.*, hypophysis; *Lg.*, lung; *K.*, larynx: *Mg.*, stomach; *P.*, pancreas; *Lbg.*, bile-duct; *Ds.*, vitelline duct; *Zg.* (in B), tongue; *All.*, allantois; *B.*, entodermic cloaca; *W.*, Wolffian duct; *N.*, hind kidney.

passages (see Development of the Ear), the second in part form the pockets in which the tonsils develop (Hammar). No traces of the remaining pouches persist in the adult, but in the embryo their epithelial lining gives origin to important organs. Thus the third pouches give origin to the *thymus*, and the fourth to the *lateral portions of the thyroid gland*, while both third and fourth supply epithelial buds which form the *parathyroid bodies*.

## ŒSOPHAGUS, STOMACH, AND INTESTINES.

Immediately behind the pharynx, the fore-gut contracts again to form the œsophagus, which is very short (fig. 203, A) in the early embryo, owing to the imperfect development of the neck. Behind the œsophagus the gut widens out into the dilatation which represents the stomach. This organ, which is at first nearly

straight (fig. 199, A, *Mg*), soon begins to show the convexity of the greater curvature on the side next the vertebral column, and the concavity of the lesser curvature on the opposite border (fig. 203, B, *Mg*), while the pyloric end becomes tilted away from the vertebral column, producing the duodenal loop (fig. 203). Finally the organ becomes turned over on what was previously its right side, which now becomes the posterior surface; and the pyloric extremity being also tilted over, the duodenal loop is thrown over to the right side of the abdomen (fig. 204). The section of the gut between the stomach and the mouth of the yolk-sac is at

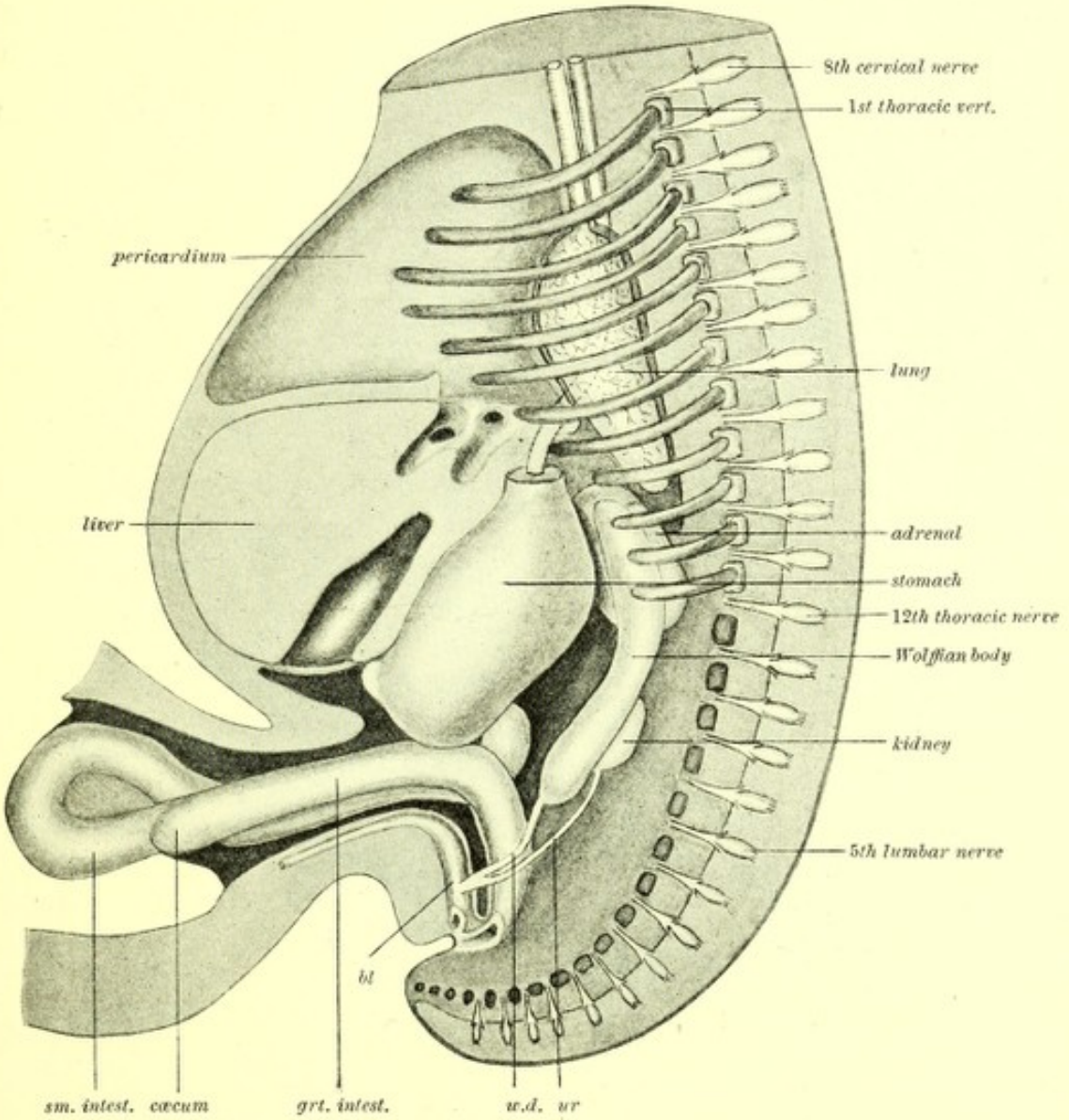



FIG. 204.—RECONSTRUCTION OF A HUMAN EMBRYO OF 17 MM. (After Mall.)
*bl*, bladder; *w.d.*, Wolffian duct; *ur*, ureter.

first short and straight. It early shows a forward directed diverticulum which is the rudiment of the liver. It gradually increases in length by the closure of the mouth of the yolk-sac, until the whole length of the intestine is laid down as a nearly straight tube which is attached to the posterior wall of the primitive abdominal cavity by a continuous mesentery (fig. 203, A). As the liver develops and comes to occupy a large section of the cavity, the intestine, increasing in length, forms a loop which extends through the wide-open umbilicus (fig. 204). This loop (*vitelline loop*) gives attachment at its extremity to the vitelline stalk (fig. 203),

and consists of a proximal descending and a distal ascending limb. As it increases in length the two limbs come close together, and the posterior extremity (afterwards the middle of the transverse colon) is brought into close relationship with the end of the duodenal loop (fig. 204). Very early a rotation of the loop commences round its long axis, which brings the distal over the proximal limb. On the distal limb an evagination develops which is the rudiment of the cæcum (fig. 204), and from now onwards it is possible to distinguish the portion of the gut which will become the small, from that which

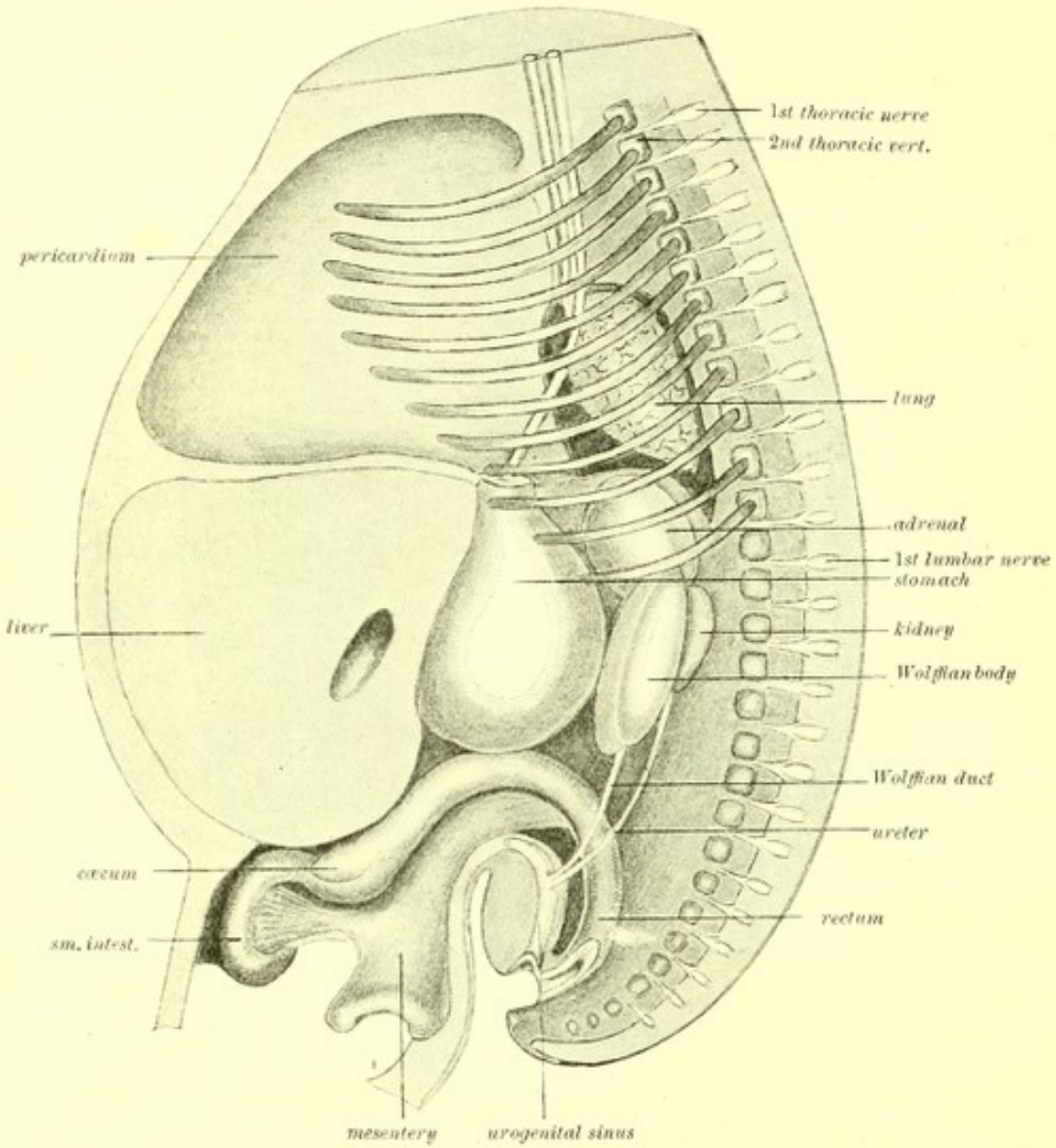



Fig. 205.—Reconstruction of a human embryo of 24 mm. (After Mall.)

will become the large intestine. The small intestine increases in length more rapidly than the large intestine, and, while still without the body-wall, it begins to be coiled (fig. 205). It shows six bends which presently become six primary circular coils (Mall). The distal coil ends at the cæcum, and from this the large intestine passes straight back in the middle line to the back wall of the abdomen, where it turns sharply down to end in the rectum (fig. 206). As the result of the continuance of the axial rotation, the small intestine becomes displaced to the left, *under* the large intestine and below the superior mesenteric artery, until it assumes its definitive position, while the large intestine, also increasing in length,

forms a U-shaped loop surrounding the coils of the small intestine (fig. 206). The small intestine is next withdrawn into the abdominal cavity, and the umbilicus is closed. The U-shaped loop of the large intestine is produced by its proximal portion being carried to the right, so that it comes to be transversely disposed, passing from right to left. As it lengthens, the cæcum descends to assume its definitive position in the right iliac fossa, and thus we have laid down an ascending and a transverse colon. The distal portion of the large intestine, at first in the mesial plane, becomes, on the other hand, displaced to the left, as the

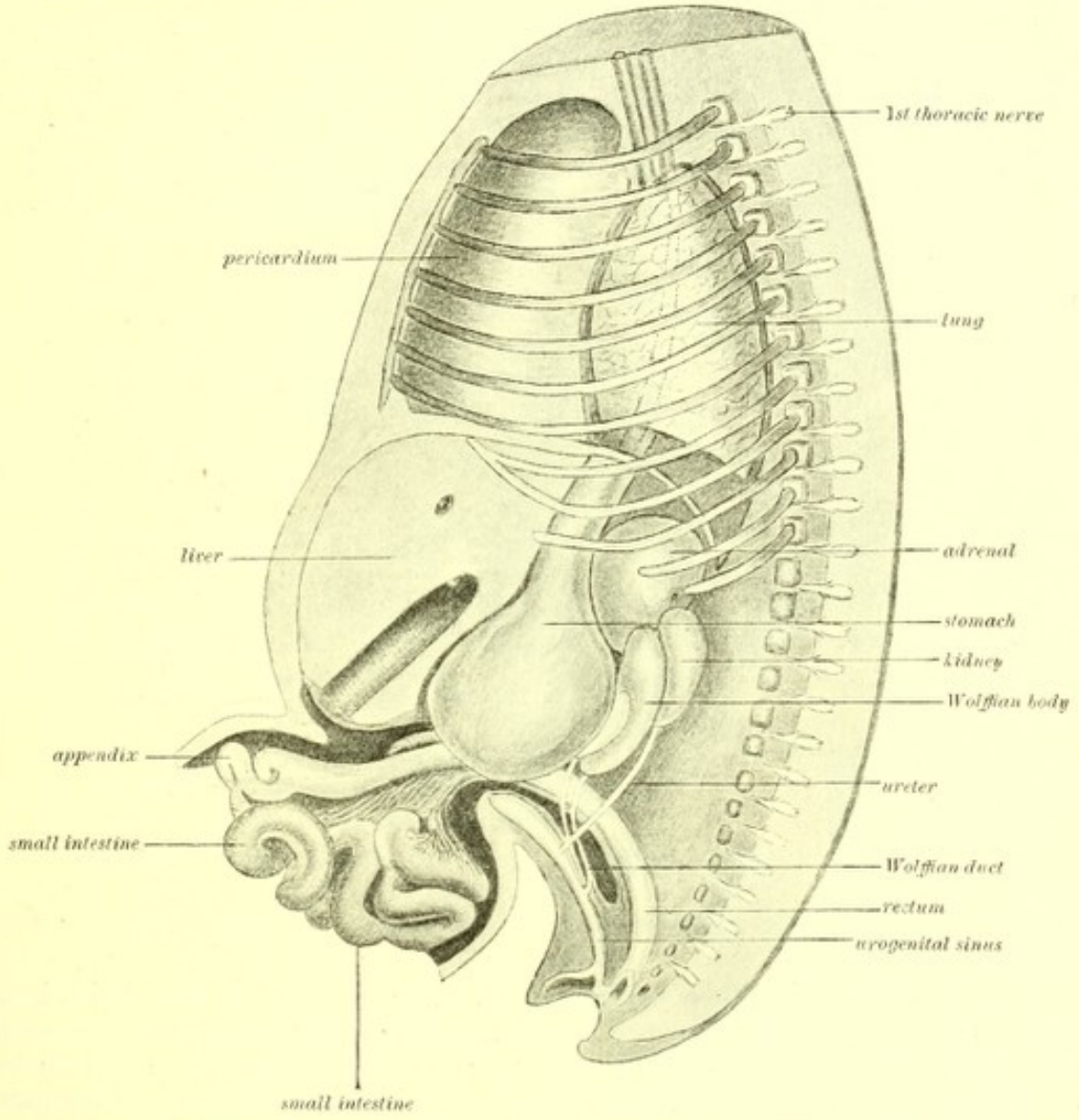



FIG. 206.—RECONSTRUCTION OF A HUMAN EMBRYO OF 24 MM. SOMEWHAT MORE ADVANCED IN DEVELOPMENT THAN THAT SHOWN IN FIG. 205. (After Mall.)

coils of the small intestine increase in number until it ultimately assumes the position of the adult descending colon. The primary coils of the small intestine become progressively more complex by the formation of secondary coils, which are arranged in definite groups so that they can be followed through all the phases of development (Mall).

The epithelium in the duodenum during the second month increases greatly in thickness by the active multiplication of the cells (fig. 170, p. 126) until the narrow lumen is nearly or quite closed (Tandler).[1] As the calibre of the gut increases in the third month the lumen is re-

[1] Anat. Anzeiger (Ergänzungsheft), xviii. 1900.

established. Cases of congenital stenosis of the gut just beyond the pylorus are possibly to be explained by the persistence of the early occlusion.

The **cæcum** is at first a uniform conical diverticulum. By the end of the first month it shows a smaller apical and a larger basal section. The former becomes the vermiform appendix, the latter the cæcum. The cæcum is at first conical (fig. 206), with the appendix passing off from its apex; but later, owing to the unequal dilatation of its anterior and right walls, the appendix comes to be attached to its posterior and left aspect.

**Formation of the entodermic cloaca and anus.**—The hind-gut ends during the third week in a dilated chamber, which also receives the openings of the Wolffian ducts (fig. 203 A, B.). This chamber, which is called the *cloaca entodermica*, is closed on its ventral aspect by a membrane derived from the persistent part of the primitive streak. This cloacal membrane consists of ectoderm and entoderm, which are here in contact with one another without the intervention of mesoderm, and it forms a septum between the cloaca and a

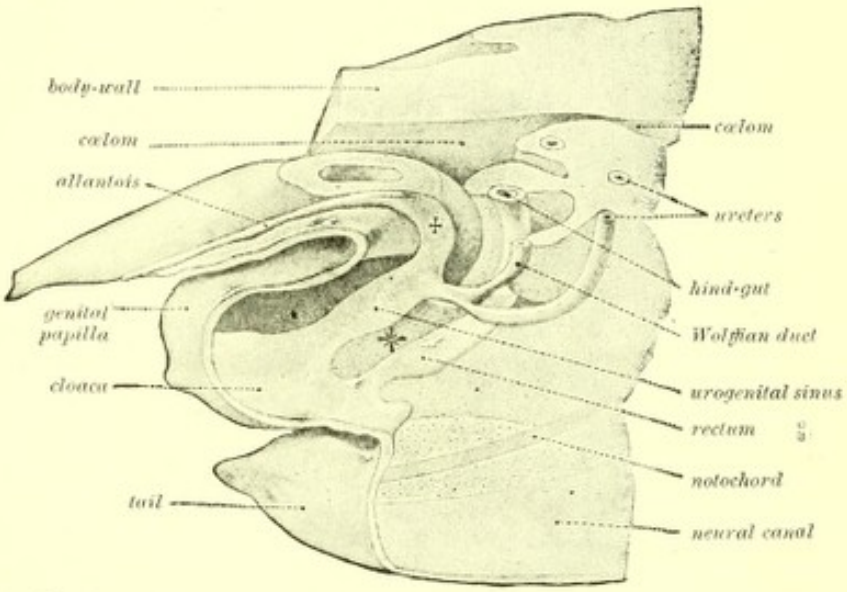



Fig. 207.—Pelvis of a human embryo of 14 mm. (five weeks). (After Keibel, from Köllmann's Entwickelungsgeschichte.)

+ bladder; * septum uro-rectale.

shallow surface depression (*urinogenital fossa*). The chamber is then divided by a septum into a dorsal and a ventral passage, becoming the *rectum* and *urogenital sinus* respectively (figs. 204, 205, 206), and these come to open on the surface by the absorption of the membrane. The opening into the alimentary canal becomes the *anus*. It does not correspond with the posterior extremity of the primitive hind-gut, for at first there is a postanal *cul-de-sac* — the tail-gut, which later becomes reduced and obliterated. The anal opening is completed during the third month. The process by which it is formed will be dealt with later.

## FORMATION OF THE GLANDS OF THE ALIMENTARY CANAL.

Under this head may be included not only those organs which are ordinarily so termed, but also the lungs, thymus, thyroid, and pituitary body, since the early development of these organs resembles that of the true secreting glands.

All the organs above enumerated are formed as epithelial involutions, either solid at first and afterwards becoming hollowed out, or hollow from the first. As

these epithelial buds grow into the mesoderm, they may either bifurcate or give off lateral branches, and in this manner all the ramifications of the ducts of the compound racemose glands are produced. The blind extremities generally end eventually in enlarged tubular or saccular dilatations. All the epithelium of the gland-saccules and ducts is derived from the original epithelial sprout, while the basement-membranes and connective tissue and blood-vessels of the gland are

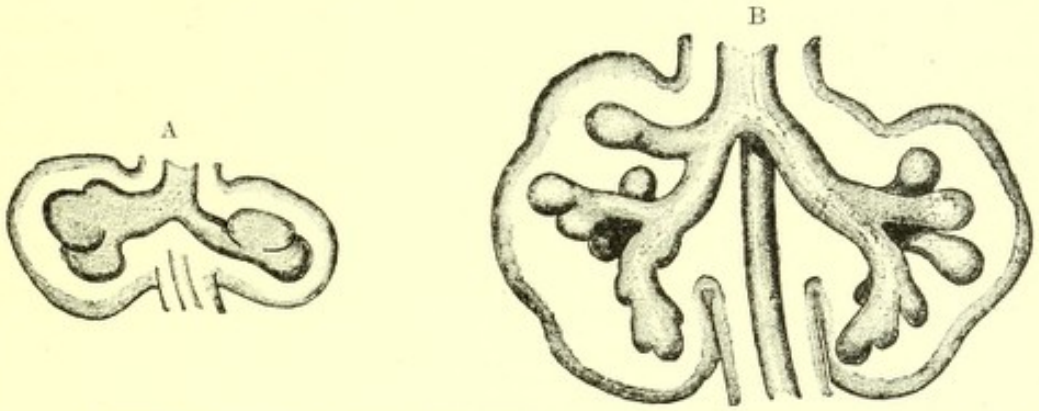



FIG. 208.—A, LUNG-RUDIMENTS OF HUMAN EMBRYO OF ABOUT FOUR WEEKS, SHOWING THE BUD-LIKE ENLARGEMENTS WHICH REPRESENT THE LOBES OF THE FUTURE LUNGS. (His.)

Three buds are seen on the right side, two on the left.

B, LUNGS OF A HUMAN EMBRYO MORE ADVANCED IN DEVELOPMENT. (His.)

derived from the surrounding mesoderm. The salivary glands and most other glands of the mouth, and part of the pituitary body, which must also be reckoned as a glandular development, are formed in this way by involution of the buccal or stomodœal ectoderm ; while the lungs, liver, pancreas, thyroid, thymus, and all the small glands of the rest of the alimentary canal are formed of involutions of the entoderm. The development of the teeth, which also first make their appearance as involutions of stomodœal ectoderm (enamel germs), will be described after their structure has been dealt with (in the part of this work which is devoted to Splanchnology).

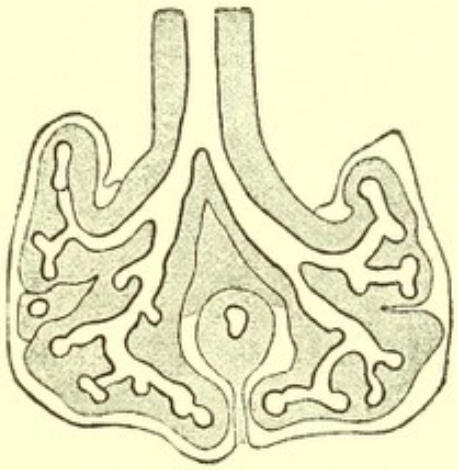


FIG. 209.—LUNGS OF A HUMAN EMBRYO STILL MORE ADVANCED. (His.)

**Salivary glands.** — The submaxillary gland appears as an epithelial sprout from the floor of the mouth towards the close of the fifth week (Sudler),[1] and the sublingual rudiment develops on its outer side in the ninth week (Hammar).[2] The parotid develops in the lateral wall of the cavity in the angle between the roof and floor of the primitive mouth. When the cheeks are formed by the union of the freed lip-portions of the mouth-opening, its duct comes to open in the cheek. According to Hammar, Stenson's duct is not formed as an epithelial sprout, as in the case of the other glands, but appears first at the end of the first month as a groove in the position specified, which afterwards closes into a canal and becomes separated from the cheek by the ingrowth of connective tissue. The duct in the tenth week runs over the masseter to the back of the mandible, where the epithelial buds are given off which form the secretory tubules of the gland.

[1] Amer. Journ. of Anat. i. 1902.

[2] *Loc. cit.*

**The lungs.**—The lungs begin to develop during the third week from the ventral part of the pharynx at its junction with the œsophagus (fig. 199, *Lg*). The lung-rudiment is at first single and median, and takes the form of an elongated vertical diverticulum of the fore-gut, communicating freely with that tube, and of course lined by entoderm. Soon the diverticulum sprouts out at its lower extremity in the form of two tubes which grow downwards on either side of the heart, into a mass of mesodermic tissue, which keeps pace in its growth with the lung-rudiment, and from which the connective tissues of the future lung become ultimately developed. The extremities of the tubes in question are early seen to be dilated and lobulated (fig. 208), three lobules being present on the right tube and two on the left. The division of the lungs into their lobes is thus early indicated.

The further outgrowth of the lobulations produces the rudiments of the principal branches of the bronchi, one for each future pulmonary lobe. Each of these branches then gradually progresses in growth, giving off as it proceeds diverticula which form the secondary bronchi, and these again giving off others until the whole complicated bronchial ramification is eventually produced. Like the first sprouts from the median diverticulum, all the secondary and other sprouts are dilated at their termination, and have a lobulated aspect (fig. 208, B; fig. 220, p. 174; fig. 268, p. 214). This is due to the fact that they are undergoing a further division or sprouting. This process goes on until the sixth month of intra-uterine life, by which time all the dilated ends of the growing and sprouting tubes have reached the surface of the lung. These dilated extremities, which now appear grouped together, and apparently springing several from a common tube, form the infundibula, but their walls are not at first beset with air-cells. The formation of these takes place when the bronchial ramification is completed (sixth month, Kölliker), as small, closely set, pouch-like protrusions of the walls of the infundibula, and of the terminal bronchial tubes.

There has been much difference of opinion as to whether the branching described above is to be regarded as *monopodial or dichotomous* (*i.e.* whether the bronchial tree is developed by the growth a chief stem from which secondary side-branches are given off, or by the continuous dichotomous division of the terminal buds. The truth seems to lie with His, who described for the human embryo a monopodial division of the primary stems, and a dichotomous division for the secondary branches. This is the view expressed in the most recent paper on the subject by Flint [1]; though he found that the secondary branches may also develop by monopodial division for two or three generations.

The trachea and larynx are formed by a separation from the œsophagus of the original median diverticulum, from the lower angles of which the bronchial rudiments have sprung, the separation commencing below and leaving a relatively small connexion between the two tubes above: this connexion is the rudimentary glottis. As development advances, both the tracheo-laryngeal and the œsophageal tubes lengthen, the latter relatively more than the former, so that the lung-rudiments no longer lie, as was the case at first, in front of and on either side of the stomach, but extend downwards somewhat short of that organ, separated from one another by the œsophagus behind and the heart and pericardium in front. As they thus grow backwards with the lengthening of the trachea, the lung-rudiments project into the anterior part of the body-cavity or cœlom (dorsal portion), and receive a covering from its lining membrane, at first only below and on the external surface, but subsequently on the internal aspect, so as to separate them from the œsophagus (fig. 220). The portions of the body-cavity into which the lungs project become shut off from the remainder on the formation of the diaphragm and pericardium, and form the pleuræ.

The rudiment of the larynx appears about the twenty-fifth day, before the trachea is separated off from the median diverticulum, in the form of two lateral swellings (*Arytänoidwülste*, Kallius), which lie behind the fourth visceral pouches, and here compress the fore-gut in a sagittal direction. They possibly represent

[1] Amer. Journ. of Anat. v. 1906. On this subject see also a recent paper on the comparative embryology of the lung by Moser, Arch. f. mikr. Anat. lxiii. 1903.

rudimentary fifth branchial arches (Kallius), but they soon lose any apparent relation to the branchial region by enlarging dorsally and by growing forwards till they reach almost to the level of the second visceral pouches. They are connected with the floor of the pharynx by two folds which run into the transverse ridge intervening between the ventral ends of the third arches. This ridge, and the lateral folds, form the furcula of His, and, as already mentioned, the epiglottis appears as a fold on the transverse ridge, while the lateral bands form the aryteno-epiglottidean folds. On the anterior margin of the arytenoid mass, external to its pointed end, a swelling, which appears very early, represents the rudiment of the cartilage of Santorini. At an early stage, after the trachea and œsophagus have separated, the slit-like cavity between the swellings is for a time partially obliterated by the cohesion of the opposed epithelial surfaces.

The connective tissue round the now slit-like glottis becomes condensed into *chondroblast*. In this precartilaginous stage the rudiments of the arytenoids, the

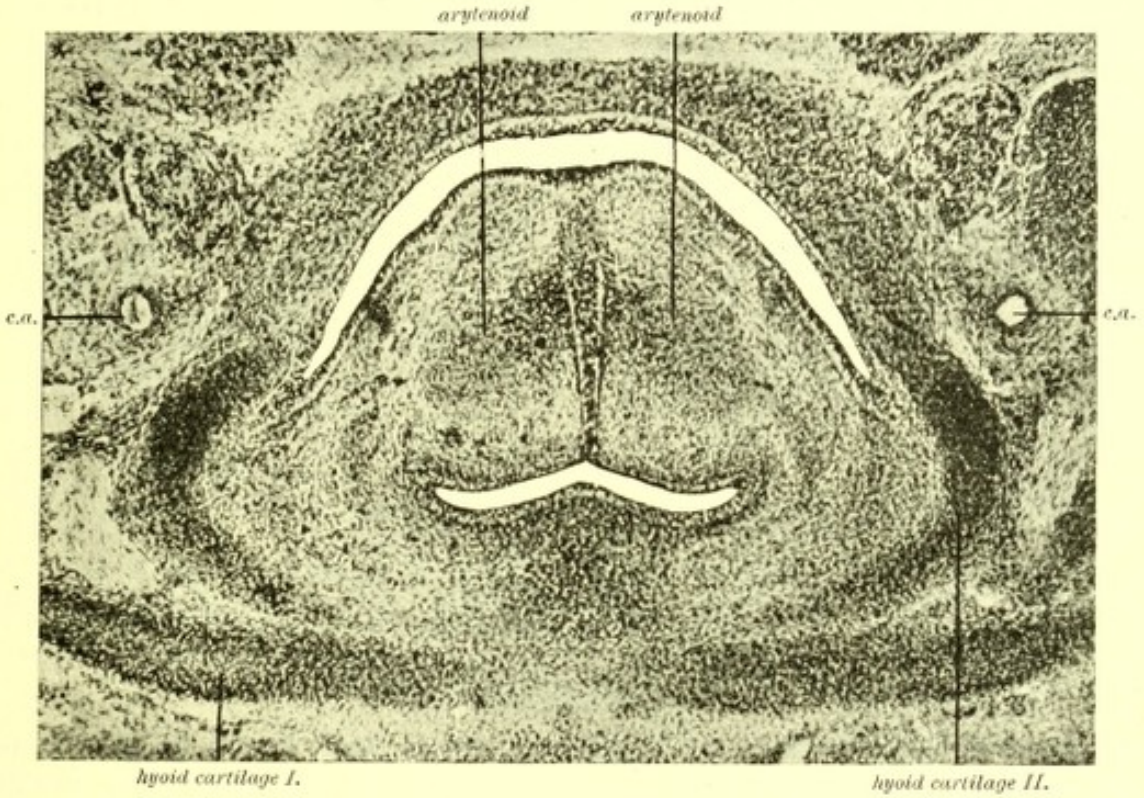



FIG. 210.—TRANSVERSE SECTION OF THE PHARYNX AND LARYNX OF A HUMAN EMBRYO OF 15·5 MM. Photograph. (T. H. Bryce.)

*c.a.*, *c.a.*, carotid arteries.

cricoid, and cartilages of the trachea are continuous laterally. The *cricoid* chondrifies by two centres, one on each side. These unite ventrally, but the ring remains open behind for a time, until completed by the extension of chondrification into the dorsal plate. The tracheal rings develop in the same way, but remain incomplete. The *arytenoids* are at first continuous with the cricoid by fibrous tissue; the *cartilages of Santorini* are portions of the arytenoids segmented off. The *epiglottis* chondrifies relatively late, and is at first continuous behind with the *cartilages of Wrisberg*, which are thus derivatives of the epiglottis (Göppert). The *thyroid* is laid down in the form of two lateral plates which are united ventrally by an intermediate nodule of cartilage (Nicolas). Each plate chondrifies from two centres, an anterior and a posterior (Kallius), possibly representing separate bars seen in Echidna, derived from the third and fourth visceral arches (Göppert).

The superior cornu is at first continuous with the great horn of the hyoid on each side, and the cartilago triticea in the lateral thyro-hyoid ligament of the adult is a remnant of the cartilaginous connexion.

The **thyroid gland** is developed partly from a median diverticulum of the pharyngeal entoderm opposite the ventral ends of the second visceral pouches (fig. 203, A, *Sd*), partly from lateral diverticula of the posterior walls of the fourth visceral pouches. The median diverticulum in most animals early becomes separated from the pharyngeal entoderm, and is thus converted into an island of epithelium imbedded in mesenchyme. In the human embryo (fig. 211, A, *thr*) it remains for some time in the form of a hollow bifid vesicle, which is connected with the upper surface of the tongue by a small duct (*ductus thyreoglossus*, *d*); subsequently, however, the vesicle becomes solid, and the duct is obliterated and disappears, with the exception of a small portion near the orifice, which becomes converted into the *foramen cæcum* of Morgagni, *f.c.*

Occasionally even in the adult a comparatively long duct is found, leading downwards and backwards from the foramen cæcum. This, which has been termed the *ductus lingualis*, is the remains of the original thyrolingual duct

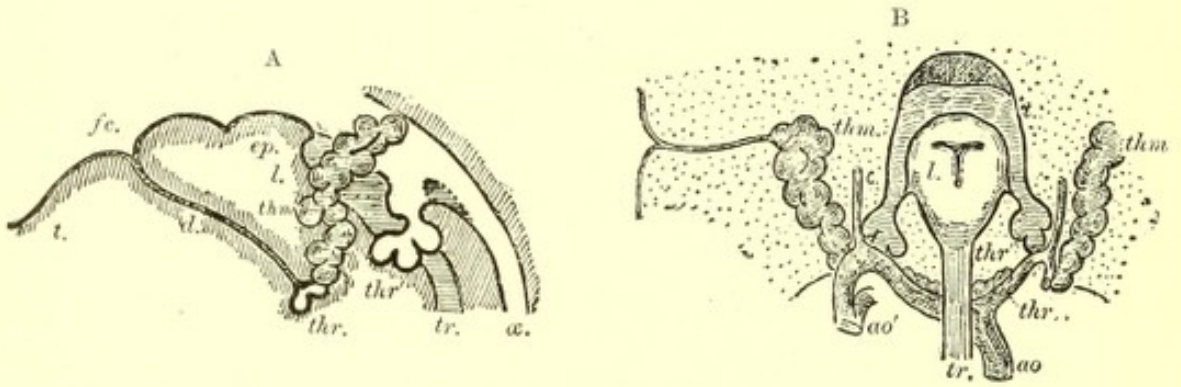



FIG. 211.—SKETCHES SHOWING THE CONDITION OF THE THYROID AND THYMUS GLANDS IN A HUMAN EMBRYO OF ABOUT FIVE WEEKS. (His.)

A, profile sketch from the left side. B, frontal sketch from behind.

*t*, tongue: *fc*, foramen cæcum; *d*, ductus thyreoglossus; *ep*, epiglottis; opposite *d*, larynx; *tr*, trachea; *œ*, œsophagus; *thr*, median rudiment of thyroid; *thr'*, lateral rudiment of thyroid; *thm*, developing thymus, seen on the left side of B to be connected with a visceral cleft; *ao* (in B), ascending aorta; *ao'*, descending aorta; *c*, carotid.

connecting the median part of the thyroid with the tongue. It may further happen that the lower part of this connexion also remains in the shape of a tubular prolongation of the median portion of the thyroid towards the root of the tongue (*ductus thryoideus*; when well developed this portion forms the *pyramid*). The so-called accessory thyroid bodies (suprahyoid, præhyoid glands, &c.) which are occasionally found near the hyoid bone are also referable to the thyrolingual duct (His). The mesial rudiment soon becomes enlarged into a lobed mass of considerable size, which, as the neck elongates, assumes the shape of a horse-shoe passing across the front of the trachea (figs. 212–214). It becomes converted into ramifying and anastomosing cell-cylinders, between which vascular connective tissue is developed. The cell-cylinders subsequently become hollowed out, and finally are subdivided by growth of the connective tissue into small vesicles, which gradually become larger from accumulation of colloid in their interior.

The two lateral diverticula, which assist in the formation of the thyroid body, spring from the fourth visceral pouches (fig. 213). They have at first the appearance of simple thick-walled saccular glands (fig. 216) partially encircling the developing larynx. In front of this they come into connexion with the median rudiment, and eventually blend with it. Like that rudiment, they become

entirely separated from the entodermic surface from which they have taken origin, and are converted into cell-cylinders in which colloid is ultimately formed.

The lateral rudiment of the thyroid apparently corresponds to a structure present in most vertebrates, and known as the *post-branchial body*. It is an entodermic pocket which gives origin to an epithelial body, but this does not yield colloid except in mammals. In Echidna (Maurer) there is colloid formation, but the body remains distinct from the primitive median thyroid. Only in placental mammals does it become united with the median rudiment. The account given above is founded on Born's original description, but it is right to say that some

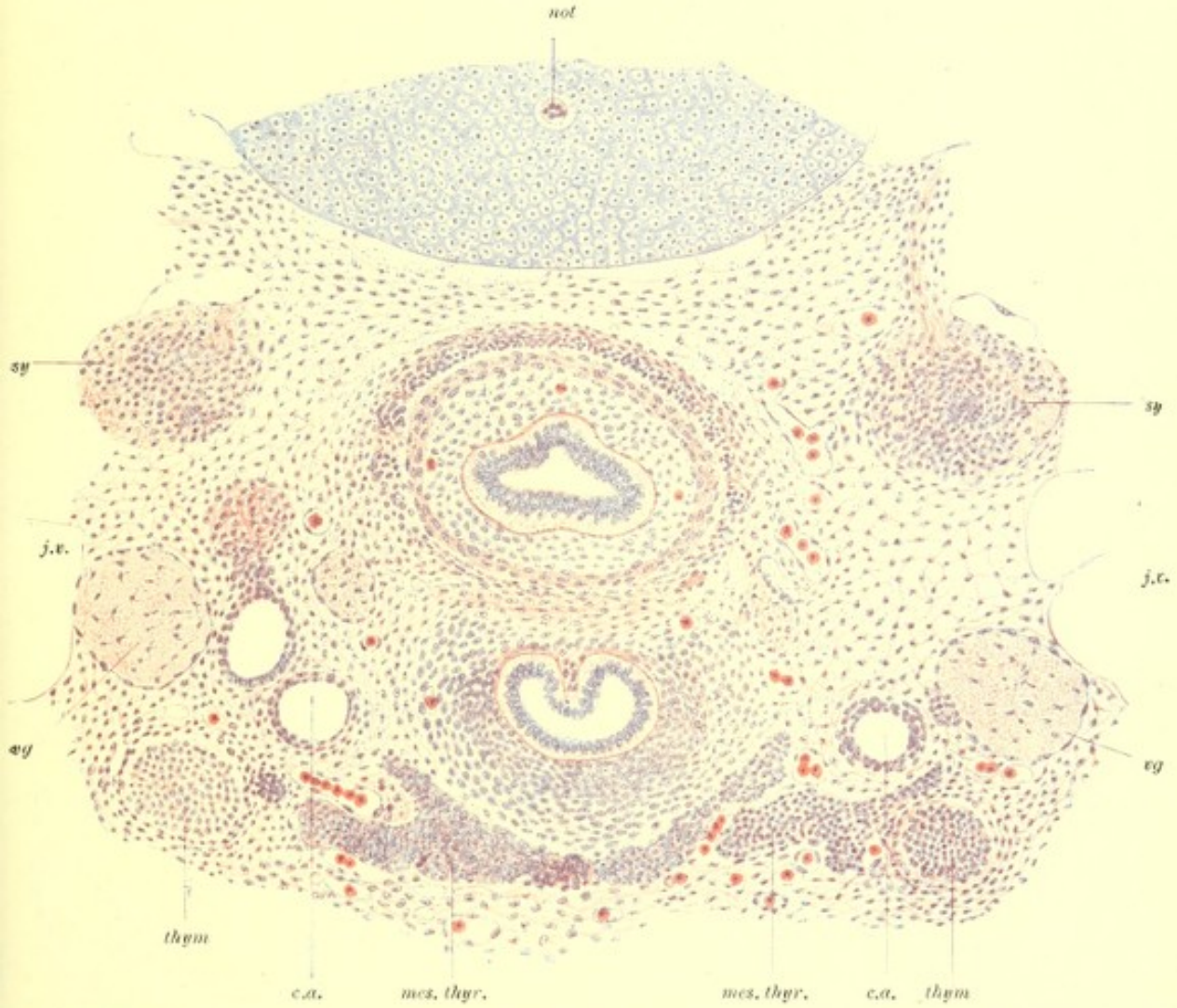



FIG. 212.—TRANSVERSE SECTION THROUGH THE NECK OF A HUMAN EMBRYO OF 15·5 MM., TO SHOW THE POSITION OF THE THYROID AND THYMUS GLANDS, AND HISTOGENESIS OF WALLS OF ŒSOPHAGUS AND TRACHEA. (T. H. Bryce.)

*not*, notochord in vertebral body; *sy*, sympathetic ganglion; *vg*, vagus; *j.v.*, jugular vein; *c.a.*, carotid artery; *thym*, thymus; *mes. thyr.*, mesial thyroid.

hold that, while the diverticulum from the fourth pouch becomes included as a vesicle in the lateral lobe of the thyroid, it takes little (Simon) or no (Verdun) share in the formation of the glandular substance.

The **thymus** in the lower vertebrates appears as a series of buds from the dorsal pockets of the branchial clefts. The number of buds differs in different forms, and the number of those which persist and enter into the formation of the adult gland varies. In birds and mammals it arises from one main rudiment related to the ventral pocket of the third visceral pouch. To this is added in birds and some mammals a rudiment from the fourth visceral pouch, but there

is an absence of agreement among those who have worked at this difficult subject as to the presence of this accessory element in man.

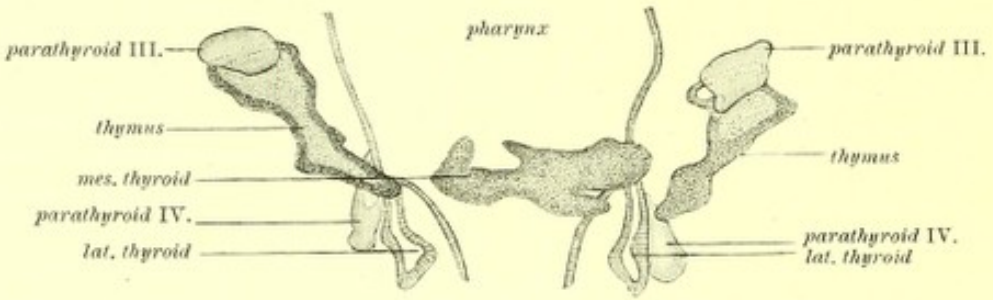



FIG. 213.—RECONSTRUCTION OF BRANCHIAL DERIVATIVES IN A HUMAN EMBRYO OF 14 MM. (After Tourneux and Verdun.)

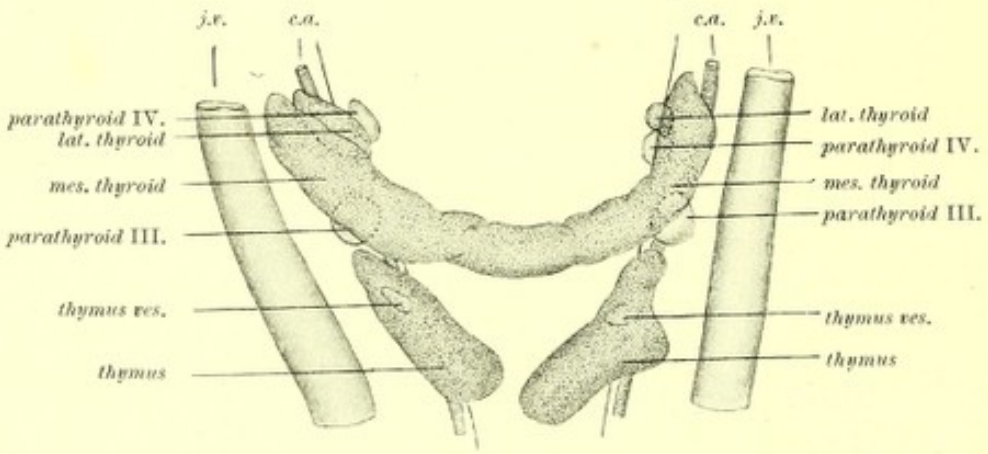



FIG. 214.—RECONSTRUCTION OF THE BRANCHIAL DERIVATIVES IN A HUMAN EMBRYO OF 16 MM. (After Tourneux and Verdun.)

*c.a.*, carotid artery; *j.v.*, jugular vein; *thymus ves.*, vesicle of thymus.

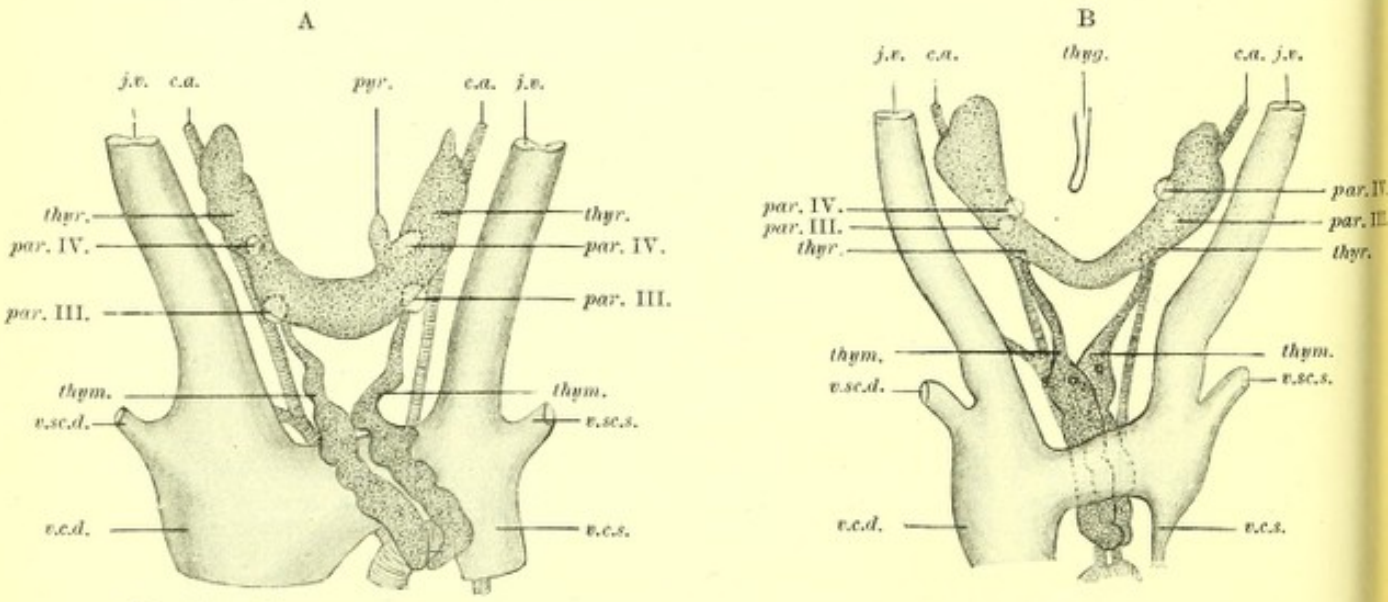



FIG. 215.—RECONSTRUCTION OF THE THYROID AND THYMUS GLANDS WITH THE VEINS AND ARTERIES. A, IN A HUMAN EMBRYO OF 26 MM.; AND B, IN ONE OF 24 MM. (After Tourneux and Verdun.)

In A the thymus lie in front, in B behind the left innominate vein.

*thyr.*, thyroid; *thym.*, thymus; *par.* IV., parathyroid of fourth pouch; *par.* III., parathyroid of third pouch; *pyr.*, pyramidal lobe of thyroid; *thyg.*, thyroglossal duct; *c.a.*, carotid artery; *j.v.*, jugular vein; *v.c.d.*, vena cava dextra; *v.c.s.*, vena cava sinistra; *v.sc.d.*, vena subclavicularis dextra; *v.sc.s.*, vena subclavicularis sinistra.

The thymus is thus in its first origin bilateral. A pocket develops from the third cleft on each side, which extends downwards as a thick-walled tubular prolongation along the carotid artery. The pocket persists as the *thymus vesicle* in the proximal section of each rudiment (fig. 216). From the lower end of the tube solid epithelial buds are given off, and from these lateral buds again come off, so that this part of the gland acquires a ramified lobular appearance like an acinous gland. The acini are, however, solid, and remain so. The two rudiments

FIG. 216.—SECTION THROUGH THE BRANCHIAL DERIVATIVES IN A HUMAN EMBRYO OF 15·5 MM. (T. H. Bryce.)

*c.a.*, carotid artery; *vg*, vagus nerve; *j.v.*, jugular vein; *mes. thyr.*, mesial thyroid; *lat. thyr.*, lateral thyroid; *thym.*, thymus; *par.* IV., parathyroid of the fourth pouch; *par.* III., parathyroid of the third pouch. It appears here as a cellular mass closely related to the thymus rudiment; in the adjoining section it becomes free, and forms a rounded cord having exactly the same structure as the parathyroid of the fourth pouch.

are brought into close contact with one another in front of the trachea (fig. 215), and unite to form a single-lobed body, which comes to lie in the anterior mediastinum in close relationship with the pericardium.

The surrounding vascular connective tissue forms a capsule to the gland, extends between the several buds so as to divide it up into lobules, and also sends processes carrying vessels with them into the interior of the lobules. Each lobule becomes differentiated into a cortical and medullary zone, but before this the gland loses its epithelial structure and assumes the appear-

ance of a lymphoid organ. The epithelial cells give rise to a reticulum (Hammar[1]) (figs. 212, 216), in the meshes of which in the cortical zone lymphoid cells collect in large numbers. The origin of these lymph-cells has been much disputed, some, following Kölliker, deriving them from the entodermic epithelial elements (Prenant, Beard, Maurer, Nusbaum, &c.); others, following Stieda and His, regarding them as invading the rudiment from without (Gulland, Kollmann, &c.). It has been proved (Hammar, Bryce,[2] Stöhr[3]) that leucocytes are already present before the lymphoid transformation of the gland, so that the thymus cannot be the original source of the leucocytes as suggested by Beard. Stöhr in a recent publication advances the thesis that the thymus is an epithelial organ throughout, and is not lymphoid, as the characters of the cells would suggest. The Hassall's corpuscles are very generally, and in all probability rightly, regarded as cell-nests derived from the epithelial cells, as are also various kinds of minute cysts, some of them with a ciliated lining, which have been described as occurring in the adult gland.

The **parathyroid bodies** develop in intimate relation with the thymus and lateral thyroid from the entodermic lining of the third and fourth visceral pouches

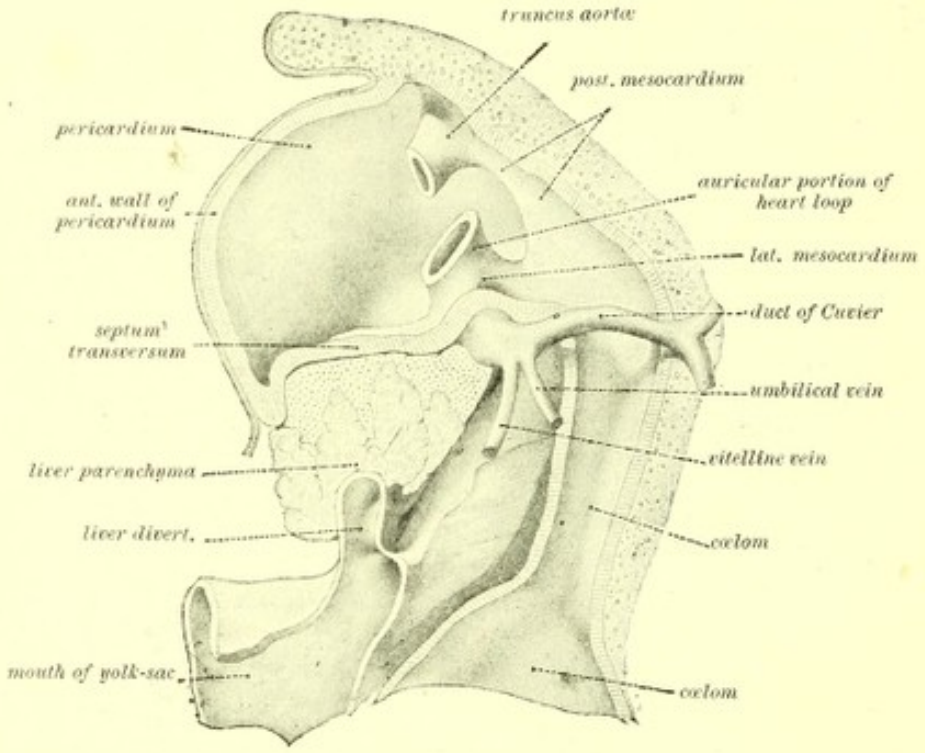



FIG. 217.—THE LIVER DIVERTICULUM AND PARENCHYME WITH SEPTUM TRANSVERSUM. HUMAN EMBRYO OF 3 MM. LONG. (After His, from Köllmann.)

of the pharynx.[4] They appear as paired epithelial buds, which soon become separated from the surface from which they have sprung, and form small isolated bodies of oval shape (fig. 213). The buds from the third pouches lie at first in front and to the outer side of the corresponding buds from the fourth pouches, but they are carried backwards with the thymus, and ultimately lie behind the others (fig. 214). The epithelial cells of each bud become loosely arranged and form a syncytial reticulum closely resembling that of the early thymus (fig. 216). Each body has a distinct capsule, and is quite independent of the other epithelial derivatives of the branchial pouches. In the early stages the parathyroids are thus quite unlike the thyroid, but resemble the thymus (fig. 216).

[1] Anat. Anzeiger. xxvii. 1905. In this paper will be found all the most important references to the literature regarding the mammalian thymus. See also Bell, Amer. Journ. of Anat. v. 1906.

[2] Bryce, Journ. of Anat. and Physiology, xl. 1905.

[3] Stöhr, Anat. Hefte, xxxi. 1906.

[4] The bud from the third pouch is often named the parathymus, while that from the fourth is called the parathyroid. Here the term parathyroid is used for both bodies in view of their relations to the thyroid gland in the adult.

**Liver.**—The primary rudiment of the liver takes the form of a diverticulum of the ventral wall of the gut immediately behind the stomach. The diverticulum first appears as a wide and elongated groove, which becomes closed, and extends

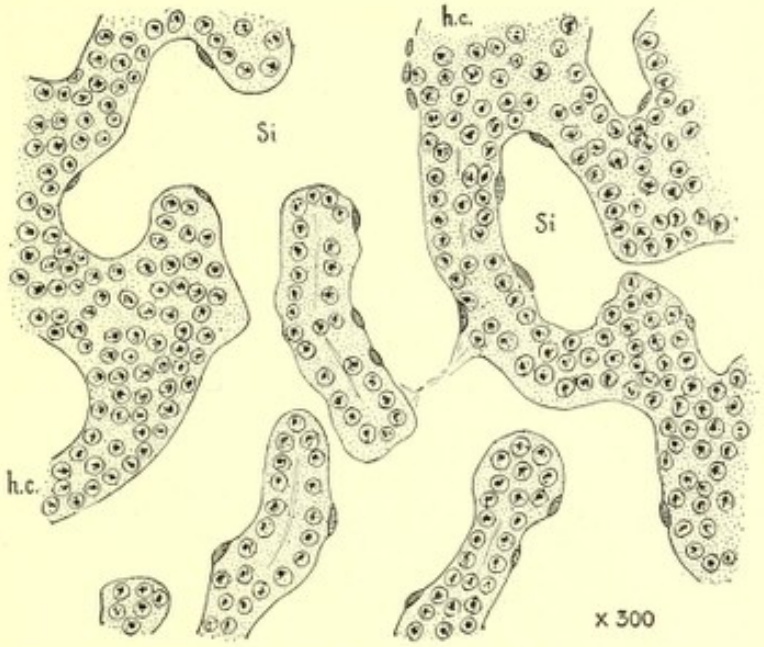



FIG. 218.—SECTION OF THE DEVELOPING LIVER, TO SHOW HOW THE HEPATIC CYLINDERS ENCROACH ON THE LUMINA OF THE SINUS-LIKE VEINS TO BREAK THEM UP ULTIMATELY INTO CAPILLARY-LIKE CHANNELS CALLED SINUSOIDS. (Minot.)

*h.c.*, hepatic cylinders; *si*, sinusoids.

forwards into the substance of the septum transversum (fig. 217). From the fore-part of the diverticulum cells are rapidly budded off from the epithelium to form the parenchyma of the gland. The hinder part of the groove does not share in

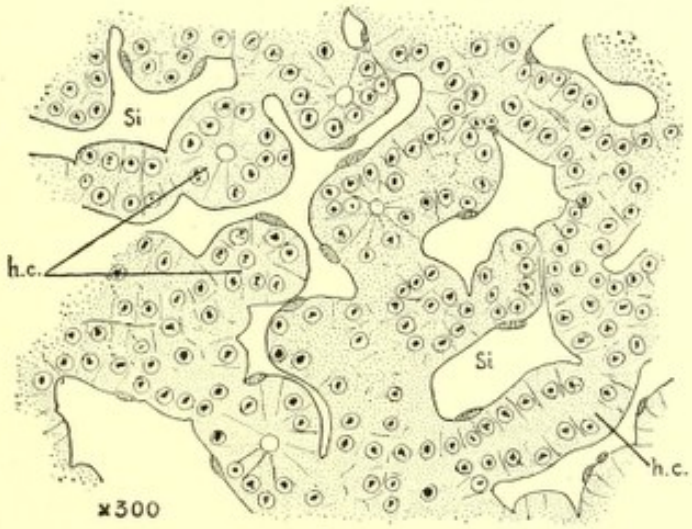



FIG. 219.—SECTION OF THE DEVELOPING LIVER AT A LATER STAGE THAN IN FIG. 218, TO SHOW THE MANNER IN WHICH THE HEPATIC CYLINDERS COME TO FORM A TRABECULAR FRAMEWORK OF PARENCHYMA WITH A NETWORK OF SINUSOIDS IN ITS MESHES. (Minot.)

*h.c.*, hepatic cylinders; *si*, sinusoids.

this proliferation, and persists as the bile-duct. Before being closed it gives off a second ventral pouch, which is ultimately converted into the gall-bladder. The mass of cells budded off from the wall of the tubular diverticulum invades the

septum transversum, the mesenchyme of which supplies the capsule and connective-tissue framework of the organ. As we have already seen, the omphalomesenteric and allantoic veins pass to the sinus venosus through this septum, and we now see the growing liver-parenchyma in the form of cellular strands or trabeculæ extending round these vessels. The cells of the trabeculæ continue to proliferate very rapidly, and the buds produced invade the lumen of the vessels, pushing the endothelial walls before them (figs. 218, 219). This process goes on until the course of the vessels is completely interrupted, and the original channels remain merely as capillary-like vessels, named by Minot 'sinusoids.' [1] The ultimate result is a system of anastomosing epithelial trabeculæ, in the meshes of which there is a

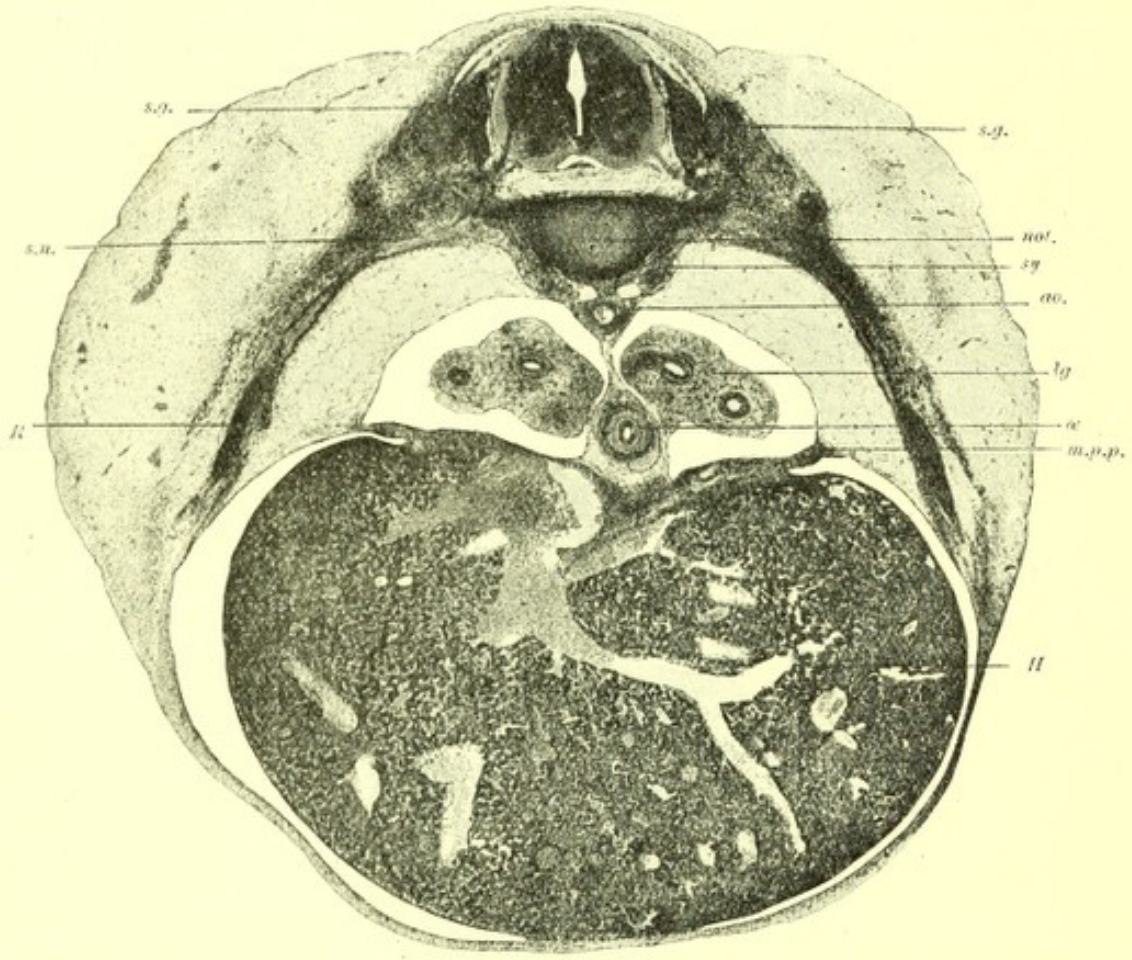



FIG. 220.—TRANSVERSE SECTION OF A HUMAN EMBRYO AT THE END OF THE FIFTH WEEK. Photograph. (T. H. Bryce.)

*s.g.*, *s.g.*, spinal ganglia, neural cartilages to their outer sides; *s.n.*, spinal nerve; *not.*, notochord in vertebral body; *sy*, sympathetic ganglion; *ao*, aorta; *lg*, lung; *œ*, œsophagus; *m.p.p.*, membrana pleuroperitonalis; *H*, liver; *R*, rib.

second network of sinusoids. The thick trabeculæ of early stages are gradually reduced to columns in which only a single layer of cells bounds the narrow lumen, which has meanwhile appeared in the solid strands. The slit-like lumen becomes the bile-capillary. From the second month onwards during the earlier months of pregnancy the liver is very actively engaged as a blood-forming organ, the vessels being crowded by young nucleated red blood-corpuscles.

Though the liver-parenchyma is laid down in higher forms as solid anastomosing strands, in some lower vertebrates (Cyclostomata, Selachians, Amphibians, and certain Reptilia) the

[1] Minot, Proc. Boston Soc. Nat. Hist. xxix. N. 10, p. 185.

trabeculæ are hollow from the first, and in Cyclostomata the arrangement is exactly like a tubular gland in respect that the branches are separate and not joined into a network.

The lobulated arrangement of the parenchyma is not completed until after birth. In the younger stages the primitive lobules are larger than those of the adult, and show an irregular arrangement of the liver trabeculæ. In each lobule there are several anastomosing branches of the hepatic vein. Later, owing to extension of branches of the portal vein with a certain amount of connective tissue into the mass, it is broken up into as many secondary lobules as there are branches of the hepatic vein. These branches become the central veins of the lobules; the trabeculæ assume a radial disposition and the intralobular venous network takes form.

The primary lobing of the liver is determined by the vessels in the septum transversum along which the cellular strands extend. Accordingly there are four primary groups of liver-tissue, two right and two left (Brachet). When the septum transversum has become fully occupied by liver-substance there is a large ventral mass and an upper lateral expansion on each side. The primary lobing is largely lost in later stages owing to the formation of secondary lobes and fissures. The organ begins to be asymmetrical by the eighth week, owing to the presence of the stomach on the left side and to a greater expansion of liver trabeculæ on the

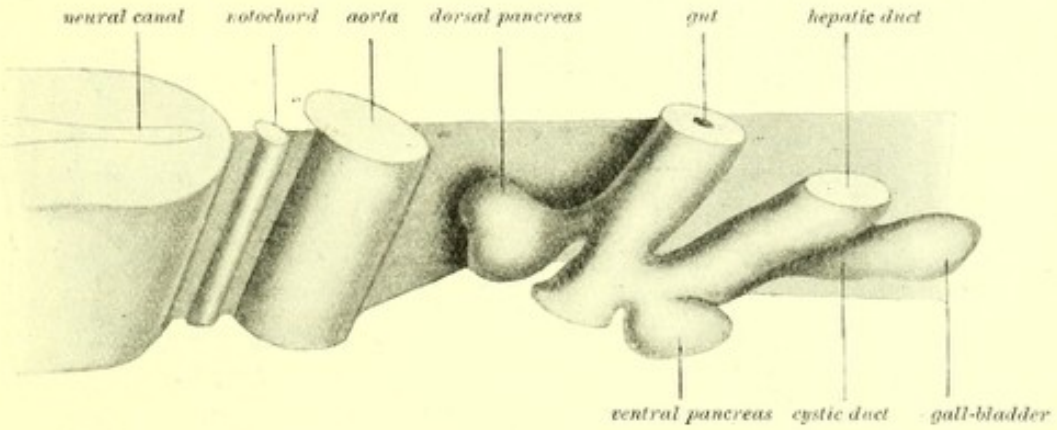



Fig. 221.—Reconstruction to show the development of the pancreas of a human embryo of 6·8 mm. (After Piper.)

right side along the vena portæ. The *lobus Spigelii* appears as a swelling on the inner face of the right lobe, the surface which forms the outer wall of the epiploic (hepato-enteric) sac (*see* Cœlom). It intervenes between the ventral mesentery (gastro-hepatic omentum) and the vena-caval fold (*see* Cœlom), and projects into the epiploic sac.

The **pancreas** is developed from two rudiments, a dorsal and a ventral. The *dorsal pancreas* arises as a diverticulum from the duodenum opposite the bile-duct; the *ventral pancreas* springs in the form of two lateral diverticula from the base of the bile-duct (fig. 221). According to some authorities, these two outgrowths both give origin to pancreatic tissue, but according to others only the right persists (Helly).[1] The dorsal diverticulum becomes the *duct of Santorini*, the persistent ventral outgrowth the *duct of Wirsung*. Each diverticulum gives off lateral offshoots which form the ducts and alveoli, as in other compound acinous glands (fig. 170, p. 126, and fig. 222). Owing to the rotation of the duodenum, the two rudiments are united with one another on the ventral aspect of the portal vein to form a single body, which extends into the mesoduodenum and mesogastrium. The

[1] Helly, Arch. f. mikr. Anat. lxvii. 1905. Other papers dealing with the mammalian pancreas which have appeared since Maurer's list (Hertwig, Entwickelungslehre II. Teil. i. and ii., p. 250) are Völker, Arch. f. mikr. Anat. lix.; Low, Proc. Anat. and Anthro. Soc. University of Aberdeen, 1900–1902; Piper, Arch. f. Anat. 1900; Ingalls, Arch. f. mikr. Anat. lxx.

opening of the duct of Santorini in the majority of instances becomes obliterated, and the duct of Wirsung persists. When the rotation of the stomach has been effected the gland loses its mesial position, and comes to lie across the back of the abdomen. In man, owing to the fusion of the mesogastrium with the transverse mesocolon (*see* Development of the Cœlom), the posterior layer

FIG. 222.—TRANSVERSE SECTION OF A HUMAN EMBRYO OF 30 MM. ABOUT THE BEGINNING OF THE THIRD MONTH. (T. H. Bryce.)

Below the spinal cord is seen the body of a vertebra; on each side of this the kidney; on the left (right of figure) below the kidney the adrenal; on the right only a small portion of the right adrenal is seen below and external to a large vein. Between the two adrenals and below the aorta (distinguished from the veins by its thick wall) some irregular groups of cells represent the abdominal sympathetic; on the right side (left of figure), just above the large vein, the two rounded clear bodies are chromaffin bodies. The liver occupies the whole abdominal cavity; its right and left lobes are separated by the ventral mesentery (falciform ligament) in which the umbilical vein passes. The stomach is twice cut in the section; between it and the adrenal is seen the mesogastrium, with the spleen. The duodenum, with its much-folded mucosa, is seen on the right; between it and the stomach the pancreatic tubules and pancreatic ducts (ducts of Santorini and Wrisberg); between stomach, pancreas, and thin portion of the mesogaster the lesser bag of the peritoneum.

of the mesenteric fold which enclosed the pancreas becomes absorbed, and the gland comes to lie entirely behind the peritoneum.

Owing to the manner in which the alveoli are budded off round the ends of the duct-rudiment, the terminal portion of duct-epithelium is as it were included in the centre of the alveolus to

form the centro-acinar cells (Laguesse). The **cell-islands of Langerhans** have been generally regarded as derivatives of the mesenchyme. This view has been advocated by Hansemann (1902), but it has been shown by Laguesse, Küster, Pearce, and Helly that they are derived from the gland-epithelium.[1] Helly has traced (in the guinea-pig) the Langerhans cells back to a stage in which the pancreas-rudiment is still a solid bud. These special cells are characterised by dense finely granular protoplasm; they do not share in the formation of the tubules, but lie loosely arranged in their walls. In the human embryo (Pearce) such cells occur in round or oval masses and in direct continuity with the epithelial cells. They bud off and form solid cell-processes which are at first connected with the acini, but later become separated from them by the ingrowth of mesenchyme. The group thus isolated is vascularised, and by further histogenetic changes becomes a fully formed cell-islet.

## DEVELOPMENT OF THE UROGENITAL SYSTEM.[2]

### EXCRETORY ORGANS.

The excretory system first appears as a longitudinal duct and a longitudinal series of epithelial tubules in that part of the mesoderm named the *intermediate cell-mass*. This forms a continuous blastema from which every part of the system takes origin. It consists at first of cells disposed, though somewhat indistinctly, in two lamellæ—outer and inner—which are connected with the outer and inner layers of the primitive segment internally, and the somatopleuric and splanchnopleuric layers of the lateral plate externally.

In the Anamnia the corresponding portion of the mesoderm forms in each segment a hollow stalk derived from the ventral part of the segment, through which the myocœl is continuous with the splanchnocœl (general body-cavity). In the mammalia, owing to the condensation of development, the stalks are solid like the segments themselves, and all traces of segmentation are lost at a very early stage.

In the nephrogenetic blastema the tubules are developed from before backwards, and are grouped, as they appear in time and place, into three systems, the *pronephros*, *mesonephros*, and *metanephros*.

**Pronephros and segmental (Wolffian) duct.**—The pronephros is developed as a functional organ in the Anamnia during the larval stage. It is rudimentary in the Amniota, and represented only by vestiges in the Mammalia. When typically developed it consists of a number of coiled tubules, which, joining one another at their outer ends, form the segmental duct, while at their inner ends they open into a chamber, the mesial wall of which is invaginated by a glomerulus—*i.e.* a tuft of capillary vessels derived from a branch of the aorta. The chamber is formed (Brauer in Gymnophiona), by a folding of the mesoderm-layers, from the ventral part of the hollow primitive segment. It becomes cut off from the myocœl, but remains connected by a passage with the splanchnocœl (body-cavity). The tubule is formed as a diverticulum of the chamber by a folding of the somatic layer of mesoderm, while the peritoneal passage becomes the *nephrostome*.

In the human embryo a very rudimentary pronephros is probably to be recognised in a longitudinal duct, some blind tubules, a peritoneal funnel, and a vestigial glomerulus, which have been described by several observers,[3] in the fifth, sixth, and seventh segments. It is possible, however, that these vestiges may represent degenerating mesonephric structures.

[1] Hansemann, Verh. deutsch. pathol. Ges. 1901; Laguesse, *loc. cit.* (Hertwig), and Arch. d'Anat. microsc. v. 1902; Pearce, Amer. Jour. of Anat. ii. 1903; Küster, Arch. f. mikr. Anat. lxiv. 1904; Helly, *ibid.* lxvii. 1905.

[2] For literature up to 1905, see Felix, Hertwig, Entwickelungslehre, III. Teil i. and ii. p. 852 *seq.*

[3] Janošik, Arch. f. mikr. Anat. xxx.; Tandler, Anat. Hefte, xxviii.; MacCallum, Amer. Jour. of Anat. i.; Gage, *ibid.* iv.; Keibel, Anat. Anzeiger (Ergänzungsheft), xxvii. 1905; Ingalls, Arch. f. mikr. Anat. lxx. 1907.

The segmental or Wolffian duct appears as a solid cord of cells, which extends backwards close under the ectoderm external to the nephrogenetic cord as far as the cloaca. It soon acquires a lumen (embryo of 3 mm.), and opens into that chamber (embryo of 4·2 mm. ; Keibel).

In the rabbit (Rabl) and marmot (Janošik) the head end of the duct arises by the fusion of cords of cells which represent rudimentary pronephric tubules, so that the mode of origin characteristic of the Anamnia is repeated, though in a very abbreviated form. It is not improbable that the head end of the duct arises in the same fashion in the human embryo. Graf Spee, Kollmann, Flemming, and others have, however, derived the duct from the ectoderm, which certainly dips in along the line of the rudiment and lies in contact with it. It is as

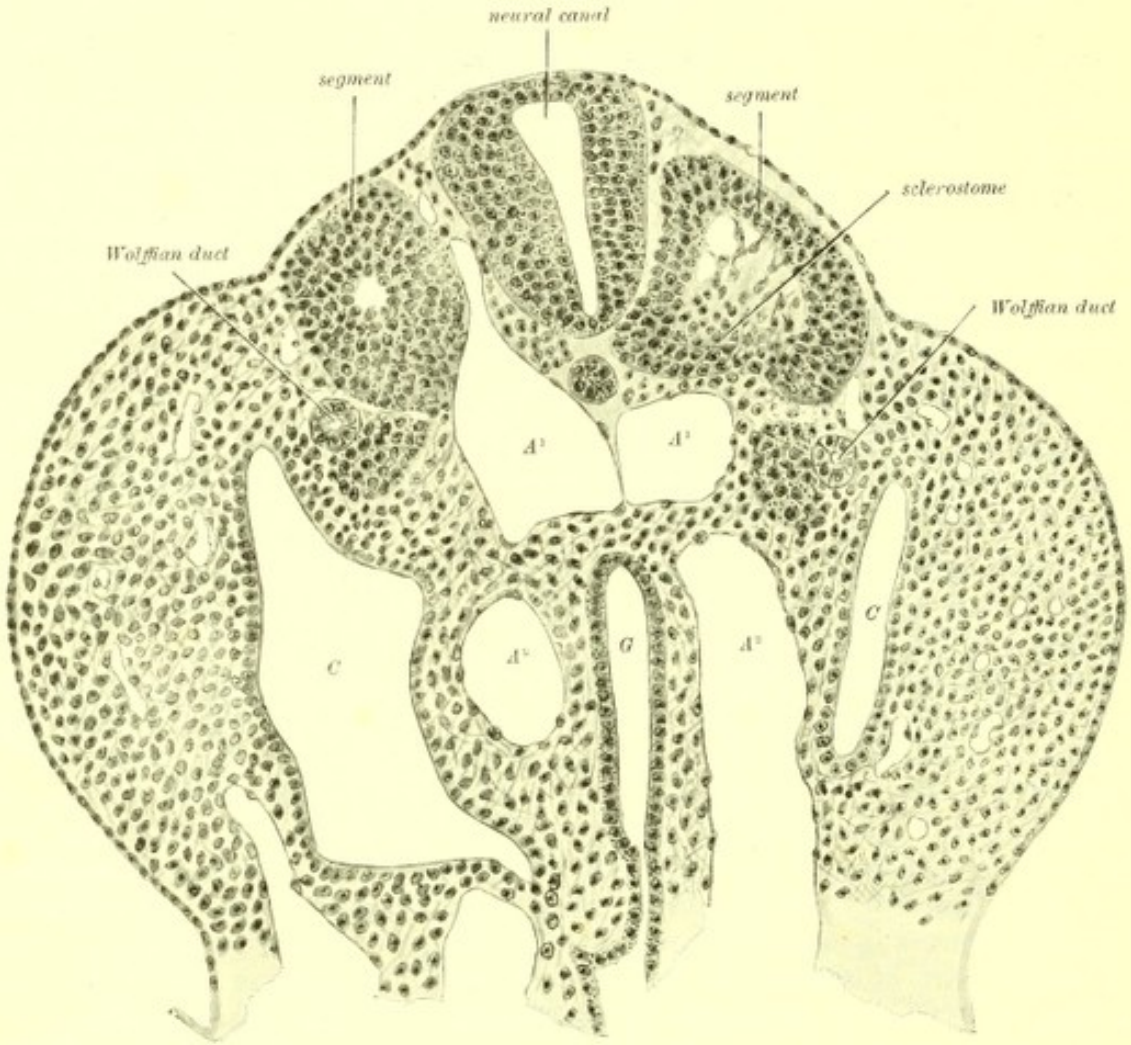



FIG. 223.—TRANSVERSE SECTION THROUGH THE TRUNK AND HIND-LIMB BUDS OF A RABBIT-EMBRYO OF THE TENTH DAY. (T. H. Bryce.) ON THE MESIAL ASPECT OF EACH WOLFFIAN DUCT THE NEPHROGENETIC CORD.

yet uncertain whether the ectoderm actually shares in the backward extension of the cellular cord, or whether the duct grows independently. An ectodermic origin would be explained in terms of Rückert's theory of the phylogeny of the duct—viz. that it is formed by a union of the outer ends of the nephridia which opened primitively on the surface.

**Mesonephros or Wolffian body.**—The mesonephros appears first as a ridge (*Wolffian ridge*) on each side of the attachment of the primitive mesentery, which extends from the fifth cervical to the fourth lumbar segment. It is formed by the enlargement of the intermediate cell-mass, as the tubules and their Malpighian corpuscles develop in its tissue. As the tubules increase in number the ridges

become prominent bodies, which increase in size until the eighth week, after which they gradually diminish owing to the fact that the tubules undergo degenerative changes. These degenerative changes commence at an early stage in the head end

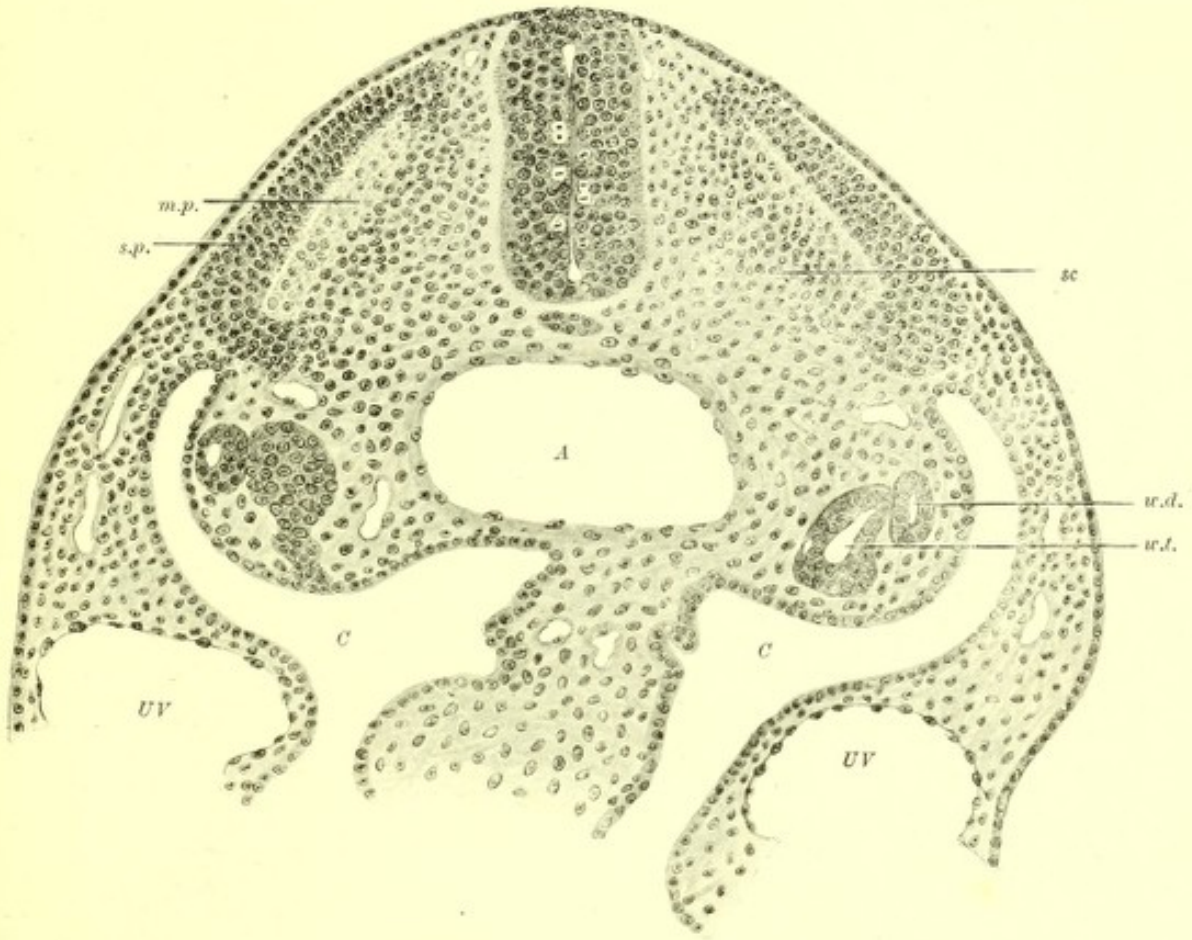



FIG. 224.—TRANSVERSE SECTION THROUGH THE TRUNK OF A RABBIT-EMBRYO OF THE ELEVENTH DAY (T. H. Bryce.)

*mc*, muscle-plate; *cp*, skin-plate of segment; *sc*, sclerotome; *w.d.*, Wolffian duct; *w.t.*, Wolffian tubule. The ridges in which the ducts and tubules lie are the Wolffian ridges. To the left the section has cut the wall of a Wolffian tubule where it is connected by a cellular cord with the cœlomic epithelium. *A*, aorta; *C*, cœlom; *U.V.*, *U.V.*, umbilical veins.

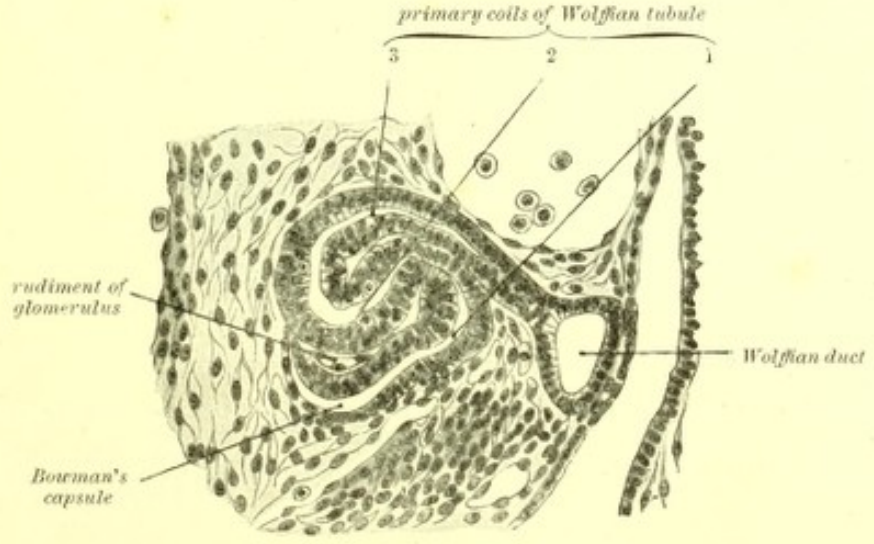



FIG. 225.—TRANSVERSE SECTION OF A WOLFFIAN TUBULE IN THE TWENTY-NINTH SEGMENT OF A RABBIT EMBRYO AT A LATER STAGE THAN THAT REPRESENTED IN FIG. 224. (After Schreiner.) × 195.

of the Wolffian body, and it is here reduced to a membranous fold which plays an important part in the formation of the primitive diaphragm, and behind that

FIG. 226.—SECTION OF THE WOLFFIAN BODY OF A HUMAN EMBRYO AT THE END OF THE FIFTH OR BEGINNING OF THE SIXTH WEEK. (T. H. Bryce.)

*gl*, *gl*, glomeruli; *w.d.*, Wolffian duct; *w.t.*, *w.t.*, Wolffian tubules; *gen.gl.*, genital gland.

structure forms the diaphragmatic fold of the Wolffian mesentery. By the fifth month the tubules have almost entirely disappeared, and in the end only persist as

accessory parts of the reproductive apparatus. The Wolffian duct lies external to the Wolffian body, enclosed in a fold of the peritoneum, which fuses posteriorly with that of the opposite side to form the genital cord (see below).

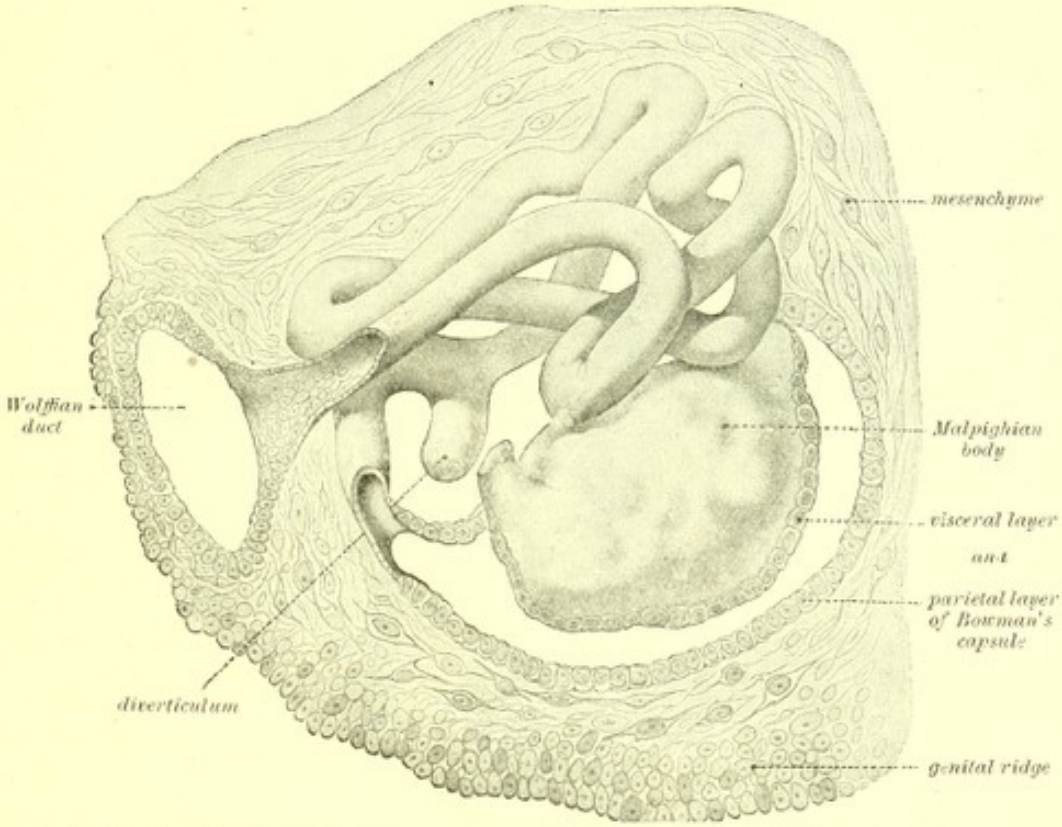



FIG. 227.—RECONSTRUCTION OF A WOLFFIAN TUBULE OF A HUMAN EMBRYO OF 10·2 MM. LONG. (From Kollmann.) × 260.

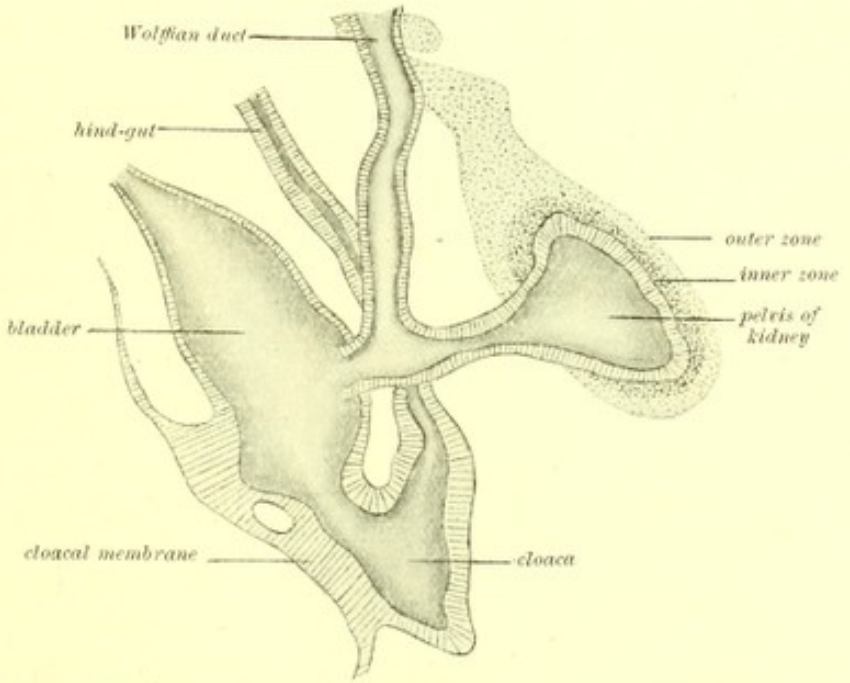



FIG. 228.—THE PRIMITIVE PELVIS OF THE KIDNEY, FROM A RECONSTRUCTION. (After Schreiner.)

The pelvis is surrounded by nephrogenetic tissue differentiated into an inner epithelial and outer mesenchymatous zone.

**Origin of the tubules.**—The intermediate cell-mass becomes differentiated (in the rabbit-embryo, fig. 223) into an inner part adjoining the segment, which has a mesenchymatous

and an outer part having more of an epithelioid character (*nephrogenetic cord*, Schreiner). This outer part forms a cord which becomes separated from the cœlomic epithelium, and secondarily segmented into a series of solid rounded bodies. These soon develop a lumen and form a series of small vesicles (fig. 224). There are several such in each segment in the rabbit, but it has been asserted (Kollmann) that the organisation is segmental in the human embryo in the early stages. In some cases it can be determined that the vesicle is connected with the cœlomic epithelium by a slender string of cells (fig. 224). From the outer and upper part of the wall a solid sprout, which is soon hollowed out to form a diverticulum of the vesicle grows against, and ultimately opens into, the Wolffian duct. This is the rudiment of the tubule proper, the original vesicle forming the Malpighian capsule. The tubule elongates and becomes S-shaped (fig. 225). Into the space between its proximal loop and the upper originally mesial wall of the now flattened, spoon-shaped vesicle, a branch grows in from the adjoining aorta. From this vessel a knot of capillaries is formed which lies in the hollow of the upper wall of the vesicle and becomes the glomerulus.

The connective-tissue framework of the Wolffian body is derived from the mesenchyme of the intermediate cell mass.

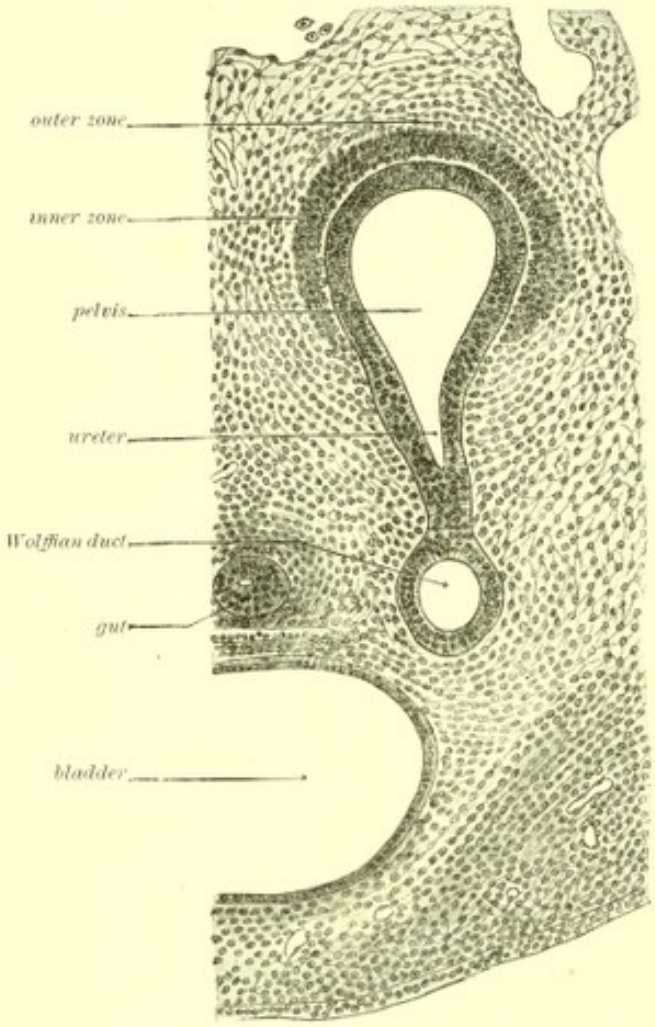



FIG. 229.—SECTION OF THE PRIMITIVE PELVIS OF THE KIDNEY OF A HUMAN EMBRYO OF FIVE WEEKS OLD. (After Schreiner.)

The inner zone of nephrogenetic tissue is sharply marked off; the outer zone passes gradually into the surrounding mesenchyme.

**Metanephros: permanent kidney.** — The metanephros arises from the posterior part of the same nephrogenetic cord as forms the blastema of the mesonephros.[1] The tissue, however, remains passive during the time when the tubules are forming in the Wolffian body, and becomes related to a diverticulum which grows out from the dorso-mesial aspect of the Wolffian duct immediately in front of its opening into the cloaca (fig. 228). As the diverticulum increases in length in a dorsal direction, the nephrogenetic tissue becomes displaced and separated from the Wolffian duct until it comes to lie dorsal and mesial to it. The diverticulum becomes expanded at its distal end to form the primitive pelvis of the kidney, while the stalk represents the future ureter. As the ureter elongates the kidney gradually changes its position relatively to the Wolffian body, until eventually it lies above and dorsal to it. The primitive pelvis is surrounded by the nephrogenetic tissue, which now shows a differentiation into an inner epithelioid and an outer mesenchymatous zone (fig. 229). The latter is continuous with the blastema of the mesonephros, but the former is quite separate

[1] This fact, first demonstrated for the chick by Sedgwick, has been substantiated for all the Amniota, including man, more especially by Schreiner, Zeitschr. f. wissen. Zool. lxxi. 1902. In a recent paper, Janošik (Arch. f. Anat. April 1907) has again thrown doubt on the ontogenetic fact, though he admits the general proposition that the kidney is merely a part of a primitive organ of which the Wolffian body is the anterior end.

from it. The primitive pelvis is at first simple, but soon becomes branched (fig. 235, p. 187) by the outgrowth from it of bulbous ampullæ, each of which

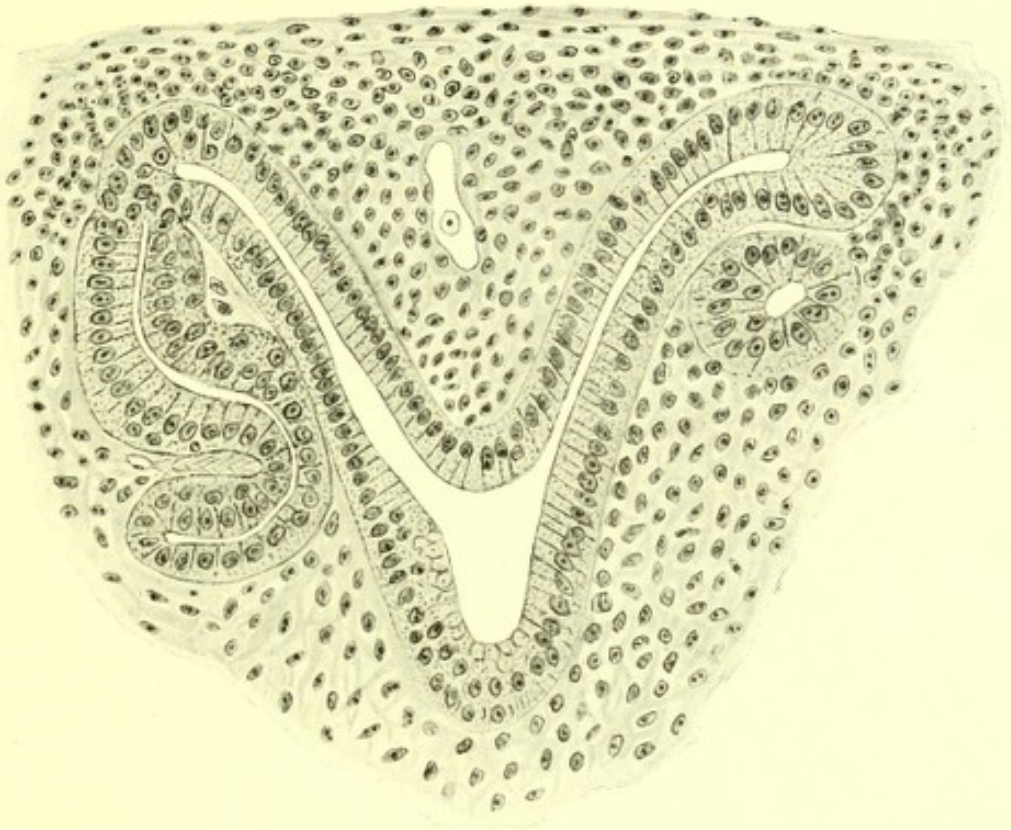


FIG. 230.—SECTION OF A PORTION OF THE COLLECTING TUBE AND TWO TUBULES IN THE DEVELOPING KIDNEY OF A RABBIT-EMBRYO. (T. H. Bryce.)

On the right the tubule is in the vesicular stage; on the left the vesicle has elongated, and is assuming the S shape, but it has not yet joined with the collecting tube.

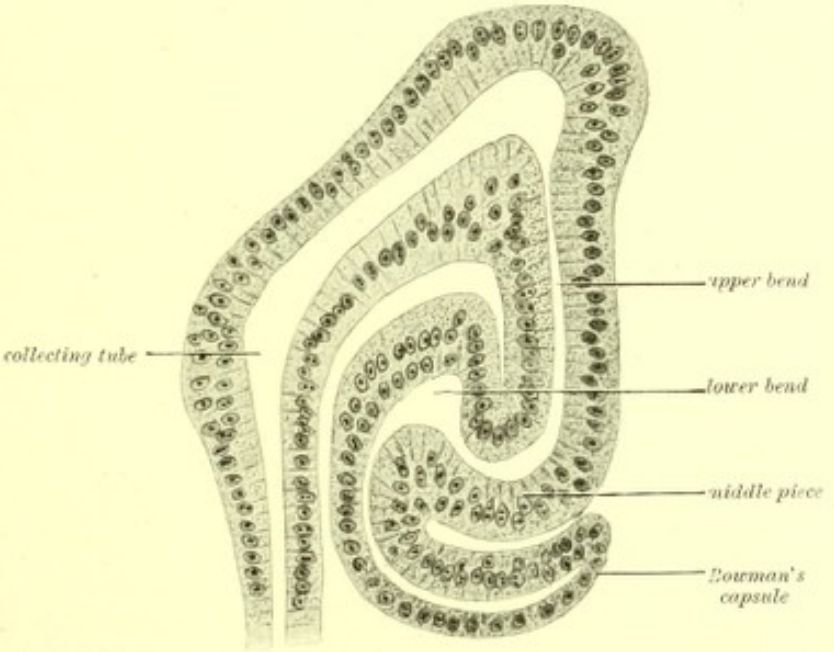



FIG. 231.—SECTION OF A DEVELOPING KIDNEY-TUBULE (RABBIT). (T. H. Bryce.)

is covered by a cap of the epithelioid inner zone, which has been broken up into separate masses during the process of branching. The collecting tubules are formed by a continuous process of dichotomous budding from the primary

branches of the pelvis. The secreting tubules, on the other hand, arise quite independently from the 'inner zone' of the nephrogenetic blastema, while the 'outer zone' provides the connective-tissue framework and capsule of the organ.

**Origin of the tubules.**[1]—At each division of the primary collecting tubules the 'inner zone' cap becomes divided into two. The peripheral part of each moiety becomes the new cap of the new branch; but the central portion of each becomes separated off as a detached oval and solid body which lies in the angle between the side branch and the main stem of the duct. This is the rudiment of the capsule of Bowman, and the further phases in the development of the tubule correspond exactly to those already described for the mesonephric tubules. A lumen appears in the solid rudiment (fig. 230), and from the upper extremity of the vesicle a diverticulum passes, which abuts against, and finally opens into the collecting duct. Briefly stated, the phases in the evolution of the vesicle are as follows. It first becomes comma-shaped by the thickening of its outer wall. The knee formed deepens into a cleft which separates the ventral part, the future capsule of Bowman, from the peripheral part, the future tubule. By a second fold, which appears in the upper part of the inner wall, the tubular portion becomes S-shaped, the one limb of the S opening from the capsule, the other ending in the collecting duct (fig. 230). The primitive capsule of Bowman, from the first hemispherical, becomes spoon-shaped by the upgrowth of its lips. Into the hollow thus produced the mesenchyme extends, and in it, either by formation *in situ*, as some think, or by ingrowth of a bud from a neighbouring blood-vessel, a glomerulus is formed. By a further great increase in length and coiling of the tubule round the Malpighian body as a more or less fixed point (Herring), the complicated adult tubule takes form. The central limb of the S becomes the first, the peripheral limb the second convoluted tubule, while the bend of the figure, lying at first in the hollow of the spoon, elongates to form the looped tubule of Henle (figs. 232, 233). As the primary branches of the ampullæ of the primitive pelvis continue to sprout and divide, it necessarily follows that the zone in which tubules are being produced is progressively displaced outwards, and thus a zone is laid down in which new tubes are formed during nearly the whole of fœtal life, only ceasing in the eighth month (Herring). As the kidney at an early stage is divided into primary lobules, corresponding to groups of branching primary collecting

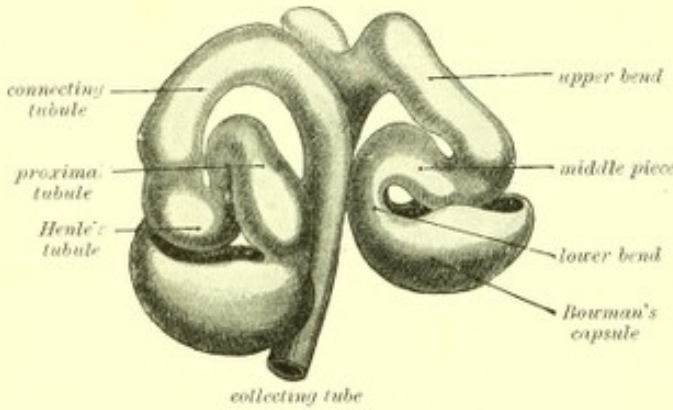



FIG. 232.—MODEL OF TWO DEVELOPING KIDNEY-TUBULES. (After Stoerk.)

On the right side the tubule is in the S-shaped stage: on the left side it is beginning to coil to form the different parts of the adult tubule.

[1] The account in the text is founded mainly on the descriptions and figures of Herring, Schreiner, and Carl Hüber, controlled by personal examination of rabbit-material. The view that the tubules have a double origin was originally advanced by Kupffer in 1865. It was substantiated by Sedgwick and adopted by Balfour. It has recently been confirmed by several observers, more especially the three named; but it should be stated that many authors have preferred the view of Remak (1855), which was maintained by Toldt and accepted by Kölliker, Waldeyer, Minot, and many others, to the effect that the tubules are in their entirety produced by budding from the original diverticulum. For references to the literature and for a history of opinion on this subject the reader is referred to Hüber's paper in the American Journal of Anatomy, vol. iv. 1905.

Janošik, in the paper referred to in the note to page 182, admits the discontinuous origin of the secreting tubules, but describes the phases of their development differently from any other observer. The process as he conceives it is one of great complexity and irregularity. The chief points are as follows: the primitive capsule and its primitive tubule connecting it with the collecting duct gives off blind processes, which may become permanent tubules when the capsule is separated from the duct, as it very early is. This separation may take place in various ways, so that the primitive capsule remains connected with the whole or part of its primitive tubule, or be isolated from it. The capsule now acquires a new connection with the collecting duct at a point nearer the cortex, either directly by some part of its own tubule, or indirectly through the medium of a different tubule. This may belong either to another capsule, in which case a double tubule results, or may be a tubule which has lost its original capsule. Further, the capsules are often double in early stages, due to a union or to a cleaving of the original rudiment. Henle's tubule cannot be recognised at an early stage as described in the text; apparently any loop may give rise to it.

tubules, the neogenic zone does not form merely a layer on the surface, but extends between the groups down to the pelvis as a series of septa, the '*primary columns of Bertin*' (Haugh). The primary collecting ducts are at first relatively far apart, but as the division progresses they come to be set at sharp angles to one another, until at last they form the straight tubules of the pyramids and medullary rays.

The **urinary bladder** is developed from the ventral portion of the cloaca entodermica, which, as we have already seen, becomes divided by a septum into rectum and urogenital sinus. The sinus and the allantois now form a tubular passage, on which a dilatation appears implicating the section derived from the cloaca, and perhaps also part of the allantois. This becomes the bladder, and the allantois is obliterated to form the urachus. When the division of the cloaca is effected

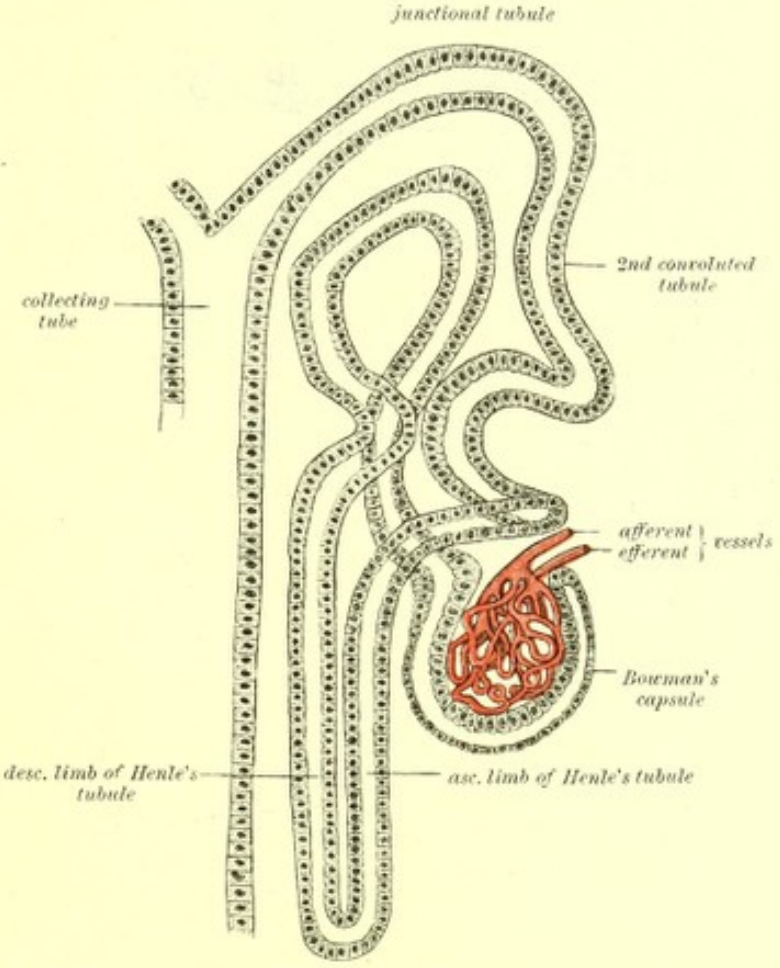



FIG. 233.—DIAGRAMMATIC SECTION OF A DEVELOPING KIDNEY-TUBULE AND GLOMERULUS. (T. H. Bryce.)

the Wolffian ducts come to open into the urogenital sinus. The openings are at first common to the ducts and the ureters, but soon they are caused to open separately by the lower ends of the Wolffian ducts being taken into the wall of the sinus. The portion of the sinus intervening between the pairs of openings then elongates, and the relations are so altered that the ureters open into the bladder dilatation, and the Wolffian ducts into the sinus proper. This ultimately forms the prostatic and membranous portions of the urethra in the male, and the whole urethra and the vestibulum vaginæ in the female. The Wolffian ducts at first open into the urogenital sinus close together, separated by an eminence in which the fused Müllerian ducts end (fig. 248, p. 196). In the male the eminence persists as the *crista urethralis*, which extends also along that section of the sinus which becomes elongated as the ureters and Wolffian ducts draw apart. When,

at a later stage of development, the bladder dilates and the ureters are drawn apart, the upper part of the crista is expanded into the *trigone* of the bladder.

## DEVELOPMENT OF THE GENITAL GLANDS AND DUCTS

The **genital glands** develop comparatively late, on the mesial aspects of the Wolffian bodies (figs. 226, 237). Here the cœlomic epithelium becomes thickened to form what is known as the *germinal epithelium* (Waldeyer). The cells become

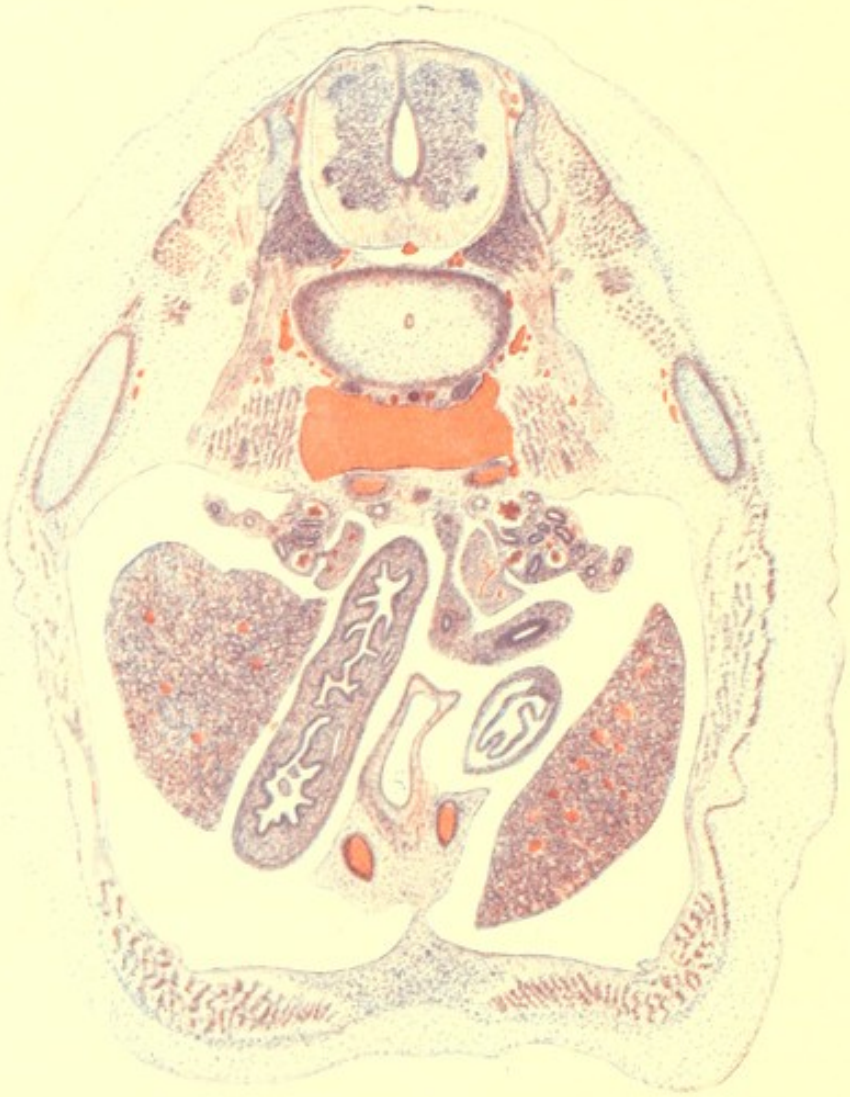


FIG. 234.—SECTION THROUGH A HUMAN EMBRYO OF 30 MM. ABOUT THE BEGINNING OF THE THIRD MONTH. (T. H. Bryce.)

On each side of the spinal cord are seen the cartilages of the neural arch; below the cord the body of the primitive vertebra with the notochord passing through it; between the two are the spinal ganglia, from which extend downwards the spinal nerves. Below the vertebra the cardinal veins are united by a large anastomosis; below this the two common iliac arteries. Between the iliac arteries the mesentery leaves the posterior abdominal wall; on each side of this the ureters. External to the ureters, the Wolffian bodies. On the mesial aspect of each is seen the genital gland connected by its mesentery; on the outer aspect of each, the Wolffian mesentery containing, to the inner side the Wolffian, to the outer side the Müllerian duct. Projecting into the abdominal cavity from below, the allantoic duct attached by a mesentery, in which the two allantoic arteries run. The intestine is cut in several places, and on each side are seen the lateral lobes of the liver.

columnar and arranged in several layers, while the underlying mesenchyme becomes somewhat thickened along a projecting ridge, the *genital ridge*. The germinal epithelium by proliferation of its cells increases in depth, and among the proper epithelial elements certain larger and more spherical cells appear (fig. 226,

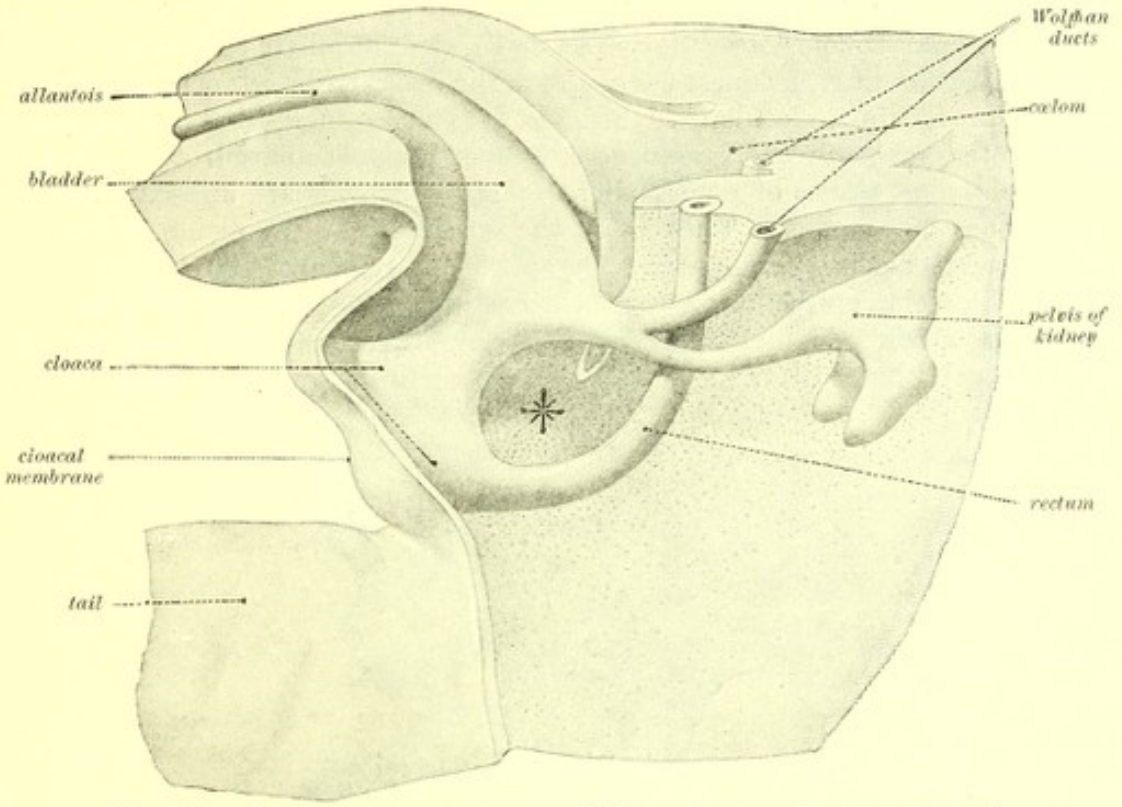



FIG. 235.—PELVIS; HUMAN EMBRYO OF 11·5 MM. (FOUR AND A-HALF WEEKS).
(After Keibel, from Kollmann's Entwickelungsgeschichte.)
* septum uro-rectale.

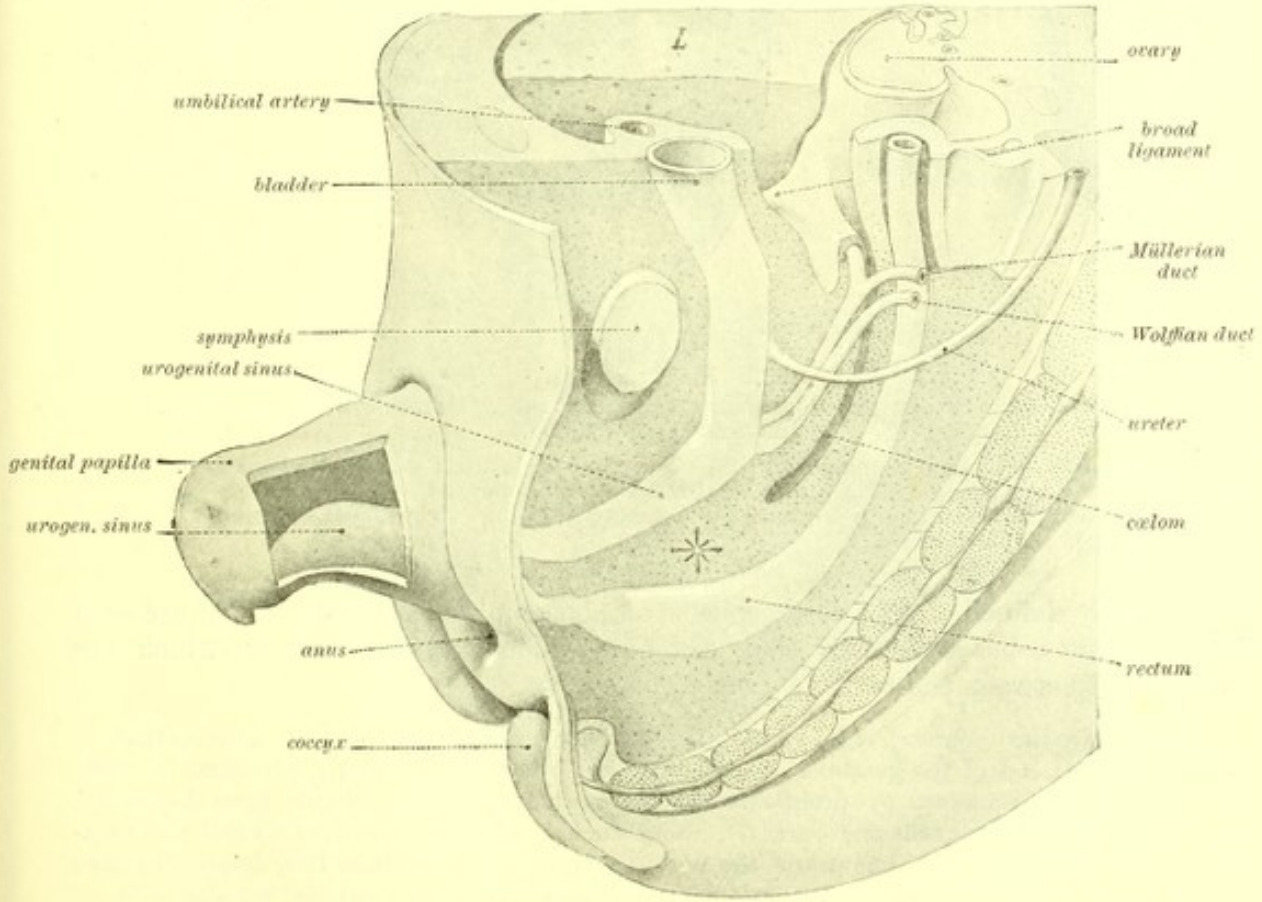



FIG. 236.—PELVIS; HUMAN EMBRYO OF 25 MM. (EIGHT AND A-HALF TO NINE WEEKS OLD).
(After Keibel, from Kollmann's Entwickelungsgeschichte.)
L, liver; *septum uro-rectale.

p. 180). These are the *primitive sex-cells*, and, as far as any evidence yet available permits conclusions, they arise from the germinal epithelium *in situ*. It is, notwithstanding, a question of great theoretical importance, which must be left to the future to decide, whether the sex-cells actually do so arise *in situ*, or whether they are only segregated here, having been set apart from the somatic cells at the earliest stages of development. Large sex-cells are already present in or under the peritoneum at the root of the mesentery in the region of the first five trunk segments in a human embryo of 4·9 mm. (Ingalls, 1907).

The proliferating epithelium now grows inwards to form strands of cells known as the *genital cords*. At first there is a very small amount of connective tissue between them, but this soon increases in amount, and the cords become

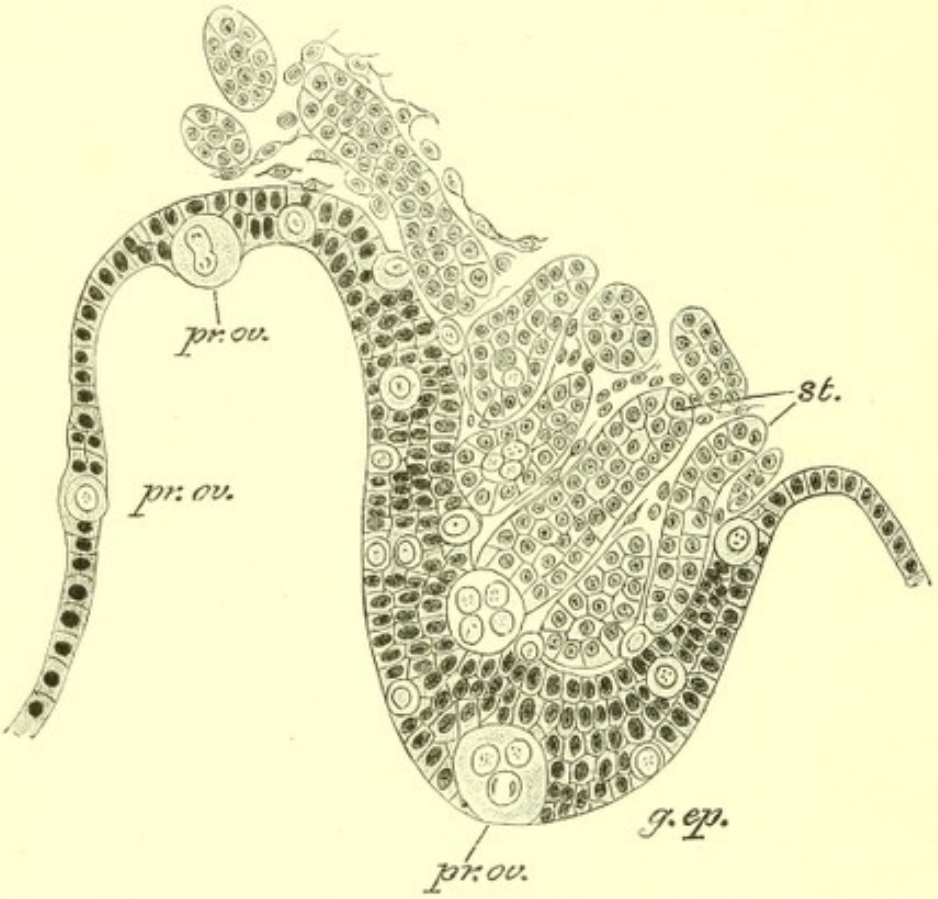



FIG. 237.—SECTION OF THE GERMINAL EPITHELIUM AND ADJACENT STROMA IN A MALE CHICK-EMBRYO. (Semon.)

*g.ep.*, germinal epithelium forming a thickened ridge-like projection; *pr.ov.*, primitive ova of various sizes, some in the germinal epithelium and others somewhat beyond the limit of this epithelium; *st.*, strands of cells which have grown from the germinal epithelium, and one of which appears connected with an enlarged primitive ovum.

more clearly defined. The cords consist of epithelial cells, among which are seen primitive sex-cells, and, it is said, elements which have characters which are transitional between the two.

According to the researches of Coert and Allen on embryos of the pig and rabbit, the epithelium over the cranial end of the genital ridge is lower than the true germinal epithelium, but here again strands are produced by proliferation which are easily distinguishable from the genital strands by their smaller cells and darker-staining nuclei. These extend inwards and also backwards between the gland-rudiment and the Wolffian body, and when later they acquire a lumen become the rete tubules (see below).

After the gland has reached this stage specialisation begins in the hitherto indifferent rudiment, and it acquires the distinctive characters of ovary or testis.

As the glands take form they become separated from the Wolffian body, remaining attached to it only by a stalk or mesentery—the *mesovarium* or *mesorchium*, as the case may be.

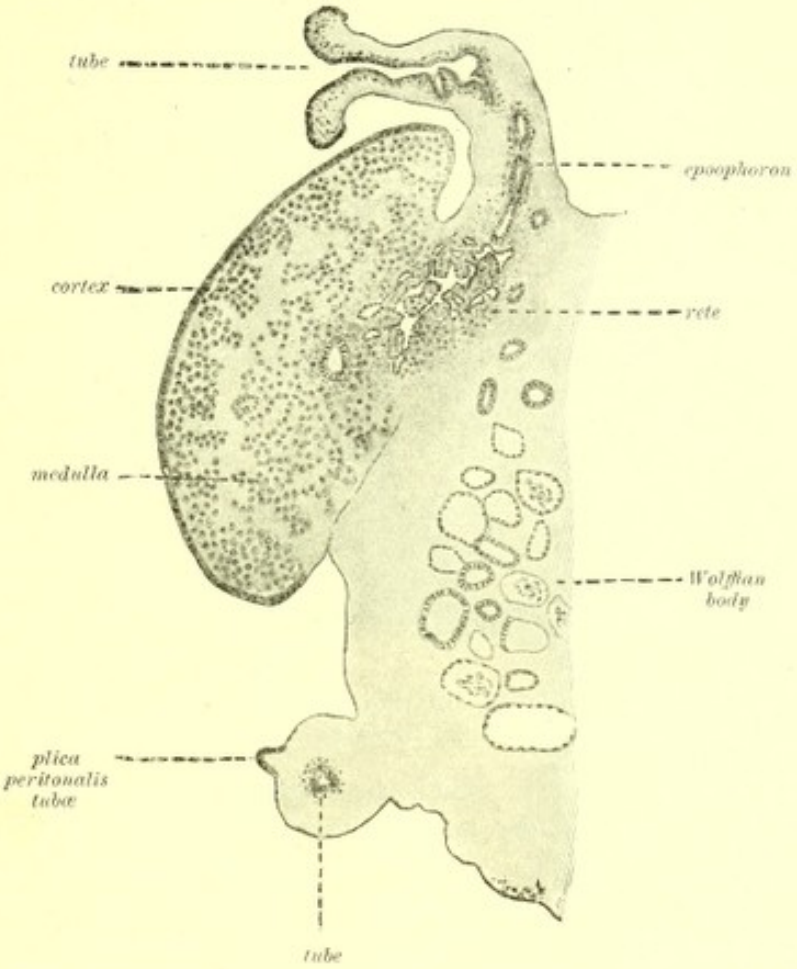



FIG. 238.—LONGITUDINAL SECTION THROUGH THE OVARY OF A CAT-EMBRYO OF 9·4 CM. LONG (SCHEMATIC). (After Coert, from Hertwig's Handbuch der Entwickelungslehre.)

FIG. 239.—SECTION OF THE OVARY OF A HUMAN FŒTUS OF THE FOURTH MONTH.

The **ovary** retains longer the primitive characters, in respect that the germinal epithelium remains many-layered, and retains its proliferative activity. The future history of the gland is explained by the fact that the mesenchyme grows

outwards into the germinal epithelium, while the epithelial strands grow inwards, so that we have an interlocking of epithelial and connective tissues. In the early

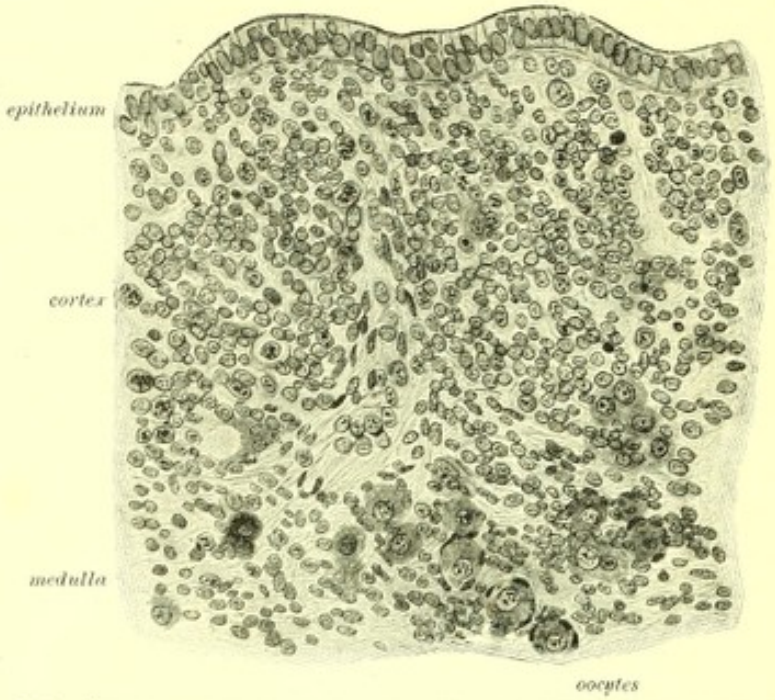



FIG. 240.—SECTION OF THE OVARY OF A HUMAN FŒTUS OF THE SEVENTH MONTH.
(Figs. 239 and 240 from Felix and Bühler, Hertwig's Handbuch der Entwickelungslehre.)

stages, a narrower *cortical zone*, in which the epithelial strands are closely pressed together and separated by a very small amount of connective tissue, is distinguished from a central *medullary zone* in which, owing to the increase in the vascular stroma, the primary genital cords are more definitely marked off from one another (fig. 239). This medullary portion of the parenchyma is gradually reduced as the cortical zone increases in thickness, and the medullary cords are reduced to a few epithelial strands, in which ova are no longer to be seen. The body of the ovary is formed from the cortical zone. The epithelial columns (egg-tubes of Pflüger) become separated, then cut up, by the growth of the stroma, into cell-islands containing one or more primitive ova; these again into smaller groups or nests of cells, until ultimately the primitive follicles are isolated, each containing a single ovum surrounded by a layer of follicular cells (fig. 241). From these the Graafian follicles are formed. This process, by which the stratum germinativum of the ovary is formed, goes

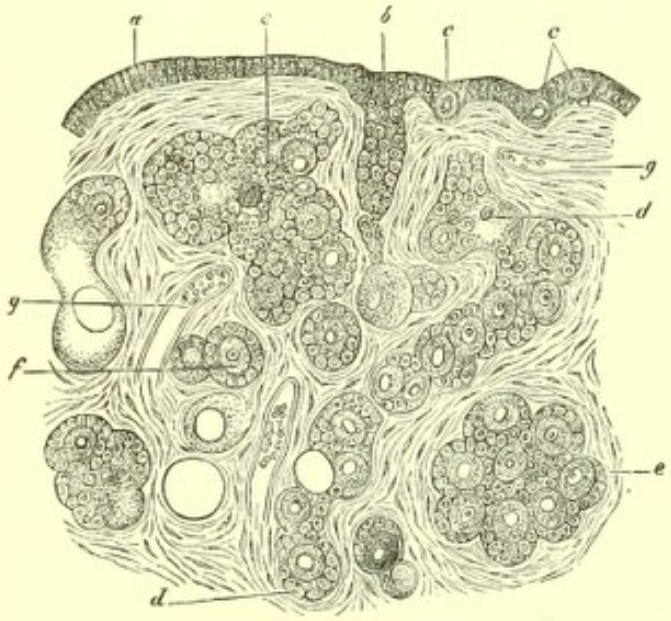



FIG. 241.—SECTION OF THE OVARY OF A NEWLY BORN CHILD. (Waldeyer.) Highly magnified.

*a*, Germinal epithelium dipping in at *b*, to form an ovarian tube; *c*, *c*, primordial ova lying in the germ-epithelium; *d*, *d*, longer tube becoming constricted so as to form nests of cells; *e*, *e*, larger nests; *f*, distinctly formed follicle with ovum and epithelium; *g*, *g*, blood vessels.

on during all the later months of fœtal life, but is completed by the time of birth or shortly after.

According to the important researches of Winiwarter,[1] the germinal epithelium comprises two layers of cells with nuclei of distinctive characters. In the superficial layer, the nuclei stain deeply as a whole, but the nuclear network is very delicate, and the nuclear membrane is indistinct; in the deeper layer the nuclei are smaller, but the network is coarser, with distinct karyosomes, and the nuclear membrane is an obvious feature. There is no true nucleolus in either variety of nucleus. Winiwarter names them '*noyaux protobroques a and b*.' In the epithelial masses invading the stroma, cells with 'noyaux protobroques b' are seen in active division, but there is also a third variety of cell with a large clear nucleus and distinct nucleolus (*noyau deutobroque*). These cells no longer divide, and are the young oocytes. In the nuclear division preceding the appearance of these cells the prophase of the heterotypical division has been initiated by the synapsis, in which the chromatin-loops fuse in pairs (see p. 17). The cells with 'noyaux protobroques b' become the follicular cells. As these gather round the oocytes they become arranged in a continuous low columnar epithelium. The cells, however, multiply, and form, soon, a many-layered investment to the oocyte. The *liquor folliculi* next gathers among the cells, and separates a mass surrounding the ovum and attached to the wall of the follicle named the discus proligerus (*cumulus oophorus*), from the cells lining the follicle or *stratum granulosum*. Outside this epithelial layer the connective tissue becomes condensed round the ovum into the *theca folliculi*, which shows two layers, an external (theca externa) more fibrous, and an internal (theca interna) more cellular. The cells in the theca interna are rounded or polygonal elements of some size, which exactly resemble the *interstitial cells* scattered in the ovarian stroma. These interstitial cells are generally regarded as being derived from the mesenchyme, but Miss Lane-Clayton[2] has supplied evidence which seems to show that they may be derived like the follicular cells from the germinal epithelium. The cells of the corpus luteum[3] are considered by some as arising from the stratum granulosum, by others from the cells of the theca interna.

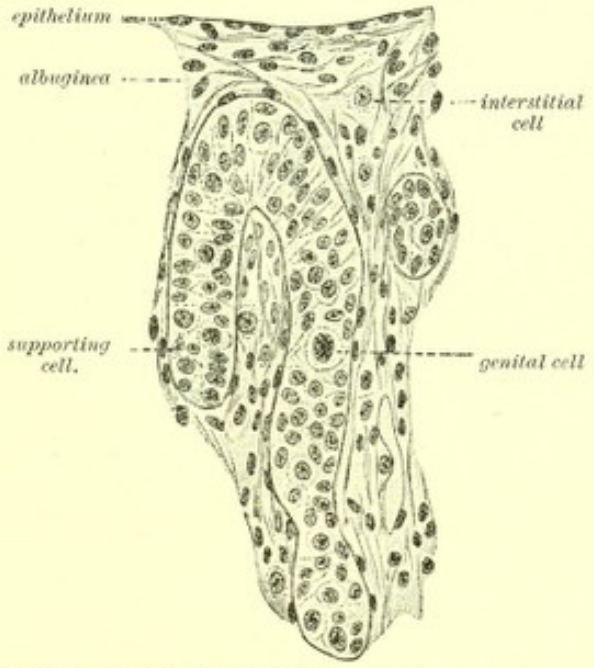



FIG. 242.—SECTION OF ONE OF THE GENITAL CORDS OF THE TESTICLE OF A HUMAN EMBRYO OF 3·5 CM. LONG. (Felix and Bühler.)

The tubules which have been observed by various authors near the hilum of the gland, and named the *rete tubules* because they are regarded as being homologous with the tubules of the rete testis, have been generally regarded as derivatives of Wolffian tubules, but according to the results of Coert and Allen, referred to above, they arise like the primary genital cords from the cœlomic epithelium.

The **testicle** is early distinguished from the ovary by the reduction that takes place in the germinal epithelium, which becomes marked off from the parenchyma of the gland by a layer of connective tissue, the future *tunica albuginea*. The genital cords of the primitive gland become the *seminal tubules*. These, which of course are at first solid, consist of smaller cells probably representing the cells of the germinal epithelium, and larger rounded sex-cells. The tubules acquire a lumen quite late in their history, and increasing in length become coiled (fig. 242). The larger rounder cells multiply, and ultimately line the greater part of the wall of

[1] Archives de Biologie, 1900.
[2] Journ. of Phys. xxxii. 1905, and Journ. of Obstet. and Gynec. xi. 1907.
[3] See 'Ovary' in volume on Splanchnology.

the tubule as *spermatogonia*. The tubules of the *rete testis* have long been regarded as probably derivatives of the Wolffian tubules, but recent work, more especially of Coert and Allen, points to their origin, as indicated above, from the cœlomic epithelium as epithelial cords which afterwards acquire a lumen. They become joined with the seminal tubules, and, growing towards the Wolffian body, they open into the capsules of Bowman of some of the anterior Wolffian tubules.

The interstitial cells of the testis are, like the corresponding cells of the ovary, generally regarded as connective-tissue elements, but some observers describe them as arising from the germinal epithelium.

**Genital ducts.**—The fate of the Wolffian body and Wolffian duct differs in the sexes. In the *male* the duct persists as the *canal of the epididymis*, the *vas deferens*, and *ejaculatory duct*; the *seminal vesicle* is formed as a diverticulum

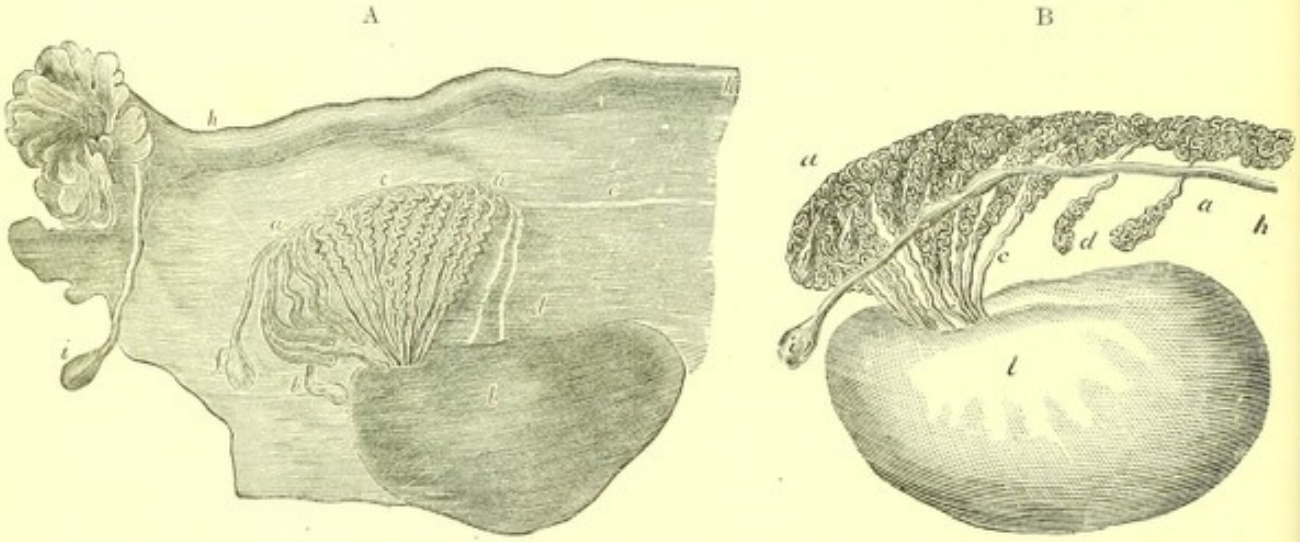



FIG. 243.—TWO FIGURES EXHIBITING A COMPARISON BETWEEN PARTS OF THE GENERATIVE ORGANS IN THE TWO SEXES. (From Farre, after Kobelt).

A. ADULT OVARY, PAROVARIUM, AND FALLOPIAN TUBE.

*a*, *a*, Epoophoron (parovarium) formed from the upper part of the Wolffian body; *b*, remains of the uppermost tubes, sometimes forming hydatids; *c*, middle set of tubes: *d*, some lower atrophied tubes; *e*, atrophied remains of the Wolffian duct; *f*, the terminal bulb or hydatid; *h*, the Fallopian tube, originally the duct of Müller; *i*, hydatid attached to the extremity; *l*, the ovary.

B. THE ADULT TESTIS AND EPIDIDYMIS.

*a*, *a*, convoluted tubes in the head of the epididymis developed from the upper part of the Wolffian body; *b* and *f*, hydatids in the head of the epididymis; *c*, coni vasculosi; *d*, vasa aberrantia; *h*, remains of the duct of Müller with *i*, the hydatid of Morgagni, at its upper end; *l*, body of the testis.

from its lower end. Certain of the anterior tubules which have been joined by the rete tubules remain as the *coni vasculosi* and *vasa efferentia* (fig. 243, B).

The organ of Giraldès or *paradidymis* represents some tubules which have lost their connexion with the duct, and the *vasa aberrantia* others which have not been connected with the rete tubules or have secondarily lost their connexion with them. The head end of the duct is said to persist as a stalked hydatid, and certain peritoneal tubules which have been described are supposed to represent the remains of nephrostomes.

In the *female* (fig. 243, A) the head end of the Wolffian body, which undergoes still greater reduction than in the male, persists as the rudimentary organ known as the parovarium. This consists of the head end of the duct and a number of tubules, which lie in the mesosalpynx (*epoophoron*), and some remains of tubules in the

broad ligament (*paroophoron*). The greater part of the duct disappears, but remnants of it are occasionally to be seen in sections across the body or cervix

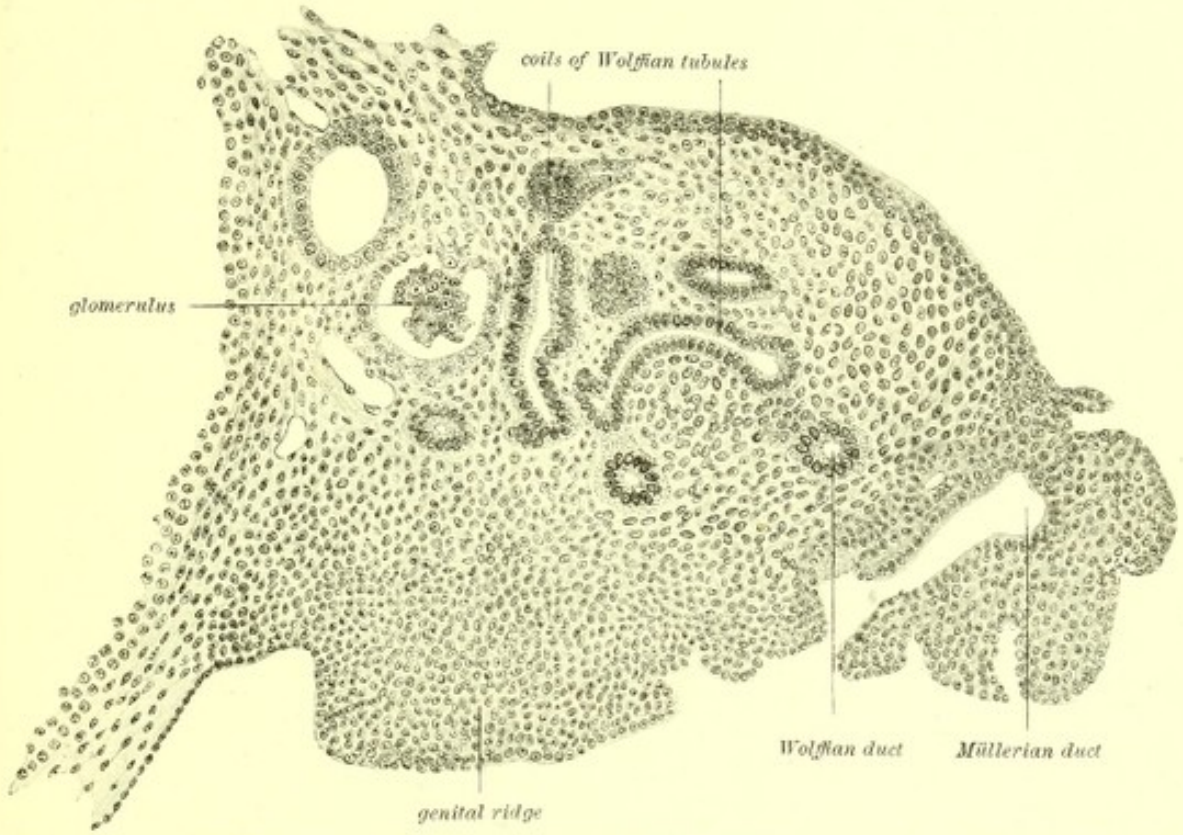



FIG. 244.—TRANSVERSE SECTION OF THE HEAD-END OF THE WOLFFIAN BODY OF A HUMAN EMBRYO AT THE END OF THE FIFTH OR BEGINNING OF THE SIXTH WEEK, SHOWING THE PERITONEAL OPENING OF THE MÜLLERIAN DUCT. (T. H. Bryce.)

of the uterus, or even lying in the vaginal wall. It persists as the *duct of Gärtner* in some mammals—*e.g.* the pig.

The **Müllerian duct** arises on the lateral aspect of the Wolffian body, and near its anterior end, as a thickening of the cœlomic epithelium. This soon shows a longitudinal depression, which, deepening at its posterior end, becomes converted into a funnel-shaped depression. From the caudal end of this the duct grows backwards in close relation to the Wolffian duct. In embryos about the middle of the second month the two ducts lie in a free fold projecting from the outer side of the Wolffian body, the Müllerian duct being to the outer side (fig. 234). Behind the Wolffian body this fold, merging with the Wolffian mesentery, passes on to the lateral wall of the contracted part of the cœlomic cavity which will form the pelvis (fig. 246). Here the folds from opposite sides meet in the middle line; the four ducts are thus brought close together, and are imbedded in a mass of tissue called the *genital cord* (figs. 245, 247). The Müllerian ducts, as they pass into the genital cord, cross over the Wolffian ducts, and come to lie close together between them. Within the cord the epithelial tubes fuse, but behind,

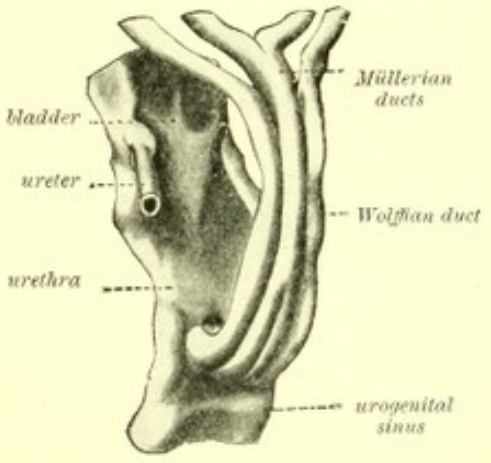



FIG. 245.—UROGENITAL SINUS, BLADDER, AND GENITAL DUCTS OF A FEMALE HUMAN EMBRYO OF 29 MM. (After Keibel.)

the lumina remain separate for a time, and the fused walls terminate in an epithelial thickening which projects into the urogenital sinus between the openings of the Wolffian ducts (*Müllerian eminence*) (fig. 248). Here, but at a much later date, the opening into the sinus is effected. The thickening in which the ducts end is produced by proliferation of the epithelial cells at their terminal growing points, the so-called *vaginal bulbs*. The future history of the ducts differs in the sexes. In the *male* they disappear throughout almost their whole length, but the head end is believed to persist as the *hydatid of Morgagni*, while their fused posterior ends remain as the prostatic utricle (*uterus masculinus*).

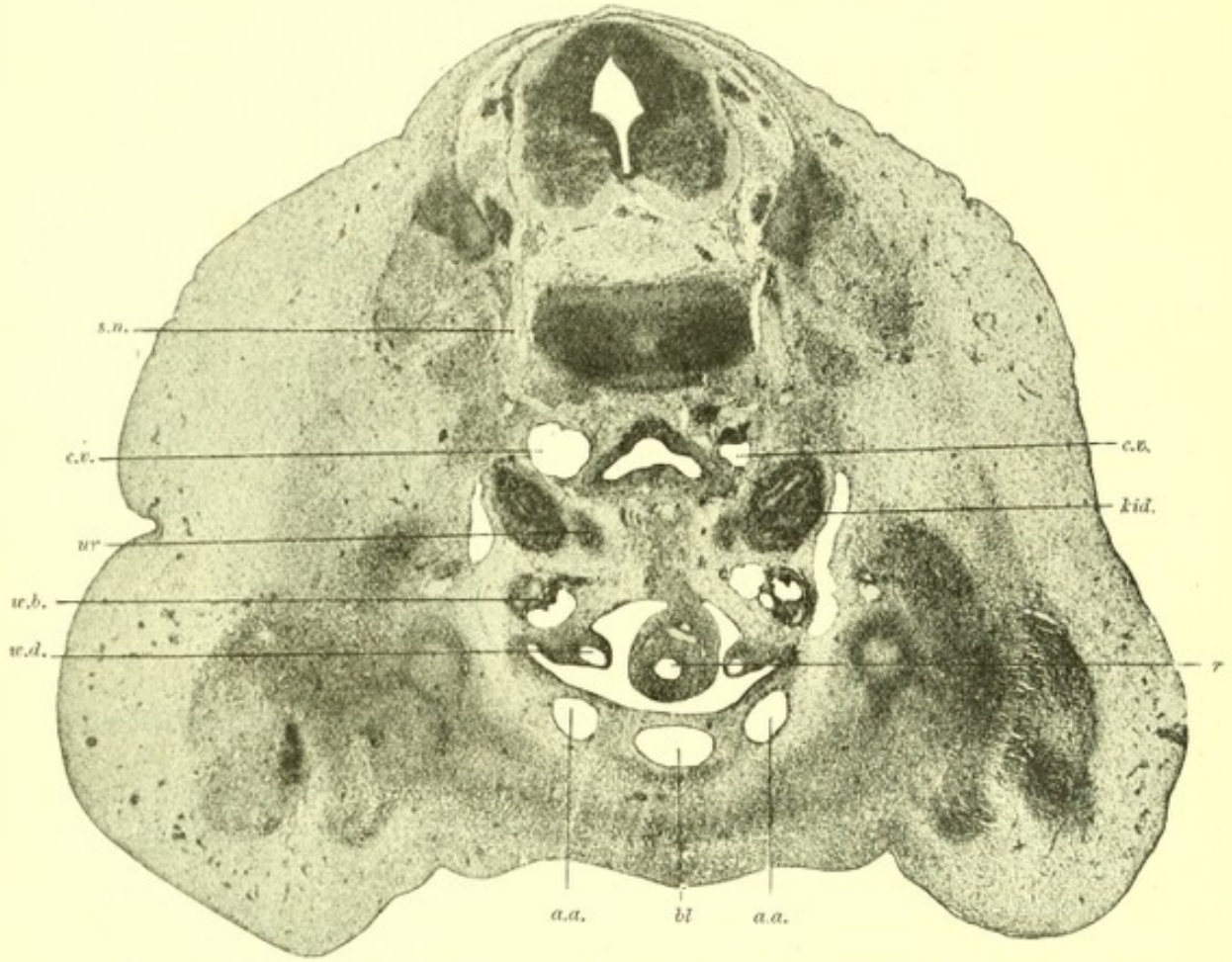



FIG. 246.—SECTION THROUGH THE TRUNK OF A HUMAN EMBRYO OF 15·5 MM. AT THE LEVEL OF THE HIND-LIMBS. (T. H. Bryce.) Photograph.

*s.n.*, spinal nerve; *c.v.*, *c.v.*, cardinal veins (between them the aorta giving off the allantoic arteries); *kid*, kidney; *ur*, ureter; *w.b.*, Wolffian body; *w.d.*, Wolffian duct in Wolffian mesentery; *r*, rectum; *bl*, bladder; *a.a.*, *a.a.*, allantoic arteries.

The glandular tissue of the **prostate** is developed as a series of epithelial sprouts from the urogenital sinus, which appear in the fourth month, proximal and distal to the opening of the Wolffian ducts. These acquire a lumen and form the parenchyma of the gland, the muscular and connective tissue being derived from the mesenchyme of the genital cord. Similar sprouts form the so-called Skene's tubules of the female urethra.

In the *female* the ducts persist, and their upper independent portions become the Fallopian tubes, while their fused posterior portions form the foundation of the uterus and vagina. The fusion begins near the lower end (fig. 245), and proceeds both downwards towards the future orifice and upwards for a certain length. The extent to which the Müllerian ducts are fused varies in different

animals, and certain malformations of the genital tract which occur in the human subject, involving a greater or lesser degree of duplicity of the tract, are explained by defective fusion of the ducts. Meanwhile the urogenital sinus shortens, the vaginal bulbs elongate, and the Müllerian eminence is brought close to the surface. It follows that when the opening out of the fused solid ends of the ducts takes place the orifice is superficial, and the urogenital sinus is only represented by the vestibule of the vagina.

For a considerable period the vagina is solid. Opinions differ as to the origin of this condition. According to one view (Nagel) it is primary, the vagina being formed from the

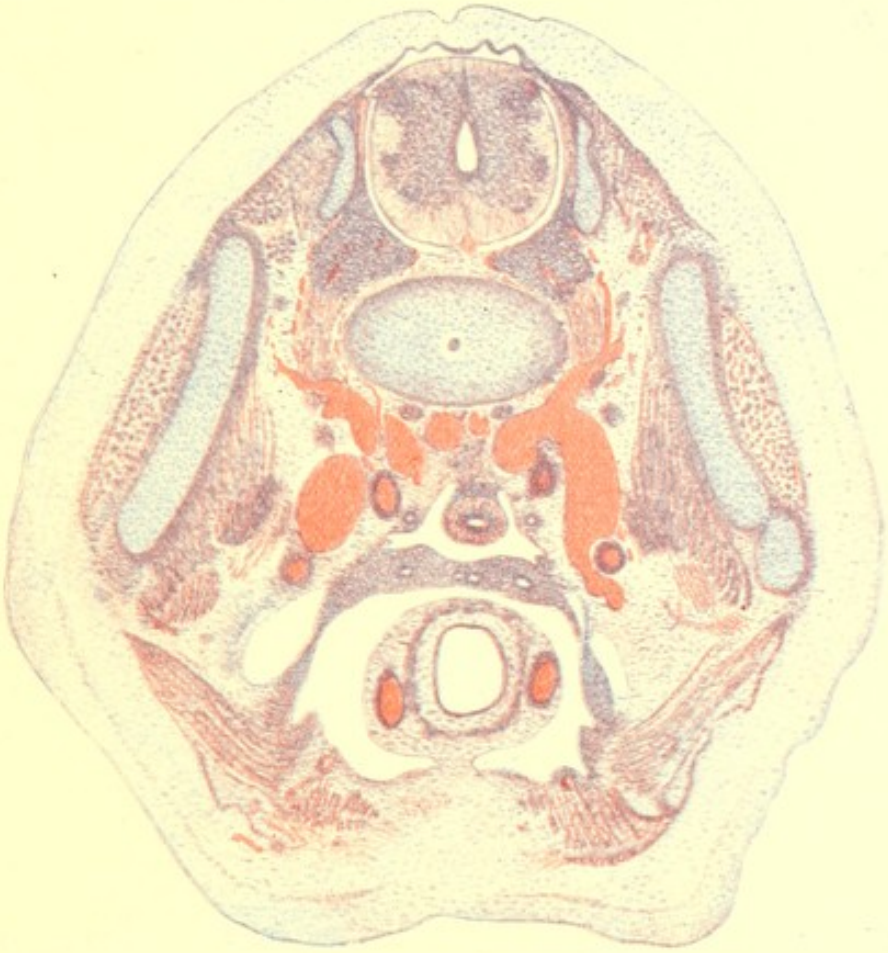


FIG. 247.—SECTION THROUGH A HUMAN EMBRYO OF 30 MM. ABOUT THE BEGINNING OF THE THIRD MONTH. (T. H. Bryce.)

Below the spinal cord is seen the body of a vertebra with the notochord, and on each side of the cord the neural arch; between them a pair of spinal ganglia. The large cartilages on each side are the ilia. The peritoneal cavity is bridged over by the genital cord formed by the fusion of the Wolffian mesenteries; in the cord are seen the two Müllerian ducts about to fuse, and externally the Wolffian ducts. Above the genital cord is the rectum; in the wall of the pelvis, one on either side, the ureters; below the cord the bladder and allantoic arteries. On each side of this the peritoneal cavity is interrupted by a fold, the plica gubernatrix extending from the Wolffian mesentery to the inguinal region. Notice how at the inguinal attachment of these folds the muscular tissue of the abdominal wall extends into the gubernaculum.

elongated epithelial mass in which the Müllerian ducts end. According to Berry Hart and F. Wood-Jones, who adopt a very similar explanation, two separate epithelial cords are formed, which fuse to give rise to the solid vagina. According to another view, the condition is secondary, and is due to the temporary fusion of the epithelial walls. The cavity is produced or restored by the shedding of the central cells after the fourth month. Opinions also differ as to the origin of the **hymen.** According to the most generally accepted view, it represents the remains of the margins of the opening of the thickened ends of the fused ducts into the urogenital sinus. Berry Hart, and also recently Kempe, have, however, derived it from the epithelium in which the genital ducts end.

The epithelial lining of the Müllerian ducts gives rise merely to the epithelium of the genital tracts. The muscular and connective-tissue elements of the mucous membrane, and of the wall of the uterus and vagina, are derived from the genital cord, which undergoes a progressive development as compared with that of the male. The lower part surrounding the ends of the ducts grows downwards, and apparently in the process occasions the shortening of the urogenital sinus already referred to. By the fifth month the muscular wall of the uterus begins to differentiate, and the mucous membrane to thicken. It is noticeable that during the later months of fœtal life the cervix bears a very large proportion to the body (fig. 249), which is very short, and it is not till puberty that the body begins to assume its proper relative proportions.

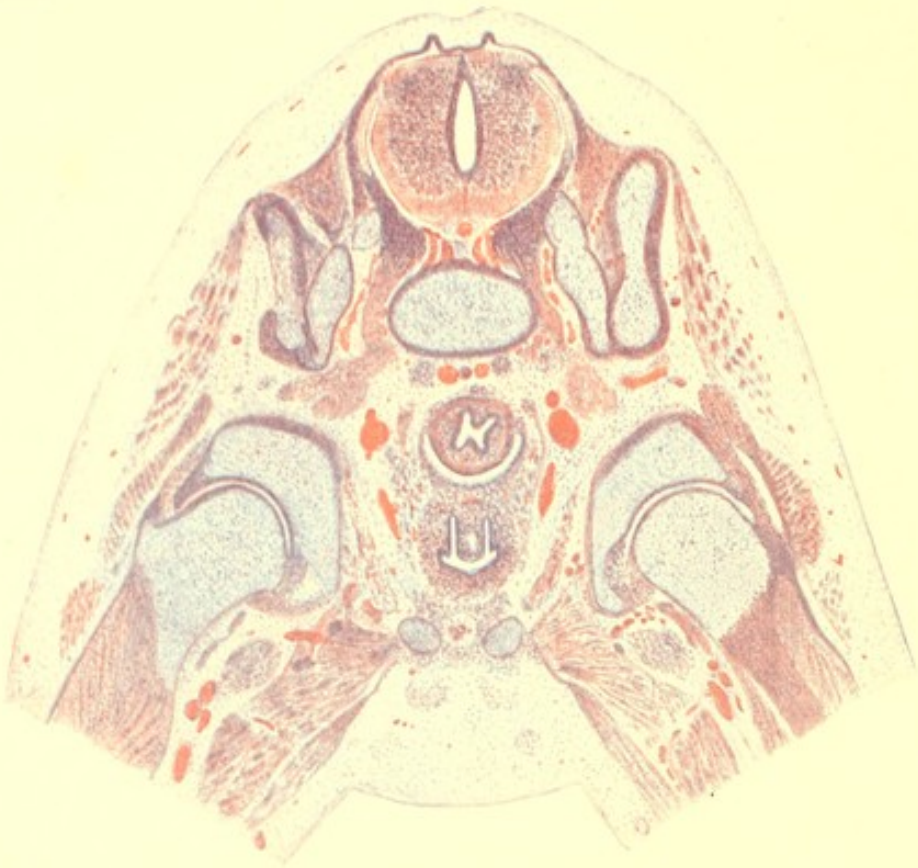


FIG. 248.—SECTION THROUGH A HUMAN EMBRYO OF 30 MM. ABOUT THE BEGINNING OF THE THIRD MONTH. (T. H. Bryce.)

Below the spinal cord is seen the body of a sacral vertebra; on each side the lateral part of the sacrum and a portion of the ilium; between the body and the lateral cartilages a pair of spinal nerves. The section passes through the hip-joints; between these ventrally the pubic cartilages. Between the two ischial cartilages the rectum, below this the urogenital sinus with the Wolffian ducts opening into it; between the Wolffian ducts the Müllerian eminence, in which is seen the irregular blind end of the fused Müllerian ducts; between the pubic cartilages the urethra.

**Descent of the ovaries and testes.**—In both sexes the genital glands undergo a displacement from their primitive position in the lumbar region and come to lie above the brim of the pelvis. From this situation in the later months of pregnancy the testicles descend into the scrotum, while the ovaries retain their secondary position until ultimately, with the enlargement of the pelvis, they sink to the definitive position. The descent of the glands is chiefly effected by the agency of a fold, in which muscular fibres develop, called the *plica gubernatrix* (fig. 247).

The change in position of the different structures is best understood by referring back to a stage reached about the end of the second month (fig. 251). The Wolffian body, on each side, is seen to be attached to the posterior abdominal wall by the

Wolffian mesente y, which is continued upwards as a fold to the diaphragm. The genital gland is fixed to its inner aspect by the *genital mesentery*, and the two ducts to its outer side by the *urogenital fold* (fig. 234). The latter merges with the Wolffian mesentery behind the Wolffian body to form the urogenital mesentery, and this in turn unites with its fellow to form the *genital cord* (fig. 247). The genital mesentery is continued upwards as the *upper*, and downwards as the *lower genital fold*. The latter joins, at the lower end of the

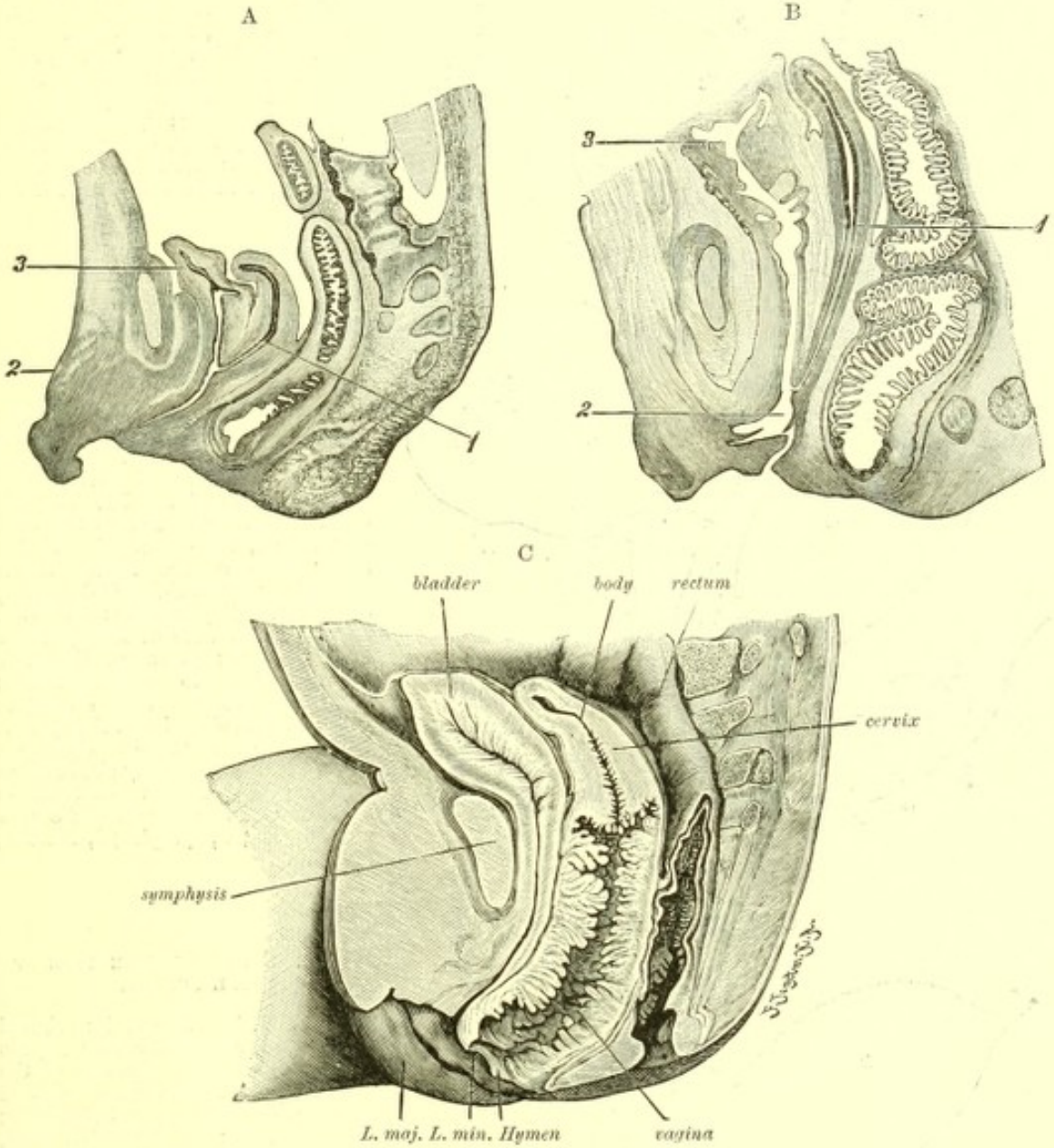



FIG. 249.—VERTICAL LONGITUDINAL SECTION OF THE PELVIS: A, OF A FŒTUS OF 6 CM.; B, OF A FŒTUS OF 10 CM.; C, OF A FŒTUS OF THE SEVENTH MONTH. (From Nagel.)

In A and B: 1, Junction of vagina and uterus; 2, sinus urogenitalis; 3, bladder.

Wolffian body, the urogenital fold, while from the same point a fold passes to the groin, the *plica gubernatrix*. In the female the adult conditions are easily deduced from this description. When the Wolffian body disappears, the Wolffian merges in the urogenital fold to form the mesosalpinx, and the mesovarium becomes an adjunct to it. The remainder of the urogenital mesentery is the primitive broad ligament; and when the Fallopian tubes and ovaries sink into the pelvis, all merge in one wing-like fold of peritoneum. The upper genital

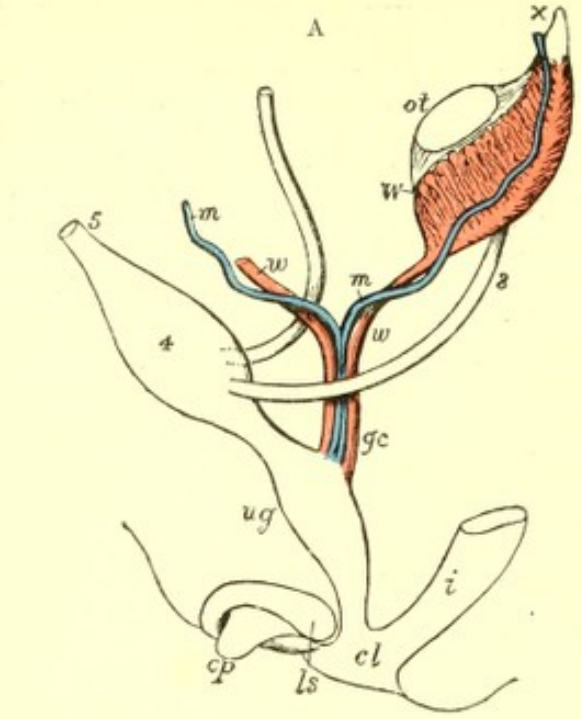
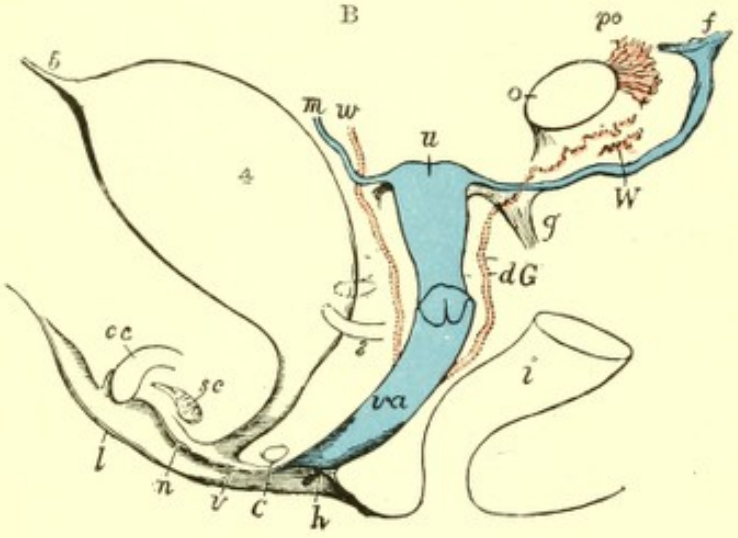



FIG. 250.—DIAGRAMS TO SHOW THE DEVELOPMENT OF MALE AND FEMALE GENERATIVE ORGANS FROM A COMMON TYPE. (Allen Thomson.)

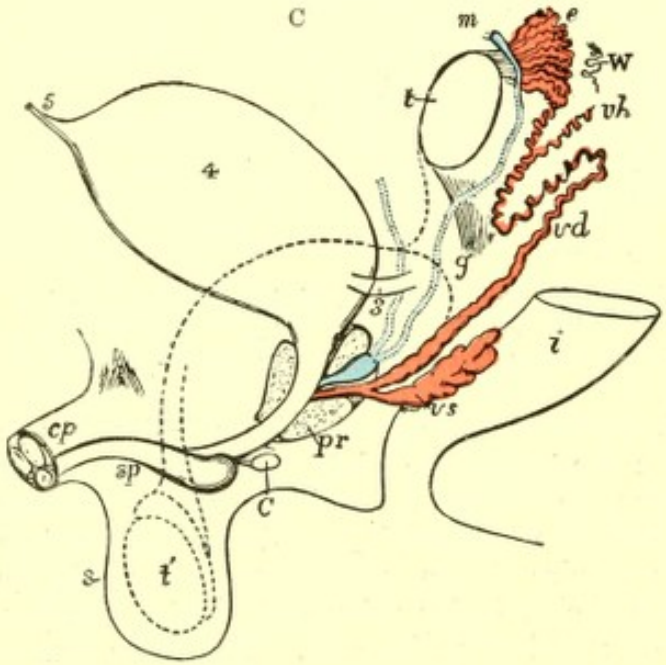
A.—DIAGRAM OF THE PRIMITIVE UROGENITAL ORGANS IN THE EMBRYO PREVIOUS TO SEXUAL DISTINCTION.

3, ureter; 4, urinary bladder; 5, urachus; *ot*, the genital ridge from which either the ovary or testicle is formed: W, left Wolffian body; *w*, *w*, right and left Wolffian ducts; *m*, *m*, right and left Müllerian ducts uniting together and running with the Wolffian ducts in *gc*, the genital cord; *ug*, sinus urogenitalis; *i*, lower part of the intestine; *cl*, cloaca; *cp*, elevation which becomes clitoris or penis; *ls*, fold of integument from which the labia majora or scrotum are formed.




B.—DIAGRAM OF THE FEMALE TYPE OF SEXUAL ORGANS.

*o*, the left ovary; *po*, parovarium (epoophoron of Waldeyer); W, scattered remains of Wolffian tubes near it (paroophoron of Waldeyer); *d G*, remains of the left Wolffian duct, such as give rise to the duct of Gartner, represented by dotted lines; that of the right side is marked *w*; *f*, the abdominal opening of the left Fallopian tube; *u*, uterus; the Fallopian tube of the right side is marked *m*; *g*, round ligament, corresponding to gubernaculum; *i*, lower part of the intestine; *va*, vagina; *h*, situation of the hymen; *C*, gland of Bartholin (Cowper's gland), and immediately above it the urethra; *cc*, corpus cavernosum clitoridis; *sc*, vascular bulb or corpus spongiosum; *n*, nympha; *l*, labium; *v*, vulva.




C.—DIAGRAM OF THE MALE TYPE OF SEXUAL ORGANS.

*t*, testicle in the place of its original formation: *e*, caput epididymis; *vd*, vas deferens; W, scattered remains of the Wolffian body, constituting the organ of Giraldès, or the paradidymis of Waldeyer; *vh*, vas aberrans; *m*, Müllerian duct, the upper part of which remains as the hydatid of Morgagni, the lower part, represented by a dotted line descending to the prostatic vesicle, constitutes the occasionally existing cornu and tube of the uterus masculinus; *g*, the gubernaculum; *vs*, the vesicula seminalis; *pr*, the prostate gland; *C*, Cowper's gland of one side; *cp*, corpora cavernosa penis cut short; *sp*, corpus spongiosum urethræ; *s*, scrotum; *t'*, together with the dotted lines above, indicates the direction in which the testicle and epididymis descend from the abdomen into the scrotum.

and upper Wolffian fold become the suspensory ligament of the ovary enclosing the ovarian vessels. The lower genital fold, and the plica gubernatrix develop involuntary muscular fibres and become the ovarian and round ligaments respectively. In the male the primitive relations are more departed from, owing to the descent of the testicle, and are further modified by the disappearance of the Müllerian ducts. The Wolffian mesentery, the genital mesentery, and the

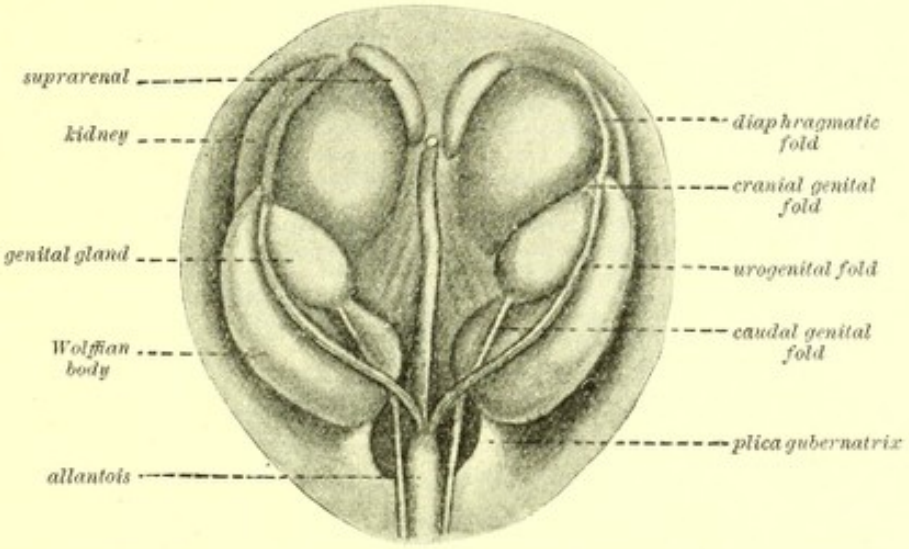



FIG. 251.—THE PERITONEAL FOLDS CONNECTED WITH THE WOLFFIAN BODIES AND GENITAL GLANDS OF A PIG-EMBRYO OF 6·7 CM. LONG. (After Klaatsch.)

urogenital fold are merged in the different portions of the adult mesorchium, but leave no trace within the abdomen. The plica gubernatrix, which after the atrophy of the Wolffian body is continuous with the Wolffian and genital mesenteries, becomes the *gubernaculum testis*. The testis descends to the iliac region in the third month, but only enters the internal abdominal ring in the seventh month. Previously to this a pouch of peritoneum—the *processus vaginalis*—has descended into the scrotum along the abdominal ring, pushing before it part of the internal

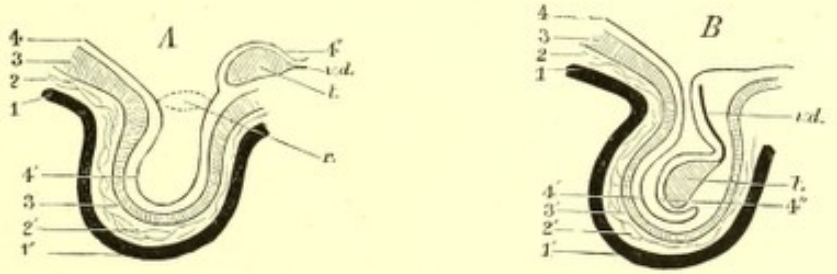



FIG. 252.—DIAGRAMS TO ILLUSTRATE THE DESCENT OF THE TESTICLE AND THE FORMATION OF ITS COVERINGS. (O. Hertwig.)

In A the testicle is lying close to the internal abdominal ring. In B it has passed into the sac of the tunica vaginalis. 1, skin of abdomen; 1′, skin of scrotum; 2, superficial abdominal fascia; 2′, Cooper's fascia; 3, muscular and aponeurotic layer of abdominal wall; 3′, cremaster muscle and spermatic fascia; 4, peritoneum; 4′, processus vaginalis; 4″, visceral layer of processus vaginalis covering testicle; *t*, testicle; *v.d.*, vas deferens; *r*, internal abdominal ring.

oblique muscle and the aponeurosis of the external oblique, which form respectively the cremasteric muscle and spermatic fascia (fig. 252). This pouch, after the descent of the testicle into it, becomes shut off from the abdominal cavity, and forms the cavity of the tunica vaginalis. The descent of the testicle into the scrotum is intimately connected with changes in the gubernaculum. The gubernaculum extends from the integument of the groin, which afterwards forms the scrotum,

upwards through the abdominal ring to the lower part of the epididymis. Round its attachment to the subcutaneous tissue a thickening is formed which includes muscular fibres from both transversalis and internal oblique muscles. The formation of this mass seems already initiated even at so early a stage as that

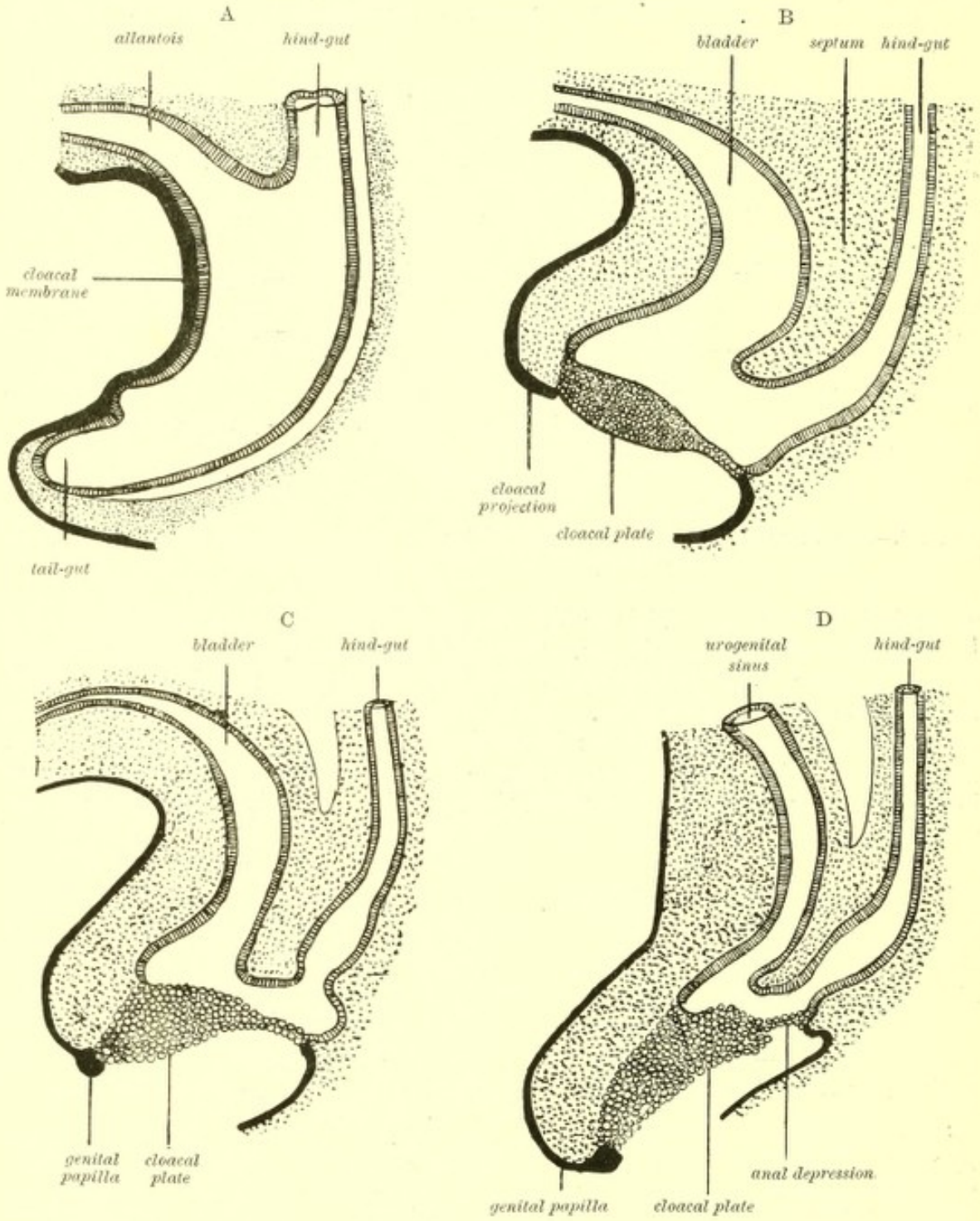



FIG. 253.—DIAGRAMS REPRESENTING FOUR STAGES IN THE DEVELOPMENT OF THE CLOACA ENTODERMICA, THE CLOACAL PLATE, AND GENITAL PAPILLA. (T. H. Bryce.)

figured in fig. 247, p. 195. The muscular tissue forming this inguinal cone occupies the base of the inguinal pouch, and it is by the outward growth of the mass that the outpushing of the abdominal wall is produced, and the processus vaginalis is carried down into the scrotum. When the processus vaginalis is formed, the gubernaculum lies behind the serous sac. The descent of the testicle

is accompanied by a shortening of the gubernacular cord, which thus *appears* to draw the organ downwards into the scrotum; the testicle, following the line originally taken by the gubernacular cord, passes down along the posterior wall of the processus vaginalis, which it therefore invaginates from behind.

In many animals the testicles remain throughout life in the abdominal cavity. In others they only descend into the scrotum during the period of 'heat.' Cases of cryptorchismus, in which one or both testicles have failed to reach the scrotum, and have remained either in the inguinal canal or within the abdominal cavity, are not unfrequent in the human subject. In rare cases the ovaries may also pass through the abdominal ring by a passage corresponding to the processus vaginalis called the *canal of Nuck*, and may even be found in the labia majora, where they resemble in position the testicles within the scrotum.

**Fate of the cloaca entodermica: Formation of external genital organs, perineum, and anus** (figs. 253, 254, 255).—The cloaca entodermica, as we have already seen, is a large chamber connected at its oral end with the allantois and hind-gut, and closed ventrally by the cloacal membrane (fig. 253, A), which extends from the umbilicus to the root of the tail. The cloacal chamber, surrounded by an investment of mesoderm, occupies the whole depth and width of the hinder part of the body-wall. By the increase in the amount of the investing mesoderm, dorsal to and on each side of the cloaca, the body-wall is caused to project between the hind limb buds as an elliptical swelling known as the cloacal tubercle. For some distance behind the umbilicus the mesoderm reaches the mid-ventral line, and an even salient surface is produced, which ends below in an angular projection. This afterwards expands into the *genital papilla*. Behind the angle the lateral sheets of mesoderm are separated by the cloacal membrane, and produce surface folds, which bound a shallow cleft. This extends towards the root of the tail, but is separated from it by a small projection, also caused by a thickening of the underlying mesoderm (*anal tubercle*), and by a slight recess behind it which marks the posterior limit of the cloacal elevation. Meanwhile important changes are taking place in the form of the cloacal chamber. Owing to the increase of the mesoderm in the tongue-like projection between the allantois and hind-gut (fig. 253, A) and also at the sides of the cloaca, the openings of the allantois and hind-gut are apparently shifted backwards—in other words, a frontal septum takes shape which separates a dorsal or rectal from a ventral or urogenital tube, and reduces the cloaca to a narrow passage between the two (fig. 253, B, C). Whether the process thus sketched involves an actual division of the chamber by lateral folds, or is merely the expression of differential growth such that the ventral part of the chamber, with the Wolffian ducts attached thereto, expands forwards, while the opening of the gut is shifted backwards to the caudal part of the dorsal wall, is not yet decided. While this urorectal septum is forming, the lumen of the ventral part of the chamber is narrowed to a sagittal cleft, and is encroached on by an epithelial mass which forms a sagittal plate named the *cloacal plate*.

The cloacal plate (Kloakalplatte, Keibel; bouchon cloacal, Tourneux; Uralplatte, Fleischmann) may be looked on as a thickening of the cloacal membrane in the future urogenital part of the cloacal fossa. According to Disse (1905) the epithelial cells are entodermic in origin, the plate being formed by the apposition of the walls of the ventral part of the cloacal chamber. The same view was advanced earlier by Fleischmann (1902–1904). Tourneux, who was the first to describe the plate (1889), looked upon it as an ectodermic thickening, and as representing, when afterwards fissured, the rudiment of an ectodermic cloaca. Otis (1906) inclines to the same opinion.

The cloacal plate extends as a keel-like thickening into the substance of the cloacal tubercle, and reaches caudally nearly, but not quite, to the anal tubercle. Here the cloacal membrane remains as a thinner lamella, which closes in the dorsal

part of the now narrow cloacal chamber, and lies at the bottom of a shallow transverse depression (ano-perineal area).

Owing to the increase of the mesoderm round the base of the cloacal elevation, the lips of the outer depression become raised into the *outer genital folds*. The increase is, however, greatest at the anterior or cranial lip, and the salient angle already alluded to grows in a ventral direction to form the *genital papilla*. The cloacal plate is necessarily displaced ventrally and rotated until it lies in the position seen in fig. 253, D, on the caudal face of the genital papilla, as a mesial ridge which runs, at the apex of the papilla, into an epithelial horn (seen in fig. 254, B) produced by a thickening of the surface-ectoderm.

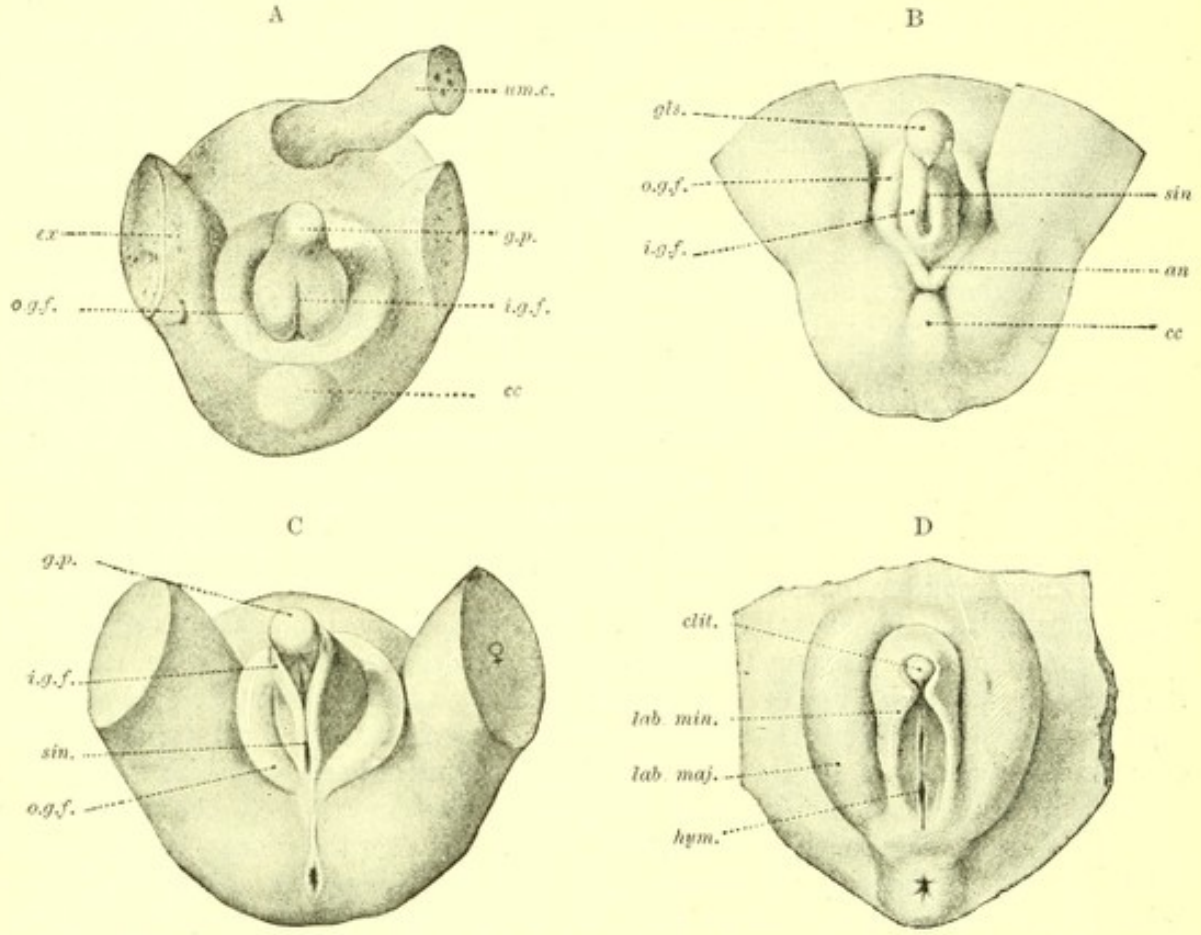



FIG. 254.—DEVELOPMENT OF THE EXTERNAL ORGANS. A, MALE EMBRYO OF 23 MM. LONG; B, MALE EMBRYO OF 29 MM. LONG; C, FEMALE FŒTUS OF 7 MM. LONG (ELEVENTH WEEK); D, FEMALE FŒTUS OF 15 CM. LONG (SIXTEENTH WEEK). (Kollmann.)

*gp*, genital papilla; *gls*, glans; *clit*, clitoris; *o.g.f.*, outer genital folds; *i.g.f.*, inner genital folds; *an*, anus; *sin*, urogenital sinus; *lab. min.*, labia minora; *lab. maj.*, labia majora; *hym*, hymen; *cc*, coccyx; *um.c.*, umbilical cord.

The cloacal plate at the base of the genital papilla now breaks through, and the urogenital opening is established. By a loosening of the central cells of the plate in front of the opening a groove is produced, running on to the caudal face of the genital papilla, and known as the urethral groove. The edges of this groove, formed by the salient lateral sheets of mesoderm, form the *inner genital folds*. The cloacal chamber has meantime been completely divided, and the mesoderm, which lies between the dorsal and ventral portions of it, is allowed to reach the surface, and here forms the perineum. A ring-shaped mesodermic thickening at the same time forms round the proctodæal depression. This at first has the form of two projections from the anal tubercle, which grow forwards round the anal depression, and gradually convert it from a transverse into a semilunar, then into a circular,

depression (Otis). In front the thickening so produced joins the mesoderm forming the perineal bridge, and forms with it the definitive perineal body separating the anus from the urogenital opening.

In the female the adult arrangement of parts is readily derived from this neutral condition described above; the inner genital folds become the *labia minora*, and the outer the *labia majora*, while the genital papilla forms the *clitoris*. The groove on the base of the papilla remains open and forms the entrance to the vestibule, which, as already mentioned, is derived from the much shortened urogenital sinus. Further, it is owing to the shortening of the sinus that the urethra comes to open separately on the surface.

In the male the inner genital folds meet to form the *bulbous urethra*, which is carried forwards on the cloacal aspect of the genital papilla, first as the solid epithelial ridge already described, then as a groove produced by the shedding of the central cells of the solid cord. This groove is closed from behind forwards, becoming the *spongy portion of the urethra*. The enlarged end of the papilla becomes the *glans penis*. In this the urethra is closed independently, so that the last part of the tube to be completed is at the junction of glans and body. The external genital folds meet in the mid-ventral line to form the *scrotum*. The prepuce in both sexes is developed by the ingrowth of a solid ridge of ectoderm (Berry Hart), which, by separating into two lamellæ, sets free a cutaneous fold as a cap to the glans.

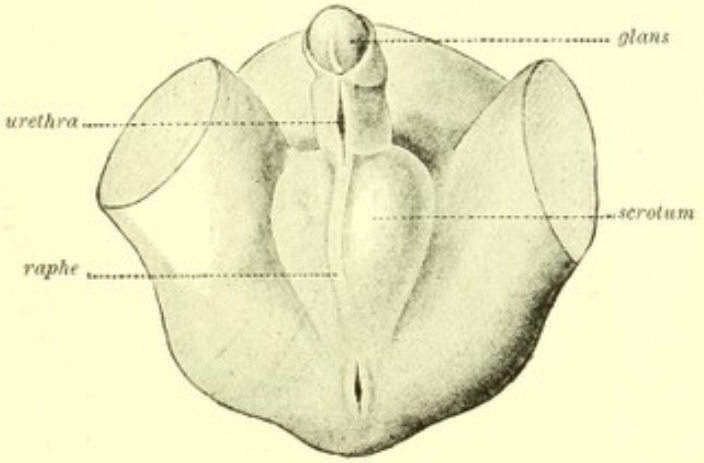



FIG. 255.—MALE FŒTUS 4½ CM. LONG (TENTH WEEK). (From Kollmann.)

The **anal opening** is formed later than the urogenital; while the urogenital opening is effected in a 15·8 mm. embryo, the anal opening is still closed in one of 29 mm. (Keibel). From the proctodæal pit the ectoderm grows inwards for a short distance and forms the short ectodermic portion of the anal canal. The remainder of that passage is derived from the terminal, last closed part, of the cloacal chamber, above which the primitive entodermal tube of the rectum ends in an ampullated dilatation (fig. 236, p. 187).

It appears from the observations of Tourneux, Retterer, Keibel, Fleischmann and his pupils, Disse, and others, that the development of the cloacal region is essentially the same in all mammals. Even in Echidna (Keibel) an entodermic cloaca is completely divided, and the rectum and urogenital sinus open independently into a secondary ectodermic invagination or ectodermic cloaca, just as they do on the surface in placental mammals in which there is no external cloaca.

Fleischmann [1] believes that the cloaca entodermica, or *Urodäum*, as he terms it after Gadow, is not divided by two lateral folds, as first suggested by Rathke. It is, perhaps, after the first frontal fold separates the rectal opening from the part of the chamber receiving the Wolffian ducts, not further divided at all, but the stage represented in fig. 235, p. 187, may be reached by differential growth, the urogenital section being pushed in a ventral and cranial direction, while the rectum retains its primitive position, and comes to open into a small dorsal chamber of the urodäum, the *pars analis*. This becomes separated from the ventral chamber to form the entodermic portion of the anal canal. Wood Jones [2] and Keith [3] deny that the cloaca has any share in the formation of the rectum. The idea involved in Wood-Jones's interpretation,

[1] Morphol. Jahrbuch, 1904. The reader will find here (p. 58) a lengthy historical *résumé* of the literature on this subject.

[2] Brit. Med. Jour. 1904, p. 1630. [3] Human Embryology and Morphology (2nd ed.), London, 1904.

which was, however, put forward before the appearance of Keibel's paper on Echidna, is that the urogenital sinus represents the *cloaca*, and the formation of the upper septum is the

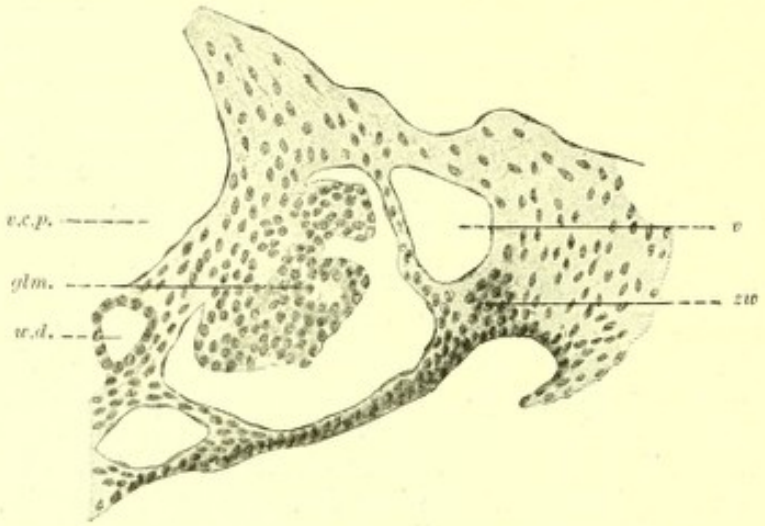



FIG. 256.—SECTION THROUGH AN EMBRYO OF TALPA EUROPÆA. (After Soulie.)

*zw*, bud from cœlomic epithelium, the rudiment of suprarenal body (cortical portion); *v.c.p.*, posterior cardinal vein; *glm*, glomerulus; *w.d.*, Wolffian duct; *v*, vein.

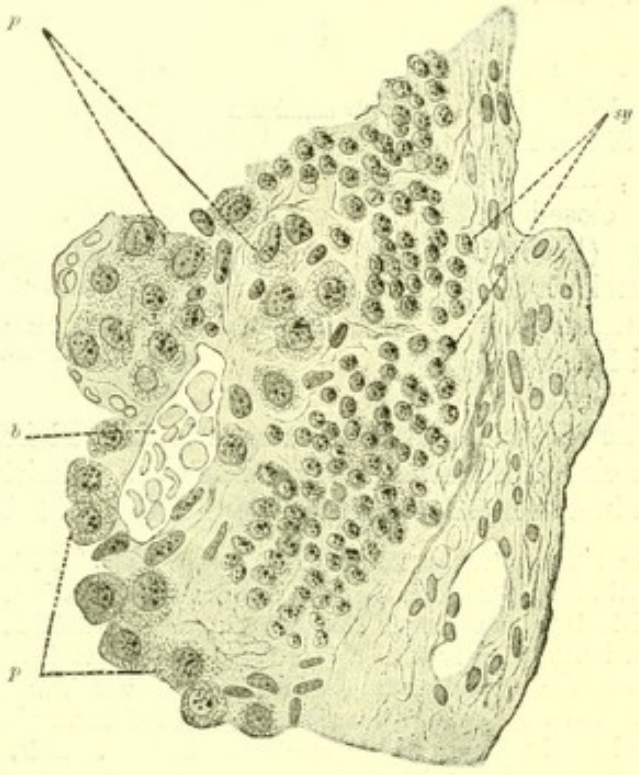



FIG. 257.—SECTION THROUGH A CHROMAFFIN-BODY IN A 44 MM. HUMAN EMBRYO, TO SHOW THE DIFFERENTIATION OF THE PRIMITIVE INDIFFERENT SYMPATHETIC CELLS. (Kohn.)

*p*, *p*, mother chromaffin-cells (Phäochromoblasts); *sy*, sympathetic cells; *b*, blood-vessel.

expression of the closure of the mouth of the hind-gut into that chamber, the rectum proper being a sub-caudal extension of the terminal part of the gut, which becomes secondarily connected with an ectodermic anal invagination.

## SUPRARENAL BODIES (ADRENALS).

The suprarenal bodies consist of two parts of totally different origin. The *cortex* is derived from the mesothelium covering the inner aspect of the fore-part of the Wolffian body, immediately lateral to the attachment of the mesentery and in front of the germinal epithelium (fig. 256). It appears as a series of buds which fuse into a cellular mass imbedded in the mesenchyme of the Wolffian ridge. The cells become arranged in columns, and the three zones characteristic of the cortex of the adult gland are early to be made out. The whole body consists

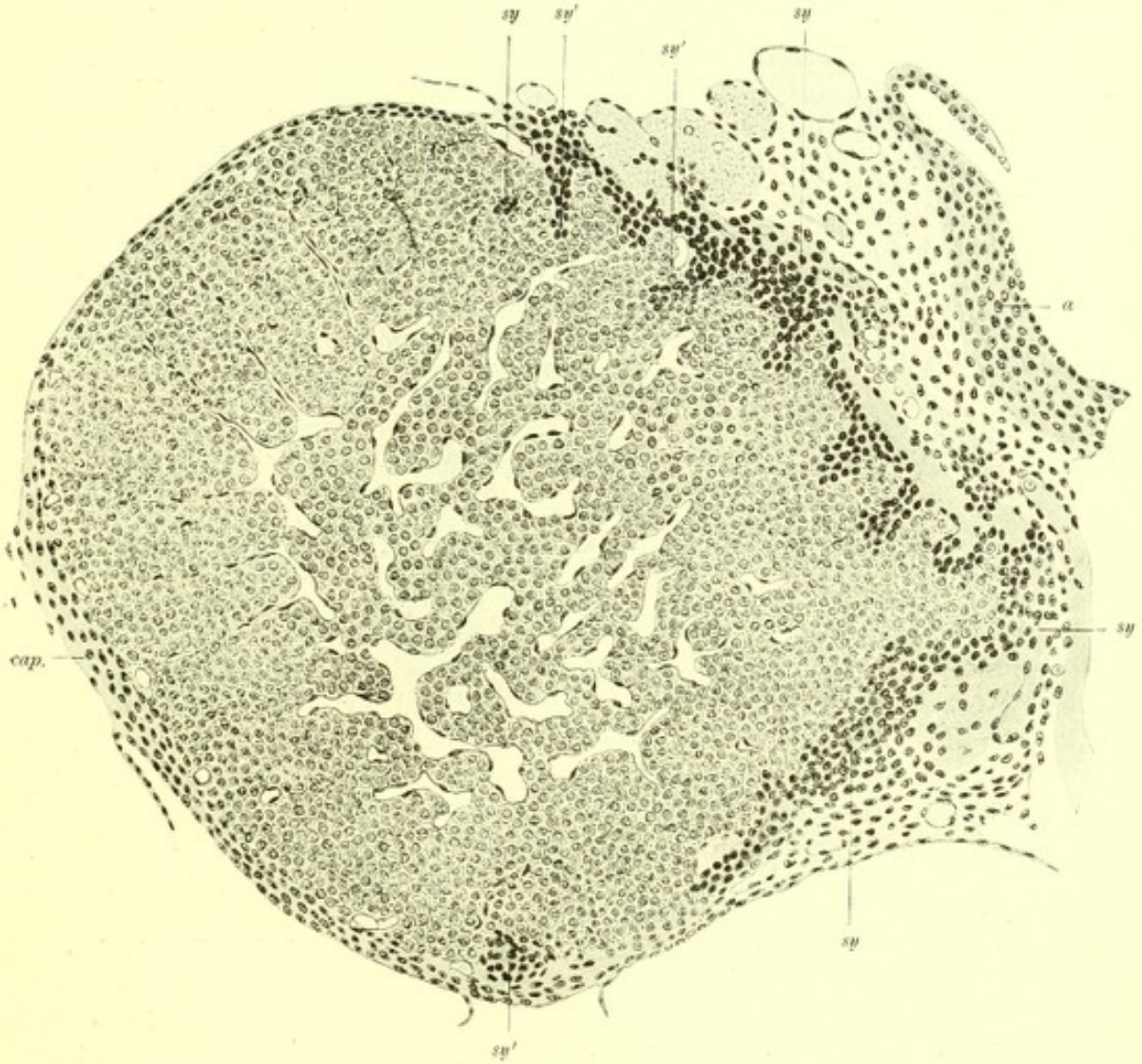



FIG. 258.—TRANSVERSE SECTION OF THE SUPRARENAL BODY OF A HUMAN EMBRYO OF 15·5 MM. (T. H. Bryce.)

*sy*, *sy*, the abdominal sympathetic; *sy'*, *sy'*, groups of cells extending from the sympathetic into the suprarenal; *cap*, capsule of the gland; *a*, aorta.

at first of cortical tissue (fig. 258), and in the centre the trabeculæ are arranged in an irregular network with vessels (sinusoid in nature) in the meshes, and opening into a central venule. The appearance is very like that of a liver lobule. The *medulla* is derived from the sympathetic, and is produced by an ingrowth of cell-groups on the mesial aspect of the gland. In an embryo at the end of the second month the abdominal sympathetic consists of numerous groups of cells in the neighbourhood of the aorta. As we have seen (p. 133), these groups of cells are derived from the ectoderm, and have wandered

from the rudiment of the spinal ganglion, or perhaps from the medullary plate, along with the ventral nerve-roots. The cellular groups in these earlier phases are not ganglia, but masses of indifferent or mother-cells which differentiate in two directions, some becoming *ganglion cells*, others *chromophil* or *chromaffin cells* (*i.e.* cells having special affinity for salts of chromic acid and staining yellow therewith). Masses of these indifferent cells invade the substance of the adrenal, undergo differentiation into chromaffin elements, and collect in the central part of the body to form the cell-groups of the medulla. The medulla begins to be marked off from the cortex in the fourth monfh. The adrenal is rounded in early stages and larger than the kidney (fig. 170). In the third month it becomes flattened and triangular in section (fig. 222), but remains relatively large all through fœtal life.

The development of the adrenals has been the subject of much discussion. Opinion has been divided both as to the cortical and medullary parts of the glands. All have agreed that the cortex arises from the mesoderm, but there have been three main views as to the exact origin of the cells, some observers tracing them to the general mesenchyme, others to the epithelium of the excretory ducts, and others to the mesothelium. The latest work of Wiesel and of Soulie, confirming that of Janošik and Inaba, affords very strong support to the view that cells are budded off from the peritoneal epithelium.[1] Recent work, more especially that of Kohn on the chromaffin elements, has thrown much light on the old problem of the medulla, and it may be now taken as proved that Balfour's view of the origin of the medulla from the sympathetic is the correct one. The close association with the sympathetic accounts also for the presence of ganglion cells under the capsule, at the hilum, and in the medulla of the organ.

## DEVELOPMENT OF THE VASCULAR SYSTEM.

### THE HEART.

In an earlier section the initial phases in the development of the vascular system have been described. We there saw that the heart was first laid down as two tubes which unite together to form a single mesial tube. This lies under the fore-gut in the pericardium, united to its dorsal wall by a double fold named the *dorsal mesocardium*. The mesial tube is divided by constrictions into three portions—the primitive auricle, ventricle, and aortic bulb. Behind it is connected with the *sinus venosus*, a transverse commissural vessel in the septum transversum which receives three pairs of veins—the vitelline, allantoic, and ducts of Cuvier. In front it is continued into a ventral stem—the *truncus arteriosus*—which divides into two vessels. These, looping round the fore-gut, are continued backwards on each side of the middle line as the primitive aortæ.

The simple heart-tube soon becomes bent on itself. This bending is due to its increasing in length disproportionately to the pericardial cavity which encloses it. The dorsal mesocardium disappears between the primitive auricle and the attachment of the bulb to the floor of the fore-gut. These two parts remain in close relationship during all succeeding phases, but the free loop, becoming enlarged and displaced backwards, comes to lie behind the original posterior end of the tube.

#### DEVELOPMENT OF THE OUTWARD FORM OF THE HEART.

In the following account we shall start with the stage reached in the human embryo by the fifteenth day (fig. 259). The auricular portion of the heart-tube lies, still attached by the mesocardium, immediately in front of the septum transversum. From this point it is directed forwards and to the left. Reaching the anterior limit of the pericardium, it turns ventrally to join, by a constricted portion named the *auricular canal*, the ventral U-shaped ventricular loop. This consists (1) of a

[1] The literature of the development of the adrenals is very completely given in the article by Poll in Hertwig's Handbuch der Entwickelungslehre, p. 603 *seq.*

descending limb which passes from left to right, from the left dorso-anterior to the right ventro-posterior extremity of the pericardium; (2) of a transverse portion directed dorsally; and (3) of a smaller ascending limb which, passing forwards,

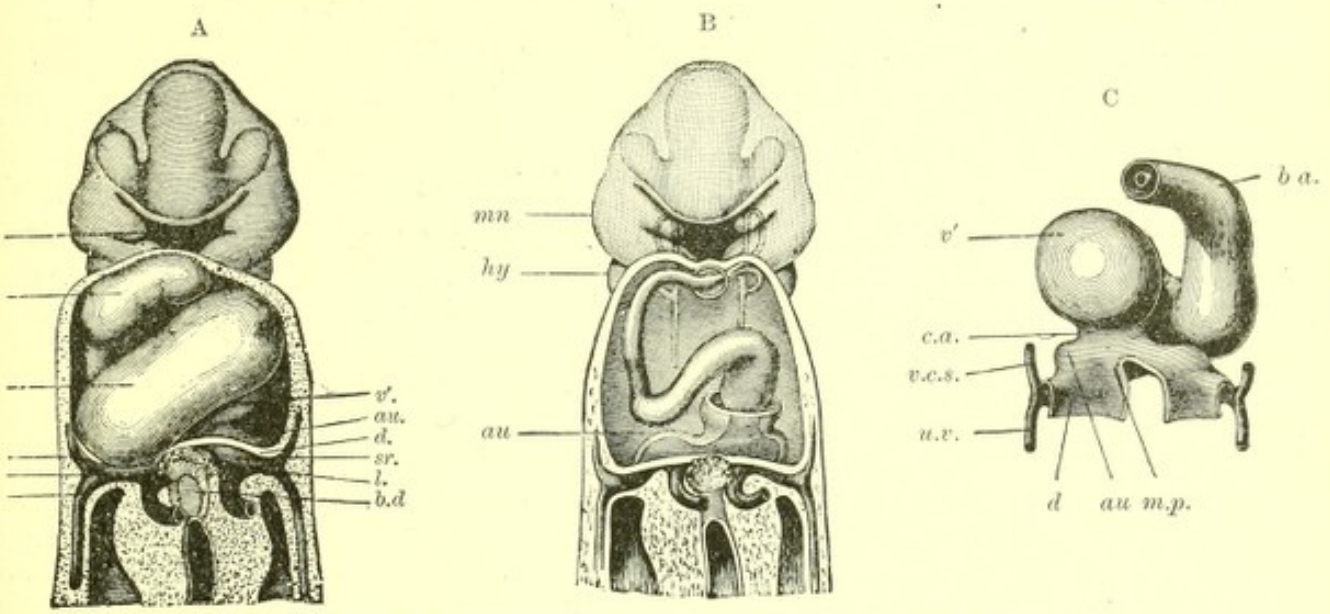



FIG. 259.—CONDITION OF THE HEART IN THE HUMAN EMBRYO OF ABOUT FIFTEEN DAYS, RECONSTRUCTED FROM SERIAL SECTIONS. (His.) $\frac{40}{1}$.

A, from before, showing external appearance of heart; B, the same with the muscular substance of heart removed showing the endothelial tube; C, from behind.

*mn*, mandibular arch with maxillary process; *hy*, hyoidean arch; *b.a.*, bulbus aortæ; *v*, right ventricle; *v'*, left ventricle; *au*, auricular part of heart; *c.a.*, canalis auricularis; *sr*, horn of sinus venosus with umbilical vein (*u.v.*), superior vena cava (*v.c.s.*), and vitelline vein entering it; *d*, diaphragm; *m.p.*, mesocardium posterius; *l*, liver; *b.d.*, bile-duct.

gradually narrows into the aortic bulb. This, finally inclining inwards, reaches the mid-dorsal line at its point of attachment to the floor of the fore-gut. The ascending limb of the loop is separated from the bulb by a slight constriction (the *fretum*

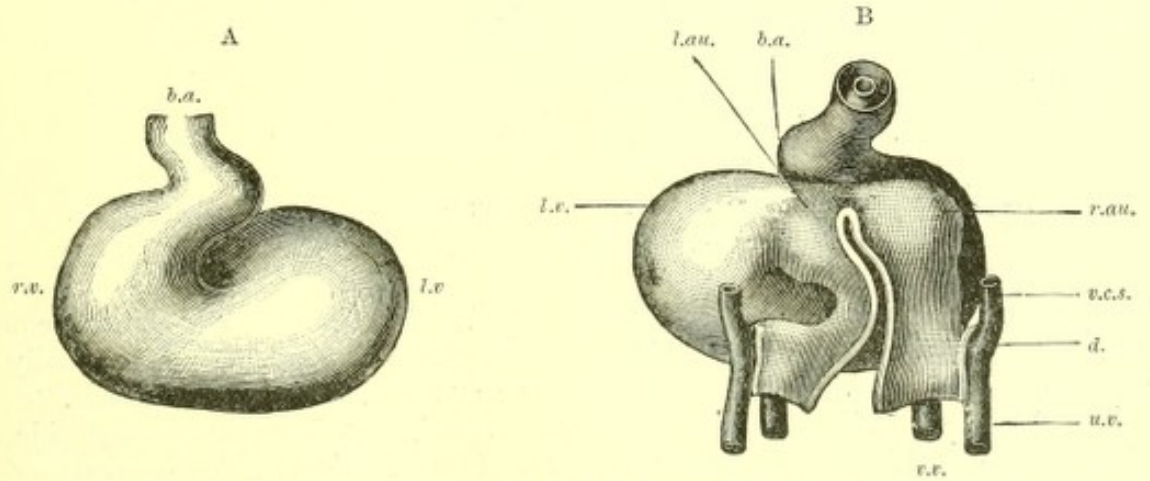



FIG. 260.—HEART OF A SOMEWHAT MORE ADVANCED HUMAN EMBRYO. (His.) $\frac{40}{1}$.

A, from before; B, from behind.

*r.v.*, right ventricle; *l.v.*, left ventricle; *b.a.*, bulbus aortæ; *r.au.*, right auricle; *l.au.*, left auricle; *v.c.s.*, vena cava superior; *u.v.*, umbilical vein; *v.v.*, vitelline vein; *d*, diaphragm.

*Halleri*), and although it ultimately becomes a portion of the right ventricle, it is to be regarded at this stage as the proximal segment of the aortic bulb, and a distinct chamber of the primitive heart (Greil).[1] In the following account we

[1] Morphol. Jahrbuch. xxxi. 1903. See also Hochstetter, in Hertwig's Handbuch der Entwickelungslehre, III. Teil II

shall speak of the ascending limb as the bulb, and of the remainder of the tube as the truncus arteriosus. As the heart-tube increases in length, and the pericardium expands in a backward direction, the sinus venosus is drawn into the cavity out of the septum transversum, necessarily of course carrying with it a covering of the connective tissue of the septum. The ducts of Cuvier undergo a similar apparent anterior displacement, and now run in lateral folds, bounding the aperture between the pericardium and the remainder of the cœlom, and named the *lateral mesocardia* (fig. 293, p. 239).

As the ventricular loop increases in size, it is more and more displaced in a backward direction, so that the auricle and its annex, the sinus venosus, which now consists of a transverse portion and a larger right and a smaller left horn, come to lie on the dorsal aspect and ultimately in front of the ventricular segment (fig. 262). The root of the bulb is thus brought into close relationship

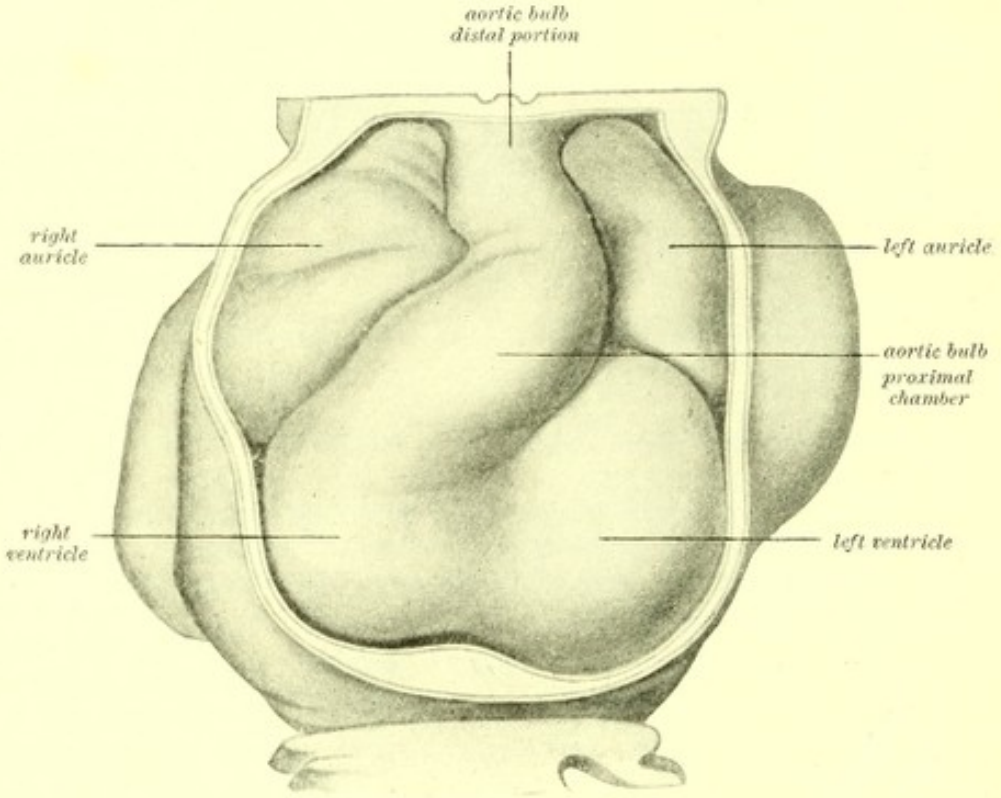



Fig. 261.—Reconstruction of the heart of a human embryo of 6·8 mm. (After Piper.)
The pericardium has been represented as opened to show the ventral aspect of the heart.

with the auricular canal. As a further result of these changes, and consequent backward expansion of the pericardium, the ducts of Cuvier take a gradually increasing antero-posterior inclination on their way to reach the sinus venosus.

Meantime the primitive auricle has thrown out ear-like dilatations on each side, and the descending limb and transverse portion of the ventricular loop have become dilated to form the primitive common ventricle. The ascending limb remains at first more tubular; but it also soon dilates, and, as a result of the increasing distension of the whole distal part of the loop, the cleft between its two limbs, representing a centre, itself stationary, round which growth is proceeding, becomes relatively shorter, until it disappears at the base of the heart, forming there a fold (bulbo-auricular fold) of the heart-wall, where the wall of the bulb passes directly into the wall of the auricular canal (fig. 263). The expansion of the loop is further accompanied by a rotation round the stationary point, of the dilating ascending limb and truncus arteriosus towards the front (fig. 261).

On the transverse portion of the loop a sulcus now appears, which corresponds to the developing interventricular septum within the ventricular chamber.

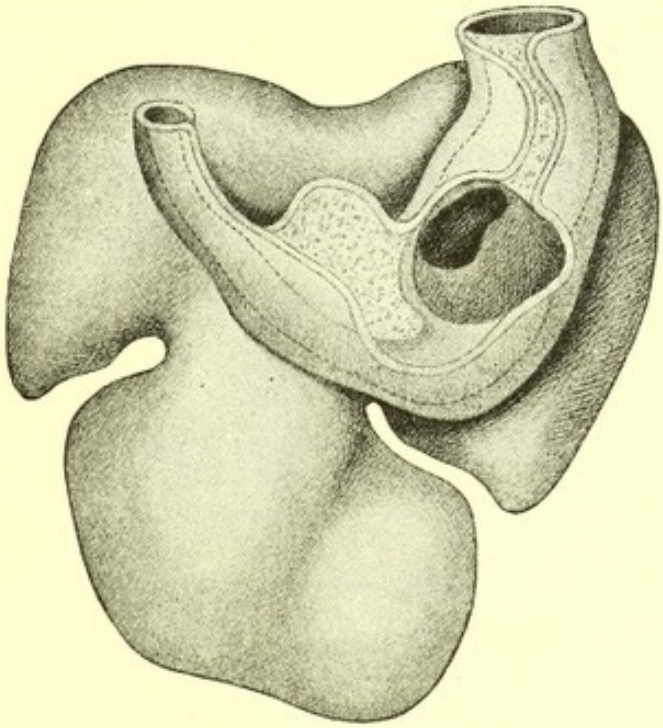


FIG. 262.—VIEW FROM BEHIND OF THE HEART OF A HUMAN EMBRYO OF ABOUT FOUR WEEKS, MAGNIFIED. (His.)

The two ducts of Cuvier and the inferior cava are seen opening separately into the sinus, which is a transversely elongated sac communicating only by a narrow orifice with the right auricle.

The appearance of this sulcus is the expression of a commencing bilateral expansion of the common ventricle. We can therefore now name the

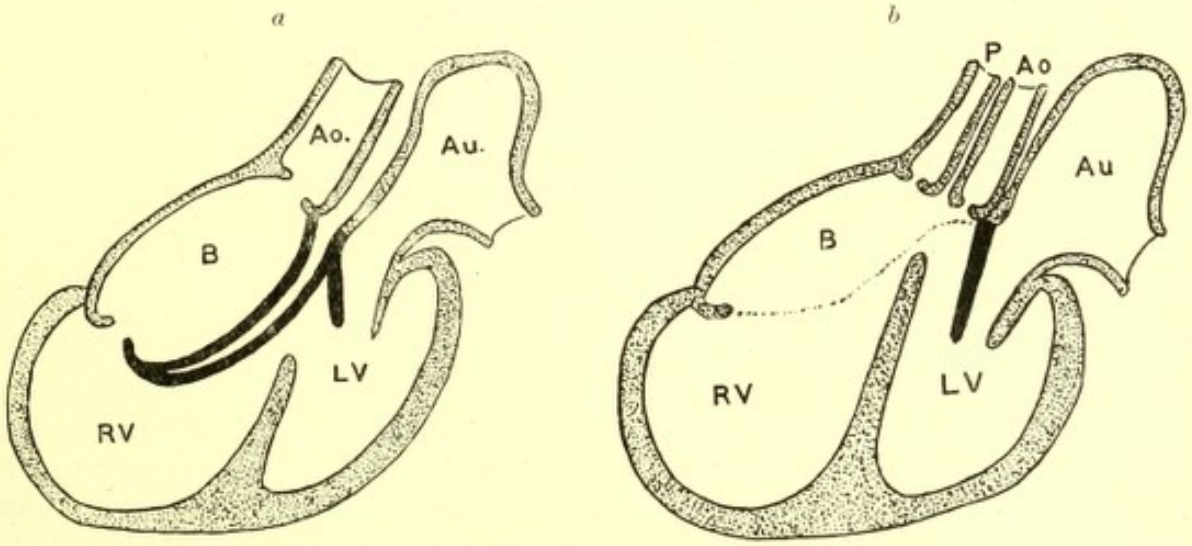



FIG. 263.—DIAGRAMS TO ILLUSTRATE HOW IN THE DISTENSION OF THE VENTRICLES THE 'LESSER CURVATURE' OF THE HEART-TUBE IS REDUCED, AND THE PROXIMAL CHAMBER OF THE AORTIC BULB (B) LOSES ITS MESIAL WALL. (After Keith.)

*a.o.*, aortic bulb (distal part); *au*, auricle; *B*, aortic bulb (proximal part); *RV*, right ventricle; *LV*, left ventricle; *P* (in *b*), pulmonary artery.

lateral dilatations the right and left ventricles. It will be observed that the right ventricle is formed from the right portion of the transverse section of the

primitive loop and its ascending limb. As this latter constitutes a special chamber, corresponding to the reptilian aortic bulb (Greil), the right ventricle has a composite character. Neither at this stage, nor later, is there any distinct demarcation between the two chambers of the right ventricle in normally developed hearts; but in certain cases, where there has been defective development, they remain in a measure distinct (Keith).[1] As the ventral rotation of the right side of the heart above mentioned proceeds, the auricular portion also undergoes a displacement, but in the opposite direction. Thus the auricular canal, which is at first on the right side, comes to be placed opposite the middle of the developing ventricles, with the bulb lying against its ventral aspect. The auricular canal

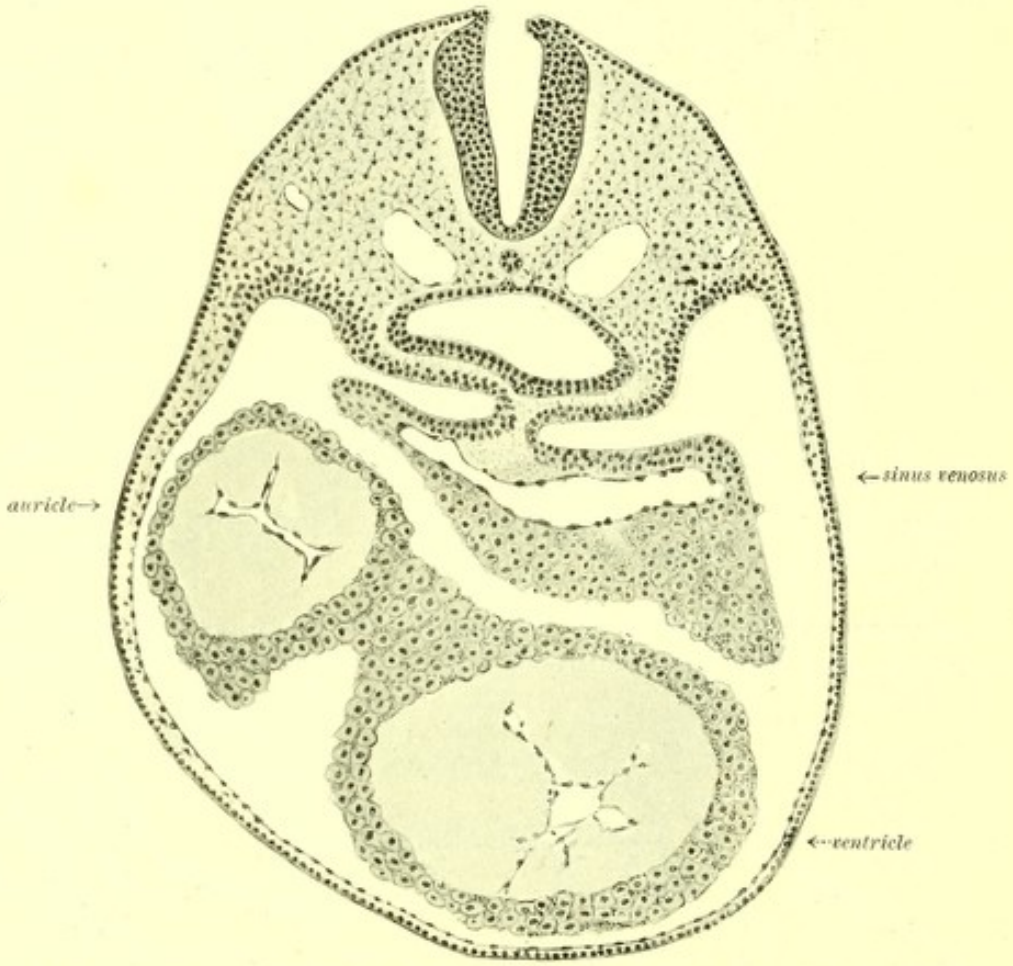



FIG. 264.—TRANSVERSE SECTION OF A HUMAN EMBRYO OF 2·4 MM. (T. H. Bryce.)

The section passes through the heart attached to the posterior wall of the pericardial cavity below the fore-gut by the posterior mesocardium. Notice the wide interval between the wall of the heart-tube and the endothelial tube.

further disappears from view by the expanding auricles coming into contact with the expanding ventricles to form the deep auriculo-ventricular sulci (fig. 262).

The relative position of the several parts now achieved is maintained throughout all subsequent phases, and the further changes will best be understood by tracing in somewhat greater detail the history of each segment.

In the early phases of the development of the interior of the heart-tube, the endothelial lining is separated by a considerable interval from the outer wall (fig. 264). This space is at first filled by a fine meshwork of connective-tissue fibrils, but in later stages by muscular columns and trabeculæ (fig. 268), over which the endothelial membrane is spread, following all the irregularities of the surface.

[1] Aberdeen University Quarter-Centenary Volume: Studies in Pathology; W. Bullock, p. 17 (1906)

Further, at the various orifices solid connective-tissue thickenings are formed, which serve in the developing heart as primitive valvular arrangements,[1] and become by changes presently to be described converted into the valves of the adult organ.

## DEVELOPMENT OF THE CHAMBERS OF THE HEART AND FORMATION OF THE SEPTA.

**Sinus venosus.**—When the sinus venosus has been drawn into the pericardium it becomes separated by a fold from the primitive auricle. This fold appears first on the left side, and though it is completed all round the tube it remains deeper on the left side. The result is that the opening of the sinus into the auricle is displaced to the right side. At first a wide opening, the ostium is converted into a narrow cleft by the drawing together of the lips corresponding to the outer folds, and these are then invaginated into the cavity of the auricle to form two flaps or valves, known as the right and left venous valves (fig. 265). The sinus at first

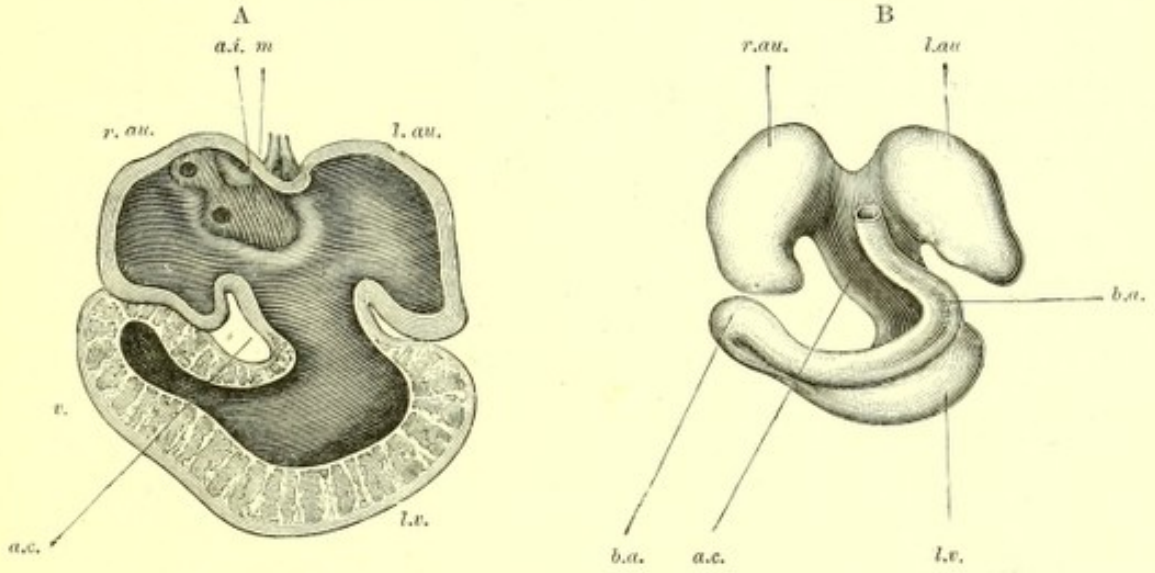



FIG. 265.—HEART OF HUMAN EMBRYO SLIGHTLY MORE ADVANCED THAN THAT SHOWN IN FIG. 166. (His.)

A, interior of auricle and ventricle displayed. B, endothelial tube.

*a.c.*, auricular canal; *a.i.*, area interposita of His; *m*, posterior mesocardium; *r.au.*, *l.au.*, right and left auricles; *l.v.*, left ventricle; *r.v.*, right ventricle; *b.a.*, bulbus aortæ.

receives three pairs of veins, but by a series of changes, afterwards to be described, the blood is ultimately returned by an unpaired vein, the inferior vena cava, and the two ducts of Cuvier. The sinus by the forward displacement of the ducts of Cuvier has meantime become horseshoe-shaped, and the lateral horns receiving the ducts become unequal in size (fig. 262). The larger right horn and transverse portion of the sinus, which become separated from the left horn by a septum, are taken into the right auricle as the *atrium* of that chamber, while the left horn becomes the *coronary sinus*.

**Auricular chamber.**—The cavity of the auricle, at first single, receives on its right side the ostium of the sinus venosus, the lips of which are invaginated into it as the *venous valves*. It opens into the left side of the common ventricle

[1] It must be borne in mind that the heart does not develop as a passive organ. It begins to beat while yet a simple tube, and the primary contraction is peristaltic. When the primitive chambers are differentiated and separated from each other by constricted portions of the tube, the peristalsis is converted into a successive contraction of auricle and ventricle. The endocardial cushions must not only tend to prevent regurgitation, but also offer an obstacle to the onflowing blood, and the increase of pressure within the chambers which will necessarily result must be the chief factor in the moulding of the heart.

through the auricular canal. It becomes distended at a very early stage into two lateral diverticula, which become the auricular appendages (fig. 265). On the outer side of the connecting portion between these appendages (the original tubular auricle) a fold now appears which indicates the position of the future primary septum. On the inner aspect another fold is also now seen running over the roof and connected with the venous valves. It is known as the septum spurium, and corresponds to a muscular fold which stretches these valves in the reptilian heart (Röse).

Immediately to the left of this the primary septum extends inwards from the dorsal wall (fig. 266). This is the *septum superius* of His, or *septum primum* of

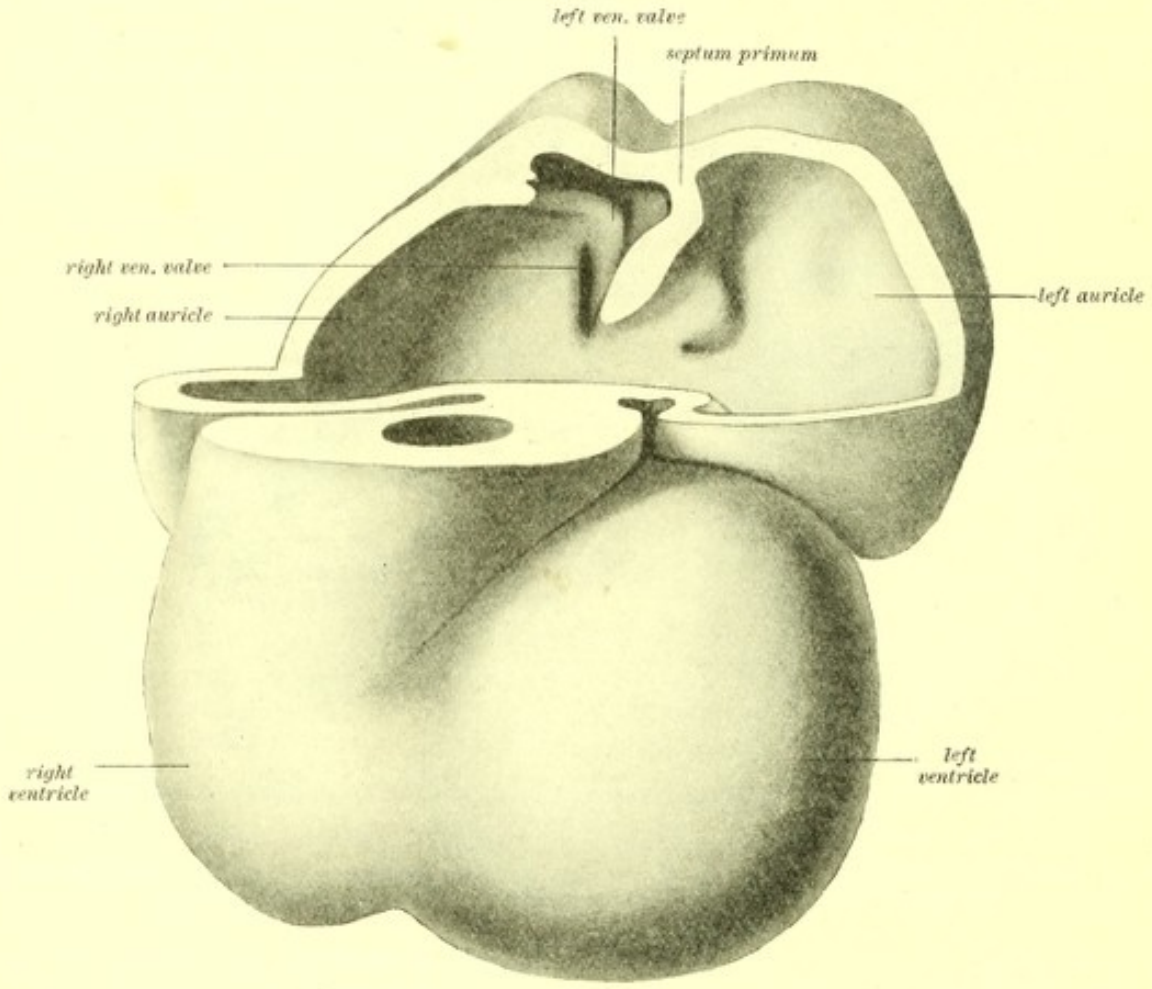



FIG. 266.—MODEL OF THE HEART OF A HUMAN EMBRYO OF 6·8 MM. (After Piper.)

The primitive auricule has been opened up to show the septum primum and the valves guarding the mouth of the opening of the sinus venosus. The fold passing on to the roof of the auricle and connected with the venous valves is the septum spurium.

Born. At first it forms only an incomplete partition, the two sides of the common auricle communicating below its free thickened lower border by the *ostium primum* (Born) (fig. 263). It soon fuses below with the endocardial thickening in the auricular canal (see below), and the ostium primum is closed, but a new opening (*ostium secundum*) appears near its dorsal attachment (fig. 268). Meantime a second septum (*septum secundum*, Born) has extended into the cavity. It is sickle-shaped, and the horns of its free semilunar border fuse with the ventral attachments of the septum primum. It overlaps the primary septum and the opening between the two is the *foramen ovale*. The aperture is bounded by the free border of the secondary septum, and the free portion of the

primary septum forms a valvular flap which closes the foramen from the side of the left auricle. In fœtal life blood passes from the right to the left auricle through the foramen ovale; but at birth, with the establishment of respiration, the valvular septum primum unites with the septum secundum and the partitional wall is complete. The *annulus ovalis* represents the edge of the septum secundum.

By the end of the first month the left venous valve and the septum secundum seem to have united with one another to obliterate a space seen in earlier stages between the left venous valve and the septum of the auricles. Further the right venous valve is continuous with the posterior horn of the septum as it passes to join the septum primum at the base of the posterior endocardial cushion. The sinus venosus thus comes to lie partly in the septum secundum as it passes forward to open into the auricle (Low).[1] The slit-like opening of the sinus venosus meanwhile opens out, and the cavity of the sinus is completely taken into that of the auricle, the junction of the two chambers being indicated merely by the *sulcus terminalis* of His. The greater part of the right venous valve is converted into the *Eustachian* valve, but its lower edge becomes the *valve of Thebesius*.

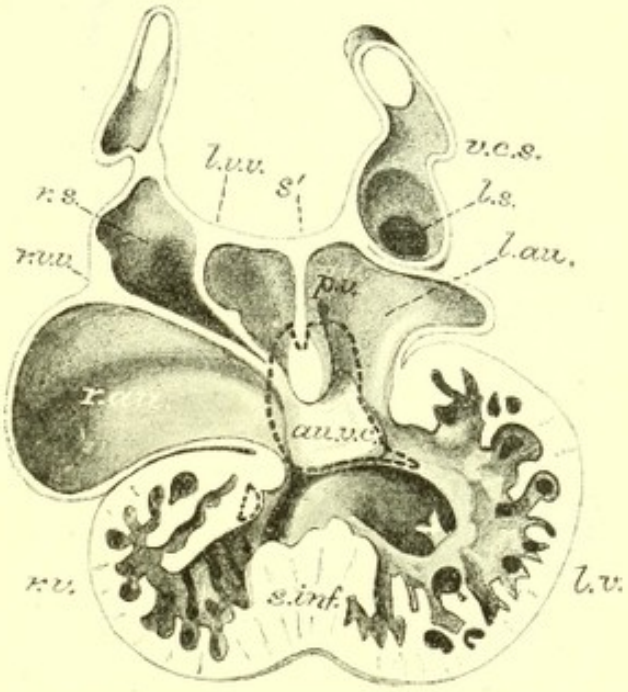



FIG. 267.—SECTION THROUGH THE HEART OF A RABBIT-EMBRYO. (Born.)

*r.s.*, *l.s.*, right and left horns of sinus receiving from above the respective ducts of Cuvier; *r.au.*, *l.au.*, right and left auricles; *r.v.*, *l.v.*, right and left parts of the ventricle; *r.v.v.*, *l.v.v.*, right and left valves guarding the orifice from the right horn of the sinus into the right auricle; *au.v.c.*, one of the two endocardial cushions which are beginning to subdivide the common auriculo-ventricular aperture. The dotted line encloses the extent of the endocardial thickening. The small oval detached area of endocardial thickening in the right ventricle, and the swelling opposite it on the septum inferius, belong to the proximal chamber of the aortic bulb, and will afterwards unite to separate the conus of the right from the aortic vestibule of the left ventricle. *s'*, septum primum growing down between the auricles and prolonged below by a thickening of endocardium. Close to this septum in the left auricle is seen the opening of the pulmonary vein; *s.inf.*, inferior septum of the ventricles.

The left auricle receives, at a stage when the primary septum is appearing, the common stem of the right and left pulmonary veins conveyed to it in the dorsal mesocardium (figs. 266, 267). In later stages the mouth of the vessel opens up like the mouth of the sinus venosus, and its proximal part is taken into the auricle as its atrium. This process of expansion proceeds in some animals until the union of the two pulmonary veins is reached, so that they come to open separately into the chamber; but in man it is carried still farther, and extends to the junction of the two main tributaries of each vein, in consequence of which the auricle comes to have four separate pulmonary veins opening into it.

**Auricular canal.**—By the overlapping of the expanding auricular and ventricular chambers the auricular canal is telescoped within the cavity of the ventricle. Its lumen becomes slit-like, and endocardial cushions develop on its dorsal and ventral walls. These fuse with one another to divide the canal into two passages, which become the auriculo-ventricular openings. When the auricular

[1] Proc. Anat. and Anth. Soc. Univ. of Aberdeen, 1900–1902.

septum joins the fused cushions these openings lead from the two auricles, but at first they both communicate with the left side of the ventricular chamber. In consequence, however, of the rotation above described, the canal is moved towards the right; and when the septum of the ventricles, presently to be described

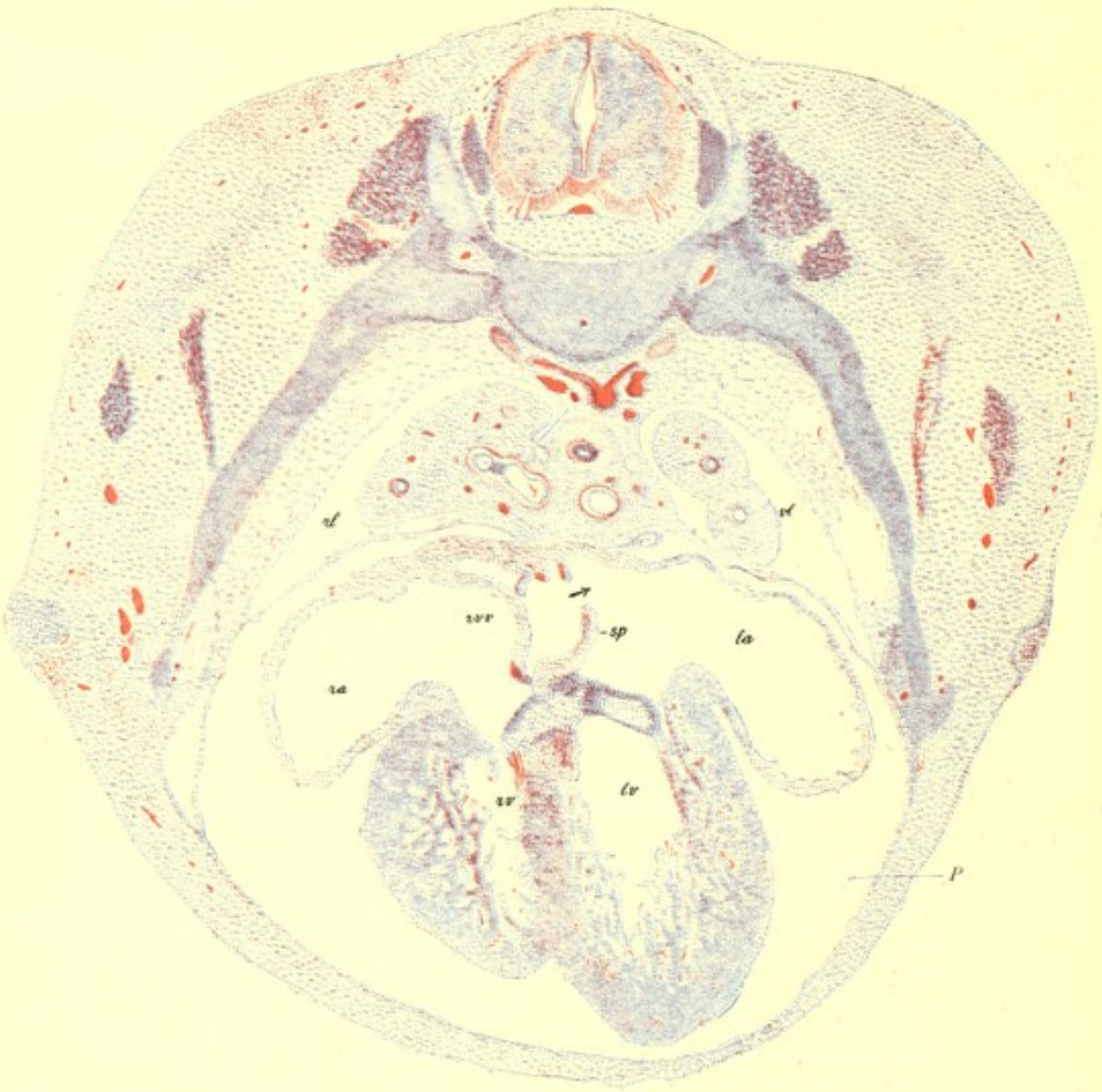



FIG. 268.—SECTION OF THE TRUNK OF A HUMAN EMBRYO OF 15·5 MM. (T. H. Bryce.)

The section cuts the pericardium, heart, and lungs. Below the neural canal is the centrum of a vertebra, which is connected with the neural arch on either side, and with a pair of ribs. To the inside of the cartilage of the neural arch are seen the spinal ganglia; outside are the myotomes separated into dorsal and ventral portions by the dorsal branches of the spinal nerves. Below the vertebra is the aorta giving off a pair of segmental arteries. On each side of the aorta the cardinal veins, and farther out the sympathetic cords. Below the aorta the œsophagus and trachea; on each side the lungs; the letters *vl* and *vl* are placed in the pleural sacs; notice how they are separated from the ribs by a thick lamella of very open connective tissue. The pleural spaces are separated from the pericardium *P* by the pleuro-pericardial membranes. The heart is attached to the mesenteric septum by the mesocardium. Attached to this on the left side by a fold is the now much reduced left duct of Cuvier. *r.v.* right, *l.v.* left ventricle; *r.a.* right, *l.a.* left auricle; *s.p.*, septum primum; the arrow marks the *ostium secundum*; *r.v.v.*, right venous valve. Above it is the opening of the sinus venosus, closed on the left by the left venous valve.

also unites with the fused endocardial cushions, they come to be connected each with its proper ventricle. The formation of the auriculo-ventricular valves will be considered in the following paragraph.

**Ventricular chamber.**—The common ventricular chamber is formed, as already stated from the descending limb and transverse portion of the ventricular

loop, while the ascending limb represents a proximal chamber of the aortic bulb afterwards taken into the right ventricle. The mesial sulcus seen on the outer aspect of the heart, representing a fold in its tubular wall, has corresponding to it, within the cavity, a projection which is the rudiment of the ventricular septum (*septum inferius* of His) (fig. 267). As the ventricular dilatations increase in size, this becomes progressively higher, its upper edge always maintaining the same relative position to a projection into the cavity from above, which corresponds to the fold between the two limbs of the primary loop, and which gradually shortens, as the chambers expand, until it is reduced to a slight crescentic ridge corresponding to the outer *bulbo-auricular fold*. By the shortening of the fold separating the two limbs of the ventricular loop, the ascending limb or bulb loses, as it were, its mesial wall and its independence as a separate chamber of the heart (fig. 263). The septum is obliquely placed and is semilunar in shape. The dorsal horn runs on to the dorsal wall of the auricular canal (fig. 268), while the ventral horn passes into a fold continuous with the projection into the ventricle just mentioned. The free edge is inclined towards the right, and the blood is conducted through the opening left between the chambers into the aortic bulb.

The space between the endothelial lining and the outer wall of the heart-tube has meantime become occupied by columns and trabeculæ springing from the outer wall; and the endothelial lining, by the distension of the endothelial tube, becomes stretched over and around these so that the greater part of the cavity becomes occupied by a spongework of muscular columns, which persist in the adult heart as the columnæ carneæ.[1] The wall of the auricular canal, at first solid, also becomes undermined from the side of the ventricle, and the inner lamella comes to hang free into the chamber, but connected to its walls by muscular trabeculæ. The septal flaps of the auriculo-ventricular valves are formed in part from the endocardial cushions, which are at first spongy but later become membranous, and the marginal flaps from the undermined wall of the auricular canal. The muscular trabeculæ which connect the inner tube with the ventricular wall become the musculi papillares and chordæ tendineæ, the muscles being the basal portions of trabeculæ which remain muscular, while the chords represent strands which have been converted into connective tissue. The ascending limb of the ventricular loop, at the stage in which it is still more or less tubular, has a uniformly thick lining. Two endocardial swellings are formed, one on the dorsal and one on the ventral wall, and then by a process of undermining, similar to that described for the auricular canal, the chamber is taken into the right ventricle. The endocardial cushions remain, however, as projections into the cavity (fig. 267). The fate of these, and the manner in which final closure of the interventricular opening takes place, will be considered after the division of the bulb has been described.

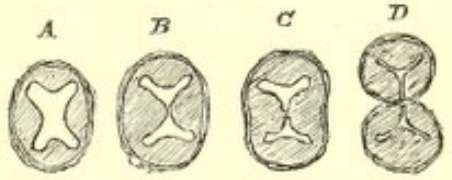



FIG. 269.—DIAGRAM SHOWING THE DIVISION OF THE LOWER PART OF THE TRUNCUS AORTÆ, AND THE FORMATION OF THE SEMILUNAR VALVES. (After Gegenbaur and His.)

A, undivided truncus arteriosus with four endocardial cushions: B, advance of the two lateral cushions resulting in the division of the lumen; C, projection of three endocardial cushions in each part; D, the separation into aorta and pulmonary trunks completed with three cushions in each.

**Distal part of aortic bulb.**—The truncus arteriosus is subdivided into two vessels, the ventral aorta and the pulmonary artery. The division of the lumen is first effected by two longitudinal endocardial thickenings which fuse with

[1] This process is interpreted rather differently by Lewis (Anat. Anzeiger, xxv. 1904). The spaces between the trabeculæ are considered as equivalent to sinusoids (Minot) produced by the breaking up of the original endothelial tube by the growing trabeculæ.

one another. Between these primary thickenings there are two smaller ridges, so that the cavity is divided into two triangular passages (fig. 269). The main folds run in a spiral direction from a point on the ventral aorta between the last two aortic arches to the base of the truncus, and as they lie dorso-ventral in front, and right and left behind, it follows that when the vessels are separated from one another they are placed dorso-ventral at their proximal, and right and left at their distal ends. The actual cleavage of the truncus arteriosus is brought about by two folds of the connective-tissue wall which correspond to the primary fused endocardial ridges. These endocardial ridges are prolonged into the part of the right ventricle

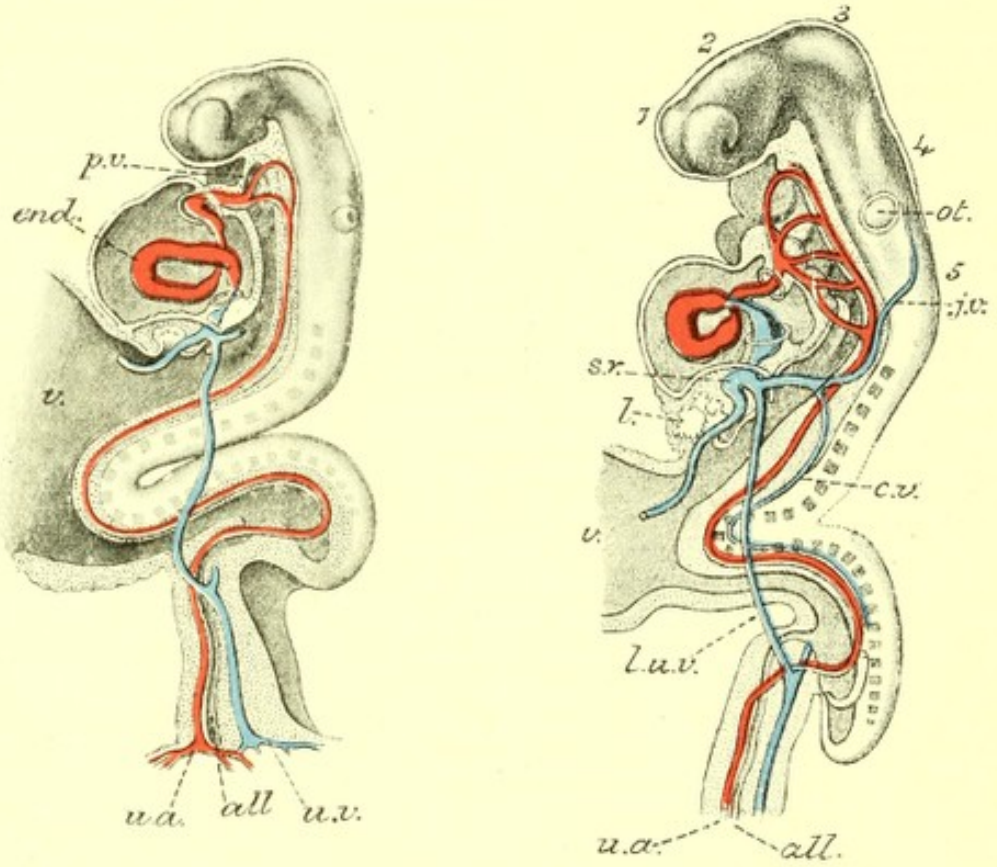



FIG. 270.—PROFILE VIEW OF A HUMAN EMBRYO OF ABOUT FIFTEEN DAYS, WITH THE ALIMENTARY CANAL IN LONGITUDINAL SECTION. (His.)

Two arterial arches are formed at this stage.

FIG. 271.—SIMILAR VIEW OF A SOMEWHAT OLDER EMBRYO, SHOWING FIVE ARTERIAL ARCHES.

1, 2, 3, 4, 5, are opposite the respective secondary cerebral vesicles; from the side of the fore-brain the primary optic vesicle is seen projecting; *ot*, otic vesicle, still open in fig. 270; *p.v.*, septum between mouth and pharynx (primitive velum). This has disappeared in fig. 271; *l*, commencing liver in septum transversum; *v*, vitelline stalk; *all*, allantois enclosed within stalk; *j.v.*, jugular vein; *c.v.*, cardinal vein; *s.v.*, sinus venosus within septum transversum; *u.a.*, left umbilical (allantoic) artery; *l.u.v.*, left umbilical vein; *end*, endothelial tube of heart. The sharp curve of the trunk of the embryo towards the yolk-sac is normal at this period of development.

formed from the ascending limb of the ventricular loop (proximal chamber of aortic bulb), and are continuous with the endocardial cushions proper to it. As these also unite with one another, the aortic septum becomes extended into the right ventricle to divide its distal portion (aortic bulb) into two passages, pulmonary and aortic. These become the conus of the right, and the aortic vestibule of the left ventricle respectively (fig. 263). The *semilunar valves* are formed by a hollowing of the endocardial cushion from the distal side at the mouths of the aorta and pulmonary artery (fig. 269).

The interventricular foramen, however, still persists. It is now closed by a somewhat complicated process. We left the interventricular septum at a

stage when its obliquely directed upper free edge bounded a relatively large interventricular foramen. This becomes constricted by the fusion of the dorsal horn of the septum with the already fused endocardial cushions of the auricular canal. This fusion takes place nearer the right than the left edge of the cushions (fig. 268), so that the septum is placed nearer the right than the left auriculo-ventricular opening. The two ventricles properly so-called are now completely separated, but a foramen still connects the left chamber with the distal part of the right ventricle or proximal chamber of the aortic bulb, meanwhile divided by the fusion of its two endocardial ridges with one another, and with the aortic septum proper. The septum of the bulb now unites with the remaining free edge of the interventricular septum, the pars membranacea septi is formed, and the two sides of the heart are finally entirely isolated.

## DEVELOPMENT OF THE ARTERIES.

The earliest stages in the development of the vessels have been already described (p. 63). We shall here begin with a stage reached in the human embryo about the fifteenth day.

**Dorsal aorta** (fig. 270).—The two dorsal aortæ of the early stages come together in the middle of their course, and fuse into a single mesial vessel. The fusion proceeds forwards and backwards, but at the head end the primitive arteries remain separate, one on either side, on the dorsal aspect of the pharynx. Behind, the vessel divides into the allantoic arteries, which are continued into the body-stalk. These vessels correspond to branches of the aorta which vascularise the allantois in lower Amniota, and which appear at a later stage after the yolk-circulation has been established.

**Aortic arches.**—By the term *aortic arches* we understand a series of vascular loops which are formed in the branchial arches, and join the ventral aortæ to the dorsal aortæ round the walls of the pharynx. They appear in succession from before backwards, one in each branchial arch. On the thirteenth day the primitive mandibular loop is alone present; by the fifteenth day a second arch is completed in the hyoid arch (fig. 270); and by the eighteenth day three others have been added (fig. 271). The first three, along with the ventral and dorsal vessels, by a series of changes presently to be described, form the carotid system of arteries, the fourth becomes the *systemic* arch, and the last the *pulmonary* arch. Between the systemic and pulmonary arches a vessel appears at a rather later stage; this has been regarded as a rudimentary fifth arch corresponding to the fifth arch of lower forms. It soon disappears, and takes no share in the formation of any adult vessels (Zimmermann and Tandler).[1] If this be so, the pulmonary arch must be the sixth of the series.

The observations on the fifth arch in mammalian embryos are not quite in complete accord, but the variations in development of the vessel, interpreted in this sense, may perhaps be due to its transitory and vestigial character; and in view of the conditions prevailing in lower forms the conclusion that there is a rudimentary fifth arch in mammals also, in front of the pulmonary, seems justified on the evidence afforded by recent research.[2]

In the majority of cases the anterior arches have already become incomplete before the last has been formed, but in the human embryo the series (with the exception of the rudimentary fifth arch) is complete for a time.

[1] Tandler, Morph. Jahrb. xxx.

[2] Zimmermann (Verh. Anat. Ges. 1887) first showed the existence of a vascular channel between the aortic and pulmonary arches in the human embryo. It took the form of a vessel springing from the systemic arch and joining it again. Tandler (*loc. cit.*) described a more complete arch (figs. 272, 273) passing from the systemic to the pulmonary arch. For detail as to the lower mammals, see Zimmermann, Anat. Anzeiger, iv. 1889; Lehmann, *ibid.* xxvi. 1905, and Zool. Jahrb. xxii.; Locy, Anat. Anzeiger, xxix. 1906; Lewis, *ibid.* xxviii. 1906. The last named holds it doubtful whether the irregular channels described as fifth arches are really of that nature.

At the stage when there are five complete arches (fig. 274) the loops arise in a radiating fashion from the truncus arteriosus, the two anterior arches being connected with an ascending, the remaining arches with a descending trunk. As

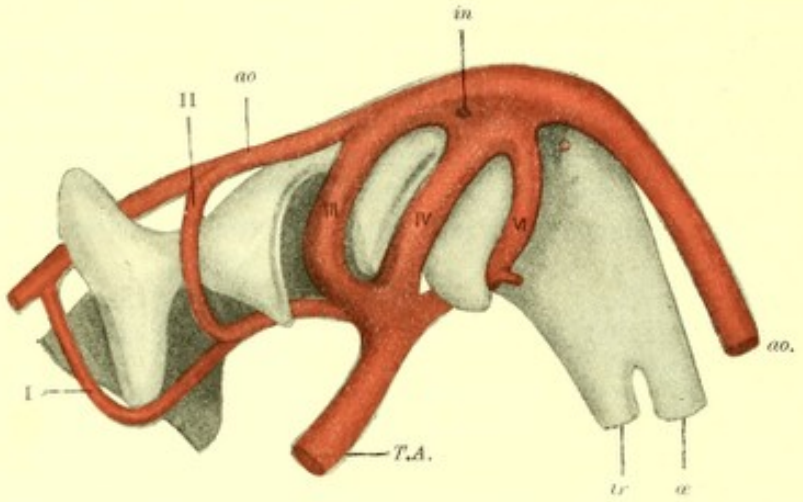



FIG. 272.—THE AORTIC ARCHES IN A HUMAN EMBRYO OF 5 MM. LONG. (After Tandler.)

The arches are represented in their relations to the visceral pouches of the pharynx. I to VI aortic arches; *T.A.*, truncus arteriosus; *ao*, dorsal aorta; *tr*, trachea; *œ*, œsophagus; *in*, island.

the heart is gradually displaced backwards, the truncus arteriosus comes to lie first opposite the third and then opposite the fourth arch, so that all save the pulmonary now spring from the ascending limb or, as it may be termed, the

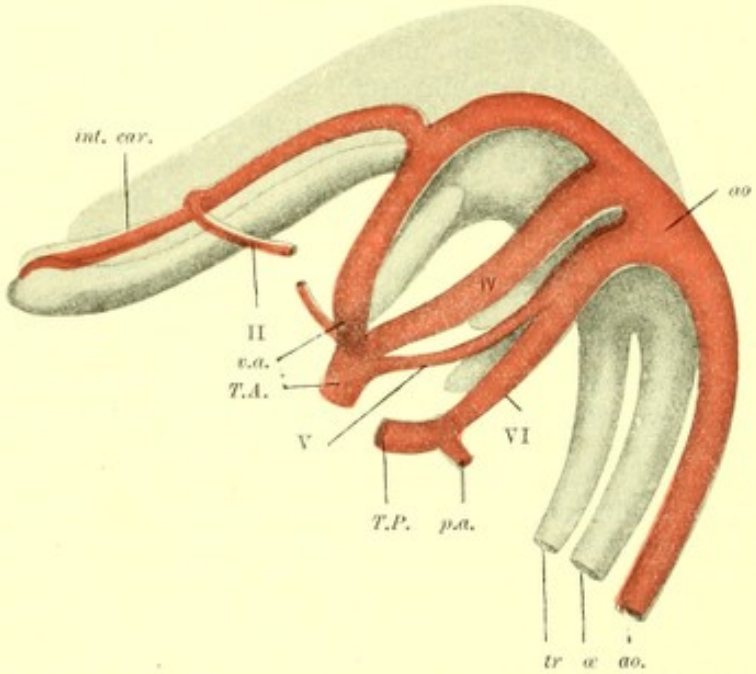



FIG. 273.—THE AORTIC ARCHES IN A HUMAN EMBRYO OF 9 MM. LONG. (After Tandler.)

I to VI aortic arches; *T.A.*, truncus arteriosus; *v.a.*, ventral aorta; *T.P.*, truncus pulmonalis *p.a.*, pulmonary artery; *int.car.*, internal carotid artery. Other lettering as in fig. 272.

ventral aorta. At the stage when the truncus lies opposite the fourth arch the aortic septum begins to develop in its lumen backwards from the interval between the systemic and pulmonary arches; when it has completed the division of the trunk into the aorta and pulmonary artery the aorta remains connected

with the four anterior pairs of arches and the pulmonary artery with the pulmonary pair alone.

The first and second arches early become interrupted in their course, but the dorsal part of the second, and possibly also of the first, persist and take part in the formation of an embryonic vessel called the *stapedial artery* (see below). The third arch remains complete, and is for a time the largest of the series. The dorsal aorta between the third and fourth arches next becomes obliterated, and the carotid system of vessels begins to take shape. The ventral aorta in front of the third arch, now disconnected from the dorsal aorta, becomes the *external carotid*; the third arch and the dorsal aorta constitute the *internal carotid*; and the ventral aorta behind the third arch is the *common carotid*. This is at first very short, but when the heart is displaced backwards, and the neck is formed it becomes much drawn out, and the internal carotid assumes a directly ascending course by the straightening out of the third arch.

The *fourth arches* persist on both sides, but the left early assumes larger proportions. When, somewhat later, the dorsal aorta on the right side is obliterated between the fourth arch and the point of fusion of the two dorsal aortæ into the descending aorta, the *left* fourth arch alone remains in connexion with that vessel and forms the aortic arch (in the strict morphological sense of that term); while the *right* fourth arch becomes the first part of the subclavian artery. At an early stage, when the truncus arteriosus has been displaced backwards to the level of the fourth arches, the proximal segment of the ventral aorta forms a common stem for the fourth and third arches. On the right side this becomes the *innominate artery*; but on the left side, though the arrangement is at first symmetrical, the common stem contracts as the fourth arch enlarges, and is only represented by the portion of the adult arch between the origins of the innominate and left common carotid arteries. The *pulmonary arch* on each side at an early stage gives off a branch which runs along the developing lung-rudiment of its own side. On the right side, the portion of the arch distal to this disappears at the same time as the section of the dorsal aortæ with which it was at first connected. On the left side, however, it persists as the *ductus arteriosus* connecting the pulmonary

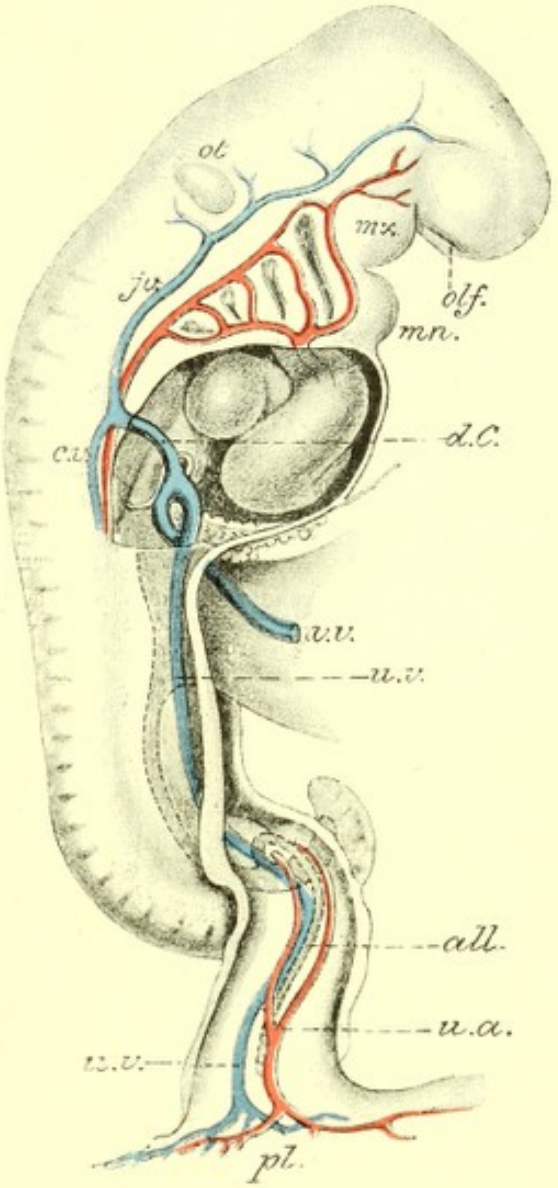



FIG. 274.—PROFILE VIEW OF A HUMAN EMBRYO OF ABOUT THREE WEEKS, SHOWING ALL THE CEPHALIC VISCERAL ARCHES AND CLEFTS.

*mx*, maxillary process; *mn*, mandibular arch; *d.C.*, duct of Cuvier; *j.v.*, jugular vein; *c.v.*, cardinal vein; *v.v.*, vitelline vein; *u.v.*, umbilical vein; *u.a.*, umbilical artery; *all*, allantois; *pl*, placental attachment of allantoic stalk; *olf*, olfactory depression; *ot*, otic vesicle.

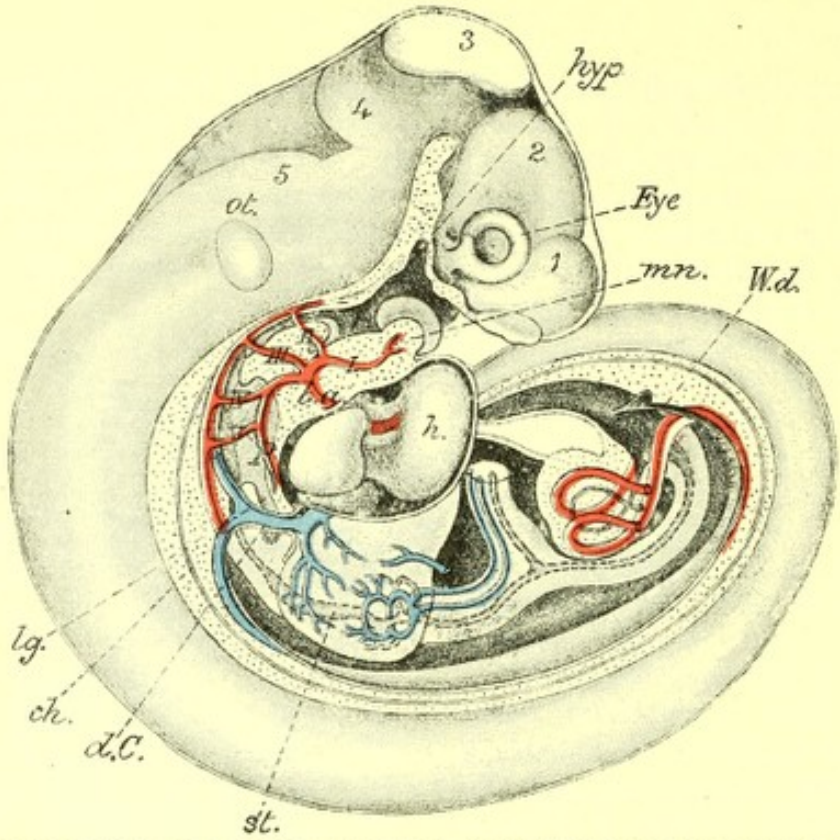



FIG. 275.—PROFILE VIEW OF A HUMAN EMBRYO OF ABOUT THREE OR FOUR WEEKS, SHOWING THE PRINCIPAL ARTERIES AND VEINS. (His.)

1, 2, 3, 4, 5, the secondary cerebral vesicles; *hyp*, hypophysis; *ot*, otic vesicle; *mn*, mandibular arch; *lg*, lung-rudiment; *st*, stomach; *W.d.*, Wolffian duct opening into cloaca; *I*, *II*, *III*, *IV*, *V*, the arterial arches springing from *b.a.*, bulbus arteriosus; *p*, pulmonary artery; *d.C.*, duct of Cuvier; *ch*, notochord.

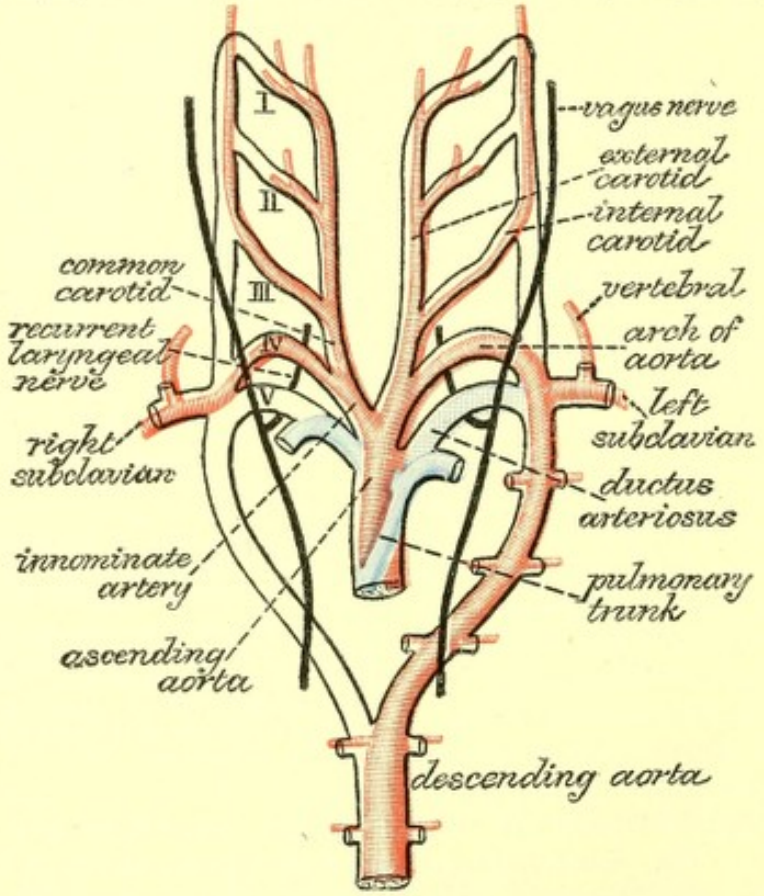



FIG. 276.—DIAGRAM TO SHOW THE DESTINATION OF THE ARTERIAL ARCHES IN MAN AND MAMMALS. (Modified from Rathke.)

The truncus arteriosus and five arterial arches springing from it are represented in outline only, the permanent vessels in colours—those belonging to the aortic system red, to the pulmonary system blue. This diagram is retained here in order to present the traditional account of the development of five aortic arches handed down from Rathke. The recent views are presented in fig. 277.

artery with the aorta. After birth this is obliterated and forms the *ligamentum arteriosum*.

The inferior laryngeal nerves at an early stage reach their destination by passing behind the pulmonary arches. When the heart is displaced backwards and the systemic and pulmonary arches are carried with it, the points of origin of the nerves from the vagus trunks are necessarily also drawn backwards, and they assume their recurrent course. On the left side the primitive relationship to the pulmonary arch is maintained—*i.e.* the nerve loops round the obliterated ductus arteriosus; but on the right side, on account of the disappearance of this part of the arch, it comes

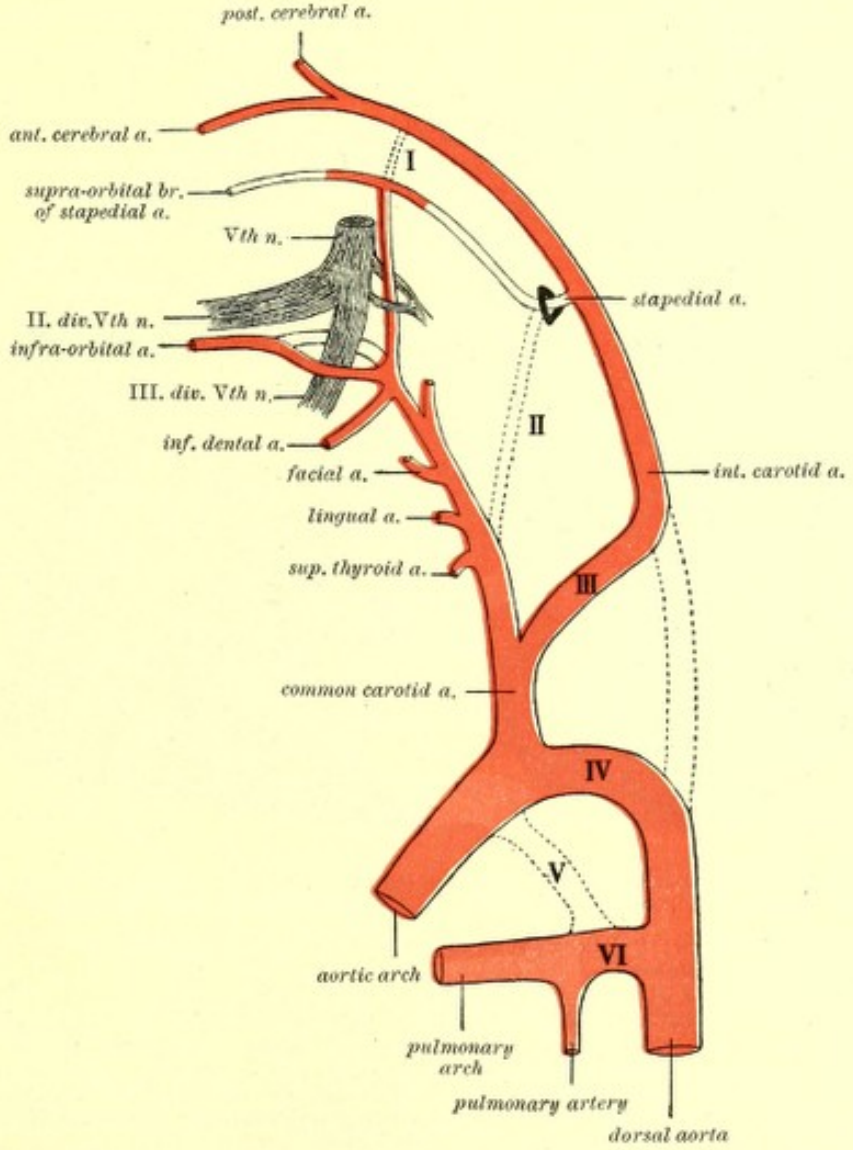



FIG. 277.—DIAGRAM TO ILLUSTRATE THE FATE OF THE AORTIC ARCHES AND THE ORIGIN OF THE MAIN BRANCHES OF THE CAROTID SYSTEM OF ARTERIES. (Founded on Tandler.)

to loop round the persistent fourth arch—*i.e.* the first portion of the subclavian artery.

**Carotid system** (fig. 277).—The *dorsal aortæ*, now the *internal carotids*, are seen at an early stage to be continued from the dorsal roots of the first arches to the developing brain. Each divides into an anterior and a posterior branch. The anterior stem ends at first in the mesial nasal process and afterwards in the septum nasi. This terminal branch is, however, afterwards obliterated, and the stem ends in the *ophthalmic* to the developing eye (the future central artery of the retina), the *anterior cerebral*, and *middle cerebral*. The posterior branch

sweeps backwards, gives branches to the brain, afterwards concentrated chiefly in the *posterior cerebral*, and joins the *cerebral portion of the vertebral* (see below) to form the *circle of Willis*.

The *ventral aortæ*, now the *external carotids*, extend forwards into the mandibular arches. In its course each gives off as secondary branches the *superior thyroid*, *lingual*, and *facial*, and then, turning backwards to reach the proximal end of Meckel's cartilage, it turns inwards and forwards on its lateral aspect to be joined to the mandibular branch of the stapedial artery by an anastomosing branch.

The *stapedial artery*, though only an embryonic vessel in man and some other mammals, persists in others, such for instance as the rat. It arises in that

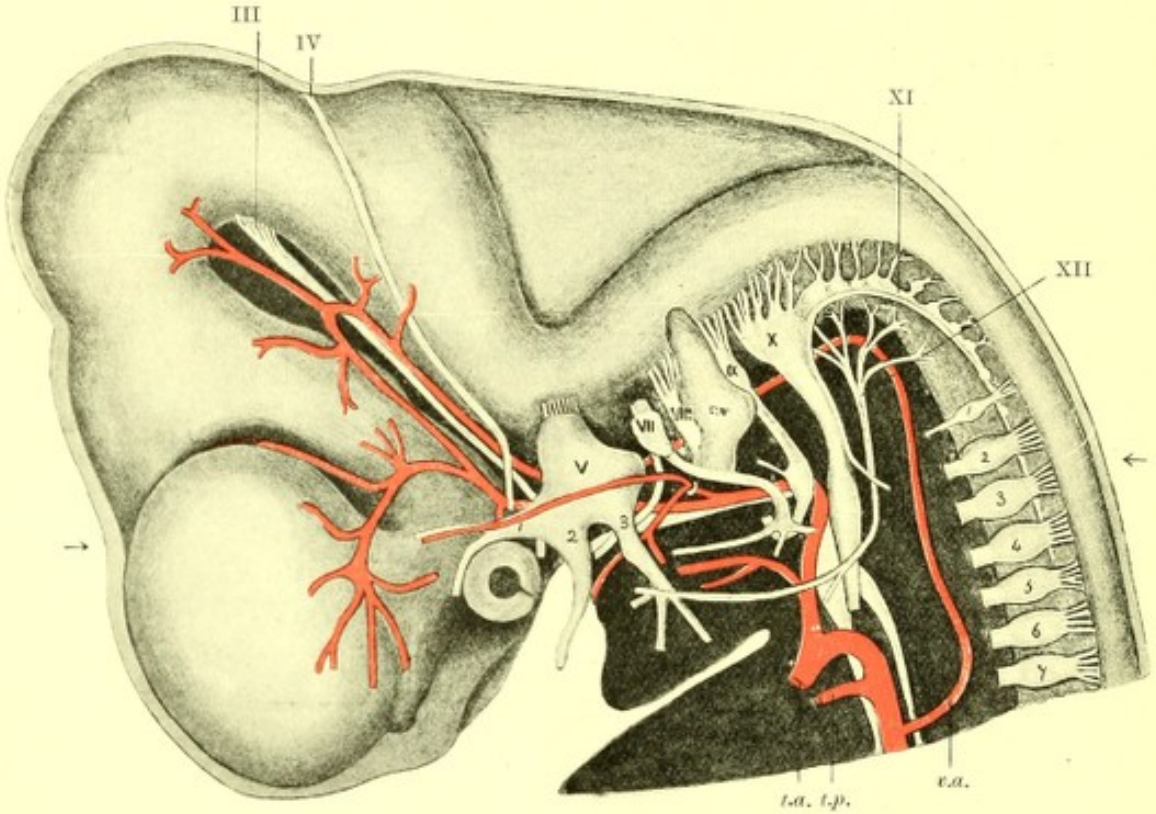



FIG. 278.—DIAGRAM REPRESENTING THE NERVES AND ARTERIES OF THE HEAD OF AN EMBRYO OF THE FIFTH WEEK, FOUNDED ON RECONSTRUCTIONS BY TANDLER, MALL, AND STREETER. (T. H. Bryce.)

I to XII, cerebral nerves; 1, 2, 3, three branches of fifth nerve; the sixth nerve is not labelled—it is seen passing forwards below 3.

The truncus arteriosus, *T.A.*, is continued forward as the common carotid, which divides into external and internal carotids. The latter arching forward between the vagus (X) and glossopharyngeal (IX) nerves passes mesial to the nerve-roots to the brain, and gives off two terminal branches—an anterior which supplies the posterior middle and anterior cerebral arteries, and a posterior which joins the vertebral, *V.A.*, to form the primitive circle of Willis. Below the auditory vesicle *av.*, the stapedial artery is seen passing through the annulus stapedialis and supplying supra-orbital, infra-orbital, and mandibular branches accompanying the three divisions of the fifth nerve.

animal (Tandler) from the dorsal persisting portion of the second arch, and is continued forwards as a longitudinal anastomosis between the second and first arches. In man its origin and course is the same (figs. 277, 278), but the share taken by the first arch is not certainly known (Tandler). At its origin it passes through the rudiment of the *stapes*, and later between the limbs of the ossicle. The artery gives off two trunks—a *superior* and an *inferior*. The superior passes forward on the mesial aspect of the Gasserian ganglion to the roof of the orbit (*supra-orbital*); the inferior divides below the Gasserian ganglion into an *infra-orbital* branch which runs forwards mesial to the mandibular root of the ganglion, and a *mandibular* which accompanies the mandibular nerve (fig. 278). The

mandibular branch becomes joined by an anastomosis with the external carotid; and later, when the stapedial artery proper becomes obliterated, this anastomosing vessel becomes the *internal maxillary artery*; thus the original branches of the stapedial become branches of that artery (fig. 277). The descending trunk, which passes between the roots of the auriculo-temporal nerve, becomes the *middle meningeal* and the *inferior dental*. The infra-orbital branch passes at first mesial to the mandibular nerve; but a vascular ring forms, in the generality of cases, on its outer side, and the deeper vessel becomes obliterated. The occasional orbital branch of the middle meningeal represents the original forward continuation of the stapedial artery to the orbit.

**Segmental vessels; vertebral and subclavian arteries.**—A series of segmental branches arise from the dorsal aortæ, and also from the common aortic stem. The first of these accompanies the hypoglossal nerve to the side of the brain (*hypoglossal artery*), and from this a vessel (*cerebral part of vertebral artery*) extends forwards to join the posterior branch of the internal carotid (*circle of Willis*). The two vertebrals fuse below the hind-brain to form the *basilar artery*. According to de Vriese, the two vessels become connected by a network, and out of this a new mesial channel is developed. The next seven segmental arteries and the hypoglossal artery are joined by an anastomosing vessel; when the heart and aortic arches are displaced backwards the arteries are obliterated, but the anastomosing vessel persists as the cervical part of the vertebral (fig. 278). From the seventh cervical segmental artery the *subclavian* arises as a lateral branch and passes into the limb-bud. As the limbs increase in size the subclavians become larger than their parent vessels; the vertebral arteries therefore now appear as branches of the subclavian stems. The upper thoracic segmental arteries likewise become obliterated, and an anastomosis developed between them becomes the *superior intercostal*. The remaining thoracic and lumbar segmental vessels become the *intercostal* and *lumbar* arteries.

**Vitelline (omphalo-mesenteric) arteries.**—The aorta at an early stage supplies a number of arteries segmentally arranged to the yolk-sac (Mall; Tandler [1]), but ultimately only one pair persists. The two arteries pass out on each side of the intestine to the yolk-sac. Later, when the embryo is cut off from the yolk-sac, only a single stem is found running to the umbilicus in the mesentery of the vitelline loop. 'Reaching the extremity of the loop, it divides into two branches which encircle the intestine, uniting again into a single trunk at the attachment of the yolk-stalk' (Bonnot and Seevers [2]). This arterial ring suggests that the two arteries have fused with one another except where they surround the intestine, rather than that one of the pair has atrophied, as has usually been stated. In either case, one side of the ring disappears and a single vitelline artery is left. When the yolk-circulation has been obliterated, the whole of the artery distal to the intestine disappears and the remainder persists as the *superior mesenteric artery*. The omphalo-mesenteric or superior mesenteric artery has thus at first several roots. These are united by a longitudinal anastomosis, which persists as the anterior roots are one by one lost. The cœliac artery represents one of the primary roots of the omphalo-mesenteric (Tandler). The remaining visceral arteries arise as secondary branches from the aorta.

The allantoic arteries run at first, closely applied to the intestine and mesial to the Wolffian ducts, to the stalks of the allantoic diverticulum. Later another channel is formed on each side external to the duct (*secondary caudal arch* of Young and Robinson), and the mesial vessels disappear. From the new

[1] Mall, Journ. of Morph. xii.; Tandler, Anat. Hefte, xxii. and xxv.
[2] Bonnot and Seevers, Anat. Anzeiger, xxix. 1906.

vessels the arteries to the posterior extremities and the vessels to the pelvic viscera arise.

**Arteries of the limbs.**—The limb-arteries are first laid down in the limb-bud in the form of a plexus of capillary loops (see fig. 223, p. 178). This plexus arises probably not from a single vessel, but from several representing a segmental series. E. Müller has described a plexus in the developing upper limb related to the nerves of the brachial plexus which he regards as being suggestive of a primitive segmental arrangement, but he did not observe a stage in which there was more than one subclavian artery.[1] As the nerves extend into the growing limb-buds, the capillary loops follow mainly the course of the nerves (De Vriese, E. Müller[2]), and the definitive arteries are formed by the enlargement of certain of these loops. The main arterial stems are at first central, but later the lateral branches assume larger proportions, and the primitive arrangement is lost. In the arm the primary brachial stem is continued to the forearm and hand, as a mesial vessel (in part the future anterior interosseous) which pierces the carpus and extends to the dorsal aspect of the hand. This artery soon recedes in importance, and the loop accompanying the median nerve becomes the main artery of the forearm. This in turn becomes a secondary stem owing to the enlargement of lateral loops which become the ulnar and radial arteries. The original artery of the lower limb accompanies the *sciatic* nerve, but a new vessel represented by the *external iliac* and the *femoral* appears later. This anastomoses above the knee with the sciatic artery, and then becomes the main artery of the limb, the original vessel becoming reduced to the *arteria comes nervi ischiatici*. The primary stem is continued to the leg and foot as an interosseous artery, which, like that of the arm, pierces the tarsus and reaches the dorsum of the foot. It is represented in part by the *peroneal artery*. The *anterior* and *posterior tibial arteries* are secondary loops enlarged to form the main arteries.

## DEVELOPMENT OF THE PRINCIPAL VEINS.

At the fifteenth day, as we have already seen (p. 63), the *ductus venosus* receives three veins on each side, the vitelline from the yolk-sac, the umbilical (allantoic) from the body-stalk, and the ducts of Cuvier, formed by the union of the anterior and posterior cardinal veins.

**Vitelline veins.**—The vitelline or omphalo-mesenteric veins enter the abdomen along the vitelline duct and ascend at first along the front of the alimentary canal, but higher up they come to lie on either side of that tube (duodenum). Here transverse communications form between the two veins, two in front of, and one behind the duodenum, so that the gut is encircled by two vascular rings (figs. 279, 280). Above these venous circles the direct communication with the sinus becomes lost, the intermediate venous vessel on either side becoming broken up within the substance of the liver (which has by this time developed around them) into a vascular network. The vascular network is produced by the breaking up of the large vessels by the hepatic epithelial cylinders which grow into and cut up the lumen into a network of capillary-like spaces (*sinusoids*, Minot).

The vessels which pass from the upper venous ring to the liver sinusoids are known as *venæ advehentes*: they become the branches of the portal vein; those which pass from it into the sinus are the *venæ revehentes*: they become the hepatic veins.

[1] That the limb-arteries are in the first instance segmentally arranged was on theoretical grounds suggested many years ago by Macalister (Journ. of Anat. and Phys. xx. 1886) and by Mackay (Memoirs and Memoranda in Anatomy, Cleland, i. 1889). Hans Rabl has recently brought forward some objective evidence in favour of this hypothesis (Arch. f. mikr. Anat. lxix. 1907).

[2] De Vriese, Bertha, Arch. de Biologie, xviii. xxi.; E. Müller, Anat. Hefte, xxii. xxvii.; see also Göppert, Ergebnisse der Anat. und Entwickelungsgeschichte, xiv. 1905.

The lower communication between the vitelline veins takes the form of a complete longitudinal fusion of the two vessels, at least for some distance. This fused part receives veins from the intestine and stomach, and becomes the

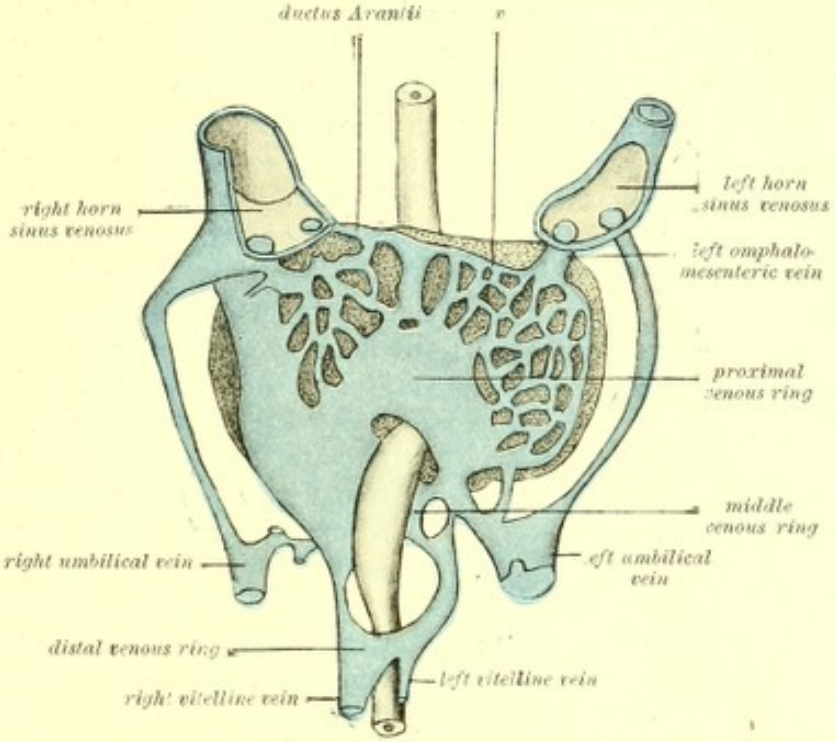



FIG. 279.—THE VEINS OF THE LIVER OF A HUMAN EMBRYO OF 6·9 MM. (After Ingalls.)

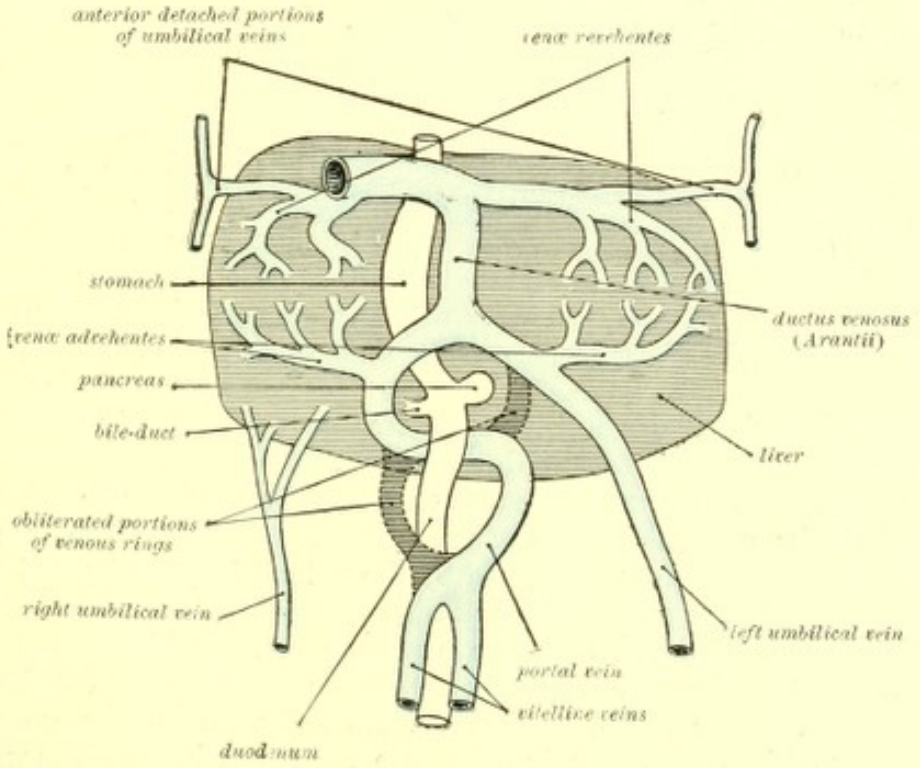



FIG. 280.—THE LIVER, AND THE VEINS IN CONNECTION WITH IT, OF A HUMAN EMBRYO, TWENTY-FOUR OR TWENTY-FIVE DAYS OLD, AS SEEN FROM THE VENTRAL SURFACE. (After His.) (Copied from Milnes Marshall's Embryology.)

commencement of the portal vein. At a later date the vitelline veins distal to this point are obliterated, and the new veins in the mesentery become the tributaries of the portal vein of the adult.

The **umbilical veins** are for a time double within the abdomen, although they have fused within the umbilical cord into a single trunk. Diverging from this, they pass to the sinus on either side in the somatopleure, just where this is becoming bent round into the amnion (fig. 81, p. 56). After a time, however, it is found that this direct communication with the sinus is partially interrupted by the development of a vascular network, and that on the left side a fresh communication has become established with the upper venous circle of the vitelline veins. The interruption subsequently becomes complete on both sides (fig. 280), and on the right side the greater part of the vein becomes atrophied (on both sides the part which originally opened into the sinus venosus remains evident for a time) (fig. 279). The left vein, on the other hand, increases in bulk with the development of the placental circulation. For a short time the whole of its blood, as well as that of the vitelline vein, passes through the capillaries of the liver. But a branch is soon seen passing from the upper venous circle direct into the right hepatic vein, near its entrance into the sinus. This forms the *ductus venosus* (Arantii) or *vena ascendens*, and it now carries most of the blood of the umbilical vein direct to the heart. Subsequently the left hepatic vein loses its direct communication with the sinus venosus, and comes to open into the right hepatic where it is joined by the ductus venosus. The channel conveying the blood from the three vessels is called the common hepatic vein, and this vein becomes later connected with the vessel which gives rise to the inferior vena cava (see below).

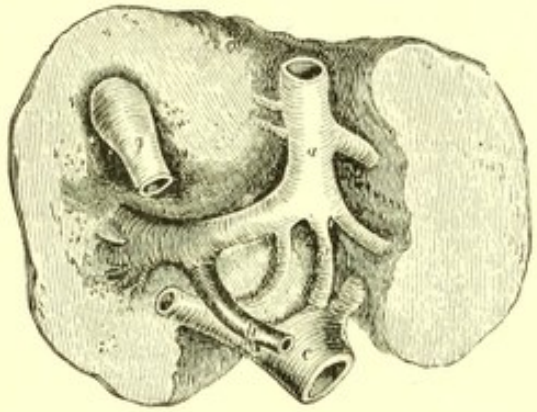


FIG. 281. — UNDER-SURFACE OF THE FŒTAL LIVER, WITH ITS GREAT BLOOD-VESSELS, AT THE FULL PERIOD.

*a*, the umbilical vein, lying in the umbilical fissure, and turning to the right side, at the transverse fissure (*o*), to join the vena portæ (*p*); *d*, the ductus venosus, continuing straight on to join the vena cava inferior (*c*); some branches of the umbilical vein pass from *a* into the substance of the liver; *g*, the gall-bladder, cut.

The lower part of the portal vein is formed, as we have seen, by the united vitelline veins. The upper part is formed as a single trunk out of the double venous annulus by atrophy of the right half of the lower ring and the left half of the upper (fig. 280). The spiral turn around the duodenum is thereby produced, and thus it is also that the portal vein at first appears more directly connected with the right venæ advehentes than with the left. Most of these embryonic veins are at first of relatively large size and have an irregular sinus-like character (fig. 279), which disappears at a later stage of development.

**Cardinal veins.**—On the thirteenth day, two short transverse venous trunks, the *ducts of Cuvier*, open, as has been above stated, one on each side, into the sinus venosus of the heart. Each is formed by the union of a superior and an inferior vein, named respectively the *anterior* and the *posterior cardinal*.

The *posterior cardinal* veins are the primitive vessels which return the blood from the Wolffian bodies and body-walls. They receive *segmental* veins all along their course, and in the region of the Wolffian body are largely broken up into sinus-like spaces (sinusoids). Behind they are continued into vessels which afterwards become the *internal iliacs*, and these receive, when the limbs develop, the *sciatic* and then the *external iliac* veins.

At first all the blood from the trunk is returned through the cardinals and ducts of Cuvier, but by a series of changes the cardinal system of veins is tapped by the hepatic system, and a new channel is opened up, which becomes the *inferior vena cava*. In the region of the Wolffian body the cardinals receive a series of

small veins from the mesentery, which are united with one another across the front of the aorta. These unite with one another on each side to form a pair of longitudinal anastomoses (*subcardinal veins*, Lewis), running parallel to the cardinal veins and united with them at both ends as well as by many small veins along their course (fig. 282). The cross-connexion between the two subcardinal veins next becomes limited to one large anastomosis below the superior mesenteric artery (fig. 283). The right subcardinal now acquires a secondary connexion with the hepatic veins on

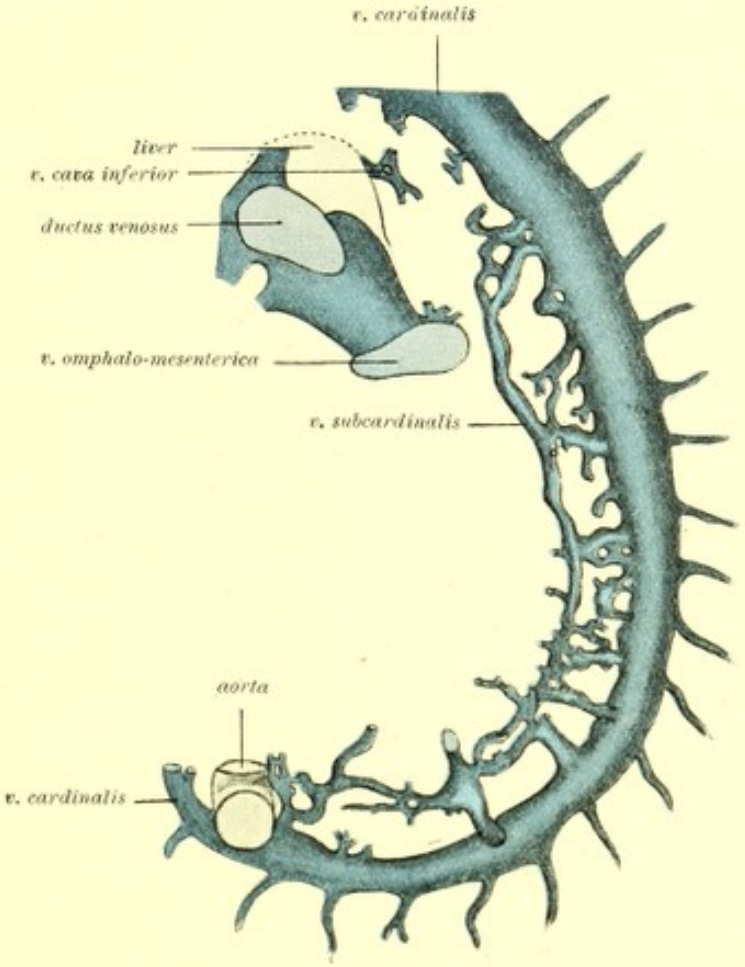



FIG. 282.—DEVELOPMENT OF THE INFERIOR VENA CAVA IN THE RABBIT-EMBRYO (FIRST STAGE). (After Lewis.)

the dorsal aspect of the liver, and as the blood comes to take this new short cut to the heart the portion in front of the anastomosis becomes rapidly enlarged.

According to Hochstetter's account [1] (with which that of Lewis here followed otherwise agrees in every essential respect), this connexion is established by a new channel which arises from the common hepatic (original right vitelline) vein, and first appears as a small vessel which passes downwards, through a cœlomic fold which is named the *caval mesentery* along the mesial surface of the Wolffian body, where it forms the vein called by Lewis the right subcardinal. A similar vessel appears simultaneously on the left side, and the two are connected by the anastomosis already mentioned.

The right subcardinal, thus enlarged, becomes a portion of the vena cova, while the disconnected anterior part of the left subcardinal probably persists as the left suprarenal vein. The portions of both subcardinals behind the cross-anastomosis diminish in size and disappear as blood-channels; the corresponding sections of the two cardinal veins, which are connected with one another across the middle

[1] For references, see Hochstetter's article in Hertwig's Handbuch III. Th. ii. and iii. p. 161 *seq.* More recent papers are Lewis (rabbit), Amer. Jour. of Anat. i.; Dexter (cat), *ibid.* i.; Miller (bird), *ibid.* ii.; Bonne (rabbit and sheep), Jour. d'Anat. et de la Phys. xxxix. 1904; Soulie et Bonne (mole), *ibid.* xli. 1906.

line through the pre-aortic subcardinal anastomosis, on the other hand, enlarge. As the permanent kidneys assume their definitive position a series of changes takes place, which need not here be entered on, until ultimately the renal veins are found opening into the cardinals at the level of the cross-anastomosis, and close to them the veins from the sex glands, spermatic or ovarian. The cardinals are at first symmetrical, but the sections behind the anastomosis are now larger than the sections in front of it.

It will be convenient to trace the fate of these portions separately. A series of *post-aortic* anastomoses is formed between the posterior and Wolffian sections of the veins. One of these (transverse iliac vein) enlarges, and now all the blood from the pelvis and limbs passes into the right cardinal, which accordingly increases in size and becomes the posterior part of the *vena cava inferior*, while the left

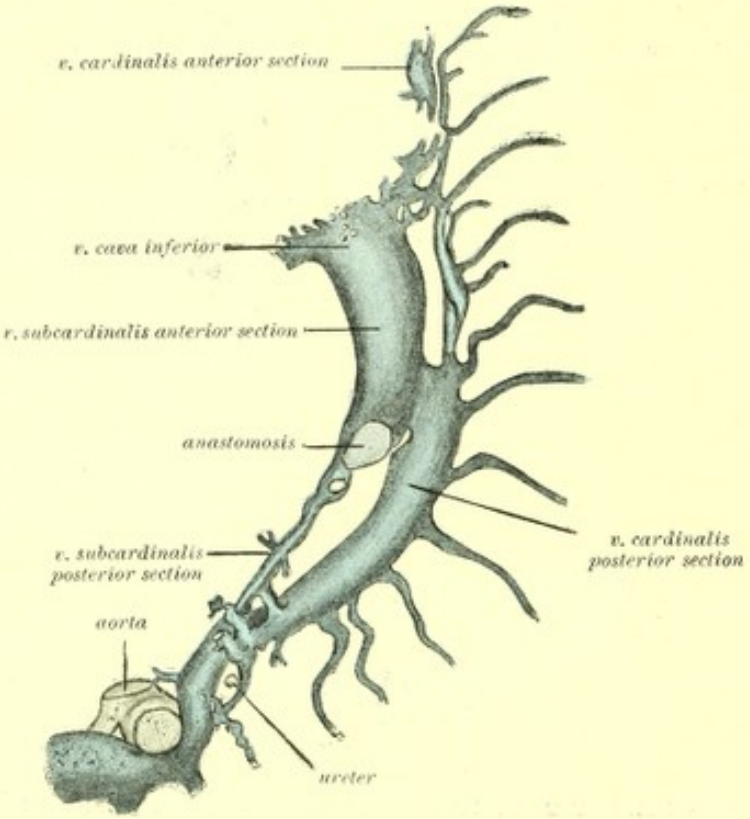



FIG. 283.—DEVELOPMENT OF THE INFERIOR VENA CAVA IN THE RABBIT-EMBRYO (SECOND STAGE). (After Lewis.)

diminishes and ultimately forms the small *ascending lumbar vein* (fig. 284). The transverse iliac vein becomes the terminal portion of the left common iliac of the adult, and the other anastomoses carry the lumbar veins over the vertebral column to the right cardinal, now the vena cava. *The inferior vena cava is thus a composite vessel formed from* (1) *the common hepatic vein ;* (2) *branches of the hepatic in the liver ;* (3) *right sub-cardinal ;* (4) *lower part of the right cardinal.*[1]

The upper portions of the posterior cardinals become the azygos veins. The right remains complete as the *vena azygos major ;* the left is interrupted by the development of one or more post-aortic anastomoses. The lower portion becomes

[1] In a preliminary note, which has appeared since the above was written, Huntington and McClure (Amer. Jour. of Anat. vi.) describe the development of the post-cava in the cat rather differently. According to them, a pair of veins develops dorso-median to the primitive posterior cardinal by longitudinal anastomosis between somatic post-cardinal tributaries. These form the post-renal parts of the post-cava by a secondary median fusion by means of post-aortic anastomoses, and also become the azygos veins, replacing the primitive cardinals. Only in its pre-renal section has the primitive cardinal any part in forming the vena cava inferior.

the *vena azygos minor*, opening through an anastomosis into the vena azygos major. The upper part becomes the *hemi-azygos superior*.

The *anterior cardinal* veins return the blood in the first instance from the developing brain. The primitive vein passes in the early stages *mesial* to the auditory vesicle and the roots of the cerebral nerves (fig. 286). Towards the end of the first month it becomes shifted to their lateral aspect by the formation of vascular rings round them, which are joined up on the outer side to form a new vein (*vena capitis lateralis*) (fig. 285). The original vein becomes the *internal jugular* behind the last cerebral nerve-roots. In front the channel where it lies mesial to the Gasserian ganglion persists as the *cavernous sinus*; between the fifth and twelfth nerves it is apparently obliterated, but is re-established at a later date as the *inferior petrosal sinus*. The vena capitis lateralis thus extends from the anterior end of the jugular vein, lateral to the nerve-roots and auditory vesicle to the fifth nerve. Near its posterior extremity it is joined by a branch accompanying the vagus (*vena cerebralis posterior*) and at its anterior extremity by a branch emerging between the fifth and seventh nerves (*vena cerebralis media*) (fig. 287). The first collects the blood from the hind-brain, the second from the region of the cerebellum. The anterior cardinal lying mesial to the trigeminal ganglion (cavernous sinus) receives a vein from the eye (*ophthalmic*), and is continued forwards as a vein (*vena cerebralis anterior*) which collects the blood from the cerebral hemisphere rudiment. Its terminal branch encircles the hemisphere and becomes the *superior longitudinal vein*. This unites with its fellow of the opposite side to form the *superior longitudinal sinus*, which early shows a dilatation marking its posterior end, the *torcular Herophili*. All the blood from the fore-part of the brain is at first returned through the anterior cerebral vein, the persistent anterior part of the cardinal (cavernous sinus), and the lateral vein, into the jugular (fig. 287); but as the hemisphere expands the connexion with the anterior cerebral is lost, and a new anastomosis is formed uniting the longitudinal sinus with the middle cerebral vein, and then with the posterior cerebral vein (fig. 288). The vena lateralis meantime becomes interrupted and finally obliterated, so that all the blood passes through the anastomosis and posterior cerebral into the internal jugular. The new channel is the *lateral sinus* (fig. 289), and the middle cerebral, which now conveys the blood from the cavernous sinus to the lateral sinus, is the *superior petrosal sinus*. Any further change is only one of position, due to the backward extension of the hemisphere.

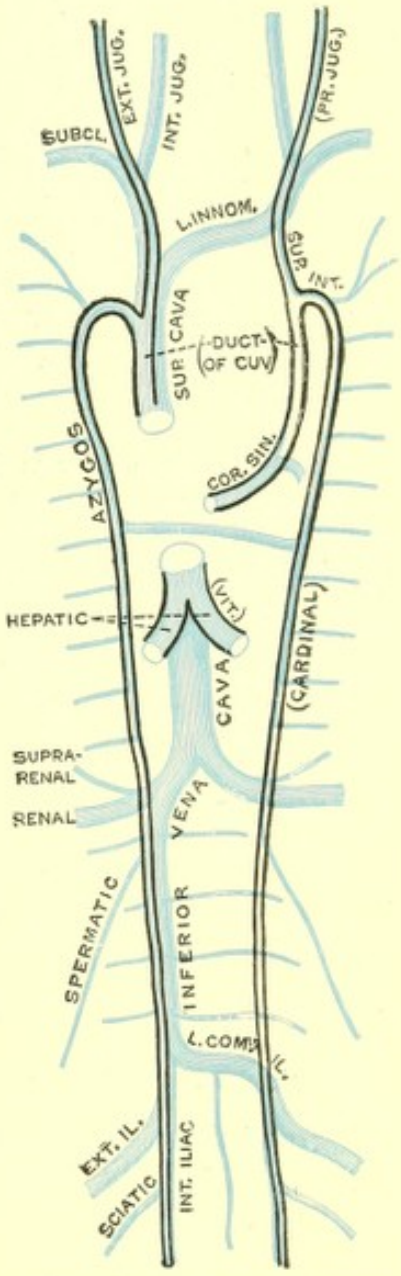



FIG. 284.—SCHEME OF THE DEVELOPMENT OF THE CHIEF VEINS OF THE BODY. (G. D. Thane.)

The primitive venous trunks are indicated by black outlines, and their names are enclosed within parentheses. The definitive veins are represented blue.

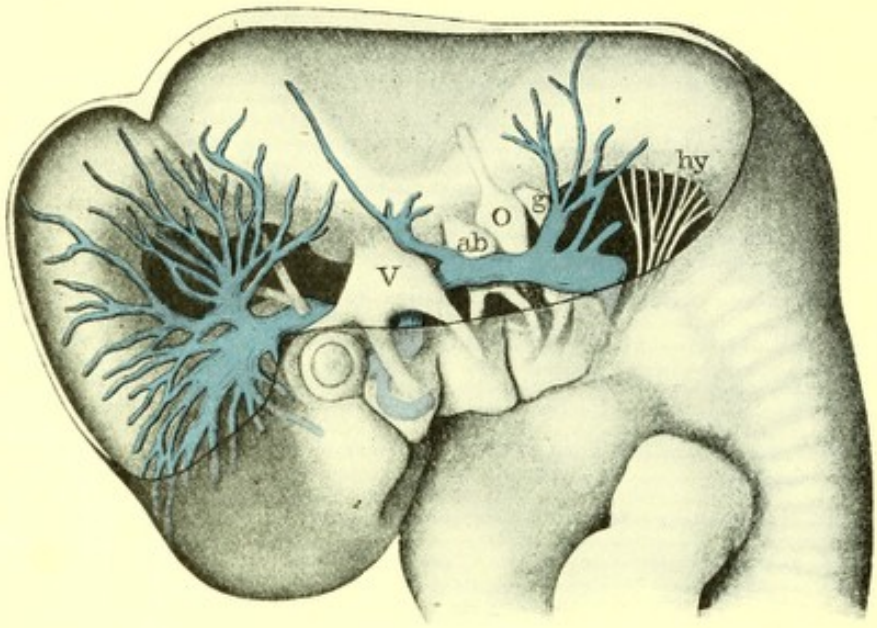



FIG. 285.—RECONSTRUCTION OF THE HEAD OF A HUMAN EMBRYO OF 9 MM. LONG. (Mall.)

The vena cerebralis lateralis is seen to pass on the outer aspect of the posterior cerebral nerve-roots and the auditory vesicle *O*. The vein on the mesial aspect of *V*, the ganglion of the fifth nerve, represents a portion of the primitive jugular. *V*, Gasserian ganglion; *ab*, acoustico-facial ganglion; *O*, auditory vesicle; *g*, glossopharyngeal; *hy*, hypoglossal.

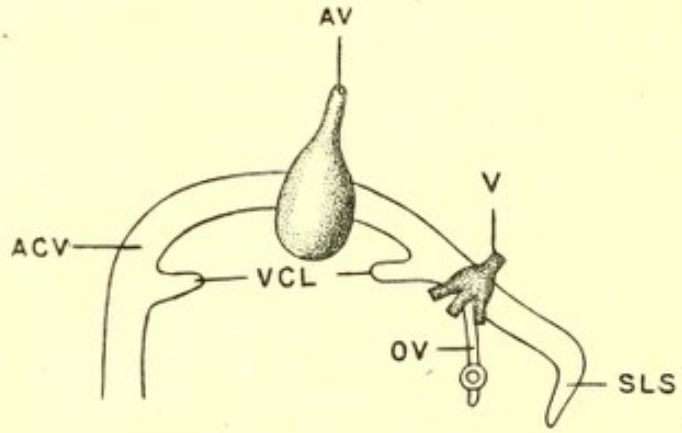



FIG. 286.—DIAGRAM OF THE VEINS OF THE HEAD OF AN EMBRYO OF FOUR WEEKS OLD. (After Mall.)

*ACV*, anterior cardinal vein; *VCL*, vena capitis lateralis; *SLS*, superior longitudinal sinus; *OV*, ophthalmic vein; *V*, fifth nerve; *AV*, auditory vesicle.

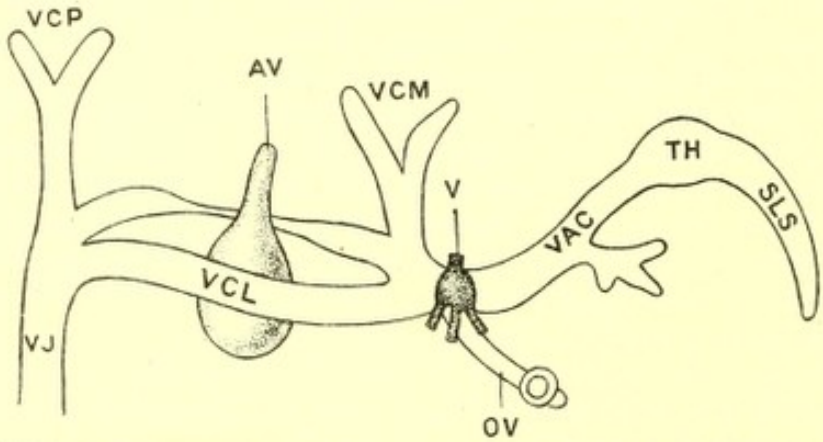



FIG. 287.—DIAGRAM OF THE VEINS OF THE HEAD OF AN EMBRYO OF FIVE WEEKS OLD. (After Mall.)

*VJ*, jugular vein; *VCP*, vena cerebralis posterior; *VCM*, vena cerebralis media; *VAC*, vena cerebralis anterior; *TH* torcular Herophili; *OV*, ophthalmic vein. Other letters as in fig. 286.

The *external jugular* is a secondary channel formed by the union of a superficial facial vein and a vein in the neighbourhood of the ear. It extends backwards and unites with the primitive or internal jugular, near its junction with the *subclavian* vein from the arm.

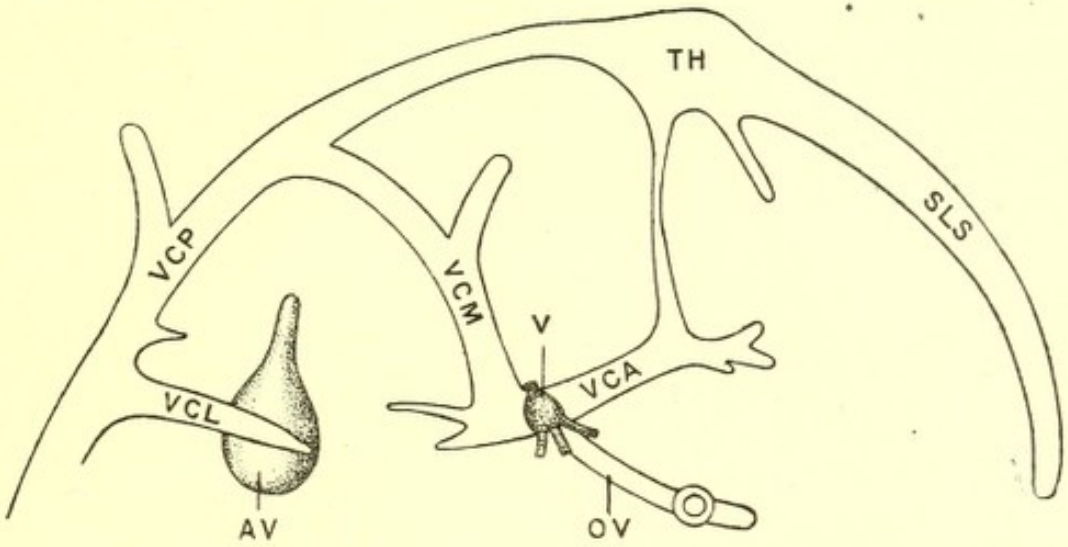



FIG. 288.—DIAGRAM OF THE VEINS OF THE HEAD AT THE BEGINNING OF THE THIRD MONTH. (After Mall.) Lettering as in fig. 287.

A secondary anastomosing vein is formed between the external jugular and the lateral sinus, which emerges through a foramen in the temporal bone (*foramen jugulare spurium*). This occasionally persists in the human adult, and in certain mammals it enlarges and, owing to the disappearance of the primitive jugular, draws all the blood from the cranial sinuses. Salzer

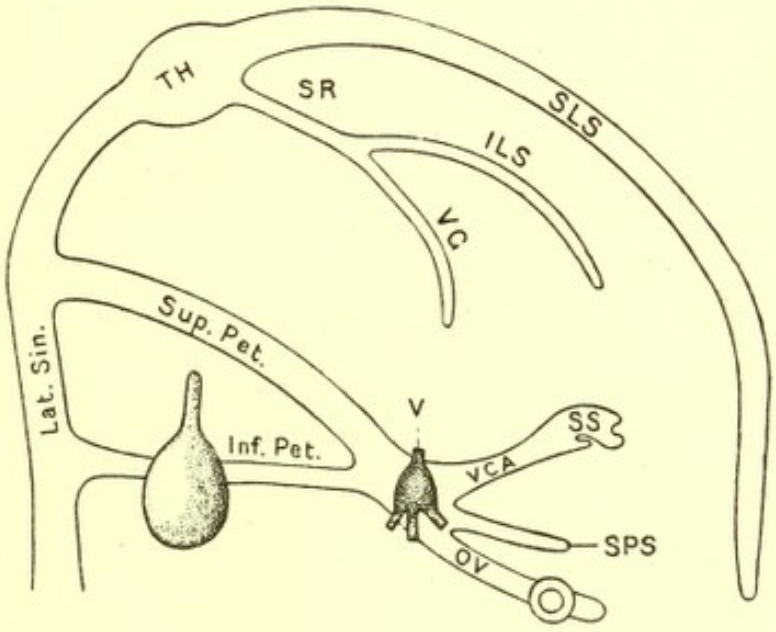



FIG. 289.—DIAGRAM OF THE VEINS OF THE BRAIN OF AN OLDER FŒTUS. (After Mall.)

*Lat.Sin.*, lateral sinus (v. cerebralis posterior); *Sup.Pet.*, superior petrosal sinus (v. cerebralis media); *SS*, Sylvian or middle cerebral vein; *SPS*, sphenoparietal sinus; *SR*, sinus rectus; *ILS*, inferior longitudinal sinus; *VG*, vena galena magna. Other letters as in fig. 287.

(1895) first showed that the view of Luschka, according to which this channel represents the primitive jugular, is untenable; and Mall, whose account has been here followed, has recently confirmed Salzer's descriptions in the case of the human embryo.[1]

[1] Salzer, Morph. Jahrb. xiii.; Mall, Amer. Jour. of Anat. iv. 1905.

The primitive jugular veins are at first symmetrical and join, as already stated, the posterior cardinals to form the ducts of Cuvier. A communicating branch is, however, formed between the point of junction of the left jugular and subclavian veins and the right jugular. This anastomosing vessel is converted into the *left innominate vein*. The portion of the right primitive jugular between the transverse vessel and the right subclavian becomes the *right innominate*, while the portion between it and the entrance of the posterior cardinal (vena azygos major), together with the duct of Cuvier, forms the definitive *superior vena cava*. On the left side the portion of the primitive jugular below the anastomosis becomes the *superior intercostal*, but the duct of Cuvier becomes obliterated (with the exception of a portion which in part forms the coronary sinus). Traces of the vessel are to be recognised even in the adult, in the form of a fibrous strand which runs over the

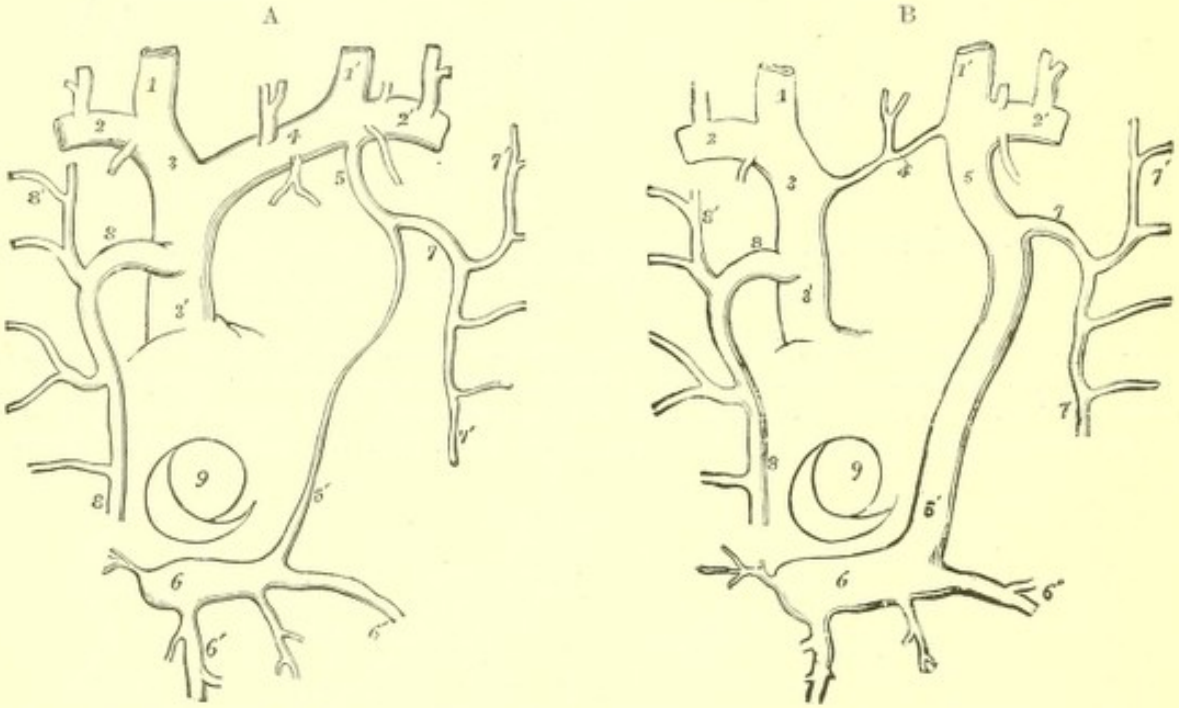



FIG. 290.—A AND B. DIAGRAMMATIC OUTLINES OF THE VESTIGE OF THE LEFT SUPERIOR CAVA AND OF A CASE OF ITS PERSISTENCE. (Sketched after Marshall.) ½.

The views are supposed to be from before, the parts of the heart being removed or seen through.

1, 1′, internal jugular veins; 2, 2′, subclavian veins; 3, right innominate; 3′, right or regular superior cava; 4, left innominate, normal in A, rudimentary in B; 5, in A, the opening of the superior intercostal vein into the innominate; 5′, vestige of the left superior cava or duct of Cuvier; 5, 5′, in B, the left vena cava superior abnormally persistent; 6, coronary sinus; 6′, coronary veins; 7, superior intercostal trunk of the left side (left cardinal vein); 8, the principal azygos (right cardinal vein); 7′, 8′, some of the upper intercostal veins; 9, the opening of the inferior vena cava, with the Eustachian valve.

back of the left auricle, and a small vein (*oblique vein* of Marshall); and in front of the root of the left lung there remains an indication of its former presence in the form of a small fold of pericardium (*vestigial fold* of Marshall).

The left duct of Cuvier has been observed persistent as a small vessel in the adult. Less frequently a right and a left innominate vein open separately into the right auricle, an arrangement which is also met with in birds and in certain mammals, and which results from the vessels of the left side being developed similarly to those of the right, while the cross-branch remains small or absent.

**Veins of the limbs.**—The veins of the limb-buds form, to begin with, a vascular loop with two marginal vessels. Of these latter the *ulnar* and the *fibular* are the primary stems. Each extends down the postaxial border of its proper limb

and over the dorsal aspect of the future hand or foot to the pre-axial border, there to become continuous with a smaller and temporary channel, the *radial* or *tibial* vein respectively. These latter veins are replaced by new (secondary) veins which become the *radial* and *cephalic* in the upper arm (opening at first into the external jugular), and the *long saphenous* in the lower limb. The primary ulnar vein persists in the upper arm as the basilic, axillary, and subclavian veins; the primary fibular, on the other hand, persists in the leg only, as the *short saphenous*. The deep veins which accompany the arteries are later formations.

## PECULIARITIES OF THE FŒTAL ORGANS OF CIRCULATION.

It may be useful here to recapitulate shortly the peculiarities of structure existing in the advanced stage of the formation of the fœtal organs of circulation, with reference to their influence in determining the course of the blood during intra-uterine life, and the changes which occur in them upon the establishment of pulmonary respiration at birth.

The **foramen ovale** has the form of a free oval opening bounded by the septum secundum, and guarded on the side of the left auricle by a valvular plate derived from the septum primum, so that the blood can only pass from the right into the left auricle, not in a contrary direction.

The **Eustachian valve** constitutes a crescentic fold of the lining structure of the heart, which is so situated as to direct the blood entering the auricle by the inferior cava towards the opening of the foramen ovale.

The **ductus arteriosus** establishes a communication between the main pulmonary artery and the aorta, by which the blood from the right ventricle is carried mainly into the dorsal aorta.

The two large **hypogastric** or **umbilical arteries**, prolonged from the iliac arteries, passing out of the body of the fœtus, proceed along the umbilical cord, to be distributed in the fœtal portion of the placenta. From the placenta the blood is returned by the **umbilical vein**, which, after entering the abdomen, communicates by one branch with the portal vein, and is continued by another, named *ductus venosus*, into one of the hepatic veins, through which it joins the main stem of the vena cava inferior.

**Course of the blood in the fœtus.**—The right auricle of the fœtal heart receives blood from the two venæ cavæ and the coronary sinus. The blood brought by the superior cava is simply the venous blood returned from the head and upper half of the body; whilst the inferior cava, which is considerably larger than the superior, conveys not only the blood from the lower half of the body, but also that which is returned from the placenta and the liver. This latter stream of blood reaches the vena cava inferior partly by a direct passage—the *ductus venosus*—and partly by the hepatic veins, which bring to the vena cava inferior all the blood circulating through the liver, whether derived from the supply of placental blood entering that organ by the umbilical vein, or proceeding from the vena portæ or hepatic artery.

The blood of the superior vena cava is believed to pass through the right auricle into the right ventricle, whence it is propelled into the trunk of the pulmonary artery. A small part is distributed through the branches of that vessel to the lungs, and returns by the pulmonary veins to the left auricle; but, as these vessels remain small up to the time of birth, by far the larger part passes through the ductus arteriosus into the descending aorta, and is thence distributed in part to the lower half of the body and the viscera, and in part along the umbilical arteries to the placenta. From these several organs it is returned by the vena cava inferior,

[1] See paper by Lewis, Amer. Jour. of Anat. v. 1905.

the vena portæ, and the umbilical vein ; and, as already noticed, reaches the right auricle through the trunk of the inferior cava.

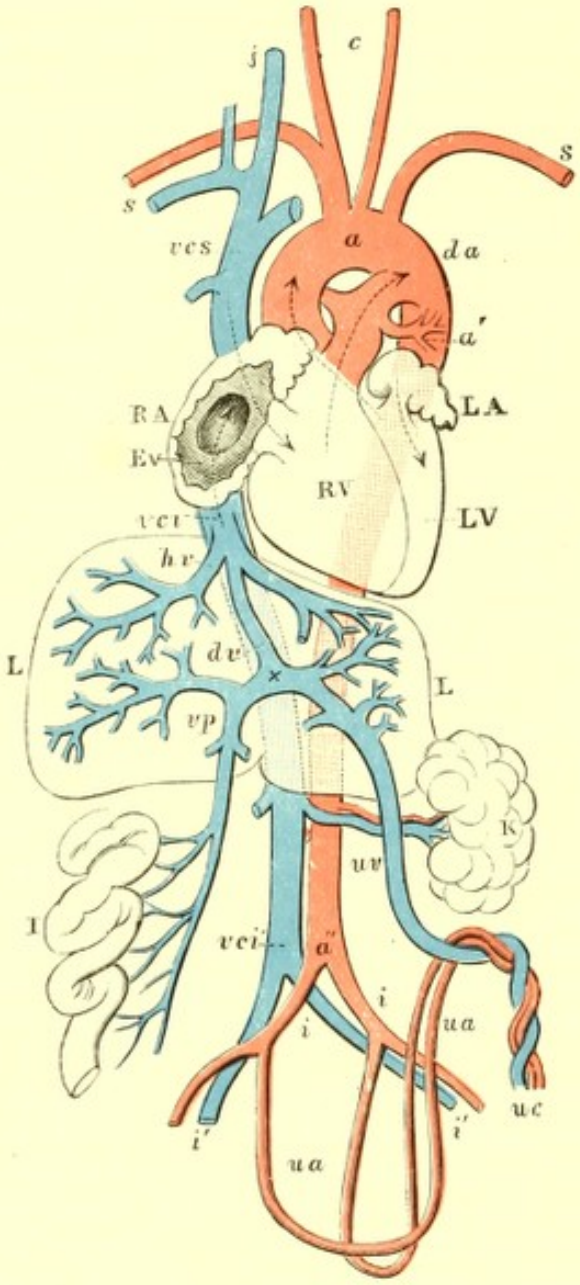



FIG. 291.—DIAGRAMMATIC OUTLINE OF THE ORGANS OF CIRCULATION IN THE FŒTUS OF SIX MONTHS. (Allen Thomson.)[1]

RA, right auricle of the heart; RV, right ventricle; LA, left auricle; Ev, Eustachian valve; LV, left ventricle; L, liver; K, left kidney; I, portion of small intestine; *a*, arch of the aorta; *a'*, its dorsal part; *a''*, lower end; *vcs*, superior vena cava; *vci*, inferior vena where it joins the right auricle; *vci'*, its lower end; *s*, subclavian vessels; *j*, right jugular vein; *c*, common carotid arteries; four curved dotted arrow lines are carried through the aortic and pulmonary opening and the auriculo-ventricular orifices; *da*, opposite to the one passing through the pulmonary artery, marks the place of the ductus arteriosus; a similar arrow line is shown passing from the vena cava inferior through the fossa ovalis of the right auricle, and the foramen ovale into the left auricle; *hv*, the hepatic veins; *vp*, vena portæ; *x* to *vci*, the ductus venosus; *uv*, the umbilical vein; *ua*, umbilical arteries; *uc*, umbilical cord cut short; *i*, *i'*, iliac vessels.

Of the blood entering the heart by the inferior vena cava, it is supposed that only a small part is mingled with that of the superior cava, so as to pass into the right ventricle ; by far the larger portion is thought to be directed by the Eustachian valve through the foramen ovale into the left auricle, and thence, together with the small quantity of blood returned from the lungs by the pulmonary veins, to pass into the left ventricle, whence it is sent into the arch of the aorta, to be distributed almost entirely to the head and upper limbs.

In earlier stages of development than those above described, it is certain that there is little or no separation of the two kinds of blood, for both the umbilical veins from the placenta and the veins from the yolk-sac and body generally, pour their blood together into the sinus venosus, and the mixed blood is then forced through a single somewhat narrowed orifice (*porta vestibuli* of His) into the auricle.

## CHANGES IN THE CIRCULATION AT BIRTH.

The changes which occur in the organs of circulation and respiration at birth, and which lead to the establishment of their permanent condition, are more immediately determined by the inflation of the lungs

[1] In this diagram the arteries are conventionally coloured red and the veins blue, but these colours are not intended to indicate the nature of the blood conveyed by the respective vessels.

with air in the first respiration, the accompanying rapid dilatation of the pulmonary blood-vessels with a greater quantity of blood, and the interruption to the passage of blood through the placental circulation. These changes are speedily followed by shrinking and obliteration of the ductus arteriosus, and of the hypogastric arteries from the iliac trunk to the place of their issue from the body into the umbilical cord; by the cessation of the passage of blood through the foramen ovale, and somewhat later by the closure of that foramen, and by the obliteration of the umbilical vein as far as its entrance into the liver, and of the ductus venosus behind that organ.

The process of obliteration of the arteries appears to depend at first mainly on the contraction of their coats, but this is very soon followed by a considerable thickening of their substance, reducing rapidly their internal passage to a narrow tube, and leading in a short time to final closure, even although the vessel may not present externally any considerable diminution of its diameter. It commences at birth, and is perceptible after a few respirations have occurred. It makes rapid progress in the first and second days, and by the third or fourth day the passage through the umbilical arteries is usually completely interrupted. The ductus arteriosus is rarely found open after the eighth or tenth day, and by three weeks it has in almost all instances become completely impervious.

The process of closure in the veins is slower; but they remain empty of blood and collapsed, and by the sixth or seventh day are generally closed.

Although blood ceases at once to pass through the foramen ovale from the moment of birth, or as soon as the left auricle becomes filled with the blood returning from the lungs, and the pressure within the two auricles tends to be more equalised during their diastole, yet the actual closure of the foramen is more tardy than any of the other changes referred to. It is gradually effected by the union of the valve of the fossa ovalis with the margin of the limbus of Vieussens on the left side; but the crescentic margin is generally perceptible in the left auricle as a free border beyond the place of union, and not unfrequently the union remains incomplete, so that a probe may be passed through the reduced aperture. In many cases a wider aperture remains for more or less of the first year of infancy, and in certain instances there is such a failure of the union of the valve as to allow of the continued passage of venous blood, especially when the circulation is disturbed by over-exertion, from the right to the left auricle; this occurs as the malformation attending the morbus cœruleus.

## THE LYMPHATIC SYSTEM.[1]

**Lymph-vessels.**—Little that is quite certain is known regarding the development of the lymph vascular system. In the lowest vertebrates there is no such system of vessels distinct from the blood vascular system, and the only channels comparable to lymph-vessels are spaces in the connective tissue. In mammals organogenesis is well advanced before there is any sign of walled and valved lymphatic vessels. Up to that stage there are spaces, in certain situations, which no doubt contain lymph, and it has been very generally held that the permanent lymphatics are such spaces round which the connective-tissue cells are arranged to form the walls of the vessels, while the communication with the veins is secondarily acquired (Gulland, Saxer, Sala). On the other hand, Klein described the lymphatics as developing by the hollowing out of mesenchyme (connective-tissue) cells (vasoformative cells), which join with one another to form protoplasmic tubes, the walls of

[1] For literature, see Hochstetter, Hertwig III. Th. ii. and iii. p. 165. Also Sabin, Amer. Jour. of Anat. vols. i. iii. and iv.; Langer (quoted by Sabin), Sitzungsber. d. k. Akad. d. Wissensch. I. Abth. 1868; MacCallum, Archiv f. Anat. u. Phys. Anat. Abth. 1902; Lewis, Amer. Jour. of Anat. v. 1905; Huntington and McClure, The Anatomical Record, Amer. Jour. of Anat. vi. No. 3, April 1907.

which are subsequently differentiated around the nuclei to produce the lymphatic endothelium. Two other views have been taken of the origin of lymphatic vessels—viz. (1) that of Budge (1880), which derives them from the cœlom, but is not supported by any satisfactory evidence, and has fallen into the background; and (2) that of Ranvier, that the lymph-vessels are derived from the veins. Miss Sabin has supplied the most complete body of evidence in support of this theory (that the lymphatics arise from the veins). According to her account (1902–3), the lymphatic system in the pig arises from the venous endothelium at four points, forming four ducts. These primary ducts dilate to form four '*lymph-hearts*,' homologous with those of the Amphibia, though not possessed of muscular walls. From these, as from centres, all the lymphatics grow first along the veins towards the skin, and second along the aorta and its branches, until they extend to every part of the body. The process of budding Miss Sabin supposes to occur as described by Langer and Ranvier—viz. solid buds are formed which are afterwards hollowed out. In the formation of plexuses the buds open into neighbouring ducts by absorption of the endothelium, and valves are formed at the point of junction. The communication between the posterior lymph-hearts and the veins is lost, but the anterior ducts persist as the right and left lymphatic ducts of the adult. The primary lymph-glands she describes as being formed from the four lymph-hearts.

Lewis also derives the lymph-vessels from venous endothelium, not, however, from four sites, but from several. The openings into the veins he believes to be secondary, not primary, and holds that the existence of structures comparable with lymph-hearts has not been demonstrated in mammals. Huntington and McClure return to the idea that the lymph-vessels are mesenchymatous spaces. They find that the main lymph-channels are formed along the early veins. They arise as oval or spindle-shaped spaces outside the intima, in an adventitious reticular tissue which takes form as the primitively redundant venous channels shrink. As the intima recedes, following the diminishing column of blood, these spaces increase in size and number, and, becoming confluent, form large irregular channels which open secondarily into the veins. They explain the adult distribution of the larger lymph-vessels by tracing them to embryonic veins, which are temporary, and subsequently entirely or in great part abandoned.

**Lymph-glands.**—The lymph-glands arise from a plexus of lymph-vessels which in section appears as a sinus broken up by connective-tissue trabeculæ. Capillary blood-vessels are formed in the trabeculæ connected with the branches of the artery of the future gland. Round the capillaries free cells (lymphocytes) gather in the connective-tissue spaces, either introduced from the vessels (Gulland) or produced *in situ* (Saxer). The lymph-follicles (*lymph-cords*) are thus laid down, and the central parts of the strands where the lymphocytes are actively multiplying are the *germ-centres*. The original plexus of lymph-vessels forms the sinus of the gland, and is necessarily connected with afferent and efferent channels.[1]

The **hæmolymph-glands** are apparently developed in a similar fashion, but the plexus is venous, not lymphatic.

## SPLEEN.[2]

The spleen appears in the mesogaster as a cellular mass produced by an aggregation of mesenchyme-cells. It lies close to the dorsal pancreas. The cellular mass becomes partially detached from the mesentery, but remains connected with it by a fold (gastro-splenic omentum), through which the vessels enter. While

[1] See further on this subject the account given in the part of this work dealing with Histology.
[2] For literature, see Hochstetter, Hertwig III. Th. ii. and iii. pp. 165-66.

still of minute size the organ shows a remarkable notching, of which traces are to be found in the adult (fig. 170, p. 126 ; fig. 222, p. 176).

The cells are at first closely packed, but spaces containing blood-corpuscles appear, and the original cellular mass is converted into a trabecular framework. The spaces become the venous sinuses of the organ. They are from the first crowded by great numbers of leucocytes of all varieties. The artery is late in developing. Round its peripheral branches lymphoid cords are formed, which become the Malpighian bodies. It is very difficult to determine the origin and fate of the free cellular elements in the spleen, owing to the minute size and crowded state of the cells in the higher vertebrates. The question whether they are produced *in situ*, or introduced from without, can only be answered indirectly, and opinion is divided on the point.

In Lepidosiren the cells are of very large dimensions, and from observations on the developing spleen the present writer [1] has been able to supply strong evidence in favour of the view that the original mesenchyme-cells of the rudiment are differentiated into both *red and white blood-corpuscles*, thus confirming the work of Laguesse and others on the Selachian spleen. The spleen sinuses are at first merely spaces in the mesenchyme-mass, which later become lined by endothelium, derived from the surface cells of the primary cellular trabeculæ. The spleen in the lower vertebrates is thus an active *hæmapoietic organ*. It is probably more than a mere *locus* (*i.e.* a site in which the primitive corpuscles collect and multiply), as there is evidence to show that blood-cells are actually formed from the indifferent cells of the rudiment. In most mammals its share in blood-formation is limited to a certain period of fœtal life, after which that function is transferred to the bone-marrow.

## DEVELOPMENT OF THE BODY-CAVITY.

The early stages in the development of the cœlom have already been described on p. 49 *seq.* It was there explained that the cœlomic space within the embryonic shield had at first the form of a U open behind, the clefts on each side of the axis being joined across the front of the shield by the precephalic cœlom. It was also shown that, while in the region of the trunk the space was continuous with the extra-embryonic cœlom, in the region of the head the future pericardial portion was separated from it by a lamina of mesoderm. It was further explained that when the head-fold is formed the precephalic cleft comes to lie below, then behind, the bucco-pharyngeal membrane. It is by the expansion of this space that the definitive **pericardial cavity** is developed, and in the following fashion. The pericardial cœlom consists at first of a mesial limb and two horns. The horns lie on either side of the open pharynx, and their splanchnopleuric mesoderm is doubled in by the primitive endothelial heart-tubes. At first on the ventral, these subsequently come to lie on the mesial aspect of the splanchnopleuric folds as they bend in towards one another. *Before* the folds meet to close in the floor of the pharynx they have already become folded-in ventrally, and the mesial cross-portion of the pericardium has come to lie below them, so that when their union is effected, and the heart-tubes are brought together, there is no ventral mesentery (Robinson, Völker, Rouvière).[2] By further extension backwards of the mesial cleft the lateral horns are taken into the cavity, and the pericardial cœlom communicates with the general cœlom only by two apertures, one on either side of the mesocardium. When this disappears in part of its extent somewhat later, there is necessarily only a single aperture extending across the middle line, and it further follows that the lateral cœlomic spaces must also communicate in this situation with one another below the free ventral edge of the gut-mesentery.

[1] Trans. Roy. Soc. Ed. xli. 1904.

[2] Robinson, Jour. of Anat. and Phys. xxxvii.; Völker, Bibliogr. Anat. x.; Rouvière, Jour. d'Anat. et de la Phys. xl.

Behind the heart the walls of the yolk-sac are nipped in, and come together, before they are folded in from the front by extension of the mesial pericardial cleft, so that here a ventral mesentery is produced, as well as a dorsal, and this continues to be formed until the union of the lateral edges of the shield has extended beyond the point where somatopleure and splanchnopleure are continuous with one another. This union primarily extends all round the front edge of the shield; when, therefore, the head-fold is formed, and the splanchnopleuric layers unite with one another, a plate of mesoderm will extend right across the body of the embryo below the gut and lateral cœlomic spaces, and behind the pericardium. This is the *septum transversum*.[1] It forms a bridge of tissue in which the allantoic and Cuverian veins pass inwards and join the vitelline, to form the sinus venosus. It is at first set nearly transversely, but as the pericardium extends backwards it becomes rotated, till it lies obliquely in an antero-posterior and dorso-ventral plane. It forms the dorsal and posterior walls

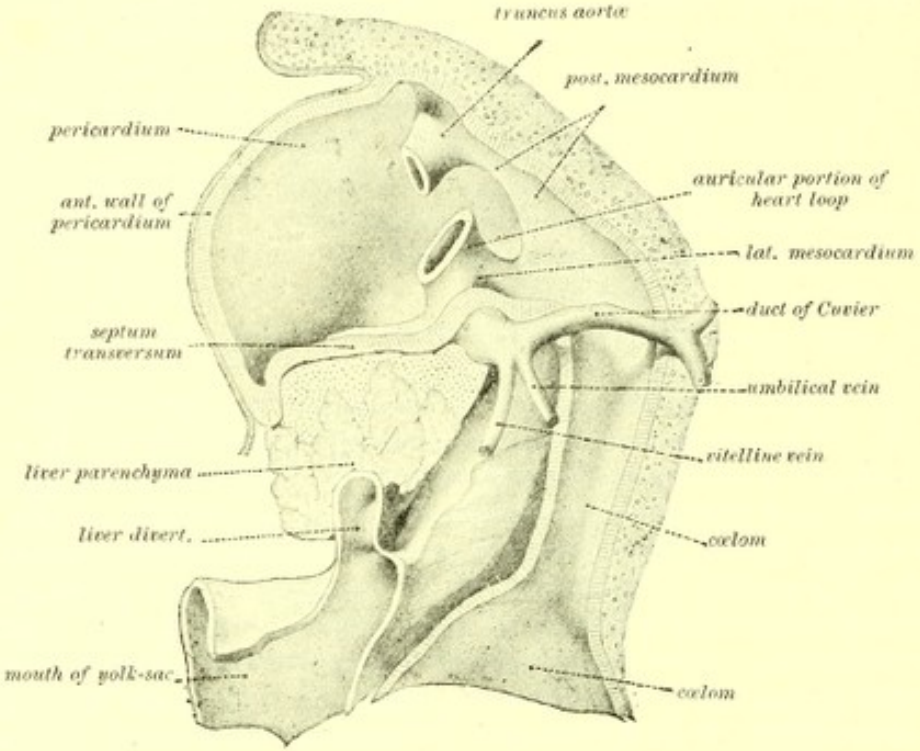



Fig. 292.—The pericardial, pleural, and abdominal portions of the cœlom and mesocardia in a human embryo of 3 mm. long. (After His, from Kollmann.)

of the pericardium, while in its anterior edge, which bounds the pleuro-pericardial opening, lie the sinus venosus and the Cuverian veins, which sweep into it from the somatopleure on each side. Between the dorsal surface of the septum and the back wall of the body-cavity stretches the mesenteric partition, containing the gut and its hepatic diverticulum, on each side of which the vitelline veins extend forwards through its substance to the sinus venosus. The septum transversum soon becomes greatly thickened by the extension into it of the epithelial trabeculæ of the liver parenchyma. These follow the walls of the veins, which they surround, imbed, and break up into the sinusoids already described (p. 174). The primary expansion takes place forwards, but does not extend to the edge containing the sinus venosus. Later the trabeculæ grow up on each side to form lateral masses of liver-substance which project into

[1] The view adopted in the text regarding the formation of the septum transversum is not shared by all embryologists. Many following Ravn consider that the somatopleure and splanchnopleure are brought secondarily into union by the enlargement of the omphalo-mesenteric vein.

the cœlom from below. Between the lateral lobes on the dorsal aspect is a groove in which the mesenteric partition is inserted. Into this partition the lung-

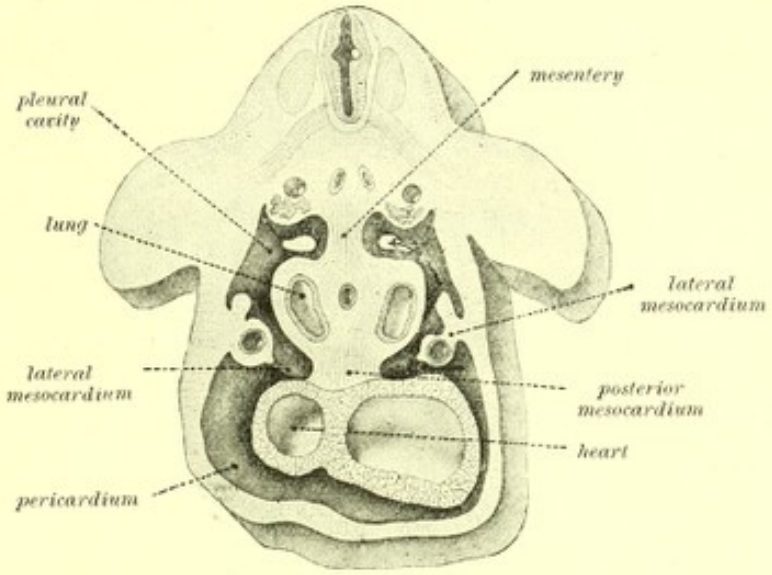



FIG. 293.—FIGURE OBTAINED BY COMBINING SEVERAL SUCCESSIVE SECTIONS OF A HUMAN EMBRYO OF 7·5 MM. (FOURTH WEEK). (From Kollmann.)

The arrow indicates the opening of the pleural cavity into the peritoneal.

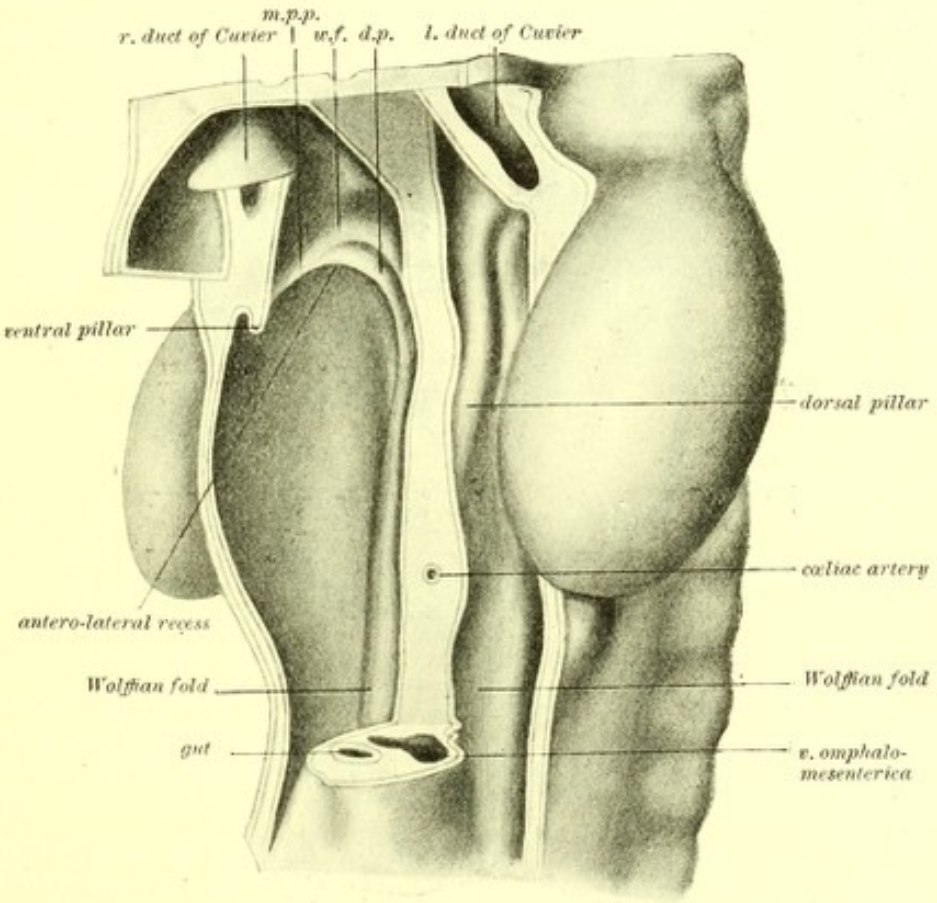



FIG. 294.—MODEL OF A HUMAN EMBRYO OF 6·8 MM., SHOWING THE DORSAL WALL OF CŒLOM. (After Piper.)

*m.p.p.*, membrana pleuro-peritonalis; *w.f.*, anterior end of Wolffian fold; *d.p.*, dorsal pillar of pleuro-peritoneal membrane.

rudiments extend from before backwards, and encroach on the cœlomic clefts. The anterior part of the cœlom of each side now becomes the primitive pleural

cavity, the posterior part the peritoneal cavity. The pleural cavities are at first only short and narrow clefts, bounded behind and on either side by certain folds which are concerned in the ultimate separation of the several portions of the cœlom from one another, and in the formation of the diaphragm.

The closure of the pleuro-pericardial opening is chiefly effected by lateral folds (*lateral mesocardia*) related to the Cuverian veins (fig. 293). The veins pass

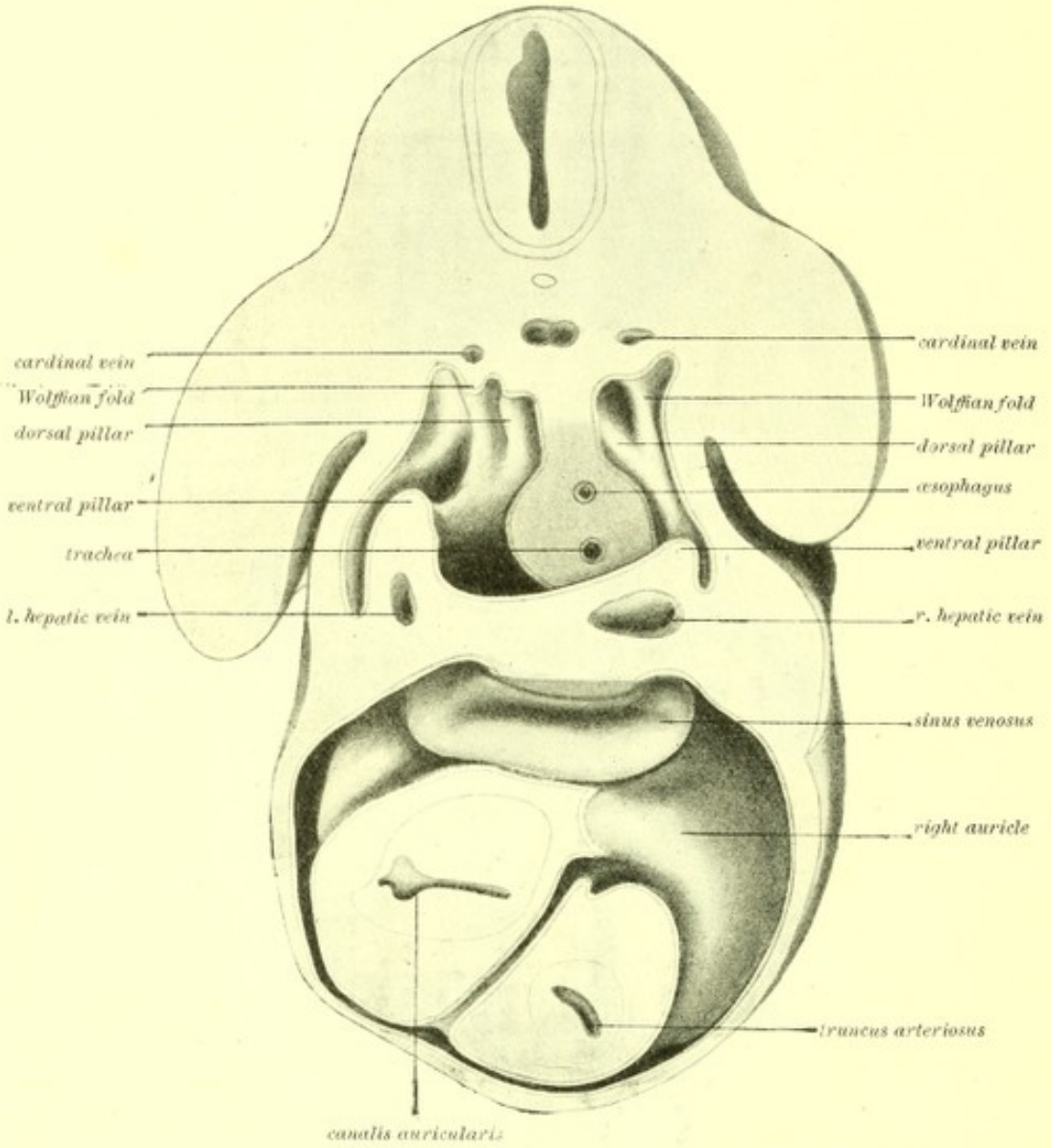



FIG. 295.—SAME MODEL AS SHOWN IN FIG. 294, IN TRANSVERSE SECTION.

The figure shows the cranial half of the model. The broad band containing the hepatic veins is the septum transversum thickened by the liver-trabeculæ. The pleuro-peritoneal membrane is seen on each side stretching between its dorsal and ventral pillars.

in a dorso-ventral direction in the lateral body-walls into the septum transversum, in which they then take a transverse direction. With the expansion of the body-wall the dorso-ventral portion of each vein comes to lie in a fold projecting into the cœlom. Owing to the backward displacement of the septum transversum and its related parts, the veins come to take an increasingly antero-posterior direction. The lateral folds, and the anterior edge of the septum transversum which is continuous with them, are necessarily brought from the transverse into a coronal plane. The terminal portions of the Cuverian veins now run parallel to one

another, and bound the pleuro-pericardial opening. The folds in which they lie (the original anterior edges of the septum transversum) become expanded owing to the enlargement of the pleural clefts and pericardial cavity, and their free margins fuse with the free ventral border of the mesenteric septum so as to shut off the pericardium from the pleural cavities (fig. 293, p. 239). The septum thus formed is known as the *pleuro-pericardial membrane*.

The closure of the pleuro-peritoneal openings is effected by a very complicated series of changes, which result in the formation of the diaphragm. The chief factor in the development of the septum is the extension of the liver trabeculæ into the septum transversum, into certain folds in connexion with it, and into the mesenteric septum, until the liver occupies the whole depth of the body-cavity. The connective-tissue sheet covering it, and derived from the several parts into which the trabeculæ extend, becomes freed from the liver-substance,

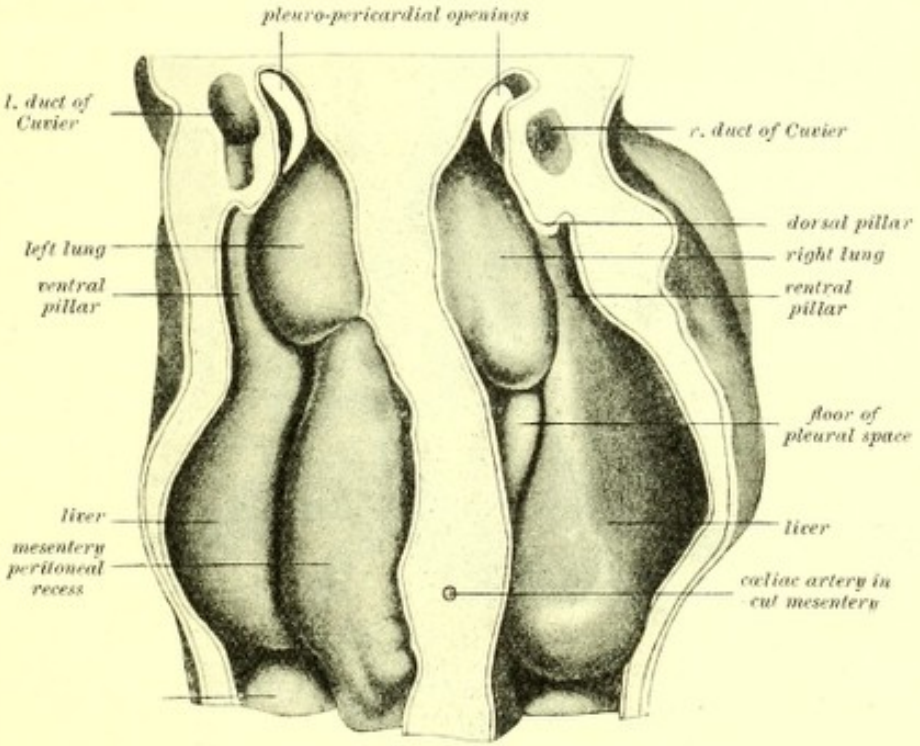



FIG. 296.—MODEL OF A HUMAN EMBRYO OF 6·8 MM. (After Piper.)

The cœlom is opened, and the dorsal wall removed by cutting through the dorsal mesentery. The lungs and liver are thus exposed from the dorsal aspect.

and forms a divisional plane which by a further series of modifications is developed into the diaphragm.

We have already seen that the liver at first consists of a mass of epithelial trabeculæ occupying the septum transversum, and that the mesenteric septum is attached to its dorsal aspect. On each side of this the pleural spaces are continuous with the peritoneal cavity. The openings are in part constricted by folds named the *pleuro-peritoneal membranes* (figs. 294–296). These lie at first in a nearly sagittal plane, with their free edges directed backwards. The dorsal pillar of each fold is continued on to the dorsal body-wall to be attached to the mesial side of the Wolffian ridge, and the ventral end is prolonged on the dorsal aspect of the liver, running behind into the attachment of the mesenteric septum to that organ. The pleuro-peritoneal membranes are in reality the anterior ends of the Wolffian ridges, here reduced to membranous folds owing to the atrophy of the head ends of the Wolffian bodies (Bertelli, Keith, Brachet, Wölfel) (fig. 297). They separate the anterior end of the pleuro-peritoneal cavity into mesial recesses

which become the pleural spaces, and lateral recesses which belong to the peritoneal cavity. These peritoneal (*antero-lateral*) recesses of course overlap the pericardium. Thus, while the anterior edge of the septum transversum internal to the pleuro-peritoneal membrane separates on each side the pleural space from the pericardium, the portion lateral to the pleuro-peritoneal fold separates the peritoneal recess from the pericardium (*peritoneo-pericardial membrane*) (fig. 297). The pleuro-peritoneal membranes soon become altered in position owing to the growth of the body-wall and the extension of the pleural cavities. Their dorsal attachments are shifted laterally until the membrane ultimately assumes an oblique position, lying in a caudo-dorsal and cranio-ventral direction. At the same time another fold has formed on the right side of the mesenteric septum, due to the formation of a cœlomic diverticulum extending inwards and then forwards

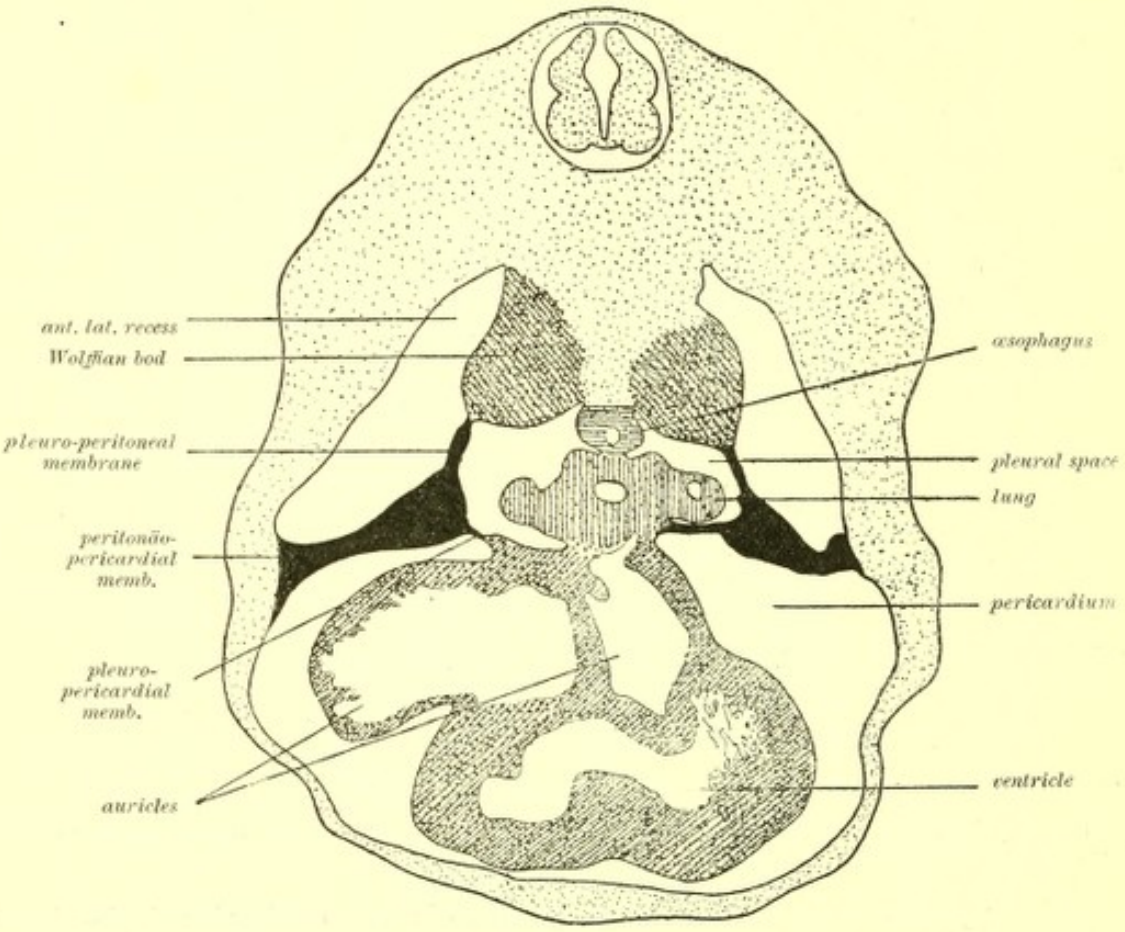



FIG. 297. – DIAGRAMMATIC SECTION OF THE TRUNK OF AN EMBRYO CALF 15 MM. LONG. (Wölfel.)

into its substance. This cleaves the mesentery into two lamellæ, of which the left follows the gut and the right passes on to the dorsal aspect of the right lobe of the liver (fig. 296). This right lamella (*mesolateral* fold of Brachet) has a free edge bounding the opening (foramen of Winslow) into the diverticulum, and it has a dorsal and a ventral pillar. The ventral column passes on to the liver to be continuous with the ventral pillar of the pleuro-peritoneal membrane; the dorsal is continued on the dorsal wall of the body-cavity in a fold in which the vena cava inferior runs, and hence is known as the *caval mesentery*. The pleuro-peritoneal openings are constricted and ultimately closed by the extension of the liver trabeculæ, first mesially into the caval and mesolateral folds on the right side, and into the dorsal mesentery round the cardia of the stomach on the left side, causing a thickening of both lamellæ of the mesenteric septum; second

laterally into the pleuro-peritoneal membranes, causing an uplifting of their ventral pillars (*cf.* fig. 295) and drawing-in of the outer and ventral margins of the openings. The ultimate result is the merging over the surface of the expanding liver on each side of the mesial layer of the pleuro-peritoneal membrane with the layer covering the thickened mesenteric septum (the mesolateral fold being considered part of this septum).

The primitive diaphragm is thus formed first of the septum transversum (including under that term a part of the pleuro-pericardial membrane); second of the thickened mesenteric septum, and third of the mesial layer of the pleuro-peritoneal membrane. It consists at first merely of a connective-tissue sheet covering the liver; it is at first continuous with the parenchyma of the liver, but soon becomes separated from it by cleaving into two layers. The cleavage, however, does not extend all round the organ, and the result is that it remains attached by suspensory bands, which afterwards become the coronary ligaments.

The diaphragm thus constituted is placed at first very obliquely, but as it descends to its definitive position it comes to lie transversely, and at the same time increases in circumference by the expansion of the pleural spaces. These, as we have already seen, are at first small, and are placed entirely dorsal to the pericardium. Owing to the development of the ribs the body-wall now becomes greatly expanded, and a thick layer of loose tissue develops on their inner side (fig. 268, p. 214). This is gradually invaded by the pleural sacs, which, pushing into the body-wall round the pericardium, gradually come to enclose that cavity, and extending behind into the tissue circumscribing the diaphragm form the costo-diaphragmatic recesses. The pleural sacs thus reach their final dimensions by excavating the body-wall, and, further, a certain portion of the circumference of the diaphragm must be referred to tissue really belonging to the body-wall (fig. 298).

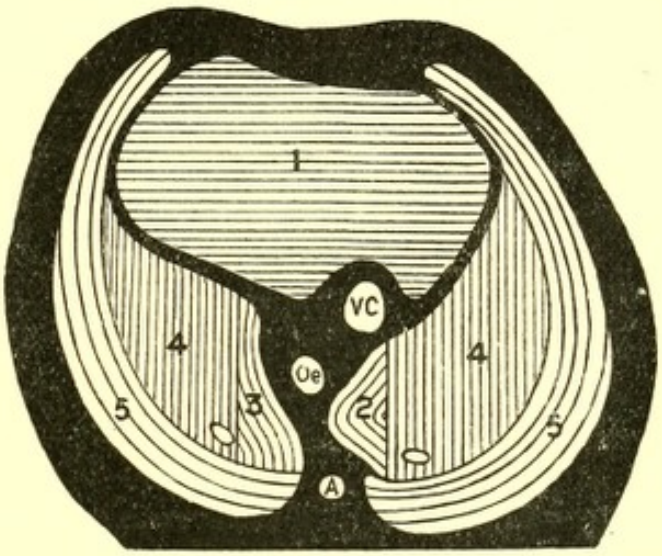



FIG. 298.—DIAGRAM OF THE PRIMITIVE DIAPHRAGM TO SHOW THE SEVERAL PARTS FROM WHICH IT IS BUILT UP. (After Broman.)

1, pericardial part derived from septum transversum; 2 and 3, parts derived from the mesentery: 4, 4, parts derived from pleuro-peritoneal membranes: between these dorsally and the mesenteric portions are the nearly closed pleuro-peritoneal openings; 5, 5, parts derived from the body-walls; 1, 2, 3, 4, 4, cover the cranial aspect (upper surface) of the liver.

Muscular tissue extends into the diaphragm derived from the *transversalis* and the *rectus* sheets (Keith). The supply of the muscle by the phrenic nerves shows that part of it is a derivative of cervical myotomes, which are displaced backwards as the diaphragm sinks to its permanent level.[1]

[1] The above account of the development of the diaphragm is a mere sketch of a very complicated process. For further detail- the reader must be referred to special works on the subject. The earlier literature will be found fully reviewed by Brachet in Merkel and Bonnet, Ergebnisse der Anatomie und Entwickelungsge-chichte, 1907. References to some more recent papers will be found in Hochstetter's article in Hertwig's Handbuch, Bd. III Th. i. and ii. p. 160. Still more recent papers are Mall, Bull. of the Johns Hopkins Hospital xii.; Broman, Anat. Anzeiger (Ergänzungsheft) xxi.; Bertelli, Arch. Anat. e Embriol. Ital iv.; Keith, Jour. of Anat. and Phys. xxxix.; Wölfel, Anat. Anzeiger xxx.; Debeyse, Bibli-graph. Anat. xiv.; Brachet, Contribution à la signification morphologique du diaphragm dorsal, Bruxelles 1906.

**Development of the mesentery and lesser sac of the peritoneum.**—A *ventral mesentery* is not developed behind the umbilicus. The fold so called in front of it is largely taken up by the liver-parenchyma (fig. 292, p. 238), and in the adult is represented by the gastro-hepatic omentum and falciform ligament. The *dorsal mesentery* extends along the whole length of the gut. It becomes drawn out into an extensive sheet when the vitelline loop is formed. As the gut increases in length the neck of the mesentery (which lies within the body while the rest of the sheet is enclosed in the cœlom of the umbilical cord) becomes narrowed until the end of the vitelline loop (the future mid-point of the transverse colon) comes into close relationship on the dorsal wall of the abdomen with the end of the duodenum. This relationship persists through all the later stages, and when the loop of the colon is formed, a twisting of the neck of the mesentery necessarily takes place in such fashion that the small gut with its mesentery, is carried to the left under the distal (colonic) part of the vitelline loop with its mesentery (fig. 301). When this rotation is complete, and the colonic loop is

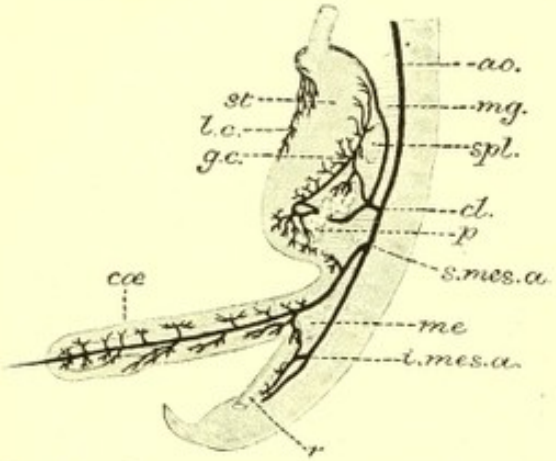



FIG. 299.—DIAGRAM OF THE MESENTERY, STOMACH, AND INTESTINE OF A HUMAN EMBRYO OF SIX WEEKS. (Toldt.)

*st*, stomach; *g.c.*, greater curvature; *l.c.*, smaller curvature; *mg*, mesogastrium; *spl*, spleen; *p*, pancreas; *c*, cæcum; *r*, rectum; *me*, mesentery; *ao*, aorta; *cl*, cœliac axis; *s.mes.a.*, *i.mes.a.*, superior and inferior mesenteric arteries.

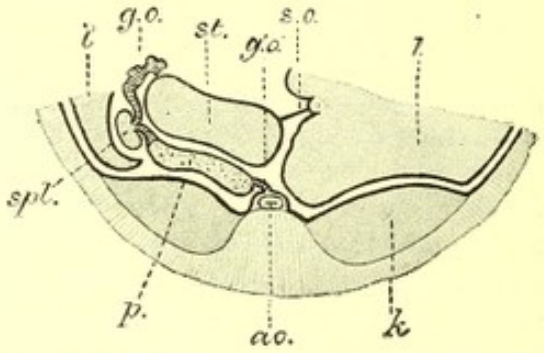



FIG. 300.—DIAGRAM OF A SECTION ACROSS THE ABDOMEN OF A HUMAN EMBRYO OF THE THIRD MONTH. (Toldt.)

*l*, *l*, liver; *k*, kidneys; *g.o.*, great omentum; *g'.o'.*, omental sac; *s.o.*, small omentum. The other letters as in fig. 299.

carried to the right, the meso-colon is necessarily stretched into a transverse plane. At the same time the portion of the gut distal to the vitelline loop being carried to the left, as the small intestine develops, the mesentery proper to it assumes a transverse position and becomes the left half of the transverse mesocolon. The ascending and the descending colon have at first a free mesentery, but they become fixed by the disappearance of the posterior layer on each side, and the adult conditions are realised.

The **lesser sac of the peritoneum**[1] is very early foreshadowed by the formation of the diverticulum in the mesenteric septum mentioned above. Some observers attribute its formation to the downward growth of the mesolateral fold, while others regard it as an actual inpushing of the cœlomic space to form a pocket. The opening into the diverticulum (foramen of Winslow) at first lies between the rudiment of the right lung and the stomach, but later, by the extension of the liver-trabeculæ into the dorsal pillar of the mesolateral fold and the formation of the caval lobe of the liver, it comes to lie between the liver and duodenum.

[1] A review of the literature of the lesser sac of the peritoneum, by Broman, will be found in Ergebnisse der Anatomie und Entwickelungsgeschichte, 1905.

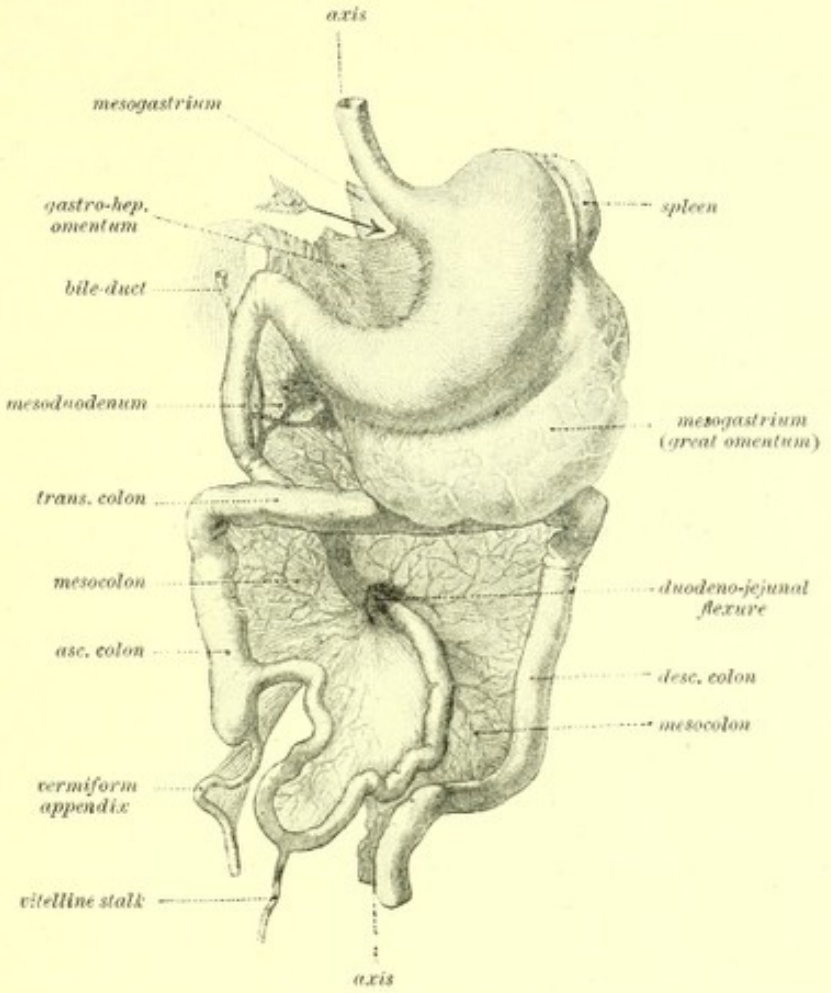



FIG. 301.—DEVELOPMENT OF THE MESENTERY IN THE HUMAN EMBRYO, SEMI-DIAGRAMMATIC. (From Kollmann.)

The arrow points to the foramen of Winslow.

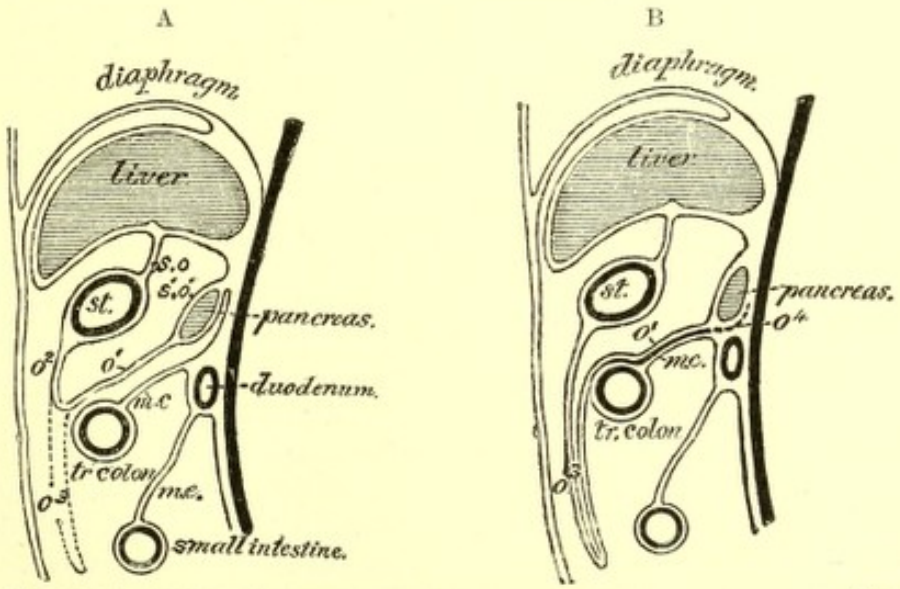



FIG. 302.—DIAGRAMS ILLUSTRATING THE DEVELOPMENT OF THE GREAT OMENTUM. (O. Hertwig.)

A, earlier stage. B, later stage.

*st*, stomach; *s.o.*, small omentum; *s'.o'.*, omental sac; *o'*, mesogastrium, springing from the posterior wall of the abdomen, near which in A it encloses the pancreas; $o^2$, attachment of mesogastrium to greater curvature of stomach; $o^3$, fold of mesogastrium or great omentum growing over coils of small intestine; *me*, mesentery; *m.c.*, transverse mesocolon; $o^4$ (in B), dotted line showing the situation of that lamella of the mesogastrium which at first assisted in enclosing the pancreas, but which has now disappeared. The next part of this lamella has coalesced with the adjacent lamella of the transverse mesocolon, and has also disappeared. The coalescence is indicated by the black line.

The cranial extension of the pocket disappears, but when the stomach turns on its axis the diverticulum enlarges horizontally between liver and stomach, and is bounded on the left by the displaced mesogaster. The mesogaster is connected with the greater curvature—*i.e.* the original dorsal border of the organ—and is thus deflected to the left. It now grows down as a double fold, containing an extension of the lesser sac, to form the *greater omentum*. This passes down at first to the left of the colonic loop, but when the definitive positions are assumed it comes to lie in front of it. An adhesion then takes place between the posterior layers and the mesocolon, so that the colon comes to be attached to the omentum. Further, by a disappearance of the posterior layer of the double mesogaster, the pancreas, which at first lies between its lamellæ, comes to lie behind the peritoneum, just above the line along which the mesogaster is joined to the mesocolon (fig. 302). The duodenum also loses its mesentery, either by fusion of the visceral and parietal layers of peritoneum, as some describe it, or by a stripping off of the peritoneum from its posterior aspect, due to the covering layer not expanding proportionately to the gut-wall.

## DEVELOPMENT OF THE MUSCULAR SYSTEM.[1]

**Muscles of the trunk.**—We have already studied the early phases in the development of the myotomes (p. 56). In the human embryo during the third week the muscle-plate is produced from the inner wall of the mesodermic segment; the axial mesenchyme is formed from the sclerotomes; the mesenchyme of the somatopleure becomes a thick layer, and the mesenchymatous thickenings on the Wolffian ridges which constitute the rudiments of the limb-buds are laid down. During the fourth week the myotomes become greatly lengthened in the trunk and extend into the somatopleure. Their inner wall has become entirely converted into muscle-cells, but the outer wall is still epithelial, and the cavity (*myocœl*) has become obliterated by the fusion of the two lamellæ (*cf.* fig. 84, p. 59). During the fifth week the outer wall also becomes muscular (Bardeen and Lewis),[2] and the myotomes are joined into a dorso-ventral sheet in which the original segmentation has largely disappeared. This sheet next becomes subdivided by ingrowing mesenchyme septa into a dorsal and a ventro-lateral mass. During the sixth week the dorsal begins to be separated from the ventro-lateral mass; the dorsal section becomes subdivided into three longitudinal columns (*ilio-costalis*, *longissimus dorsi*, *spinalis dorsi*); and the ventral-lateral into mesial and lateral portions, of which the mesial forms the *rectus*, and the lateral, cleaving into three strata, the *obliquus externus* and *internus* and *transversalis*. It is in the thorax alone that any segmental arrangement is retained, the ventral projections of the myotomes being separated by the rudiments of the ribs and giving origin to the *intercostal* muscles. By the seventh week the premuscular tissue is all resolved into its definitive divisions (Bardeen and Lewis).

The rectus-muscle rudiments are at first separated by a considerable interval (Mall), the body-wall between them being formed only by the membrana reuniens or fused somatopleuric layers. The muscle-sheets ultimately grow towards the middle line, and come into apposition, carrying their nerves with them.

**Muscles of the limbs.**—In the early stages the limb-buds consist of a mass of mesenchyme continuous with that of the Wolffian ridges and lateral to the line of the myotomes (fig. 82, p. 57). As the buds increase in length this becomes differentiated into a skeletal core and a premuscule sheath. It is not definitely

[1] The literature of the development of the muscles will be found collected by Maurer in Hertwig's Handbuch III. Th. i. p. 76 *seq.*; also in Kollmann's Handatlas, Appendix, p. 45 *seq.*

[2] Bardeen and Lewis, Amer. Jour. of Anat. i.

known whether in man this premuscular tissue is derived from the myotomes or arises *in situ*. In some lower forms there is clear evidence of a growth of muscle-buds from the myotomes into the limb (fig. 303), while in others it seems to be formed by a budding-off of cells individually from the myotomes into the mesenchymatous matrix. While *a priori* we should expect the striped limb-muscles to be derived from the myotomes in one way or another, there is no decisive proof

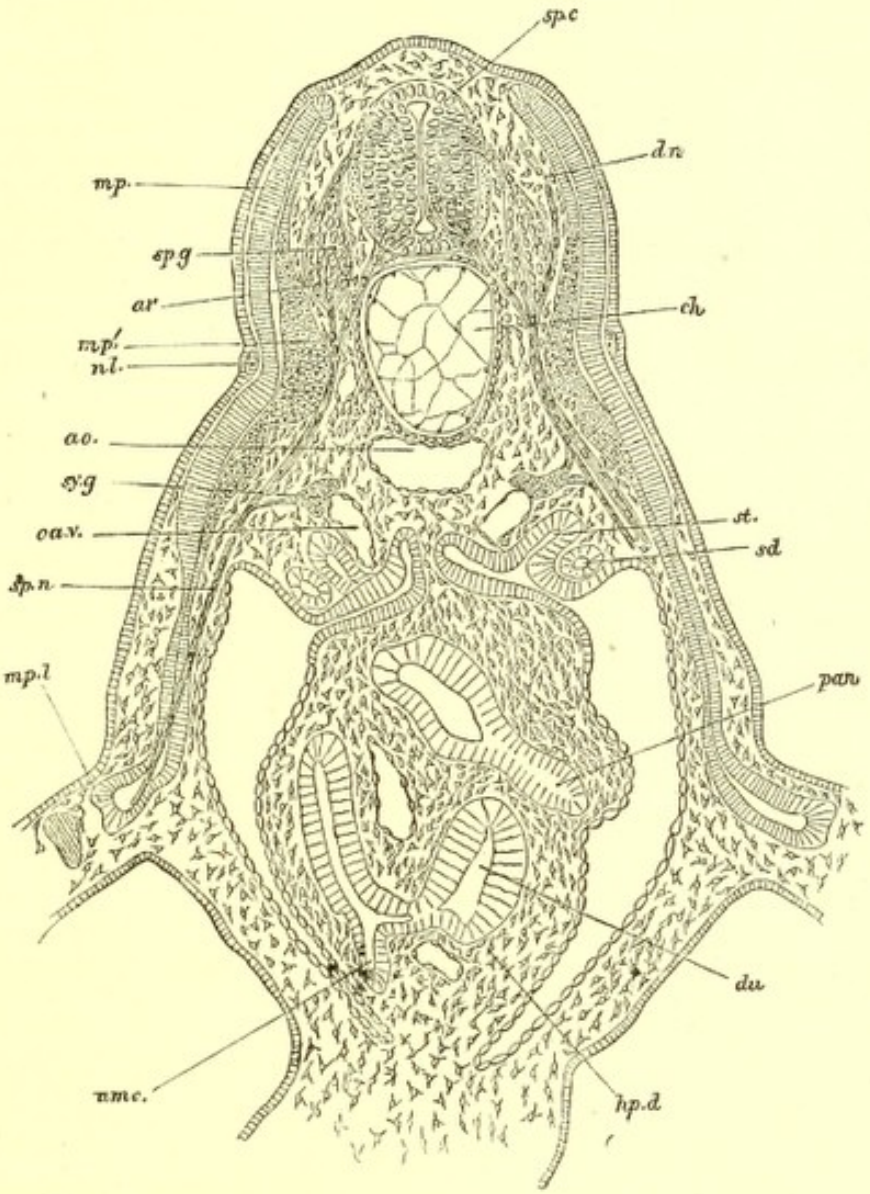



FIG. 303.—TRANSVERSE SECTION THROUGH THE ANTERIOR PART OF THE TRUNK OF AN EMBRYO OF SCYLLIUM. (Balfour.)

*sp.c*, spinal cord; *sp.g*, ganglion of posterior root; *ar*, anterior root; *dn*, dorsal; *sp.n*, ventral branch of spinal nerve; *mp*, muscle-plate; *mp'*, part of muscle-plate already converted into muscle; *mp.l*, part of muscle-plate extending into the limb; *nl*, nervus lateralis; *ao*, aorta; *ch*, notochord; *sy.g*, sympathetic ganglion; *ca.v*, cardinal vein; *sd*, segmental duct; *st*, segmental tube; *du*, duodenum; *hp.d*, junction of hepatic duct with it; *pan*, rudiment of pancreas connected with another part of duodenum; *umc*, opening of umbilical canal (vitelline duct).

that this is the case in higher forms; some observers therefore conclude that the premuscular tissue is a differentiation *in situ* (Paterson, Lewis, Bardeen, and others). Ingalls,[1] in a very well-preserved human embryo of 4·9 mm., describes a distinct budding off of cells from the myotomes into the limb-buds. A stream of cells seems first to proceed from the outer plate, as was described by Kollmann, but later the

[1] Arch. f. mikr. Anat. lxx. 1907.

inner lamella apparently also contribute cells to the limb-bud. The cleavage of the premuscule sheath into the rudiments of the adult muscles is completed by the seventh week (Lewis).[1]

The premuscule sheath is the rudiment, not only of the muscular tissue proper, but of the connective-tissue framework, fasciæ, and tendons of the muscles. There is no distinction at first between the cells which will become muscle-cells and those which will give rise to connective-tissue elements. In quite early stages, according to Bardeen,[1] areas are to be made out which will become muscles, and areas which represent intermuscular spaces. As differentiation proceeds these spaces become more definite; the premuscular masses become divided up into individual muscle-rudiments, and these again into the fasciculi of the individual muscles by the growth of connective-tissue septa, which are more abundant in embryonic than in fully developed muscles. The main nerve-paths follow the spaces between the rudiments of the muscle-groups, and the larger branches of the nerve supplying a muscle-group lie in the septa, between the members of the group. Differentiation of a muscle-rudiment usually begins at the point of entrance of the nerve into it. According, further, to Bardeen, 'Metameric segmentation in the innervation of the limb-muscles is not due to ingrowth into the limb of myotomes, accompanied by nerves, but to the fact that a given region in the developing musculature is in the more direct path of fibres extending into the limb from one or two specific spinal nerves.'

**Muscles of the head.**—We have already seen that there are three primitive segments in the occipital region, but that in front of this point there is no trace of cleavage of the mesoderm. The tongue-muscles supplied by the hypoglossal (occipito-spinal nerves), and formed in the floor of the primitive mouth, are probably derived from these occipital myotomes, and come into the same category with the trunk-musculature. The remaining head-muscles fall into two groups, the muscles of the eye and the branchial musculature.

The **eye-muscles** are developed from a cell-complex which appears between the jugular vein and carotid artery, mesial to the trigeminal ganglion (Reuter). This mass is sickle-shaped, and has three limbs—two anterior which embrace the optic stalk on the inner side, and a posterior. Each limb has its own nerve connected with it, the upper being associated with the trochlear, the inferior with the oculo-motor, and the posterior with the abducens. The rudiment moving forward surrounds the optic stalk, and the two anterior limbs uniting into a ring (Reuter) the whole complex forms a sort of cup embracing the optic vesicle; out of the walls of this the straight and oblique muscles are developed.

The eye-muscles in the mammal are developed in the unsegmented head-mesoderm, but in the lowest vertebrates (Cyclostomata and Selachia) they are formed in connexion with the so-called *head-cavities*, which are supposed to represent primitive segments in the prechordal part of the head. The first of these gives rise to the muscles supplied by the oculo-motor nerve, the second to the superior oblique, and the third to the external rectus. The three limbs of the premuscle-cell-complex in mammals would represent, arguing from their relation to the three nerves, the three head-cavities of lower forms.

The muscles of the **branchial group**, which may be termed the visceral musculature, are derived from the unsegmented mesoderm of the branchial region. All are supplied by the lateral motor-roots of the cranial nerves.

The masticatory muscles develop in the mandibular arch near the angle which it forms with the maxillary process (Reuter), appearing as a cell-complex round the branches of the mandibular division of the fifth nerve. The mass resembles in shape an inverted Y, the limbs embracing the rudiment of the ramus of the mandible. The stem forms the *temporal*, the outer limb the *masseter*, and the inner the *pterygoids* (Reuter for pig).

The muscles supplied by the facial are derivatives of the hyoid arch. The platysma and all the mimetic muscles wander from this site. There are few develop-

[1] Lewis, Amer. Journ. of Anat. i. Regarding the development of the arm-muscles, see also Gräfenberg, Anat. Hefte xxx.; of the leg-muscles, Bardeen, Amer. Jour. of Anat. vi. 1907.

mental data regarding the remaining head-muscles; but it is probable that the series supplied by the motor roots of the glossopharyngeal, vagus, and spinal accessory nerves, which are primarily branchial in their distribution, are to be looked on as muscles of the branchial arches, corresponding to those originating in connexion with the branchial sacs of the lower vertebrates. The sternomastoid and trapezius, though they wander far back in development, may with some reason be regarded as, in part at least, branchial derivatives.

**Segmentation of the head.**—The foregoing paragraphs necessitate here a brief statement on this obscure and intricate subject.

In the higher Amniota there is certain evidence of segmentation in the occipital region. Here at an early stage there are three myotomes, and, related to these, three or four occipito-spinal nerves, which are primarily segmental, but united into a single trunk, the hypoglossal. In front of this clearly segmented portion of the head there is no trace of segmentation except in the lower vertebrates. In Selachia the number of 'head-segments' has been very variously estimated; but according to the classical account of van Wijhe there are in all nine, four metotic (the occipital) and five pre-otic. The pre-otic are much modified, and their claim to rank as segments has been disputed. They are cavities the walls of which give rise to muscles. The first three provide the eye-muscles, while the fourth and fifth disappear. In the branchial arches there is a series of cavities regarded as representing the lateral plates of certain segments. Their walls give origin to the branchial muscles. The evidence of typical segmentation is more striking in the Cyclostomata. In Petromyzon (Koltzoff) typical segments occur, the anterior only being modified in having no side-plates. They are derived from pouches of the archenteron, and the lateral plates show cavities, one in each branchial arch. There are two main views regarding the head-segmentation. The first, maintained by van Wijhe, Miss Platt, Koltzoff, and others, represents the whole series of segments as belonging to the head proper, and corresponding to trunk-segments. The anterior or pre-otic are rudimentary and greatly modified, the posterior or metotic are more complete. Their dorsal portions persist and give rise to myotomes supplied by the occipital nerves (hypoglossal). Their ventral portions give rise to the muscles of the branchial arches, and their splanchnic and sensory nerves are collected into the vagus-complex. The second view, maintained by Gegenbaur, Froriep, Fürbringer, and others, represents the series of 'head-segments,' as divided into two distinct categories. The metotic are segments belonging to a part of the trunk which has become included in the head comparatively recently in phylogeny. The pre-otic are primarily segments of the head proper, and to them belongs the mesoderm of the branchial arches which have been displaced backwards, while the occipital segments have been displaced forwards, so that the two regions overlap. There are thus two genetically distinct parts of the head; the palingenetic and cœnogenetic of Gegenbauer, palæocranium and neocranium of Fürbringer, the prespinal and spinal of Froriep. The occipital nerves (hypoglossal) belong to the occipital myotomes, and therefore to the neocranium; the vagus-complex (including the glossopharyngeal in lower forms as well as the accessory), belongs to the palæocranium, being formed by the coalescence at their proximal ends of the splanchnic fibres of the segmental nerves of the posterior palingenetic segments, of which only the splanchnic or branchial portions now remain. According to Agar in a recent paper on the anterior mesoderm in Lepidosiren,[1] the preponderance of evidence is in favour of the Gegenbauer-Fürbringer view. It seems quite certain that the occipital myotomes really belong to the trunk, but with regard to the palæocranium the matter is more doubtful. It is not yet proved that the prechordal 'head-segments' and branchial segmentation correspond to the trunk-segmentation, and the ontogenetic facts which have induced Hubrecht and others to attribute a radial symmetry to the fore-part of the head must not be left out of sight.

[1] Trans. Roy. Soc. Ed. xlv. Part III. 1907

## DEVELOPMENT OF THE SKELETON.[1]

In the following brief account of the development of the skeleton only the more general features of the early stages will be considered. The details of ossification and many points which relate to the morphology of the parts will be dealt with in other parts of this work.

The **vertebral column** is developed from the mesenchyme which invests the notochord and neural canal, and is derived from the sclerotomes. This is also the blastema from which the membranes investing the spinal cord and the ligaments of the vertebræ are produced. The appearance of the skeletal elements is preceded by a stage in which a series of paired cellular thickenings is laid down in the mesenchyme. It has been shown by v. Ebner and others in the reptilian, and by O. Schultze, Weiss, and others in the mammalian embryo, that each sclerotome is divided into a cranial and a caudal portion by a narrow transverse cleft (fig. 304). This appears in man in the thoracic region about the end of the third week (Bardeen).[2] The intervals between the sclerotomes disappear, and the dividing cleft is soon obliterated, but the two portions remain distinguishable owing to the fact that the caudal half consists of more densely cellular tissue. The mesenchyme immediately round the notochord loses all trace of segmental cleavage, and becomes condensed into a continuous notochordal sheath. As Weiss has shown in the rat, the myotome extends as a keel-shaped thickening into the cleft, and pushes the two portions of the sclerotome apart, so that the *caudal* portions of each sclerotome pair come to lie obliquely, embracing on their mesial aspect the *cranial* portions of the succeeding pair. The thickenings are slowly pushed into the intervals between the myotomes to which they properly belong and the succeeding pair, and thus ultimately come to have an intersegmental position (Bardeen). It must be remembered that these thickenings are merely areas of condensation in a general blastema; but it is customary to speak of them as primitive vertebræ (or *scleromeres*, Bardeen). Each scleromere (fig. 305 A) has a pair of dorsal or neural processes (primitive arch), a pair of ventral or costal processes which extend outwards between the myotomes, and a mesial plate which is continuous with the condensed mesenchyme of the notochordal sheath. These plates do not form the future bodies of the vertebræ; they occupy rather the position of the future intervertebral discs. Between the intervertebral plates the notochordal sheath is invested by

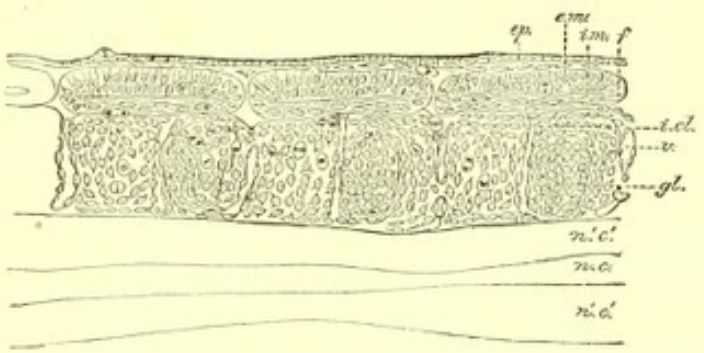



FIG. 304.—HORIZONTAL LONGITUDINAL SECTION OF THREE PROTOVERTEBRÆ IN A SNAKE-EMBRYO. (v. Ebner.)

*ep*, cutaneous ectoderm; *e.m.*, outer wall of segment; *f*, its margins folded round into *i.m.*, muscle-plate composed of flattened cells which are becoming elongated into muscular fibres; *n.c.*, neural canal, in outline only; *n'.c'.*, neural ectoderm forming its walls. Between these and the muscle-plate is a continuous mass of mesenchyme which has been derived from the inner parts of the primitive segments, partly interrupted by the ganglion-rudiments, *gl*. The original intervals between the primitive segments here are still indicated by vessels, *v*. *i.cl.*, cleft in the mesenchyme (according to Ebner this is the remains of the original cavity of the segment).

[1] The literature of the development of the skeleton will be found collected by Braus (skeleton of limbs), Schauinsel (vertebral column, ribs, and sternum), and Gaup (skull), in Hertwig's Handbuch III. Th. ii. and iii. pp. 331 *seq.*, 562 *seq.*, and 855 *seq.*

[2] Amer. Journ. of Anat. iv. 1904.

looser mesenchyme, which is derived, like the tissue intervening between the neural processes, from the anterior portions of the sclerotomes. The plates are at first relatively thick, but the tissue forming them becomes loosened posteriorly, and is added to the loose investment of the notochordal sheath, while in front it is condensed where it adjoins the fissure of Ebner. This thickened band is the rudiment of the permanent disc, and the looser tissue intervening between adjoining discs is converted into the body of the permanent vertebra. It follows from this description that the future body is contributed to by the anterior portions of a sclerotome pair, and also by the posterior portions (primitive plates) of the preceding pair, so that a new segmentation of the skeletal axis is effected which alternates with the primary myotomic segmentation. The formation of the vertebral body is brought about

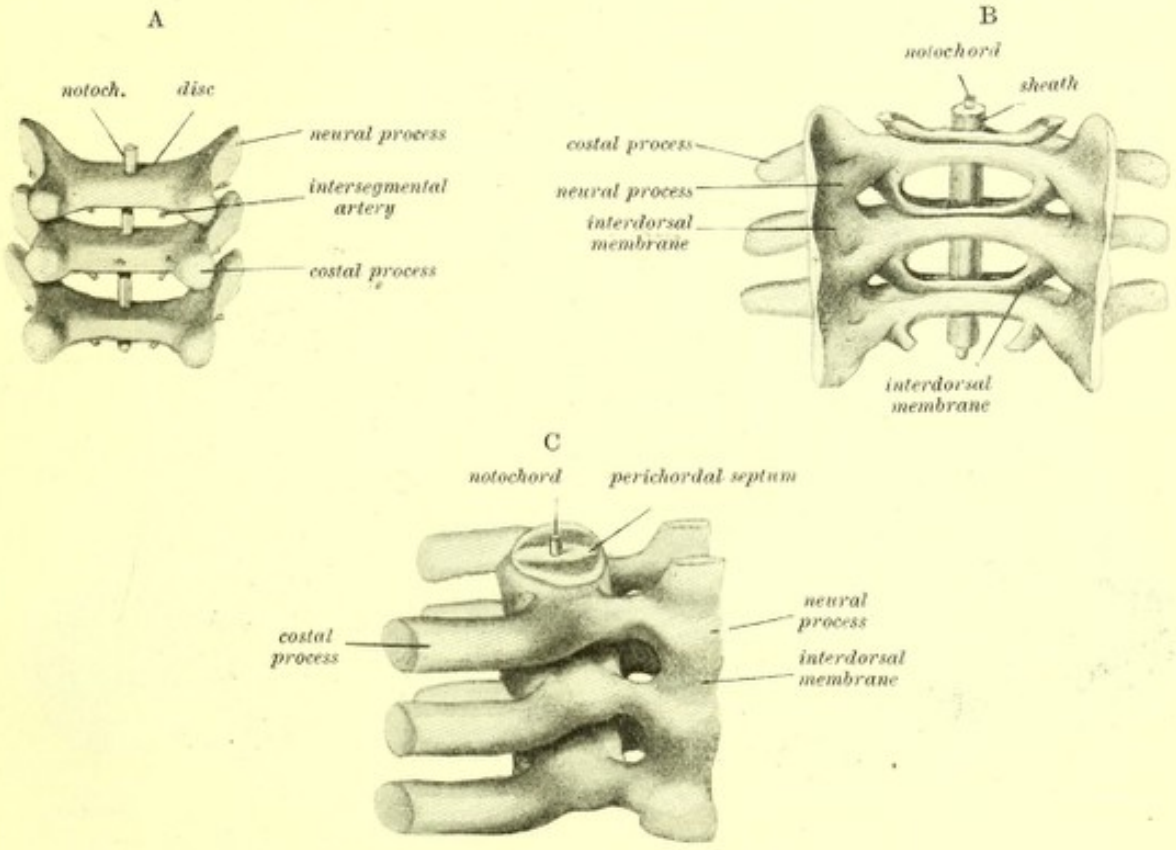



FIG. 305.—VIEWS OF MODELS OF BLASTEMAL (MEMBRANOUS) STAGE OF VERTEBRAL COLUMN: A. FROM AN EMBRYO OF 7 MM., VENTRAL ASPECT. × 33⅓ diameters. B. FROM AN EMBRYO OF 9 MM., DORSAL ASPECT. × 25 diameters. C. FROM AN EMBRYO OF 11 MM., LATERAL ASPECT. × 25 diameters. (After Bardeen.)

as follows: the notochordal sheath becomes prolonged dorso-ventrally into a kind of septum (fig. 305, C), which extends between the primitive plates and separates the loose mesenchyme, alluded to above, into a right and left moiety; at the same time the superficial layers of the intervening tissue become condensed into a continuous lamella uniting the plates, and enclosing the looser tissue on each side of the septum. This enclosed tissue now becomes converted into cartilage. There are necessarily at first two chondrogenetic centres, but soon the septum becomes implicated, and the notochord is enclosed in a continuous cartilaginous ring. According to O. Schultze, the cartilage formation extends also through the primitive intervertebral plates, so that the column becomes for a time a continuous rod of cartilage, and the permanent discs are formed in this secondarily by the conversion of the hyaline into fibro-cartilage, the only persistent portion of the primitive membranous plates being the *annulus fibrosus* of the intervertebra

discs. Bardeen did not observe this stage in the human embryo. Within the discs the notochord is enlarged and afterwards converted in each along with the surrounding tissue into the *nucleus pulposus*. Within the bodies, on the other hand, the chorda becomes constricted and ultimately disappears.

The neural arches retain their primitive position, and while the costal processes are extending between the myotomes to form the membranous ribs, a transverse process appears on each side in the angle between it and the neural process, opposite the attachment of the scleromere to the notochordal sheath. A chondrogenetic centre appears in each side of the primitive arch, and another in each costal process. The arch becomes joined to the body, and the cartilaginous vertebra is completed. The arches, however, remain for a long time open (figs. 306, and 234, 268, pp. 186, 214). It is not till the fourth month that they are

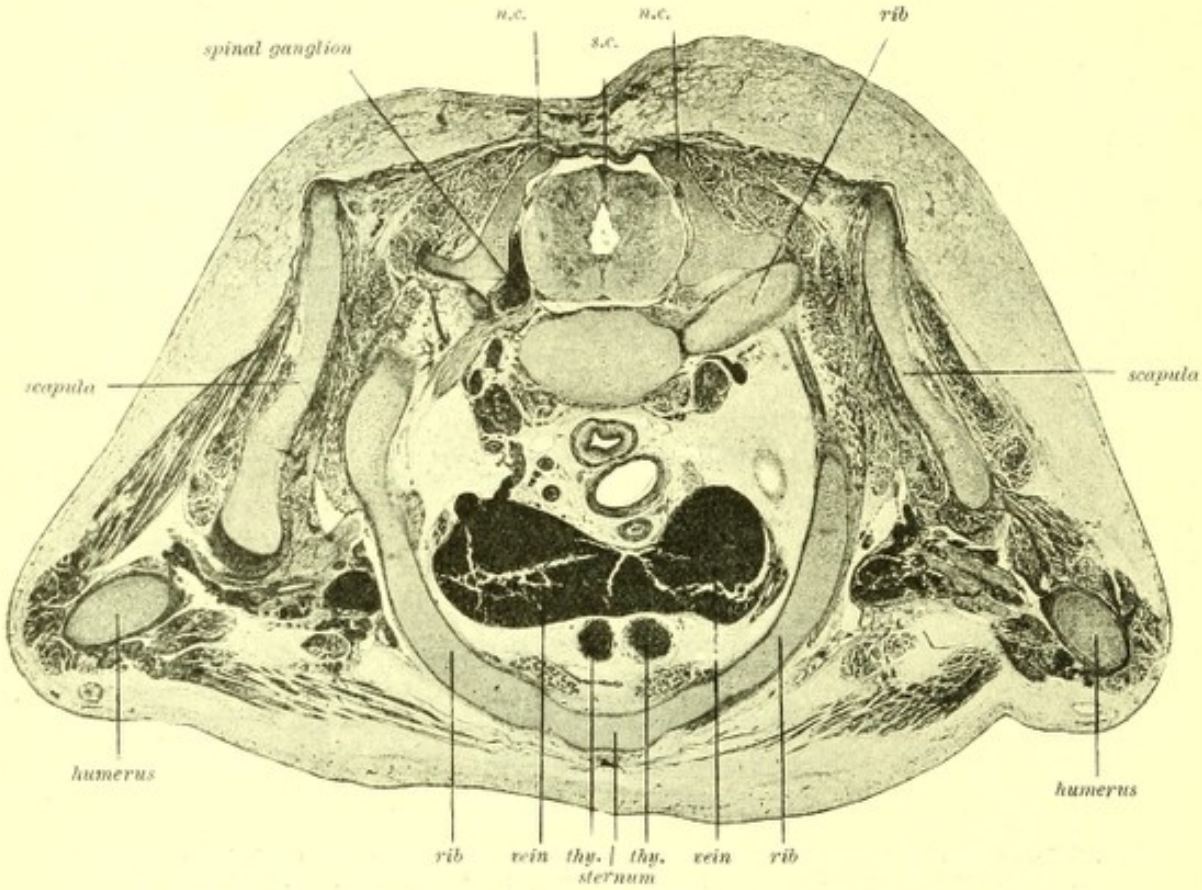



FIG. 306.—SECTION OF A HUMAN EMBRYO OF 30 MM. Photograph. (T. H. Bryce.)
*s.p.*, spinal cord; *n.c.*, cartilages of neural arch still separate; *thy*, *thy*, thymus.

closed in over the cord to complete the spinal canal. The articular processes are produced by the growth of cartilaginous rudiments, backwards and forwards, from the neural processes into the intervening layer of tissue. The primitive membranous plate at an early stage becomes much thickened ventrally. This thickened band corresponds to the hypochord rod of lower forms. It is not a separate structure at any time (rat, Weiss; man, Bardeen), except in the case of the atlas, in which, loosened from the body, it persists as the ventral bar of that bone. It becomes chondrified by two lateral centres (Weiss). The body of the atlas remains free from the bases of the arches, and is secondarily fused with the axis as its odontoid process.

**Ribs and sternum.**—Each vertebra is provided with a rib-process. In the blastema stage there is no separation between rib and primitive vertebra, and the

same is true, according to some authorities (O. Schultze), for the cartilaginous stage. The processes remain attached to and become parts of the vertebræ in the cervical, lumbar, and sacral regions, but in the thoracic region they grow round the body-wall to form the free ribs. The costo-central joints are produced by absorption in the matrix between ribs and vertebræ, the surrounding mesenchyme giving origin to the costo-vertebral ligaments. The rib-process and growing transverse process are at first united by a continuous blastema. This is absorbed as anastomoses are established between the segmental arteries (Bardeen), but between the end of the process and the rib a joint-cavity is formed and the surrounding mesenchyme gives rise to costo-transverse ligaments (see fig. 268, p. 214).

The ventral ends of the ribs become continuous with two longitudinal cellular bands (sternal bands), which are laid down from before backwards. The cellular strands are derived according to some from the rib-ends, but according to others they are independent formations; opposite the first seven pairs of ribs they fuse by differentiation of the intervening tissue to form the sternum (fig. 306). This remains cellular for some time after the ribs are converted into cartilage. The

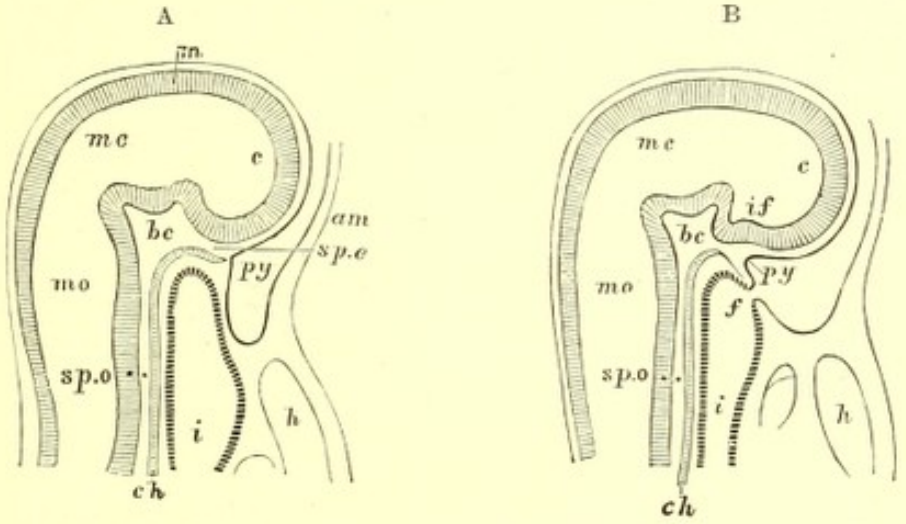



FIG. 307.—MEDIAN SAGITTAL SECTION OF THE HEAD IN EARLY EMBRYOS OF THE RABBIT. Magnified. (From Mihalkovics.)

A, from an embryo 5 mm. long. B, From an embryo 6 mm. long.

In A, the faucial opening is still closed; in B, the septum is perforated at *f*; *c*, anterior cerebral vesicle; *mc*, mesencephalon; *mo*, medulla oblongata; *m*, medullary epiblast; *if* (in B), infundibulum; *sp.e*, spheno-ethmoidal; *bc*, sphenoidal; and *sp.o*, spheno-occipital parts of the basis cranii; *i*, fore-gut; *ch*, notochord; *py*, buccal pituitary involution; *am*, amnion; *h*, heart.

process of chondrification begins in the upper lateral angles of the presternum and in the mesosternum between the ribs (Paterson); it proceeds from the margin inwards, repeating the process by which the chondroblast sternum is formed. The metasternum is developed separately, but also from independent lateral rudiments in all probability.

The usual view adopted regarding the development of the sternum is that of Ruge, who derives the sternal bands from the ventral ends of the ribs, which unite with one another, as it were, from before backwards to form the bands. According to Paterson, they are at first quite separate and independent of the ribs, and are only united with them secondarily. He describes an early stage in which the primitive sternum is separate from the ribs, but connected with the rudiments of the shoulder-girdles, and believes, therefore, that ontogenetically the sternum is an independent structure connected with the limb-girdles. It is not yet clear whether, or in what degree, the limb-girdles contribute to the formation of the manubrium, and the relations of the chondroblastic areas to the cartilaginous skeleton are not yet sufficiently elucidated to warrant a more definite statement than that contained in the text.

**Skeleton of extremities.**—The skeletal core of the limb-buds is produced by a condensation of the vascular mesenchyme in the axis of the developing limbs, and at their bases. The skeletal blastema becomes still further condensed in the situation of the future bones, and distally into a hand or foot plate. This stage is named the blastema or prechondral stage. The cellular blastema is then converted into cartilage by the appearance of centres of chondrification in the precartilaginous blastema of the several skeletal parts. During this chondrogenetic stage the limbs acquire the main features of the adult form. The joints are at first represented by areas of mesenchymatous condensation, which directly join the cartilages, but by the end of the second month the joint-cavities have appeared (fig. 248, p. 196) and the surrounding mesenchyme is condensed and thickened into the capsular ligaments. Intra-articular structures are derived from the primary blastema. Centres of ossification next appear in the

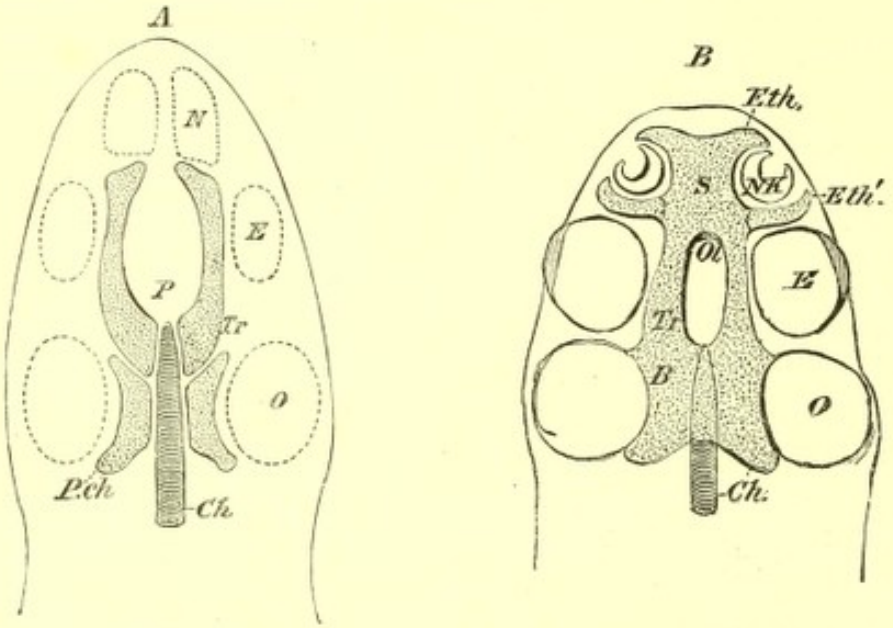



FIG. 308.—DIAGRAMS OF THE CARTILAGINOUS CRANIUM. (Wiedersheim.)

A, First stage.

*Ch*, notochord; *Tr*, trabeculæ cranii; *P.ch*, parachordal cartilages; *P*, situation of pituitary body; *N*, *E*, *O*, situations of olfactory, visual, and auditory organs.

B, Second stage.

*B*, basilar cartilage (investing mass of Rathke); *S*, nasal septum and ethmoidal cartilage; *Eth*, *Eth'*, prolongations of ethmoidal around olfactory organ, completing the nasal capsule; *Ol*, foramina for passage of olfactory nerve-fibres; *N*, *E*, *O*, *Ch*, *Tr*, as before.

cartilages, and they closely correspond to the preceding centres of chondrification (Bardeen.)

**Development of the skull.**—As in the trunk, so in the head, the notochord is at first the only supporting structure. As we have seen in an earlier section, it extends forwards to the flexure of the mid-brain, and then returns on itself to end at the attachment of the buccopharyngeal membrane (fig. 307). Cartilage begins to be laid down, during the second month, in the mesenchyme on each side of this part of the notochord, and a *basicranial* plate is formed enclosing the chorda and extending from the future foramen magnum to the stalk of the pituitary body, where it ends in a plate or process which becomes the *dorsum sellæ*.

It appears from the work of Jacoby, Levi, Robinson, and others that there are no definite parachordal nor trabecular cartilages in the human embryo such as occur in lower forms (fig. 308). Levi describes the appearance of a number of chondroblastic centres, which ultimately fuse to form the continuous chondrocranium. The basicranial plate is chondrified in two sections,

an anterior related to the auditory capsule and a posterior or occipital segment. The otic portion shows no trace even in the membranous stage of any segmentation; but regarding the occipital portion, Levi confirms for man the accounts given by Froriep for the calf and recently by Weiss for the rat. Froriep holds that the occipital region represents the fusion of four rudimentary vertebræ, corresponding to the three primary roots of the hypoglossal nerve. Of these only the posterior is at all independent. Its development in the early stages resembles that of the vertebræ, and it loses its identity only when fused with the parts in front of it. The anterior portion of the occipital blastema shows faint traces of segmentation, but only in the earliest phases, by

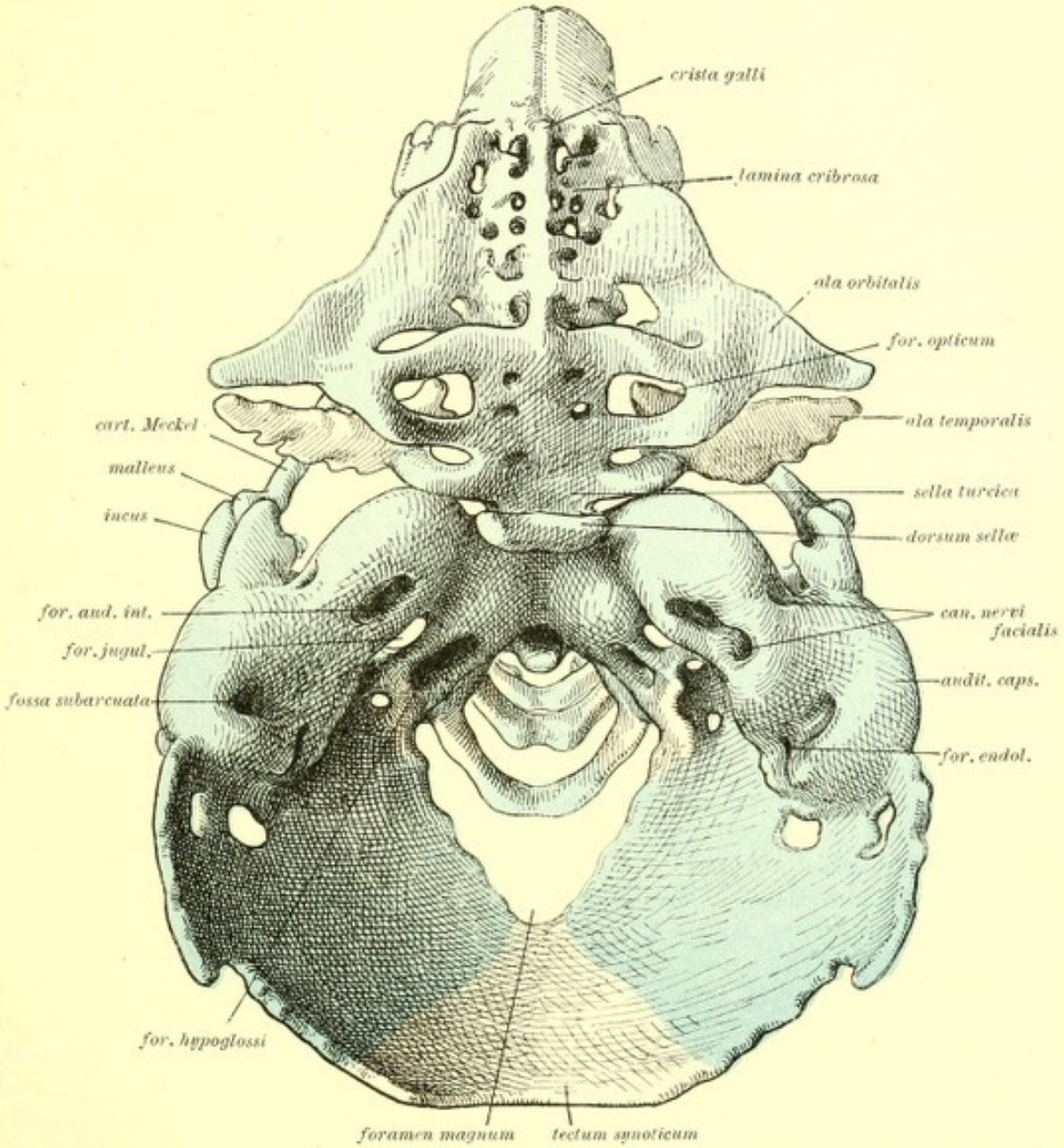



FIG. 309.—MODEL OF THE CHONDROCRANIUM OF A HUMAN EMBRYO, 8 CM. (From Hertwig's Handbuch der Entwickelungslehre.)

The membrane-bones are not represented.

the presence of three rudimentary cellular masses (primitive arches) which extend outwards between the myotomes. After the cartilaginous elements are formed, all trace of segmentation is lost. The relation of the basicranial plate to the notochord (see below) in mammals makes the significance of this early segmentation doubtful (Robinson).

The chondrocranium forms only an incomplete case for the brain. The cranial vault consists of bones which are laid down directly in membrane, and in the region of the visceral skeleton numerous investing bones are added to complete

the adult skull. As these will be fully dealt with in the volume on Osteology, it will suffice here if a brief account be given of the chondrocranium as a basis for that description.

The cartilaginous cranium consists of two parts, the *neurocranium* and the *visceral skeleton*. The **neurocranium** consists of two sections, a *parachordal* and a *prechordal*. The auditory capsule becomes an integral part of the parachordal, and the olfactory capsule of the prechordal section. The basicranial plate encloses the notochord, which ends at the dorsum sellæ in a rounded process, its anterior hooked portion having disappeared. According to Froriep, Robinson, and others,[1] the chorda lies on the ventral aspect of the middle portion of the basicranial plate, being completely invested by cartilage only behind and in the dorsum sellæ. The plate consists, as mentioned above, of an otic and an occipital segment. From the latter there extends on each side a lateral plate (occipital pillar, Gaup), which in man is not vertical, as in lower mammals, but is laid out horizontally. This becomes continuous with the posterior edge of the auditory capsule behind a gap which is left as the jugular foramen. In each lateral plate which represents the fused occipital arches is the foramen for the hypoglossal nerve. At first the skull is wide open behind the hind-brain, being covered merely by the membrana reuniens; but into this, from the auditory capsule and occipital pillars on each side, a plate of cartilage extends to close in the foramen magnum and form the supra-occipital. The anterior part of the basicranial plate becomes continuous with the auditory capsule. This is an oval mass of cartilage with its long axis directed inwards and forwards, and divided into an upper and posterior vestibular portion, and a lower and anterior cochlear portion. Between these is a groove on the upper aspect for the facial nerve, which in the figure is seen partially bridged over to form a canal. On the mesial aspect of the capsule is seen the internal auditory meatus, and a deepish fossa (*fossa subarcuata*) which extends below the superior semicircular canal. On the outer aspect a shelf-like process extends which ultimately forms the tegmen tympani. The prechordal or trabecular portion of the skull stands at first at a considerable angle from the posterior portion (Hagen). There are, as already mentioned, no separate trabecular cartilages formed in man. Chondrification occurs in an already continuous mesial blastema, which is interrupted by the stalk of the pituitary body. The cartilage extends directly forwards into the mesial nasal process as the nasal septum. On the upper aspect of the cartilage in front of the dorsum sellæ is a shallow fossa—the future sella turcica, the floor of which is incomplete for a time where the stalk of the pituitary body passes through it. A process projects from the cartilage on either side of the fossa; between this and the auditory capsule the internal carotid artery enters the skull. To this process is attached an obliquely placed plate of cartilage (*ala temporalis*), arising from a separate centre (Levi), which is the rudiment of the great wing of the sphenoid. As it extends backwards it surrounds the mandibular division of the trigeminal nerve and the middle meningeal artery so as to form the foramen ovale and foramen spinosum. Between it and the orbital wing is a wide gap through which the maxillary division of the fifth and all the nerves entering the orbit pass. By the formation of a bridge of cartilage the maxillary division is separated from the rest of the nerves; thus the foramen rotundum is formed, while the main fissure becomes the sphenoidal fissure. In front of the sella turcica a broad bar of cartilage expands laterally on each side into the orbital or lesser wings (*ala orbitalis*). From the posterior borders of each orbital wing a bar is developed which is attached to the side of the central cartilage in front of the pituitary fossa and completes the optic foramen. From the anterior border of each orbital wing a

[1] See Robinson, Jour. of Anat. and Phys., xxxviii.

broad process projects forwards to be attached to the roof of the nasal capsule. In later stages this is largely reabsorbed. The ethmoidal region of the human skull is peculiar in respect that the nasal capsules are so rotated that the apertures of communication between the cranial cavity and the nasal fossæ are placed horizontally. Each aperture is at first single, but is afterwards converted into the cribriform plate by the formation of cartilaginous bridges. The central cartilage is continued forwards as the septum nasi, and its upper edge projects between the olfactory openings as the crista galli. The side walls of the nasal capsules bend inwards in front to be continuous with the edge of the septum and so complete the roof of the nasal fossæ, but the floor is deficient, and only completed when the palatal processes have met with the lower free edge of the septum. From the mesial aspect of the outer wall of the nasal capsule on either side project the cartilaginous rudiments of the several turbinate processes.

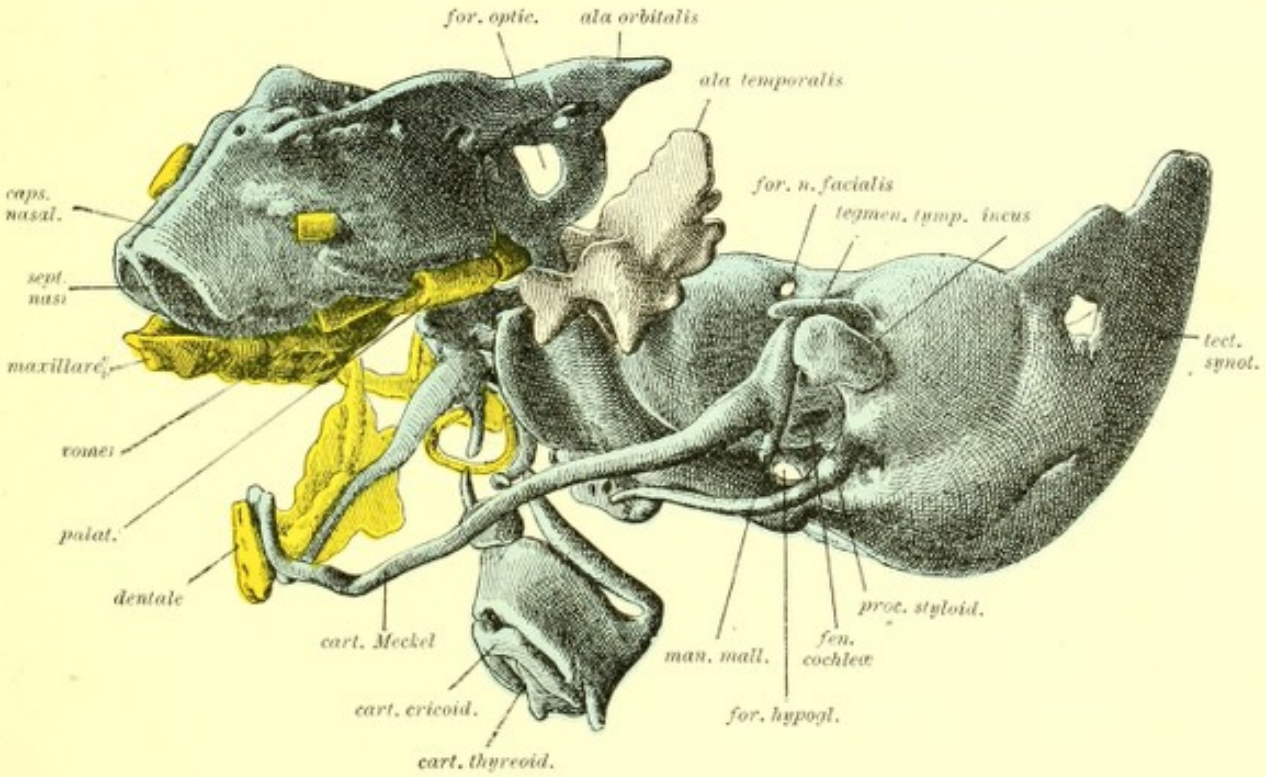



FIG. 310.—THE SAME MODEL AS SHOWN IN FIG. 309, FROM THE LEFT SIDE.
Certain of the membrane-bones of the right side are represented in yellow.

The **visceral skeleton** consists of a number of skeletal elements which occupy the mandibular, the hyoid, and first branchial arches. In the mandibular arch a bar of cartilage is laid down, known as *Meckel's cartilage*. This represents the primitive mandible; but it in great part disappears, being displaced by a membrane bone, the os dentale. A small portion of its ventral end, however, directly ossifies and forms a part of the lower jaw, and its proximal end is developed into the *malleus*. Close to this a separate formation in the blastema in the base of the arch gives rise to the *incus*. In the hyoid arch are formed the *stapes*, the *styloid process* of the temporal bone, the *stylohyoid ligament*, and the *lesser cornu of the hyoid bone*; while in the first branchial arch a short bar of cartilage is deposited which becomes the *greater cornu* of that bone. The body of the hyoid bone is an intermediate formation between the ventral ends of the second and third arches. The development of the visceral skeleton is specially interesting as providing the proof that proximal portions of the first two arches, which in lower vertebrates

form a suspensory apparatus for the mandible, are in higher vertebrates, as it were, annexed by the organ of hearing to provide an apparatus for sound-transmission.

**Formation of the auditory ossicles.**—The development of the auditory ossicles in the human subject has in recent years been investigated again in great

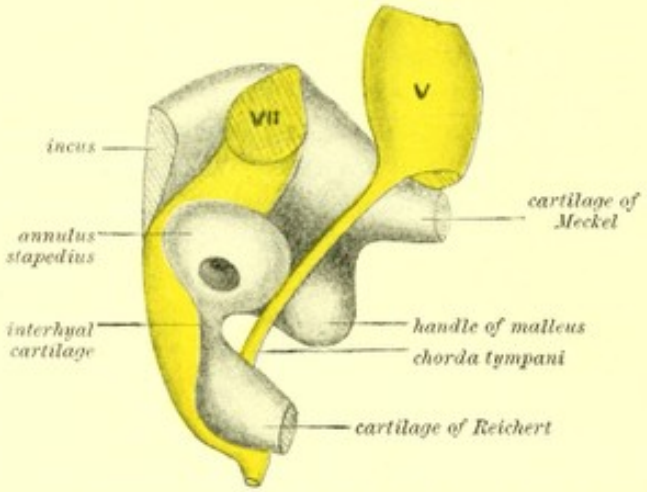



FIG. 311.—RECONSTRUCTION OF THE PROXIMAL ENDS OF THE FIRST AND SECOND BRANCHIAL ARCHES OF A HUMAN EMBRYO OF 16 MM. LONG; LEFT SIDE, INNER ASPECT. (After Broman.)

*V.*, fifth nerve; *VII.*, facial nerve.

detail by Broman, and also incidentally by Hammar. The following account summarises the chief points of Broman's researches. They confirm in the main the views first enunciated by Reichert in 1837.[1] In the middle of the second month the rudiments of the ossicles appear as chondroblast thickenings in a common

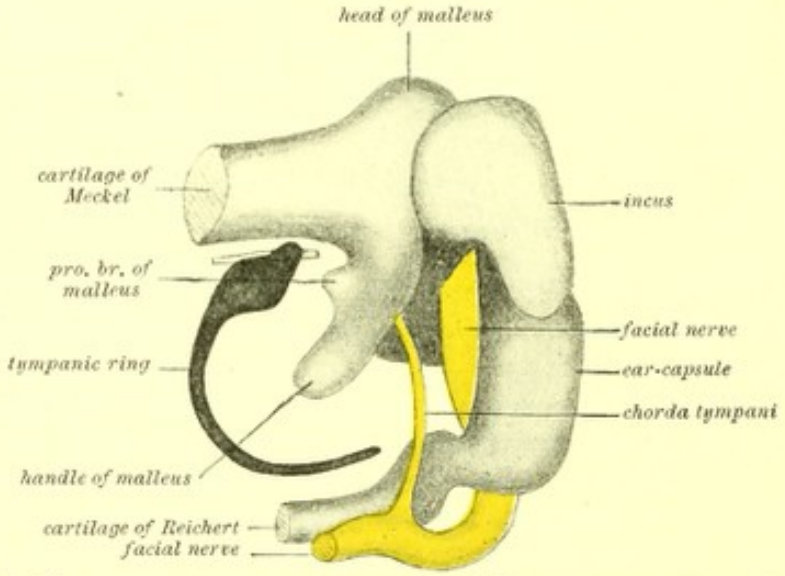



FIG. 312.—THE SAME MODEL AS SHOWN IN FIG. 311, SEEN FROM THE OUTER SIDE.

blastema outside the first visceral pouch. This blastema is divided in the mandibular arch by the trigeminal nerve, and in the hyoid arch by the facial nerve, into mesial and lateral portions. In the mandibular arch the proximal part of the lateral mass becomes the rudiment of the *incus*, while the corresponding part in the hyoid arch represents the *laterohyal cartilage*. The distal portions of the lateral

[1] Meckel discovered the cartilage which bears his name in the human embryo in 1820. He observed its continuity with the malleus, but the interpretation of the facts was due to Reichert.

masses, from the first continuous over the first branchial cleft, become separated from the visceral skeleton, and form the cartilage of the outer ear. The proximal portion of the *mesial* thickening in the mandibular arch does not develop farther, but the distal portion forms the chondroblast of *Meckel's cartilage*. Its upper end early enlarges and becomes the rudiment of the *malleus*. The proximal part of the mesial thickening in the hyoid arch becomes thickened round the stapedial artery, and gives rise to the primitive *stapes*. This is connected with the incus by a strand of the common blastema which persists as the rudiment of the long process of that bone. The distal part of the mesial portion of the hyoid blastema becomes the hyoid bar. It is at first connected with the stapes by a membranous strand (*pars interhyalis*), which soon disappears, so that the stapes is separated from the rest of the hyoid arch.

In these chondroblast areas cartilage is now developed. Meckel's cartilage is deposited as a single piece. Its enlarged upper end is the malleus, which has meantime developed a projection which becomes its handle, and another which becomes its external process. Between the malleus and incus, which chondrifies

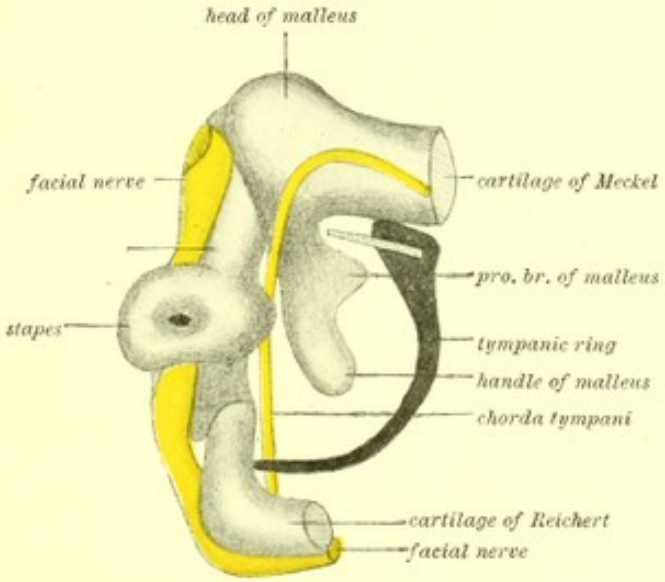



FIG. 313.—RECONSTRUCTION OF THE SAME PARTS AS ARE SHOWN IN FIGS. 311, 312 OF AN EMBRYO OF 55 MM. LONG; LEFT SIDE, INNER ASPECT. (After Broman.)

from a separate centre, there is at first a membranous layer which is afterwards absorbed to give rise to the joint between the bones. In the same manner the original union between the stapes and the long process of the incus is broken to form the joint between them. The incus in its chondroblastic stage becomes attached to the auditory capsule, but is separated from it again when the cartilage is formed, the original intervening tissue becoming the ligament of the bone. The stapes is at first free from the ear-capsule, but later becomes attached to it and ultimately, when in the end of the second month it begins to lose its ring-shape and assume the adult form, the base takes form in the fenestra ovalis, where the wall of the capsule is reduced to a layer of perichondrium over it. The stapes and hyoid cartilage chondrify separately, as does also the laterohyal cartilage mentioned above. This becomes fixed to the ear-capsule, and by an extension of the cartilage between it and the hyoid cartilage the latter obtains a direct secondary attachment to the capsule. The bar thus formed becomes the styloid process. Its basal part lies in the wall of the tympanum and takes part in the formation of the facial canal. Its lower part is represented by the styloid ligament and lesser cornu of the hyoid bone. The ossicles ossify each by a single centre. When the malleus has become

converted into bone the cartilage of Meckel disappears, but meantime on its proximal end a small membranous ossicle appears, which joins the malleus as its anterior process.

The tympanic ring is also a membrane bone. It appears in the third month below and lateral to Meckel's cartilage, and is secondarily attached at a later date to the petrous and squamous. When this union is effected the ossicles originally on the outer side of the ear-capsules are included in the tympanic cavity.

Among other recent writers who have worked at this old problem, J. F. Gemmill [1] agrees with Broman in respect of the stapes, but Fuchs,[2] working on rabbit-material, has come to conclusions shared also by Drüner,[3] which revert to those of Parker in his earlier papers (1877), and

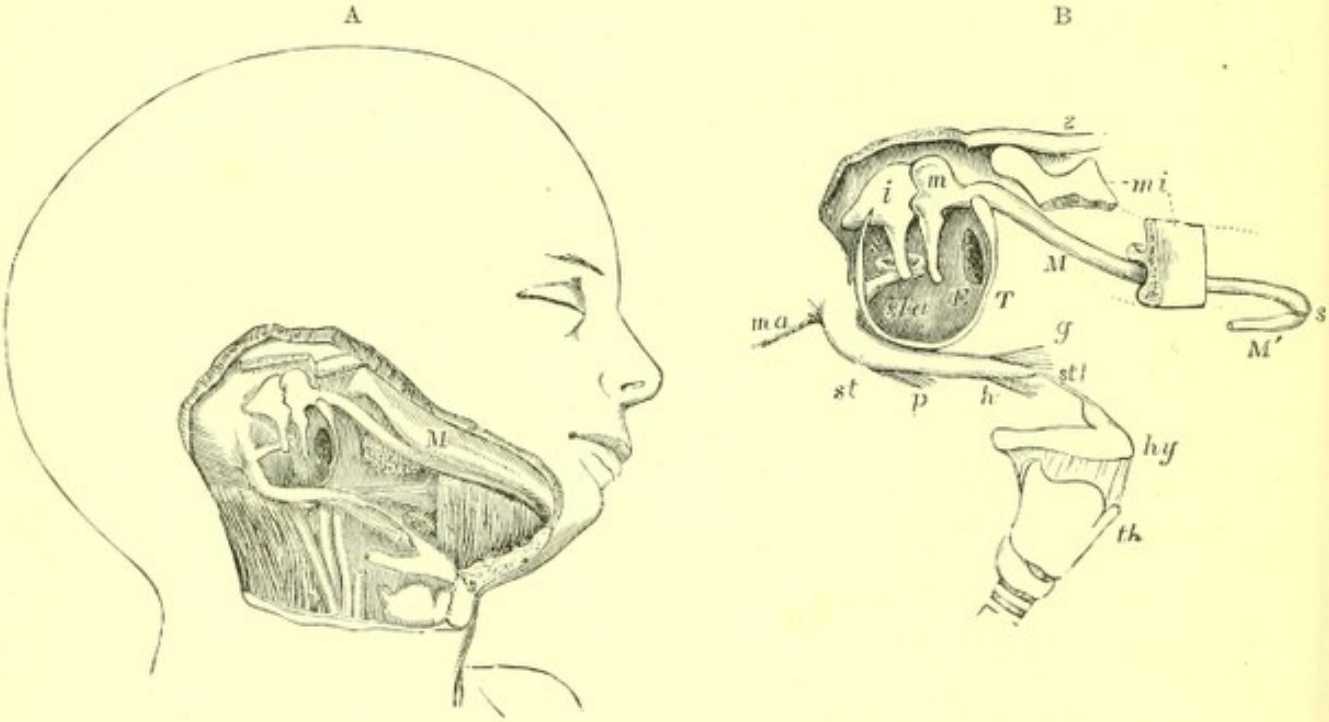



FIG. 314.—CONDITION OF MECKEL'S CARTILAGE AND THE HYOID BAR IN THE HUMAN FŒTUS OF ABOUT EIGHTEEN WEEKS. (Kölliker.)

B is an enlarged sketch by Allen Thomson, showing the relationship of the several parts better than in A.

*z*, zygomatic arch; *ma*, mastoid process; *mi*, portions of the lower jaw left *in situ*, the rest having been cut away; *M*, Meckel's cartilage of the right side, continued at *s*, the symphysis, into that of the left side *M'*, of which only a small part is shown; *T*, tympanic ring; *m*, malleus; *i*, incus; *s*, stapes; *sta*, stapedius; *st*, styloid process; *p*, *h*, *g*, stylopharyngeus, stylohyoid, and styloglossus muscles; *stl*, stylohyoid ligament attached to the lesser cornu of the hyoid bone, *hy*; *th*, thyroid cartilage.

of Gruber (1877)—viz. that the stapes blastema is primarily connected with the auditory capsule and is only secondarily connected with the hyoid arch. Fuchs and Drüner also believe that the connection of the malleus and incus with Meckel's cartilage is a secondary one.

The ontogenetic history of the auditory ossicles, as described by Broman, affords additional evidence that the incus is a separate element, and confirms the view that it represents the quadrate bone of lower forms; while the malleus is the upper end of the primitive mandible, and when ossified is the homologue of the os articulare (Gaup).

[1] Brit. Assoc. Report, 1901. [2] Archiv f. Anat. Suppl. 1905. [3] Anat. Anzeiger xxiv. 1904.

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