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TEXT-BOOK
OF THE
EMBRYOLOGY OF MAN AND MAMMALS

CORRIGENDA.

Page 82, line 5, *dele* "folds of the small intestine."
,, 85, ,, 7 from bottom, *for* "body" *read* "abdominal."
,, 91, ,, 16 ,, ,, *for* "thickness" *read* "volume."
,, 156, ,, 2 ,, ,, *for* "physiological" *read* "histological."
,, 174, ,, 11 ,, ,, *dele* comma after "segment."
,, 309, ,, 1 ,, ,, *for* "*sp*" *read* "*zp*."

TEXT-BOOK

OF THE

EMBRYOLOGY OF MAN AND MAMMALS

BY

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TRANSLATED FROM THE THIRD GERMAN EDITION

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With 339 Figures in the Text and 2 Lithographic Plates

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TRANSLATOR'S PREFACE.

The rapidly increasing recognition of the importance of Embryology in all morphological studies makes it desirable that the most valuable text-books upon the subject, in whatever language, be made available for those who are beginning its study. Although the English-reading student already has at command a number of text-books upon this subject, it is evident to any one familiar with HERTWIG'S *Lehrbuch der Entwicklungsgeschichte des Menschen und der Wirbelthiere* that this work covers the field of Vertebrate Embryology in a more complete and satisfactory way than any book heretofore published in English.

Two important objects to be accomplished in a text-book are: first, a clear and methodical exposition of the well-established facts of the science; and, secondly, such a presentation of unsettled questions as shall stimulate the reader to further inquiry and research. I believe it is far too common for the second of these aims to be overlooked. The present work fulfils both requirements in an eminent degree, and in its historical surveys exhibits an exceptional fairness of treatment, notwithstanding the author has been one of the foremost contestants in several of the fields reviewed. The summaries which follow the discussions of the several topics serve a useful purpose in directing attention to the more important conclusions drawn from each subject.

I have aimed to give a clear and accurate reproduction of the author's ideas; while I have endeavored—not always successfully—to avoid awkward renderings and German idioms, I have preferred to err on the side of a too literal rather than a too liberal translation. There are a few points that demand a brief explanation. The German word *Anlage* has heretofore been variously rendered into English by *rudiment*, *origin*, *beginning*, *basis*, *foundation*, etc., while some writers, recognising the inadequacy of any of these words to express the idea, have incorporated the German word itself in their English.

The *Anlage* of a structure is its beginning or its undifferentiated state—the object in a simple condition which is destined to be followed by a more complicated one. The use of rudiment in this sense is undesirable, because, in the interest of scientific accuracy, it is important to restrict its meaning, as in German, to a structure which is *not destined to become* more complicated, but which *may have been*, either ontogenetically or phylogenetically, even more highly developed than it now is. Origin and beginning are abstract terms, whereas *Anlage* is more frequently used in the concrete; basis and foundation (*Grundlage*) convey a wrong impression—that of the substratum *upon* which the structure is erected. The need of a new word, which shall be used in the sense of *Anlage*, is evident. I suggest the adoption of an already existing word,—*fundament*,—used at present only in a sense with which the proposed usage will not produce confusion. This word has been uniformly employed in the present translation, and the reader will see how readily and naturally it lends itself to this use. Fundament would thus bear the same relation to foundation that *Anlage* does to *Grundlage.*

I have also departed from authorised usage by sometimes employing for *Bindegewebe* and *Stützgewebe* the term *sustentative* (in a mechanical sense) tissue, instead of connective tissue. My reason for this is the narrower meaning of connective as compared with sustentative.

In deference to a custom still followed in Human Anatomy, the author, in describing the relative positions of parts, has very generally used anterior and posterior for dorsal and ventral, etc. Instead of converting these expressions into terms which are independent of the temporary position of the organism, as I should have preferred, it has seemed better to indicate the direction by a bracketed word in those cases where a misunderstanding was most likely to occur. It has of course not been necessary to repeat this after each term of direction, but only after the first one of a series, the reader's attention being thus sufficiently directed to the matter to prevent any misconception.

The rapid advances in Embryology make it impossible for a book two years old to be a faithful reflection of the science of to-day in all its branches; there are some topics in which even radical changes must be recognised. I have thought best, however, to reproduce the book as it left the hands of its author, and to content myself with calling the reader's attention to some of the topics in which the most important advances have been made, such as the metamerism of the head, and the plan and metamorphoses of the vessels of the visceral arches.

I am under very great obligations to my colleague, Dr. C. B. Davenport, for kind assistance and valuable criticism, but for which many defects of the translation would have been overlooked. I am also indebted to Drs. T. G. Lee, H. B. Ward, and W. McM. Woodworth for aid in reading portions of the proof.

E. L. MARK.

CAMBRIDGE, MASS.

AUTHOR'S PREFACE

TO THE FIRST EDITION.

"Die Entwickelungsgeschichte ist der wahre Lichtträger für Untersuchungen über organische Körper."—C. E. v. **Baer**, "Ueber Entwickelungsgeschichte der Thiere" (Bd. I., S. 231).

The Embryology of Animals, although one of the youngest shoots of morphological research, has, nevertheless, grown up in the course of sixty years, along with the cell-doctrine and that of the tissues, to a vigorous and stately tree. The comprehension of the structure of organisms has been extended in a high degree by numerous developmental investigations. The *study of the human body* has also derived great advantage from the same. In the newer anatomical text-books (**Gegenbaur**, **Schwalbe**) Embryology is receiving more and more attention in the description of the separate systems of organs. To what extent many things may be more clearly and attractively described in this manner is best shown by a comparison of the descriptions of brain, eye, heart, etc., in the older and the more recent anatomical text-books.

Although it is generally recognised that *Embryology* constitutes "a foundation-stone of our comprehension of organic forms," nevertheless the attention which its importance warrants is not yet given to it; it is especially true that it has not become as extensively as it should be a component of well-rounded medical and natural-history instruction, to which it is indispensable. The cause of this is perhaps in part to be sought in the fact that in student-circles the study of Embryology is often held to be especially difficult and a comprehension of it to be laborious. And thus many do not venture into this apparently obscure realm.

But ought the development of an organism to be really more difficult to comprehend than the complicated finished structure?

To a certain extent this was the case at a time when the most divergent and contradictory opinions prevailed concerning many of the most important processes of development, such as the formation of the germ-layers, the protovertebræ, etc., which the lecturer had to take into account, and when many processes were not yet understood in their essence and their significance. But, thanks to the results of Comparative Embryology, the number of the unintelligible processes has been every year diminished, and in the same ratio the study of Embryology even for the beginner has been rendered easier.

At least, it is not in any way an essential feature of the process of development that it should be more difficult to understand than the structure of the completed form. For every development begins with a very simple condition, from which the more complicated is gradually derived and by which it is explained.

Inasmuch as I have for twelve years pursued the study of Embryology with especial interest, both in annually recurring academic lectures and in a series of scientific investigations, the desire has been awakened in me to acquire for Embryology a broader and more secure foundation in education, and to procure for it admission into larger circles of medical men and well-educated naturalists. As the result of this there has come into existence the book which is before us, in which the especial problem has been to make the complicated structure of the human body more intelligible through the knowledge of its development.

For the solution of this problem I have in the present text-book placed *the comparative method of investigation* in the foreground. I do not thereby find myself in any way in opposition to another direction of embryological research, which places the objective point in the *physiological or mechanical explanation of the form of the animal body*. Such a direction I hold to be fully warranted, and I believe that, instead of being opposed to a comparative-morphological direction, it can be of the most permanent value to it in the solution of its problems. One will find that I have here given full attention to the mechanico-physiological explanation of forms. Compare the sections on cell-division and Chapter IV., "General Discussion of the Principles of Development," in which the laws of unlike growth and the processes of the formation of folds and evaginations are treated.

In the presentation of the separate processes of development, in the main the important things only have been selected, the subsidiary left out, in order thus to make the introduction into embryological study easier. In the case of fundamental theories I have gone into their history extensively, because it is of great interest, and under certain circumstances operates as a stimulus, for one to see in what way the state of a scientific question for the time being has been attained. In pending controversial questions

I have, it is true, employed chiefly as the foundation of my presentation the views which appear to me the most entitled to acceptance, but have not left unmentioned opposing conceptions.

Numerous figures in the text, as well as some colored plates, will contribute materially to the easier comprehension of the various developmental processes.

I submit, then, this text-book to physicians and to students of medicine and the natural sciences, with the desire that it may promote and facilitate the study of Embryology in wider circles, and that it may thereby contribute to a deeper insight into the structure of our own bodies.

OSCAR HERTWIG.

JENA, *October* 1886.

AUTHOR'S PREFACE

TO THE SECOND EDITION.

THE friendly reception which the "Text-book of the Embryology of Man and Mammals" has found, is an indication of the increased interest which this branch of Morphology now meets with.

Even more than a year ago, after the first part of the text-book appeared and while the second part was in the press, the necessity of preparing a second edition became evident.

In this edition fundamental changes have not been undertaken; the text has, however, undergone an expansion in some places, owing to the attention given to several works which have recently appeared. This has been the case with the section on the first developmental processes of the egg (WEISMANN, BLOCHMANN); that on the origin of the vascular system (RABL, RÜCKERT); that on the development of the fœtal membranes (DUVAL, OSBORN); and that on the human placenta (KASTSCHENKO, WALDEYER, RUGE).

As the second part of the text-book has just appeared, it has been possible to incorporate it in the second edition without alteration.

It has, furthermore, seemed to me expedient in the second edition to distribute at the ends of the several chapters the synopses of the literature, which in the first edition were brought together at the close of the whole work. Finally, there has been added an index of subjects, by which a more rapid orientation concerning the separate topics will be facilitated; this will increase the usefulness of the work.

May the book in this form make for itself new friends, not only among students of medicine and the natural sciences, but also with all those who have a fondness for and a comprehension of studies in natural science.

OSCAR HERTWIG.

JENA, *February* 1888.

AUTHOR'S PREFACE
TO THE THIRD EDITION.

In the two years which have elapsed since the appearance of the second edition of this text-book, our knowledge of the embryology of Vertebrates has experienced many important enrichments, thanks to the numerous investigations which are annually published. Therefore, as the problem of preparing a third edition of the text-book confronted me, I was compelled to make extensive changes in many places. Thus the second and third chapters, concerning the processes of fertilisation and cleavage of the egg, have undergone expansion, owing to the presentation of the important discoveries which have been made on the the egg of Ascaris megalocephala. I have given an entirely new wording to the ninth chapter on the development of connective substance and blood, also to the sections on the origin of the urinary organs and the development of the peripheral nervous system, and, finally, to the account of the development of the heart and the venous system. Also at other places one will often recognise the hand of improvement.

The third edition has been essentially improved by the addition of thirty new figures, which I have taken from the investigations of VAN BENEDEN, BOVERI, DUVAL, FLEMMING, HERMANN, HIS, BORN, GEGENBAUR, NAGEL, VAN WIJHE, GRAF SPEE, BONNET, and KEIBEL. Through the friendliness of Professor VAN BENEDEN I was also put in a position to employ for my text-book three figures out of his hitherto unpublished extensive work on the development of the germinal layers of the Rabbit. By means of the increase in the number of figures I hope that I have been able to render still easier the comprehension of many of the processes of development.

And so I close the preface to the third edition by expressing my thanks to all those who have rendered me friendly aid, and especially to the publisher, who in the further equipment of the text-book has met my wishes with the greatest willingness.

OSCAR HERTWIG.

BERLIN, *March* 1890.

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INTRODUCTION.

The history of the development of the individual, or Ontogeny (Embryology), is the science of the growth of an organism; it describes the morphological changes which an organism passes through from its origin in the ovum up to its complete maturity, and presents these in their natural connection. We can regard the fertilisation of the egg-cell as the beginning of the process of development for Vertebrates, as it also is for all the rest of the higher animals.

In giving an account of the changes of the egg-cell, which begin with fertilisation, one may choose between two different methods.

According to one method a particular organism is made the basis of the account, and one describes the changes which its germ undergoes from the moment of fertilisation onward, from hour to hour, and from day to day. It is in this way that the embryology of the Chick has been worked out by C. E. von Baer in his classical paper, and by Foster and Balfour in their "Elements of Embryology." This method has the advantage that the reader acquires a view of the total condition of an organism in the separate stages of its development.

A book of that kind is especially suitable for such persons as desire to acquaint themselves, by their own observation, with the embryology of a single animal, as, for example, the Chick, by repeating the investigations of others. It is, on the contrary, less adapted to those who wish to acquire a connected view of the development of the separate organs, as the eye, the heart, the brain, etc. For the formation of these will of course be treated of at different places in describing younger and older embryos. In order to procure a general survey of the course of development of an organ, the reader must consult various places in the text-book, and collect for himself what relates to the subject.

For beginners, and for the needs of theoretical instruction in Embryology, the *second* method commends itself, in which the separate organs are considered in succession, each for itself, and the changes which a single organ has to pass through during development are set forth connectedly from beginning to end. It is in this way that **Kölliker**'s "Embryology of Man and the Higher Animals" is written.

The second method is, moreover, the only one applicable when the problem is to investigate in a comparative way the development of several organisms, and to fill up the gaps which exist in our knowledge of one by that which we know concerning nearly related animals. But it is precisely in this position that we find ourselves, when we wish to acquire a survey of the development of the human body. An account which should limit itself to that which we know about Man would exhibit numerous and extensive gaps. For up to the present the eye of man has not seen how the human ovum is fertilised, how it divides, how the germ-layers are formed, or how the establishment of the most important organs is effected. It is especially the period of the first three weeks, during which the greatest variety of fundamental processes of development take place, concerning which we know next to nothing; there is also little prospect that a change will soon occur in this regard. The time will therefore perhaps never come when a complete embryology of Man in the strict sense of the word will be possible.

However, the existing gaps can be filled out in another manner, and one which is entirely satisfactory. The study of the most widely differing Vertebrates teaches us that they are developed according to a common plan, that the first processes of development agree in all really important points, and that the differences which we encounter here and there are produced by causes of a subordinate kind, as, *e.g.*, by the egg's possessing a greater or less amount of yolk.

When we see that the establishment of the central nervous system, of the eye, of the spinal column, of the viscera, etc., takes place in Mammals on the whole just as it does in Amphibia, Birds, and Reptiles, the conclusion is near at hand, and justified, that Man also in his development is no exception to this general phenomenon. Thus in the study of Embryology we are naturally led to the *comparative method*. What, owing to the nature of the difficulties, we cannot learn directly about the development of Man, we seek to deduce by the investigation of other Vertebrates.

In earlier decennia the Hen's egg was the favorite object, and it is upon this that we possess the most numerous and most complete series of observations. During the last twenty years research has also been directed to Mammals,—in the investigation of which the greatest difficulties have to be surmounted,—as well as to Reptiles, Amphibia, Fishes, etc. Only through the observation of such various objects has insight been acquired into many processes, which in their essence remained unintelligible to us from the study of the Chick alone. For it was thus that one first learned to distinguish the important from the accessory and unimportant, and to understand the laws of development in their generality.

In this text-book, therefore, I shall not confine myself to a single object, such as the egg of the Hen or the Rabbit, but from more general comparative standpoints shall endeavour to present what, through extensive series of investigations, we have thus far recognised as the rule in regard to the real nature of the processes of fertilisation and cleavage, the formation of the germ layers, etc.

However, let no one expect a text-book of comparative Embryology. The purpose and the problem is first of all to learn to comprehend the development and the structure of the human body. What we know about that has been placed before everything else, and the embryology of the remaining Vertebrates has been cited, and, as it were, fully utilised, only in so far as was necessary for the purpose indicated.

In the division of the embryological material proposed by us, according to the separate systems of organs, there is a long series of processes, with which the development begins, which do not permit of an arrangement, because at the beginning the fundaments of definite, afterwards differentiated organs, are not recognisable in the germ. Before there is any formation of organs, the egg is divided into numerous cells, and these then arrange themselves into a few larger complexes, which have been called the germ-layers, or the primitive organs of the embryo. Further, in the higher Vertebrates there are formed certain organs, which are useful only during embryonic life, and are subsequently lost—namely, the fœtal membranes and fœtal appendages. All of the processes of that nature we shall treat of connectedly, and by themselves. In accordance with this, we can divide *our theme into two main sections*, the first of which will deal with the initial processes of development and the embryonic membranes, the second with the origin of the separate systems of organs. In order to facilitate for the advanced a more thorough study, and a penetration into embryological literature, a survey of the more important original works is given at the close of the separate chapters. On the other hand, text-books of Embryology may be mentioned in this place. [Compare also the larger monographic works cited at the end of the book.]

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PART FIRST.

CHAPTER I.

DESCRIPTION OF THE SEXUAL PRODUCTS.

EGG-CELL AND SEMEN-CELL.

In most animals, and without exception in all Vertebrates, the development of a new being can take place only when reproductive elements, produced by two sexually different individuals,—the egg by the female, and the seminal corpuscle or seminal filament by the male,—are at the proper time brought into union as the result of the procreative act.

The egg and the seminal filament are simple elementary parts or cells, which are produced in special glandular organs, the egg-cells in the ovary of the female, and the semen-cells in the testis of the male. After the beginning of sexual maturity at definite periods, they detach themselves within the sexual organs from their union with the remaining cells of the body, and form, under suitable conditions of development, among which the union of the two sexual cells is the most important, the starting-point for a new organism.

First of all, therefore, we have to acquaint ourselves with the peculiarities of the two kinds of sexual products.

1. The Egg-cell.

The egg is by far the largest cell of the animal body. At a time when nothing was known of its cell-nature, its separate components were given special names, which remain in use even at the present time. The contents were called egg-yolk, or *vitellus*; the cell-nucleus was called *vesicula germinativa*, or germinative vesicle, discovered by the physiologist PURKINJE; the nuclear corpuscles, or nucleoli, were called germinative spots, or *maculæ germinativæ* (WAGNER); and, finally, the cell-membrane was called the yolk-membrane, or *membrana vitellina*. All these parts vary in not unimportant ways from the ordinary condition of the protoplasm and nucleus of most animal cells.

The **vitellus** (figs. 1 and 3 *n.d*) rarely appears homogeneous, mucilaginous, and translucent, like the protoplasm of most cells; it is ordinarily opaque and coarsely granular. This results from the fact that the egg-cell, during its development in the ovary, stores up in itself nutritive materials, or *reserve stuffs.* These consist of fat, of albuminous substances, and of mixtures of the two, and are described, according to their form, as larger and smaller yolk-spherules, yolk-plates, etc. Later, when the process of development is in progress, they are gradually used up in the growth and for the increase of the embryonic cells. The fundamental substance of the egg, in which the reserve stuffs just now referred to are imbedded, is *protoplasm*, physiologically the most interesting and important of substances, because in it take place, as we infer from many phenomena, the essential life-processes.

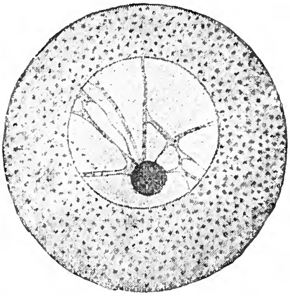

Fig. 1.—Immature egg from the ovary of an Echinoderm. The large germinative vesicle shows a germinative dot, or nucleolus, in a network of filaments, the nuclear network.

We must therefore distinguish in the yolk, in accordance with the suggestion of VAN BENEDEN, (1) the *egg-protoplasm*, and (2) the *yolk-substance*, or *deutoplasm*, which is of a chemically different nature, and is stored up in the former.

When the deposition of reserve materials takes place to a great degree, the really essential substance, the egg-protoplasm, may become almost entirely obscured by it (figs. 3, 4). The protoplasm then fills up the small interstices between the closely packed yolk-globules, yolk-cakes, or lamellæ, as mortar does those between the stones in masonry, and appears in sections only as a delicate network, in the smaller and larger meshes of which lie the yolk-elements. Only at the surface of the egg is the egg-plasm constantly present as a thicker or thinner continuous cortical layer.

The **germinative vesicle** usually occupies the middle of the egg. It is the largest nuclear structure in the animal body, and its diameter generally increases with the size of the egg.

The germinative vesicle (figs. 1, 2) is separated from the yolk by a firm *membrane*, which may often be distinctly demonstrated, and which surrounds various included components: *nuclear liquid* (Kernsaft), *nuclear network*, and *nucleoli*. The **nuclear liquid** is more fluid than the yolk, in the fresh condition usually as clear as water, and when coagulated by the addition of reagents, absorbs only a little or no coloring matter. It is traversed by a *network of delicate filaments* (*kn*), which attach themselves to the nuclear membrane. In this network are enclosed *nucleoli*, or **germinative spots** (*kf*), small, for the most part spherical, homogeneous, lustrous structures, which consist of a substance akin to protoplasm—nuclear substance or nuclein. *Nuclein* is distinguishable from protoplasm—in addition to certain other chemical reactions—especially by the fact that it absorbs with great avidity pigments such as carmine, hæmatoxylin, aniline, etc., on account of which it has also received from Flemming the name *chromatin*.

The number of the nucleoli in the germinative vesicles of different animals is highly variable, but it is tolerably constant for each species; sometimes there is only a single nucleolus present (fig. 1), sometimes there are several or even very many of them (fig. 2 *kf*). Accordingly one may with Auerbach distinguish uninucleolar, plurinucleolar, and multinucleolar germinative vesicles.

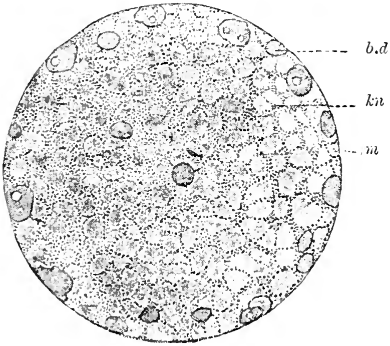

Fig. 2.—**Germinative vesicle of a Frog's egg that is still small and immature.** It shows very numerous mostly peripheral germinative spots (*kf*), in a fine nuclear network (*kn*). *m*, Nuclear membrane.

At their surfaces eggs are surrounded by protective **envelopes**, the number and condition of which are exceedingly variable throughout the animal kingdom as well as among Vertebrates. It is best to divide them, as Ludwig has done, according to their method of origin, into two groups, into the *primary* and the *secondary egg-membranes*. Primary egg-membranes are such as have been produced either by the egg itself or by the follicular cells within the ovary and the egg-follicle. Those produced by the yolk of the egg are called *vitelline membrane*; those formed by the follicular epithelium, *chorion*. All which take their origin outside of the ovary, as a result of secretions on the part of the wall of the oviduct, are to be designated as secondary egg-membranes.

In their details the eggs of the various species of animals differ from each other in a high degree, so that they must really be considered as the most characteristic for the species of all the kinds of animal cells. Their size, which is due to a greater or less accumulation of deutoplasm, varies so extensively that in some species the egg-cells can be only barely recognised as minute dots, whereas in others they attain the considerable dimensions of a Hen's egg, or even of an Ostrich's egg. The form is usually globular, more rarely oval or cylindrical. Other variations arise from the method in which protoplasm and deutoplasm are constituted and distributed within the limits of the egg; there are in addition the differences of the finer structure of the germinative vesicle and the great variability of the egg-membranes.

Some of these conditions are of great significance from their influence on the manner of subsequent development. They have been employed as a basis for a **classification of the various kinds of eggs.**

It is most expedient to divide eggs into two chief groups,—into *simple* and into *compound eggs,*—the first of which is divisible into several sub-groups.

A. *Simple Eggs.*

Simple eggs are such as are developed in an ovary out of a single germinal cell. The eggs of all the Vertebrates and most of the Invertebrates belong to this group.

In this chief group there occur, according to the *manner in which protoplasm and deutoplasm are distributed within the egg, three modifications, which are of very great importance in the determination of the first processes of development.*

In the simplest case the *deutoplasm,* which ordinarily is present only to a limited amount in the correspondingly small egg, is *more or less uniformly distributed in the protoplasm* (fig. 1). In other cases there has arisen out of this original condition, in conjunction with an increase in the bulk of the yolk-material, an inequality in the distribution of the two egg-substances previously distinguished. *The egg-plasma has accumulated in greater abundance at certain regions of the egg-territory, and the deutoplasma at other regions.* Consequently, a contrast has arisen between portions of the egg-cell which are richer, and those which are poorer, in protoplasm. A further accentuation of this contrast exercises an extraordinarily broad and profound influence on the first processes of development, which take place in the egg after fertilisation. That is to say, the changes, which further on are embraced under the process of cleavage, make their appearance only at the region of the egg which is richer in protoplasm, whereas the region which is more voluminous and richer in deutoplasm remains apparently quite unaltered, and is not divided up into cells. By this means the contrast, which was already present in the unsegmented egg, becomes during development disproportionately greater and more obvious. The one part undergoes changes, is divided into cells, and out of these produces the individual organs; the other part remains more or less unaltered, and is gradually employed as nutritive material. Following the example of Reichert, the part of the yolk which is richer in protoplasm, and to which the developmental processes remain confined, has been designated *formative* yolk, and the other *nutritive* yolk.

The unequal distribution of *formative yolk* (*vitellus formativus*) and of *nutritive yolk* (*vitellus nutritivus*) within the egg is accomplished in two different ways.

In the *one case* (fig. 3) the formative yolk is accumulated at one pole of the egg as a *flat germ-disc* (*k.sch*). Inasmuch as its specific gravity is less than that of the nutritive yolk (*n.d*) collected at the opposite pole, it is always directed upward, and it spreads itself out on the yolk just like a drop of oil on water. In this case, therefore, the egg has undergone a *polar differentiation*; when at rest it must always assume a definite position, owing to the unequal weight of the two poles. *The dissimilar poles are distinguished: the upper, lighter pole, with the germ-disc, as the animal* (*A.P*); *the under, heavier and richer in yolk, as the vegetative pole* (*V.P*). The polar differentiation of eggs is often encountered in Vertebrates, and is especially prominent in the classes of Bony Fishes, Reptiles, and Birds.

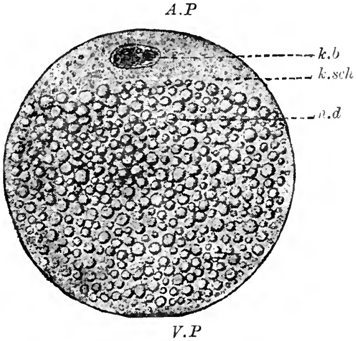

Fig. 3.—Diagram of an egg with the nutritive yolk in a polar position. The formative yolk constitutes at the animal pole (*A.P*) a germ-disc (*k.sch*), in which the germinative vesicle (*k.b*) is enclosed. The nutritive yolk (*n.d*) fills the rest of the egg up to the vegetative pole (*V.P*).

In the *second case* (fig. 4) *the formative yolk* (*b.d*) *is accumulated over the whole surface of the egg*, and surrounds the centrally placed nutritive yolk (*n.d*) as a uniformly thick, finely granular cortical layer. The egg exhibits central differentiation, and therefore does not assume a constant position when at rest. As in the former case the yolk was polar in position, so here it is *central.* Such a condition is never encountered in Vertebrates, but it is characteristic of Arthropods.

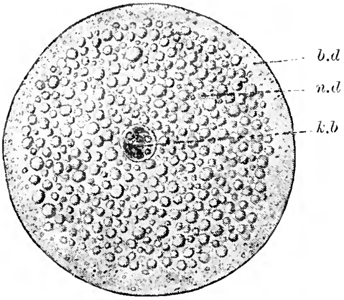

Fig. 4.—Diagram of an egg with the nutritive yolk in the centre. The germinative vesicle (*k.b*) occupies the middle of the nutritive yolk (*n.d*), which is enveloped in a mantle of formative yolk (*b.d*).

In order to distinguish the three modifications, Balfour has made use of the expressions alecithal, telolecithal, and centrolecithal. He calls those eggs alecithal in which the deutoplasm, in small amount, is uniformly distributed through the protoplasm ; telolecithal, those in which it is accumulated at the vegetative pole ; centrolecithal, those in which the accumulation of deutoplasm has taken place at the centre. In what follows, we shall speak of (1) *eggs with uniformly distributed yolk*, (2) *eggs with polar deutoplasm, and* (3) *eggs with central deutoplasm.*

It is now expedient to illustrate what has just been said by typical examples, and for this purpose the eggs of Mammals, Amphibia, Birds, and Arthropods have been selected. We shall also frequently recur to these in the presentation of the subsequent phases of development.

The egg of Mammals and of Man is exceedingly small, since it measures on the average only 0·2 mm. in diameter. It is for this reason that it was not discovered until the present century—in 1827, by Carl Ernst von Baer. Previously the much larger Graafian follicle of the ovary, in which the smaller true egg is enclosed, had been erroneously taken for the latter. The Mammalian egg (fig. 5) consists principally of a finely granular protoplasmic substance, which contains dark, fat-like spherules and granules (deutoplasm), and which is turbid and opaque in proportion to the amount of these. The germinative vesicle (*k.b*) contains a large germinative dot (*k.f*), located, together with a few smaller accessory dots, in a nuclear network (*k.n*). The egg-membrane is called *zona pellucida* (*z.p*), because it surrounds the yolk as a relatively thick and clear layer. It is a primary membrane, for it is formed within the Graafian follicle, by the follicular cells. Under high magnification the zona pellucida

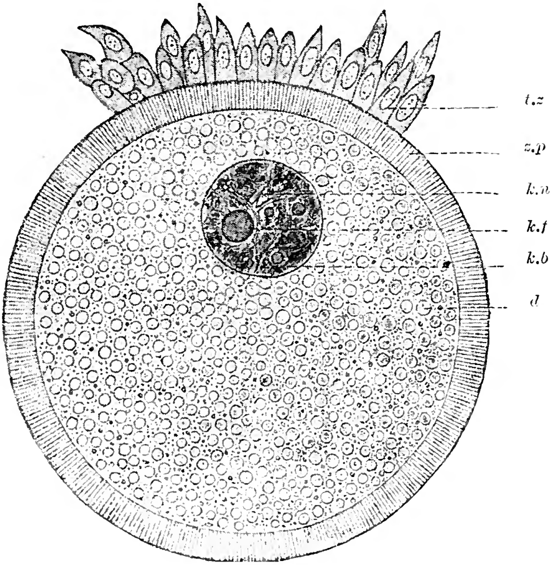

Fig. 5.—Egg from a Rabbit's follicle which was 2 mm. in diameter, after Waldeyer. It is surrounded by the zona pellucida (*z.p*), on which there rest at one place follicular cells (*f.z*). The yolk contains deutoplasmic granules (*d*). In the germinative vesicle (*k.b*) the nuclear network (*k.n*) is especially marked, and contains a large germinative dot (*k.f*).

(*z.p*) appears radially striate, since it is traversed by numerous pore-canals, into which, as long as the egg remains in the Graafian follicle, very fine projections of the follicular cells (*f.z*) penetrate. These fuse with the egg-plasm, and are probably concerned in the nutrition and growth of the contents of the egg. (Retzius.)

The *human ovum* is wonderfully like the egg of Mammals in size, in the condition of its contents, and the nature of its membranes. However, it always can be distinguished by means of special, though trifling, characteristics, as the careful investigations of Nagel have shown. Whereas in the Rabbit lustrous, fat-like spherules render the yolk cloudy, the human ovum retains its transparency during all stages of development, so that one may recognise most accurately all its structural details, even on the living object. The yolk is divided into two layers. The *inner layer* contains principally deutoplasm, which produces in this case, contrary to most of the Mammals, only a slight cloudiness; it consists in part of feebly lustrous, in part of highly refractive fragments, some coarser, some finer; but it is not possible to recognise the mutual boundaries of the individual components, as is the case in other Mammals and lower animals, where one distinguishes with great ease granules and distinct drops. The *outer layer* or peripheral zone of the yolk is more finely granular and still more transparent than the central part, and contains the germinative vesicle with a large germinative dot, in which NAGEL was able to observe amœboid motions. The zona pellucida is remarkably broad; it is striate, and is separated from the yolk by a narrow (perivitelline) space. There are two or three layers of follicular cells attached to the periphery of the egg when it is set free from the GRAAFIAN follicle. The long diameters of these cells are arranged in a radial direction around the egg, as is general in Mammals, and it is due to this circumstance that they have received the name *corona radiata*, introduced by BISCHOFF. The human egg without the follicular epithelium measures, on the average, 0·17 mm. in diameter.

The eggs of many Worms, Molluscs, Echinoderms, and Cœlenterates agree with the Mammalian egg in their size, and in the method in which protoplasm and deutoplasm are uniformly distributed through the egg.

The *eggs of Amphibia*, which were cited as the second example, form a transition from simple eggs, with uniform distribution of yolk-material, to eggs with distinctly expressed and externally recognisable polar differentiation. Already these have deposited in themselves a large amount of deutoplasm, and have thereby acquired a very considerable size. The Frog's egg, for example, is stuffed full of closely compacted, fatty-looking yolk-lumps (Dotterschollen) and yolk-plates. The egg protoplasm is in part distributed as a network between the little yolk-plates; in part it forms a thin cortical layer at the surface of the egg. Upon closer examination, however, the beginning of a polar differentiation is most distinctly recognisable even here. It manifests itself in this way: at one pole, which at the same time appears black on account of a deposit of superficial pigment, the yolk-plates are smaller and enveloped in more abundant egg-plasm; and also, probably as a consequence of this, slight differences in specific gravity are distinguishable between the pigmented and the unpigmented, or the animal and the vegetative, halves of the egg.

The germinative vesicle (fig. 2) lies in the middle of the immature egg, is exceedingly large, even visible to the naked eye, and multinucleolar, inasmuch as there are a hundred or more large germinative dots (*kf*) distributed immediately under the nuclear membrane.

The envelopes exhibit, in comparison with the Mammalian egg, an increase in number, for to the zona pellucida (zona radiata), which is produced in the follicle, there is subsequently added still another, a secondary envelope. This is a thick, viscid, gelatinous layer, which is secreted by the wall of the oviduct, and which becomes swollen in water.

The polar differentiation, taken, as it were, in the very process of developing in the case of the Amphibia, is found sharply expressed in our third example, the *Bird's egg*.

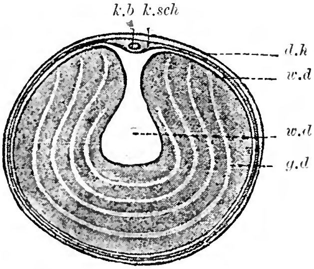

Fig. 6a.—Egg-cell (yolk) of the Hen taken from the ovary. *k.sch*, Germinative disc; *k.b*, germinative vesicle; *w.d*, white yolk; *g.d*, yellow yolk *d.h*, vitelline membrane.

In order to form a correct picture of the condition of the egg-cell in the case of the Hen, or of any other bird, we must seek it while still in the ovary, at the moment when it has finished its growth, and is ready to be set free from the follicle. It is then ascertained that only the spheroidal yolk, the so-called yellow of the egg, which in itself is an enormously large cell (fig. 6a), is developed in the botryoidal ovary. It is enclosed in a thin but tolerably firm pellicle (*d.h*), the vitelline membrane, the rupture of which is followed by an extrusion of the soft pulpy contents. By careful examination one will discover upon the latter a small white spot, the germinative disc (*k.sch*), or *discus proligerus*, also called scar or *cicatricula.*. It has a diameter of about 3 or 4 mm., and consists of formative yolk,—a finely granular protoplasm with small yolk-spherules,—which alone is involved in the process of cleavage. In the flattened germinative disc is also found the germinative vesicle, fig. 6a (*k.b*) and fig. 6b (*x*), which is likewise somewhat flattened and lenticular.

The remaining chief mass of the egg-cell is nutritive yolk, which is composed of numberless yolk-spherules united by slight traces of egg-plasm, as though by a cement. Information concerning its finer structure is to be gained from thin sections through the hardened egg, which should be cut perpendicularly to the germinative disc. According to differences in staining and in elementary composition, there are now to be distinguished *the white and the yellow nutritive yolk* (fig. 6a).

The white yolk (*w.d*) is present in the egg-cell only in a small quantity; it forms a thin layer over the whole surface, the white yolk-rind; secondly, it is accumulated in somewhat greater quantity under the germinative vesicle, for which it at the same time forms a bed or cushion (Pander's nucleus); and, thirdly, from this region it penetrates in the form of a mortar-pestle into the very centre of the yellow yolk, where it terminates in a knob-like swelling (latebra, Purkinje). Upon boiling the egg, it is less coagulated, and remains softer than *the yellow yolk.* In the coagulated condition the latter discloses upon sections a lamellated condition, in that it consists of smaller and larger spherical shells, which envelope the *latebra.*

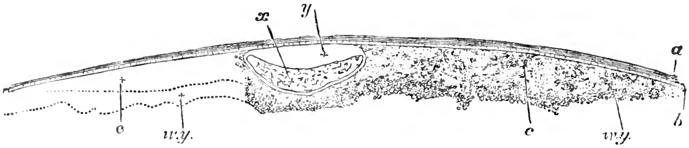

Fig. 6b.—**Section of the germ-disc of a mature ovarian Hen's egg still enclosed in the capsule,** after Balfour.

a, Connective-tissue capsule of the egg; *b*, epithelium of the capsule, on the inside of which lies the vitelline membrane reposing upon the egg; *c*, granular substance of the germinative disc; *w.y*, white yolk, which passes imperceptibly into the finely granular substance of the disc; *x*, germinative vesicle enclosed in a distinct membrane, but shrivelled up; *y*, space originally occupied by the germinative vesicle, but made empty by its shrivelling up.

The two kinds of yolk also differ from each other in respect to the condition of their elementary particles. The yellow yolk consists of soft plastic spherules (fig. 7 A) from 25 to 100 μ in diameter, which acquire a punctate appearance from the presence of numerous exceedingly minute granules. The elements of the white yolk are for the most part smaller (fig. 7 B), and likewise spherical, but contain one or several large highly refractive granules.

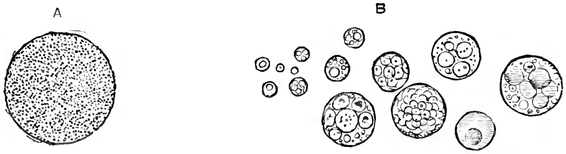

Fig. 7.—**Yolk-elements from the Fowl's egg,** after Balfour. A, Yellow yolk; B, white yolk.

At the boundary between the two kinds of yolk there are present spherules which effect a transition between them.

The freshly laid Hen's egg (fig. 8) has a different appearance from that of such an ovarian egg. This results from the fact that there is deposited around the yolk, when it detaches itself from the ovary and is taken up by the oviduct, several secondary envelopes derived from the wall of the oviduct, viz., the white of the egg, or the albumen, the shell-membrane, and the calcareous shell. Each of these parts is formed in a special region of the Hen's oviduct. The latter is divided into four regions: (1) A narrow ciliated initial part, into which the liberated egg is received, and where it is fertilised by the spermatozoa already accumulated there; (2) a glandular region, covered with longitudinal furrows, from which the albumen is secreted and spread around the yolk in a thick layer; (3) a somewhat enlarged part, covered with small villi, the cells of which secrete calcareous salts, and thus cause the formation of the shell; (4) a short narrower region, through which the egg passes rapidly, and without undergoing any further change, when being deposited.

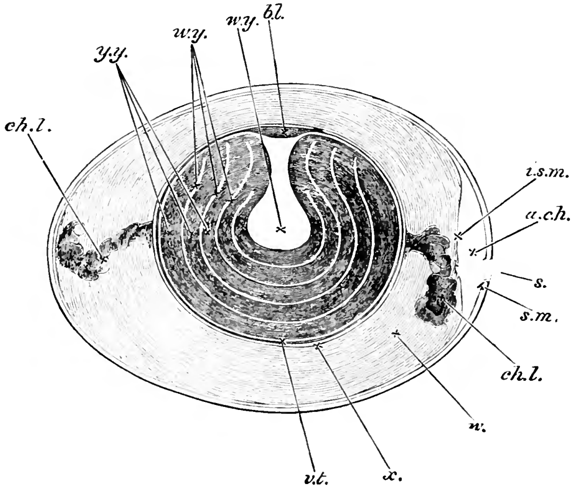

Fig. 8.—Diagrammatic longitudinal section of an unincubated Hen's egg, after ALLEN THOMSON. (Somewhat altered.)

b.l. Germ-disc; *w.y.* white yolk, which consists of a central flask-shaped mass and a number of concentric layers surrounding the yellow yolk (*y.y.*); *v.t.* vitelline membrane; *x.* a somewhat fluid albuminous layer, which immediately envelopes the yolk; *w.* albumen composed of alternating layers of more and less fluid portions; *ch.l.* chalazæ; *a.ch.* air chamber at the blunt end of the egg—simply a space between the two layers of the shell-membrane; *i.s.m.* inner, *s.m.* outer layer of the shell-membrane; *s.* shell.

The envelopes furnished in succession by the oviduct have the following composition:—

The white of the egg, or albumen (*w*), is a mixture of several materials: according to chemical analyses, it contains 12% albumen, 1·5% fat and other extractive materials, 0·5% salts (potassic chloride, sodic chloride, sulphates, and phosphates), and 86% water. It surrounds the yolk in several layers of varying consistency. There is a layer quite closely investing the latter, which is firmer and especially noteworthy because it is prolonged into two peculiar spirally twisted cords, the *chalazæ* (*ch.l*), which consist of a very compact albuminous substance, and which make their way through the albumen to the blunt and to the pointed poles of the egg.

The albumen is enclosed by the thin but firm shell-membrane (*s.m*) (membrana testæ), which is composed of felted fibres. It may be separated into two lamellæ—an outer, which is thicker and firmer, and an inner, which is thinner and smooth. Soon after the egg is laid the two layers separate from each other at the blunt pole, and enclose between them a space filled with air (*a.ch*),—the so-called air-chamber, which continues to increase in size during incubation, and is of importance for the respiration of the developing Chick.

Finally, the shell, or testa (*s*), is in close contact with the shell-membrane; it consists of an organic matrix (2%), in which 98% calcareous salts are deposited. It is porous, being traversed by small canals, through which the atmospheric air may gain entrance to the egg. The porosity of the calcareous shell is an absolute necessity for the normal development of the egg, since the vital processes in the protoplasm can take place only when there is a constant supply of oxygen. If the porosity of the shell be destroyed, either by soaking it in oil or closing its pores with varnish, the death of the incubated egg ensues in a very short time.

B. *Compound Eggs.*

Compound eggs are found only in a few subdivisions of the invertebrated animals, as in the Cestodes, Trematodes, etc.; they are noteworthy in this respect, that they are produced by the union of numerous cells, which are formed in two different glands of the sexual apparatus of the female,—in the germarium and in the vitellarium. In the *germarium* is developed the *egg-cell* in the *restricted sense.* This is always very small, and consists almost exclusively of egg-plasm. When this cell at its maturity is set free from its surroundings and comes into the sexual outlets, it is obliged to pass the opening of the *vitellarium;* here there are associated with it a number of yolk-cells, which, owing to deposition of reserve material in the protoplasm, appear turbid and coarsely granular, and which constitute the dower that is given by the maternal organism to the developing germ on its way. Thereupon the whole is enclosed in one or several secondary egg-membranes, and now constitutes the compound egg, in which, however, the developmental processes manifest themselves exclusively on the simple germ cell; it is that alone which is fertilised and segments, while the yolk-cells gradually degenerate and are employed as nutritive material. Thus in this case also, upon closer examination, the general law, that the descendent organism takes its origin from a *single cell* of the maternal body, suffers no exception.

2. The Seminal Filaments.

In contrast with eggs, which are the largest cells of the animal body, the sperm-cells or sperm-filaments (spermatozoa) are the smallest elementary parts; they are accumulated in great multitudes in the seminal fluid of the male, but can be recognised in it only by the aid of high magnification, being, for the most part, slender motile filaments. Inasmuch as every cell consists of at least two parts, namely, nucleus and protoplasm, we must look for these parts in this case also. We shall take for description the spermatozoa of Man.

In Man the seminal filaments (fig. 9) are about 0·05 mm. long. One may distinguish as head (*k*) a short but thick region, which marks the anterior end, as tail a long thread-like appendage (*s*), and between the two a so-called middle piece (*m*).

The head (*k*) has the form of an oval plate, which is slightly excavated on both surfaces, and is somewhat thinner toward the anterior end. Seen from the side (*B*) it presents a certain resemblance to a flattened pear. Chemically considered, it consists of nuclear substance (nuclein or chromatin), as microchemical reactions show. To the head is united, by means of a short part called the middle piece (*m*), the long thread-like appendage (*s*), which is composed of protoplasm, and is best compared to a flagellum, because, like the latter, it executes peculiar serpentine motions in virtue of its contractile properties. By means of these motions the spermatozoön moves forwards in the seminal fluid with considerable velocity.

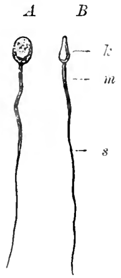

Fig. 9.—Mature spermatozoa of Man, seen in two different positions. Each consists of a head (*k*), a middle piece (*m*), and tail (*s*).

The spermatozoa have often been designated—and it seems to us with entire justice—as ciliate, or still better as flagellate, cells.

The spermatozoa of the remaining Vertebrates have a similar structure to that of Man; on the whole, the diversity of form which is encountered in the comparative study of the egg-cell in the animal kingdom is wanting here.

That spermatozoa are in reality metamorphosed cells cannot be more clearly demonstrated than by their development. According to the extended observations of LA VALETTE and others, each spermatozoön is formed from a single seminal cell or *spermatid*, and, to be more precise, *the head is formed from the nucleus, the contractile filament from the protoplasm.*

The metamorphoses which take place in the development have been investigated with the greatest detail by FLEMMING and HERMANN in the case of Salamandra maculata, the spermatozoa of which are characterised by their very great size. The individual spermatozoön here consists of: (1) a very long head, which has the form of a finely pointed skewer, and takes up stains with avidity; (2) a short cylindrical middle piece, which differs from the first part in chemical properties also; (3) the motile caudal filament, which in the Salamander exhibits the additional peculiarity that it is provided with a contractile undulating membrane. Of these three regions the skewer-like head, and probably also the middle piece, arise from the nucleus of the spermatid, whereas the contractile filament is differentiated out of the protoplasm. In the development of the head the nucleus of the seminal cell is seen to become more and more elongated (fig. 10 *A*, *B*); at first it takes the form of a pear (fig. 10 *A k*); then it grows out into an elongated cone (fig. 10 *B k*), the base of which serves as the point of attachment for the middle piece (*mst*). The cone becomes elongated and narrowed into a rod (fig. 11 *A*, *B*), which is finally converted into the characteristic form of a skewer. With this elongation of the nucleus the chromatic network becomes more and more dense, and at last assumes a quite compact and homogeneous condition, as in the mature spermatozoön. The fundament (Anlage) of the middle piece (figs. 10, 11, *A*, *B*, *mst*) makes its appearance early—when the nucleus begins to elongate—at that end of the nucleus which was called its base, in the form of a small oval body, which at first takes up stains like the head, but afterwards loses this property. Its first appearance demands still further elucidation.

Why are the male sexual cells so small and thread-like, and so differently constituted from the eggs?

The dissimilarity between the male and the female sexual cells is explained by the fact that a division of labor has arisen between the two, inasmuch as they have adapted themselves to different missions.

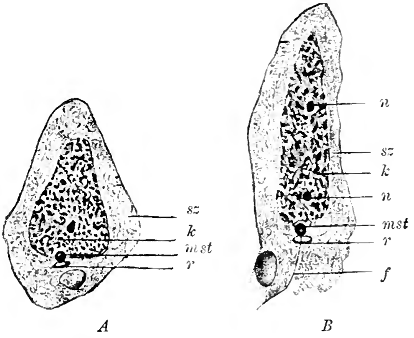

Fig. 10 A and B.—Initial stages of the metamorphosis of the seminal cell into the seminal filament, after Hermann.

A, Seminal cell with pear-shaped nucleus; *B*, seminal cell with cone-shaped nucleus; *sz*, seminal cell; *k*, nucleus with chromatin network, and nucleoli (*n*); *mst*, body out of which the middle piece is developed *r*, ring-like structure, which is in contact with th middle piece, and is claimed to have relation to the formation of the spiral membrane of the filament; *f*, caudal appendage of the seminal filament.

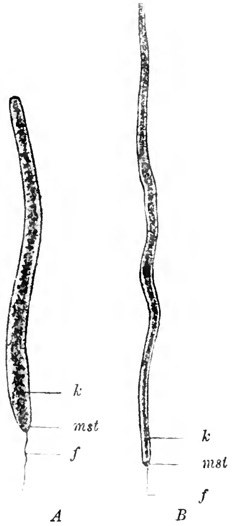

Fig. 11 A and B.—Two terminal stages in the metamorphosis of the seminal cell into the seminal filament, after Flemming.

k, Nucleus, which has become elongated to form the head of the spermatozoön; *mst*, its middle piece; *f*, its caudal filament.

The female cell has assumed the function of supplying the substances which are necessary for that nutrition and growth of the cell protoplasm which a rapid accomplishment of the process of development demands. It has therefore, while in the ovary, stored up in itself yolk-substance, reserve material, for the future; and consequently has become large and incapable of motion. But inasmuch as it is necessary for the accomplishment of a process of development that union with a second cell from another individual should take place, and since non-motile bodies cannot unite, therefore the male element has been suitably modified to meet this second requirement.

For the purpose of locomotion and in order to make possible the union with the non-motile egg-cell, it has become metamorphosed into a contractile filament, and has rid itself completely of all substances, as, for example, yolk-material, which would interfere with this principal requirement. At the same time it has assumed the form best adapted for passing through the envelopes with which, as a means of protection, the egg is surrounded, and for penetrating the yolk.

The conditions especially in the vegetable kingdom confirm the accuracy of this interpretation. There are plants of the lowest forms in which the two copulating sexual cells are entirely alike, both being small and motile; and there are other related species in which a gradual differentiation is brought about by the fact that one of the cells becomes richer in yolk and incapable of motion, while the other becomes smaller and more active. From this it is evident that the stationary egg must now be sought out by the migratory cell.

A few physiological statements may be in place in this connection. In comparison with other cells of the animal body, and especially in comparison with the eggs, the seminal filaments are characterised by greater duration of life and power of resistance, a fact which is frequently of importance for the success of fertilisation. The mature spermatozoa, after they are set free from their connection with other cells, remain for months in the testes and vasa deferentia without losing their fertilising power. They also appear to remain active for a long time after having been introduced into the sexual passages of the female, perhaps for several weeks in the case of Man. For some animals this is demonstrable to a certainty. For example, it is known that the semen of Bats remains alive in the uterus of the female during the whole winter; and in the case of the Fowl it is known that fertilised eggs can be laid up to the eighteenth day after the removal of the Cock.

In the presence of external influences semen shows itself to be much more resistent than the egg-cell, which is easily injured or killed. For example, when semen is frozen and then thawed out, the motion of the seminal filaments comes back again. Many salts, if they are employed not too strong, have no deleterious influence. Narcotics in strong concentration, and when employed for a long time, make the filaments motionless, without immediately killing them, because after removal of the injurious substance they can be revived.

Very weak alkaline solutions stimulate the motions of seminal filaments; on the contrary, acids, even when they are very dilute, produce death. Accordingly the motion becomes more lively in all animal fluids of alkaline reaction, whereas in acid solutions it soon dies out.

HISTORY.—The discovery that egg and seminal filament are simple cells is of far-reaching import for the comprehension of the whole process of development. In order to appreciate this to its full extent, it will be necessary to make a digression into the historical field. Such a digression will acquaint us with some fundamental transformations, which have affected our conception of the essentials of developmental processes.

In the last century, and even in the beginning of the present, ideas about the nature of the sexual products were very indistinct. The most distinguished anatomists and physiologists were of opinion that eggs agreed in their structure in every particular with the grown-up organism, and therefore that they possessed from the beginning the same organs in the same position and connection as the latter, only in an extraordinarily diminutive condition. But inasmuch as it was not possible, with the microscopes of the time, actually to see and demonstrate in the eggs at the beginning of their development the assumed organs, recourse was had to the hypothesis that the separate parts, such as nervous system, glands, bones, etc., must be present, not only in a very diminutive, but also in a transparent condition.

In order to make the process more intelligible, the origin of the blossoms of plants from their buds was cited as an illustrative example. Just as already in a small bud all the parts of the flower, such as stamens and coloured petals, are enveloped by the green and still unopened sepals,—just as the parts grow in concealment and then suddenly expand into a blossom, so also in the development of animals it was thought that the already present but small and transparent parts grow, gradually expand, and become discernible. The doctrine which has just been outlined was consequently called the *Theory of unfolding, or evolution.* However, a more appropriate designation for it is the one introduced during recent decennia—*preformation theory*. For the characteristic feature of this doctrine is, that at no instant of development is there anything new formed, but rather that every part is present from the beginning, or is preformed, and consequently that the *very essence of development—the becoming*—is denied. "There is no such thing as becoming!" is the way it is expressed in the "Elements of Physiology" by HALLER. "No part in the animal body was formed before another; all were created at the same time."

As the necessary consequence of a rigid adherence to the preformation theory, it follows, and indeed was formulated by LEIBNITZ, HALLER, and others, that in any germ the germs of all subsequent offspring must be established or included, since the animal species are developed from one another in uninterrupted sequence. In the extension of this *box-within-box doctrine* (*Einschachtelungslehre*) its expounders went so far as to compute how many human germs at the least were concentrated in the ovary of mother Eve, and thereby arrived at the number 200,000 millions.

The evolution theory offered a point of attack for a scientific feud, inasmuch as every individual among the higher organisms is developed by means of the coöperation of two separate sexes. When, therefore, the seminal filament as well as the animal egg became known, there soon arose the actively discussed question, *whether the egg or the seminal filament was the preformed germ.* Decennium after decennium the antagonistic camps of the *ovists* and of the *animalculists* stood opposed to each other. Those who followed the latter thought they saw, with the aid of the magnifying glasses of the times, the spermatozoa of man actually provided with a head, arms, and legs. The animalculists recognised in the egg only a suitable nutritive soil, as it were, which was necessary to the growth of the spermatozoön.

In the face of such doctrines there dawned a new period for Embryology, when in 1759 CASPAR FRIEDRICH WOLFF in his doctor's dissertation opposed the dogma of the evolution theory, and, casting aside preformation, laid down the scientific principle that what one could not recognise by means of his senses was certainly not present preformed in the germ. *At the beginning*, so he maintained, *the germ is nothing else than an unorganised material eliminated from the sexual organs of the parent*, which gradually becomes organised, but only during the process of development, in consequence of fertilisation. According to WOLFF, the separate organs of the body differentiate themselves one after another out of the hitherto undifferentiated germinal material. In individual cases he endeavoured, even at this time, to determine more exactly, by means of observations, the nature of the process. Thus C. F. WOLFF was the founder of the *doctrine of epigenesis*, which, through the discoveries of the present century, has proved to be the right one.*

WOLFF'S *doctrine of unorganised germinal matter* has been compelled since then to give way to more profound knowledge, thanks to the improved optical aids of recent times, and to the establishment of the cell-theory by SCHLEIDEN and SCHWANN. A better insight into the elementary composition of animals and plants was now acquired, and especially into the finer structure of the sexual products, the egg-cell and the seminal filament.

So far as regards the *egg-cell*, a series of important works began with PURKINJE'S investigation of the Hen's egg in 1825, in which the germinative vesicle was described for the first time. This was soon (1827) followed by C. E. v. BAER'S celebrated discovery of the Mammalian egg, which had been hunted for, but always without success. Extensive and comparative investigations into the structure of the egg in the animal kingdom were published in 1836 by R. WAGNER, who also discovered at the same time in the germinative vesicle the germinative dot (macula germinativa).

With the establishment of the cell-theory there naturally arose the question as to how far the egg was in its structure to be regarded as a cell,—a question which was for years answered in widely different ways, and which even now from time to time is brought up for discussion in an altered form. Even at that time SCHWANN, albeit with a certain reservation, expressed it as his opinion that the egg was a cell, and the germinative vesicle its nucleus; but others, his cotemporaries (BISCHOFF and others), regarded the germinative vesicle as a cell,

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* Historical presentations of the theory of evolution and the theory of epigenesis, which are worth the reading, have been given by A. KIRCHHOFF in his interesting paper, "CASPAR FRIEDRICH WOLFF. Sein Leben und seine Bedeutung für die Lehre von der organischen Entwicklung." *Jenaische Zeitschrift für Medicin und Naturwissenschaft*, Bd. IV., Leipzig, 1868; and by W. HIS, "Die Theorien der geschlechtlichen Zeugung." *Archiv für Anthropologie*, Bd. IV. u. V.

and the yolk as a mass of enveloping substance. A unanimity of views in this matter was brought about only after the general conception of "cell" had received in Histology a more precise definition. This was due especially to more accurate knowledge of the processes of cell-formation gained through the works of NÄGELI, KÖLLIKER, REMAK, LEYDIG, and others.

The interpretation of eggs with separate formative and nutritive yolk, and with partial cleavage, occasioned especial difficulty. Two antagonistic views in this matter have existed for a long time. According to one view, eggs with polar nutritive yolk (the eggs of Reptiles, Birds, etc.) are compound structures, which cannot be designated as simple cells. Only the formative yolk, together with the germinative vesicle, is comparable with the Mammalian egg; the nutritive yolk, on the contrary, is something new, superposed upon the cell from without, a product of the follicular epithelium. The spherules of the white yolk are explained as uninuclear and multinuclear yolk-cells. The formative and nutritive yolk together are comparable with the entire contents of the GRAAFIAN vesicle of Mammals. H. MECKEL, ALLEN THOMSON, ECKER, STRICKER, HIS, and others, have expressed themselves in favour of this view with slight modifications in the details.

According to the opposite view of LEUCKART, KÖLLIKER, GEGENBAUR, HAECKEL, VAN BENEDEN, BALFOUR, and others, the Bird's egg is just as truly a simple cell as the egg of a Mammal, and the comparison with a GRAAFIAN follicle is to be rejected. The yolk never contains enclosed cells, but only nutritive components. As KÖLLIKER, especially in opposition to HIS, has shown, the white-yolk spherules contain no structures comparable with genuine cell-nuclei; and therefore cannot be interpreted as cells. As GEGENBAUR already in 1861 sharply formulated it: "The eggs of Vertebrates with partial cleavage are on that account essentially no more compound structures than those of the remaining Vertebrates; they are nothing else than enormous cells peculiarly modified for special purposes, but which never surrender this their real character." There would be no change in this interpretation, even if it should prove to be that the yolk was formed in part from the follicular epithelium, and was set free from the latter as a sort of secretion. In that event we should have to do with a special method of nutrition of the egg, the cell-nature of which cannot on that account be called in question.

Various components of the yolk have received special names. REICHERT first distinguished as formative yolk the finely granular mass, which, in the Bird's egg, contains the germinative vesicle, and forms the germ-disc, because it alone undergoes the process of cleavage, and produces the embryo. The other chief mass of the egg he called nutritive yolk, because it does not break up into cells, and because subsequently, enclosed in a yolk-sac, it is consumed as nutritive material. Afterwards HIS introduced for these the names chief germ and accessory germ (*Haupt- und Nebenkeim*).

Whereas the nomenclature of REICHERT and HIS is applicable only to eggs with polar arrangement of nutritive yolk, VAN BENEDEN (1870) has undertaken the division of the substance of the egg from a more general standpoint. He distinguishes between the protoplasmic matrix of the egg, in which, as in every cell in general, the vital processes take place, and the reserve and nutritive materials, which are stored up in the protoplasm in the form of granules, plates, and balls, and which he designates as deutoplasm. Every egg possesses both components, only in different proportions, in varied forms and distribution. BALFOUR has selected this latter condition as a basis for division; and has consequently made the three groups of alecithal, telolecithal, and centrolecithal eggs, for which I have selected the designation eggs with little or uniformly distributed yolk, eggs with polar, and eggs with central yolk.

In recent times investigation has been directed to the finer structure of the germinative vesicle, in which KLEINENBERG (1872) was the first to observe a special protoplasmic nuclear trestle (*Kerngerüst*) or nuclear network, which since then has been shown by numerous researches to be a constant structure. In the case of the germinative dot I have myself designated two chemically and morphologically distinguishable substances as nuclein and paranuclein, the investigations concerning the importance and the *rôle* of which in the development of the egg are not yet concluded.

The history of the spermatozoa begins with the year 1677. A student in Leyden, HAMM, in the microscopic examination of semen, saw the briskly moving bodies, and communicated his observation to his teacher, the celebrated microscopist LEEUWENHOECK, who instituted more accurate investigations, and published them in several papers, which soon attracted general attention. The sensation caused was all the greater because LEEUWENHOECK declared the seminal filaments to be the preëxisting germs of animals, and maintained that at fertilisation they penetrated into the egg-cell and grew up in it. Thus arose the school of animalculists.

After the refutation of the preformation theory, it was thought that no importance was to be ascribed to the seminal filaments in fertilisation, it being held that it was the seminal fluid that fertilised. Even during the first four decennia of the present century, the seminal filaments were almost universally held to be independent parasitic creatures (spermatozoa) comparable with the Infusoria. Even in JOH. MÜLLER'S "Physiology" (1833-40) occurs this statement: "Whether the semen-animalcules are parasitic animals, or animated elements of the animals in which they occur, cannot for the present be answered with certainty."

The settlement of the question was accomplished by comparative histological investigations of the semen in the animal kingdom, and by physiological experiment.

In two essays—"Beiträge zur Kenntniss der Geschlechtsverhältnisse und der Samenflüssigkeit wirbelloser Thiere," and "Bildung der Samenfäden in Bläschen"—KÖLLIKER showed that in many animals, *e.g.*, in the Polyps, the semen consists of filaments only, the fluid being entirely absent; and that in addition the filaments are developed in cells, and consequently are themselves elementary parts of animals. REICHERT discovered the same to be true in Nematodes. By means of physiological experiment it was recognised that seminal fluid with immature and motionless filaments, and likewise mature but filtered semen, did not fertilise. This was decisive for the view that the seminal filaments are the active part in fertilisation, and that the fluid, which is added thereto in the case of the higher animals under complicated sexual conditions, "can be regarded only as a menstruum for the seminal bodies which is of subordinate physiological significance."

Since then our knowledge (1) of the finer structure, and (2) of the development of the seminal filaments, has made further advances. So far as regards the first point, we have learned, especially through the works of LA VALETTE and SCHWEIGGER-SEIDEL, to distinguish between head, middle piece, and tail, and to know their different chemical and physical properties. The view expressed by KÖLLIKER, that ordinarily the seminal filaments were the metamorphosed and elongated nuclei of the seminal cells, underwent a modification. According to the researches of LA VALETTE, only the head of the seminal filament arises from the nucleus, the tail, on the contrary, from the protoplasm of the spermatid. Finally FLEMMING brought forward convincing proof that it is only the chromatin of the nucleus that is metamorphosed into the head of the seminal filament. Important investigations concerning the development of the seminal filaments in various animals have recently been made by VAN BENEDEN ET JULIN, PLATNER, HERMANN, and others.

SUMMARY.

The most important results of this chapter may be briefly summarised as follows :—

1. Male and female sexual products are simple cells.

2. The seminal filaments are comparable to flagellate cells. They are usually composed of three portions, head, middle piece, and contractile filament.

3. The seminal filament is developed out of a single cell, the spermatid; the head, and probably also the middle piece, from the nucleus ; the contractile filament from the protoplasm.

4. The egg-cell consists of egg-plasm and yolk-particles, which are reserve material (deutoplasm), imbedded in it.

5. The quantity and distribution of the deutoplasm in the egg-cell is subject to great variation, and exercises the greatest influence on the course of the first processes of development.

   (*a*) The deutoplasm is small in amount, and uniformly distributed in the egg-plasm.

   (*b*) The deutoplasm is present in greater quantity, and, in consequence of unequal distribution, is more densely accumulated either at one pole of the egg or in its middle. (Polar and central deutoplasm.)

   (*c*) In eggs with polar deutoplasm (eggs with polar differentiation) the pole with more abundant deutoplasmic contents is designated as the vegetative, the opposite one as the animal pole.

   (*d*) In the case of eggs with polar differentiation, the more abundant protoplasm of the animal pole may be sharply differentiated as germ-disc (formative yolk) from the portion which is richer in deutoplasm (nutritive yolk). The developmental processes take place only in the formative yolk, while the nutritive yolk remains on the whole passive,

6. Eggs may be divided into several groups and sub-groups according to their development from cells of the ovary alone, or from cells of the ovarium and vitellarium, as well as according to the distribution of the deutoplasm, as exhibited in the following scheme:—

- I. Simple eggs. (Development from cells of the ovary.)
  - A. Eggs with little deutoplasm uniformly distributed through the egg (alecithal*). (Amphioxus, Mammals, Man.)
  - B. Eggs with abundant and unequally distributed deutoplasm.
    - (1) Eggs with polar differentiation (telolecithal), with deutoplasm having a polar position, with animal and vegetative poles. (Cyclostomes, Amphibia.)
    - (2) Eggs with polar differentiation, which are distinguished from the preceding sub-group by the fact that with them there has been effected a still sharper segregation into formative yolk (germ-disc) and nutritive yolk—into a part which is active during development and a part that is passive. (Eggs having polar differentiation with a germ-disc. Fishes, Reptiles, Birds.)
    - (3) Eggs having central differentiation with central deutoplasm (centrolecithal) and superficially distributed formative yolk (blastema, *Keimhaut*). (Arthropods.)
- II. Compound eggs. (Double origin from cells of the ovarium and vitellarium.)

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* The translator has been accustomed for several years to use the word homolecithal instead of alecithal, heterolecithal being employed as a coördinate term to embrace telolecithal and centrolecithal eggs.

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CHAPTER II.

THE PHENOMENA OF THE MATURATION OF THE EGG AND THE PROCESS OF FERTILISATION.

1. The Phenomena of Maturation.

EGGS, such as have been described in the previous chapter, are not yet capable of development, even if they have acquired the normal size. Upon the addition of mature semen they remain unfertilised. In order that they may be fertilised they must first pass through a series of changes, which I shall group together as *the phenomena of maturation.*

The maturation-phenomena begin with changes of the germinative vesicle, which have been followed out the most carefully on the small transparent eggs of invertebrated animals, such as the Echinoderms and Nematodes (the maw-worm of the horse). The germinative vesicle gradually moves from the middle of the egg—the egg of an Echinoderm may serve as the basis of the description—towards its surface, shrivels a little (fig. 12 *A*), in that fluid escapes from it into the surrounding yolk, its nuclear membrane disappears, and the germinative dot becomes indistinct and breaks up into small fragments (fig. 12 *B kf*). During this *degeneration of the germinative vesicle a nuclear spindle* (fig. 12 *B sp*) *is formed,* as can be recognised only after appropriate treatment with reagents; *there arises out of parts of the germinative dot, or out of a part of the nuclear substance of the germinative vesicle, a nuclear spindle* (fig. 12 *B sp*),—a form of the nucleus which one encounters in the animal and vegetable kingdoms in stages preparatory to cell-division.

The nuclear spindle, the more precise structure of which will be described later, in discussing the process of cleavage, pursues still further the direction already taken by the germinative vesicle, unti it touches with its apex the surface of the yolk, where it assumes a position with its long axis in the direction of a radius (fig. 13 *I sp*). A genuine process of cell-division soon takes place here, which is to be distinguished from the ordinary cell-division only by this, that the two products of the division are of very unequal size. To be more exact, therefore, we have to do here with a *cell-budding*. At the place where the nuclear spindle touches the surface with one of its extremities the yolk arches up into a small knob, into which half of the spindle itself advances (fig. 13 *II*). The knob thereupon becomes constricted at its base, and with the half of the spindle—from which subsequently a vesicular nucleus is again formed—is detached from the yolk as a very small cell (fig. 13 *III* rk^1). Hereupon exactly the same process is repeated, after the half of the spindle which remains in the egg, without having previously entered into the vesicular quiescent stage of the nucleus, has restored itself to a complete spindle (fig. 13 *IV*).

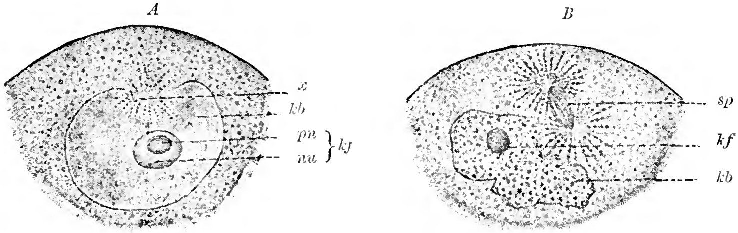

Fig. 12.—Portions of eggs of Asterias glacialis. They show the degeneration of the germinative vesicle.

In figure *A* it begins to shrivel, in that a protuberance of protoplasm (*x*), with a radial structure inside of it, penetrates into its interior, and dissolves the membrane at that point. The germinative dot (*kf*) is still visible, but separated into two substances, nuclein (*nu*) and paranuclein (*pn*).

In figure *B* the germinative vesicle (*kb*) is entirely shrivelled, its membrane is dissolved, and only small fragments of the germinative dot (*kf*) remain. In the region of the protoplasmic protuberance of figure *A* there is a nuclear spindle (*sp*) in process of formation.

There now lie close together on the surface of the yolk two spherules, which consist of protoplasm and nucleus, and therefore have the value of small cells (fig. 13 *V* rk^1, rk^2), and which are often to be identified in an unaltered condition, even after the egg has been divided into a number of cells. They were already known in earlier times under the name of *direction bodies*, or *polar cells.* They have acquired the latter name because, in the case of eggs in which an animal pole is to be distinguished, they always arise at that pole. After the conclusion of the second process of budding, one half of the spindle, the other half of which was employed in the formation of the second polar cell, is left in the cortical layer of the yolk (fig. 13 *V* and *VI ek*). From this arises a new, small, vesicular nucleus, which consists of a homogeneous, tolerably fluid substance without distinctly segregated nucleoli, and attains a diameter of about 13 μ. From the place of its formation it usually migrates slowly back again toward the middle of the egg (fig. 14 *ek*).

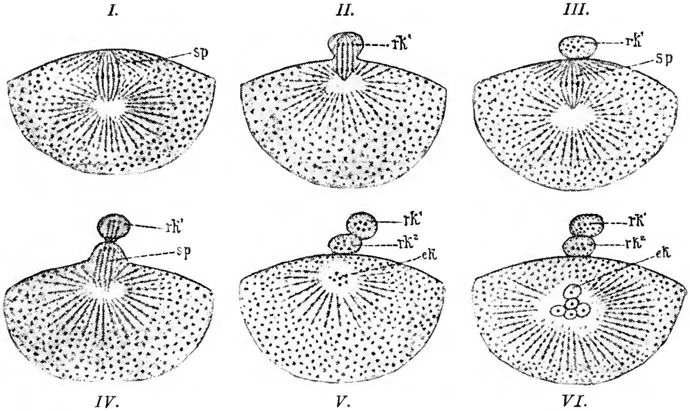

Fig. 13.—Formation of the polar cells in Asterias glacialis.

In figure *I.* the polar spindle (*sp*) has advanced to the surface of the egg. In figure *II.* there has been formed a small elevation (rk^1), which receives a half of the spindle. In figure *III.* the elevation is constricted off, forming a polar cell (rk^1). Out of the remaining half of the previous spindle a second complete spindle (*sp*) has arisen. In figure *IV.* there bulges forth beneath the first polar cell a second elevation, which in figure *V.* has become constricted off as the second polar cell (rk^2). Out of the remainder of the spindle is developed (figure *VI.*) the egg-nucleus (*ek*).

The nucleus of the mature egg (fig. 14 *ek*) has been designated by me as **Egg-nucleus**, by VAN BENEDEN as female pronucleus. It is not to be confounded with *the germinative vesicle of the unfertilised egg.* Compare the figures of the immature egg (fig. 15) and the mature egg (fig. 14) of an Echinoderm, both of which are drawn with the same magnification. The germinative vesicle is of very considerable size, the egg-nucleus remarkably small: in the case of the former one distinguishes a clearly developed nuclear membrane, a nuclear network, and a nucleolus; the latter is almost homogeneous, without nucleolus, and not separated from the protoplasm by any fixed membrane. Similar distinctions in the condition of the germinative vesicle and the egg-nucleus recur throughout the animal kingdom.

The formation of polar cells, and the accompanying metamorphosis of the germinative vesicle into such an extraordinarily reduced egg-nucleus, is a phenomenon of very wide, probably, indeed, of general occurrence. Polar cells have been observed throughout the Cœlenterates, Echinoderms, Worms, and Molluscs. In the ripening of the eggs of Arthropods, according to the earlier observations, they appeared never to be present; but recently they have been found in numerous species by a number of observers, especially by Blochmann and Weismann. Among Vertebrates polar cells are always encountered in Cyclostomes and Mammals, whereas in Fishes and Amphibia they have been identified only in some cases, and in Reptiles and Birds not at all as yet. They arise either some time before or else during fertilisation.

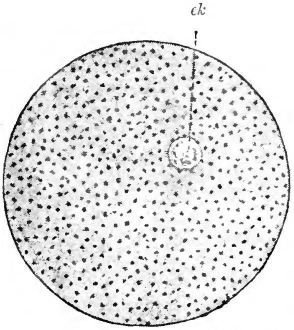

Fig. 14.

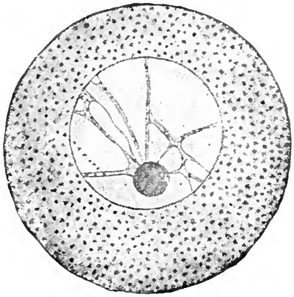

Fig. 15.

Fig. 14.—Mature egg of an Echinoderm. It encloses in the yolk the very small homogeneous egg-nucleus (*ek*).

Fig. 15.—Immature egg from the ovary of an Echinoderm.

In the case of Mammals (Rabbit and Mouse) the process has been very carefully investigated by van Beneden, and recently by Tafani. Several weeks before the rupture of the Graafian follicle the germinative vesicle ascends to the surface of the egg; some days before that epoch it there disappears, and at the place where it disappeared there are formed the egg-nucleus and, under the zona pellucida, one or two (Tafani) polar cells. The egg after it has escaped from the ovary always exhibits egg-nucleus and polar cells.

Also in the case of Fishes, Amphibia, Reptiles, and Birds, whose eggs are of considerable size and with few exceptions opaque, the germinative vesicle, distinguished by its numerous nucleoli, undergoes a regressive metamorphosis. As has been followed step by step in Teleosts by **Oellacher**, and in Amphibia by the author, it always ascends from the middle of the yolk to its surface, and in fact without exception to its animal pole: in the case of the Frog (fig. 16 *kb*) this occurs many weeks before the beginning of maturation. Here immediately under the vitelline membrane, it becomes flattened to a disc-like body, being at the same time somewhat shrunken. Further changes, which it is very difficult to follow in detail, take place in a comparatively short time; these occur in the case of the Amphibia at the time when the eggs are detached from the ovary. For if one examines eggs which have already escaped into the abdominal cavity, or have entered the oviduct, it is uniformly found that the germinative vesicle with its dots has disappeared. In this case, too, there are subsequently formed from a part of the chromatic substance of the germinative vesicle two polar cells and an egg-nucleus, as has been proved by the fine investigations of **Hoffmann** for some species of Teleosts, of **O. Schultze** for several Amphibia (Siredon, Triton), and of **Kastschenko** for certain Selachians.

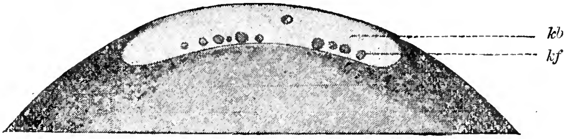

Fig. 16.—Frog's egg in process of ripening.
The germinative vesicle (*kb*), with numerous germinative dots (*kf*), lies quite at the surface of the animal pole as a flattened lenticular body.

Weismann and **Blochmann** have discovered a very interesting fact in the Arthropods. In eggs, namely, which develop parthenogenetically (in summer eggs of Polyphemus, Bythotrephes, Moina, Leptodora, and Daphnia, as well as in Aphidæ) *only a single* polar cell is eliminated, whereas in eggs which require fertilisation for their further development there are always two formed. At present, however, this contrast cannot be established as a general law. For **Platner** found that in the case of Liparis dispar there are formed in parthenogenetic eggs, as well as in those which are fertilised, *two* polar cells, the first of which again divides. **Blochmann** arrived at the same result from the investigation of unfertilised eggs of bees, from which drones are developed.

Although the researches on the phenomena of maturation of the egg in animals still present numerous gaps, nevertheless *it can be regarded as already well-established, that eggs with a germinative vesicle are never capable of fertilisation, that the germinative vesicle is without exception dissolved, and that there is formed out of components of it* (as regards the details there are still many processes to be more carefully studied) *a very small egg-nucleus. During the metamorphosis there arise, probably without exception, polar cells.*

The *polar differentiation* of many eggs rich in yolk, which was pointed out in the first chapter, may be brought into causal connection with the phenomena of maturation. Without exception the animal pole is the part of the egg-sphere to which the germinative vesicle ascends, and where the polar cells are subsequently formed. That the protoplasm is accumulated here in greater quantity is in part referable to the fact that it comes to the surface of the egg along with the nucleus, which most certainly furnishes a centre of attraction for the protoplasm.

The insight into the phenomena of the maturation of the egg, as they have been connectedly presented in the preceding pages, has been acquired only by many roundabout ways and after the removal of many misconceptions. As early as the year 1825 PURKINJE, the discoverer of the germinative vesicle in the Hen's egg, found that in eggs which were taken from the oviduct this vesicle had disappeared, and from this concluded that it was ruptured by the contractions of the oviduct, and that its contents (a lympha generatrix) were mingled with the germ. Whence the name vesicula germinativa. Similar observations were made on this and other objects by C. E. v. BAER, OELLACHER, GOETTE, KLEINENBERG, KOWALEVSKY, REICHERT, and others. But on the other hand the positive statements were made for many eggs (by JOH. MÜLLER for Entoconcha mirabilis; by LEYDIG, GEGENBAUR, and VAN BENEDEN for Rotifers, Medusæ, etc.) that the germinative vesicle did not disappear, but remained and gave rise by direct division at the time of segmentation to the daughter-nuclei.

There were therefore in previous decennia two opposing parties: the one asserted the continuance of the germinative vesicle and its division during the process of cleavage; the other maintained that the egg-cell in its development passed through a condition *without nucleus*, and again acquired a nucleus in consequence of fertilisation.

The controversial points were cleared up by investigations which BÜTSCHLI and the author had undertaken at the same time.

I showed in my first "Beiträge zur Kenntniss der Bildung, Befruchtung und Theilung des thierischen Eies," that in all the older writings there had been no distinction made between the nucleus of the immature, the mature, and the fertilised egg, but that these nuclei had been often confounded and held to be identical, and I first established the differences between germinative vesicle, egg-nucleus, and cleavage-nucleus, the latter being the names which were introduced by me. In addition I showed that the disappearance of the germinative vesicle and the origin of the egg-nucleus preceded fertilisation, and thus I distinguished between the phenomena of maturation and fertilisation of the egg-cell, which generally had been interchanged and confounded. I also endeavoured to make it probable that the egg-nucleus descended from the germinative vesicle, and in fact from a nucleolus of the vesicle, and defended the thesis that the egg during its maturation did not pass through a non-nuclear condition. In this I fell into an error: I overlooked, like all previous observers, the connection between the formation of the polar cells and the disappearance of the germinative vesicle,—a process which it was the more difficult to establish in the object which I studied because it takes place in the ovary.

The excellent investigations of **Bütschli**, which brought the changes of the germinative vesicle into connection with the formation of the polar cells, now made their appearance, supplementing my results. The polar cells were discovered in the year 1848 by **Fr. Müller** and **Lovén**, and were named by the former directive vesicles (Richtungsbläschen), because they always lie at the place where subsequently the first cleavage-furrow makes its appearance. Their wide distribution in the animal kingdom had also been established by many investigators; **Bütschli** was the first, however, to direct attention to the peculiar processes which take place in the yolk, in the interpretation of which he, nevertheless, committed several errors. He maintained that the whole germinative vesicle is converted into a spindle-shaped nucleus, which moves to the surface, and, while becoming constricted in the middle, is thrust outside by the contractions of the yolk in the form of two directive bodies. By this process the egg became non-nuclear, and again acquired a nucleus only in consequence of fertilisation.

In two further articles on the Formation, Fertilisation, and Cleavage of the Animal-Egg, I modified the teachings of **Bütschli**, and brought them into unison with my previous investigations, inasmuch as I pointed out that the germinative vesicle is not as such directly converted into the nuclear spindle, but in part is dissolved; that the spindle takes its origin from the nuclear substance in a manner which it is very difficult to investigate; that the polar cells are formed, not by the elimination of the spindle, but by a genuine process of division or budding; that in consequence of this the egg is not destitute of a nucleus even after the constricting off of the second polar cell, but that the egg-nucleus arises from the half of the divided polar spindle which remains in the yolk, and therefore, in its ultimate derivation, from components of the germinative vesicle of the immature egg.

Soon afterwards **Bütschli** also interpreted the development of the directive bodies as cell-budding, likewise **Giard** and also **Fol**, who has produced a very extensive and thorough investigation on the phenomena of the maturation of the egg in animals. Recently **van Beneden**, supported by researches on Nematodes, has combatted the interpretation of the process as cell-budding; however, **Boveri** and **O. Zacharias**, who have established a complete agreement between the formation of directive bodies and the process of cell-division in the case of the Nematodes also, are unable to subscribe to his conclusion in this matter.

As a new advance is to be recorded the discovery by **Weismann** and by **Blochmann**, that in eggs which are developed parthenogenetically *only a single polar cell* arises.

If the original obscurity on the morphological side, in which the phenomena of the maturation of the egg were enveloped, has been in general cleared up, the same is not the case if we inquire after its physiological meaning. That the germinative vesicle undergoes a regressive metamorphosis into component parts is easily comprehensible, for a firm membrane and a rich accumulation of nucleoplasm certainly cannot be necessary to the interaction of protoplasm and active nuclear substance in the processes of division. Its dissolution is, as it were, the preliminary requirement for the renewed activity of the nuclear contents. But what function shall one ascribe to the polar cells?

Concerning this several hypotheses have been proposed.

BALFOUR, SEDGWICK MINOT, VAN BENEDEN, and others, are of opinion that the immature egg, like every other cell, is originally hermaphroditic, and that by the development of polar cells it rids itself of the male constituents of its nucleus, which afterwards are replaced by fertilisation. BALFOUR thinks that, if no polar cells were formed, parthenogenesis must normally occur.

WEISMANN, supported by his discovery in the case of eggs developing parthenogenetically (p. 34), ascribes a different function to the first and the second polar cells. He distinguishes in the germinative vesicle two different kinds of plasma, which he designates ovogenetic and germinal plasma. He maintains that by the formation of the first polar cell the ovogenetic plasma is eliminated from the ovum; by that of the second polar cell, half of the germinal plasma. In the latter case the ejected germinal plasma must be replaced by fertilisation.

These hypotheses appear to me upon closer examination to present many vulnerable points. To me appears more promising an interpretation of BÜTSCHLI, who compares the egg, as had already often been done, to the mother-cell of spermatozoa. Just as the latter gives rise to many spermatozoa, so also the egg must have once possessed the capability of dividing itself into many eggs. In the formation of the polar cells, which are eggs that have become rudimentary, as it were, there has been preserved a trace of these original conditions. Also BOVERI regards the polar cells as *abortive eggs*. I have likewise always conceived of the conditions in this manner.

2. The Process of Fertilisation.

The union of egg-cell and spermatic cell is designated as the process of fertilisation. This process is to be observed, sometimes with great difficulty, sometimes with considerable ease, according to the choice of the animal for experimentation. The investigator ordinarily encounters great difficulties in cases where the ripe eggs are not laid, but where a part, if not the whole, of their development is effected within the sexual ducts of the maternal organism. In such cases the fertilisation also must evidently take place in the ducts of the female sexual apparatus, into which the semen is introduced in the act of copulation.

An *internal fertilisation* takes place in nearly all Vertebrates except the greater part of the Fishes and many Amphibia. Usually the egg and the spermatozoa meet, in the case of Man and Mammals, in the beginning of the oviduct; likewise in the case of Birds they meet in the first of the four regions previously (p. 17) distinguished, and at a time when the yolk is not yet surrounded with its albuminous envelope and calcareous shell.

In contrast to internal fertilisation stands *external fertilisation*, which is the simpler and more primitive method, and which occurs in the case of many Invertebrates that live in the water, as well as ordinarily in Fishes and Amphibia. In this method, while male and female keep near together, both kinds of sexual products, which are for the most part produced in great number, are evacuated directly into the water, where fertilisation takes place outside of the maternal organism. The whole procedure is therefore much more easily observable. The experimenter has it within his power to effect fertilisation artificially, and thus to determine precisely the point of time at which egg and semen are to meet. He needs only to collect in a watch-glass containing water ripe eggs from a female, likewise in a second watch-glass ripe semen from a male, and then to mingle the two in a suitable manner. In this way artificial fertilisation is extensively practised in fish-breeding. For the purpose of scientific investigation the selection of the particular species of animal is of the greatest importance. It is manifest that animals with large opaque eggs do not commend themselves, whereas those species are especially suitable whose eggs are so small and transparent that one can observe them under the microscope with the highest powers, and at the same time pass in review every least speck. Many species of Echinoderms

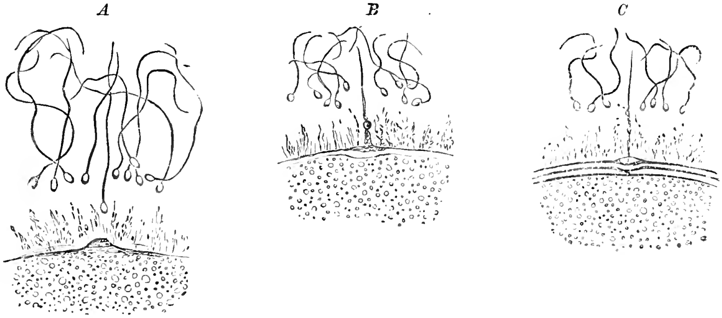

Fig. 17 A, B, C.—Small portions of eggs of Asterias glacialis, after Fol.
The spermatozoa have already penetrated into the gelatinous envelope which covers the eggs. In *A* there begins to be raised up a protuberance toward the most advanced spermatozoön. In *B* the protuberance and spermatozoön have met. In *C* the spermatozoön has penetrated into the egg. A vitelline membrane, with a crater-like orifice, has now been distinctly formed.

are in this respect most excellent objects for investigation. Consequently it was by means of them that an accurate insight into the processes of fertilisation was first secured. They may therefore serve in the following account as the foundation of our description.

If ripe eggs with egg-nucleus are removed from the ovary into a watch-glass containing sea-water, and a small quantity of seminal fluid is added, a very uniform result is obtained, since in the course of five minutes every one of many hundreds or thousands of eggs is normally fertilised, as can be accurately observed by means of high magnification.

Although spermatozoa attach themselves to the gelatinous envelope of an egg in great numbers,—many thousands of them when concentrated seminal fluid is employed,—still only a single one of them is concerned in fertilisation, and that is the one which by the lash-like motion of its filament first approached the egg. Where it strikes the surface of the egg with the point of its head the clear superficial expanse of the egg-protoplasm is at once elevated into a small knob that is often drawn out to a fine point, the so-called receptive prominence (*Empfängnisshügel*), or cone of attraction. At this place the seminal filament, with pendulous motions of its caudal appendage, bores its way into the egg (fig. 17 *A*, *B*). At the same time a fine membrane (fig. 71 *C*) detaches itself from the yolk over the whole surface, beginning at the cone, and becomes separated from it by an ever-increasing space. The space probably arises because, in consequence of fertilisation, the egg-plasma contracts and presses

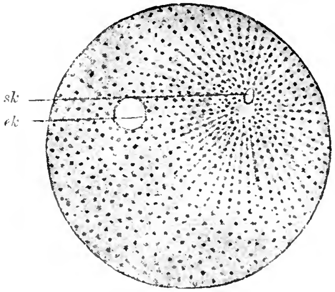

Fig. 18.

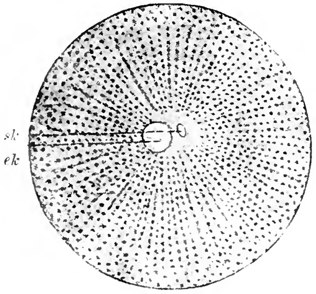

Fig. 19.

Fig. 18.—Fertilised egg of a Sea-urchin.
The head of the spermatozoön which penetrated has been converted into a sperm-nucleus (*sk*) surrounded by a protoplasmic radiation, and has approached the egg-nucleus (*ek*).

Fig. 19.—Fertilised egg of a Sea-urchin.
The sperm-nucleus (*sk*) and the egg-nucleus (*ek*) have come close to each other, and both are surrounded by a protoplasmic radiation.

out fluid (probably the nuclear fluid which was diffused after the disappearance of the germinative vesicle).

The formation of a vitelline membrane is in so far of great significance for the fertilisation, as it makes the penetration of another male element impossible. No one of the other spermatozoa swinging to and fro in the gelatinous envelope is able after that to get into the fertilised egg.

The one which has penetrated thereupon undergoes a series of changes. The contractile filament ceases to vibrate, and soon disappears; but out of the head—which, as was previously stated, is derived from the nucleus of a sperm-cell (spermatid), and consists of nuclein—there is soon developed a very small spheroidal or oval corpuscle, which afterwards becomes somewhat larger, the semen- or sperm-nucleus (fig. 18 *sk*). This slowly moves deeper into the yolk, whereupon it exerts an influence upon the surrounding protoplasm. For the latter is arranged radially around the sperm-nucleus (*sk*), so that there is formed a radiate figure, which is at first small, but afterwards becomes more and more sharply expressed and more extended.

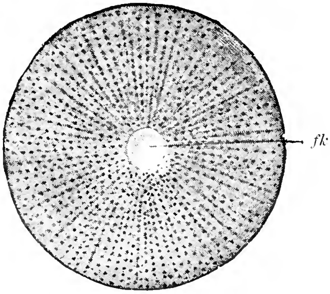

Fig. 20.—Egg of a Sea-urchin immediately after the close of fertilisation. Egg-nucleus and sperm-nucleus are fused to form the cleavage-nucleus (*fk*), which occupies the centre of a protoplasmic radiation.

Now an interesting phenomenon begins to hold the attention of the observer (figs. 18, 19, 20). Egg-nucleus and sperm-nucleus mutually attract each other, as it were, and migrate through the yolk toward each other with increasing velocity. The sperm-nucleus (*sk*), enveloped in its protoplasmic radiation, changes place more rapidly than the egg-nucleus (*ek*). Soon the two meet, either in, or at least near, the middle of the egg (fig. 19); become surrounded by a common radiation, which now extends through the whole yolk-substance; are firmly juxtaposed, and then mutually flattened at the surface of contact; and finally fuse with each other (fig. 20 *fk*). The product of their fusion is the first *cleavage-nucleus* (*fk*), which undergoes the further alterations leading to cell-division.

This whole interesting process of fertilisation has consumed in the present object of investigation the short time of about ten minutes only.

The phenomena of fertilisation discovered in the Echinoderms were soon observed, either completely or at least partially, in numerous other animals also—in Cœlenterates and Worms (NUSSBAUM, VAN BENEDEN, CARNOY, ZACHARIAS, BOVERI, PLATNER), and in Molluscs and Vertebrates. As regards the last, it has been possible to follow accurately in the case of Petromyzon the penetration of a *single* spermatozoön into the egg through a special preformed micropyle in the vitelline membrane (CALBERLA, KUPFFER, BENECKE, and BÖHM). Likewise in the Amphibia, proof has been brought forward that after fertilisation a sperm-nucleus is formed at the animal pole, and that, surrounded by a pigmented area, derived from the cortex of the yolk, it moves toward another more deeply imbedded nucleus (egg-nucleus), and fuses with it (O. HERTWIG, BAMBEKE, BORN). In Mammals the fertilisation takes place in the beginning of the oviduct. Evidence has also been produced in their case that after the liberation of the polar cells two nuclei are temporarily to be seen in the egg-cells, and that these unite in the centre of the egg to form the cleavage-nucleus (VAN BENEDEN, TAFANI).

This is the proper place in which to mention briefly the so-called **micropyle**. In many animals (Arthropods, Fishes, etc.) the eggs are enclosed before they are fertilised in a thick firm envelope, which is impenetrable for spermatozoa. Now, in order to make fertilisation possible, there are found in these cases at a definite place on the egg-membrane sometimes *one*, sometimes several, small openings (micropyles), at which the spermatozoa accumulate in order to glide into the interior of the egg.

The egg of Nematodes has for several years rightly played an important rôle in the literature of the process of fertilisation. But this is especially true for the egg of the Maw-worm of the Horse (Ascaris megalocephala), which VAN BENEDEN has made the subject of a celebrated monograph. It is an excellent object, in so far as it not only can be had for study everywhere and at all seasons of the year, but also allows one to follow step by step, in the most accurate manner, the penetration and subsequent fate of the spermatozoön. Since, moreover, the process of fertilisation in Ascaris megalocephala presents many peculiarities in its details, an extended presentation of them is both warranted and desirable.

In the case of this Worm, in which the sexes are separate individuals, there is a copulation, and the fertilisation of the egg takes place within the sexual passages of the female. In one region, which is expanded into a kind of uterus, mature spermatic bodies are met with in great numbers. The appearance of these differs greatly from that which the male seminal elements ordinarily present in the animal kingdom: for they are apparently motionless; are comparable in form to a cone, a conical ball, or a thimble (fig. 21); and consist in part of a granular substance (*b*), in part of a homogeneous lustrous substance (*f*), and of a small spherical body of nuclear substance (*k*), which is imbedded in the granular substance at the base of the cone.

When the small naked eggs enter into the region designated as uterus, fertilisation takes place at once. *One* spermatic body, which can execute feeble amœboid motions with its basal end (SCHNEIDER), attaches itself to the surface of the yolk (fig. 22 *sk*). Where contact with the egg first takes place, there is formed, exactly as in the Echinoderms, a special cone of attraction. Here the spermatic body, without essential change of form, gradually glides deeper into the yolk, until it is completely enclosed therein (fig. 23).

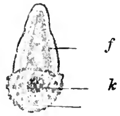

Fig. 21.—Spermatic body of Ascaris megalocephala, after VAN BENEDEN.
k, Nucleus; *b*, base of the cone, by which the attachment to the egg takes place; *f*, lustrous substance resembling fat.

While the two sexual products are thus externally fused, the egg itself is not yet ripe, because it still possesses the germinative vesicle (fig. 22 *kb*), but it now promptly begins to enter upon the maturation stage by preparing to form the polar cells. The germinative vesicle, which is of small size in the case of the Maw-worm of the Horse, loses its sharp delimitation from the yolk, moves toward that surface of the egg which is opposite to the cone of attraction (figs. 23, 24), and is gradually converted into a nuclear spindle (*sp*), the origin of which may be traced upon this object with considerable precision. The most important part of the process consists in the formation, out of the chromatic substance, of numerous short, rod-like pieces (figs. 23, 24, *ch*), which form directly the chromatic elements of the spindle, the *chromosomes* (WALDEYER). As in the case of the Echinoderms, there then arise at the surface of the yolk two small polar cells (fig. 25 *pz*); as in that case, a vesicular egg-nucleus (fig. 25 *ei*) arises from the half of the second polar spindle which remains in the peripheral portion of the yolk.

Meanwhile the spermatic body has moved farther and farther from the place of its entrance into the egg (figs. 22, 23, *sk*), and finally comes to lie in the middle of the yolk (fig. 24 *sk*), approximately in the position occupied by the germinative vesicle before its migration to the surface. During this period the spermatic body has gradually lost its original form and its sharp delimitation; out of its nuclear substance, which was described as a small, deeply stainable spherule, there arises a vesicular nucleus (fig. 25 *sk*), which acquires the same size and condition as the egg-nucleus.

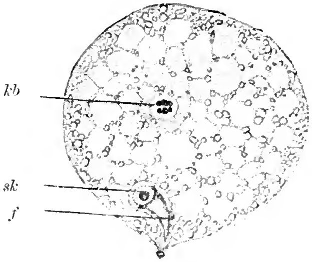

Fig. 22.

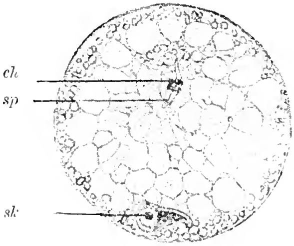

Fig. 23.

Fig. 22.—An egg of Ascaris megalocephala just fertilised, after VAN BENEDEN.
sk, Spermatic body, with nucleus, which has entered the egg; *f*, fat-like substance of the spermatic body; *kb*, germinative vesicle.

Fig. 23.—A stage of a fertilised egg of Ascaris megalocephala, somewhat older than that of fig. 22, after VAN BENEDEN.
sk, Spermatic body, which has penetrated deeper into the cortex of the yolk; *sp*, polar spindle, which has arisen from the germinative vesicle; *ch*, chromosomes of the spindle.

After the rapid and continuous accomplishment of these processes, the egg of the Worm usually enters on a longer or shorter period of rest. It now presents (compare fig. 25, which represents a stage already further developed) at its surface within the vitelline membrane two polar cells (*pz*), and in its interior two large vesicular nuclei, the spermatic nucleus (*sk*) and the egg-nucleus (*ei*), the

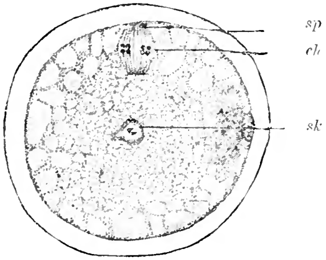

Fig. 24.

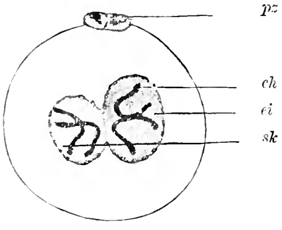

Fig. 25.

Fig. 24.—A still older stage of development, following that of fig. 23, of the egg of Ascaris megalocephala, after BOVERI.
sp, Polar spindle, which has ascended to the surface of the yolk; *ch*, 2 × 4 chromosomes; *sk*, spermatic nucleus, which has migrated into the middle of the egg.

Fig. 25.—Egg of Ascaris megalocephala in preparation for the process of cleavage, after E. VAN BENEDEN.
pz, Two polar cells which have arisen from the polar spindle (*sp*) of fig. 24 by a repetition of the process of budding; *ei*, egg-nucleus; *sk*, spermatic nucleus already preparing to divide; *ch*, nuclear loops or chromosomes.

latter of which has come close up to the former, without, however, fusing with it. A union of the male and female nuclear substances into a common nuclear figure takes place in the case of the Maw-worm, when the process of egg-cleavage is beginning.

The processes of fertilisation just described can be designated as typical for the animal kingdom. But they appear to recur in exactly the same manner throughout the vegetable kingdom also, as has been shown by the thorough investigations of STRASBURGER. We are therefore in a better position now than formerly to advance a *theory of fertilisation* based upon an important array of facts :—

In fertilisation clearly demonstrable morphological processes take place. Of these the important and essential one is the union of two cell-nuclei which have arisen from different sexual cells, a female egg-nucleus and a male spermatic nucleus. These contain the fructifying nuclear substance, which is an organised body and comes into activity as such in fertilisation.

Recently the attempt has been made to expand the *fertilisation theory* into a *theory of transmission.* Important reasons may be urged, as appearing to indicate that the fructifying substance is at the same time the bearer of the transmissible peculiarities. *The female nuclear substance transmits the peculiarities of the mother, the male nuclear substance the peculiarities of the father, to the nascent creature.* Perhaps there is in this theory a morphological basis for the fact that offspring resemble both progenitors, and in general inherit from both equally numerous peculiarities.

If we accept these two theories, the nucleus, which, despite its constant presence, previously had to be described as a problematic structure of unknown significance, acquires an important rôle in the life of the cell. *It seems to be the cell's especial organ of fertilisation and transmission,* inasmuch as there is stored within it a substance (idioplasma of NÄGELI) which is less subject to cell metastasis.

In connection with the consideration of the process of fertilisation may be permitted a slight digression to the realm of pathological phenomena.

As follows from numerous observations in both the animal and vegetable kingdoms, *in the normal course of fecundation only a single spermatic filament penetrates into an egg,* when the encountering sexual cells are entirely healthy. *But with an impaired condition of the egg-cell, superfetation by means of two or more seminal filaments* **(polyspermia)** *takes place.*

Superfetation may be produced artificially, if by way of experiment one injures the egg-cell. This may be accomplished either by exposing it temporarily to a lower or a higher temperature, and thus producing cold-rigor or heat-rigor, or by affecting it with chemical reagents,—chloroforming it, or treating it with morphine, strychnine, nicotine, quinine, etc.,—or by doing violence to it in a mechanical way, such as shaking it. It is interesting to observe how, with all of these means, the degree of superfetation is, to a certain extent, proportional to the degree of the injury; how, for example, a small number of spermatozoa penetrate into eggs which have been slightly affected with chloral, whereas a greater number penetrate those which have been more strongly narcotised.

In all unfertilised eggs the whole course of development becomes abnormal. But whether, as claimed in Fol's hypothesis, the origin of double and of multiple organisms is referable respectively to the penetration of two and many spermatozoa, must still be regarded as doubtful. Certainly the question suggested richly deserves to be still more thoroughly tested experimentally.

HISTORY.—The facts here given concerning the theory of fecundation are acquisitions of very recent times. To omit the older hypotheses, it was generally assumed up to the year 1875 that the spermatozoa penetrate in great numbers into the substance of the egg, but that they there lose their activity and become dissolved in the yolk.

I succeeded in my study of the eggs of Toxopneustes lividus in finding an object in which all the internal phenomena of fertilisation may be determined with ease and certainty, and in establishing (1) that in consequence of fertilisation the head of a spermatic filament surrounded by a stellate figure makes its appearance in the cortex of the yolk, and is metamorphosed into a small corpuscle, which I called spermatic nucleus; (2) that within ten minutes egg-nucleus and spermatic nucleus copulate; (3) that normally fertilisation is accomplished by only a *single* spermatic filament, whereas in pathologically altered eggs several spermatozoa may penetrate. I was therefore able at that time to announce the proposition, that fertilisation depends upon the fusion of two sexually differentiated cell-nuclei.

A few months later, VAN BENEDEN announced that in the case of Mammals the segmentation-nucleus arises from the fusion of two nuclei,—as had previously been observed by AUERBACH and BÜTSCHLI in the case of numerous other objects,—and expressed the conjecture that one of them, which has at first a peripheral position, might in part result from the substance of the spermatozoa, which, in great numbers, as he maintained, fuse and become commingled with the cortical portion of the yolk. An advance was soon after this made by FOL, who investigated with the greatest detail the eggs of Echinoderms at the very moment of the penetration of a spermatic filament into the egg, and discovered the formation of a cone of attraction. Since then it has been established by means of numerous researches (those of SELENKA, FOL, HERTWIG, CALBERLA, KUPFFER, NUSSBAUM, VAN BENEDEN, EBERTH, FLEMMING, ZACHARIAS, BOVERI, PLATNER, TAFANI, BÖHM, and others) that in other objects also, and in other branches of the animal kingdom, the processes of fertilisation take place in essentially the same manner. At the same time the comprehension of the processes of fertilisation was essentially advanced, especially by the works of VAN BENEDEN on the egg of Ascaris megalocephala, to which have been added the important investigations of BOVERI and others on the same object. STRASBURGER has established in a series of excellent researches the identity of the processes of fertilisation in the animal and vegetable kingdoms.

Finally, the phenomena of fertilisation were utilised simultaneously by STRASBURGER and myself for the foundation of a theory of heredity, in our endeavor to prove—what others (KEBER, HAECKEL, HASSE) had previously expressed as a conjecture—that the male and the female nuclear substances are the bearers of the peculiarities which are transmitted from parent to offspring. KÖLLIKER, ROUX, BAMBEKE, WEISMANN, VAN BENEDEN, BOVERI, and others have since expressed themselves in a similar manner.

SUMMARY.

1. At maturation the germinative vesicle gradually rises to the animal pole of the egg, and thereby undergoes a regressive metamorphosis (degeneration of the nuclear membrane and the fibrous network, mingling of the nuclear fluid—Kernsaft—with the protoplasm).

2. A nuclear spindle (polar spindle or direction-spindle) is developed out of remnants of the germinative vesicle, principally, indeed, out of the substance of the germinative dot, which breaks up into chromosomes.

3. At the place where the spindle encounters the surface of the yolk with one of its ends, there are formed two polar cells or direction-bodies (*Richtungskörper*) by means of a process of budding, which is repeated.

4. At the second budding, half of the nuclear spindle remains in the cortex of the yolk, and is metamorphosed into the egg-nucleus The egg is then ripe.

5. In the case of eggs which develop parthenogenetically (Arthropoda), ordinarily only *one polar cell* is formed.

6. At fertilisation only a single spermatozoön penetrates a sound egg (formation of a *cône d'attraction*, detachment of a vitelline membrane).

7. The head of the spermatozoön is converted into the spermatic nucleus, around which the neighbouring protoplasmic particles are radially arranged.

8. Egg-nucleus and spermatic nucleus migrate toward each other, and in most instances immediately fuse to form the segmentation-

nucleus; in many objects they remain for a considerable time near each other, but not united, and only later are together metamorphosed into the segmentation-spindle.

9. In some animals fertilisation of the egg takes place only after completion of its maturation, but in others it is inaugurated at the very beginning of maturation, so that the two phenomena overlap each other.

10. *Fertilisation theory.* Fertilisation depends on the copulation of two cell-nuclei, which are derived from a male cell and a female cell.

11. *Theory of heredity.* The male and female nuclear substances contained in the spermatic nucleus and the egg-nucleus are the bearers of the peculiarities which are transmissible from parents to their offspring.

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CHAPTER III.

THE PROCESS OF CLEAVAGE.

FERTILISATION is in most instances immediately followed by further development, which begins with the division of the egg-cell—the simple elementary organism—into an ever-increasing number of small cells—the process of cleavage. We shall begin the study of cleavage with a very simple case, and here also choose as a foundation for the presentation of the subject the egg of an Echinoderm and the egg of the common Ascaris of the Horse.

In the living egg of the Echinoderm the cleavage-nucleus (fig. 26 *fk*), which arose from the fusion of egg-nucleus and spermatic nucleus, is at first spheroidal, and lies exactly in the middle of the egg, where it forms the centre of a radiation which affects the whole yolk-mass; but it soon begins to be slightly elongated, and at the same time to become less and less distinct, so that with the living object one might be misled into assuming that it had been completely dissolved. Before this, very regular changes in the distribution and arrangement of the protoplasm around the nucleus have taken place. The monocentric radiation resulting from fertilisation is divided. The two newly formed radiations thereupon move to the poles of the elongated nucleus. At first small and insignificant, they rapidly extend, and finally each occupies a half of the egg (fig. 27), and the rays of the two systems meet at a sharp angle in the median plane of the egg.

Just in proportion as the two radiations become more distinct, there arises, within the granular yolk, as the starting-point and centre of the radiations, a figure, which may be appropriately compared (fig. 27) with a *dumb-bell.* It arises by the accumulation of a large amount of homogeneous protoplasm around the poles of the elongating nucleus, forming the two ends of the dumb-bell; the poles may be regarded as if they were two centres of attraction. The non-granular streak, representing the handle of the dumb-bell, is the nucleus, which has meanwhile undergone a peculiar metamorphosis and has become indistinct.

A more accurate knowledge of the nuclear metamorphosis may be got by employing suitable reagents and dyes. By means of intermediate stages, which may be disregarded here, there arises out of the vesicular nucleus the *nuclear spindle* (fig. 31 *B*), which is a typical structure for cell-division throughout the organic world. This (*sp*) consists of two substances, both of which, in my opinion, are derived from the quiescent condition of the nucleus—namely, (1) of a *non-chromatic substance,* which does not show affinity for any dyes, and (2) of the stainable *nuclein* or *chromatin.* The non-chromatic substance forms extraordinarily fine, and therefore at times scarcely discernible, "*spindle-fibres,*" which are united into a bundle, and give rise to a spindle by the convergence of their ends to points. The chromatin, on the contrary, has assumed the form of small individual granules or *chromosomes,* which correspond in number with the spindle-fibres, and are so arranged that each granule adjoins a spindle-fibre at its middle point. In its totality, therefore, it constitutes at the middle of the spindle a plate composed of individual

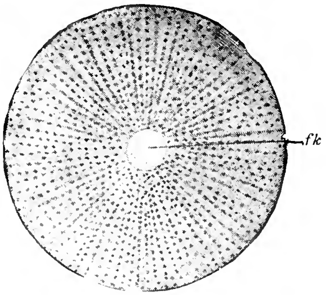

Fig. 26.

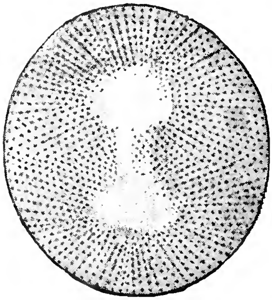

Fig. 27.

Fig. 26.—Egg of a Sea-urchin immediately after the conclusion of fertilisation. *fk*, Cleavage-nucleus.

Fig. 27.—Egg of a Sea-urchin in preparation for division. The nucleus is no longer to be seen; there has arisen in its place a dumb-bell figure.

Both figures are drawn from the living object.

granules—the *nuclear plate* of Strasburger. That which in the case of the Sea-urchin ordinarily appears as a chromatic granule is found, upon the employment of the highest magnifying powers,—but especially in the study of objects (fig. 28 *A*) more suitable for this purpose,—to be a small V-shaped loop. The number of the loops or chromosomes appears to be very definite, and subject to law for each species of animal.

At the tips of the spindle there may be demonstrated, in addition, two special and exceedingly minute bodies, one of which occupies the exact centre of each of the two previously mentioned systems of rays; they are, in fact, to be regarded as the cause of the latter. Inasmuch as during the elongation of the nucleus they are to be found at each of its two poles, they may be especially designated as *polar corpuscles* [or *centrosomes*]. During the whole process of the division of nucleus and cell-body, it appears as though a directing influence belongs to the two polar corpuscles.

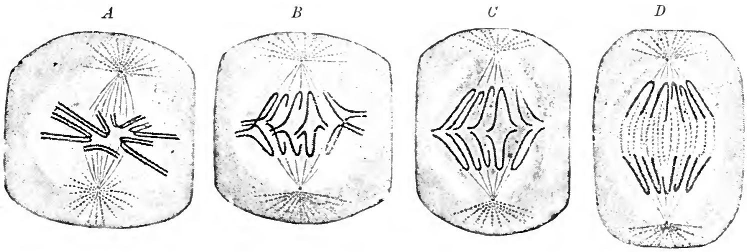

Fig. 28.—Diagram of nuclear division, after Rabl.
In figure *A* one sees the spindle, composed of delicate non-chromatic fibres, with the protoplasmic radiations at its tips and the chromatic loops at its middle. The splitting of the filaments of the latter has already taken place. In figure *B* the daughter-loops resulting from the fission have moved apart in opposite directions. In figure *C* they begin to arrange themselves in a regular manner into two groups of loops. In figure *D* the groups of daughter-loops lie near the two poles of the spindle.

Important changes in the nuclear loops of the spindle take place during later stages of the process of division. Each loop is split lengthwise into two *daughter-loops* (fig. 28 *A*), as discovered by Flemming and as confirmed since then by numerous other investigators (Strasburger, Heuser, van Beneden, Rabl, and others). These daughter-loops soon move apart toward the opposite ends of the spindle (figs. 28 *B*, *C*; see also the explanation of the figures), and approach very closely to the polar corpuscles at their tips (fig. 28 *D*).

Thus by a complicated process a division of the stainable nuclear substance into similar halves is brought about. As the immediate consequence of this the protoplasmic parts of the cell also begin at this time to be divided into halves by means of the process of cleavage, which is already recognisable externally. There is formed at the surface of the egg (fig. 29 *A*), in a plane passing between the two groups of loops through the middle of the spindle perpendicular to its long axis, a circular furrow, which rapidly cuts deeper and deeper into the substance of the egg, and in a short time divides it into two equal parts. Each of these contains half of the spindle with half of the loops, half of the dumb-bell, and a protoplasmic radiation.

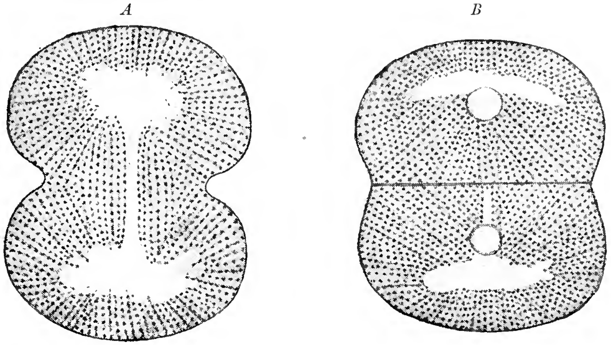

Fig. 29 A.—Egg of a Sea-urchin at the moment of division.
A circular furrow cuts into the yolk and halves it in a plane which is perpendicular to the middle of the nuclear axis and to the long axis of the dumb-bell.

B.—Egg of a Sea-urchin after its division into two cells.
In each resultant of the division a vesicular daughter-nucleus has arisen. The radial arrangement of the protoplasm begins to become indistinct.
Both figures are drawn from the living object.

The resulting halves of the egg, still surrounded in common by the vitelline membrane, then closely apply to each other the surfaces resulting from the division, and become so flattened that each one of them forms approximately a hemisphere (fig. 29 *B*). Internally, however, nucleus and protoplasm enter upon a brief transitory resting stage. There is developed out of the half of the nuclear spindle with its daughter-loops a vesicular homogeneous daughter-nucleus like the first, but in the protoplasm the radial arrangement becomes less and less distinct and at last entirely disappears.

The egg of the common Maw-worm of the Horse is also a very instructive object for the study of the process of cleavage, as it was for the study of fertilisation, for it allows a still deeper insight into this process. As has already been stated, the egg-nucleus and the spermatic nucleus remain for a time separate, even after they have approached each other. After a brief period of rest both of them begin to exhibit simultaneously the changes which precede the formation of the nuclear spindle. In each the chromatic substance is metamorphosed into a fine thread, which is arranged within the nuclear membrane in numerous windings. Each filament is thereupon divided into two equally large coiled loops, the chromosomes (fig. 25 *ch*). Now the two vesicular nuclei lose their delimitation from the surrounding yolk, in which there arise at a little distance from each other two polar corpuscles [centrosomes], surrounded by a system of rays, which is at first faint, but subsequently becomes more distinct. Between the two centrosomes, the method of whose development no one has as yet succeeded in observing, there are formed spindle-fibres, and the four loops (chromosomes), set free by the dissolution of the two nuclear membranes, so arrange themselves that they lie upon the outside of the spindle at its equator.

In the case of the egg of the Maw-worm, therefore, the union of the two sexual nuclei, which terminates the act of fertilisation, takes place only at the time of the metamorphosis to form the cleavage-spindle, in which metamorphosis they take an equal share. In consequence of this remarkable deviation from the ordinary course of the process of fertilisation, VAN BENEDEN has been able to establish the interesting and important fact that half of the chromosomes of the first cleavage-spindle are derived from the egg-nucleus, and half from the spermatic nucleus, and that consequently they may be distinguished as female and male chromosomes. Since in this instance, just as in nuclear division ordinarily, the four loops are split lengthwise and then move apart toward the two polar corpuscles (centrosomes), there are formed two groups of four daughter-loops each, of which two are of male origin and two of female. Each group is then metamorphosed into the quiescent nucleus of the daughter-cell. This furnishes incontestable proof, that *to each daughter-nucleus in each half of the egg, which arises as the result of the first cleavage, there is transmitted exactly the same amount of chromatic substance from the egg-nucleus as from the spermatic nucleus.*

The first division is followed after a brief period of rest by the second, this by the third, the fourth, etc., during which are repeated the same series of changes in nucleus and protoplasm that have just been described. Thus in quick succession the 2 first daughter-cells are divided into 4, these into 8, 16, 32, 64, etc. (fig. 30), until there has resulted a large spheroidal mass, which has received the name *morula* or *mulberry-sphere*, because the cells protrude as small elevations at its surface.

During the second and third stages of cleavage there is easily recognisable *a rigidly observed order in the direction which the planes of cleavage sustain to each other.* The second plane of cleavage always halves the first and cuts it perpendicularly; the third plane, again, is perpendicular to the first two, and passes through the middle of the axis formed by their intersection. If one regards the ends of this axis as the poles of the egg, the first two planes of division may be designated as meridional, the third as equatorial.

This uniformity is caused by the mutual relation which subsists between nucleus and protoplasm, in which connection the two following laws are to be noted: (1) *The plane of division always cuts the axis of the spindle perpendicularly at its centre.* (2) *The position of the axis of the nuclear spindle in turn depends on the form and differentiation of the protoplasmic body which envelops it, and in such a manner that the two poles of the nucleus take the direction of the greatest protoplasmic masses.* Thus, for example, in a sphere in which the protoplasm is uniformly distributed, the centrally situated spindle may come to lie in any radius; but in an ovoid protoplasmic body, only in the longest diameter. In a circular protoplasmic disc the nuclear axis lies parallel to its surface in any diameter whatever of the circle, but in an oval disc, as before, in the longest diameter only.

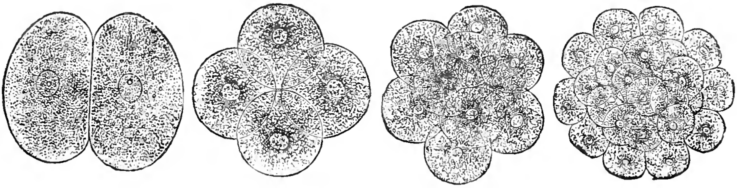

Fig. 30.—Various stages of the process of cleavage, after GEGENBAUR.

Let us return now, after these general remarks, to the case under consideration. Each daughter-cell forms at the close of the first segmentation a hemisphere. According to the rule, the daughter-spindle cannot assume a position perpendicular to the flat surface of the hemisphere, but must lie parallel to it, so that a division into two quadrants must result. At the next segmentation the axis of the spindle must coincide with the long axis of the quadrant, whereby this becomes divided into two octants.

There are some important deviations from the process of division just described, which affect the form of the cleavage products, although leaving unaltered the finer processes relating to the nucleus. The deviations are induced, as we shall show more in detail in the individual cases, by the variation in the amount of deutoplasm contained in the eggs, and by the previously described variability in its distribution. One may appropriately separate the various forms of the process of cleavage into two classes, and each class into two subclasses, although the forms merge into one another by means of transitional conditions.

To the first class we assign such eggs as *are completely divided into segments* by the process of cleavage. The cleavage itself we designate as *total*; and according as the segments are of equal or unequal size, we distinguish as subdivisions *equal* cleavage and *unequal* cleavage.

With total is contrasted *partial cleavage*. This occurs in the case of eggs which are provided with very abundant deutoplasm, and are consequently of considerable size, and in which, at the same time, the previously described separation into formative yolk and nutritive yolk has been distinctly established. In this case the formative yolk alone undergoes a process of cleavage, whereas the chief mass of the egg, the nutritive yolk, remains undivided, and in general unaffected, by the processes of embryonic development; hence the name *partial cleavage*. This, in turn, is resolvable into the two subtypes of *discoidal* and *superficial cleavage*, according as the formative yolk rests as a disc upon the nutritive yolk, or envelops the latter as a thick cortical layer. Remak has designated eggs with total segmentation as *holoblastic*, those with partial segmentation as *meroblastic*.

We may therefore present the following scheme of cleavage :—

I. Type— Total cleavage: (*a*) Equal cleavage (*b*) Unequal cleavage	Holoblastic eggs.
II. Type— Partial cleavage: (*a*) Discoidal cleavage (*b*) Superficial cleavage	Meroblastic eggs.

I$^{a.}$ Equal Cleavage.

In the general consideration of the process of cleavage we have already become acquainted with the phenomena of equal segmentation. It remains to be added to what has been previously said, that this type is most frequent in the case of Invertebrates, and is to be encountered among Vertebrates only in the cases of Amphioxus and Mammals. With the latter, however, there early appears a slight difference in the size of the segments; this has induced many investigators to designate the cleavage of Amphioxus and Mammals as unequal also. If I have not followed this suggestion, it is because the differences are of a trivial nature, because the nucleus in the egg-cell and also in its segments still occupies a central position, and because the different methods of cleavage are in general not sharply definable, but connected by transitional conditions.

Concerning Amphioxus, **Hatschek** states that at the eight-cell stage four smaller and four larger cells are to be distinguished, and that from that time forward in all the subsequent stages there is to be observed a difference in size, and that the process of cleavage takes place in a manner similar to that which will be subsequently described for the Frog's egg. The egg of the Rabbit, concerning which we have the painstaking investigations of **van Beneden**, divides at the very outset into two segments of slightly different size; moreover, from the third stage of division onward there occurs a difference in the rapidity with which the divisions follow each other in the different segments. After the four cleavage-spheres have been divided into eight, there is a stage with twelve spheres; this is followed by another with sixteen, and afterwards another with twenty-four.

I^b. Unequal Cleavage.

As a basis for the description of unequal cleavage we may employ the Amphibian egg, the structure of which has already been considered. As soon as the egg of the Frog or Triton is deposited in the water and is fertilised, and while the gelatinous envelope is swelling up, its black pigmented hemisphere or animal half becomes directed upward, because it contains more protoplasm and small yolk-spherules, and is specifically lighter. The want of uniformity in the distribution of the various components of the yolk also induces an altered position of the segmentation-nucleus. Whereas the latter assumes a central position in all cases in which the deutoplasm is uniformly distributed, it invariably alters its location whenever one half of the egg is richer in deutoplasm and the other richer in protoplasm; it then migrates into the more protoplasmic territory.

In the case of the Frog's egg, consequently, we find it in the black pigmented hemisphere, which is turned upward.

When in this case the nucleus prepares to divide, its axis can no longer assume the position of any and every radius of the egg. In consequence of the want of uniformity in the distribution of the protoplasm, the nucleus comes under the influence of the more protoplasmic pigmented part, which rests on the more deutoplasmic portion like an inverted cup, and, on account of its less specific gravity, floats at the surface, and is spread out horizontally. But in a horizontal protoplasmic disc the nuclear spindle comes to occupy a horizontal position (fig. 31 *A* *sp*). Consequently the plane of division must be formed in a *vertical direction*. A small furrow now begins to show itself—at the animal pole first, because the latter is more under the influence of the nuclear spindle, which lies nearer to it, and because it contains more protoplasm, from which proceed the phenomena of motion during division. The furrow gradually deepens downward, and cuts through to the vegetative pole.

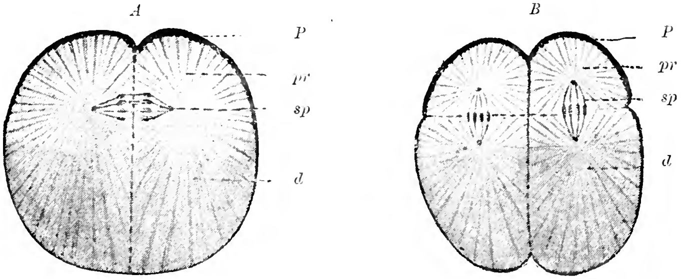

Fig. 31.—Diagram of the division of the Frog's egg.
A, Stage of the first division. *B*, Stage of the third division. The four segments of the second stage of division are beginning to be divided by an equatorial furrow into eight segments. *P*, pigmented surface of the egg at the animal pole ; *pr*, the part of the egg which is richer in protoplasm ; *d*, the part which is richer in deutoplasm ; *sp*, nuclear spindle.

By the first act of division we get two hemispheres (fig. 32 ²), each of which is composed of a quadrant richer in protoplasm and directed upward, and another poorer in protoplasm and directed downward. By this means both the position of the nucleus and the direction of its axis are again determined, when it prepares for the second division. According to the rule previously laid down, the nucleus is to be sought in the quadrant which contains the more protoplasm ; the axis of the spindle must take a position parallel to the long axis of the quadrant, and must therefore come to lie horizontally

The second plane of division is consequently, like the first, vertical, and cuts the latter at right angles.

After the conclusion of the second segmentation the Amphibian egg consists of four quadrants (fig. 32^{4}), which are separated from one another by vertical planes of division and possess two dissimilar poles,—one richer in protoplasm, lighter, and directed upwards; the other richer in yolk, heavier, and directed downwards. In the case of equal segmentation we saw that at the stage of the third segmentation the axis of the nuclear spindle becomes parallel to the long axis of the quadrant. The same thing occurs here also, although in a somewhat modified manner. On account of the greater accumulation of protoplasm in the upper half of the quadrant, the spindle cannot, as in the case of equal segmentation, lie in the middle of it, but must lie nearer to the animal pole of the egg (fig. 31 *B sp*). Moreover, it is exactly vertical, because the four quadrants of the Amphibian egg are definitely oriented in space on account of the difference in specific gravity of their halves. In consequence of this *the third plane of division must be horizontal, and must also lie above the equator of the egg-sphere* more or less toward its animal pole (fig. 32^{8}). *The segments are very unlike both in size and composition;* and this is the reason why this form of segmentation has been called unequal. The four upper segments are smaller and contain less yolk, the four lower ones are much larger and richer in yolk. They are also distinguished from each other as *animal cells* and *vegetative cells*, according to the poles near which they lie.

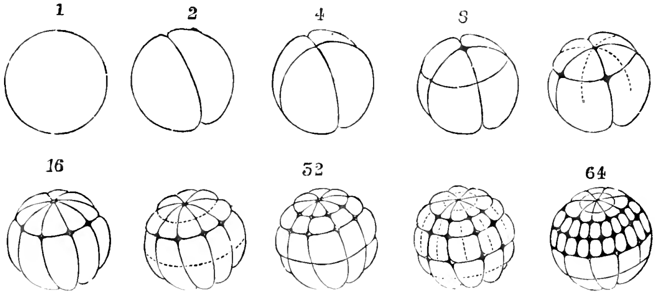

Fig. 32.—Cleavage of Rana temporaria, after Ecker.
The numbers placed above the figures indicate the number of segments present in the corresponding stage.

In the course of further development, the distinction between animal and vegetative cells constantly increases, for the richer the cells are in protoplasm the more quickly and the more frequently do they divide. At the fourth stage the 4 upper segments are first divided by vertical furrows into 8, and then after an interval the 4 lower ones are divided in the same manner, so that the egg is now composed of eight smaller and eight larger cells (fig. 32^{16}). After a short resting stage the eight upper segments are again divided, this time by a horizontal furrow, and somewhat later a similar furrow divides the eight lower segments also (fig. 32^{32}). In the same manner the 32 segments are divided into 64 (fig. 32^{64}). In the stages which follow this, the divisions in the animal half of the egg are still more accelerated relatively to those of the vegetative half. While the 32 animal cells are divided into 128 segments by two divisions which follow each other in quick succession, there are still found in the lower half only 32 cells which are preparing for cleavage. It thus comes to pass that, as the final result of the process of cleavage, there exists *a spheroidal mass of cells with entirely dissimilar halves,*—an upper, animal half with small, pigmented cells, and a vegetative half with larger, clear cells, containing more abundant yolk.

From the nature of the progress of unequal cleavage, as well as from a series of other phenomena, one may lay down a general law, first formulated by BALFOUR, that *the rapidity of cleavage is proportional to the concentration of protoplasm in the segment.* Cells which are rich in protoplasm divide more rapidly than those in which protoplasm is more scanty and deutoplasm more abundant.

As we have seen, the Frog's egg, by reason of the difference in specific gravity between its animal and vegetative halves, by reason of the heterogeneous pigmentation of its surface, by reason of the unequal distribution of protoplasm and deutoplasm, and by reason of the eccentric position of its nucleus, allows us to pass fixed and easily determinable axes through its spherical body. On this account it is an especially favourable object upon which to determine the question whether the egg allows one to recognise in the position of its parts, even before fertilisation, immediately after the same, and during the process of cleavage, fixed relations to the organs of the fully developed organism. This question has been tested by means of ingenious experiments, especially by PFLUEGER and ROUX, by the latter in his "Beiträge zur Entwicklungsmechanik des Embryo."

These have resulted in determining that the first cleavage plane of the egg corresponds to the median plane of the embryo, so that it separates the material of the right half of the body from that of the left. Secondly, according to ROUX, the position of the head- and tail-ends of the embryo may be determined in the fertilised egg. That half of the egg, namely, through which the spermatic nucleus migrates to reach the egg-nucleus, becomes the tail-end of the embryo; the opposite half becomes the head-end. Every egg, however, can be fertilised in any meridian whatever, as was demonstrable experimentally, and thereby the tail-end of the embryo may be located at any chosen position in the egg. Thirdly, the plane in which the two sexual nuclei meet each other (copulation-plane) corresponds with the first plane of segmentation.

IIa. Partial Discoidal Cleavage.

The Hen's egg serves us as the classical example for the description of discoidal segmentation. In this instance the whole process of cleavage takes place while the egg is still in the oviduct, during the period in which the yolk is being surrounded by the albuminous envelope and the calcareous shell. It results simply in a cleavage of the germ-disc of formative yolk, whereas the greater part of the egg, which contains the nutritive yolk, remains unsegmented, and becomes subsequently enclosed in an appendage to the embryo,—the so-called yolk-sac,—and is gradually consumed as nutritive material. Just as in the case of the pigmented, animal half of the Frog's egg, so also in the case of the Hen's egg, turn it in whatever direction one will, the germ-disc floats on top, because it is the lighter part. As in the Frog's egg the first plane of cleavage is vertical and begins at the animal pole, so in the case of the Hen's egg (fig. 33 *A*) a small furrow (*b*) makes its appearance in the middle of the disc, and advances from above downward in a vertical direction. But

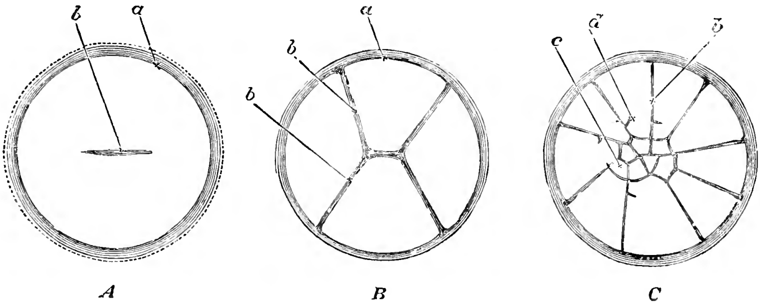

Fig. 33.—Surface view of the first stages of cleavage in the Hen's egg, after Coste.
a, Border of the germ-disc; *b*, vertical furrow; *c*, small central segment; *d*, large peripheral segment.

whereas in the case of the Frog's egg the first plane of cleavage cuts through to the opposite pole, in the case of the Hen's egg it divides only the germ-disc into two similar segments, which like two buds rest upon the undivided yolk-mass with a broad base, by means of which they still have a physical connection with each other. Soon after this, there is formed a second vertical furrow, which crosses the first at right angles, and likewise remains limited to the germ-disc, which is now divided into four segments (fig. 33 *B*).

Each of the four segments is again divided into halves by a radial furrow. The segments thus formed correspond to sectors, which meet in the centre of the germ-disc with pointed ends, and have their broad ends turned toward the periphery. The apex of each of the segments is then cut off by a cross furrow, *i.e.*, by one which is parallel to the equator of the egg (fig. 33 *C*), in consequence of which there are formed smaller central (*c*) and larger peripheral (*d*) segments. Since from this time forward radial furrows and those that are parallel to the equator make their appearance alternately, the germ-disc is subdivided into more and more numerous segments, which are so arranged that the smaller lie at the centre of the disc,—therefore immediately around the animal pole,—the larger toward its periphery. With the advancing cleavage the smaller segments are entirely constricted off from the underlying yolk, whereas the larger peripheral ones still remain at first in continuity with it (fig. 34). In this way we finally get a disc of small embryonic cells, which, toward the middle, are arranged in several superposed layers.

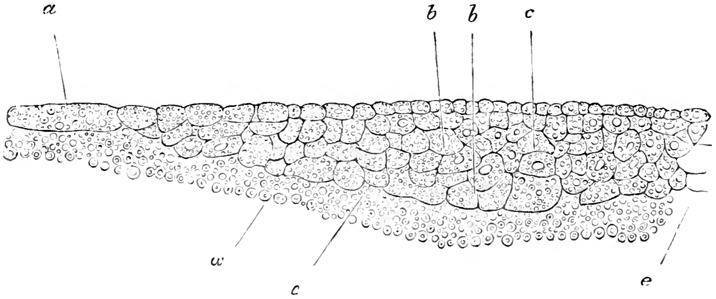

Fig. 34.—**Section through the germ-disc of the Hen's egg during the later stages of segmentation** after Balfour.

The section, which represents rather more than half the breadth of the blastoderm (the middle line is at *c*), shows that the segments of the surface and of the centre of the disc are smaller than those below and toward the periphery. At the border they are still very large. One of the latter is indicated at *a*.

a, Large peripheral cell ; *b*, larger cells of the lower layers ; *c*, middle line of the blastoderm ; *e*, boundary between the blastoderm and the white yolk, *w*.

The layer of yolk which immediately adjoins the periphery of the cellular disc, and which is very finely granular and especially rich in protoplasm, still merits particular consideration, for in it lie isolated nuclei (fig. 35 *nx'*), the *much-discussed yolk-nuclei or parablast-nuclei* (the "*merocytes*" of RÜCKERT). In the case of the Chick they are less striking than in Teleosts and Selachians, in which they have been accurately investigated by BALFOUR, HOFFMANN, RÜCKERT, and KASTSCHENKO. Formerly these were held to arise spontaneously (free formation of nuclei) in the yolk, an assumption which in itself is very improbable, since, according to our present knowledge, the free formation of nuclei does not appear to occur anywhere in either animal or vegetable kingdom. Consequently *the yolk-nuclei are now rightly held to be derived from the cleavage-nuclei.* They are probably produced even at an early period, when the first-formed segments, which remain, as we have seen, for a long time in connection with the yolk, begin to be constricted off from the latter. This probably takes place in the following manner: there arise in the segments nuclear spindles, the halves of which go into the completely isolated embryonic cells at the time of their separation from the yolk, while the remaining halves go into the underlying yolk-layer, and are there converted into vesicular yolk-nuclei.

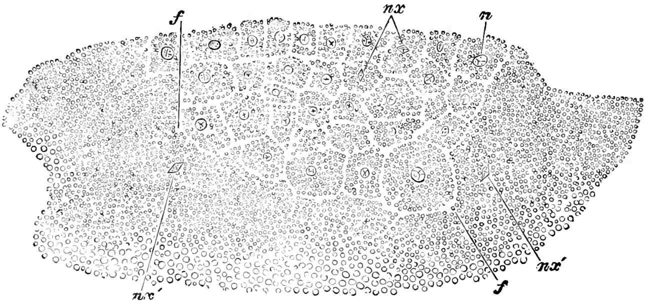

Fig. 35.—Section through the germ-disc of a Pristiurus embryo during segmentation, after BALFOUR.

n, Nucleus; *nx*, modified nucleus prior to division; *nx'*, modified nucleus in the yolk; *f*, furrows which appear in the yolk adjacent to the germ-disc.

Their number subsequently increases by means of indirect division, as is established by the fact that in sections nuclear spindles have been observed in the yolk-layer (fig. 35 *nx'*).

While, on the one hand, there is an increase in the number of the yolk-nuclei, so, on the other hand, there is also a diminution in their *number*, as is asserted by several authors (Waldeyer, Rückert, Balfour, etc.). This takes place by the constricting off of nuclei and surrounding protoplasm, which go to enlarge the cellular disc. We may, with Waldeyer, designate these as *secondary cleavage*-cells, and regard the whole process as a kind of *supplementary segmentation*.

By means of this a part of the voluminous yolk-material continues to be gradually individualised into cells. These annex themselves to the border of the germ-disc, which with their aid increases in extent and grows over a continually increasing territory of the unsegmented yolk-sphere. In still later stages of development, long after the cellular germ-disc has been differentiated into the germ-layers, the supplementary segmentation continues to go on at the margin of the disc in the neighbouring yolk-mass, and to furnish new cell-material. *Therefore the layer which encloses the yolk-nuclei forms an important connecting link between the segmented germ and the unsegmented nutritive yolk;* I shall come back to this subject later.

The appearance of merocytes and the supplementary cleavage which proceeds from them are phenomena which are induced by the vast accumulation of yolk-material, and which allow the latter to be divided up into cells, even though the process is a slow one.

The eggs of Selachians (Kastschenko, Rückert) deviate a little from the usual method of partial cleavage in meroblastic eggs, and in a manner which recalls to a certain extent the processes of superficial cleavage, which are to be treated of later. The cleavage-nucleus, namely, is divided into two nuclei, these again into four and even a greater number, without an accompanying division of the germ-disc into a corresponding number of segments. In this case, therefore, there arises at first a multinuclear protoplasmic mass,—a plasmodium,—in which the nuclei are distributed at regular intervals. Subsequently furrows appear, generally in great numbers and all at once, by means of which the germ-disc becomes divided into cells from the centre to the periphery. Some of the nuclei always remain in the periphery outside the territory of cleavage, here undergo further division, migrate out of the germ-disc into the surrounding nutritive yolk, and constitute the yolk-nuclei or merocytes. These cause and maintain in the yolk for a long time the process of supplementary cleavage.

When we institute a comparison between partial and unequal cleavage,—for the descriptions of which we have made use of the eggs of the Hen and the Frog,—it is not difficult to derive the former from the latter, and to find a cause for the origin of the former.

It is the same as that which produced unequal cleavage from equal cleavage; it is the great accumulation of nutritive yolk, the inequality in the distribution of the egg-substances which goes hand in hand with it, and the alteration in the position of the cleavage-nucleus. The process of differentiation, which is still in a stage of transition in the case of the Frog's egg, is carried to an extreme in the case of the Hen's egg. Protoplasmic substance was already abundantly accumulated at the animal pole in the former case, but in the latter it is still more concentrated, and at the same time has become differentiated from the nutritive yolk as a disc enclosing the segmentation-nucleus. The yolk, accumulated to an enormous extent at the opposite pole, is, in consequence of this separation, relatively poor in protoplasmic substance, which only scantily fills the interstices between the large yolk-spheres.

Inasmuch as the phenomena of motion during the process of division emanate from the protoplasm and nucleus, whereas the deutoplasm remains passive, *the active substance in the case of meroblastic eggs can no longer master the passive substance and cause it to participate in the cleavage.* Even in the case of the Frog's egg a preponderance of the animal pole during cleavage is observable; within its territory the nucleus lies, the radial figures of the protoplasm appear, and the first and second planes of division begin to arise, whereas they cut through at the vegetative pole last of all; moreover the process of division during the later stages takes place there with greater rapidity, so that a distinction arises between the smaller animal cells and the larger vegetative ones. In the case of the Hen's egg, the preponderance of the animal pole is still further increased, and the contrast with the vegetative pole is most sharply expressed. The cleavage-furrows not only begin there, but they remain restricted to the territory immediately surrounding it. Thus we get on the one hand a disc composed of small animal cells, on the other an immense undivided yolk-mass, which corresponds to the larger vegetative cells of the Frog's egg. *The yolk-nuclei* enclosed in the periphery of the germ-disc *are equivalent to the nuclei of the vegetative cells of the Frog's egg.*

II$^{b.}$ Partial Superficial Cleavage.

The second sub-type of partial cleavage is prevalent in the phylum of Arthropods, and occurs in centrolecithal eggs, where a central yolk-mass is enclosed in a cortical layer of formative yolk. Manifold variations are possible here, as well as transitions to equal and unequal cleavage. When the course pursued is quite typical, the segmentation-nucleus, surrounded by a mantle of protoplasm, lies in the middle of the egg in the nutritive yolk; here it is divided into two daughter-nuclei, without the occurrence of a corresponding division of the egg-cell. The daughter-nuclei, in turn, undergo division into 4, these into 8, 16, 32 nuclei, etc., while the egg as a whole still remains unsegmented. Subsequently the nuclei move apart, the greater number gradually migrate to the surface, and penetrate into the protoplasmic cortical layer, where they arrange themselves at uniform distances from each other. It is only at this stage that the process of egg-segmentation takes place, for now *the cortical layer is divided into as many cells as there are nuclei in it, while the central yolk remains undivided.* The latter is therefore suddenly enclosed in a sac formed of small cells—a *blastoderm* (Keimhaut). Instead of a polar (telolecithal) yolk, we have a central (centrolecithal) yolk. Ordinarily yolk-nuclei or merocytes remain behind in the yolk, as in the meroblastic eggs of Vertebrates.

Now that we have become acquainted with the various forms of the process of segmentation, it will be expedient to dwell for a moment on its results. According as the process of cleavage takes place by one or the other of the four methods described, there arises a mass of cells with corresponding characteristics. From equal segmentation there arises a spherical germ with cells approximately uniform in size (Amphioxus, Mammals) (fig. 30, p. 56); from unequal segmentation, as well as from discoidal, there is produced a form of the germ with polar differentiation. This manifests itself in the first case (Cyclostomes, Amphibia) in the production of small cells at the animal pole and large yolk-laden elements at the opposite, vegetative pole (fig. 32 ^{64}, p. 60). In the other case (fig. 35, p. 64) the vegetative pole is occupied by an unsegmented yolk-mass, in which at definite regions nuclei are found (Fishes, Reptiles, and Birds). Finally there is developed from superficial cleavage a germ composed of a mantle of cells, which envelops an unsegmented yolk-mass in which also there are nuclei (Arthropods).

The multicellular germ undergoes further changes, sometimes in the earlier stages of the cleavage-process, sometimes only in the later stages, in that a small, fluid-filled *cleavage-cavity* is developed in its centre, by the separation of the embryonic cells. At first small, this cavity increases more and more in size, so that the surface of the whole germ is augmented, and the cells which were at first central come to the surface.

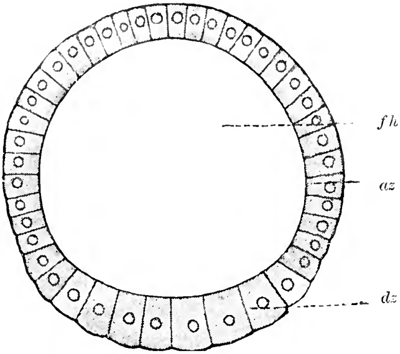

Fig. 36.—Blastula of Amphioxus, after HATSCHEK. *fh*, Segmentation-cavity ; *az*, animal cells ; *dz*, cells with abundant yolk.

Different names have been given to the solid and to the hollow mass of cells. A *morula* or *mulberry-sphere* is spoken of as long as the segmentation-cavity is either wanting or only slightly developed. But when a larger cavity has been formed, as is almost always the case toward the end of the cleavage-process, the germ is called a *blastula* or *blastosphere* (Keimblase). The latter in turn exhibits a four-fold variation of form, according to the abundance of yolk in the original egg and the method of the antecedent segmentation.

In the simplest case (fig. 36) the wall of the blastula is only *one* layer thick; the cells are of uniform size and cylindrical, and are closely united to one another to form an epithelium (many of the lower animals, Amphioxus). In the case of lower, aquatic animals the blastulæ at this stage abandon the egg-envelopes, and, since their cylindrical cells develop cilia at the surface, swim about with rotating motion in the water as ciliate spheres or blastospheres.

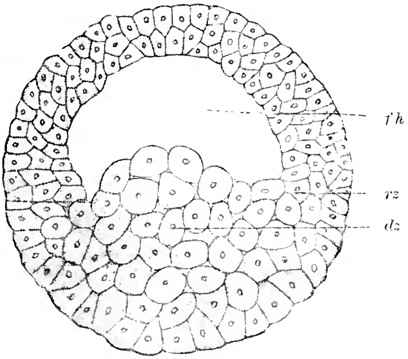

Fig. 37.—Blastula of Triton tæniatus. *fh*, Segmentation-cavity ; *rz*, marginal zone ; *dz*, cells with abundant yolk.

In eggs with unequal segmentation the blastula is ordinarily formed of several layers of cells, as in the case of the Frog and Triton, and at the same time it exhibits in different regions different thicknesses (fig. 37). At the animal pole the wall is thin; at the vegetative pole, on the contrary, it is so much thickened that an elevation, composed of large yolk-cells, protrudes from this side far into the cleavage-cavity, thus considerably diminishing it.

The eggs with partial discoidal segmentation (fig. 38) are modified most of all, and are therefore scarcely to be recognised as blastulæ. In consequence of the immense accumulation of yolk on the ventral (vegetative) side, the cleavage-cavity (*B*) is extraordinarily constricted, and is still preserved only as a narrow fissure filled with albuminous fluid. Dorsally its wall consists of the small embryonic cells (*kz*) resulting from the process of cleavage, which are accumulated in several superposed layers; at the surface they join each other closely, deeper they lie more loosely associated. The floor of the cleavage-cavity is formed of a yolk-mass, scattered through which are to be found the yolk-nuclei or merocytes (*dk*), which likewise result from the cleavage-process. It is to be seen that they are especially numerous at the place of transition from the germ-disc to the yolk-mass.

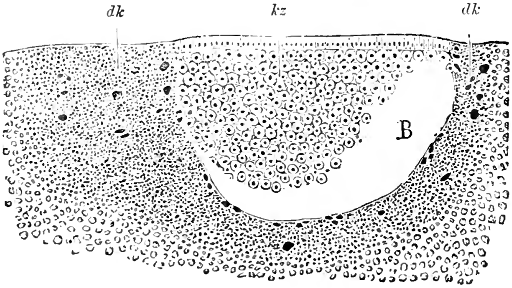

Fig. 38.—Median section through a germ-disc of Pristiurus in the blastula stage, after RÜCKERT.
B, Cavity of the blastula; *kz*, segmented germ; *dk*, finely granular yolk with yolk-nuclei.

This nucleated yolk-mass very evidently corresponds to the large vegetative cells which constitute the floor of the cleavage-cavity in the case of the Amphibian egg (fig. 37).

In the case of superficial cleavage there is formed, strictly speaking, no blastula, since the place where the segmentation-cavity should be developed is filled with nutritive yolk. The latter either remains unsegmented or is subsequently divided, as in the Insects, into individual yolk-cells.

HISTORY OF THE PROCESS OF CLEAVAGE.

The investigation and right comprehension of the process of cleavage have been attended with manifold difficulties. A voluminous literature has arisen on this subject. We limit ourselves to pointing out the most important discoveries and the chief questions which have been discussed.

The first observations on the process of segmentation were made on the Frog's egg. Aside from short statements by SWAMMERDAM and RÖSEL VON

ROSENHOF, it was PREVOST ET DUMAS who were the first to describe, in 1824, the manner in which regular furrows arise on the Frog's egg, and how by means of these the whole surface is divided into smaller and smaller areas. According to the French investigators, the furrows were restricted to the surface of the egg. However, only a few years later, RUSCONI (1826) and C. E. v. BAER recognised that the furrows visible at the surface correspond to fissures which extend through the whole mass of the yolk, and divide it into separate parts. Even in his time VON BAER rightly characterised the whole process of segmentation, in which he discerned the first impulse of life, as an automatic division of the egg-cell, but subsequently he abandoned this, the right path, since he sought for the meaning of division in the dictum: that "all yolk-masses are subject to the influence of the fluid and volatile components of the fertilising material."

In the next decennary there followed numerous discoveries of the process of segmentation in other animals. During this period acquaintance was also gained with partial segmentation. After RUSCONI and VOGT had seen it in the case of fish eggs, KÖLLIKER gave, in the year 1844, the first detailed description of it as seen in the eggs of Cephalopods, and four years later COSTE described it in the Hen's egg.

The question of the significance of the cleavage-process has engaged the earnest attention of investigators, and has given rise to many controversies. The discussion first took a definite turn upon the establishment of the cell-theory. The question was, to determine whether and in what manner cleavage was a process of cell-formation. Although there were already many observations on the division of eggs, SCHWANN himself took no definite position on this question. The views of other investigators were at variance for years. There was a difference of opinion as to whether the egg or the germinative vesicle was a cell, whether the segments resulting from cleavage possessed a membrane or not, and whether these segments were to be regarded as cells or not. In the earlier literature the germinative vesicle and the nuclei of the cleavage-spheres were often designated as embryonic cells, and the surrounding yolk-mass as an enveloping sphere. The difficulty of comprehending the process of segmentation was also aggravated by the false doctrine of free cell-formation from an organic matrix—the cytoblastema—founded by SCHWANN. It remained for a long time a controverted point whether the tissue-cells of the adult organism were the direct descendants of the segmentation-spheres, or whether they arose at a later period by means of free cell-formation from cytoblastema. After NÄGELI on the botanical side had adopted the right course, it was the service of KÖLLIKER, REICHERT, REMAK, and LEYDIG to have paved the way to a comprehension of cleavage, and to have shown that free cell-formation does not take place, but that all cellular elements arise in uninterrupted sequence from the egg-cell.

As far as regards the different kinds of cleavage, KÖLLIKER designated them as total and partial. VAN BENEDEN has given in his "Recherches sur la composition et la signification de l'œuf" a more exhaustive review of the subject, and has also expounded in a clear way the signification of the deutoplasm for the different kinds of cleavage. Subsequently HAECKEL materially simplified the categories of segmentation recognised by VAN BENEDEN, and proposed in his "Anthropogenie" and in his paper "Die Gastrula und die Eifurchung" the classification of the methods of cleavage on which is based the scheme previously given, and according to which total cleavage is divided into equal and unequal, and partial into discoidal and superficial. At the same time HAECKEL endeavoured to derive the different methods of cleavage from one another, and apropos of this directed attention to the important rôle of the nutritive yolk.

The processes which take place within the yolk have eluded observation and a correct interpretation even more than the external phenomena of cleavage, so that it is only in the most recent times that we have acquired a satisfactory insight into them. It is true that the problem, as to what part the nucleus plays in segmentation, has had the uninterrupted attention of investigators, but without any solution having been found. For years there were in the literature two opposing views: sometimes one of them, sometimes the other, attained temporarily greater currency. According to one view—which was almost universally adopted by the botanists, and was defended on the zoölogical side principally by REICHERT, and even recently by AUERBACH—the nucleus disappears before every division, and is dissolved, to be afterwards formed anew in each daughter-segment; according to the other view the nucleus, on the contrary, is *not* dissolved, but is constricted, becomes dumb-bell-shaped, and is divided into halves, and thereby induces cell-division. This view was taught especially by such zoölogists and anatomists as C. E. v. BAER, JOH. MÜLLER, KÖLLIKER, LEYDIG, GEGENBAUR, HAECKEL, VAN BENEDEN, and others, who were supported by the observations which they had made on transparent eggs of the lower animals.

Light was first thrown on the disputed question at the moment when suit able objects were studied with the aid of higher magnifications, and especiall with the employment of modern methods of preparation (fixing and staining reagents).

The works of FOL, FLEMMING, SCHNEIDER, and AUERBACH on the cleavage of the eggs of various animals mark a noteworthy advance. They still maintained, it is true, that the nucleus is dissolved at the time of cleavage, but they gave a detailed and accurate description of the striking radiation which arises in the yolk upon the disappearance of the nucleus, and which during the constriction of the egg soon becomes visible in the region of the daughter-nuclei.* SCHNEIDER observed parts of the spindle-stage.

Soon after this a more exact insight into the complicated and peculiar nuclear changes was obtained by means of three investigations, which were carried out independently and simultaneously on different objects, and were published in rapid succession by BÜTSCHLI, STRASBURGER, and the author. It was definitely established by these observations that there is no dissolution of the nucleus at the time of division, but a metamorphosis, such as has been described in the preceding pages. At the same time I likewise proved that the egg-nucleus is not a new formation, but is derived from parts of the germinative vesicle. From this resulted *the important doctrine that, just as all cells, so also all nuclei of the animal organism are derivatives in an uninterrupted sequence, the one from the egg-cell and the other from its nucleus.* (Omnis cellula e cellula, omnis nucleus e nucleo.) Through these researches there was furnished for the

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* Radiating structures had already been observed in the yolk before this, but in an incomplete manner, by different authors—by GRUBE in the Hirudinea, by DERBES and MEISSNER in the Sea-urchin, by GEGENBAUR in Sagitta, by KROHN, KOWALEVSKY, and KUPFFER in Ascidians, by LEUCKART in Nematodes, by BALBIANI in Spiders, and by OELLACHER in the Trout.

first time a scheme of nuclear division and cell-division, which has since proved to be correct in all essentials, even though it has undergone important improvements and additions at the hands of FOL, FLEMMING, VAN BENEDEN, and RABL.

FOL published an extended monographic investigation of the process of cleavage, which he had observed in many invertebrated animals. FLEMMING, starting with nuclear division in tissue-cells, distinguished with great acumen the non-chromatic and the chromatic parts of the nuclear figure, the non-stainable nuclear spindle-fibres, and the stainable nuclear filaments and loops, which are located upon the surface of the former. He made the interesting discovery concerning the latter, that they become split lengthwise. Light was soon thrown upon this peculiar phenomenon, when HEUSER, VAN BENEDEN, and RABL, independently of each other, discovered that the halves of the split filaments moved apart toward the poles of the nucleus, and furnished the fundament for the daughter-nuclei. VAN BENEDEN at the same time made the additional and important observation on the egg of Ascaris megalocephala, that of the four chromatic loops, which are constantly to be observed in the case of the cleavage-nucleus, two are derived from the chromatic substance of the spermatic nucleus, the other two from the chromatic substance of the egg-nucleus; and that, in consequence of the longitudinal splitting, each daughter-nucleus receives at the time of division two male and two female nuclear loops. In addition there have appeared many other recent works of value on the process of cleavage by NUSSBAUM, RABL, CARNOY, BOVERI, PLATNER, and others.

Within the last few years PFLÜGER has endeavored to prove by interesting experiments that gravitation exercises a determining influence on the position of the planes of cleavage. BORN, ROUX, and the author, on the contrary, thought they were able to explain division from the organisation of the egg-cell itself. In the author's article, "Welchen Einfluss übt die Schwerkraft auf die Theilung der Zellen?" he recognised the causes which determine the various directions of the planes of division, (1) in the distribution of the lighter egg-plasm and the heavier deutoplasm, and (2) in the influence which the spatial arrangement of the egg-plasm exercises on the position of the nuclear spindle, and that which the position of the latter exercises upon the direction of the plane of cleavage.

SUMMARY.

1. In the process of cleavage *the internal and the external* phenomena of segmentation are to be distinguished from each other.

2. The internal phenomena of cleavage find expression in changes (*a*) of the nucleus, (*b*) of the protoplasm.

3. The nucleus while in the process of division consists of a non-chromatic and a chromatic nuclear figure. The non-chromatic figure is a spindle composed of numerous fibres. The chromatic figure is formed of bent, V-shaped nuclear filaments (chromosomes), which lie upon the surface of the middle of the spindle. At the two ends of the spindle there is found a special polar corpuscle [centrosome].

4. The division of the nucleus takes place in the following manner: the nuclear filaments split lengthwise, and their halves move apart in opposite directions toward the ends of the spindle, and are there converted into vesicular daughter-nuclei.

5. The protoplasm arranges itself around the ends of the spindle in filaments having the form of a stellate figure (an aster), so that a double radiation or an amphiaster arises in the egg.

6. The external phenomena of cleavage consist in the division of the egg-contents into individual parts, the number of which corresponds to that of the daughter-nuclei. They exhibit various modifications, which are dependent on the arrangement and distribution of the egg-plasm and the deutoplasm, as is to be seen from the following scheme of segmentation.

Scheme of the Various Modifications of the Process of Cleavage.

I. Total Cleavage. (Holoblastic eggs.)

The eggs, which for the most part are small, contain a small or moderate amount of deutoplasm, and are completely divided into daughter-cells.

1. *Equal Cleavage.*

This takes place in eggs with meagre and uniformly distributed deutoplasm (alecithal). By the process of cleavage there are formed segments which, in general, are of uniform size. (Amphioxus, Mammalia.)

2. *Unequal Cleavage.*

This occurs in eggs in which a more abundant deutoplasm is unequally distributed, being concentrated toward the vegetative pole, and in which the cleavage-nucleus is located nearer the animal and more protoplasmic pole. Usually the segments become unequal in size only with and after the third act of division. (Cyclostomes, Amphibia.)

II. Partial Cleavage. (Meroblastic eggs.)

The eggs, which are often very large, ordinarily contain considerable quantities of deutoplasm. In consequence of the unequal distribution of this, the egg-contents are separated into a formative yolk, in which alone the process of cleavage is manifested, and a nutritive yolk, which remains undivided, and is used up during embryonic development for the growth of the organs.

1. *Discoidal Cleavage.*

This takes place in eggs with nutritive yolk in a polar position The process of cleavage remains confined to the formative yolk accumulated at the animal pole, which has the form of a disc and contains only a small amount of deutoplasm. There is formed, consequently, a cellular disc. (Fishes, Reptiles, Birds.)

2. *Superficial Cleavage.*

This occurs in the case of eggs with central yolk. In typical cases the nucleus alone, which occupies the middle of the egg, undergoes repeated division. The numerous daughter-nuclei which arise in this manner migrate into the layer of protoplasm which invests the central nutritive yolk, and the protoplasm is thereupon divided into as many segments as there are nuclei lying in it. There is formed a germ-membrane (Keimhaut). (Arthropods.)

7. Eggs with total cleavage are designated as holoblastic, eggs with partial cleavage as meroblastic.

8. The direction and position of the first cleavage-plane are strictly conformable to laws which are founded in the organisation of the cell; they are determined by the following three factors:—

First factor. The cleavage-plane always divides the axis of the nucleus which is preparing for division perpendicularly at its middle.

Second factor. The position of the axis of the nucleus during division is dependent upon the form and differentiation of the enveloping protoplasm.

In a protoplasmic sphere the axis of the nuclear spindle, occupying the centre of the sphere, can lie in the direction of any radius whatever; but in an oval protoplasmic body, only in the longest diameter. In a circular disc the nuclear axis lies parallel to its surface in any diameter of the circle, but in an oval disc only in the longest diameter.

Third factor. In the case of eggs of unequal segmentation, which, in consequence of their unequally distributed, polar deutoplasm, are geocentric, and therefore assume when in equilibrium a particular position, the first two planes of cleavage must be vertical, and the third must be horizontal and placed above the equator of the sphere.

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CHAPTER IV.

GENERAL DISCUSSION OF THE PRINCIPLES OF DEVELOPMENT.

A SIMPLE principle has exclusively controlled the embryonic processes hitherto considered. By means of the cleavage of the egg-substance, or cell-division, alone the originally simple elementary organism has been converted into a cell-colony. This presents the simplest conceivable form, inasmuch as it is a hollow sphere, the wall of which is composed of *one* or several layers of epithelial cells. But the principle of cell-division is not adequate for the production, out of this simple organism, of more complicated forms with dissimilar organs, such as the adult animals are; further progress in development can be brought about from this time forward only by the supervention of two other principles, which are likewise simple; namely, the principle of unequal growth in a cell-membrane, and the principle of the division of labour, together with the histological differentiation connected with it.

Let us consider first the **principle of unequal growth.** When in a cell-membrane the individual elements continue to divide *uniformly*, the result will be either a thickening or an increase in the surface of the membrane. The former takes place when the plane of division has the same direction as the surface of the membrane, the latter when it is perpendicular to the surface. With the increase in the extent of surface the cells which were at first present are uniformly and gradually crowded apart by the introduction of the new daughter-cells, inasmuch as they are soft and plastic, and are joined together only by means of a soft cementing substance. Were we to assume that only such a growth took place in the case of the blastula during its further development, nothing else could come of it except an ever larger and thicker-walled hollow sphere of cells.

The operation of an *unequal* growth of the surface produces quite another result. When in the middle of a membrane the cells of a single group within a short time repeatedly undergo "division" by vertical planes, they will be suddenly compelled to claim for themselves much greater surface, and they will consequently exert a vigorous pressure, due to growth, upon the cells in their vicinity, and will tend to push them apart. But in this case a separation of contiguous cells, such as takes place with gradual and uniformly distributed interstitial growth, will be impossible; for the surrounding cells, remaining in a passive condition, will constitute, as it were, a rigid frame, as HIS has expressed it, around the extending part, which, in consequence of accelerated growth, demands an increased area. It must therefore secure room for itself in another manner, and increase its surface by abandoning the level of the passive part through the formation of a fold in either one direction or the other. The fold will be still further increased, and forced farther from the original level, if the increased activity of the process of cell-division in it continues. Thus by means of unequal growth there has now arisen out of the originally uniform membrane a new recognisable part, or a special organ.

When the folding membrane encloses a cavity, as is the case with the blastula, there are *two cases conceivable in the formation of folds.* In the first place, the membrane may be folded into the interior of the body, a process which in embryology is called invagination or involution. Secondly, there may arise by evagination a fold, which projects free beyond the surface of the body.

In the *first case* numerous variations in the details are possible, so that the most various organs, as, *e.g.*, the glands of the animal body, parts of the sensory organs, the central nervous system, etc., are formed.

In the origin of glands a small circumscribed circular part of a cellular membrane is infolded as a hollow cylinder (fig. 39 [1] and [4]), towards the interior of the body, into the underlying tissue, and by continuous growth may attain considerable length. The invagination develops into either the tubular or the alveolar form of gland (FLEMMING). If the glandular sac possesses from its mouth to its blind end nearly uniform dimensions, we have the simple tubular gland (fig. 39 [1]),—the sweat glands of the skin, LIEBERKÜHN's glands of the intestine. The alveolar form of gland differs from this in that the invaginated sac does not simply increase in length, but expands somewhat at its end (fig. 39 [5], *db*), while the other part remains narrow and tube-like and serves as its duct (*a*). More complicated forms of glands arise, when the same processes to which the simple glandular sac owes its origin are repeated on the wall of the sac—when on a small tract of it a more vigorous growth again takes place, and a part begins to grow out from the main tube as a lateral branch (fig. 39 ² and ⁶). By numerous repetitions of such evaginations, the originally simple tubular gland may acquire the form of a much-branched tree, upon which we distinguish the part formed first as trunk, and the parts which have arisen by outgrowths from it as chief branches and branchlets of first, second, third, and fourth order, according to their ages and correlated sizes. According as the lateral outgrowths remain tubular or become enlarged at their tips, there arise either the compound tubular glands (fig. 39 ²) (kidney, testis, liver), or the compound alveolar glands (fig. 39 ⁶) (sebaceous glands of the skin, lungs, etc.).

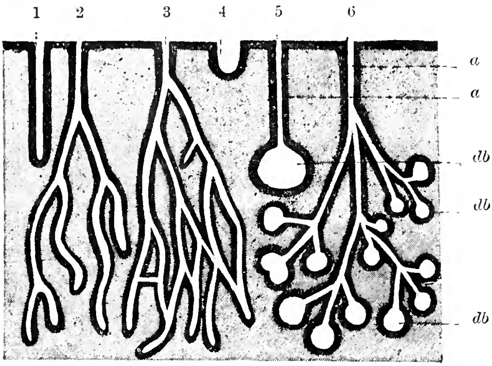

Fig. 39.—Diagram of the formation of glands.
1, Simple tubular gland; 2, branched tubular gland; 3, branched tubular gland with anastomosing branches; 4 and 5, simple alveolar glands; *a*, duct; *db*, vesicular enlargement; 6, branching alveolar gland.

Again, the invaginating part of an originally flat membrane assumes other forms in the *production of sense organs and the central nervous system.* For example, the part of the organ of hearing which bears the nerve terminations—the membranous labyrinth—is developed out of a small tract of the surface of the body, which becomes depressed into a small pit (fig. 40) in consequence of its acquiring an extraordinary vigor in growth. The edges of the auditory pit then grow toward one another, so that this is gradually converted into a little sac, which still opens out at the surface of the body by means of a narrow orifice only (fig. 40 *a*). Finally, the

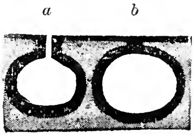

Fig. 40.—Diagram of the formation of the auditory vesicle.
a, Auditory pit; *b*, auditory vesicle, which has arisen by a process of constriction, and still remains connected with the outer germ-layer by means of a solid stalk of epithelium.

narrow orifice closes. Out of the auditory pit there has arisen a closed auditory sac (*b*), which then detaches itself completely from its parent tissue, the epithelium of the surface of the body. Afterwards, simply by means of the unequal growth of its different regions, by means of constrictions and various evaginations, it acquires such an extraordinarily complicated form, that it has justly received the name of membranous labyrinth, as will be shown in detail in another chapter.

The development of the central nervous system may serve as the last example of invagination. Spinal cord and brain take their origin at an early epoch from the layer of epithelial cells which limits the outer surface of the body of the embryo. A narrow band of this epithelium lying along the axis of the back becomes thickened, and is distinguished from the thinner part of the epithelium, which produces the epidermis, as the medullary plate (fig. 41 *A mp*). Inasmuch as the plate grows more rapidly than its surroundings, it becomes infolded into a gutter which is at first shallow, the medullary groove. This becomes deeper as a result of further increase of substance. At the same time the edges (fig. 41 *B mf*), which form the transition from the curved medullary plate to the thinner part of the cellular membrane, become slightly elevated above the surrounding parts, and constitute the so-called medullary folds. Subsequently these grow toward each other, and become so apposed that the furrow becomes a tube, which still remains temporarily open to the outside by means of a narrow longitudinal fissure. Finally, this fissure also disappears (fig. 41 *C*); the edges of the folds grow together; the closed medullary tube (*n*), like the auditory vesicle, then detaches itself completely along the line of fusion (suture) of the cell-membranes of which it was originally a component part and becomes an entirely independent organ (*n*).

Let us now examine somewhat more closely the mechanism of the fusion and detachment of the neural tube.

The two medullary folds are each composed of two layers, which are continuous with each other at the edge of the fold,—the thicker medullary plate (*mp*), which lines the furrow or tube, and the thinner epidermis (*ep*), which has either a more lateral or a more superficial position. When, now, the folds come into contact, they fuse, not only along a narrow edge, but over so extensive a tract that epidermis is joined to epidermis, and that the edges of the medullary plate are joined to each other. The medullary tube thus formed, and the continuous sheet of epidermis that stretches across it, are by means of an intermediary cell-mass still in continuity along the suture produced by the concrescence. But a separation soon takes place along this line, inasmuch as the intermediary band of substance becomes narrower and narrower, and one part of it unites with the

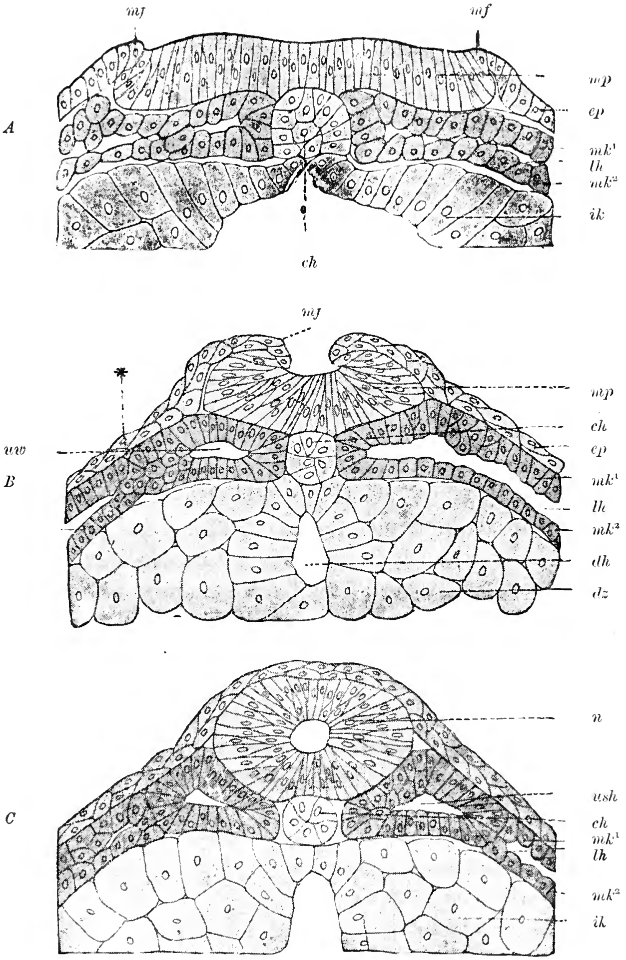

Fig. 41—Cross sections through the dorsal halves of three Triton larvæ.
A, Cross section through an egg in which the medullary folds (*mf*) begin to appear.
B, Cross section through an egg whose medullary furrow is nearly closed.
C, Cross section through an egg with closed neural tube and well-developed primitive segments.
mf, Medullary folds; *mp*, medullary plate; *n*, neural tube (spinal cord); *ch*, chorda; *ep*, epidermis, or corneal layer; *mk*, middle germ-layer; *mk*¹, parietal, *mk*², visceral subdivision of the middle germ-layer; *ik*, inner germ-layer; *ush*, cavity of primitive segment.

epidermis, while the other part is annexed to the medullary tube. Thus in the *formation of the suture* processes of fusion and of separation occur almost simultaneously, a condition which often recurs in the case of other invaginations, as in the constricting off of the auditory vesicle, the vesicle of the lens, etc.

The neural tube having once become independent is subsequently segmented in manifold ways by the formation of foldings, in consequence of inequalities in the rate of surface growth, especially in its anterior enlarged portion, which becomes the brain. There are formed out of this by means of four constrictions five brain-vesicles, which lie in succession one after another; and of these the most anterior, which becomes the cerebrum with its complicated furrows and convolutions of first, second, and third order, serves as a classical example when one desires to show how a highly differentiated organ with complicated morphological conditions may originate by the simple process of folding.

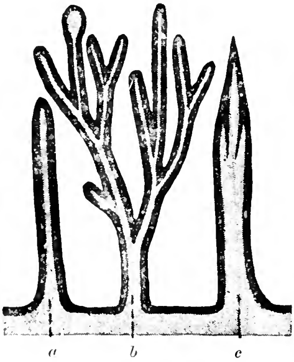

Fig. 42.—Diagram of the formation of papillæ and villi.
a, Simple papilla; *b*, branched papilla or tufted villus; *c*, simple papilla, the connective-tissue core of which runs out into three points.

In addition to invagination *the second method in the formation of folds*, which depends upon a *process of evagination*, plays a no less important part in the determination of the form of animal bodies, giving rise to protuberances of the surface of the body, which may likewise assume various forms (fig. 42). As a result of exuberant growths of small circular territories of a cell-membrane there arise rod-like elevations, resembling the papillæ on the mucous membrane of the tongue (*c*), or the fine villi (*a*) in the small intestine (villi intestinales), which are so closely set that they give a velvety appearance to the surface of the mucous membrane of the intestine. Just as the tubular glands may be abundantly branched, so tufted villi are here and there developed out of simple villi, since local accelerations of growth cause the budding-out of lateral branches of a second, third, and fourth order (fig. 42 *b*). We recall the external tufted gills of various larvæ of Fishes and Amphibia, which project out from the neck-region free into the water, or the villi of the chorion in Mammals, which are characterised by still more numerous branchings. The formation of the limbs is also referable to such a process of external budding.

When the growth of the membrane takes place along a line, the free edges form ridges or folds directed outward, such as the valves of KERKRING folds of the small intestine or the gill-plates on the gill-arches of Fishes.

From the examples cited it is clearly to be seen how the greatest variety of forms may be attained by the simple means of invagination and evagination alone. At the same time, the forms may be modified by two processes of subordinate importance, by *separations* and by *fusions* which affect the cell-layers. Vesicular and sac-like cavities acquire openings by the thinning out of the wall at a place where the vesicle or sac lies near the surface of the body, until there is a breaking through of the separating partition. Thus in the originally closed intestinal tube of Vertebrates there are formed the mouth-opening and the anal opening, as well as the gill-clefts in the neck-region.

The opposite process—fusion—is still more frequently to be observed. It allows of a greater number of variations. We have already seen how the edges of an invagination may come in contact and fuse, as in the development of the auditory vesicle, the intestinal canal, and the neural tube. But concrescence may also take place over a greater extent of surface, when the facing surfaces of an invaginated membrane come more or less completely into contact, and so unite with each other as to form a single cell-membrane. Such a result ensues, for example, in the closure of the embryonic gill-clefts, in the formation of the three semicircular canals of the membranous labyrinth of the ear, or, as a pathological process, in the concrescence of the surfaces of contact of serous cavities. Moreover fusions may take place between sacs which come in contact with their blind ends, as very often occurs in the compound tubular glands (fig. 39 ^{3}). Of the numerous lateral branches which sprout out from the tubule of a gland, some come in contact at their ends with neighboring branches, fuse with them, and establish an open communication with them by the giving way of the cells at the place of contact. It is by this means that branched forms of tubular glands pass into the net-like forms to which the testis and the liver of Man belong.

In addition to the *formation of folds in epithelial layers*, which under a great variety of modifications determine in general the organisation of the animal body, there were mentioned, as a *second* *developmental principle of fundamental significance, division of labor and the histological differentiation associated with it.* In order to understand fully the significance of this principle in development, we must proceed from the thesis that the life of all organic bodies expresses itself in a series of various duties or functions. Organisms take to themselves substances from without; they incorporate in their bodies that which is serviceable, and eliminate that which is not (function of nutrition and metastasis); they can alter the form of their bodies by contraction and extension (function of motion); they are capable of reacting upon external stimuli (function of sensibility); they possess the ability to bring forth new organisms of their own kind (function of reproduction). In the lowest multicellular organisms each of the individual parts discharges in the same manner as the others the enumerated functions necessary for organic life; but the more highly an organism is developed, the more do we see that its individual cells differentiate themselves for the duties of life,—that some assume the function of nutrition, others that of motion, others that of sensibility, and still others that of reproduction,—and that with this division of labor is likewise joined a greater degree of completeness in the execution of the individual functions. The development of a specialised duty likewise leads invariably to an altered appearance of the cell: *with the physiological division of labor there always goes hand-in-hand a morphological or histological differentiation.*

Elementary parts which are especially concerned in the duties of nutrition are distinguished as gland-cells; again others, which have developed the power of contractility to a greater extent, have become muscle-cells, others nerve-cells, others sexual cells, etc. The cells which are concerned in one and the same duty are for the most part associated in groups, and constitute a special tissue.

Thus the study of the embryology of an organism embraces chiefly two elements: one is the study of the development of form, the second the study of histological differentiation. We may at the same time add that in the case of the higher organisms the morphological changes are accomplished principally in the earlier stages of development, and that the histological differentiation takes place in the final stages.

A knowledge of these leading principles will materially facilitate the comprehension of the further processes of development.

CHAPTER V.

DEVELOPMENT OF THE TWO PRIMARY GERM-LAYERS. (GASTRÆA-THEORY.)

THE advances which are brought about during the next stages in the development of the blastula depend primarily upon *processes of folding.* By these means there arise larval forms, which are at first composed of two, and afterwards of four epithelial membranes, or *germ-layers.*

The larval form which is composed of two germ-layers is called the gastrula. It possesses an important developmental signification, because, as HAECKEL has shown in his celebrated Gastræa-Theory, it is to be found in each of the six chief branches of the animal kingdom, and thus furnishes a common starting-point from which along diverging lines the separate animal forms may be derived. As with blastulæ, so in the case of the gastrula four different kinds can be distinguished, according to the abundance and the method of distribution of the yolk. Starting from a simple fundamental form, three further modifications have arisen, all of which, with the exception of a single one which is characteristic of many Arthropods, are to be encountered within the phylum of Vertebrates.

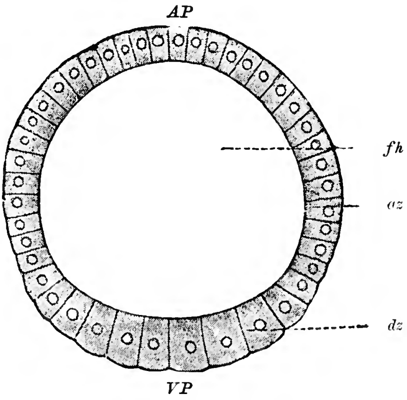

Fig. 43.– Blastula of Amphioxus lanceolatus, after HATSCHEK. *fh*, Cleavage-cavity; *az*, animal cells; *vz*, vegetative cells; *AP*, animal pole; *VP*, vegetative pole.

The simplest and most primitive form, with the consideration of which we have to begin, *is found only in the development of Amphioxus lanceolatus.*

As has been previously shown, its blastula is composed of cylindrical cells, which are closely joined into a single-layered epithelium (fig. 43). At one place, which may be designated as the vegetative pole

(*VP*), the cells (*vz*) are somewhat larger and more turbid, owing to the yolk-granules lodged in them. The process of the formation of the gastrula commences at this place. The vegetative surface begins at first to be flattened, and then to be pushed in toward the middle of the sphere. By the advance of the invagination the depression grows deeper and deeper, while the cleavage-cavity becomes to the same degree diminished in size. Finally, the invaginated portion (fig. 44 *ik*) comes in contact with the inner surface of the uninvaginated portion (*ak*) of the blastula, and completely obliterates the cleavage-cavity. As a result there has been formed out of the hollow sphere with a single wall a cup-shaped germ with double walls—the gastrula.

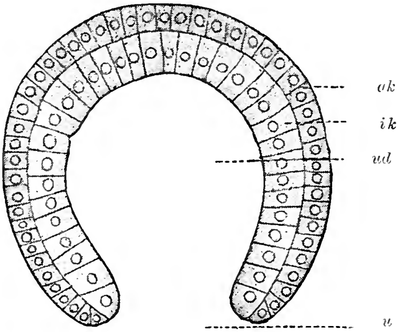

Fig. 44.—Gastrula of Amphioxus lanceolatus, after Hatschek.
ak, Outer germ-layer; *ik*, inner germ-layer; *u*, blastopore, or mouth of archenteron (*ud*).

The cavity of the gastrula, which results from the invagination and is not to be confounded with the cleavage-cavity which it has supplanted, is the primitive intestine (archenteron) (*ud*), or the intestine-body cavity (cœlenteron). This opens to the outside through the primitive mouth (mouth of the archenteron, blastopore) (*u*).

Inasmuch as the names primitive intestine and primitive mouth might easily give rise to erroneous conceptions, let it be remarked, in order to preclude from the start such an event, that the cavity and its external opening which arise by this first invagination are not equivalent to the intestine and mouth of the adult animal. The archenteron of the germ, it is true, furnishes the fundament for the intestinal tube, but there are also formed out of it a number of other organs, the chief of which are the subsequently formed thoracic and body cavities. The future destination of the cavity will therefore be better expressed by the term "*cœlenteron.*" Finally, the primitive mouth is only an evanescent structure among vertebrated animals; later it is closed and disappears without leaving a trace, while the permanent or secondary mouth is an entirely new structure.

The two cell-layers of the cup, which are continuous with each other at the edge of the blastopore, are called the *two primary* *germ-layers*, and are distinguished according to their positions as the outer (*ak*) and the inner (*ik*). Whereas in the blastula the individual cells differ only a little from one another, with the process of gastrulation a division of labor begins to assert itself, a fact which may be recognised in the case of the free-swimming larvæ of Invertebrates. *The outer germ-layer* (*ak*) (also called *ectoblast* or *ectoderm*) serves as a covering for the body, is at the same time the organ of sensation, and effects locomotion when cilia are developed from the cells, as is the case with Amphioxus. *The inner germ-layer* (*ik*) (*entoblast* or *entoderm*) lines the cœlenteron and provides for nutrition. The cell-layers thus stand in contrast to each other both as regards position and function, since each has assumed a special duty. In view of this fact they have been designated by C. E. VON BAER as the two *primitive organs* of the animal body. They present us with a very instructive, because very simple, illustration of the manner in which two organs originate from a single fundament. By invagination the undifferentiated cells of the surface of the blastula are brought into different relations to the outer world, and have consequently been compelled to follow different courses in their development, and to adapt themselves to special duties corresponding to the new relations.

The separation of the embryonic cell-material into the two primitive organs of VON BAER is of decisive significance for the whole subsequent course of the development of the individual cells. For a very definite portion of all the ultimate organs of the body is referable to each of the two primitive organs. In order to put this important condition in the proper light at once, let it be stated that the outer germ-layer furnishes the epithelial covering of the body, the epidermis with the glands and hair, the fundament of the nervous system, and that part of the sense organs which is functionally most important. On this account the older embryologists imposed upon it the name of dermo-sensory layer. The inner germ-layer, on the contrary, is converted into the remaining organs of the body—into the intestine with its glands, into the body-cavity, into the muscles, etc.; by far the greater mass of the body, therefore, is differentiated out of it, and it has to pass through the most numerous and the most trenchant metamorphoses.*

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* The practice of distinguishing the outer and the inner germ-layers as animal and vegetative, which was formerly in vogue and is followed even now, is not proper, and ought therefore to be given up. For the transversely striped musculature of the body, which belongs to its animal organs, does not arise from

Larval forms quite like that of Amphioxus have also been observed in the case of Invertebrates belonging to the phyla of Cœlenterata, Echinodermata, Vermes, and Brachiopoda. For the most part they quit the egg-envelope, even in the gastrula stage, to swim about in the water by means of their cilia; and they can now take nutritive substances—small infusoria, algæ, or remnants of larger animals—through the primitive mouth into the digestive cavity, and make use of them in the further growth of their bodies. Likewise the substances which are not serviceable because indigestible are ejected from the body through the same orifice. In the case of the higher animals the ingestion of food is not only impossible at this time, but also superfluous, because the egg and the embryonic cells arising from it still contain yolk-granules, which are gradually consumed.

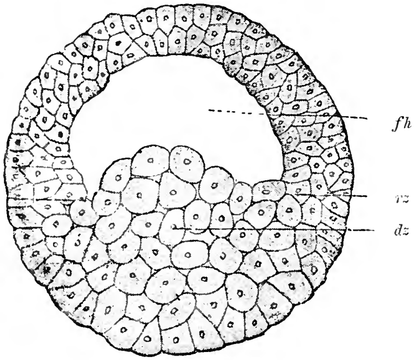

Fig. 45.—Blastula of Tritontæniatus.
fh, Cleavage-cavity; *dz*, yolk-cells; *rz*, marginal zone.

The modifications which *gastrulation undergoes in the Amphibia* are easily referable to the simpler conditions in Amphioxus. In the case of the Water-Salamander, which is to serve as an illustration in this description, one half of the blastula (fig. 45), which is called the animal half, is thin-walled and composed of small cells, which lie in two or three layers one above another, and in the case of the Frog contain black pigment. The other, or vegetative half (*dz*), exhibits a greatly thickened wall, composed of much larger, more deutoplasmic, polygonal cells (*dz*), which, loosely associated in several layers, cause a protuberance into the cavity (*fh*) of the blastula, which is proportionally diminished in size. Where the differentiated halves meet, a transition is effected by means of cells, forming what Goette has designated *marginal zone* (*rz*). Inasmuch as the specific gravity of the animal half is much less than that of the opposite half, it is without exception directed upward in water. The former

the outer germ-layer, as, in consequence of false observations, was formerly believed, but rather from the primary inner germ-layer, as has now been established by many observations.

constitutes the thinner roof, the latter the highly thickened floor, of the excentrically placed cleavage-cavity.

When the gastrula begins to be developed, the invagination takes place on one side in the marginal zone (fig. 46 *u*), and is distinguishable externally by means of a sharp, afterwards horseshoe-shaped furrow, which is bounded on one side by small cells, which in the case of the Frog contain black pigment, on the other side by large unpigmented elements. At the fissure-like blastopore there are infolded into the interior of the blastula (fig. 47 *u*) along its dorsal lip (*dl*) small cells, along its ventral lip (*vl*) the large deutoplasmic elements of the vegetative half; the former constitute the roof, the latter the floor, of the cœlenteron (*ud*). The latter appears in the first stages of the invagination simply as a narrow fissure alongside the capacious cleavage-cavity (*fh*); soon, however, it causes a complete obliteration of this cavity, the fundus of the invagination becoming enlarged into a broad sac, while the entrance always remains narrow and fissure-like. Since the cœlenteron of the Amphibia was first observed by the Italian investigator, Rusconi, it is ordinarily mentioned in the older writings as Rusconi's digestive cavity, and the blastopore likewise as the Rusconian anus.

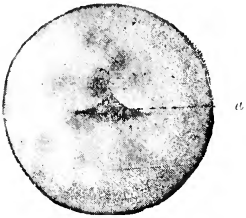

Fig. 46. Egg of Triton, which is developing into a gastrula, seen from the surface.
u, Primitive mouth (blastopore).

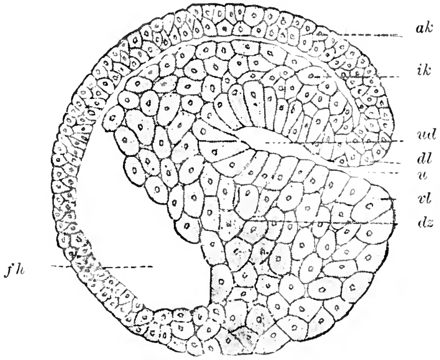

Fig. 47.—Longitudinal [sagittal] section through an egg of Triton at the beginning of gastrulation.
ak, Outer germ-layer; *ik*, inner germ-layer; *fh*, cleavage-cavity; *ud*, cœlenteron; *u*, blastopore; *dz*, yolk-cells; *dl* and *vl*, dorsal and ventral lips of the cœlenteron.

At the close of the process of invagination the whole yolk-mass, or the vegetative half of the blastula, has been taken into the interior to form the lining of the cœlenteron, being at the same time overgrown by a layer of small cells (fig. 48). In the case of the Frog the whole surface of the germ, with the exception of a small place about as large as the head of a pin, which corresponds to the blastopore, now appears black, because the small cells are deeply pigmented. At the place excepted a part of the unpigmented yolk-mass protrudes through the blastopore and closes the entrance to it as if with a stopper (*d*), by reason of which it bears the significant name of vitelline plug.

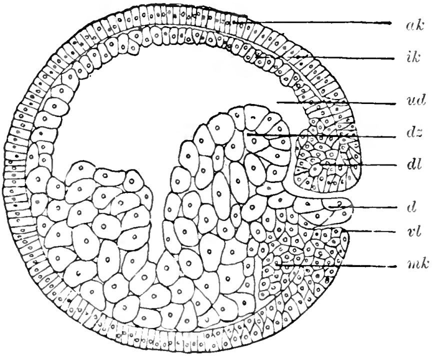

Fig. 48.—Sagittal section through an egg of Triton after the end of gastrulation.
ak, *ik*, *dz*, *dl*, *vl*, *ud*, as in fig. 47; *d*, vitelline plug; *mk*, middle germ-layer.

Of the two germ-layers of the gastrula the outer subsequently becomes reduced in thickness in the case of the Water-Salamander to a single layer of regularly arranged cylindrical cells, whereas in the case of the Frog it is composed of two or three layers of small, in part cubical, deeply pigmented elements. The inner germ-layer in the roof of the cœlenteron likewise consists of small (in the Frog, pigmented) cells, but in the floor it is composed of large yolk-cells, which, heaped together in many layers, produce an elevation that projects far into the cœlenteron and partly fills it. For this reason the gastrula in Amphibia is compelled to adopt in water a definite position of rest, because the yolk-mass, being the heavier part, always assumes the lowest position (fig. 48).

The germ of the Amphibia is already a bilaterally symmetrical body. The thickened, yolk-containing wall of the gastrula becomes the ventral side of the adult animal; the opposite wall, or roof of the cœlenteron, becomes the dorsum. The blastopore indicates, as the sequel shows, the posterior end, the opposite part the head-end. There may therefore be passed through the gastrula a longitudinal, a dorso-ventral, and a transverse axis, which correspond with the axes of the adult animal. This bilateral symmetry, which appears so early in the Amphibia, is solely attributable to the accumulation of yolk-material, and to the piling up of it on the ventral side of the cœlenteron.

The development of Amphibia furnishes us with a transitional condition, which is serviceable for the comprehension of the much more highly altered form[1] which the *gastrula acquires in the case of eggs with partial cleavage in the classes of Selachii, Teleosts, Reptiles, and Birds.*

The conditions are the most readily intelligible in the case of the *Selachians.* That which we have described in the blastula of the Amphibia as the roof of the cleavage-cavity is in the blastula of the Selachians a small disc of embryonic cells (fig. 49 *kz*), continuous at its margin with the extraordinarily voluminous yolk-mass (*dk*), which contains nuclei, although it is not divided up into cells. This yolk-mass corresponds to the yolk-cells of the Amphibia, and, like the latter, forms the floor of the cleavage-cavity (*B*). Germ-disc and yolk thus together constitute a sac with an almost obliterated cavity (*B*), and with walls differing in thickness and in differentiation. A very small part of the wall, the germ-disc, consists of cells. The much larger and thicker portion is yolk-mass, which in the vicinity of the cavity contains nuclei, but is not divided into cells.

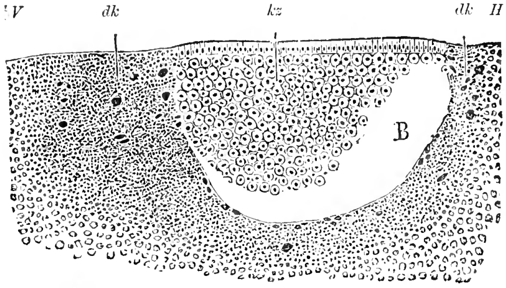

Fig. 49. Median section through a germ-disc of Pristiurus in the blastula stage, after RÜCKERT. The posterior end of the embryo lies at the right. *B*, Cleavage-cavity; *dk*, yolk-nuclei; *kz*, germ-cells; *V* and *H*, front and hind margins of the germ-disc.

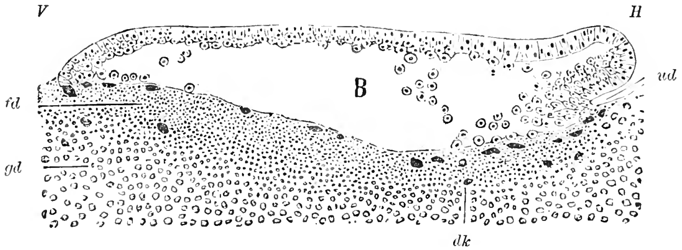

Fig. 50.—Median section through a germ-disc of Pristiurus, in which the gastrular invagination has begun, after RÜCKERT.
ud, First rudiment of the cœlenteron; *B*, cleavage-cavity; *dk*, yolk-nuclei; *fd*, finely granular yolk; *gd*, coarsely granular yolk; *V* and *H*, front and hind margins of the germ-disc.

As in the Amphibia, so here, the gastrulation begins at what is subsequently the hind end (*H*) of the embryo, at a region in the zone of transition or margin of the germ-disc, in which the most superficial cells have assumed the cylindrical form, and are closely joined together (fig. 49). The margin of the disc is folded in (fig. 50) toward the cleavage-cavity (*B*), so that a small cœlenteron (*ud*), shown in the accompanying section, and a fissure-like blastopore are distinctly recognisable. The neighboring yolk also participates in the invagination, since in the territory of the zone of transition the yolk-nuclei (*dk*), enveloped in protoplasm, become detached from the yolk, grow into the cleavage-cavity along with the invaginated cells, and contribute to the formation of the inner germ-layer in a similar manner to that in which, in the case of the Amphibia, the vegetative cells at the lower lip of the blastopore are carried in with the invagination into the cleavage-cavity. The cleavage-cavity (*B*) is being continually encroached upon by the ingrowth of the cells originally in its roof, which form a continuous layer projecting from behind forward. Consequently in the Selachians also the germ-disc becomes two-layered as the result of the invagination. It lies so close upon the yolk, that the cœlenteron appears at most as a fissure. Moreover, the invagination in the Selachians does not remain limited to one region of the original margin of the germ-disc, but soon stretches itself out over its whole posterior perimeter. The blastopore then appears as a large semicircular or horseshoe-shaped fissure at the future posterior end of the embryonic fundament.

The enormous thickness of the yolk causes an important difference between the gastrulation of the Selachii and that of the Amphibia. In the case of the latter the mass of the yolk-cells was quite rapidly carried in with the invagination, and employed in the formation of the ventral wall of the cœlenteron. In the Selachians the taking up of the yolk into the interior of the body ensues only at a slow rate (in a manner to be more accurately explained later), so that for a long time only the dorsal side of the gastrula consists of two cell-layers, whereas the ventral wall is formed by the yolk-mass.

The eggs of Teleosts are very nearly related to those of Selachians in their whole method of development. The same cannot be said to be true to the same extent for the eggs of Reptiles and Birds. The latter, indeed, also belong to the meroblastic type, since they have developed a large amount of yolk, and in consequence undergo partial segmentation; but in the formation of the germ-layers, they exhibit many peculiarities, so that they require a separate treatment. In Birds and Reptiles the investigation is accompanied with greater difficulties than in the Selachians. Particularly the development of the germ-layers in the Chick, notwithstanding the fact that the best investigators have given it their attention, has for a long time been the subject of very divergent descriptions. At the present moment, however, the main facts in the case have been established for the Bird's egg also by the very recent and excellent work of Duval, and upon this as a basis the gastrulation in Birds is easily to be correlated with that of the Vertebrates hitherto described. Since the Bird's egg has played such an important rôle in the history of embryology, and has even been called a classical object for investigation, it appears necessary to go briefly into the *conditions which it presents in the gastrula-stage*, and in connection therewith to consider some of the important results drawn from the study of the eggs of Reptiles.

The blastula arises and the germ-layers begin to be developed out of it while the Bird's egg tarries in the terminal region of the oviduct.

The blastula arises in a manner which was first correctly described by Duval. When by the process of segmentation a small disc of cells has been formed, there appears in the latter a narrow fissure, the *cleavage-cavity* (fig. 51 *fh*), and the cell-material is separated into an upper layer (*dw*) and a lower layer (*vw*), which are continuous with each other at the margin of the disc. The upper layer consists of fully isolated cleavage-spheres, which are flattened at their surfaces of contact and arranged into an epithelium-like layer. They correspond to the thin-walled half of the blastula in Triton (fig. 45), which has already been designated as the animal half. The lower layer is composed of larger cleavage-spheres, which are still in great part continuous by means of their lower halves with the white yolk (*wd*), which is spread out beneath the germ-disc and is known as Pander's nucleus. Yolk-nuclei (merocytes) are also found here in great

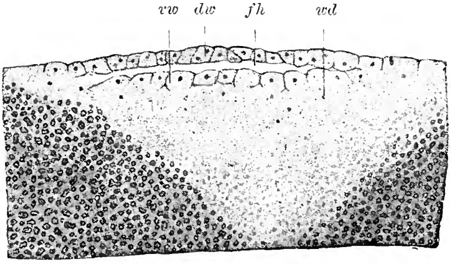

Fig. 51.—Section through the germ-disc of a freshly laid unfertilised Hen's egg, after Duval.
fh, Cleavage-cavity ; *wd*, white yolk ; *vw*, lower cell-layer ; *dw*, upper cell-layer of the blastula.

numbers, especially around the whole periphery of the germ-disc. Since they increase in number by nuclear division, and since some of them, enveloped in protoplasm, become detached from the yolk, they contribute to the continuous growth of the germ-disc, a process which has already (p. 65) been described as supplementary cleavage. The lower cell-layer, together with the whole yolk-mass with its free nuclei, must be compared to the vegetative half of the blastula of Triton (fig. 45 *dz*).

The gastrulation proceeds from the posterior margin of the germ-disc, and begins even some time before the egg is laid. The study of it is coupled with great difficulties, and demands, most of all, that, in the investigation of the disc by means of sections, one should be accurately informed concerning the position of its anterior and posterior margins. The orientation is essentially facilitated by the fact that, in the case of every Hen's egg, with rare exceptions, the side toward which the front end of the embryo is directed can be stated accurately before opening the shell. This results from the following rule established by KUPFFER, KOLLER, GERLACH, and DUVAL.

When one so places an egg in front of him that the blunt pole is turned to the left, the more pointed one to the right, then a line uniting the two poles divides the germ-disc into a half on the side toward the observer, which becomes the hind end of the embryo, and a forward half, which is developed into the head-end. By taking into account this rule, one can establish a difference on the germ-disc even during the process of cleavage. In the anterior region the cleavage takes place more slowly than in the posterior half. Consequently larger embryonic cells are found in front, smaller and more numerous ones behind (OELLACHER, KÖLLIKER, DUVAL).

The difference between anterior and posterior becomes more evident at the beginning of gastrulation. If one now examines carefully the thickened margin of the germ-disc (Randwulst of German writers, bourrelet blastodermique of DUVAL), it is seen that the disc is limited in front and on the sides by a notched and indistinct boundary, but behind, on the contrary, by a sharper contour. The latter is caused by the fact that the marginal ridge, in consequence of a more vigorous growth of the cells, has become thickened and more opaque, and has assumed a whiter colour. It is distinctly recognisable from its surroundings as a whitish crescentic figure (fig. 52 *A s*). Often there is also observable in the crescent a narrow furrow, the crescentic groove (Sichelrinne, KOLLER), by means of which the germ-disc acquires a still sharper limitation behind.

Duval has proved by means of sections, part of which was made in a transverse direction, and part in the sagittal, that the Bird's egg is now in the gastrula stage. Especially instructive are the two median sections, figs. 53 and 54. As is to be seen at once in fig. 53, which represents the somewhat younger stage, the crescentic groove described as occupying the posterior part of the marginal ridge (*vl*) is continued in the form of a narrow fissure (*ud*). Whereas in the blastula stage (fig. 51) the lower cell-layer passed over continuously into the white yolk, it is now sharply separated from it as far as the fissure extends. In fig. 53 this separation has been completed only in the posterior half of the germ-disc; in the anterior half, on the contrary, embryonic cells (*dk*) and yolk are still continuous. However, in the somewhat older stage (fig. 54) the connection is terminated in this region also, since the fissure (*ud*) has extended itself nearly to the anterior margin of the disc (*vr*). In consequence of this process the part of the white yolk which lies beneath the fissure has become destitute of cells and nuclei, with the exception of the marginal territory, where,

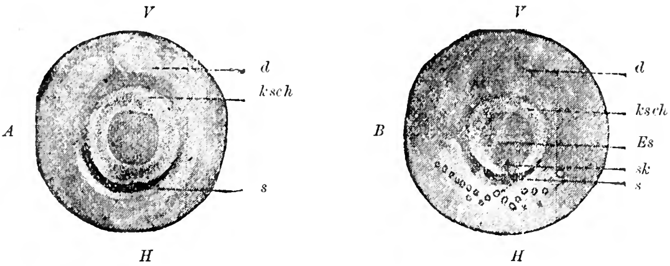

Fig. 52 A.—**The unincubated germ-disc of a Hen's egg,** after Koller.
d, Yolk; *ksch*, germ-disc; *s*, crescent; *V* and *H*, anterior and posterior margins of the germ-disc.

B.—**The germ-disc of a Hen's egg during the first hours of incubation,** after Koller.
d, Yolk; *ksch*, germ-disc; *Es*, embryonal shield; *s*, crescent; *sk*, knob of the crescent; *V* and *H*, anterior and posterior margins of the germ-disc.

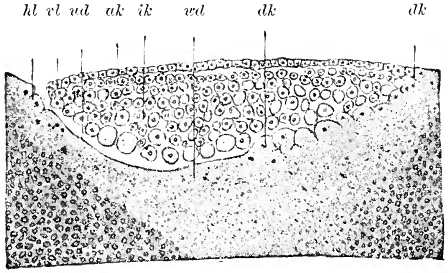

Fig. 53.—**Longitudinal section through the germ-disc of an unincubated egg of the Siskin (Carduelis spinus),** after Duval.
ak, Outer, *ik*, inner germ-layer; *wd*, white yolk; *dk*, yolk-nuclei; *ud*, cœlenteron; *vl*, anterior lip, *hl*, posterior lip at the place of invagination (crescentic groove or blastopore).

especially behind (*hl*) the crescentic groove, free nuclei are constantly to be found keeping up the supplementary cleavage.

Owing to the appearance of the new fissure (subgerminal cavity) (fig. 53 *ud*), the cleavage-cavity (fig. 51 *fh*) is almost completely obliterated. The two cell-layers of the blastula-stage (fig. 51 *dw*, *vw*), described as lying one above and one below the cleavage-cavity, have come close together (figs. 53 and 54), being separated from each other by only a narrow fissure. In the upper layer (*ak*) the cells have assumed a cubical, and at a somewhat later stage a cylindrical, form, and constitute a compact epithelial membrane. The lower layer (*ik*) is composed of larger roundish and loosely arranged cells in several layers. The former is the primary outer germ-layer, the latter the inner layer. In the region of the posterior marginal ridge (*vl*), where the cells are at the same time engaged in more active proliferation, the two layers are continuous with each other.

The highly important processes, by means of which are produced the conditions represented in figs. 53 and 54, present many points of comparison with the gastrulation of the Selachians and Amphibia. We can conceive that the newly appearing fissure has arisen, as in the case of the germ-disc of Pristiurus (fig. 50), by an infolding, in such a way that, as in the former case, cells grow inward from the posterior marginal ridge; and that at the same time, at the deep part of the invagination, the cells which are originally continuous with the yolk (fig. 53 *dk*) detach themselves from the latter, and are employed for the increase of the inner germ-layer.

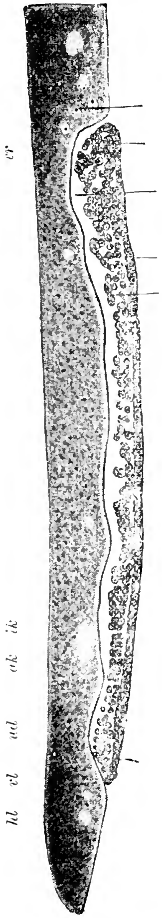

Fig. 54.—Longitudinal section through the germ-disc of a fertilised unincubated egg of the Nightingale, after Duval.
ak, Outer, *ik*, inner germ-layer; *ud*, cœlenteron; *vl*, anterior, *hl*, posterior lip of the blastopore (crescentic groove).

If this explanation is correct, the fissure (*ud*) which now exists between the inner germ-layer and the floor of the yolk corresponds to the cœlenteron, as Goette and Rauber have already remarked, and as Duval has for the first time demonstrated; moreover, the crescentic groove (fig. 52 *s*) corresponds to the blastopore; the thickened portion of the marginal ridge (fig. 53 *vl*) which lies in front of the crescentic groove, within whose territory the two primary germ-layers are continuous with each other, is the anterior or dorsal lip of the blastopore; and the yolk (*hl*) which lies behind the crescentic groove, and which at this early stage contains numerous free nuclei, may be designated as the posterior or ventral lip of the blastopore.

The development of the cœlenteron is the cause of the gradual reduction of the cleavage-cavity, and of its persisting only as a narrow fissure separating the primary germ-layers.

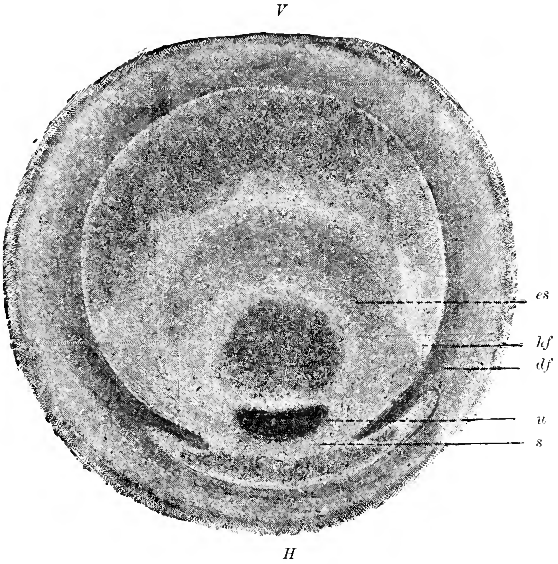

Fig. 55.—Embryonic fundament of Lacerta agilis, after Kupffer.
hf, Area pellucida; *df*, area opaca; *u*, blastopore; *s*, crescent; *es*, embryonic shield. *V*, anterior, *H*, posterior end.

The points of comparison with the gastrula of Triton (fig. 47) are made evident as soon as we replace the mass of yolk-cells with unsegmented yolk, and imagine nuclei imbedded in the latter in the region of the ventral lip of the blastopore.

Through the exposition given by Duval, it appears to me that the contest concerning the origin of the two primary germ-layers in Birds has been happily settled. For a long time there have existed on this very question two irreconcilable views.

According to the older view, to which many investigators still cling, the germ-disc which results from the process of cleavage is divided by *fission* into an upper and a lower layer (Pander, von Baer, Remak, Kölliker, His, and others). According to the other one (Haeckel, Goette, Rauber, Duval, and others), the lower layer has arisen by an infolding. Only by means of the theory of infolding can be explained the different conditions of the anterior and posterior margins of the germ-disc, the more active cell-growth in the territory of the crescent, the existence of a crescentic groove, and the continuity of the two primary germ-layers which is demonstrable in that region. Only by means of this theory, finally, is the relation of Birds to the lower classes of the Vertebrates made possible.

The discoveries which KUPFFER UND BENECKE have made in their investigations of Reptiles, which are so closely related to Birds, also contribute to the elucidation of the pending controversy. In the case of Lacerta agilis (fig. 55), Emys europæa, etc., there is found, as in the case of the Hen at a corresponding stage of development, at the boundary of the pellucid and opaque areas of the posterior end of the germ-disc, an exuberant cell-growth in the form of a crescent (*s*). In the middle plane and slightly in front of this crescent there is to be seen a *small, transversely placed, fissure-like opening* (*u*), *which leads into a blind sac and is comparable to the crescentic groove.* KUPFFER rightly interprets the opening as the blastopore, which is enclosed between an anterior and a posterior lip, and the cavity as the cœlenteron. He also draws a comparison between the corresponding structures in Birds and Reptiles.*

Let us now direct our attention to the succeeding developmental stages of the germ-disc of the Chick. These consist, chiefly, in a constant increase of the superficial extent of the disc.

In the freshly laid, unincubated egg (fig. 54) the outer germ-layer (*ak*) is composed of a single sheet of closely united cylindrical cells; the inner layer (*ik*), on the contrary, consists of a two-layered to three-layered bed of somewhat flattened elements, which are only loosely associated.

Under the influence of incubation the superficial extension of the germ-disc makes rapid advances (fig. 56). In this process the outer germ-layer (*ak*) outstrips the inner, and terminates in a region of the

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* In the interpretation of the manner in which the invagination takes place in the case of the eggs of Reptiles and Birds, I differ from other investigators who also maintain that a gastrulation takes place (GOETTE, HAECKEL, RAUBER, BALFOUR, and others). They regard the whole margin of the germ-disc as the blastopore, at which the outer germ-layer bends over to become continuous with the inner layer. According to my interpretation, the invagination occurs at a small circumscribed place of the margin. The blastopore is from the beginning surrounded by cells both on its anterior and its posterior lip. The relation of the blastopore as well as that of the germ-layers to the yolk will be more fully dealt with hereafter.

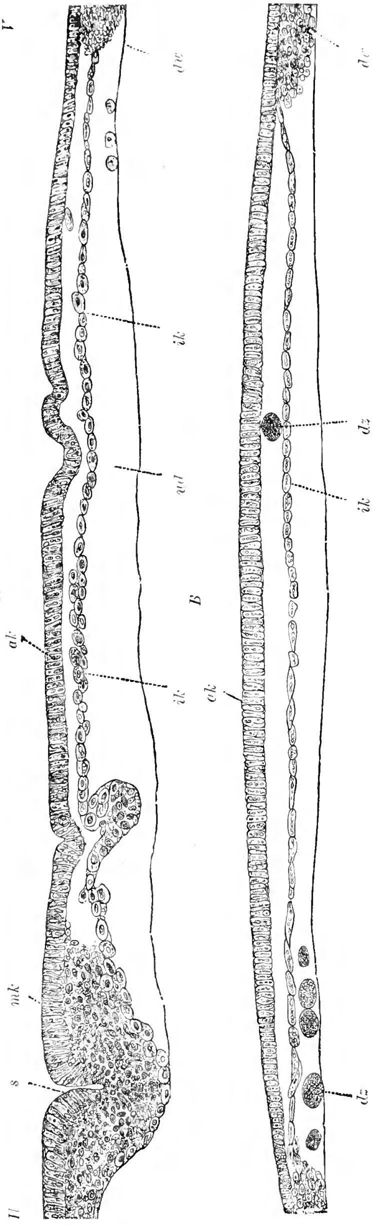

Fig. 56 A.—Longitudinal section through the germ-disc of a Hen's egg that had been incubated a few hours, after Koller. B, Cross section through the germ-disc of a Hen's egg that had been incubated a few hours, after Koller.
ak, Outer; *ik*, inner, *mk*, middle germ-layer; *dw*, yolk-wall; *dz*, yolk-cells; *s*, crescentic groove; *ud*, cœlenteron; *V*, anterior, *H*, posterior end of the germ-disc.

yolk where the latter has not yet undergone division into entodermic cells. In the form of its cells it is, in every respect, in sharp contrast with the inner layer. While the ectodermic cells (fig. 56 *ak*) attain their greatest height in the middle of the germ-disc, they gradually decrease in height toward the margin, and undergo a transition into cubical and finally into flattened elements (fig. 57). The reverse is the case with the inner germ-layer; the latter has now become converted in the middle of the germ-disc (fig. 56 *ik*) into a single layer of much flattened scale-like cells, which are closely united into a thin membrane. Toward the periphery they become somewhat larger and more polygonal (fig. 57), and here, at some distance inside the free margin of the outer germ-layer, they become merged in the white yolk (*dw*), which is abundantly provided with yolk-nuclei (*dk*) in the region of the transition. This region of the yolk is designated as the yolk-wall (vitelline rampart). It serves for the augmentation of the inner germ-layer, in that the free nuclei increase in number by division, and keep up the process of supplementary cleavage already mentioned.

During incubation the liquefaction of the yolk makes further progress (fig. 56) and leads to the formation of a depression (*ud*), which continually increases in depth and breadth, and over which the germ-disc arches like a watch-glass. Upon examination from the surface its middle, as far as the fluid reaches under it, appears clear and translucent, whereas the marginal area, which lies upon the opaque yolk, appears dark. Such a distinction is still more observable when one detaches the whole germ-disc from the yolk, for in the region of the fluid-filled space the thin and transparent germ-layers come off easily and clean from their substratum, whereas at the rim, from the point where the inner germ-layer merges with the yolk-wall outward, turbid yolk-substance remains clinging to the germ-disc. For a long time the middle, clear, circular area has been designated in embryology as the clear germinal area (area pellucida), and the more cloudy, ring-like rim as the opaque germinal area (area opaca).

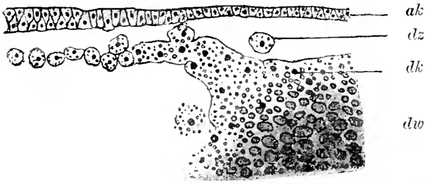

Fig. 57.—Section through the margin of the germ-disc of a Hen's egg that had been incubated for six hours, after DUVAL.
ak, Outer germ-layer ; *dz*, yolk-cells ; *dk*, yolk-nuclei ; *dw*, yolk-wall.

In the next chapter I shall treat more in extenso of the important changes which take place—up to the time when the egg is laid and during the first hours of incubation—in the vicinity of the crescentic groove and the anterior lip of the blastopore, because they are connected with the development of the middle germ-layer.

It is still more difficult than in the case of the Chick to interpret in its details the *development of the germ-layers in Mammals*, and to refer it back to the gastrulation of the other Vertebrates. Especial service has been rendered through the painstaking investigation of these conditions: in the earlier times by BISCHOFF, in later years by HENSEN, LIEBERKÜHN, VAN BENEDEN, KÖLLIKER, and HEAPE. The object of investigation which has been made use of in this work, and which we shall employ as the basis of our description, has usually been the Rabbit; besides this, the Bat and the Mole have also been employed.

While the Mammalian egg is gradually impelled through the oviduct toward the uterus by the ciliary motion of the epithelium, it becomes converted by the cleavage process into a spherical mass of small cells (fig. 58 *A*). Then there arises within it, by the secretion of a fluid, a small fissure-like cleavage-cavity (fig. 58 *B*). The germ has consequently entered upon the vesicular or blastula stage. The wall of the blastula, or vesicula blastodermica, is composed of a single layer of polygonal cells, arranged, as has been known since Bischoff's works, in mosaic, with the exception of a small region, where the wall, as in the case of the Amphibian blastula, is thickened by an accumulation of somewhat more granular and darker cells, which produce a knob-like elevation that projects far into the cleavage-cavity.

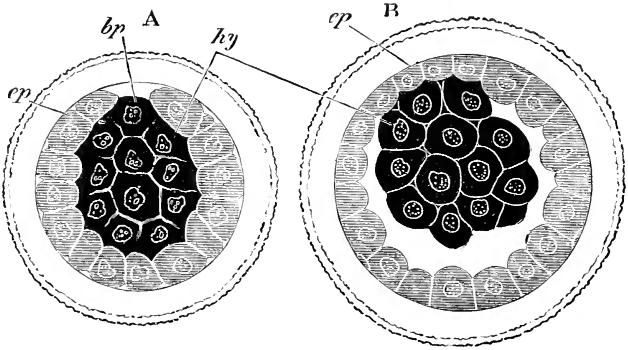

Fig. 58.—Optical sections of a Rabbit's egg in two stages immediately following cleavage, after Ed. v. Beneden. Copied from Balfour's "Comparative Embryology."

A, Solid cell-mass resulting from cleavage.

B, Development of the blastula by the formation of a cleavage-cavity in the cell-mass. (According to van Beneden's interpretation, *ep* is epiblast; *hy*, hypoblast; *bp*, blastopore.)

A peculiarity preëminently characteristic of the further development of Mammals is that here, as in no other Vertebrate, the blastula increases enormously in size (fig. 59), by the accumulation of fluid which contains much albumen and produces a granular coagulum upon the addition of alcohol; it soon acquires a diameter of 1·0 mm. Of course, with these processes of growth the zona pellucida is altered and distended into a thin membrane. A gelatinous layer (*zp*) already secreted by the oviduct envelops the latter.

In Rabbits' eggs which are a millimetre in diameter the wall of the blastula has become very thin. The mosaic-like cells arranged in a single layer have become very much flattened. Also the knob of cells, which projects into the cleavage-cavity, has become metamorphosed and has spread itself out more and more in the form of a disc-like plate, which is continuous at its attenuated margins with the thin wall of the blastula. The further processes of development take place principally in this plate. Its most superficial cells are flattened out to thin scales, such as also form the wall of the blastula elsewhere; its remaining elements, on the contrary, arranged in from two to three superposed layers, are larger and richer in protoplasm.

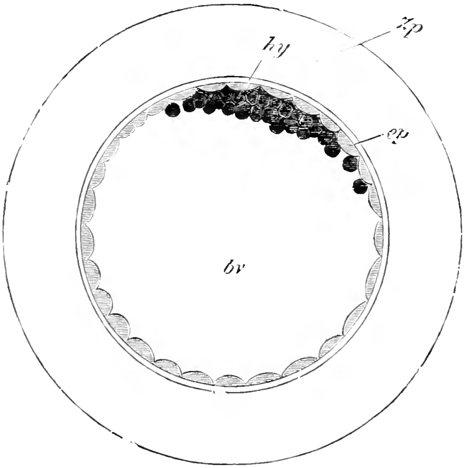

Fig. 59.—Rabbit's egg, 70-90 hours after fertilisation, after ED. V. BENEDEN. Copied from BALFOUR'S "Comparative Embryology."

br, Cavity of the blastula; *zp*, [gelatinous layer surrounding the] zona pellucida; *ep*, *hy*, as in Fig. 58.

Up to this time the embryo of the Mammal is in the blastula stage. It still consists everywhere of a single germ-layer. For the view which has been advanced by many persons, that the germ-disc in this stage of development is already in the two-layered condition, and that the outer layer of flat cells constitutes the outer germ-layer and the more protoplasmic cells lying under it the inner germ-layer, is, in my opinion, untenable. Opposed to this are, first, the fact that the flattened and the thicker cell-layers are firmly joined together and are not separated from each other even by the narrowest fissure, and, secondly, the further course of the development.*

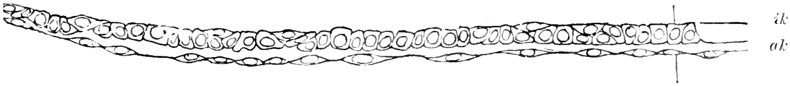

Fig. 60.—Cross section through the almost circular germinal area of a Rabbit's egg 6 days and 9 hours old (diameter 0·8 mm.), after BALFOUR.

ak, Outer, *ik*, inner germ-layer. The section shows the peculiar character of the upper layer with a certain number of flattened superficial cells. Only about half of the whole breadth of the germinal area is represented.

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* Holding to this interpretation, I am of course also unable to agree with a view of VAN BENEDEN'S, according to which the gastrulation takes place at the

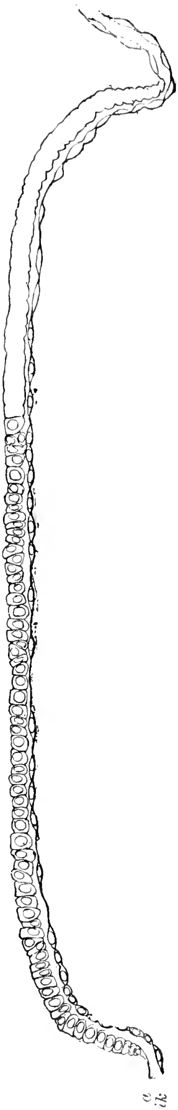

Fig. 61.—Cross section through an oval blastula of a Rabbit of the seventh day. Length of the germinal area about 1·2 mm., breadth of the same 0·86 mm. After Balfour.
The flattened cells of the outer germ-layer (*ak*), represented in Fig. 60, are no longer present.

Two germ-layers first appear in eggs which have already attained a diameter of more than 1 mm. and are about five days old. At the place where the cell-plate previously lay, one sees by inspection from the surface a whitish spot, which is at first round, but later becomes oval or pear-shaped. It is generally designated at this stage as area embryonalis, or as *embryonic spot.* It consists of two germ-layers (fig. 60), which are separated by a distinct fissure, and may be detached from each other. The inner germ-layer (*ik*) is a single sheet of greatly flattened cells. The outer germ-layer (*ak*), on the contrary, is considerably thicker, and shows that it is composed of two sheets of cells: (1) a deeper layer of cubical or roundish, larger elements, and (2) a superficial layer of isolated flatter cells, which were first accurately described by Rauber, and which have been named after him Rauber's *layer.* Toward the margins of the embryonic spot the outer layer becomes thinner and possesses only a single layer of cells; these are continuous with the large flattened elements which, as we have seen, alone constitute the greater part of the wall of the sac in the blastula stage. The inner germ-layer is at first developed on only a small part of the wall of the sac—at the embryonic spot and its immediate vicinity; it terminates with a free notched margin, where there are to be found *loosely associated amœboid cells,* which by their increase in number and migration probably cause the further growth

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end of the first stages of cleavage. He interprets in the originally solid sphere of cells (fig. 58 *A*) the darker and larger centrally located elements (*hy*) as entoderm, the layer of smaller and clearer cells (*ep*) surrounding the latter as ectoderm, and a small vacuity in this investing layer as the blastopore (*bp*). I, on the contrary, believe that the gastrulation takes place in the manner described on page 104.

of the layer. This on older eggs slowly spreads itself from the embryonic spot toward the opposite pole, and thereby the whole blastodermic vesicle gradually becomes two-layered. While this is taking place, changes also proceed at the embryonic spot, which has become oval and somewhat larger. **Rauber's** layer disappears * (fig. 61); the underlying cubical or spherical cells have become cylindrical and more closely crowded together. Each of the primary germ-layers is now composed of a single layer of cells.

The two accompanying figures, which represent in two different positions a Rabbit's egg seven days old, will serve for the illustration of these conditions. *In looking down from above* (fig. 62 *A*) one sees the embryonic spot (*ag*), now become oval. It is produced exclusively by a definitely limited thickening of the outer germ-layer, and indicates the place at which the cells are cylindrical; in that respect it corresponds to the embryonic shield of reptilian and avian embryos, and is not to be confounded with the cell-plate (fig. 59), which was described as a thickening of the one-layered blastula. *In looking at it from the side* (fig. 62 *B*) one can distinguish on the blastula three regions: (1) the embryonic spot (*ag*); (2) a region which includes the upper half of the vesicle and reaches to the line *ge*, in which the wall is still composed of two layers, but in which the cells of both the outer and inner germ-layers are very much flattened; and (3) a third portion lying below the line *ge*, where the wall is composed exclusively of the outer germ-layer.

There now arises the important question, in what manner the two-layered condition in Mammals arises out of the single-layered form. One has reason to expect that gastrulation takes place here in the same way as with the remaining Vertebrates, by means of an invagination or an ingression of cells which proceeds from a definite territory of the thickened cell-plate of the blastula; in this connection attention must be directed to the posterior end of the embryonic spot.

When the embryonic spot has acquired a pear-shaped appearance (fig. 63), there is at its posterior end a somewhat less transparent, because thickened, place (*hw*), which **Kölliker** has designated the terminal ridge (Endwulst). It is comparable with the opacity

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* Two views are held concerning the manner in which **Rauber's** layer disappears. According to **Balfour** and **Heape**, the flat cells become metamorphosed into cylindrical cells, which are interposed between the other cylindrical cells; according to **Kölliker**, on the contrary, they disintegrate and disappear.

at the posterior margin of the germ-disc of Reptiles and Birds, when their gastrulation begins. An invagination proceeding from this point, such as **Duval** has established for the Chick, is unfortunately not as yet proven with sufficient certainty in the case of Mammals; the origin of the two-layered stage is also still involved in obscurity.

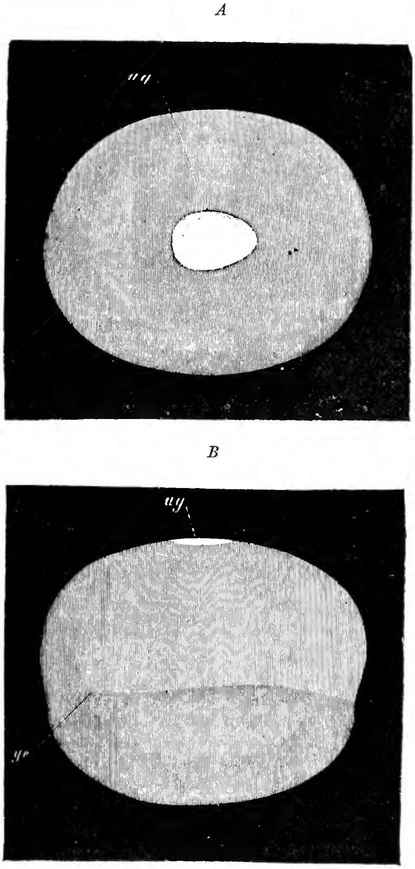

Fig. 62.—Blastula of the Rabbit 7 days old without the outer egg-membranes. Length 4·4 mm. After Kölliker. Magnified 10 diameters.
Seen in *A* from above, in *B* from the side.
ag, Embryonic spot (area embryonalis); *ge*, the line up to which the blastula is two-layered.

However, there are in the literature some observations, which, fragmentary as they are, appear to me to be worthy of special regard.

At the stage at which the blastula has become for a certain distance two-layered (fig. 62), there has been discovered by **Heape** in the case of the Mole, by **Selenka** in the Opossum, and by **Keibel** in the Rabbit, at one place of the embryonic spot (probably in the region just described as terminal ridge), *a small opening* (fig. 64 *u*), *which is possibly to be interpreted as blastopore and to be compared with the crescentic groove of Birds. Here the two primary germ-layers are continuous with each other, and from here, as well as from the primitive streak, the middle germ-layer takes its origin. I assume that, beginning at this place, the lower germ-layer has in a still earlier stage been developed by an infolding of a small territory of the single-layered blastula* (fig. 59).

One circumstance is especially characteristic of the gastrulation of Mammals: that the invaginating membrane is not a closed blind sac, but possesses a free margin, with which it grows along on the inner surface of the outer germ-layer, until it has completely lined the blastodermic vesicle. The reader will please compare with this the statements on page 102. But the absence of a ventral closure becomes intelligible, when we imagine that the yolk-mass, which constitutes in meroblastic eggs or in Amphibian eggs the floor of the cœlenteron, has degenerated and wholly disappeared. In this case cœlenteron and cleavage-cavity become one and the same, as is the case with Mammals.

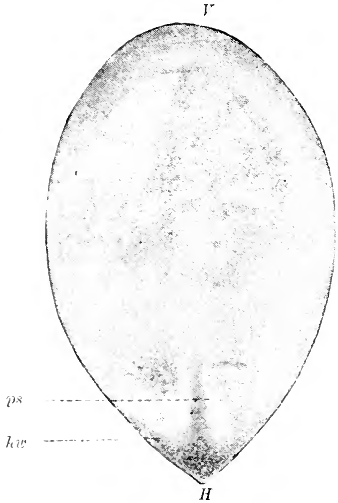

Fig. 63.—Pear-shaped embryonic spot of a Rabbit's egg 6 days and 18 hours old, after Kölliker.

ps, Short primitive streak; *hw*, crescent-shaped terminal ridge; *V*, anterior, *H*, posterior end.

Moreover we are induced to assume that in the eggs of Mammals a regressive metamorphosis of originally abundant yolk-contents must have taken place, on account of many phenomena in their development, which would be unintelligible without this assumption. These phenomena will be considered more at length in a subsequent chapter.

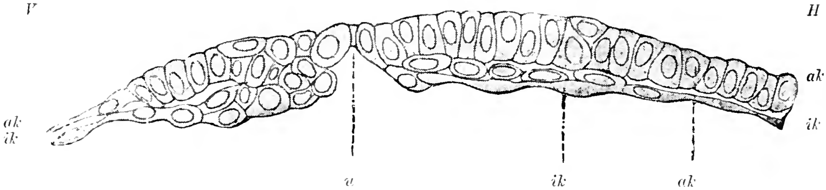

Fig. 64.—Median section of the embryonic fundament of a Mole's egg through that part in which the primitive streak has begun to be formed, after Heape.

u, Blastopore; *ak*, outer, *ik*, inner germ-layer; *V*, anterior, *H*, posterior end.

CHAPTER VI.

DEVELOPMENT OF THE TWO MIDDLE GERM-LAYERS. (CŒLOM-THEORY.) *

After the completion of the gastrula stage the processes of development become more and more complicated, so that the attention of the observer from this time on must be directed to a series of changes which take place at the same time and in various parts of the embryo. For a *transformation now ensues, due to the simultaneous folding of both the inner and outer germ-layers*, whereby four new chief organs of the vertebrate body are called into existence. Out of the inner primary germ-layer arise (1) the two middle germ-layers, which enclose between them the body-cavity; (2) the secondary entoderm or entoblast (Darmdrüsenblatt), which lines the secondary intestine of vertebrated animals; and (3) the fundament of the axial skeleton, the chorda dorsalis, or notochord. At the same time there is developed from the outer germ-layer, as its only system of organs, the fundament of the central nervous system. Since these four processes in the development are in part most intimately involved in one another, they cannot be separated in their treatment.

Here again we have to do with a problem which is one of the most difficult in the embryology of vertebrated animals—the history of the development of the two middle germ-layers. Notwithstanding a voluminous literature which has grown out of this theme, there are many conditions, especially among the higher classes of Vertebrata, which are not yet explained in an entirely satisfactory manner. We shall therefore enter somewhat more minutely into this topic, which, like the question as to the origin of the two primary germ-layers, possesses a fundamental significance for the comprehension of the organisation of Vertebrates.

The presentation of what follows will be essentially facilitated, if we allow ourselves a short digression into the history of the development of the Invertebrata, and take under consideration a case in which the middle germ-layers and the body-cavity are established in a manner similar to that which obtains in the case of Vertebrata, but which is easier to investigate and to understand. Such an

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* In figs. 66-89 the individual germ-layers are represented in different depths of shade, so as to make their relations to one another more evident. The middle germ-layer is darkest.

example is presented to us in the *development of arrow-worms* (*Sagitta*) or *Chætognatha*, concerning which observations have been published by KOWALEVSKY, BÜTSCHLI, and the author.

After the process of cleavage there arises a typical blastula, which after some time is converted into a typical gastrula. While the latter elongates, two folds of the inner germ-layer arise at the bottom of the cœlenteron, and grow up parallel to each other (fig. 65).

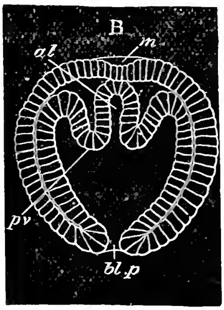

Fig. 65.

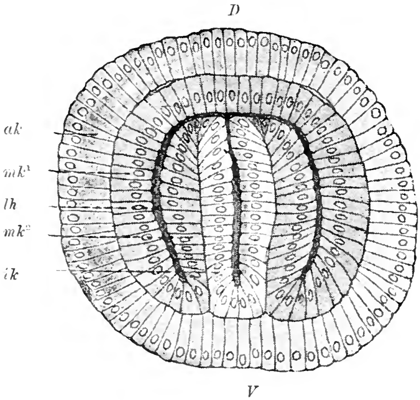

Fig. 66.

Fig. 65.—A stage in the development of Sagitta, after KOWALEVSKY, from BALFOUR'S "Comparative Embryology."

Optical longitudinal section through a gastrula at the beginning of the formation of the body-cavity.

m, Mouth; *al*, alimentary cavity; *pv*, body-cavity; *bl.p*, blastopore.

Fig. 66.—Optical cross section through a larva of Sagitta.

The cœlenteron is separated by means of two folds, which protrude from its ventral wall (*V*), into the intestinal canal proper and the two lateral body-cavities (*lh*), all of which are still in communication with one another on the dorsal side (*D*).

D, Dorsal side; *V*, ventral side; *ak*, outer, *ik*, inner germ-layer; mk^1, parietal, mk^2, visceral middle layer; *lh*, body-cavity.

They grow larger and larger, and at the same time stretch over on to the ventral wall of the larva. From here the free edges finally grow on the one hand up to the dorsal wall, on the other up to the blastopore, and thereby completely divide the cœlenteron into a middle and two lateral spaces (fig. 66 *lh*), which for a time communicate with each other near the blastopore and along the subsequent dorsum (*D*) of the embryo. After a short time this communication is lost; the blastopore becomes closed, and the edges of the folds fuse with the adjacent surfaces of the cœlenteron. Of the three cavities the middle becomes that of the permanent intestinal tube, the two lateral ones (*lh*) become those of the two body-cavity sacs which separate the intestine from the wall of the body. They appropriately take the name *enterocœl,* since they are formed from the cœlenteron by a process of constriction, and are genetically distinguishable from other cavities which arise in other animals between the wall of the intestine and that of the body by simple splitting, and to which is given the name *fissicœl* or *schizocœl.*

By the process of infolding the number of the germ-layers in Sagitta has been increased from two to three. The primary inner germ-layer is thereby divided into (1) a cell-layer (*ik*) which lines the intestinal tube, and (2) a cell-layer which serves to enclose the two body-cavities (mk^1 and mk^2). The first is designated as the *secondary inner germ-layer or entoblast,* the second as the *middle germ-layer* (*mesoblast*). One part of the latter is adjacent to the outer germ-layer, the other part to the intestinal tube; accordingly the division is carried still further—into a *parietal* (mk^1) *and a visceral layer* (mk^2) *of the mesoblast.* For the sake of brevity the former may be called the parietal (mk^1), the latter the visceral (mk^2) middle layer. *Consequently, one may now speak of two middle germ-layers instead of one, the total number of the germ-layers being, naturally, raised by this from three to four.*

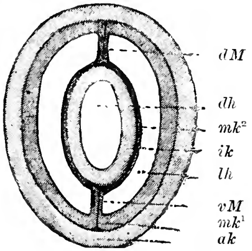

Fig. 67.—Diagrammatic cross section through a young Sagitta. *dM,* Dorsal, *vM,* ventral mesentery; *dh,* intestinal cavity; *lh,* body-cavity; *ak,* outer, *ik,* inner germ-layer; mk^1, parietal, mk^2, visceral middle layer (middle germ-layers).

In regard to the course of the further development it may be stated that, while the larva elongates into a worm-like body, the two body-sacs (fig. 67 *lh*) are increased to a greater extent than the intestinal tube (*ah*) which they embrace. They everywhere crowd the latter away from the wall of the body, grow around it from above and below, where their thin walls come into direct contact. By the fusion of the two body-sacs along their surfaces of contact there are formed two delicate membranes, a dorsal (*dM*) and a ventral (*vM*) mesentery, by means of which the intestinal tube is attached to the dorsal wall and to the ventral wall of the trunk.

Processes very similar to those of Sagitta occur in the development of Vertebrata also, but in the latter case they are combined with the development of the neural tube and the chorda dorsalis. In the presentation of these we shall proceed as in the foregoing chapter, which treated of the formation of the gastrula, and consider separately the processes in Amphioxus, Amphibia, Selachians, Birds, and Mammals, since they differ somewhat from one another.

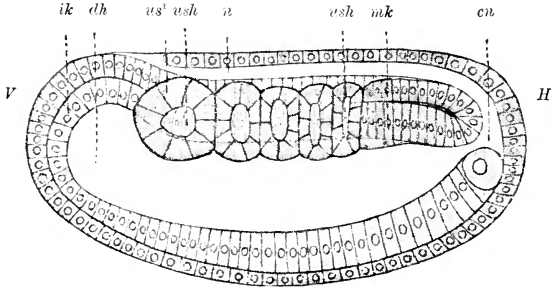

Fig. 68.—Optical longitudinal [sagittal] section through an embryo of Amphioxus with five primitive segments, after Hatschek.
V, Anterior, *H*, posterior end; *ik*, inner, *mk*, middle germ-layer; *dh*, intestinal cavity; *n*, neural tube; *cn*, neurenteric canal; us^1, first primitive segment; *ush*, cavity of primitive segment.

The history of the development of Amphioxus lanceolatus is very instructive. The gastrula elongates, whereby the cœlenteron is turned a little towards the future dorsal surface, and here terminates in the blastopore, which marks the future hind end of the worm-shaped body. Then the dorsal surface becomes somewhat flattened; the cells in this region increase in height, become cylindrical, and form the medullary or neural plate (fig. 69 *mp*). By a slight infolding of the latter, there arises a medullary groove, which forces downward the roof of the cœlenteron in the form of a ridge (*ch*). At the place where the thickened medullary plate joins the small-celled part of the outer germ-layer, or the horn-layer (*hb*), an interruption in the continuity now takes place, and the epidermis grows over the curved neural plate from both sides, until its halves meet in the middle line and fuse. Thus there arises along the back of the embryo (fig. 70) a canal, the lower wall of which is formed by the curved medullary plate (*mp*), and the upper wall by the overgrowing epidermis (*ak*). It is only at a later stage that the medullary plate in Amphioxus, lying under the epidermis, is converted into a neural tube (fig. 72 *n*) by the bending up of its edges and their fusion. As the fundament of the nervous system becomes differentiated, it extends so far toward the posterior end of the embryo, that the blastopore, which is located there, still falls within its territory, and with the closure of the neural tube is included within the end of the latter. In this manner it occurs that neural tube and intestinal tube, as Kowalevsky first observed, are now, by means of the blastopore, in continuity (fig. 68 *cn*) at the posterior end of the body. The two together constitute a canal composed of two arms, the form of which is comparable with a siphon. The upper arm, which is the neural tube, continues, for a time, to open to the outside world at its anterior end. The bent portion of the siphon, or the blastoporic region, by means of which the neural and the intestinal tube are united, is called *canalis neurentericus* (fig. 68 *cn*), a structure which we shall again encounter in the development of the remaining Vertebrata.

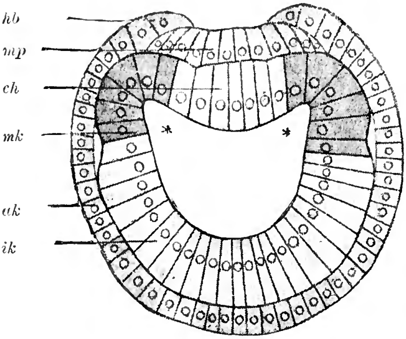

Fig. 69.—Cross section of an Amphioxus embryo, in which the first primitive segment is being formed, after HATSCHEK.
ak, Outer, *ik*, inner, *mk*, middle germ-layer; *hb*, epidermis; *mp*, medullary plate; *ch*, chorda; *, evagination of the cœlenteron.

Simultaneously with the neural tube are developed the two *middle germ-layers* and the *chorda dorsalis* (figs. 69 and 70). At the front end of the embryo there arise in the roof of the cœlenteron close to each other two small evaginations, the body-sacs (*mk*), which grow dorsally and laterally at either side of the curved medullary groove. These are slowly enlarged, since the process of evagination progresses from the anterior toward the posterior end of the larva, and finally reaches the blastopore. The narrow strip of the wall of the cœlenteron which is found between them and separating them (its limits marked by two stars * * in figs. 69 and 70), and which lies under the middle of the medullary groove, represents the *fundament of the chorda* (*ch*).

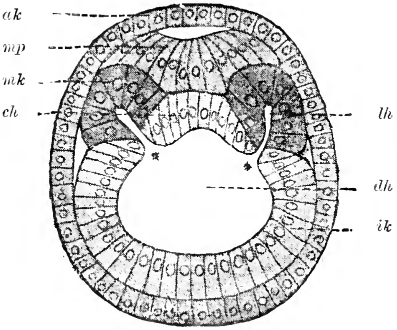

Fig. 70.—Cross section of an Amphioxus embryo, in which the fifth primitive segment is in process of formation, after HATSCHEK.
ak, Outer, *ik*, inner, *mk*, middle germ-layer; *mp*, medullary plate; *ch*, chorda; *, evagination of the cœlenteron; *dh*, intestinal cavity; *lh*, body-cavity.

The primary inner germ-layer therefore has now undergone division into four different parts: (1) *the fundament of the chorda* (*ch*), (2) *and* (3) *the cells* (*mk*) *which line the two body-sacs* (*lh*) *and represent the middle germ-layer, and*

(4) *the remaining part, which, since it is destined to form the bounding wall of the subsequent intestine* (*dh*), *is to be designated as permanent entoderm* (Darmdrüsenblatt) (*ik*).

The succeeding processes of development have as their objective point the detachment from one another, by means of constriction and fusion, of the parts which are still in continuity, and the formation of discrete cavities. The processes of constriction begin at the anterior end of the embryo, and progress thence to the blastopore (figs. 70 and 71). At first the body-sacs become deeper (fig. 70 *lh*), and then lose their connection with the main cavity (*dh*) by the close apposition of the cells which surround the entrances to them (fig. 71). By this process the margin of the secondary entoderm (*ik*) comes to abut directly on the margin of the *chordal fundament* (*ch*). The latter has meanwhile also undergone changes; the plate-like fundament has become so curved by the elevation of its lateral margins, that there has arisen a deep *chordal groove*, which is open along its ventral side. Subsequently the lateral walls of the groove come into close contact, and are thereby converted into a solid rod of cells, which temporarily shares in the closure of the roof of the secondary intestine, and appears as a ridge-like thickening of the latter. Then the cell-rod (*ch*) becomes detached (fig. 72) from the wall of the intestine; the latter now, for the first time, becomes completely closed in the form of a tube. To effect this the margins of the entoderm, indicated in

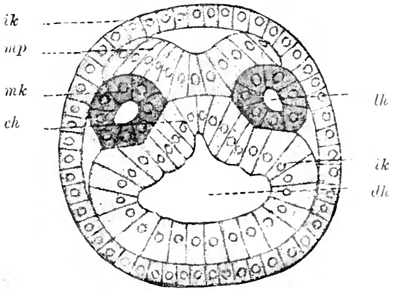

Fig. 71.

Fig. 71.—Cross section through an Amphioxus embryo with five well-developed primitive segments, after HATSCHEK.

ak, Outer, *ik*, inner, *mk*, middle germ-layer; *mp*, medullary plate; *ch*, chorda; *dh*, intestinal cavity; *lh*, body-cavity.

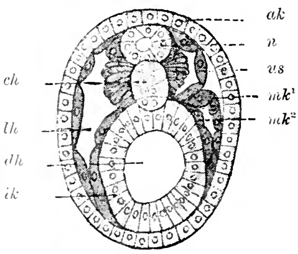

Fig. 72.

Fig. 72.—Cross section through the middle of the body of an Amphioxus embryo with eleven primitive segments, after HATSCHEK.

n, Neural tube; *vs*, primitive segment. For the meaning of the other letters see Fig. 71.

fig. 70 by stars (* *), grow toward each other under the chorda and fuse into a median raphe.

The final result of all these processes is shown in the cross section fig. 72: the original cœlenteron has become divided into three cavities —into the ventral permanent intestine (*dh*), and into the two body-cavities (*lh*), which are situated dorso-laterally to it, and which continue to increase in size. Between these there has been interpolated the chorda (*ch*), upon which the intestine abuts below and the neural tube (*n*) above. The cells which have been cut off from the cœlenteron by constriction—and which are more deeply shaded in figs. 69 to 72, and enclose the body-cavities (*lh*)—constitute the middle germ-layer (*mk*). The part which lies in contact with the outer germ-layer (fig. 72) is recognisable as the parietal middle layer (mk^1); the part which is in contact with the neural tube, chorda, and intestine as the visceral middle layer (mk^2).

Inasmuch as the process of differentiation just described begins, as has been already stated, at the front end of the embryo and extends slowly step by step toward the hind end, by an examination of a series of sections one may follow the various stages of metamorphosis on a single object.

In the description given I have presented the conditions as though in Amphioxus there arose two simple body-sacs, one on either side of the intestinal tube. The processes are, however, somewhat more complicated, for in the case of the embryo of fig. 70 the body-sacs, while increasing in size posteriorly, undergo further changes in the anterior region, and through repeated infoldings are divided into separate compartments, the primitive segments (*us*), which lie one behind the other. I content myself with this statement, since for didactic reasons I shall defer the treatment of the development of the primitive segments until I come to a subsequent chapter.

While in the case of Amphioxus lanceolatus there is no doubt but *that the body-cavity and the middle germ-layer are formed by an outpocketing of the wall of the cœlenteron*, opinions upon the origin of the same parts in the case of the remaining Vertebrata are still very divergent. This results, in the first place, from the fact that the investigation, which can be carried out only by means of serial sections, is coupled with greater technical difficulties, and, secondly, because the conditions are somewhat altered, owing to the greater abundance of yolk in the eggs, and furnish less clear and intelligible views. Where in the gastrula of Amphioxus a great cavity is present, we see in the case of the remaining Vertebrates a great mass of yolk-material collected, and the cœlenteron more or less completely filled with it. Consequently there are formed in these cases for the production of the body-cavity *no hollow evaginations, but solid cell-growths, in that the parietal and the visceral lamellæ of the middle germ-layer have the surfaces which in Amphioxus bound the body-cavity pressed together at the beginning of the development and separated only at a rather late stage.* In order to make easier the comprehension of the somewhat dissimilar appearances furnished by an investigation of the separate classes of Vertebrates, let us describe first, with the aid of two diagrammatic figures, how, according to a series of investigations which I have undertaken, the development of the middle germ-layer and the body-cavity would take place in the case of the vertebrated animals.

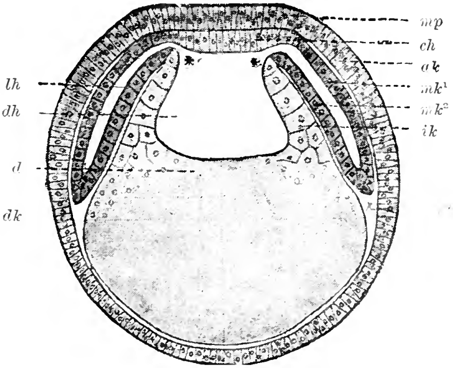

Fig. 73.—Diagram to show the development of the middle germ-layers and the body-cavity in Vertebrata.

Cross section of an embryo in front of the blastopore.

mp, Medullary plate; *ch*, fundament of the chorda; *ak*, outer, *ik*, inner germ-layer; mk^1, parietal, mk^2, visceral lamella of the middle germ-layer; *d*, yolk-mass; *dk*, yolk-nuclei; *dh*, intestinal cavity; *lh*, body-cavity.

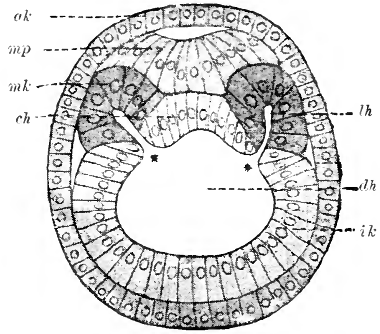

Fig. 74.—Cross section of an Amphioxus embryo. See explanation of Fig. 70.

ak, Outer, *ik*, inner, *mk*, middle germ-layer; *ch*, chorda.

One of the diagrams (fig. 73) represents a cross section in front of the blastopore. It exhibits the inner germ-layer (*ik*) extensively thickened on the ventral side by the deposition of yolk (*d*), so that the cœlenteron is reduced to a small cavity (*dh*). In the roof of the cœlenteron there lies a single layer of cells (*ch*), the fundament of the chorda, characterised by their cylindrical form. On both sides of it the inner germ-layer has developed evaginations, the two body-sacs (*lh*), which have grown down some distance between the yolk-mass and the outer germ-layer. Their wall (mk^1 and mk^2) is composed of small cubical or polygonal elements, shaded darker in the diagram. The cœlenteron is distinctly separated by means of the two cœlenteric folds (* *) into a median or intestinal cavity proper (*dh*), lying beneath the chordal fundament, and the two narrow body-sacs (*lh*), which communicate with the former only by means of narrow fissures (* *) at the right and left of the chordal fundament. The figure is easily reducible to the preceding (p. 113) cross section of an Amphioxus embryo (fig. 74), if we conceive the simple epithelium on the ventral side of the latter thickened by an accumulation of yolk, and the two small body-sacs grown down a certain distance between yolk-mass and outer germ-layer.

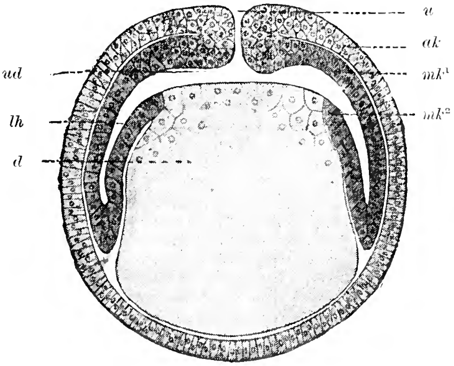

Fig. 75.—Diagram to show the development of the middle germ-layers and the body-cavity in Vertebrata. Cross section through the blastopore of an embryo.
u, Blastopore ; *ud*, cœlenteron ; *lh*, body-cavity ; *d*, yolk ; *ak*, outer germ-layer ; mk^1, parietal, mk^2, visceral lamella of the middle germ-layer.

In the second diagrammatic cross section, which is through the blastopore (fig. 75), the cœlenteron (*ud*) is wholly filled up with the yolk-mass (*d*). The body-sacs (*lh*) described in the first diagram are to be seen here also, as they crowd themselves downwards between yolk and outer germ-layer. Their walls are composed of small cells, and the outer or parietal layer (mk^1) merges into the outer germ-layer at the blastopore, while the inner or visceral layer (mk^2) is continuous with the yolk-mass or the inner germ-layer.

Were the conditions in Vertebrates such as the two diagrams represent, there could no longer be any doubt in regard to *them*, any more than in the case of Amphioxus, that the body-cavity is developed out of two evaginations of the cœlenteron, and that its walls constitute the two middle germ-layers. But there is not a single Vertebrate which presents such clear and convincing evidence. The distinctness is everywhere diminished, most of all by the fact that *the parts which are to be interpreted as body-sacs no longer enclose cavities,* because their walls are firmly pressed together, in consequence of the fact that the greater collection of yolk requires the space for itself. Consequently we find, *in place of the body-sacs exhibited in the diagram, solid masses of cells, for which it remains to be established that they correspond to the sacs in position and development.*

In order to see what condition would result in consequence of a disappearance of the body-cavity, we will imagine that in the two diagrams the parietal and the visceral layers of the body-sacs are firmly pressed together. In the first diagram (fig. 73) we should then have a mass several cells thick, which would be everywhere distinctly separated from the two germ-layers—in between which it had grown—with the exception of the place indicated by a star, which marks the entrance to the body-sac; this is the important region whence the evagination or the outgrowth of the middle germ-layer from the inner layer has taken place. At this point the cell-mass is continuous, on the one side with the fundament of the chorda, on the other with the entoderm. In the second diagram (fig. 75) we should likewise see the thick cell-mass everywhere isolated, except in the vicinity of the blastopore, where a transition to the outer as well as to the inner germ-layer takes place. If, in addition to this, we should imagine that the two lips of the blastopore were here pressed together from right to left, we should have in the middle of the cross section a thick, many-layered cell-mass, which on both sides is resolved into the three germ-layers, or, in other words, *at the blastopore all three germ-layers by their fusion meet together in a single mass of cells.*

By careful investigation it is, in fact, demonstrable that similar conditions to those which we have produced by changes in the diagrams are found in the investigation of the several classes of Vertebrates. For this purpose we must make sections through three different regions of the embryo: (1) through the region in front of the blastopore, (2) through the region of the blastopore itself, and (3) behind it. *The agreement appears most prominent in the development of the Amphibia,* among which the Tritons again furnish the most instructive objects.

When in the case of Triton the gastrulation, with the accompanying obliteration of the cleavage-cavity, is fully completed, the embryo becomes slightly elongated; the future dorsal surface (fig. 76 *D*) becomes flattened, and gives rise to a shallow furrow (*r*), which stretches from the anterior to the posterior end nearly up to the blastopore (*u*). The latter has now assumed the form of a longitudinal fissure. A cross section made through the middle of the embryo in front of the blastopore (fig. 77) corresponds in every particular to our first diagram (fig. 73), if we conceive that the body-cavity in this case has disappeared. The outer germ-layer (*ak*) consists of a single sheet of cells, which on the back of the embryo are cylindrical, but become shorter toward its ventral side. The cells enclosed within the outer layer exhibit a differentiation in three ways, and therefore are subsequently converted into three different organs—into chorda, entoderm, and middle germ-layer. First, there is to be found on the roof of the cœlenteron (*dh*) under the medullary groove, even close up to the blastopore, a narrow band of long cylindrical cells (*ch*); it corresponds in every respect to the fundament of the chorda in our diagram (fig. 73 *ch*), and in the cross section through Amphioxus (fig. 74 *ch*). Secondly, the fundament of the chorda is flanked on either side by two bands (mk^1, mk^2) of small oval cells, which extend downwards to about the middle of the lateral region of the embryo. They do not share in bounding the cœlenteron, since a third kind of cells (*ik*), large and rich in yolk, lie along their inner surfaces. The latter begin at the margin of

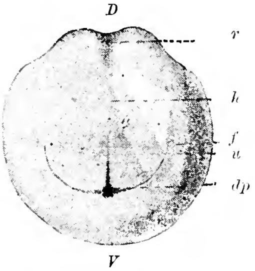

Fig. 76.

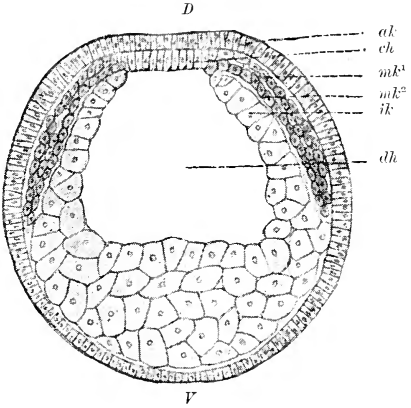

Fig. 77.

Fig. 76.—Egg of Triton with distinctly developed medullary groove, seen from the blastopore, 53 hours after artificial fertilisation.

D, Dorsal, *V*, ventral region; *u*, blastopore; *h*, elevation between blastopore and medullary groove (*r*); *f*, semicircular furrow, which encloses the blastoporal area; *dp*, yolk-plug.

Fig. 77.—Cross section of an egg of Triton with feebly expressed medullary groove.

ak, Outer, *ik*, inner germ-layer; mk^1, parietal, mk^2, visceral lamella of the middle germ-layer; *ch*, chorda; *dh*, intestinal cavity; *D*, dorsal, *V*, ventral.

the chordal fundament as a single layer, become two layers thick farther down, and thus merge into the more voluminous accumulation of yolk-cells, which, in all Amphibian embryos, occupy the ventral side and restrict the gastrula-cavity. They correspond, to continue with our comparison, with the entoderm, whereas the small-celled masses, which, starting from the fundament of the chorda, have crowded themselves out between the entoderm and the outer germ-layer, are comparable with the cells which in Amphioxus and in our diagram form the wall of the body-sacs, or the middle germ-layer. The conclusion is therefore justified and very obvious, that in *Triton the two middle germ-layers have arisen in the anterior territory of the embryonic body by a process of evagination at both sides of the chordal fundament, just as in Amphioxus, except that in one case the evaginated cell-mass contains a cavity, in the other case none.*

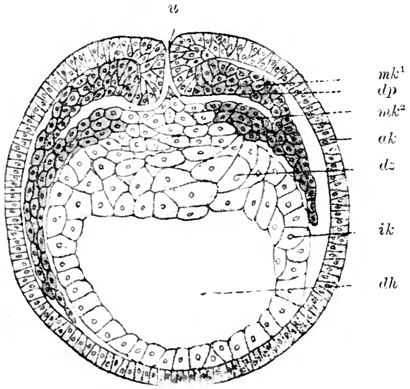

Fig. 78.—Cross section through the blastopore of an egg of Triton with feebly expressed medullary groove.

ak, Outer, *ik*, inner germ-layer; *mk*^{1}, parietal, *mk*^{2}, visceral lamella of the middle germ-layer; *u*, blastopore; *dz*, yolk-cells; *dp*, yolk-plug; *dh*, intestinal cavity.

A cross section through the blastopore of the Triton embryo (fig. 78) is to be compared with our second diagram (fig. 75). The hollow body-sacs of the latter correspond to the solid cell-bands, which are the fundament of the middle germ-layer. Near the blastopore (*u*) they are split into two lamellæ. Of these the outer (*mk*^{1}) merges, as in our diagram, into the inner layer of the blastoporic lip, and becomes continuous at the edge of the blastopore with the outer germ-layer (*ak*); the inner lamella (*mk*^{2}), on the contrary, is connected with the mass of yolk-cells (*dz*), which lies like a wall in front of the blastopore and even projects into it as the RUSCONIAN yolk-plug (*dp*).

Posteriorly to the blastopore, the middle germ-layer stretches itself out for some distance, but here only as a single connected mass.

According to the region from which the middle germ-layer is developed, we may divide it into two portions, and call that part which is produced on both sides of the chorda the gastral mesoderm, and that which arises from the blastopore the peristomal mesoderm (Rabl).

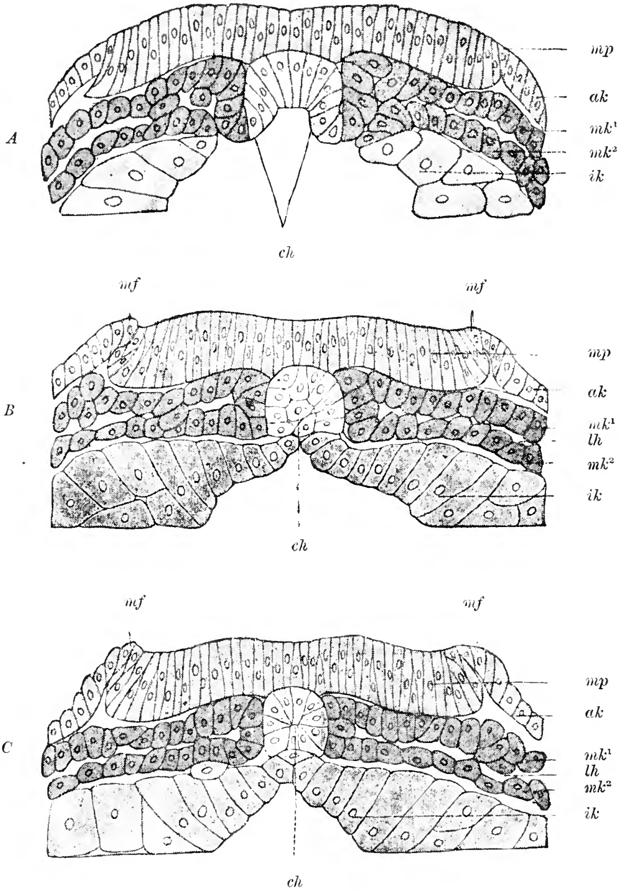

Fig. 79.—Three cross sections from a series through an egg on which the medullary ridges begin to appear. The sections illustrate the development of the chorda out of the chordal fundament, and the constricting off of the two halves of the middle germ-layer.
ak, Outer, *ik*, inner germ-layer; mk^1, parietal, mk^2, visceral lamella of the middle germ-layer; *mp*, medullary plate; *mf*, medullary folds; *ch*, chorda; *lh*, body-cavity.

The further development of the fundaments of mesoderm, chorda, and intestine, which subsequently become entirely separated from one another at the places where they now remain in connection, causes the agreement with the conditions found in Amphioxus to appear in stronger relief. The process of separation is introduced by the curving of the *chordal plate*, and its conversion into the *chordal groove* (fig. 79 *A ch*). Inasmuch as it is continuous at its edges with the parietal lamella of the middle germ-layer (mk^1), there arise in the roof of the cœlenteron the two small chordal folds, which enclose between them the chordal groove. Its free margins abut directly upon the folded edge, where the visceral lamella of the middle germ-layer (mk^2) bends around into the entoderm (*ik*) to produce the cœlenteric fold.

In the next following stage (fig. 79 *B*) the thickened medullary plate, consisting of long cylindrical cells, becomes distinctly marked off from the now still smaller cubical elements of the ectoderm. Meanwhile the middle germ-layer begins to detach itself from its previous connections in the vicinity of the place of evagination; the parietal lamella becomes separated from the fundament of the chorda, the visceral lamella from the entoderm, and thereupon their detached edges become fused to each other. By means of this process the fundament of the body-sac, or of the middle germ-layer, becomes closed on all sides, and is separated from the other germ-layers. At the same time the entoderm (*ik*) and the fundament of the chorda (*ch*) have come into contact along their free margins, so that the chorda appears like a thickening of the entoderm, and for a time shares in bounding the intestinal cavity on the dorsal side. This is changed by a second process of detachment.

The fundament of the chorda, now converted into a solid rod, is gradually excluded from participation in lining the intestine (fig. 79 *C*), by the fact that the halves of the entoderm (*ik*), composed of large yolk-cells, grow toward each other underneath it, and fuse in a median raphe.

The closure of the permanent intestine on the dorsal side, the constricting off of the two body-sacs from the inner germ-layer, and the origin of the chorda dorsalis are therefore in Amphibia, as in Amphioxus, processes which are most intimately related with one another. Here, too, constricting off of the parts mentioned begins at the head-end of the embryo, and advances slowly toward the posterior end, where there exists for a long time a zone of growth, by means of which the increase in the length of the body is effected. Soon after this, the moment arrives when in the embryos of Triton the body-cavity becomes visible. For after the detachment of the organs previously mentioned is completed, the two middle germ-layers at the head-end of the body, and on both sides of the chorda, separate from each other, and thus cause to appear a right and a left body-cavity (enterocœl), which, according to my interpretation, were not previously recognisable, simply on account of the intimate mutual contact of their walls.

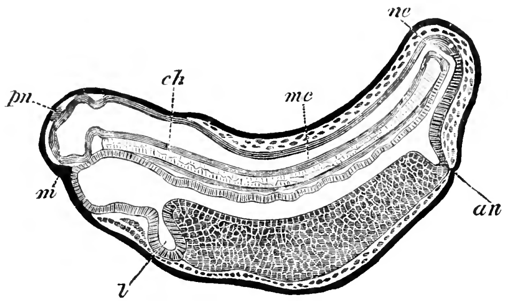

Fig. 80.—**Longitudinal [sagittal] section through an advanced embryo of Bombinator,** after Goette.
m, Mouth ; *an*, anus ; *l*, liver ; *ne*, neurenteric canal ; *mc*, medullary tube ; *ch*, chorda ; *pn*, pineal gland.

Meanwhile the medullary plate has become converted, by the process of folding already described, into the neural tube (fig. 80 *mc*), which lies beneath the epidermis. Since the neural tube subsequently encloses the blastopore, and is thereby in communication with the intestinal tube (as the preceding longitudinal section of an advanced embryo of Bombinator most distinctly shows), it follows that there is also in the Amphibia a structure (fig. 80 *ne*) corresponding to the neurenteric canal of Amphioxus (compare fig. 68 *cn*).

More fundamental differences in the development of the middle germ-layer are met with in the eggs of Fishes, Reptiles, and Birds, which are more abundantly provided with nutritive yolk and undergo partial cleavage, and also in the eggs of Mammals. However, the variations appear in these cases to be of a subsidiary nature, whereas in the chief points the unity of the developmental processes for all vertebrated animals has been the more firmly established the more accurately the individual stages have been investigated by means of improved methods.

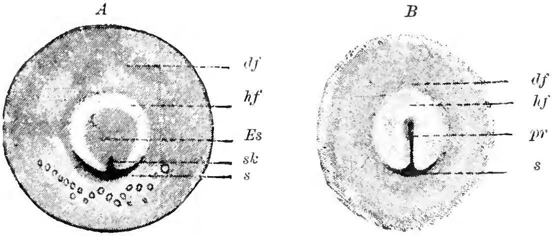

Fig. 81 A and B.—**Two germ-discs of Hens' eggs in the first hours of incubation,** after Koller.
df, Area opaca ; *hf*, area pellucida ; *s*, crescent ; *sk*, crescent-knob ; *Es*, embryonic shield ; *pr*, primitive groove.

In the presentation of these difficult conditions, we shall describe first the changes which may be recognised in viewing the germ-disc from the surface, and to these shall add, secondly, the more important results acquired by series of cross sections.

At the posterior margin of the germ-disc of the Chick (fig. 81 *A*), which consists of two layers lying on the yolk like a watch-glass, we had distinguished—not only a short time before incubation, but also during the early hours of that process—the crescent (*s*) and the crescentic groove, and had learned to recognise that this was the place from which the inner germ-layer arose by a process of folding under.

When, during the first hours of incubation, the germ-layers grow out farther on the yolk, the crescentic groove (fig. 81 *B*) is converted into the primitive groove (*pr*), a structure of far-reaching significance.

The metamorphosis, according to the excellent researches of Duval, takes place in the following manner: In the middle of the anterior blastoporic lip, where the outer germ-layer bends over to become continuous with the inner, there arises a small notch, which is directed forwards (fig. 81 *A sk*); this gradually elongates into a groove (fig. 81 *B*), corresponding with the future longitudinal axis of the embryo, and by the following method: the right and the left halves of the [anterior] blastoporic lip, together with the part which bounds the first notch, grow toward each other, and come in contact with each other in the median plane, with the same rapidity with which the disc increases in superficial extent. For a time, therefore, the blastopore has the form of a short longitudinal groove, which, at its posterior end, is bent around into two short transversely placed crescentic horns (*s*). Finally these also have disappeared; they, too, have grown toward each other, toward the median plane, and have thus contributed largely to the posterior elongation of the primitive groove. By this remarkable process of growth the whole blastopore is converted from a transverse fissure into a longitudinal one.

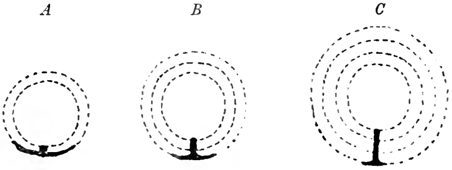

Fig. 82.—Diagrams to elucidate the formation of the primitive groove, after Duval.
The increasing size of the germ-disc in the course of the development is indicated by dotted circular lines. The heavy lines represent the crescentic groove, and the primitive groove which arises from it by the fusion of the edges of the crescent.

The accompanying diagrams (fig. 82) serve to illustrate this highly important process. The increase which the germ-disc has undergone during successive stages is indicated by dotted lines. The margin of the fold, where the upper germ-layer passes over into the lower layer, or the anterior lip of the blastopore, is denoted by a heavy black line. In the figures *A*, *B*, *C*, one observes how, with the increasing extent of the germ-disc, the right and left halves of the blastoporic lip come together in the median plane in ever-increasing extent, and form the primitive groove.

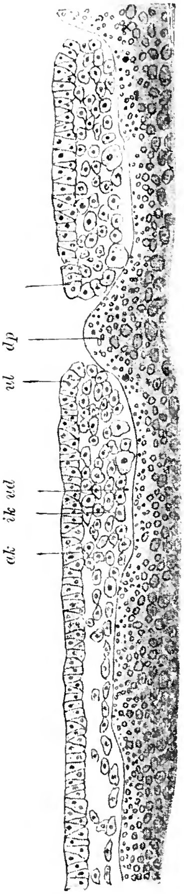

Fig. 83.—A somewhat oblique cross section through the primitive groove of a Hen's egg 2-6 hours after fertilisation, after Duval.
ak, Outer; *ik*, inner germ-layer; *ud*, cœlenteron; *ul*, lip of the blastopore; *dp*, yolk-plug.

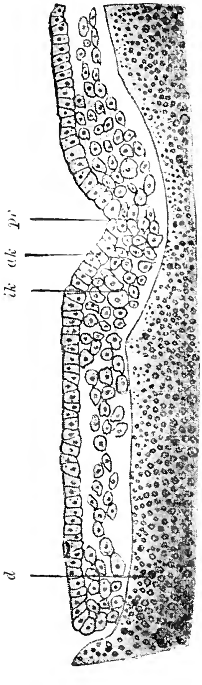

Fig. 84.—Cross section through the same germ-disc, but somewhat farther forward than in Fig. 83, after Duval.
ak, Outer, *ik*, inner germ-layer; *pr*, primitive groove; *d*, yolk.

In figs. 83 and 84 are presented instructive cross sections through the primitive groove in the first stages of its development. The first shows us the two lips of the blastopore (fig. 83 *ul*), separated by a small space, into which there projects from below a small elevation (*dp*) of yolk-substance, containing a number of nuclei (merocytes), comparable with the Rusconian yolk-plug in the Amphibian larva (fig. 78 *dp*). At the lips, the upper germ-layer, a single cell thick, bends around into the lower germ-layer, composed of loosely associated cells. The blastopore leads into the cœlenteron, which lies between yolk and germ-disc. In fig. 84 the margins of the two folds have come into close contact, and have fused to form the anterior part of the primitive streak, above which the primitive groove is still to be found.

When the last remnant of the crescentic groove has been employed for the elongation of the primitive groove, the margin of the germ-disc, which continues all the time to spread itself out uniformly over the yolk, exhibits everywhere one and the same condition; it has become at all points a *circumcrescence-margin*, now that the *invagination-margin* has detached itself from it as primitive groove.

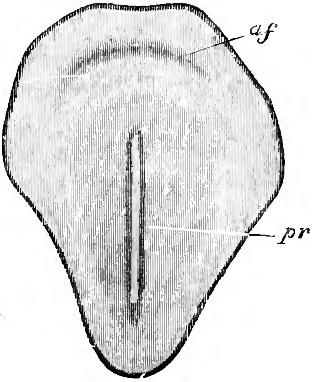

Fig. 85

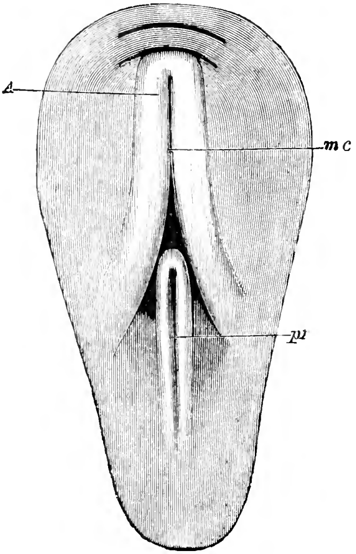

Fig. 86.

Fig. 85.—Surface view of the area pellucida in the blastoderm of a Chick, soon after the formation of the primitive groove, after Balfour.

pr, Primitive streak with primitive groove; *af*, amniotic fold. The darker shading surrounding the primitive streak indicates the extent of the mesoblast.

Fig. 86.—Surface view of the area pellucida of a blastoderm of 18 hours, after Balfour.

The area opaca is omitted; the pear-shaped outline marks the limit of the area pellucida. At the place where the two medullary folds are continuous with each other there is to be seen a short curved line, which represents the head-fold. In front of it there lies a second line concentric with it, the beginning of the amniotic fold. *A*, Medullary folds; *mc*, medullary furrow; *pr*, primitive groove.

When subsequently the pellucid and opaque areas become more distinctly separated, the primitive groove comes to lie in the posterior part of the pellucid area. By careful examination of a surface preparation (figs. 85 and 86 *pr*), one sees that it is bounded, both on the right side and on the left, by two small folds, which are derived from the blastoporic lips, and which appear darker and more opaque because the cells are multiplying rapidly and are more closely crowded. Since the two primitive folds, or the two blastoporic lips,

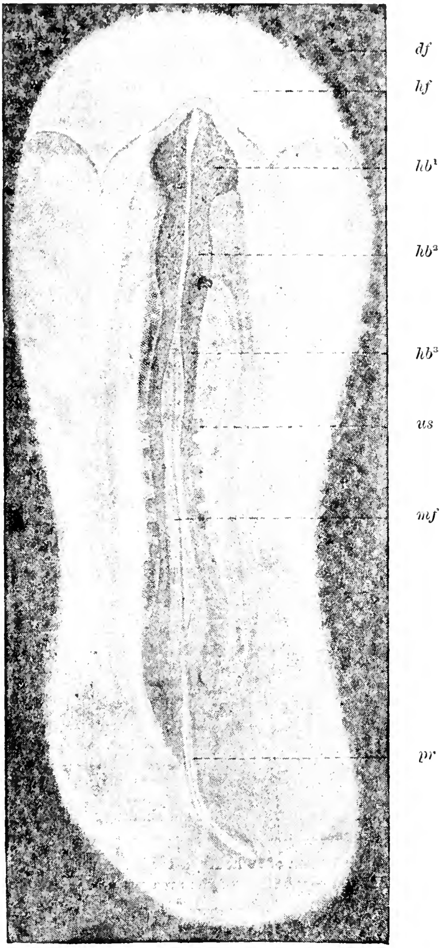

Fig. 87.—Blastoderm of the Chick, incubated 33 hours, after DUVAL.

The area pellucida (*hf*) is surrounded with a portion of the opaque area (*df*). The fundament of the nervous system is nearly closed in front and segmented into the three brain-vesicles hb^1, hb^2, hb^3; behind, the medullary furrow (*mf*) is still open. On either side of the latter there are six primitive segments (*us*). The posterior end of the embryonic fundament is occupied by the primitive streak and the primitive groove (*pr*).

are closely in contact at the bottom of the groove, and indeed are in places completely fused, they together produce in the pellucid area a dark streak of substance, which is about a millimetre long and 0·2 mm. broad. With the earlier embryologists, to whom it was already known, we designate this as the primitive streak of the germ-disc.

In the vicinity of the primitive streak there are to be distinguished in surface views, now and during the following stages of development, some additional changes, which are caused by the beginnings of special organs. In the first place, there is to be seen in the anterior region of the area pellucida, and in the direct continuation of the primitive streak, a narrow, dark streak of cells, which has been designated by KÖLLIKER as the head-process of the primitive streak, and which gradually increases in length. Secondly, there appears an increasing opacity (fig. 85) in the vicinity of the primitive streak and its head-process, which afterward stretches out farther laterally: it is connected with the origin of the middle germ-layer.

In a still later stage of development (fig. 86), at the beginning of the second day of incubation, the first fundament of the central nervous system makes its appearance in the anterior portion of the germ-disc. Over the head-process there arise at some distance from each other the two medullary folds (*A*), which are continuous with each other at their anterior ends, and which bound the broad medullary furrow (*mc*); posteriorly they become less prominent, and they here embrace between them the anterior end of the primitive streak (*pr*). Medullary furrow (*mc*) and primitive groove (*pr*) must not be confounded with each other, as occurred in the earlier days of embryology; they are two entirely distinct and dissimilar structures, which exist at the same time, and independently of each other, as fig. 86 shows.

Primitive streak and primitive groove are preserved for a long time without undergoing important changes (fig. 87 *pr*). They always occupy the posterior end of the embryonic body, which is characterised by its slightly differentiated condition even in stages when the development of the separate organs of the body is already in full progress. On the contrary, the embryonic territory lying in front of it, which is so small at the time of the appearance of the head-process, becomes greatly elongated and, at the same time, differentiated into the separate organs of the body. This process of differentiation begins in front, and proceeds posteriorly toward the primitive groove, just as in Amphioxus and the Amphibia. The margins of the medullary folds come into contact with each other and begin to fuse, forming the neural tube (hb^1, hb^2, hb^3, *mf*), the fusion progressing from the head- toward the tail-end. There are also to be recognised now in the interior of the body, at either side of the neural tube, the protovertebræ or primitive segments (*us*), which we shall investigate more minutely further on. The number of these is constantly increased by the growth which is taking place at the tail-end.

When a large number of primitive segments has arisen, the primitive groove begins on surface-views to disappear; for it is surrounded by the medullary folds, and inasmuch as these fuse here as well as elsewhere, it is enclosed in the terminal part of the neural tube. A notable condition, and one of great importance for the interpretation of the primitive groove, has been discovered at this stage in the embryos of several species of Birds by Gasser, Braun, HOFFMANN, and others. At the front end of the primitive groove a narrow canal has arisen, which leads obliquely from the neural tube under the entoderm, and unites the two in the same manner in which the blastopore does in Amphioxus and the Amphibia. A diagrammatic longitudinal section through the hind end of a Chick (fig. 88) shows us this important union (*n.e*), which exactly corresponds to the condition of an Amphibian embryo presented in fig. 80.

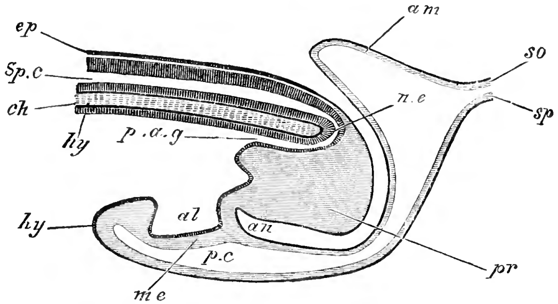

Fig. 88.—Diagrammatic longitudinal section through the posterior end of an embryo Chick at the time of the formation of the allantois, after BALFOUR.

The section shows that the neural tube (*Sp.c*) is continuous at its posterior end with the post-anal intestine (*p.a.g*) by means of the neurenteric canal (*n.e*). The latter traverses the remnant of the primitive streak (*pr*), which is folded over on to the ventral side. *ep*, Outer germ-layer; *ch*, chorda; *hy*, entoderm; *al*, allantois; *me*, middle germ-layer; *an*, the place where the anus will arise; *am*, amnion; *so*, somatopleure; *sp*, splanchnopleure.

Such a neurenteric canal has been observed still more distinctly in Selachians and Reptiles and at even earlier stages, whereas in Teleosts it does not come to development on account of special subsidiary conditions.*

The investigation of the embryonic fundaments of a Mammal furnishes us with views quite similar to those respecting the Chick. When

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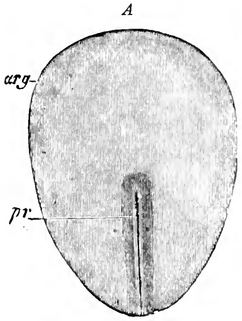
* In Selachians the blastopore is very early enclosed within the medullary folds, and then assumes the condition of a long-persisting canal-like passage to the intestinal cavity through the floor of the medullary groove, and later through that of the neural canal.

In the case of Reptiles, the primitive streak is very short and triangular, and in many species soon discloses, before other organs have been differentiated, an opening at its anterior end which leads to the cavity under the germ-disc, which is filled with yolk. Subsequently the opening is converted into a canal, the wall of which is composed of cylindrical cells, and is in continuity above with the outer germ-layer, and below with the inner germ-layer. Then the medullary folds, which are being formed in front of the orifice, grow around it; the orifice now becomes a genuine neurenteric canal, which in many cases appears to become obliterated even before the closure of the medullary tube, but in other cases persists for a long time.

the embryonic area has assumed an oval form, the opacity at the posterior end, or the terminal ridge (fig. 63 *hw*), which was compared with the crescent of the Bird, elongates into the primitive streak; the latter occupies the posterior half of the embryonic area (fig. 89 *A pr*), and exhibits a distinct groove, that is flanked by a right and a left ridge-like fold. (Compare with this the Chick as shown in fig. 85.)



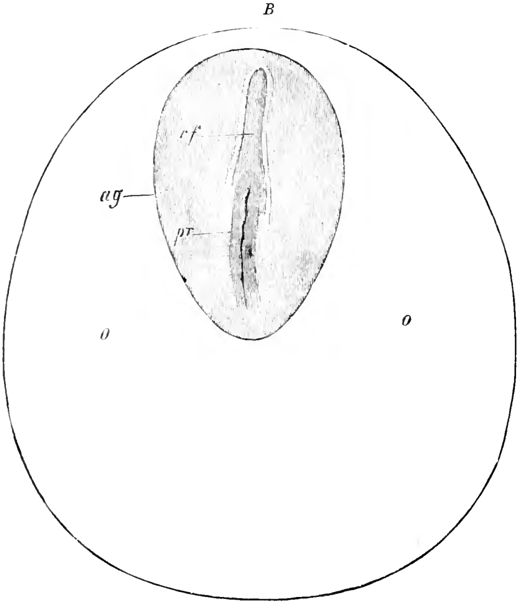


Fig. 89 A.—Embryonic fundament of an 8-days Rabbit, after Kölliker.
arg, Fundament of the embryo; *pr*, primitive streak.

Fig. 89 B.—Vascular area (*o*) **and embryonic fundament** (*ag*) **of a 7-days Rabbit's egg,** after Kölliker.
o, Vascular area (area opaca); *ag*, embryonic fundament; *pr*, primitive groove; *rf*, medullary furrow.

Afterwards there appears in this instance, just as with the Chick, a narrow opaque streak in the forward prolongation of the primitive streak,—its head-process,—and this divides the anterior portion of the germ into a right and a left half (fig. 90 *kf*). After some time there are developed on both sides of the head-process the medullary folds (fig. 89 *B*), which bound the broad medullary furrow (*rf*), and which, by forming a bow at their anterior ends, become continuous with each other; but posteriorly they diverge somewhat from each other, and embrace the primitive groove (*pr*). This stage corresponds to the condition of the Chick presented in fig. 86.

From this time forward the anterior part of the embryonic area grows in length much more rapidly than the hind part with its primitive groove; the latter remains almost unaltered in Mammals up to late stages of development, and then diminishes in length, not only relatively, but also absolutely.

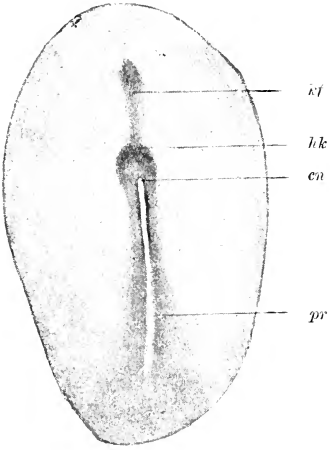


Fig. 90.

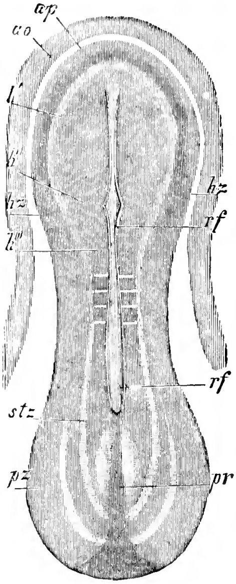


Fig. 91.

Fig. 90.—Germ-disc of an embryo Rabbit with primitive streak, after E. van Beneden.
pr, Primitive streak; *kf*, head-process; *hk*, Hensen's node; *cn*, canalis neurentericus.

Fig. 91.—An embryo Rabbit with a part of the area pellucida 9 days after fertilisation. Magnified 22 diameters. After Kölliker.
ap, Area pellucida; *ao*, area opaca; *h'*, medullary plate in the region of subsequent first brain-vesicle; *h''*, the same in the region of the subsequent mid-brain, where the medullary furrow (*rf*) exhibits a widening; *h'''*, the same in the region of the subsequent third brain-vesicle; *hz*, fundament of the heart; *stz*, trunk zone (Stammzone); *pz*, parietal zone; *pr*, remnant of the primitive streak.

At the same time the embryonic area passes from the oval to a pronounced guitar-shaped outline. Such an embryo is represented in fig. 91. The primitive streak (*pr*) is to be seen at its posterior end, partly embraced by the medullary folds (*rf*). The middle germ-layer is already fully developed, and in the future neck-region three pairs of primitive segments have already been differentiated at the sides of the chorda.

Just as there has been up to this stage an agreement with Birds and Reptiles in other points, so there also is in the existence of a neurenteric canal. At a rather early stage there is already noticeable, at the anterior end of the primitive streak, a small spot, at which, in consequence of cell-proliferation, a large amount of material is accumulated. It is known under the name of HENSEN's node (fig 90 *hk*). This is important chiefly because a narrow canal, the canalis neurentericus (*cn*), passes through it, and leads from the outside into the interior of the blastodermic vesicle. The presence of this canal has already been established by several investigators—by VAN BENEDEN in the Rabbit and the Bat, by BONNET in the Sheep, by HEAPE in the Mole, and by GRAF SPEE in a young human embryo. The latter exhibited a still widely open medullary furrow. At the beginning of the primitive groove there was a wide, roundish, triangular orifice, which traversed the germ-disc, and was surrounded by a ring-like elevation corresponding in position to HENSEN's node.

I have dwelt upon the primitive streak more at length, and have considered more in detail its first appearance and its topographic relations to other organs, because from a developmental standpoint it is a very important structure, and one the significance of which is still much discussed. For it corresponds to the blastopore of the lower Vertebrates, and is important as the region from which the middle germ-layer takes its origin. While I postpone an exposition of the grounds which warrant us in designating the primitive groove as blastopore, I shall at once consider the development of the middle germ-layer. Information concerning this is to be got from cross sections, which should be made, as in the Amphibians, (1) in front of the primitive groove, (2) in the region of the groove, and (3) back of it, both in younger and older embryos.

In embryonic fundaments which have reached the stages represented in figs. 81 *B*, 85, and 89, the middle germ-layer is already begun in the immediate vicinity of the primitive groove, and causes the opacity which appears upon both sides and in front of it. Cross sections through the cephalic process of the primitive streak now allow the establishment of a complete agreement in *one* fundamental point between Amphioxus and the Amphibia on the one hand, and Selachians, Reptiles, Birds, and Mammals on the other.

Along a narrow median streak, in the former groups in front of the blastopore, in the latter in front of the primitive groove, the embryonic fundament is composed of only two germ-layers, of which the lower is destined to become the chorda. At both sides of these regions the two-layered condition passes abruptly in all Vertebrates into a three-layered *one*, the outer germ-layer being followed by the middle layer, and this by the inner germ-layer.

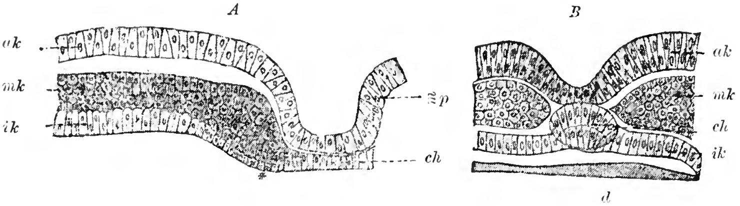


Fig. 92 A and B.—Cross sections through the germ-disc of a Selachian. Copy after Balfour's **Monograph, Pl. IV., Fig. 8a, and Pl. IX., Fig. 1a.**
Only the left half of section *A* is represented.
ak, Outer, *ik*, inner, *mk*, middle germ-layer; *ch*, chorda; *mp*, medullary plate; *d*, yolk.

The conditions in detail assume in Selachians, Birds, and Mammals the forms indicated by the accompanying figures (92-95).

In the Selachians the medullary fold is well marked in cross sections (fig. 92 *A mp*). Beneath it there lies, as in Amphioxus and Triton, only a single layer of tall cylindrical cells (*ch*), the fundament of the chorda; laterally this merges into a many-layered mass of small cells, which is soon divided by means of a fissure into two distinctly separated lamellæ—into the middle layer (*mk*), composed of small polygonal cells, and into the inner layer (*ik*), which here consists of a single layer of tall columnar cells. At the point indicated by a star, the fundament of the chorda and the middle and inner germ-layers are continuous with one another. At a later stage (fig. 92 *B*) a separation of the three fundaments takes place, as in Triton, and we then have (1) a round chordal rod (*ch*), which has been formed by infolding in the manner previously described; (2) at either side of it the small-celled mass of the middle germ-layer (*mk*), divided into halves by the chorda; (3) the inner germ-layer (*ik*), the halves of which, separated in the previous stage, are now growing under the chorda, and are about to fuse into a single layer.

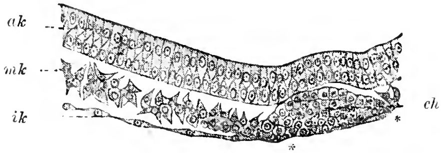


Fig. 93.—Cross section through the blastoderm of a Chick in which the first traces of the chorda and the medullary furrow are to be seen, after Balfour and Deighton.
The section passes through the fundament of the chorda in front of the primitive streak. The part of the section at the right of the fundament of the chorda is not figured.
ak, Outer, *mk*, middle, *ik*, inner germ-layer; *ch*, fundament of the chorda.

A similar view is furnished by a cross section through the cephalic process of the germ of the Chick (fig. 93). Under the outer germ-layer there is found in the median plane, in front of the primitive groove, only the fundament of the chorda (*ch*); at the point indicated by a star it is continued laterally into the small-celled middle germ-layer, and into the entoderm, which is composed of a single layer of very much flattened cells.

The same is true for cross sections of Mammals (fig. 94) in corresponding stages of development. Thus, for example, the fundament of the chorda (*ch*) in the cross section through the embryo of a Mole figured by HEAPE is a single layer of cylindrical cells; it has already become curved into a chordal groove, such as has been represented in fig. 79 *A* for Triton. Laterally it is continuous with a mass of small cells, which is resolved into two layers at the point indicated by a star: (1) into the middle germ-layer (*mk*), composed of several layers of small cells; and (2) into the inner germ-layer, which, as before, appears as a single layer of flattened cells (*ik*).

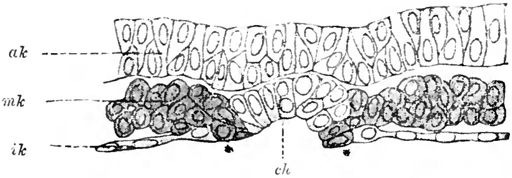


Fig. 94.—Cross section through the embryonic area of a Mole which is in about the stage of the Rabbit represented in Fig. 89 *B*. After HEAPE.

The section passes through the chordal groove (*ch*) somewhat farther forward than the section represented in Fig. 97, which has encountered a region that is to be interpreted as the blastopore.

ak, Outer, *mk*, middle, *ik*, inner germ-layer; *ch*, fundament of the chorda.

In a still more convincing manner VAN BENEDEN has shown, in his investigations upon the development of Mammals, that conditions exist in the formation of the middle germ-layer and of the body-cavity in this class which agree with those in Amphibia. The cross section (fig. 95) through the germ-disc of the Rabbit, taken from his work, is especially convincing. It shows the fundament of the chorda (*ch*) as a single layer of cylindrical cells, flanked on the right and left by the middle and inner germ-layers. The middle germ-layer consists of a parietal (mk^1) and a visceral (mk^2) lamella of flat cells, the former of which is continuous with the fundament of the chorda, while the latter bends around at the point indicated by a star to become continuous with the single-layered epithelium of the inner germ-layer (*ik*). The place where the bend occurs even protrudes distinctly as a lip into the cœlenteron, as in the case of the Amphibia. Except for these unions at the sides of the chordal fundament, the middle germ-layer is everywhere sharply separated by a fissure from the other two germ-layers.*

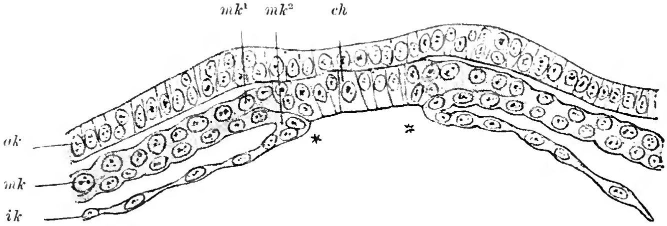


Fig. 95.—Cross section through the germ-disc of an embryo Rabbit, after E. VAN BENEDEN.
ak, Outer, *ik*, inner, *mk*, middle germ-layer; mk^1, parietal, mk^2, visceral lamella of the middle germ-layer; *ch*, chorda.

Further agreement with the conditions which the investigation of Triton has furnished is afforded by a series of cross sections *through the primitive streak—the obliterated blastopore. In the case of all Vertebrates, this is the only place in the whole embryonic area where all three germ-layers, although for only a short distance, are fused with one another, and cannot be distinguished as separate layers, whereas at the sides of this region they are separated by distinct fissures.*

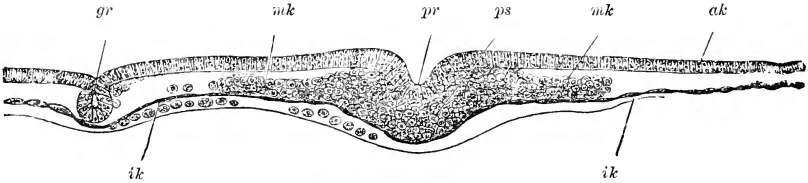


Fig. 96.—Cross section through the middle of the primitive streak of a Chick's germ-disc, which is in the stage of development represented in Fig. 81 *B*. After KOLLER.
At some distance from the primitive groove is to be seen upon the left side of the figure in cross section the marginal groove of HIS. Upon the right side it is as yet little developed.
ak, Outer, *ik*, inner, *mk*, middle germ-layer; *pr*, primitive groove; *ps*, primitive streak; *gr*, marginal groove.

Figure 96 represents a cross section through the embryonic area of a Chick in which the primitive groove is distinctly developed,

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* In the development of Mammals there has been observed at certain stages under the fundament of the chorda a peculiar structure, the so-called chordal canal, which is not found in the other classes of Vertebrates. I mention it here only incidentally, because the publication of VAN BENEDEN'S investigations will doubtless furnish the desired explanation of its origin and significance.

but in which no traces of the medullary folds are to be observed. The outer germ-layer (*ak*) is composed of a single layer of tall cylindrical cells, the inner germ-layer (*ik*) of a single sheet of greatly flattened elements. In the space between the two there penetrates at both sides of the primitive groove a mass of small cells in many superposed layers, the middle germ-layer (*mk*). In the region of the primitive groove (*pr*) this goes over continuously into the outer germ-layer, the cells of which are here found in proliferation, whereas its lateral wings are separated from the outer layer by a fissure. The lower germ-layer is drawn by KOLLER—from whose work the accompanying figure is taken—as being everywhere a separate sheet of flattened cells. It is clear, however, from other drawings and descriptions by DUVAL, RABL, and others, as well as from the accounts in regard to the similar development of Reptiles, that for a certain distance underneath the primitive groove the middle germ-layer is as little to be distinguished as a separate structure from the lower as it is from the upper germ-layer.

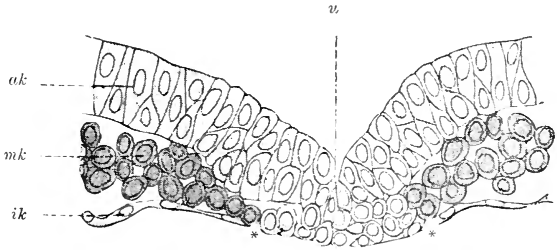

Fig. 97.—Cross section through the embryonic area of a Mole, which is in a stage corresponding approximately with that of the Rabbit represented in Fig. 89 *B*. After HEAPE.
The section passes through the primitive groove, somewhat behind the one represented in Fig. 94. *ak*, Outer, *ik*, inner, *mk*, middle germ-layer ; *u*, primitive groove.

Cross sections through the primitive groove of mammalian embryos are very instructive (fig. 97). According to HEAPE's investigations on the Mole, the groove (*u*) cuts deeply into a mass of small cells. At this place all three layers are fused together ; and it is only laterally to this that they are separated by means of a distinct fissure, and that each is distinguishable by its characteristic kind of cells—the outer (*ak*) by its tall, the inner (*ik*) by its much-flattened, and the middle (*mk*) by its small, more spherical or polygonal cells.

The conditions of the germ-disc of the Rabbit found by VAN BENEDEN are especially distinct (fig. 98). At the deep incision of the primitive groove (*pr*) all three germ-layers are joined to one another for a certain distance by means of a common cells mass. At the same time one may observe, with tolerable distinctness, how the outer germ-layer (*ak*) bends around into the parietal middle layer (mk^1) at the primitive fold (*ul*), while the visceral lamella (mk^2) is continuous with the entoderm (*ik*), which is only one cell thick. Indeed, in embryos of Rabbits and Bats, VAN BENEDEN in some cases observed between the primitive folds, or blastoporic lips, a structure corresponding to the yolk-plug of Amphibia.

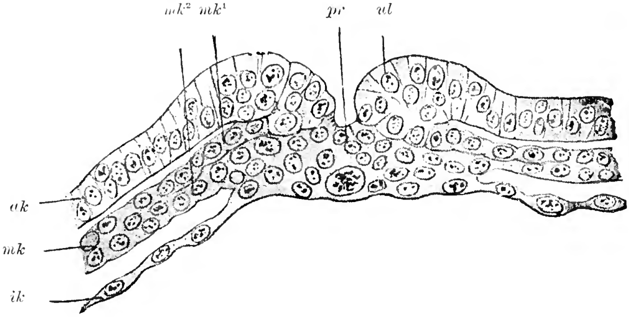

Fig. 98.—Cross section through the primitive groove (blastopore) of a Rabbit's germ-disc, after ED. VAN BENEDEN.
ak, Outer, *ik*, inner, *mk*, middle germ-layer; mk^1, parietal, mk^2, visceral lamella of the middle germ-layer; *ul*, lateral lip of the blastopore; *pr*, primitive groove.

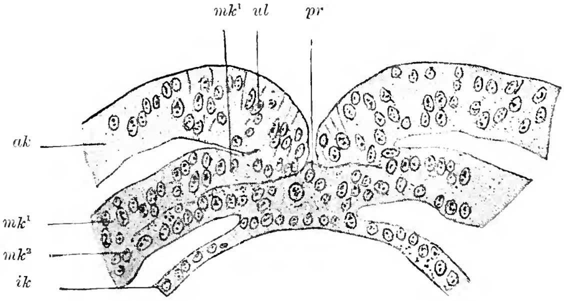

Fig 99.—Cross section through a human germ-disc, with open medullary groove, in the vicinity of the neurenteric canal (*pr*), after GRAF SPEE.
ak, Outer, *ik*, inner germ-layer; mk^1, parietal, mk^2, visceral lamella of the middle germ-layer; *ul*, lateral lip of the blastopore; *pr*, primitive groove.

It is certainly of great general interest that the investigation of an extraordinarily young human germ-disc at the hands of GRAF SPEE has furnished a cross section (fig. 99) which is near enough like the one of the Rabbit here figured to be mistaken for it. In the case of the human embryo, one sees a deep-cutting primitive groove, and at the easily recognisable blastoporic lip (*ul*) the bending over of the outer germ-layer (*ak*) into the parietal lamella (mk^1). The visceral lamella (mk^2) is well separated from the latter for some distance; under the primitive groove it is merged with the inner germ-layer, the edges of the potential folds of the two sides being fused into a mass of cells, which forms the floor of the primitive groove.

Finally an agreement with the development of the Amphibia is not wanting in sections which are made through the embryonic areas of Birds, Reptiles, and Mammals *behind* the primitive groove. The middle germ-layer begins to spread itself out backward also, not, however, as in the anterior part of the embryonic area, in the form of paired fundaments, but rather as a single continuous cell-mass. This outgrowth too is united to the two primary germ-layers only in the region of the posterior end of the primitive streak, being elsewhere distinctly separated from both of them.

For the completion of the previous account, some statements about the further growth of the middle germ-layer may now be added, concerning which cross sections through embryos of various ages afford evidence. The middle germ-layer spreads itself out on all sides between the two primary germ-layers, farther and farther from the place of its first formation—the vicinity of the primitive groove. At first it is limited to the fundament of the embryo itself, then it makes its way into the area pellucida, and, finally, it is encountered in the opaque area. Everywhere and constantly in its extension it appears as an entirely independent layer, at least two cells thick, which is separated from its surroundings by fissures. It is found to be united for a short distance with the inner and outer germ-layers, but only at the primitive groove, which persists for a long time,—in older embryos even,—as we have already learned from surface-views. Even in the stage when the neurenteric canal traverses the primitive streak, and puts the cœlenteric cavity (under the entoderm, fig. 100 *hy*) in communication with the neural tube, we see the cellular lining of the canal and the middle germ-layer fused, so that in this region a connection still exists between all three germinal layers. Compare the accompanying cross sections through embryos of Lacerta muralis.

After the statement of the actual conditions, the questions remain to be answered: (1) What is the meaning of the primitive groove? (2) How is the middle germ-layer developed?

In the interpretation of the primitive groove I place myself, as is to be seen from what precedes, wholly on the side of those investigators who, like **Balfour**, **Hatschek**, **Kupffer**, **Hoffmann**, **van Beneden**, **L. Gerlach**, **Rückert**, and others, recognise in it a structure equivalent to, but somewhat modified from, the blastopore of lower Vertebrates, and who compare the *primitive folds* to lateral *blastoporic lips* closely pressed together. In my description of a previous stage I have already designated as blastopore the crescentic groove of Birds (fig. 52 *B s*) and the prostoma (fig. 55 *u*) of Reptiles, because that is the place where the lower germ-layer is infolded. In my opinion both grooves are identical structures, which, by changes in position and form, have been so evolved, the one from the other, *that the fissure, which was at first transverse, has become converted into a longitudinal one.* For Reptiles **Kupffer** has established this to a certainty. According to his figures in Emys Europæa, *e.g.*, the transverse depression (*u*) represented in fig. 101 *A* is converted at a later stage into the form shown in the adjacent figure (101 *B u*). For the Birds the investigations of **Duval** previously recounted (p. 121, fig. 82) are convincing. There is also to be taken into account the additional fact, that even as early as in the Amphibia an exactly corresponding metamorphosis of the blastopore takes place. As the accompanying cuts (fig. 101 *C* and *D*) show, the blastopore of the Amphibian is, at its first appearance, a transverse fissure (fig. 101 *C u*). Then it becomes circular, and embraces with its lips a protruding portion of the otherwise enclosed yolk-mass,—the yolk-plug,—becomes narrower, and is continued forward into a longitudinal groove. Finally it appears (fig. 101 *D u*) as a deep groove, situated at the end of the

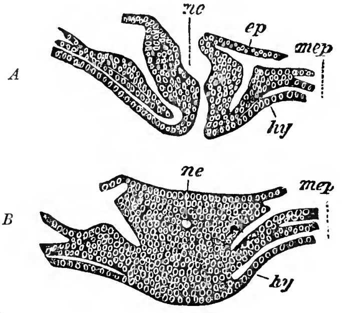

Fig. 100.—Cross sections through the posterior end of a young embryo of Lacerta muralis, after Balfour.

In figure *A* the neurenteric canal is cut lengthwise; in figure *B* only an evagination of it, which is directed backward. Since the sections probably have not cut the chief axis of the embryo perpendicularly, the middle germ-layer is fused with the wall of the canal only on the right side in figure *A*, whereas in figure *B* the connection is present on both sides.

ne, Neurenteric cana ; *ep*, outer, *mep*, middle, *hy*, lower germ-layer.

medullary furrow, with its small circular opening filled up with a yolk-plug.

In addition there are three important considerations which may be urged in support of the interpretation of the primitive groove as blastopore.

First, the primitive streak, even when an open canal is wanting, is the only place in the whole germ-disc where a connection between all the germ-layers is constantly present, as at the Amphibian blastopore.

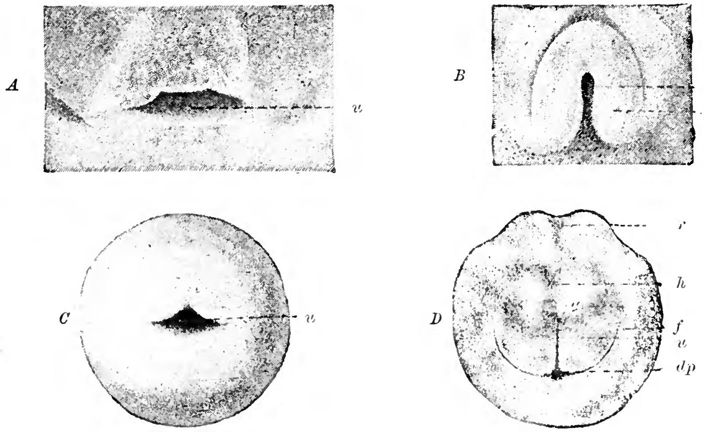

Fig. 101. A and B.—A portion of a younger and of an older embryonic fundament of Emys Europæa, with the prostoma or blastopore (*u*), after Kupffer.

ul, Lip of the blastopore.

C and D.—Two eggs of Triton tæniatus seen from the blastopore, one 30 hours, the other 53 hours after artificial fertilisation.

u, Blastopore ; *h*, elevation between blastopore and dorsal groove ; *f*, semicircular furrow, which encloses the blastoporic area ; *dp*, yolk-plug.

Secondly, the chief organs of the body, such as the chorda, the neural tube, and the primitive segments, are developed in front of the primitive streak in the case of the higher Vertebrates, just as they arise in front of the blastopore in Amphioxus and the Amphibia. Both blastopore and primitive streak occupy the posterior end of the body. The so-called cephalic process of the primitive streak is nothing else than the first rudiment of the chorda.

Thirdly, one may still recognise in the openings—canales neurenterici—which have been pointed out in the primitive streak at an earlier or later stage in its development, in the case of Birds, Reptiles, and Mammals, an indication that an open communication has existed here from the beginning between the inner and the outer germ-layers; further, that this communication has disappeared through the fusion of the blastoporic lips, but that it can be in part reëstablished in consequence of more favorable processes of growth. At the same time the neurenteric canal, in cases where it reappears in the primitive streak, effects a very characteristic union between the posterior ends of the neural and intestinal tubes, in exactly the same manner in which the blastopore of Amphioxus, the Amphibia, and the Selachii does (compare fig. 80 with fig. 88 *n.e*).

In the interpretation of the primitive groove as blastopore I am compelled to oppose a somewhat different view. Certain investigators (BALFOUR, RAUBER, and others) recognise in the primitive groove and the crescentic groove of meroblastic eggs only a small part of the blastopore; they interpret as the major part of it the region which is encircled by the whole rim of the germ-disc and is occupied by the yolk-mass, and to which they give the name yolk-blastopore.* According to their conception, as also according to the original assumption of HAECKEL, the two-layered germ-disc is a flattened-out gastrula,—its blastoporic rim lying upon the yolk-sphere,—which gradually grows around the yolk, and finally takes the latter wholly inside itself, just as if it were a ball of food. The primitive groove is a small detached part of the blastopore, which is connected with the development of the middle germ-layer. The two parts become completely separated from each other, and are closed at different times, each for itself, the yolk-blastopore often late, at the pole of the yolk-sac which is opposite to the embryo.

Such an assumption of a double blastopore appears to me to be untenable. *I propose that only that place of the germ be designated as blastopore at which, as in the gastrulation of Amphioxus and the Amphibia, there actually occurs an invagination of cells, by means of which the cleavage-cavity is obliterated.* Such a process takes place in the Selachii only at the crescentic hinder part of the margin of the germ-disc, in the Reptiles and Birds at the small place designated as crescentic groove. It is also from this place alone that subsequently the development of the middle germ-layer proceeds.

The anterior margin of the germ-disc in Selachians, and, after the conversion of the crescentic groove into the primitive groove, the whole

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* RAUBER has suggested for the various regions which he assumes for the blastopore the designations *prostoma sulcatum longitudinale* (primitive groove), *prostoma sulcatum falciforme* (crescentic groove), and *prostoma marginale* (yolk-blastopore).

margin of the germ-disc in Birds and Reptiles, have an entirely different signification. This margin exhibits a very different relationship from that of the primitive streak or blastopore; it is a peculiarity of meroblastic eggs, which is most intimately associated with the origin of partial cleavage. It indicates the place at which the segmented portion of the germ meets the unsegmented portion—the place at which there lie in the yolk free nuclei, by means of which a supplementary cleavage is kept up until late stages in the process of development, until, in fact, the time when the two primary germ-layers have been formed by means of the invagination which occurs at the blastopore. At the expense of the cell-material, which is constantly being augmented by supplementary cleavage, the germ-layers increase in extent at their place of transition into the yolk, and thus gradually grow over the unsegmented part. *Whereas at the blastopore an invagination of cells already present takes place, there ensues at the margin of the germ-disc a formation of new cells, and thereby an increase of the marginal part and an overgrowth of the yolk.* I therefore propose for it the name *circumcrescence-margin of the yolk-sphere.* There can be no such thing as a separate opening or a yolk-blastopore, because the yolk is an organic part of the germ, and is in continuity with the segmented part of it by means of the layer which contains the yolk-nuclei.

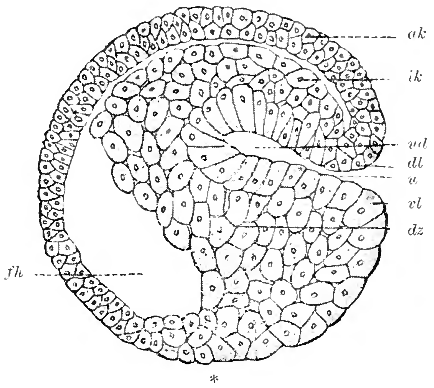

Fig. 102.—Longitudinal section through a gastrula of Triton. *ak*, Outer, *ik*, inner germ-layer; *fh*, cleavage-cavity; *vd*, cœlenteron; *u*, blastopore; *dz*, yolk-cells; *dl*, dorsal, *vl*, ventral lip of the cœlenteron.

If we would institute a comparison between animals with meroblastic eggs and the Amphibia at a stage when gastrulation is not yet completed, then the blastopore of the Amphibia, which is indicated by the letter *u* in the accompanying section through the gastrula of a Triton (fig. 102), corresponds to the prostoma of Reptiles, and to the crescentic and primitive grooves of Birds; the still exposed mass of yolk-cells corresponds to the yolk-material which is not yet overgrown by germ-layers; the place marked by a star, at which in the Amphibia the transition from the small-celled layer to the mass of yolk-cells occurs, or the marginal zone of GOETTE, is comparable to the margin of circumcrescence in meroblastic eggs.

In the second place, the question arises: *How is the middle germ-layer of Vertebrates developed?* The answer is: By a process of folding similar to that in the case of Amphioxus lanceolatus. This answer is substantiated by the fact that the individual processes in the development of the middle germ-layer may be correlated with corresponding processes in Amphioxus.

In view of the fundamental importance of the matter, I formulate in a synoptic and precise manner in six paragraphs the points in reference to which it has been possible to establish an agreement in all Vertebrates.

1. Before the chorda is formed, the germ in all Vertebrates is composed of two layers in the region of a median streak which lies in front of the blastopore and primitive groove. It is here composed of the medullary plate and the fundament of the chorda, which then shares in bounding the intestinal cavity.

2. At both sides of this median streak the germ is three-layered, if we regard the middle germ-layer as a single one; it is four-layered, if we allow that the latter consists of a parietal and a visceral cell-layer, which are originally pressed firmly together, and only later actually separated by the appearance of the body-cavity.

3. In no Vertebrate do the middle germ-layers arise by fission, either from the outer or the inner germ-layers, because they are everywhere, except in a very limited region of the germ, sharply separated from both by means of a fissure.

4. A connection of the middle germ-layers with the neighbouring cell-layers takes place only: (*a*) at the blastopore or primitive groove, where all four (or three) germ-layers are joined together, and (*b*) at both sides of the fundament of the chorda.

5. One observes the first fundament of the middle germ-layers at the region of the germ just mentioned, and sees it spread itself out from here—*i.e.*, from the periphery of the blastopore or the primitive groove, and from both sides of the fundament of the chorda —forward, backward, and ventrad or laterad. In front of the blastopore it appears in the form of paired fundaments separated by the fundament of the chorda; behind the blastopore, on the contrary, as a continuous structure.

6. While the chorda is being developed, the two paired fundaments

of the middle germ-layers detach themselves from the adjacent cell-layers at the sides where their ingrowth took place, and at the same time the halves of the permanent entoderm grow together, whereby the dorsal closure of the intestine is effected.

In view of these facts there is only *one* explanation at which we can arrive. If it is certain that the middle germ-layers do not arise by a fission *in loco* from either of the primary germ-layers, then their gradual spreading out from a definite region of the germ can result only from an ingrowth of cells, which occurs from those places where a connection with other cell-layers has been demonstrated. The middle germ-layers draw the principal material for their growth from cells which, at the blastopore or at the primitive groove, migrate between the two primary germ-layers.

But this immigration of cells may be interpreted as a process of infolding of the primary germ-layers, as in the case of Amphioxus. In the method of the infolding there exists, it is true, *one* very striking and apparently important difference between Amphioxus and the remaining Vertebrates. In Amphioxus the middle germ-layer arises as a hollow sac, by means of the folding of the inner germ-layer—in the remaining Vertebrates as a solid mass of cells. This undeniable difference is, however, easily explained in the following manner: In the solid fundaments of the middle germ-layer a cavity is wanting, because the cellular walls of the sac are from the beginning firmly pressed together, in consequence of the yolk-mass which fills the cœlenteron. In addition to other striking agreements with the conditions in Amphioxus lanceolatus, there are three points of view which in particular commend this interpretation:—

(1) In all vertebrated animals there early arises in the middle germ-layer a fissure, which is surrounded by cells, often cubical or cylindrical, having an epithelial arrangement. The parietal and visceral layers then take the form of epithelial lamellæ, as is to be seen in an especially striking manner in the case of the Selachii at a very early stage of development. (2) From these epithelial layers there arise in the adult genuine epithelial membranes, like the ciliated peritoneal epithelium of many Vertebrates, and, in addition, glands that in many respects resemble the glands derived from epithelial membranes [of the other germ-layers] (kidney, testis, ovary). (3) The objection that the middle germ-layer of Vertebrates arises as a single cell-mass, and therefore cannot be equivalent to two layers of epithelium, loses its weight with every one who knows the numerous analogous phenomena of development

occurring elsewhere, in which organs that should be hollow are at first developed as solid masses of cells. We shall hereafter cite as such the solid fundament of the neural tube in Bony Fishes, many sensory organs and the most of the glandular sacs, which latter arise as solid buds of epithelial lamellæ, and only later, when they become functionally active, acquire a cavity by the separation of their cells.

SUMMARY.

A. The blastula.

1. Out of the mass of cleavage-cells (morula) there is developed in all Vertebrates a sac-like germ (blastula) with cleavage-cavity.

2. There are four different kinds of blastulæ in Vertebrates, according to the amount and distribution of yolk.
   - (*a*) In Amphioxus the cleavage-cavity is very large, and its wall consists of a single layer of cylindrical cells of nearly uniform size.
   - (*b*) In Cyclostomes and Amphibia the cleavage-cavity is small: one half of the wall of the blastula is thin, and composed of one or several layers of small cells; the other half is considerably thickened, and formed of large yolk-cells arranged in many superposed layers.
   - (*c*) In Fishes, Reptiles, and Birds (meroblastic eggs) the cleavage-cavity is small and fissure-like or wanting. Only its roof or dorsal wall consists of cells (germ-disc); its floor or ventral wall, on the contrary, consists of the yolk-mass which has not been divided into cells, but which contains yolk-nuclei in the vicinity of the margin of the germ-disc.
   - (*d*) In Mammals the cleavage-cavity is very spacious, and filled with an albuminous fluid; its wall is composed of a single layer of greatly flattened hexagonal cells, with the exception of a small thickened place, where larger cells in several superposed layers cause an elevation which projects into the cavity.

B. The cup-shaped larva or gastrula with two germ-layers.

1. There is formed out of the blastula, by the invagination of a portion of its surface, a two-layered form, the beaker-larva or gastrula.

2. The two layers of the double beaker are the outer and the

inner germ-layer (ectoblast, entoblast); the fissure separating the two layers is the obliterated cleavage-cavity; the cavity resulting from the invagination is the cœlenteron, its external opening the primitive mouth (blastopore, prostoma, crescentic groove, primitive groove).

3. The four kinds of gastrulæ correspond to the four kinds of blastulæ.

(*a*) In Amphioxus the cœlenteron is wide, and each germ-layer is made up of a single sheet of cylindrical cells.

(*b*) In Cyclostomes and Amphibia the mass of yolk-cells is accumulated on the ventral wall of the cœlenteron in the inner germ-layer, and causes a protuberance, by means of which the cœlenteron is reduced to a fissure.

(*c*) In Fishes, Reptiles, and Birds the process of invagination remains confined to the germ-disc, since the unsegmented yolk, on account of its considerable volume, cannot be made to share in the invagination. The *germ-disc* becomes two-layered by means of an ingrowth of cells at the crescentic groove (blastopore). The yolk acquires a cellular boundary very slowly and at a late period; it is overgrown by the margin of the germ-disc, when the supplementary cleavage (yolk-nuclei) takes place.

The outer germ-layer spreads itself out and envelops the yolk most rapidly; then follows the inner, and finally the middle layer.

(*d*) In Mammals the inner germ-layer is developed from the thickened region of the blastula, probably by means of an invagination, because at a later stage an orifice of invagination, comparable with the primitive groove of Birds, or a blastopore, can be demonstrated. At the beginning of its development the inner germ-layer terminates below in a free margin, so that the cœlenteron is for a time closed in on the ventral side by the outer germ-layer only, a peculiarity which is comparable with the conditions in Reptiles and Birds, if we conceive the yolk-material to have disappeared in this instance before it is completely surrounded by the inner germ-layer.

4. In Vertebrates the gastrula presents a sharply expressed bilateral symmetry, so that one can easily distinguish the future

head- and tail-ends, the future dorsal and ventral sides of the body. The blastopore (crescentic groove, primitive groove) marks the posterior end. The ventral side is characterised by being the place where the segmented or unsegmented yolk-material comes to lie.

C. *The embryo with four germ-layers and a body-cavity.*

1. In all Vertebrates there are formed from the roof of the cœlenteron two lateral evaginations of the inner germ-layer, by means of which the cœlenteron is divided into a median cavity, the secondary intestine, and two lateral cavities, the two body-sacs.

2. The primary inner germ-layer is resolved in consequence of this process of evagination into three parts :—

First, the epithelial lining of the intestinal tube (secondary inner germ-layer—Darmdrüsenblatt).

Secondly, the epithelial lining of the body-cavity, or the middle germ-layer, in which a parietal and a visceral layer are distinguishable.

Thirdly, the chorda, which takes its origin from the portion of the primary inner germ-layer which lies between the lateral evaginations from the roof of the cœlenteron.

3. Two modifications of the process of evagination can be recognised in the case of Vertebrates.

(*a*) In Amphioxus the evaginations are small, numerous, and segmentally arranged; provided from the first with a cavity; and, beginning in the fundus of the cœlenteron, developed toward the blastopore.

(*b*) In the remaining Vertebrates, instead of hollow sacs, there grow out from the inner germ-layer two solid masses of cells :—

(1) In the vicinity of the blastopore (primitive groove, peristomal mesoblast).

(2) From here forward along the roof of the cœlenteron, at a slight distance from the median plane, at both sides of the fundament of the chorda (gastral mesoblast).

The paired fundaments spread themselves out from their place of origin between the two primary germ-layers farther forward and ventralward.

4. The three organs derived from the primary inner germ-layer (middle germ-layer, fundament of the chorda, secondary inner germ-layer) are separated from one another by constrictions.

First, the body-sacs are detached from the fundament of the chorda and the entoblast, whereupon the edges of the parietal and visceral lamellæ, thus set free, fuse with each other.

Secondly, the fundament of the chorda is bent into a chordal groove, and this is converted into a solid rod, which is completely isolated from the entoblast.

Thirdly, the entoblast closes together into a tube with a dorsal raphe.

5. The development of the three fundaments, as also that of various other organs, begins at the head-end of the embryo, and advances from here toward the blastopore, where for a long time a continual formation of new parts and an increase in the longitudinal growth of the body take place.

6. During the development of the middle germ-layer, the blastopore of the Amphibians, Fishes, Reptiles, Birds, and Mammals has been metamorphosed into a groove occupying the longitudinal axis of the embryo (primitive groove of the higher Vertebrates).

7. The blastopore and the primitive groove in later stages of development undergo degeneration, and are not converted into any organ of the adult. (For the details of this, see Part II.)

8. Before their disappearance the blastopore and primitive groove are surrounded by the medullary folds and taken into the terminal part of the neural tube, whereby a direct communication between neural tube and intestinal tube—the neurenteric canal—is effected. The two organs, which communicate with each other for a long time, are later separated by its closure.

CHAPTER VII.

HISTORY OF THE GERM-LAYER THEORY.

The fundamental facts of the sheet-like structure of the vertebrate body, which have been treated of in the two preceding chapters, are epitomised as the doctrine of the germ-layers, or the germ-layer theory. Since this theory is of the most far-reaching significanc for the comprehension of the evolution of form in animals, and can be placed side by side with the cell-theory as coëqual with the latter, I devote a separate chapter to its history.

The very earliest establishment of the germ-layer theory is associated with the most celebrated names in the field of embryology: CASPAR FRIEDRICH WOLFF, PANDER, and CARL ERNST VON BAER.

CASPAR FRIEDRICH WOLFF, the discoverer of the metamorphosis of plants, who, even before GOETTE, had clearly and distinctly stated that the various organs of the plant, as, for example, the separate parts of the flower, have been developed by various modifications of leaf-like fundaments, also established the metamorphosis of animals, for which he endeavoured to found a similar law of development.

He showed in his important work on the formation of the intestinal canal of the Chick, that it originally appeared in the egg as a leaf-like structure, and that this afterwards became folded into a groove, and finally converted into a tube.

He conjectured that the remaining systems of organs might arise in a similar way, and appended to the account of the development of the intestinal canal the significant assertion: "It appears as though at different periods, and many times in succession, various systems might become formed after one and the same type, and as if they might be on that account similar to one another, even though they are in reality different. The system which is first produced, which is first to take on a specific form, is the nervous system. When this is concluded, then the fleshy mass, which really makes up the embryo, is formed after the same type; then appears a third, the vascular system, which certainly . . . is not so unlike the first ones that the form described as common to all systems could not be easily recognised in it. After this follows the fourth, the intestinal canal, which, again, is formed after the same type, and appears as a completed independent whole, similar to the first three."

WOLFF's article, written in Latin, made no impression on his contemporaries; it had to be rescued from oblivion by MECKEL, who published a German translation of it in 1812. It was probably by means of this translation that the attention of PANDER was directed to WOLFF. PANDER, under the stimulus and direction of his celebrated teacher, DÖLLINGER, further developed the doctrine, the germ of which was contained in WOLFF's paper.

In his publication, "Beiträge zur Entwicklung des Hühnchens im Ei," issued in the year 1817, PANDER distinguished in the blastoderm, as early as the twelfth hour of incubation, two thin separable lamellæ as the serous layer and the mucous layer, and maintained that subsequently a third, the vascular layer, was developed between them. "Whatever noteworthy may subsequently occur," he remarks, "it is never to be regarded as anything else than a metamorphosis of *the blastoderm and its layers*, endowed as they are with an inexhaustible store of formative energy." A few years later the germ-layer theory reached at the hands of CARL ERNST VON BAER a preliminary completion, which served for some time. VON BAER, likewise a pupil of DÖLLINGER, had observed in Würzburg the beginning of the investigations of his young friend, PANDER. In laborious studies pursued for many years, BAER followed with wonderful accuracy the origin of the germ-layers and their metamorphosis into the individual organs of the adult body, principally in the case of the Chick, but also in the case of some other Vertebrates, and recorded his investigations in his classical work, "Ueber Entwicklungsgeschichte der Thiere, Beobachtung und Reflexion," which is unsurpassable both in observations and in its general standpoints.

BAER differs from PANDER in maintaining that each of the two primary germ-layers, which he distinguishes as animal and vegetative, subsequently divides into two sheets. The animal germ-layer divides itself into dermal lamella and sarcous lamella (Hautschicht, Fleischschicht), the vegetative into mucous lamella and vascular lamella, so that now four secondary germ-layers have arisen. The individual organs are developed out of the germ-layers by morphological and histological differentiation.

A further advance beyond that of BAER could not be attained until, with the establishment of the cell-theory, entirely new points of view were introduced into morphology and, with improved construction in microscopes, methods of investigation were refined. It is chiefly REMAK and KÖLLIKER who have promoted the germ-layer theory in this direction.

REMAK took in hand successfully in his noted investigations on the development of Vertebrates the very important question, how the originally similar cells of the germ-layers are related to the tissues of the completed organs. He showed that out of the lowest of the four germ-layers there proceed only the epithelial and glandular cells of the intestinal tube and its appendages, that from the uppermost layer the epithelial cells of the epidermis, the sensory organs, and the nervous tissue arise, whereas the two middle layers furnish the mechanically sustentative substances and the blood, the muscular tissue, and the urinary and sexual organs.

In regard to the manner in which the four secondary germ-layers arise, REMAK differs from BAER. Out of the two primary germ-layers he first makes a third one, the middle germ-layer, arise, and indeed he derives it exclusively from the lower germ-layer by a process of fission. He designates the three layers as the upper or sensorial, the middle or motor-germinative, and the lower or trophic. The four secondary germ-layers of von Baer come into existence subsequently by a repetition of the fission, whereby the middle germ-layer is split, at least in its lateral portions (lateral plates), into the dermo-fibrous layer and the intestino-fibrous layer (Hautfaser- und Darmfaserblatt), between which arise the thoracic and body-cavities.

Remak in his account approximates the true state of affairs, as detailed in the preceding chapters, more nearly than von Baer; however, both made the same mistake of interpreting the formation of the germ-layers as always a process of disassociation or fission. That is also the rock on which were wrecked the researches of numerous other investigators, who in the decennary succeeding Remak dealt with the important question of the origin of the germ-layers. It was difficult to decide this question for the higher Vertebrates, which have been most frequently investigated; so that very contradictory opinions were expressed relative to the development of the middle layer—whether it was exclusively from the lower (Remak), exclusively from the upper, or from both layers.

This question could be clearly understood only upon the establishment of new general standpoints. These could be acquired only by the *comparative method, and by the study of lower Vertebrates and the Invertebrates.*

Two fundamental processes needed to be better comprehended:—

(1) *How are the two primary germ-layers developed?*

(2) *How are the two middle germ-layers developed?*

By means of the comparative developmental method, one question has been brought nearer to a solution in the gastræa-theory, the other in the cœlom-theory.

In the study of the first problem, which was the earlier solved, Huxley and Kowalevsky, Haeckel and Ray Lankester, have shown especial merit. They demonstrated, partly through anatomical, partly through embryological studies, that, with the exception of the Protozoa, the body of every invertebrated animal is constructed of layers, which may be compared with the primary germ-layers of Vertebrates.

The highly gifted English zoölogist Huxley distinguished as early as the year 1849 two membranes in the Medusæ, an outer and an inner layer, out of which alone their bodies are constructed; and at the same time expressed the happy idea that physiologically they were equivalent to the serous and the mucous layers of BAER. Soon after this (1853) ALLMAN introduced for the layers of the Cœlenterates the names, which are now so much employed, *ectoderm* and *entoderm*; subsequently use was also made of these for designating the embryonic layers.

The germ-layer theory was promoted to a still greater degree by the Russian zoölogist KOWALEVSKY, who made us acquainted in numerous excellent detailed investigations with a profusion of important facts concerning the embryology of Worms, Cœlenterates, Molluscs, Brachiopods, Tunicates, and Arthropods. He produced evidence that in all the Invertebrates which he investigated two germ-layers are formed at the beginning of development, and that in almost all cases, when the process of cleavage is at an end, a cellular sac arises, and that this, by the infolding of a part of the wall, becomes converted into a double cup, the cavity of which, enclosed by two germ-layers, communicates with the outside by means of an opening. He succeeded in establishing the existence of this very important cup-shaped larva (gastrula) in many branches of the animal kingdom.

In this connection should be mentioned the services of several other embryologists, who at a still earlier period had observed in isolated cases the *cup-shaped larva and its origin by means of invagination*. RUSCONI and REMAK had described the cup-shaped larva of Amphibia, GEGENBAUR that of the Sagittæ or arrow-worms, MAX SCHULTZE that of Petromyzon.

Whereas KOWALEVSKY by his series of investigations enriched our knowledge of material facts, HAECKEL first sought to utilise the same for a *general theory*, since by the process of morphological comparison he brought into association hitherto disconnected observations. Starting from the development and the anatomy of the Sponges, he compared the layer-like structure of the embryos of all animals with the layer-like structure of the Cœlenterates, and produced as the fruit of this study the celebrated *gastræa-theory*, which, attacked on many sides at the time of its publication, has now found in its essential substance general acceptance, and has given the impetus to numerous investigations. HAECKEL showed that in the development of the various classes of animals from the Sponges up to Man a single form of the germ makes its appearance, the gastrula, which consists of two cell-layers, and that the two cell-layers of the various embryonic forms are comparable to one another or homologous. The gastrula in its simplest condition presents, as he endeavored to establish, the form of a double cup with a cœlenteric cavity and a primitive mouth, but may be greatly altered, as in the most of the Vertebrates, by the deposition of yolk-material in the egg, so that the original fundamental form is scarcely recognisable. Consequently he distinguished, according to the kind of modification, *different forms of the gastrula, as bell-shaped, cap-shaped, disc-shaped, and vesicular gastrulæ.* He made the various forms arise by a process of invagination from a still simpler fundamental form, the *blastula*, which is the final result of the cleavage process.*

HAECKEL published his excellent gastræa-theory in two articles in the *Jenaische Zeitschrift*: (1) "Die Gastræatheorie, die phylogenetische Classification des Thierreichs, und die Homologie der Keimblätter," (2) "Nachträge zur Gastræatheorie."

At the same time with HAECKEL, RAY LANKESTER in England was led to a similar theory, which he had worked out in a paper full of new ideas: "On the Primitive Cell-layers of the Embryo as the Basis of Genealogical Classification of Animals."

Both HAECKEL and LANKESTER failed to point out how the formation of the gastrula takes place in some of the divisions of Vertebrates—in Fishes, Reptiles, Birds, and Mammals. Essential service in the establishment and explanation of numerous questions of detail, which remained unsettled in the gastræa-theory, has been rendered by BALFOUR, VAN BENEDEN, GERLACH, GOETTE, HOFFMANN, KOLLER, RAUBER, RÜCKERT, SELENKA, DUVAL, and others.

Thus through HAECKEL'S gastræa-theory the following points were gradually cleared up: (1) The two primary germ-layers, which form the foundation for the development of both Invertebrates and

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* It should be here stated that even OKEN and C. ERNST V. BAER had set forth, although in a very indefinite manner, the importance of the *vesicular* form for the development of the animal body. OKEN was an opponent of the germ-layer theory of WOLFF. In a criticism of PANDER'S investigations he exclaimed with emphasis and a certain justice: "The facts cannot be so. The body arises out of vesicles and never out of layers," and he added the very pertinent remark: "It appears to me as if it had been entirely forgotten that the yolk and the yolk-membrane, which is a vesicle, belong *essentially to the body* of the germ; that the embryo does not swim upon it like a fish in the water, nor lie upon it like a funnel on a cask."

In a similar manner BAER remarks, but without further expounding the relation to the germ-layers: "Since the germ is the undeveloped animal itself, one can affirm, not without reason, that the simple vesicular form is the common fundamental form, out of which all animals are developed, not only ideally, but historically."

Vertebrates, arise, not through disassociation or fission, but through infolding of an originally simple cell-layer.* (2) These are comparable with one another or homologous, because they are developed according to the same process, and because the two fundamental organs of the body, the layer which limits the body externally (the ectoderm) and the layer which lines the digestive cavity (the entoderm), arise from them. (3) The intestinal canal of all animals arises by invagination.

In the question as to the development of the middle germ-layer **Haeckel** remained at the traditional standpoint, and inclined most to **C. E. von Baer**'s view that the parietal lamella arose by fission from the outer primary layer, and the visceral lamella from the inner germ-layer. Most embryologists, who worked on the development of Vertebrates, entertained, on the contrary, **Remak**'s view, and made the whole middle germ-layer arise from the inner by fission.

They regarded the body-cavity as a fissure in the middle germ-layer, and compared it with other lymphatic spaces, such as occur in the connective tissue at various places in the body.

The correction of this view was undertaken by various persons in the same manner as in the case of the primary germ-layers. By detailed study of the formation of the germ-layers in the Chick and Mammals, **Kölliker** found that the middle germ-layer did not simply split itself off from the inner, but that it arose from a limited region of the blastoderm, namely, from the primitive groove, where the two primary germ-layers are continuous. He maintained that from this region it grew out between the two primary germ-layers as a solid cell-mass, and that subsequently the body-cavity appeared in it by means of its fission into two layers. This was an essential advance in the representation of the actual state of affairs.

But a deeper insight into these embryonic processes in Vertebrates was first acquired in this case also through the study of Invertebrates, especially through the important discoveries of **Metschnikoff** and **Kowalevsky** concerning the formation of the body-cavity in Echinoderms, Balanoglossus, Chætognathi, Brachiopods, and Amphioxus. The former found that in the larvæ of Echinoderms and in Tornaria, the larva of Balanoglossus, the walls of the body-cavity are formed from evaginations of the intestinal canal. But a still greater sensation

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* It is still affirmed by several authors for certain Invertebrates that the inner germ-layer develops, not by infolding, but by a splitting off or delamination from the outer germ-layer.

was created when Kowalevsky in 1871 published his "Embryology of Sagitta," and showed how the cœlenteron of the gastrula was divided by two folds into three cavities,—into the secondary intestinal cavity and into the body-cavities: this discovery was afterwards fully confirmed by the investigations of Bütschli and the author. After a short interval, Kowalevsky's account of the development of Sagitta was followed by his work on Brachiopods, in which he again enriched science with the new and important fact, that in this class also the body-cavity was formed in the same way as in the case of the Chætognaths. This was followed by his fundamental work on Amphioxus.

Through the important discoveries made on Invertebrates, Huxley, Lankester, Balfour, my brother and I were stimulated to theoretical speculations concerning the origin of the body-cavity and the middle germ-layer in the animal kingdom.

Huxley distinguished three kinds of body-cavity according to their origin: (1) an *enterocœl*, which arises as in Sagitta, etc., from evaginations of the cœlenteron; (2) a *schizocœl*, which is developed by means of fission in a mesodermal connective substance lying between the integument and the intestine; (3) an *epicœl*, which is formed by an invagination of the surface of the body like the perithoracic space of the Tunicates. The last kind, Huxley thinks, may perhaps correspond to the pleuroperitoneal cavities of the Vertebrates.

Lankester makes Huxley's paper his starting-point. He gives preference to the hypothesis of the common origin of the body-cavity in all animals until decisive proof of diverse origins is produced; and, in fact, he makes the schizocœl arise out of the enterocœl in the following manner. Evaginations of the cœlenteron have lost their lumen, and therefore are begun as solid cell-masses, which only subsequently acquire a cavity. While Lankester in this, as well as in a second publication, overlooks existing differences in his effort to reduce everything to a single scheme, Balfour in various essays takes more fully into account in his speculations the actual condition of affairs; he also limits himself chiefly to the explanation of the conditions in Vertebrates. In investigating the development of Selachians, he made the important discovery that the middle germ-layer arises from the lateral margins of the primitive mouth, and at first consists of two separate masses of cells, which grow out forwards and laterally into the space between the two primary germ-layers. Since in each cell-mass a separate cavity soon makes its appearance, he designates the body-cavity as from the beginning a paired structure, and compares it to the body-sacs which are developed in Invertebrates by evagination from the cœlenteron. BALFOUR justly alleges that the originally solid condition of the two fundaments can have no weight against his interpretation, since in numerous instances organs which ought properly to contain cavities are developed solid, and subsequently become hollow, as, for example, in many Echinoderms one encounters solid cell-masses in place of hollow evaginations of the cœlenteron.

Led by theoretical considerations similar to those of the English morphologists, my brother and I, by a thorough comparison of developmental and anatomical conditions, and with due regard to the morphological and histological structure of organisms, then endeavored to bring to a solution this question of the day,—the question of the development of the body-cavity and the middle germ-layers,—by systematic investigations (published in "Studien zur Blättertheorie"), which extended over Invertebrates and Vertebrates. The results of these series of investigations were published in two articles: (1) in the "Cœlomtheorie, Versuch einer Erklärung des mittleren Keimblattes," and (2) in the "Entwicklung des mittleren Keimblattes der Wirbelthiere."

In the first paper, in order to prepare the way, we were compelled to give the *term germ-layer a more precise definition.* We designated as such *a layer of embryonic cells which are arranged like an epithelium and serve for the limitation of the surfaces of the body.* At the close of segmentation there is only **one** *germ-layer present;* namely, the *epithelium of the blastula. The remaining germ-layers arise from it by the processes of invagination and evagination. The inner germ-layer is formed by means of gastrulation, the two middle germ-layers by the formation of the body-cavities, in that two body-sacs are evaginated from the cœlenteron, and grow out between and separate the two primary germ-layers.* There are, in the first place, animals which are formed of two germ-layers, and possess in their bodies only *one* cavity, a cœlenteron, produced by invagination (Cœlenterata and Pseudocœlia), and, secondly, animals with four germ-layers, a secondary intestine, and a body-cavity derived from the cœlenteron—an enterocœl. To the two-layered animals belong the Cœlenterates and the Pseudocœls, but all four-layered animals are Enterocœls.

From this standpoint we endeavored to prove that hitherto there had been confused under the conception "middle germ-layer" two things which are genetically, morphologically, and histologically entirely different.

Besides the cell-layers which arose by invagination there had been assigned to the middle germ-layer cells which detach themselves individually from the primary germ-layers, and give rise between the epithelial layers of the body to the sustentative substances, and also to the blood, when such exists. Embryonic cells of that kind, which are formed by emigration into the space surrounded by the germ-layers, we named the *mesenchymatic* germ, and the tissue produced from them *mesenchyme.* This occurs as well in two-layered as in four-layered animals. In our opinion a sharp distinction must be made between the formation of germ-layers, which is correlated with the morphological differentiation of the body, and the formation of mesenchyme,—which will especially engage our attention in one of the next chapters,—if clearness and a uniform principle are to be introduced into the whole germ-layer theory.

In the second article it was our aim to show that in the Vertebrates a middle germ-layer is developed by infolding. For that purpose the development of Amphibia, Fishes, Reptiles, Birds, and Mammals was compared with the development of Amphioxus, and thus was acquired the foundation upon which is based the account of the development of the middle germ-layer given in the preceding chapter.

After the publication of these two papers, there appeared numerous articles by van Beneden, Duval, Heape, Hoffmann, Kölliker, Kollmann, Rabl, Rückert, Strahl, Waldeyer, and others, through which valuable facts concerning the development of the middle germ-layer in the different classes of Vertebrates have been made known. In some of these the chief points of view of the cœlom-theory were in general recognised as correct, attempts were made to modify details, but especially was the question of the formation of the mesenchyme of the Vertebrates actively discussed.

The mechanical principle of the process of development, by means of which the germ-layers are formed, and out of these the separate organs, is appreciated in its full significance by only a few, and in text-books particularly has not been adequately presented.

Among the founders of the germ-layer theory, Pander best comprehended this principle. "The blastoderm," he says in one place, "forms, exclusively through the simple process of folding, the body and the viscera of the animal. A delicate thread attaches itself as the spinal cord to it, and scarcely has this taken place, when the blastoderm sends the first folds, which themselves necessarily designate the position of the spinal cord, as an envelope over the exquisite filament, thus forming the first foundation of the body. Hereupon it produces new folds, which, in contradistinction to the first, give shape to the abdominal and thoracic cavities, together with their contents. And for the third time it sends out folds to envelop in suitable membranes the fœtus, which is formed out of it and by means of it. Therefore it need not surprise any one if, in the course of our narration, so much is said about folds and envelopes." And in order to avoid misunderstandings he adds in another place the important statement that "wherever anything is said about the folds of the skin, one is not to imagine a lifeless membrane, whose mechanically produced folds would necessarily spread themselves over the whole surface, without allowing themselves to be limited to a definite space. The folds which cause the metamorphosis of the skin are rather themselves of organic origin, and are produced at the appropriate place, either through increase in the size of the spherules already present there, or through an accession of new spherules, without the remaining part of the blastoderm being thereby altered."

PANDER's successors have expressed themselves concerning the mechanism of foldings much less clearly; the most of them, indeed, not at all. The whole doctrine was in fact condemned by RUDOLPH WAGNER as positively erroneous. "It will occur to no one," he says in his "Lehrbuch der Physiologie," "to imagine the three germ-layers to be like the leaves of a book. No one will entertain the mechanical conception that the embryo arose by a folding process of these three layers."

After PANDER, LOTZE was the next to be occupied with the "Mechanik der Gestaltbildung," as has been pointed out by RAUBER in a meritorious history of this topic. He designates "unequal growth" or "unequal vegetation" as the cause of the changes of place, which in part only appear to be shiftings, out-pocketings, invaginations, or extensions, but in part are actually such, being brought about in this way by mechanical traction and pressure.

In very recent times HIS has prosecuted the study of embryology from the mechanico-physiological standpoint more intensely than all his predecessors, and has also particularly emphasised the significance of the process of folding for the formation of the body. The two principal writings of HIS in this connection are: "Untersuchungen über die erste Anlage des Wirbelthierleibes" (1868), and "Unsere Körperform und das physiologische Problem ihrer Entstehung" (1874). While I refer for details to the original papers, I remark that, notwithstanding manifold agreements, I cannot in important points assent to HIS's view. When, for example, HIS (1874, p. 50) seeks to reduce the mechanics of form to the simple problem of the form-changes in an unequally stretched elastic plate, in my opinion he overlooks the fact that a plate composed of cells, even if it possess elastic properties, is, nevertheless, a much more complicated structure, and that the processes of folding and evagination are primarily produced by the energy of the growth of special groups of cells, and are therefore not to be compared with the bendings and stretchings of elastic plates. As PANDER has already emphatically stated, one is not to imagine in the folding processes a lifeless membrane, but rather the folds are themselves of organic derivation, called forth at the proper place by a cell-multiplication at that place. For this reason, too, HAECKEL in his polemic, "Ziele und Wege der heutigen Entwicklungsgeschichte," has attacked this method of treating embryology, introduced by HIS.

That the morphological differentiation of the animal body primarily rests upon a process of folding of epithelial lamellæ, my brother and I have endeavored, by means of an abundant series of observations, to demonstrate in a still more exhaustive manner than our predecessors. In our "Studien zur Blättertheorie" we have, in the first place, directed attention to the Cœlenterates as the animal organisms in which the principle of the formation of folds is most clearly shown throughout the whole organisation, even into details; and, secondly, we have endeavored to establish for Vertebrates that organs like the body-cavity, chorda, and primitive segments, which it was claimed arose by a separating and splitting of cell-layers, likewise come into existence through the typical process of foldings and constriction.

Finally we have endeavored to point out a physiological cause for the unequal growth of a cell-membrane, and have found such in the Cœlenterates in the unlike functional activity of its various regions. Parts of a membrane will grow more rapidly and must become infolded, when in consequence of their position they are called upon to accomplish more than neighboring regions.

In concluding this historical sketch attention should be called to the fact that C. E. VON BAER, in the general discussion of embryological processes, was the first to distinguish clearly between the events of morphological differentiation, which take place in the beginning of development, and those of physiological differentiation, which occur later.

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CHAPTER VIII.

DEVELOPMENT OF THE PRIMITIVE SEGMENTS.

THE more one pursues the development of Vertebrates into later stages, the more numerous become the changes which simultaneously appear in the different regions of the embryonic body. We cannot here undertake to describe step by step the processes which are simultaneously accomplished, for by that method the presentation would become fragmentary and the comprehension of the separate processes would be made more difficult; but it is necessary, in the interest of a didactic method, to select from all the manifold phenomena a single process of the development, and to follow it up until it has come to a preliminary termination.

After the formation of the middle germ-layer two important processes take place in the embryonic fundament. One process leads to a division of the middle germ-layers into the two lateral plates and into two series of cuboidal bodies, which are situated at the right and the left of the chorda, and which, under an erroneous interpretation, were formerly called *protovertebræ*, but for which one should now substitute exclusively the more accurate name *primitive segments* [mesoblastic somites]. The other process, which occurs at about the same time, at least in the case of the higher Vertebrates, leads to the origin of those cells from which the sustentative substances and the blood of Vertebrates are derived.

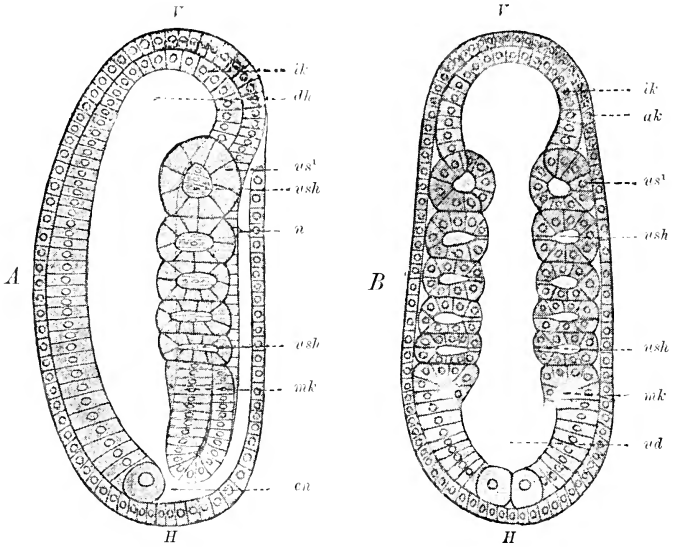

Fig. 103.—Amphioxus embryo with five pairs of primitive segments in optical section, after Hatschek.

A Seen from the side. *B* Seen from the dorsum.

In figure *B* are indicated the openings of the cavities of the primitive segments into the intestinal cavity, which can be seen by deeper focussing. *V*, Anterior, *H*, posterior end; *ak*, outer, *ik*, inner, *mk*, middle germ-layer; *dh*, intestinal cavity; *n*, neural tube; *cn*, neurenteric canal; *us*¹, first primitive segment; *ush*, cavity of primitive segment; *ud*, cœlenteron.

In this chapter we shall take into consideration the *formation of the primitive segments* first in the eggs of Amphioxus and the Amphibians, and then in those of Fishes, Birds, and Mammals.

In Amphioxus the formation of the primitive segments is more nearly simultaneous with the development of the middle germ-layer than in the remaining Vertebrates. As soon as the two cœlomic sacs begin to grow out from the cœlenteron at the front end of the embryo, there begins a division of them into two rows of small sacs lying one behind the other (fig. 103 *A*, *B*, *us*), and this division proceeds from in front backwards. Here again we have to do with a process of folding, which repeats itself many times in the same manner.

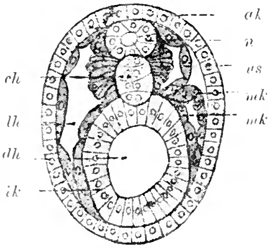

Fig. 104.—Cross section through the middle of the body of an Amphioxus embryo with 11 primitive segments, after Hatschek.

ak, Outer, *ik*, inner germ-layer ; mk^1, parietal, mk^2, visceral lamella of the middle germ-layer ; *us*, primitive segment ; *n*, neural tube ; *ch*, chorda ; *lh*, body-cavity ; *dh*, intestinal cavity.

The wall of the groove-like cœlomic evagination, composed of cylindrical cells, becomes, at a little distance from its head-end, folded transversely to the longitudinal axis of the embryo ; this fold grows from above and from the side downwards into the body-cavity ; in the same manner a second transverse fold is soon formed on either side of the body at a little distance behind the first ; behind the second a third, a fourth, and so on, at the same rate as that at which the embryonal body elongates and the fundament of the middle germ-layer increases by the progress of the evagination toward the blastopore.

In the embryo represented in fig. 103 five sacs may be counted on either side of the body. The evagination is taking place at the region marked *mk* ; it advances still farther toward the blastopore and gives rise to a considerable series of primitive segments, the number of which in a larva only twenty-four hours old has already increased to about seventeen pairs. The primitive segments exhibit at first an opening, by means of which their cavities (*ush*) are in communication with the intestinal cavity. But these openings soon begin to be closed in succession, by their margins growing toward each other and then coalescing; this takes place in the same sequence as that in which the detachment of the parts takes place, from before backwards. At the same time the primitive segments (fig. 104) gradually spread out both dorsally and ventrally, while their cells increase in number and become altered in form. They grow upward more and more at the side of the neural tube, which has meanwhile detached itself completely from its matrix, the outer germ-layer.

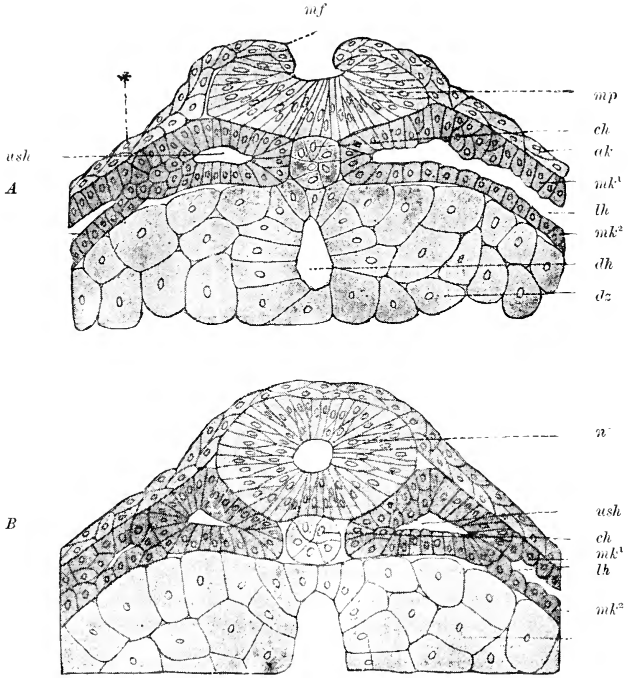

Fig. 105—Two cross sections through a Triton embryo.

A, Cross section through the region of the trunk in which the neural tube is not yet closed an the primitive segments begin to be constricted off from the lateral plates.

B, Cross section through the region of the trunk in which the neural tube is closed and the primitive segments have been formed.

mf, Medullary folds; *mp*, medullary plate; *n*, neural tube; *ch*, chorda; *ak*, outer, *ik*, inner germ-layer; mk^1, parietal, mk^2, visceral middle layer; *dh*, intestinal cavity; *lh*, body-cavity *ush*, cavity of primitive segment; *dz*, yolk-cells.

Toward the ventral side they insert themselves between the secondary intestine and the outer germ-layer.

Finally, it might be further mentioned here that at a still later stage, as is to be seen on the right side of fig. 104, the dorsal portions of the primitive segment are constricted off from the ventral. The former lose their lumina and furnish the transversely striped musculature of the body, but from the cavities of the latter originates the real unsegmented body-cavity, since the partitions which at first separate them become thinner, break through, and finally disappear.

Similar processes take place in a somewhat modified manner in the case of the remaining Vertebrates.

In the Tritons the middle germ-layer (fig. 105 *A*) becomes thickened on both sides of the chorda (*ch*) and of the fundament of the central nervous system (*n*), which is not yet closed into a tube, and at the same time there appears a cavity (*ush*) in its thickened part, caused by the separation of the visceral and parietal lamellæ. The thickening is not produced by an increase in the number of the layers of cells, but simply by the fact that the cells increase in height and grow out into long cylinders, which are arranged around the cavity like an epithelium. We distinguish these thickened parts of the middle germ-layer, which lie on either side of the chorda and the nervous system, as the *primitive-segment plates*, from the lateral parts, or the *lateral plates*. In the territory of the latter the cells are lower, and ordinarily there is no distinctly marked cavity between visceral and parietal layer.

Whereas in Amphioxus the process of forming somites extends itself over the whole of the middle germ-layer, in the case of the Amphibians, and likewise all the remaining Vertebrates, it affects only the part which is next to the chorda and the neural tube, leaving the lateral plates, on the contrary, untouched. The segmentation begins at the head-end, and proceeds slowly toward the blastopore; it is accomplished by folding and constricting off. The epithelial lamella next to the neural tube and the chorda, being composed of cylindrical cells, is raised up into small transverse folds, which, separated from each other by intervals of uniform size, grow into the cavity of the primitive-segment plate, and give rise to small sacs lying one behind the other (fig. 106).

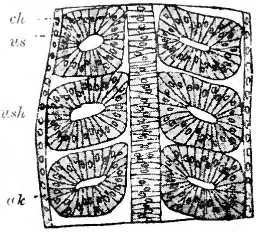

Fig. 106.—**Frontal section through the dorsum of an embryo Triton with fully developed primitive segments.**
One sees on both sides of the chorda (*ch*) the primitive segments (*us*) with their cavities (*ush*).

Soon afterwards each little sac is constricted off from the lateral plates (fig. 105 *A* and *B*). Consequently one now meets, both in transverse and frontal sections at the right and left of chorda and neural tube, cubical sacs the walls of which are formed of cylindrical cells; these sacs are everywhere surrounded by a fissure-like space, and they enclose a small cavity (the primitive-segment cavity), which is a derivative of the body-cavity. From the front layer of the fold is produced the posterior wall of the newly formed segment, from its posterior layer the front wall of the remnant of the primitive-segment plate, or of the sac which is next to be constricted off.

Of the Vertebrates which are developed out of meroblastic eggs, the Selachians appear to exhibit most clearly the original mode of the formation of primitive segments. A distinct body-cavity is formed on either side of the trunk by the separation of the parietal and visceral lamellæ of the middle germ-layer (fig. 110). The dorsal portion of the cavity, which flanks the neural tube, acquires thickened walls (*mp*), and corresponds to the part previously designated as the primitive-segment plate, which at the same time with the appearance of the body-cavity begins to be divided into primitive segments. In the anterior part of the body a series of transverse lines of separation become visible (fig. 195 mp^1), the number of which is continually increased toward the hind end of the body. For a long time the cavities of the primitive segments, which are separated from one another by these transverse furrows, remain in communication ventrally with the common body-cavity by means of narrow openings. One may therefore describe this state of affairs by saying that the body-cavity is provided toward the back of the embryo with a series of small sac-like evaginations, which lie close together one after the other. Afterwards the primitive segments are entirely constricted off from the body-cavity, and then their thickened walls come into close contact, and thus cause the disappearance of the cavities of the segments (fig. 111 *mp*).

Whereas in the Selachians it is still evident that the formation of the primitive segments depends upon folding and constricting off, the process is obscured even to obliteration in the case of Reptiles, Birds, and Mammals; this is referable simply to the fact that the two lamellæ of the middle germ-layer remain for a long time firmly pressed together, only subsequently beginning to separate, and that they are composed of several layers of small cells. *The process of folding and constricting off appears here as a splitting up of a solid cell-plate into small cubical blocks.*

The part of the middle germ-layer that is next to the chorda and neural tube appears in a cross section of a Chick embryo (fig. 107) as a compact mass (*Pv*) consisting of many superposed small cells, which, as far as it is not divided up into separate blocks, is designated as primitive-segment plate or protovertebral plate. In fig. 107 it is still connected at the side by means of a thin isthmus of cells with the lateral plates, in whose territory the middle germ-layers are thinner and separated from each other by a fissure.

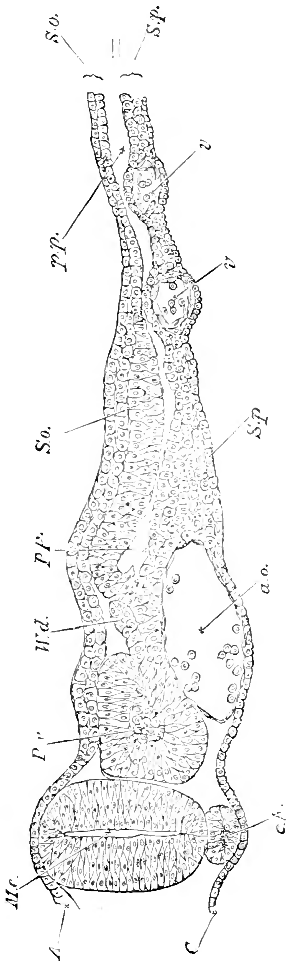

Fig. 107.—Cross section through the dorsal region of an embryo Chick of 45 hours, after Balfour.
The section shows the middle germ-layer partially separated into the primitive segment (*Pv*) and the lateral plate, which embraces within it the body-cavity (*up*).
Mc, Medullary tube; *Pv*, primitive segment; *So*, somatopleure; *Sp*, splanchnopleure; *up*, body-cavity (pleuroperitoneal cavity); *ch*, chorda; *A*, outer germ-layer; *C*, inner germ-layer; *ao*, aorta; *v*, blood-vessel; *Wd*, Wolffian duct.

In observing the blastogerm from the surface the region of the primitive-segment plates, as is to be seen in the posterior part of a nine-days-old Rabbit embryo (fig. 108), appears darker than the region of the lateral plate; so that the two are distinguished from each other; one is stem-zone (*stz*), the other parietal zone (*pz*).

The development of the primitive segments is observable in the Chick at the beginning of the second day of incubation, in the Rabbit at about the eighth day. Clear transverse streaks appear in the stem-zone at some distance from the primitive streak, about in the middle of the embryonic fundament, both on the right and the left of the chorda and neural tube (fig. 108). They correspond to transverse fissures, by means of which the primitive-segment plates are divided into the small and solid cubical primitive segments (*uw*). In the nine-days-old Rabbit embryo represented in fig. 108 these plates are resolved in front into eight pairs of primitive segments (*uw*), whereas in the hind end of the embryonic area they still have the form of a continuous mass of cells, the stem-zone (*stz*), which in surface-views appears darker than its surroundings.

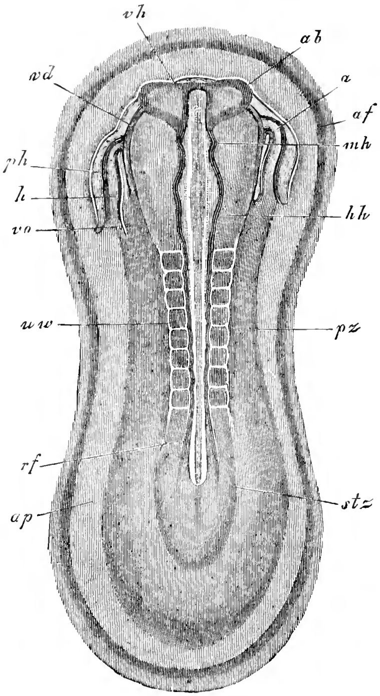

Fig. 108.—Rabbit embryo of the ninth day, seen from the dorsal side, after Kölliker. Magnified 21 diameters.

The stem-zone (*stz*) and the parietal zone (*pz*) are to be distinguished. In the former 8 pairs of primitive segments have been established at the side of the chorda and neural tube.

ap, Area pellucida ; *rf*, medullary groove ; *vh*, fore brain ; *ab*, eye-vesicle ; *mh*, mid brain ; *hh*, hind brain ; *uw*, primitive segment ; *stz*, stem-zone ; *pz*, parietal zone ; *h*, heart ; *ph*, pericardial part of the body-cavity ; *vd*, margin of the entrance to the head-gut (*vordere Darmpforte*), seen through the overlying structures ; *af*, amniotic fold ; *vo*, vena omphalomesenterica.

In a somewhat more advanced stage the primitive segment, which probably secretes at the same time fluid, develops in its interior, as in the case of the Amphibia and Selachii, a cavity, around which the cells group themselves in a radial manner. This cavity, too, is at first in communication laterally with the fissure of the body-cavity, until the primitive segment has been fully constricted off.

In Vertebrates, besides the trunk-region, a part of the head-region of the embryo is also affected by this process of segmentation which we have been considering. We must therefore speak in the one case of head-segments, and in the other of trunk-segments. Up to the present time the number and condition of the head-segments have been made out (by Balfour, Milnes Marshall, and van Wijhe) most accurately for the Selachians. In this instance there are nine pairs of hollow head-segments. In the higher Vertebrates such segments, although fewer in number, have also been described ; however, the less sharply differentiated structures of the latter demand still further investigation.

But, in any event, the accurate study of the earliest embryonic segmentation of the body into a large number of metameres yields this result of the highest importance for the general morphology of the Vertebrate body, that *the head not less than the trunk represents a segmented portion of the body and has in no wise been produced from a single primitive segment.*

SUMMARY.

1. In Vertebrates the middle germ-layers immediately after their origin are differentiated into several fundaments by processes of folding and constricting off.

2. The process of differentiation in the middle germ-layer exhibits two modifications.

(*a*) In Amphioxus the middle germ-layers are, at the time of their first appearance, *completely* separated into primitive segments lying one behind the other.

It is only later that each primitive segment is divided into a dorsal portion (the real primitive segment) and a ventral portion.

The dorsal portion, or primitive segment proper, furnishes the transversely striped musculature of the trunk.

The ventral segments form the body-cavity, which is at first segmented, but afterwards with the disappearance of the partitions becomes a single cavity.

(*b*) In all other Vertebrates the fundaments of the middle germ-layers are divided first into a dorsal and a ventral region—into the primitive-segment plates and the lateral plates.

The *lateral plate* remains unsegmented. The body-cavity, which becomes visible in it by separation of the parietal and the visceral lamellæ of the middle layer, is from the beginning on each side of the body a single space.

The *primitive-segment plate* alone is divided into successive primitive segments.

3. The segmentation of the middle germ-layers also extends over the future head-region of the embryo. One therefore distinguishes—

(*a*) *Head-segments*, the number of which amounts to nine;

(*b*) *Trunk-segments*, the number of which is constantly being increased during the development of the posterior trunk-region.

CHAPTER IX.

DEVELOPMENT OF CONNECTIVE SUBSTANCE AND BLOOD. (THE MESENCHYME-THEORY.)

WITH the question of the origin of connective or mechanically sustentative substance and blood we enter a very difficult field, the cultivation of which has now been taken in hand successfully by many persons. Here also we shall acquaint ourselves with a simple case from the development of Invertebrates, before we begin with the conditions in Vertebrates, which are more difficult to comprehend.

In Cœlenterates and Echinoderms there is developed between the germ-layers, which are composed of epithelial cells, a sustentative tissue. It consists of a homogeneous jelly, in which are scattered a few isolated spheroidal or stellate cells, which are capable of changing position by virtue of their amœboid motion. It is usually developed very early; in the Echinoderms, for example, as early as the blastula-stage (fig. 109).

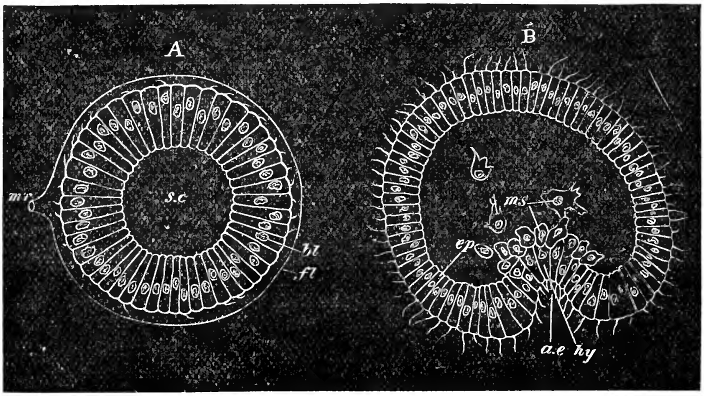

Fig. 109.—Two stages of development of Holothuria tubulosa, in optical section (after SELENKA), from BALFOUR.

A, Blastosphere-stage at the end of cleavage.

B, Gastrula-stage.

mr, Micropyle; *fl*, chorion; *s.c*, segmentation-cavity, in which gelatinous substance is early secreted as a gelatinous core; *bl*, blastoderm; *ep*, outer, *hy*, inner germ-layer; *ms*, amœboid cells arising from the inner germ-layer; *a.e*, cœlenteron (archenteron).

Into the cavity of the blastula (*A*) a homogeneous soft substance, the jelly-core (*s.c*), is secreted by the epithelial cells. Into this jelly there migrate from the epithelium, and indeed from the particular region which at the time of gastrulation is infolded (fig. 109 *B*) as the inner germ-layer (*hy*), numerous cells (*ms*), which loose their epithelial character, and send out processes in the manner of lymph-corpuscles. They soon distribute themselves as migratory cells everywhere in the jelly.

In the gastrula-stage and subsequently, the cell-containing jelly between the outer and the inner germ-layers represents a third sheet, which is distinguished from the latter histologically, and, according to the definition previously given, cannot be designated as a middle germ-layer; for by that definition we understand the term to be limited to a sheet of embryonic cells, having an epithelial arrangement and bounding a surface. The jelly-like sheet is a *product of the germ-layers*, which may be distinguished from them by the name *mesenchyme* or *intermediate layer* (Zwischenblatt).

Once formed, the mesenchyme continues to grow as an independent tissue, in that the cells which at first migrated into the jelly at a definite stage of development, to which one may give the name *mesenchyme-germ*, continue to increase uninterruptedly by means of cell-division. In its growth it penetrates into all the interstices which arise when the germ-layers, as happens in many Cœlenterates, produce the most complicated structures by the formation of folds and evaginations; it furnishes everywhere a support for the epithelial layers which repose upon it. At the same time some of the mesenchyme-cells can alter their original histological character as simple trophic or nutritive cells of the intermediate substance. Thus here and there they differentiate contractile substance at their surface, and become, as is to be seen in Ctenophores and Echinoderms, smooth muscle-cells, the ends terminating either in *one* fine point, or dividing themselves into *several* processes, as is more frequently the case with Invertebrates.

In Vertebrates also, after the two primary germ-layers have arisen, a process similar to that which we have just considered appears to lead to the formation of connective tissue and blood, two tissues which correspond morphologically and physiologically to the mesenchyme of Invertebrates.

In the first two editions of the "Lehrbuch" I set forth that the whole mesenchyme-question in the Vertebrates was still in a nascent condition, that the account therefore presented nothing final, but bore in many respects the *character of the provisional.* Since that time an essential advance has been made in this field. Thanks to the investigations of HATSCHEK and RABL, of RÜCKERT, ZIEGLER, and VAN WIJHE, we have acquired more accurate explanations concerning the origin of the connective substances; the question of the origin of the vascular endothelium and of the blood, on the contrary, is one that is less cleared up. This determines me to treat the two questions separately in the following account.

A. The Origin of the Connective Tissues.

Selachian embryos appear to be the most suitable objects on which to trace the origin of the connective substances. Here the *middle germ-layer* serves as the matrix for the mesenchymatic tissue. At the time when the primitive segment is still connected below with the lateral plates, and when the body-cavity is visible in the latter, there appears a cell-growth at the lower border of each primitive segment on the side which is directed toward the chorda. It is ordinarily designated as *sclerotome*. It contains at first a small evagination of the body-cavity (fig. 258 *A sk*). At the restricted place designated, which is marked off from its surroundings, and which recurs on each primitive segment, cells in large numbers (fig. 110 *sk*) individually detach themselves from the epithelial layer, remove by active migration from their place of origin, like the mesenchymatic cells of Invertebrates, and distribute themselves in the space which is limited on the one side by the inner wall (*mp*) of the primitive segment, and on the other by the chorda (*ch*) and the neural tube (*nr*).

At the time of their appearance the amœboid cells are separated by only a small amount of inter-cellular substance: they increase rapidly in number, and thereby soon crowd chorda, neural tube, and primitive segment farther apart (fig. 111). The segmental arrangement which the growths exhibit at their first appearance (fig. 195 *Vr*) very early ceases to exist, since by their extension they become fused together into a continuous sheet.

The mesenchyme, which thus grows forth out of the middle germ-layer on both sides of the chorda, furnishes the *foundation for the whole axial skeleton*; it produces the skeletogenous tissue by the growing toward each other and the fusion of the masses which are formed on the right and left sides. As fig. 111 shows, the mesenchyme (*sk*) grows around the chorda (*ch*) both dorsally and ventrally, and envelops it with a connective-tissue sheath, which is continually becoming thicker. In the same manner it encloses the neural tube (*nr*) and forms the membrana reuniens superior of the older embryologists, the foundation out of which subsequently the connective-tissue envelopes of the neural tube and the vertebral arches with their ligaments are differentiated.

Conditions similar to those of Selachians are also to be observed, although less distinctly, in Reptiles, Birds, and Mammals; they have been described by Remak, Kölliker, and others, and have been brought into connection with the formation of the vertebral column. The primitive segments, which are at first solid, soon acquire a small cavity (fig. 116), around which the cells are arranged into a

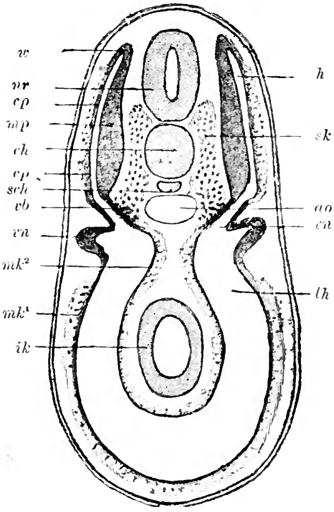

Fig. 110.

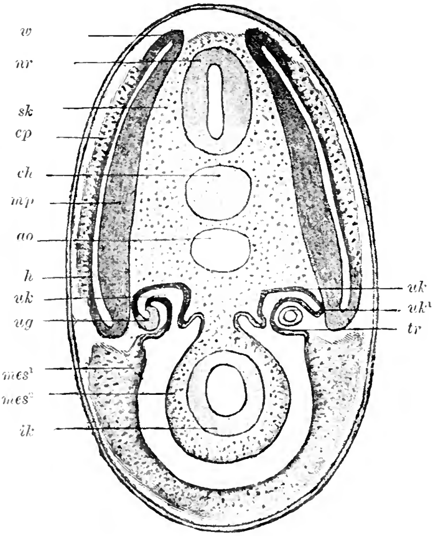

Fig. 111.

Figs. 110 and 111.—Diagrams of cross sections through younger and older Selachian embryos to illustrate the development of the principal products of the middle germ-layer. After van Wijhe, with some changes.

Fig. 110.—Cross section through the region of the pronephros of an embryo, in which the myotomes (*mp*) are in process of being constricted off.

Fig. 111.—Cross section through a somewhat older embryo, in which the myotomes have just been detached.

nr, Neural tube; *ch*, chorda; *ao*, aorta; *sch*, subnotochordal rod; *mp*, muscle-plate of the primitive segment; *w*, zone of growth, at which the muscle-plate bends over into the cutis-plate (*cp*); *vb*, portion connecting the primitive segment with the [walls of the] body-cavity, out of which are developed, among other things, the mesonephric tubules *uk* (fig. 111); *sk*, skeletogenous tissue, which arises as an outgrowth from the median wall of the connecting portion (*vb*); *vn*, pronephros; mk^1, parietal, mk^2, visceral middle layer, from the walls of which mesenchyme is developed; *lh*, body-cavity; *ik*, entoderm; *h*, cavity of the primitive segment; *uk*, mesonephric tubule, arisen from the connecting portion *vb* of the diagram 110; uk^1, place where the mesonephric tubule has detached itself from the primitive segment; *ug*, mesonephric duct, with which the mesonephric tubule has united on the left side; *tr*, union of the mesonephric tubule with the body-cavity (nephridial funnel); mes^1, mes^2, mesenchyme, which has arisen from the parietal and visceral lamellæ of the middle layer respectively.

continuous epithelium. Then a part of the wall of the primitive segment lying at its lower and median angle begins to grow with extraordinary rapidity, and to furnish a mass of embryonic connective tissue, which spreads itself around the chorda and neural tube in the manner previously described. The dorsal and lateral parts of the primitive segment (fig. 116 *ms*), which subsequently loses its cavity, are not involved in this growth; out of them arise principally the fundaments of the trunk-musculature. This part is consequently now distinguished as *muscle-plate* (*ms*).

Mesenchyme arises from three other places of the middle germ-layer besides the primitive segments—from the visceral lamella, from the parietal lamella, and finally from that wall of the primitive segment which is turned toward the epidermis and has been given by Rabl the name *cutis-plate.* Here also the conditions are best followed in Selachii.

Individual cells migrate out from the visceral lamella (Darm-faserblatt), which in early stages is composed partly of cubical, partly of cylindrical cells (fig. 110 mk^2), and distribute themselves upon the surface of the entodermic layer; they are found at places where no trace of a vessel is observable. They furnish the mesenchyma of the intestinal wall, which is ever becoming more abundant, and which is subsequently converted partly into connective tissue, partly into the smooth muscle-cells of the tunica muscularis (fig. 111 mes^2).

A similar process is repeated in the parietal lamella (Haut-faserblatt). Emigrating cells produce between the epithelium of the body-cavity and that of the epidermis an intermediate layer of mesenchyme-cells (fig. 110 mk^1, fig. 111 mes^1).

An important region for the production of connective tissue is, finally, the cutis-plate, *i.e.*, the epithelial layer of the original primitive segment, which is in contact with the epidermis (fig. 110 *cp*). The process occurs here later than at the other places mentioned, and begins with an active cell-growth, which gradually leads to a complete disintegration of the epithelial lamella. "The disintegration," as Rabl remarks, "proceeds in such a manner that the cells, which hitherto exhibited an epithelial character, separate themselves from one another, and thereby lose their epithelial character." It is probably from this part of the mesenchyme that the corium is derived.

That the mesenchyme-cells scattered between the epithelial lamellæ are capable of executing extensive migrations, after the fashion of migratory cells, is perhaps best shown in the investigation of transparent embryos of Bony Fishes. "One sees distinctly," thus WENKEBACH describes it, "how the cells by means of amœboid motions, and of sometimes extraordinarily long protoplasmic processes, move themselves about independently in the body of the embryo and upon the yolk, which is not yet clothed with hypoblast, and creep toward definite places, as if they acted voluntarily and consciously." By virtue of this peculiarity, the mesenchyme-cells actively penetrate into all larger and smaller fissures which exist between the germ-layers and the fundaments of organs which have arisen from them. Everywhere they form a filling and connecting mass between these structures, which afterwards acquires a still greater importance as the bearer of blood- and lymph-courses as well as nerves.

In comparison with the earlier editions of the "Lehrbuch," I have here given an essentially different presentation of the development of the mesenchyme. Formerly, supported by the investigations of HIS, WALDEYER, KOLLMANN, and others on meroblastic eggs, I thought it necessary to refer the chief source of the mesenchyme to a limited territory of the germ, to the area opaca, and made the cell-material arise by delamination from the entodermic layer, especially from the yolk-wall. But now I assume a manifold origin from various regions of the middle germ-layer. Thus I come back again to an interpretation which I had already propounded as probable in "Die Cœlomtheorie" (p. 80) and "Die Entwickelung des mittleren Keimblattes" (p. 122),—to the interpretation, namely, that mesenchyme-germs in Vertebrates are perhaps formed by an emigration of cells at several distinct places at the same time. Whether this or that be the real mode, the essence of the mesenchyma-theory is not thereby affected, for the essential part of that theory consists in this, that it establishes in the earliest development of tissue a contrast between the epithelial germ-layers and a packing tissue, produced by a dissolution of the epithelial continuity, which spreads itself out between the germ-layers, and soon appears as an independent structure.

Indeed, with this theory as a basis, it would not be surprising if *the production of mesenchymatic tissue should not be limited simply to the middle germ-layer, and if the entoderm by the contribution of cell-material should participate in its formation.*

B. The Origin of the Vascular Endothelia and the Blood.

The question of the origin of the tissues represented in the above heading is one of the most obscure in the realm of comparative embryology. The very investigators who have endeavored most recently and with the most reliable methods to elucidate this matter do not hesitate to emphasise the uncertainty in the interpretation of the conditions presented to them. Even the lowest Vertebrate, which is distinguished by the greater simplicity of its structure, and by the greater ease with which all its processes of development are understood, has failed us in this question. For HATSCHEK, who knows the development of Amphioxus better than any one else, designates the blood-vessels as the only system of organs concerning which he was unable to arrive at a clear understanding.

Consequently in the field now to be examined there are many views and observations which in part stand in the most direct antagonism to each other. To give a comprehensive review of them is not possible without the greatest fulness, which would be contrary to the plan of this Text-book; I therefore limit myself, first, to giving a survey of the various possibilities by which the origin of the vessels and the blood might take place, and, secondly, to presenting a series of observations which have been made on Selachians, Birds, and Mammals; still it is always to be kept in mind that much remains doubtful here, and that coming years may bring about many a change in our interpretations.

According to one view, the vascular cavities are developed out of fissure-like spaces between the germ-layers which remain unoccupied at the time the fundament of the mesenchyme is produced. These cavities acquire a boundary in this way: the neighboring mesenchyme-cells begin to penetrate into them, and then unite into a vascular endothelium. "The system of blood-vessels and that of lymphatic vessels," observes ZIEGLER, "are produced in their first fundaments from remnants of the primary body-cavity (the space between the primary germ-layers), which at the general distribution of the formative tissue (mesenchyma) remain behind as vessels, lacunæ, or interstices, and are enclosed by that tissue and incorporated in it." The formed elements [corpuscles] arise at separate places in the blood-courses by the growth and detachment of mesenchymatic cells.

According to another view, the vessels are constructed in this manner: cells in the mesenchymatic tissue arrange themselves in rows, and these cell-cords become hollowed out; thereby the more superficial cells furnish the endothelial wall, whereas the remaining cells become blood-corpuscles. The blood-vessels are therefore nothing else than cavities which have been secondarily produced in the mesenchymatic tissues by means of their own cells. Both views agree in this, that they cause the group of sustentative substances to be brought into genetic connection with the blood, and the latter to figure as a product of the metamorphosis of the mesenchyma.

Moreover, both views may present variations in the details, according as they ascribe to the mesenchyme a different origin and make it arise either out of the middle germ-layer alone, or out of the entoblast alone, or by the migration of cells out of both layers and their union into a single fundament. Still other variations result from the first fundament of the blood-course being sometimes referred to a limited territory of the germ, sometimes to several places. Thus, for the meroblastic eggs of Birds, the area opaca is designated by some observers as the place where vessels and blood are first formed. From here they grow out as it were at first into the embryonic body proper. The opposite is reported of Bony Fishes, in which the first vessels, heart, aorta, caudal veins, and sub-intestinal veins, together with blood-corpuscles, arise earliest in the embryonic body itself, whereas they appear on the yolk only subsequently. Finally, for the Selachians a local origin of the vessels is maintained both for the area opaca and also for the embryonic body in the restricted sense.

In opposition to the two views hitherto presented, a third view assumes a separate origin for the connective substances on the one hand, and for the vascular endothelium and the blood on the other. Whereas the former are produced by the emigration of cells from the middle germ-layer, the vascular endothelium is maintained to arise from cells of the entoblast. It is held that an endothelial sac is formed (perhaps by constriction) as an independent fundament, which by budding gives rise to the whole vascular system.

After this brief survey of the various possibilities concerning the origin of the blood-course, I turn to a description of certain conditions, concerning the signification of which it must be admitted that the views are also often very divergent.

The *area opaca of the meroblastic eggs* of Fishes, Reptiles, and Birds has always played an important rôle in the literature on the question of the origin of the blood. Notwithstanding the frequency with which it has been investigated, the researches concerning it cannot be regarded as concluded. It is from this standpoint that I beg the reader to judge what follows.

In the case of the Chick, on which especially we shall base our account, the opaque area is composed of only the two primary germ-layers at the time when the middle germ-layer begins to be formed from the region of the blastopore by the production of folds.

The outer germ-layer, as has already been described in Chapter V., has in general a simple structure, since it is composed of a single layer of small cubical cells. The inner germ-layer (fig. 56 *ik* and fig. 112), on the contrary, alters its condition the more we approach the margin of the disc. In the area pellucida and in the immediately surrounding parts it appears as a single layer of greatly flattened cells, and is separated from the yolk-floor by a cavity filled with an albuminous fluid; in the opaque area it reposes directly upon the yolk; its cells here become higher, cubical, or polygonal, and finally it terminates with a greatly thickened marginal zone, the previously mentioned yolk-wall (*dw*). This is the important region of the germ with which we now have especially to deal.

The yolk-wall consists in the Chick partly of embryonic cells, which are separable from one another, partly of yolk-material in which are enclosed numerous large and small nuclei enveloped in protoplasm (the merocytes), as at the final stages of the process of cleavage.

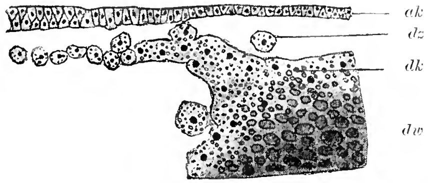

Fig. 112.—Section through the margin of the germinal disc of a Hen's egg incubated for six hours, after Duval. *ak*, Outer germ-layer; *dz*, yolk-cells; *dk*, yolk-nuclei; *dw*, yolk-wall.

Such free nuclei have also been demonstrated with perfect certainty in the marginal territory of the yolk during the course of the formation of the germ-layers in Selachians, Teleosts, and Reptiles (Kupffer, Hoffmann, Rückert, Strahl, Swaen).

The most accurate description of the yolk-nuclei has been given by Rückert for the eggs of Selachians (fig. 113). They are present in this case at the marginal portion of the germ-disc, embedded in the yolk in not inconsiderable numbers, and are remarkable for their size, sometimes reaching a diameter ten-fold as great as that of an ordinary nucleus (k^1, k^*). From the protoplasm enveloping the nucleus k^* there proceeds a richly branched network of processes. In the interstices of the net are lodged yolk-elements (*d*) in great numbers, from the size of the ordinary yolk-plates down to the finest granules. The former are often in process of disintegration. One may conclude from this, as well as from other phenomena, that a vigorous consumption of deutoplasm is taking place at the margin of the germ. This deutoplasm is taken up as nutritive material by the protoplasmic net surrounding the nucleus, and employed by means of intra-cellular digestion for its growth. Consequently one also sees the yolk-nuclei in active increase.

Toward the surface of the yolk small clusters of nuclei (fig. 113 *k*) arise out of the large deeper-lying yolk-nuclei. From these there are finally produced genuine cells of the germ (*z*), by the small nuclei surrounded by a layer of protoplasm detaching themselves from the yolk, as it were by an act of supplementary cleavage. "*Since the merocytes thus on the one hand uninterruptedly take up nutritive material out of the yolk, and on the other continually surrender it in the form of cells to the germ-layers of the nascent embryo, they present an important link between the latter and the yolk.*" (RÜCKERT.)

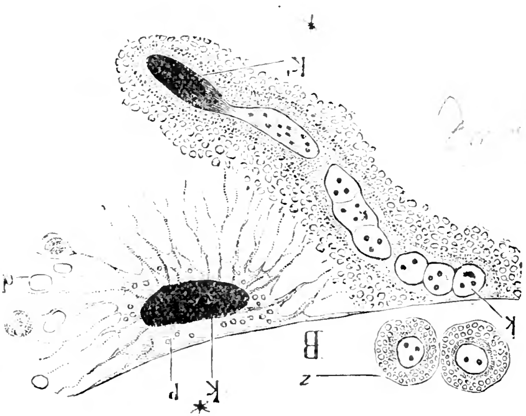

Fig. 113.—Yolk-nuclei (merocytes) from Pristiurus, lying underneath the germ-cavity *B*, after RÜCKERT.

z, Embryonic cells; *k*, superficial clear nuclei; *k'*, deeper nuclei; *k**, marginal nuclei rich in chromatin, largely freed from the surrounding yolk, in order to show the processes of the protoplasmic mantle; *d*, yolk-plates.

The views of investigators on the significance of the yolk-wall and of the merocytes enclosed in it are very divergent. Indeed there is unanimity only in this, that the yolk-wall contributes to the increase of the lower germ-layer by single cells becoming independent and attaching themselves at the margin to the elements which already have an epithelial arrangement. On the other hand it appears less certain how far the yolk-wall is concerned in the formation of the blood. According to the observations of HIS, DISSE, RAUBER, KOLLMANN, RÜCKERT, SWAEN, GENSCH, HOFFMANN, and others, it does share in this process during a limited period of development in the case of Selachians, Teleosts, Reptiles, and Birds.

In the Selachians the anterior margin of the germ-disc is the first to be metamorphosed into a vascular zone. RÜCKERT could find here numerous and unequivocal indications that the previously described peculiar cell-elements of the yolk (merocytes) provided with large nuclei contribute to the formation of blood-islands, in that they break up into clusters of small cells, detach themselves from the yolk-containing part of the lower germ-layer, and become differentiated on the one hand into the migratory cells of the first blood-vessels, and on the other into the blood-corpuscles. **Rückert** further maintains that the *material destined for the production of blood is supplemented by means of cells freshly cleft off from the yolk.*

Swaen remarks with the same positiveness, "Les premiers îlots sanguins se développent *aux dépens des éléments de l'hypoblaste.* Ces derniers constituent à la fin de ce développement les parois de cavités vasculaires closes et les cellules sanguines qui les remplissent." Likewise **Gensch** makes the large cells in the yolk responsible for the formation of the blood in the case of the Bony Fishes. **Hoffmann** also finds in Reptiles that the blood and the endothelial wall of the vessels, as well as the spindle-shaped cells which lie between the vessels, are a product of the inner germ-layer, and that they appear at definite places of the germ-disc at a time when the middle germ-layer has not yet been formed in those regions.

Finally, it is stated concerning the germ of the Chick that at the end of the first day of incubation the cells in the yolk-wall have become very numerous, through the multiplication of the nuclei enclosed in the latter, and that afterwards the abundance of the cells diminishes. For part of the cells which have been formed by the active proliferation now detach themselves from the yolk-wall, get into the space between the outer and inner germ-layers, and there produce a third independent layer, which is continually increasing in thickness, whereas the remaining part becomes modified into an epithelium of large cylindrical cells containing yolk-granules. This middle layer is judged by several investigators to be an independent fundament of the germ, and has in this sense been described by **His** as *parablast*, by **Disse** and others as *vascular layer*, by **Rauber** as *desmohæmoblast*, and by **Kollmann** as marginal germ or *acroblast.*

All of these accounts need still more precise confirmation, since they have often been called in question, even up to most recent times. Thus **Kölliker** has always defended the position that not only the connective substances, but also the vessels and the blood, are products of the middle germ-layer, and are generated by it in its peripheral regions. **Kastschenko**, in his study of the Selachii, could not convince himself that the merocytes have special importance in the formation of blood and vessels, but was not, however, willing to deny it. So much the more positively do Wenkebach and Ziegler, on the strength of their investigations on Teleosts, express themselves against the mode of blood-formation given by Gensch. According to Ziegler, the blood-corpuscles are developed in the blood-vessels of the embryonic body itself. The free nuclei of the yolk, the merocytes, on the contrary, it is maintained, do not share in the formation of embryonic tissues, but, in adaptation to the function of resorbing the yolk, undergo peculiar modifications, which "cause the frequently affirmed but never proved production of blood-corpuscles [by them] to appear improbable."

Under this condition of affairs, I must regard the question of the source of the cell-layer in which, in the region of the opaque area, the formation of blood takes place as not yet ready for final judgment.

So far as regards the further changes, by means of which the cell-layer under consideration is converted into connective substance and blood, on the whole I subscribe, in this difficult field of investigation, to Kölliker's representation.

At the end of the first day of incubation, the masses of cells which lie between the inner and the outer germ-layers arrange themselves in cylindrical or irregularly limited cords, which join themselves together into a close-meshed network; they are the first fundaments both of the vessels and also of their contents, the blood. In the spaces of the net are to be found groups of indifferent cells, which afterwards become embryonic connective tissue, and which are the *Substanzinseln* (fig. 114) of authors.

At the beginning of the second day of incubation, the solid fundaments of the vessels become more distinct, in proportion as they become bounded superficially by a special wall, and acquire an internal cavity. The wall of the vessels is developed out of the most superficial cells of the cords, and is composed during the first days of incubation of a single layer of very much flattened polygonal elements, on account of which the first vessels of the embryo are often designated as *endothelial tubes* (fig. 114 and fig. 115 *gw*).

The cavity of the vessel is probably formed by the penetration of fluid into the originally solid cord from its surroundings, thus forming the plasma of the blood, by which the cells are pressed apart and to the sides. The cells then constitute here and there thickenings of the wall, and project into the fluid-filled cavities as elevations of loosely united spherical elements (fig. 114, Blood-islands). Consequently the vessels which are just becoming permeable are very irregular, since narrow places and wider ones, often provided with evaginations, alternate (fig. 114) with one another, and since the vessels are sometimes wholly excavated, fluid-filled, endothelial tubes, and sometimes remain more or less impassable, owing to the variously formed cell aggregates which project from the wall.

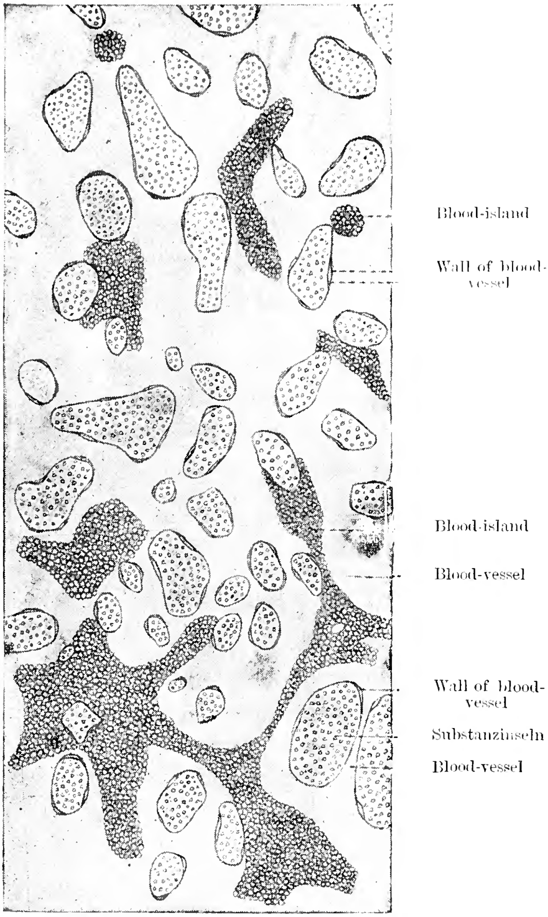

Fig. 114.—A portion of the vascular area of the germ-disc of an embryo Chick, in which 12 primitive segments are developed, after Disse. One sees the more darkly shaded blood-courses, in which lie the "blood-islands," the centres whence the blood-corpuscles arise. The clear spaces in the vascular network, the walls of which are formed of flat endothelial cells, are the "substance-islands" (Substanzinseln).

The aggregations of cells themselves are simply *the centres where the formed components of the blood are produced.* The small spherical nucleated cells, which still enclose dark yolk-granules, become at first homogeneous by the dissolution of the latter, and then, owing to the formation of the coloring matter of the blood in them, they take on a slightly yellowish color, which gradually becomes more intense.

If one at this time examines a blastoderm which has been removed from the yolk, the zone in which the formation of blood takes place appears flecked with more or less intensely colored blood-red spots, some of which are roundish, others elongated, and others branched. The spots are known as the *blood-points* or *blood-islands* of the blastoderm (fig. 114). From these formative areas the superficial cells now detach themselves and enter the blood-fluid as the isolated red blood-corpuscles. Here, as well as in the blood-islands, they multiply by means of cell-division, during which the nucleus is metamorphosed into the well-known spindle-figure.

As REMAK first showed, *divisions of blood-cells* are to be observed in the Chick in great numbers up to the sixth day of incubation, whereas they later become more rare, and then wholly disappear. *Also in the case of Mammals and of Man* (FOL) *the first embryonic blood-corpuscles, which are at this time provided as in the other Vertebrates with a genuine cell-nucleus, possess the power of division.*

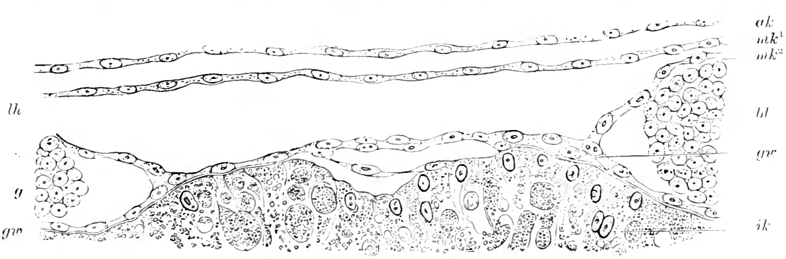

Fig. 115.—Cross section through a portion of the vascular area, after DISSE.
ak, Outer, *ik*, inner germ-layer ; *mk*¹, parietal, *mk*², visceral lamella of the middle germ-layer ; *lh*, extra-embryonic body-cavity ; *gw*, wall of blood-vessel formed of endothelium ; *bl*, blood-cells ; *g*, vessels.

In proportion as blood-corpuscles still further detach themselves from the blood-points, the latter become smaller and smaller, and finally disappear altogether ; but the vessels without exception then contain, instead of a clear fluid, red blood with abundant formed elements (fig. 115 *bl*).

Subsequently there occur changes in the *Substanzinseln* which lead to the formation of *embryonic connective substance.* The germinal cells, at first spheroidal, separate farther from one another, at the same time secreting a homogeneous inter-cellular substance ; they become stellate (fig. 116 *sp*), and send out processes by means of which they are united into a network, which stretches all through the gelatinous secretion ; other cells apply themselves to the endothelial tubes of the vessels.

After the formation of vessels and blood is completed, the territory of the area opaca, in which the processes just described take place, is sharply delimited at its periphery (fig. 117) in all meroblastic eggs, as well as in those of Mammals. For the close network of blood-vessels ends abruptly at its periphery in a broad, circular, marginal vein (the vena or sinus terminalis, *S.T.*).

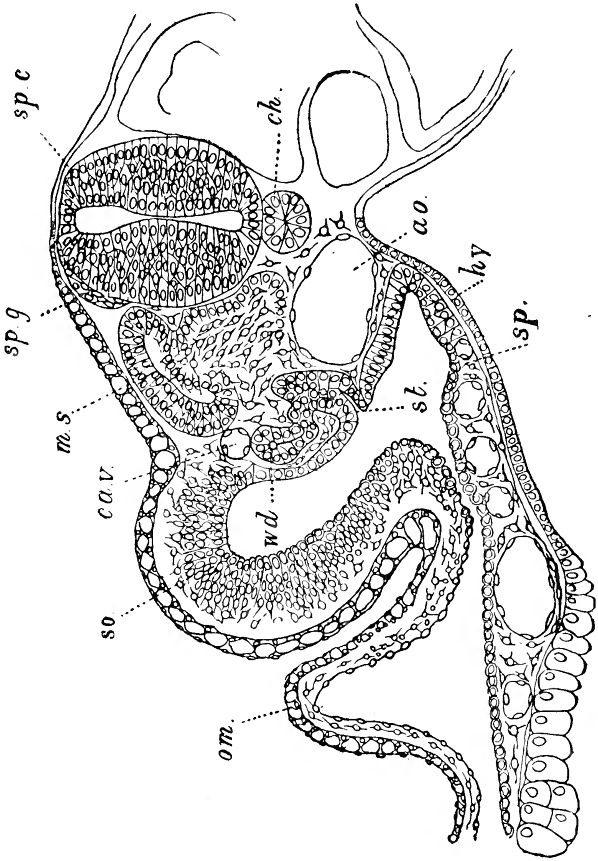

Fig. 116.—Cross section through the trunk of an embryo Duck with about 24 mesoblastic somites, after Balfour. One sees the four original germ-layers, and the organs which have arisen from them, separated from one another by a small amount of embryonic connective substance which contains stellate cells, and likewise the beginnings of blood-vessels.

om, Amnion; *so*, parietal lamella; *sp*, visceral lamella of the middle germ-layer; *wd*, Wolffian duct; *st*, segmental canal; *ca.v*, cardinal vein; *m.s*, muscle-plate; *sp.g*, spinal ganglion; *sp.c*, neural tube (spinal cord); *ch*, chorda; *ao*, aorta; *hy*, inner germ-layer (hypoblast).

Beyond the sinus terminalis, there is formed on the yolk neither blood nor blood-vessels. Nevertheless, the two primary germ-layers spread themselves out laterally over the yolk still farther, the outer layer more rapidly than the inner, until they have grown entirely around it.

We must therefore now distinguish in the opaque area (Plate I., fig. 2, page 213) two ring-like areas, *the vascular area (gh) and the yolk-area (dh), area vasculosa* and *area vitellina*. Since, moreover,

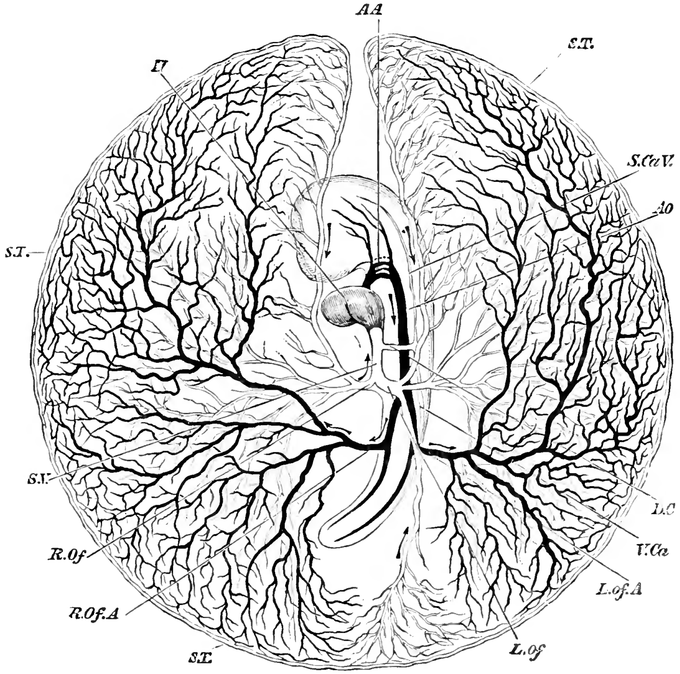

Fig. 117.—Diagram of the vascular system of the yolk-sac at the end of the third day of incubation, after BALFOUR.

The whole blastoderm has been removed from the egg and is represented as seen from below. Therefore what is really on the left appears on the right, and *vice versâ*. The part of the area opaca in which the fine vascular network has been formed is sharply limited at the periphery by the sinus terminalis, and represents the vascular area; outside of it lies the yolk-area. The immediate vicinity of the embryo is destitute of a vascular network, and is designated now, as at an earlier stage, by the name area pellucida.

H Heart; *AA*, aortic arches; *Ao*, dorsal aorta; *L.Of.A*, left, *R.Of.A*, right vitelline artery; *S.T*, sinus terminalis; *L.Of*, left, *R.Of*, right vitelline vein; *S.V*, sinus venosus; *D.C*, ductus Cuvieri; *S.Ca.V*, superior, *V.Ca*, inferior cardinal vein. The veins are drawn in outline, the arteries in solid black.

the area pellucida is still recognisable, being traversed by only a few chief trunks of blood-vessels leading to the embryo, the body of the embryo is enclosed altogether by three zones or areas of the extra-embryonic part of the germ-layers.

Up to the present we have pursued the formation of blood in the *opaque area*. But how do the vessels in the body of the embryo itself arise? Here, too, the uncertainty of our present knowledge is to be emphasised.

According to the representation of HIS, to which KÖLLIKER also adheres, and which the author himself has made the foundation of his account in the first edition of this Text-book, blood-vessels in the embryo are not independently formed, but take their origin from those already existing in the opaque area. According to HIS, the germ of the blood and connective substances, originally a peripheral fundament, makes its way from the opaque area at first into the pellucid area, and from there into the body of the embryo itself, and is distributed everywhere in the spaces between the epithelial germ-layers and the products that have arisen by constriction from them. Into the spaces migrate first of all amœboid cells, which send out in front of them branched processes; on the heels of these follow endothelial vascular shoots.

At variance with the teachings of HIS are noteworthy investigations of recent date,—not only the previously mentioned accounts of the manifold origin of the connective substances from the middle germ-layers, but also particularly the more recent observations concerning the independent origin of vessels and the endothelial sac of the heart in the body of the embryo itself. (RÜCKERT, ZIEGLER, MAYER, RABL, KASTSCHENKO, and others.)

For Selachian embryos the question, whether the repository of the material for the blood-vessels of the embryo is to be sought exclusively on the nutritive yolk, is, as RÜCKERT remarks, to be answered definitely in the negative. The vessels arise in the embryo itself within the territory of the mesenchyme, from cells which are sometimes loosely, sometimes compactly arranged (RÜCKERT, MAYER).

RÜCKERT derives the cells that form the vessels from two different sources, partly from the inner germ-layer of the yolk-wall, partly from the adjoining mesoblast, and their double origin appears to him a natural process of development, in so far as the two layers which bound the first vessels also furnish the material for their walls.

To the same purport are the accounts concerning the formation of the endothelial sac of the heart. At first it consists of a rather irregular mass of cells, in which there appear separate cavities, that gradually unite to form a single cardiac space. The cell-material of the fundament of the heart is developed *in situ* (RÜCKERT, ZIEGLER, MAYER, RABL, and of the earlier investigators GÖTTE, BALFOUR, HOFFMANN) from the wall of the bounding germ-layers; however, uncertainty prevails as to whether the inner germ-layer alone, or the middle, or both, are concerned in the production of the fundament.

When once the first vessels have been formed, they grow further independently, and continually give rise to new lateral branches by means of a kind of budding process.

It can be observed that from the walls of vessels that are already hollow, solid, slender sprouts go out, which are formed of spindle-shaped cells, and by means of cross-branches join others to form a network. The youngest and most delicate of these sprouts consist of only a few cells arranged in a row, or indeed of only a single one, which, reposing upon the endothelial tube like a knob, is drawn out into a long protoplasmic filament. Into the solid sprout there now projects from the already completed vessel a small evagination, which gradually elongates and at the same time enlarges into a tube, the wall of which is formed of the separated cells of the fundament. The formation of blood-corpuscles no longer takes place in this process, all the cells of the sprout being employed to form the wall of the vessel. Since out of the vessels thus produced new sprouts are formed, and so on, the fundaments of the vessels spread themselves out everywhere in the spaces between the germ-layers and the organs which have by constrictions been formed from them.

There are, moreover, two different opinions about the manner in which the sprouting takes place. Are the solid vascular shoots formed exclusively by growth of cells in the wall of the endothelial tube, or do neighboring connective-tissue cells take part in their formation? While RABL holds to the proposition that new vascular endothelia always take their origin from such as are already in existence, KÖLLIKER, MAYER, and RÜCKERT make statements which appear to prove that the endothelial vascular tubes both continue to grow by themselves alone, and also to elongate through the participation of the connective-tissue cells of the surrounding tissue.

In the preceding pages we have endeavored to show in detail how in Vertebrates the material of the cleavage-cells is differentiated into the separate fundamental or primitive organs. As such we must designate the outer and the inner germ-layers, the two middle germ-layers, and the mesenchyme or intermediate layer.

In order properly to estimate at once *the significance and the rôle of these fundamental organs,* we will glance at the final result of the process of development—propound the question, What organs and tissues take their origin in the separate germ-layers and the mesenchyme? A definite answer to this question is possible, except on a few points concerning which the accounts of the different observers are still contradictory, and which therefore will be indicated by a mark of interrogation.

From the *outer germ-layer* arise: the epidermis, the epidermoidal organs, such as hair and nails, the epithelial cells of the dermal glands, the whole central nervous system with the spinal ganglia, the peripheral nervous system (?), the epithelium of the sensory organs (eye, ear, nose), and the lens of the eye.

The *primary inner* germ-layer is differentiated into:—

1. The secondary inner germ-layer, or entoblast;
2. The middle germ-layers;
3. The fundament of the chorda;
4. The germ of the mesenchyme, which forms the intermediate layer.

The *entoblast* (Darmdrüsenblatt) furnishes the epithelial lining of the whole intestinal canal and its glandular appendages (lung, liver, pancreas), the epithelium of the urinary bladder, and the taste buds.

The *middle germ-layers* undergo extremely various metamorphoses after having been differentiated into primitive segments and lateral plates.

From the *primitive segments* are derived the striated, voluntary muscles of the body and a part of the mesenchyme.

From the *lateral plates* arise the epithelium of the pleuroperitoneal cavity; the epithelium of ovary and testis (primitive ova, mother-cells of the spermatozoa); in general, the epithelial components of the sexual glands and their ducts, as well as those of the kidney and ureter; and finally mesenchymatic tissue.

The *fundament of the chorda* becomes the chorda dorsalis, which in the higher Vertebrates is reduced, during later stages of development, to insignificant remnants.

The *mesenchyme-germs*, which produce *the intermediate layer*, undergo manifold differentiations, for they spread themselves out in the body between the epithelial components as the intermediate mass. From them are derived: the multiform group of sustentative (connective) tissues (mucous tissue, fibrillar connective tissue, cartilage, bone), vessels (?) and blood (?), the lymphoid organs, the smooth, involuntary muscles of the vessels, of the intestine, and of various other organs.

HISTORY OF THE PARABLAST- AND MESENCHYME-THEORIES.

The older investigators, as, for example, **REMAK**, grouped together all the cells which are inserted between the two primary germ-layers under the common name of the middle germ-layer, and assumed for them a common origin. To this conception **HIS** opposed in the year 1868 in "Die erste Entwicklung des Hühnchens im Ei" his "*parablast-theory*," in which, influenced principally by histogenetic considerations, he distinguished two fundaments of different origin, an *archiblastic* and a *parablastic*.

As archiblastic fundament he designated the part of the middle germ-layer which lies in the body of the embryo itself, the axial cord (Achsenstrang) and the animal and vegetative muscle-plates, and he made them arise by delamination from the primary germ-layers, and therefore ultimately from the embryonic cleavage-cells.

He gave the name parablast to a peripheral fundament, lying originally outside the embryo, which is the source of all the connective substances, the blood and the vascular endothelium, and which grows from the margin, or more specifically from the opaque area, into the body between the archiblastic tissues.

The division of the middle germ-layer into archiblast (chief germ) and parablast (accessory germ), proposed by **HIS** and carried out in several of his writings, found at the time no approbation, and encountered decided and successful opposition, especially on the part of **HAECKEL**, because the correct views contained in the doctrine were obscured and covered up by peculiar conceptions about the origin of the parablast. The parablast, it was claimed, is not derived from the egg-cell, but from the white yolk, a product of the granulosa-cells, which, according to the earlier teachings of **HIS**, penetrate into the primordial ovum in great numbers and become the white yolk-cells and the yellow spherules. But the granulosa-cells in turn, it was maintained, arise from the connective tissue (leucocytes) of the mother; consequently after their migration into the egg they are capable of producing again only connective tissue and blood.

HIS thought it was necessary to assume a fundamental difference between *chief germ* and *accessory germ*; the former alone had experienced the influence of fertilisation, since it alone was descended from cleavage-cells, whereas the latter, since it issued from the white yolk (a derivative of the maternal connective tissue), was "purely a maternal dower."

RAUBER, in a short communication, accepted the conclusions of **HIS**, in so far as he also assumed a common origin for blood and connective tissue, a special "hæmo-desmoblast," but differed from him in that he derived them from the cleavage-cells.

GOETTE (1874) is also to be mentioned in this connection, since he maintained that the blood is developed out of yolk-cells, which break up into clusters of smaller cells (Amphibia and Birds).

Proceeding from other standpoints, and induced by observations on Invertebrates, my brother and I were led in our *Cœlom-Theory* (1881) to a result similar to that of **HIS**, namely, that two entirely different structures had been hitherto embraced under the expression middle germ-layer, and that it was necessary to introduce in the place of the old indefinite conception two new and more precise ones, "*middle germ-layer in the restricted sense*" and "*mesenchyme-germ*." But our conception, notwithstanding many points of agreement, took in detail a form very different from the doctrine of **HIS**.

All fundaments of the animal body are derived from embryonic cells, which have been produced from the egg-cell by the process of cleavage. The distinction between middle germ-layer and mesenchyme-germ is to be sought in another direction than in that indicated by HIS. *The middle germ-layers are sheets of embryonic cells, having an epithelial arrangement, which arise by a process of folding from the inner germ-layer, just as the latter does by a folding of the blastula* (compare the historical part of Chapter VII.). *The mesenchymatic germ, on the contrary, embraces cells, which have been individually detached from epithelial union in the inner germ-layer, and furnish the foundation for connective substance and blood by spreading themselves out in the system of spaces between the epithelial germ-layers.*

After the appearance of the Cœlom-Theory, HIS entered again into an explanation of his parablast-theory, and modified it in his paper, "Die Lehre vom Bindesubstanzkeim," in so far as he no longer laid weight on the question whether the fundament of the connective substance was derived from the segmented or the unsegmented germ.

The *theory of the double origin of the middle germ-layers*, established by HIS and by us in different ways, met with opposition on the part of KÖLLIKER who held to the older interpretation; but by many others it was accepted; attempts were made further to confirm and also to modify it by KUPFFER, DISSE, WALDEYER, KOLLMANN, HEAPE, and others, who defended the existence of a special connective-tissue germ.

KUPFFER and his followers furnished important observations concerning the presence of *yolk-nuclei* in a definite zone of the embryonic fundament, and their relation to the formation of blood in Fishes and Reptiles.

HOFFMANN and RÜCKERT showed that the yolk-nuclei do not arise by free [spontaneous] formation of nuclei, but are descendants of the cleavage-nucleus.

DISSE investigated the germ-wall of the Hen's egg.

KOLLMANN named the cells which migrate out between the germ-layers poreuts (Poreuten), and the whole fundament the acroblast.

Finally, WALDEYER endeavored to derive the connective-tissue germ from a special part of the cleavage-material, which he divided into an archiblast and a parablast.

According to WALDEYER'S theory, the cleavage of the eggs of all those animals in which there is any blood and connective substance does not take place uniformly up to the end, but one must distinguish a *primary and a secondary cleavage*. "The former divides the egg, so far as it is in any way capable of cleavage, into a number of cells, which are ready for the production of tissues. These then form the primary germ-layers. A remnant of immature cleavage-cells (in the case of holoblastic eggs), or of egg-protoplasm, which is not yet converted into the cell-form (in meroblastic eggs), is left remaining. Neither the immature cells, nor the protoplasm still unconverted into cells, enter for the present into the integrating condition of the germ-layers. On the contrary, it is only afterwards that there is effected on this material a further formation of *cells*, the *secondary cleavage*. The immature cells of the holoblastic eggs, over-loaded with nutritive yolk, divide themselves, or, if one prefers, 'cleave' themselves further, or the parts which are most richly provided with protoplasm constrict themselves off from the eggs, whereas the remnant of the nutritive material is consumed,—the unformed remnants of the protoplasm (germ-processes) of meroblastic eggs become divided up into cells. The cell-material thus secondarily acquired migrates in between the primary germ-layers, and becomes blood and connective substance."

According to the recent investigations of RABL, ZIEGLER, VAN WIJHE, RÜCKERT, and others, the mesenchyme is produced from various regions of the middle germ-layer. A participation of the inner germ-layer in the formation of the blood-vessels is rendered probable.

SUMMARY.

1. Besides the four germ-layers, which have the form of epithelial lamellæ, special germs are developed in the higher Vertebrates for the sustentative substances and the blood,—the mesenchyme-germs. The latter together make up the intermediate layer.
2. The mesenchyme-germs arise by cells detaching themselves from epithelial union with the germ-layers, and penetrating as migratory cells into the fissure between the four germ-layers (the remnant of the original cleavage-cavity) and spreading themselves out in this space.
3. Germ-layers and mesenchyme-germ (intermediate layer) exhibit a difference in the method of their origin: the former are developed by foldings of the wall of the blastula, the latter by emigration of isolated cells from definite territories of the germ-layers.
4. Mesenchyme-germs arise from the wall of the primitive segment, from the cutis-plate, and at certain regions of the parietal and visceral lamellæ of the middle germ-layer.
5. Blood-vessels are developed both in the body of the embryo itself, in a manner which still remains to be accurately determined, and also in the territory of the area opaca of meroblastic eggs.
6. The source of the cells from which the vessels and blood of the opaque area arise is at present a matter of controversy.
7. In the formation of vessels in the opaque area the following phenomena are to be regarded:—
    (*a*) The embryonic cells of the intermediate layer arrange themselves:—
        First into a network of cords, and
        Secondly into the substance-islands (Substanzinseln).
    (*b*) There are developed out of the cell-cords, at the same time with the secretion of the fluid portions of the blood, the endothelial wall of the primitive blood-vessels and their cellular contents, the blood-corpuscles (blood-islands).
    (*c*) The Substanzinseln become embryonic connective substance.

(*d*) The place where blood-vessels and connective substance at first arise in the opaque area is sharply limited at the periphery by a circular vessel, the sinus terminalis.

(*e*) Since the outer and the inner germ-layers further continue to spread themselves out over the yolk after the development of the intermediate layer, the body of the embryo becomes surrounded by three areas:—

First by the *area pellucida*,
Secondly by the *vascular area* ending in the sinus terminalis,
Thirdly by the *yolk-area*, which is coëxtensive with the margin of the overgrowth.

8. The red blood-corpuscles of all Vertebrates possess in the earliest stages of development the power of increase by means of division. The red blood-corpuscles of Mammals have at this time a nucleus.

9. The following table gives a survey of the fundamental organs of the embryo, and the products of their further development:—

I. Outer Germ-layer.

Epidermis, hair, nails, epithelium of dermal glands, central nervous system, peripheral nervous system, epithelium of sensory organs, the lens.

II. Primary Inner Germ-layer.

1. *Entoblast, or secondary inner germ-layer.*
   Epithelium of the alimentary canal and its glands, epithelium of urinary bladder.
2. *Fundament of the chorda.*
3. *The middle germ-layers.*

A. Primitive Segments.

Transversely striped, voluntary muscles of the body. Parts of the mesenchyme.

B. Lateral Plates.

Epithelium of the pleuroperitoneal cavities, the sexual cells and epithelial components of the sexual glands and their outlets, epithelium of kidney and ureters. Parts of the mesenchyme.

4. *Mesenchyme-germ.*
   Group of the connective substances, blood-vessels and blood, lymphoid organs, smooth involuntary muscles.

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CHAPTER X.

ESTABLISHMENT OF THE EXTERNAL FORM OF THE BODY.

After having investigated in the preceding chapters the fundamental organs of the body of vertebrated animals, or the germ-layers, and their first important differentiations into neural tube, chorda, and primitive segments, as well as the origin of the blood and connective tissues, it will be our next undertaking to make ourselves acquainted with the *development of the external form of the body*, and with the *development of the embryonic membranes*, the latter being intimately connected with the former.

There exists an extraordinary difference in these respects between the lower and higher Vertebrates. When the embryo of an Amphioxus has passed through the first processes of development, it elongates, becomes pointed at both ends, and already possesses in the main the worm-like or fish-like form of the adult animal. But the higher we ascend in the series of Vertebrates, the more are the embryos, when they attain the stage of development corresponding to the Amphioxus embryo, unlike the adult animals: at this stage they assume very singular and strange forms, inasmuch as they become surrounded by peculiar envelopes and are provided with various appendages, which subsequently disappear.

The difference is referable, *first of all, to the more or less extensive accumulation of nutritive yolk*, the significance of which for the nascent organism is twofold.

From a *physiological point of view*, the nutritive yolk is a rich source of energy which alone makes it possible for the embryological processes to take place in uninterrupted sequence, until at length an organism, with an already relatively high organisation, begins its independent existence.

From a *morphological point of view*, on the other hand, the yolk plays the rôle of ballast, which exerts a restrictive and modifying influence on the direct and free development of those organs which are entrusted with the reception and elaboration of it. Even at the very beginning of development we could see how the cleavage-process and the formation of the germ-layers were retarded, altered, and to a certain extent even suppressed by the presence of yolk. In what follows we shall again have occasion to point out the same thing,—how, owing to the presence of yolk, the normal formation of the intestinal canal and of the body can be attained only gradually and by a circuitous process.

In the *second place*, the great difference which the embryos of Vertebrates present is produced by the medium in which the eggs undergo development. Eggs which, like those of water-inhabiting Vertebrates, are deposited in the water, are developed in a more simple and direct manner than those which, provided with a firm shell, are laid upon the land, or than those which are enclosed in the womb up to the time of the birth of the embryos.

In the two latter cases the growing organism attains its goal only by very indirect ways. At the same time with the *permanent organs* there are also developed others which have no significance for the post-embryonic life, but which serve during the egg-stage of existence either for the *protection* of the soft, delicate, and easily injured body, or for *respiration*, or for *nutrition*. These either undergo regressive metamorphosis at the end of embryonic life, or are cast off at birth as useless and unimportant structures. But inasmuch as they are developed out of the germ-layers, they are also properly to be regarded as belonging immediately to the nascent organism—as being its *embryonic organs*, and as such they too are to be treated in morphological descriptions.

The extensive material which has to be mastered in this connection I shall present grouped into *two parts*.

In *the first part* we shall inquire how the embryo overcomes the obstacle which it encounters in the presence of the yolk and acquires its ultimate form.

In *the second* and likewise more extensive part we must concern ourselves more minutely with the embryonic enveloping structures and appended organs, which subserve various purposes.

The collection of yolk-material disturbs the course of development least in the case of the Amphibia. The latter therefore stand, as it were, midway between Amphioxus with direct development and the remaining Vertebrates, and constitute a transition between them. In the Amphibia the yolk shares in the process of cleavage; after the close of this process it is found accumulated for the most part in the large yolk-cells which form the floor of the blastula (fig. 45); at the time of the differentiation into germ-layers it is taken up into the cœlenteron, which it almost completely fills (fig. 47); after the formation of the body-sacs the large yolk-cells lie in a similar manner in the ventral wall of the intestine proper (fig. 118 *yk*). Here they are in part dissolved and employed for the growth of the remaining parts of the body, in part they share directly in the formation of the epithelium of the ventral wall of the intestine.

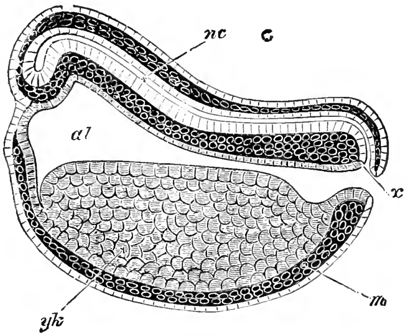

Fig. 118.—Diagrammatic longitudinal section through the embryo of a Frog, after GOETTE, from BALFOUR. *nc*, Neural tube; *x*, communication of the same with blastopore and cœlenteron (*ai*); *yk*, yolk-cells; *m*, middle germ-layer. For the sake of simplicity the outer germ-layer is represented as if composed of a single layer of cells.

In consequence of the presence of the great accumulation of yolk-cells, the Amphibian embryo acquires a shapeless condition at a time when the Amphioxus larva has already become elongated and fish-like. The body, which is spherical during gastrulation, later becomes egg-shaped, owing to its elongation. Thereupon the head-end and the tail-end begin to be established at the two poles as small elevations (figs. 118 and 80). The middle or trunk-part lying between the latter becomes somewhat incurved along its dorsal region, in which neural tube, chorda, and primitive segments are developed, so that the cephalic and caudal elevations become joined by means of a concave line. The ventral side of the trunk-region, on the contrary, is greatly swollen and bulges out ventrally and laterally like a hernia, since it is filled with yolk-cells. This swelling is therefore called the *yolk-sac.*

In the further progress of development the embryo continually acquires a more fish-like shape. The anterior and the posterior ends of the body, especially the latter, increase greatly in length, and the middle of the trunk becomes thinner, for with the consumption of the yolk-material the yolk-sac becomes smaller and finally disappears altogether, its walls being incorporated into the ventral wall of the intestine and that of the body.

The interferences in the normal course of development become greater in the same ratio as the yolk increases in amount, as it does in the case of the meroblastic eggs of Fishes, Reptiles, and Birds. With the latter the yolk is no longer broken up into a mass of yolk-cells, as in the case of the Amphibia; it participates in the process of cleavage, but only to a slight extent, inasmuch as nuclei make their way into the layer of yolk which is adjacent to the germ, and, surrounded by protoplasm, continue to increase in number by division. The gastrula-form is altered until it becomes unrecognisable; only a small part of its dorsal surface consists of cells, which are arranged into the two primary germ-layers, whereas the whole ventral side, where in the Amphibia the yolk-cells are found, is an unsegmented yolk-mass.

Thus we acquire in the case of the Vertebrates mentioned a peculiar condition; the embryo, if we regard the yolk as not belonging to the body, appears to be developed from layers that are spread out flat instead of from a cup-like structure (Plate I., fig. 1, page 213). Moreover we see even a greater distinction effected between the dorsal and ventral surfaces of the egg during development than was the case with the Amphibians. The fundaments of all important organs, the nervous system, the chorda, the primitive segments (Plate I., figs. 2, 8), are at first produced exclusively on the former, whereas on the ventral side few and unimportant changes only are to be observed. These consist principally in the extension of the germ-layers, which spread out farther ventrally, grow over the yolk-mass (Plate I., figs. 2-5), and form around it a closed sac consisting of several layers. This circumcrescence of the unsegmented yolk by the germ-layers is accomplished, on the whole, very slowly, the more voluminous the accumulated yolk-material, the more time it requires: thus, for example, in the case of Birds it is completed at a very late stage of development, when the embryo has already attained a high state of perfection (Plate I., fig. 5).

In the case of meroblastic eggs, the part of the germ-layers on which the first fundaments of the organs (neural tube, chorda, primitive segments, etc.) appear has been distinguished as the *embryonic area* from the remaining part, or the *extra-embryonic area.* The distinction is both fitting and necessary; but the names might have been more appropriate than "embryonic and extra-embryonic," since obviously everything that arises from the egg-cell, and consequently even that which originates in the extra-embryonic area, must be reckoned as belonging to the embryo. The differentiation into two areas persists in the course of further development, and becomes expressed still more sharply (fig. 119). The embryonic area, by means of the folding of its flattened layers into tubes, alone forms the elongated, fish-like body which all Vertebrates at first exhibit; the extra-embryonic area, on the contrary, becomes a sac filled with yolk (*ds*), which, like an enormous hernia, is united to the embryo (*Em*) by means of a stalk (*st*) attached to its belly, sometimes even while the embryo is still remarkably small.

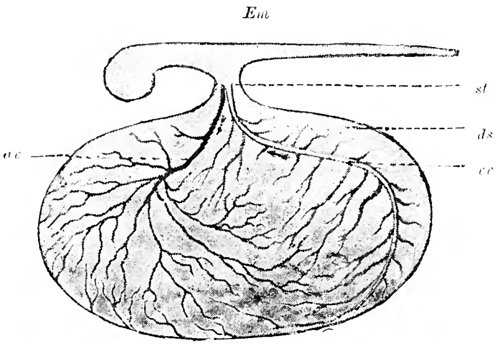

Fig. 119.—Advanced embryo of a Shark (Pristiurus), after BALFOUR.
Em, Embryo; *ds*, yolk-sac; *st*, stalk of the yolk-sac; *ac*, arteria vitellina; *vc*, vena vitellina.

We must now explain more minutely the details of the processes of development which take place in this connection: first the metamorphosis of the flattened embryonic area into the fish-like embryonal body, and secondly the formation of the yolk-sac.

In the presentation we shall adhere chiefly to the Hen's egg, but for the time being we shall leave out of consideration the formation of the embryonic membranes.

The body of the Chick is developed by a folding of the flattened layers, and by the constricting off of the tubular structures thus formed *from the area pellucida.* The beginning of the process of folding is recognisable upon the surface of the blastoderm by means of certain furrows, the *marginal grooves* (Grenzrinnen) of His. These appear earlier in the anterior than in the posterior region of the embryonic fundament, in correspondence with the law previously enunciated, according to which the anterior end of the body anticipates in development the posterior end.

At first that part of the embryonic fundament which is destined to become the head is marked off by means of a crescentic groove (fig. 120). In the case of the Chick this is indicated during the first day of incubation, at a time when the first trace of the nervous system becomes visible. It lies immediately in front of the curved anterior end of the medullary ridges, with its concavity directed backward.

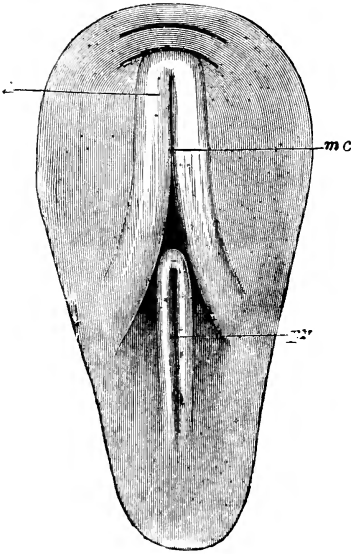

Fig. 120.—**Surface-view of the area pellucida of a blastoderm of 18 hours,** after Balfour.

In front of the primitive groove (*pr*) lies the medullary furrow (*mc*), with the medullary ridges (*A*). These diverge behind and fade out on either side in front of the primitive groove; anteriorly, on the contrary, they are continuous with each other, and form an arch behind a curved line, which represents the anterior marginal groove. The second curved line, lying in front of and concentric with the first, is the beginning of the amniotic fold.

At a later stage the embryonic area is marked off laterally. In the case of the embryo seen from the surface in fig. 121, in which the neural tube is already partly closed and segmented into three brain-vesicles, and in which six pairs of primitive segments are laid down, there may be recognised at some distance from these primitive segments two dark streaks, the two lateral marginal grooves. They become less distinct in passing from before backward, and wholly disappear at the end of the primitive groove.

Finally, the tail-end of the embryo is marked off by the posterior marginal groove, which like the anterior is crescentic, but has its concavity directed toward the head.

In this manner a small part of the germ-layers, which alone is required for the construction of the permanent body, is separated by a continuous marginal furrow from the much more extensive extra-embryonic area, which serves for the formation of evanescent organs like the yolk-sac and the embryonic membranes.

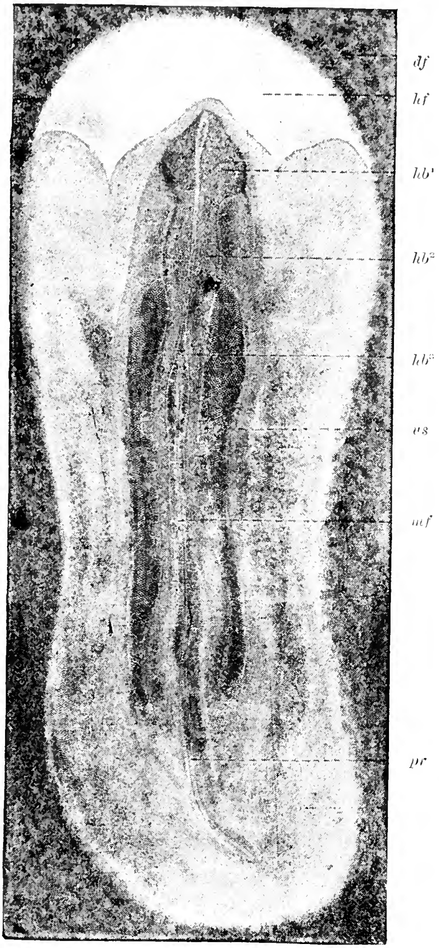

Fig. 121.—Blastoderm of the Chick, incubated 33 hours, after Duval.

One sees the pellucid area, *hf*, surrounded by a portion of the opaque area, *df*. The fundament of the nervous system is closed anteriorly and segmented into three brain-vesicles, *hb*^{1}, *hb*^{2}, *hb*^{3}; behind, the medullary fold *mf* is still open. On either side of it lie six primitive segments, *us*. The posterior end of the fundament of the embryo is occupied by the primitive streak with the primitive groove, *pr*.

The marginal grooves are formed by the infolding of the outer germ-layer and the parietal middle layer, which are together called the *somatopleure*, and in such a manner that the ridge of the original small fold is directed downward toward the yolk (Plate I., fig. 8 *sf*). The space enclosed by the two folded layers is the marginal groove (*gr*). As we have distinguished on the latter several regions, which are developed at different times, so must we here distinguish the corresponding folds, and we consequently speak of a *headfold*, a *tail-fold*, and the *two lateral folds*.

The *headfold* appears, first of all, even on the first, but more distinctly on the second, day of incubation. By means of it the head-end of the embryonal fundament is formed and separated from the extra-embryonic part of the germ-layers. At the moment of its origin it is turned directly downward toward the yolk; but the more it enlarges,—whereby the anterior marginal groove is deepened into a pit,—the more its ridge is turned backwards.

Two diagrammatic longitudinal sections, one of which is shown in fig. 122, the other on Plate I., fig. 11, may serve to illustrate this process.

In fig. 122 there is shown, projecting above the otherwise smooth flat surface of the germ-layers, a small protuberance, which encloses the anterior end of the neural tube (*N.C*) and the simultaneously forming intestinal tube (*D*), and which has arisen by the formation of the fold *F.So.* The upper sheet of the fold, by directing itself backwards, furnishes the ventral wall of the cephalic elevation; the lower sheet forms the floor of the marginal groove.

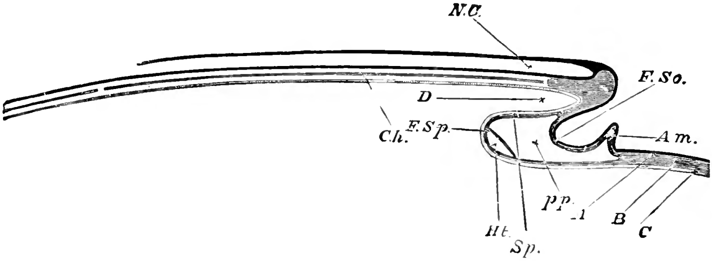

Fig. 122.—Diagrammatic longitudinal section through the axis of an embryo Bird, after Balfour.

The section represents the condition when the head-fold has begun, but the tail-fold is still wanting.

F.So, Head-fold of the somatopleure; *F.Sp*, head-fold of the splanchnopleure, forming at *Sp* the lower wall of the front end of the mesenteron; *D*, cavity of the fore gut; *pp*, pleuroperitoneal cavity; *Am*, fundament of the anterior fold of the amnion; *N.C*, neural tube; *Ch*, chorda; *A*, *B*, *C*, outer, middle, inner germ-layer, everywhere distinguished by different shading; *Ht*, heart.

In the second figure, in which there is represented a diagrammatic longitudinal section through an older embryo, the head-fold (kf^1) has extended still farther backward. The head has thereby become longer, since its under surface has increased in consequence of the advance in the process of folding.

Whoever desires to make this process, which is very important for the comprehension of the construction of animal forms, clearer and more intelligible, may do so with the help of an easily constructed model. Let him stretch out his left hand on a table, and spread flat over the back of it a cloth, which is to represent the blastoderm; then let him fold in the cloth with his right hand by tucking it a little way under the points of his left fingers. The artificially produced fold corresponds to the head-fold previously described. The points of the fingers, which by the tucking under of the cloth have received a covering on their lower sides, and which project above the otherwise flattened cloth, are comparable to the cephalic elevation. In addition we can represent the backward growth of the head-fold by tucking the cloth still farther under the left fingers toward the wrist.

The hinder end of the embryo develops in the same manner as the front end, only somewhat later (compare fig. 11, Plate I.). Corresponding to the posterior marginal groove (*gr*), the *tail-fold* is so formed that its ridge is directed forward and that it grows toward the head-fold.

Where in surface-views of the blastoderm the lateral marginal grooves are to be seen (fig. 121), one recognises on cross sections the *lateral folds* (Plate I., fig. 8 *sf*). They grow at first directly from above downwards, thus producing the lateral walls of the trunk. Afterwards their margins bend somewhat toward the median plane (Plate I., fig. 9 *sf*), thereby approaching each other, and in this way gradually draw together to form a tube (Plate I., fig. 10). By their infolding the trunk acquires its ventral wall.

In order to avoid misconceptions, let it be further remarked that only at the beginning of their formation are head-, tail-, and lateral folds somewhat separated from one another, but that when they are more developed they are merged into one another, and thus are only *parts of a single fold*, which encloses the fundament of the embryo on all sides.

As the separate parts of this fold increase, they grow with their bent margins from in front and from behind, from right and from left, toward one another, and finally come near together in a small territory, which corresponds approximately with the middle of the surface of the embryo's belly, and is designated on the figure of the cross section through this region (Plate I., fig. 10) by a ring-like line (*hn*). Thus a small tubular body is formed (Plate I., fig. 3), which lies upon the extra-embryonic area of the blastoderm and is united to it by means of a hollow stalk (*hn*). The stalk marks the place where the margins of the folds, growing toward one another from all sides, have met, but a complete constricting off of the embryonic territory from the extra-embryonic does not take place.

We can also represent these conditions, if, in the previously mentioned model, we in addition fold in the cloth that covers the tips of the fingers along the sides of the hand and the wrist, and then carry the circular fold thus artificially formed still farther under, even to the middle of the palm. Then the cloth forms around the hand a tubular sheath, which is continuous at one place by means of a connecting cord with the flattened remaining portion of the cloth.

A process similar to the externally visible one just described, by which the lateral and ventral walls of the body are produced from the sheet-like fundaments, takes place at the same time within the embryo in the splanchnopleure. There are developed from it, as from the somatopleure, an anterior, a posterior, and two lateral intestinal folds.

First, at the time when the head is differentiated (fig. 122), the part of the splanchnopleure corresponding to it (*F.Sp.*) is folded together into a tube, the so-called *cavity of the fore gut* or *head-gut* (*D*).

The same process repeats itself on the third day of incubation at the posterior end of the embryonal fundament, where, upon the appearance of the caudal part (Plate I., fig. 11), there is formed within it and out of the splanchnopleure the *cavity of the hind gut.*

Both parts of the intestine at first terminate with blind ends directed toward the outer surface of the body. At the head-end the mouth-opening is still wanting, at the posterior end the anus. When, however, one raises the blastoderm with the nascent embryo from the yolk, and examines it from the under side, the anterior and posterior portions of the intestinal canal exhibit openings (*vdpf* and *hdpf*), through which one can look from the yolk-side into the blind-ending cavities. One of these is called the *anterior*, the other the *posterior*, *intestinal portal* or *intestinal entrance* (Plate I., fig. 11 *vdpf* and *hdpf*).

Between the two portals the middle region of the intestinal canal remains for a long time as a leaf-like fundament. Then by its becoming somewhat bent downwards (Plate I., figs. 9 and 2) there arises under the chorda dorsalis an *intestinal groove* (*dr*), which lies between fore and hind gut. Owing to the further increase of the lateral intestinal folds (*df*), the groove becomes deeper and deeper, and finally, by the approximation of the edges of the folds from in front, from behind, and from both sides, becomes closed into a tube in the same manner as the wall of the body.

At only one small place, which is indicated by the ring-like line *dn* in Plate I., figs. 3 and 10, the folding and constricting-off process is not completed, and here the intestinal tube too remains continuous, by means of a hollow stalk, with the extra-embryonic part of the splanchnopleure, which encloses the yolk.

The part of the germ-layers which is not employed in the formation of the embryo furnishes in the case of the Reptiles and Birds the yolk-sac and certain embryonic membranes. I shall speak of the development of these in the next chapter.

The fate of the extra-embryonic area of the blastoderm in Fishes is more simple, since there is formed from it only a sac for the reception of the yolk.

Fig. 123 exhibits the embryo (*Em*) of a Selachian, which has arisen by the infolding of a small area of the germ-layers in the manner described for the Chick. All the remaining part of the egg has become a great yolk-sac (*ds*), which is united with the middle of the belly by means of a long stalk.

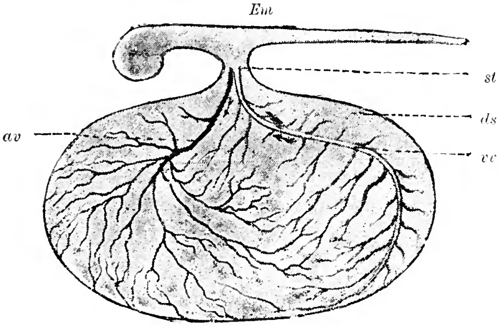

Fig. 123.—Advanced embryo of a Shark (Pristiurus), after Balfour.
Em, Embryo ; *ds*, yolk-sac ; *st*, stalk of the yolk-sac ; *av*, arteria vitellina ; *vc*, vena vitellina.

The Teleosts (Plate I., fig. 6) show us transitions from this condition to one in which the yolk-sac, as in Amphibians, is not separated by a stalk from the mesenteron, but represents only a capacious enlargement of the latter and of the belly-wall.

Let us now examine more carefully the *structure of the yolk-sac.* As has been remarked already, all four of the germ-layers spread themselves out one after another around the unsegmented yolk-mass of meroblastic eggs (Plate I., figs. 6 and 7). As in the embryonal body the two middle germ-layers separate from each other and allow the body-cavity to appear between them, so, too, at a later stage the same process occurs in the extra-embryonic area. Throughout the region of the middle germ-layer there is formed a narrow fissure, for which the name "extra-embryonic body-cavity," or *blastospheric cœlom* (cavity of the blastoderm, Kölliker), would be most suitable. It separates the envelope of the yolk into two layers, of which the inner is the immediate continuation of the intestinal wall (splanchnopleure), the outer, on the contrary, that of the body-wall (somatopleure). Therefore, to be exact, we have before us a double sac formed around the yolk, which we can distinguish as intestinal yolk-sac and dermal yolk-sac. The former is simply a hernia-like evagination of the intestinal canal, and, like it, is composed of three layers:—

(1) The intestino-glandular layer (*ik*),—the entoblast or secondary entoderm, which encloses the yolk;

(2) The visceral middle layer, or the pleuroperitoneal epithelium (mk^2); and

(3) The intermediate layer (Zwischenblatt), in which have been developed the vitelline blood-vessels, which at the beginning of the circulation of the blood have to conduct the liquefied nutritive material from the yolk-sac to the places of embryonic growth.

The dermal yolk-sac is, as a continuation of the body-wall, likewise composed of three layers—the epidermis (*ak*), the parietal middle layer (mk^1), and the connective-tissue intermediate substance (Zwischensubstanz).

It has already been stated that the constricting-off of the yolk-sac from the embryonal body is quite variable in extent, and can go so far that the connection between the two is kept up only by means of a narrow stalk. A more careful examination shows that in the latter case the stalk itself is composed of two narrow tubes one within the other (Plate I., fig. 7), of which the outer unites the dermal yolk-sac (*hs*) to the ventral wall of the body, and the inner the intestinal yolk-sac to the intestinal canal. The former is called the dermal stalk, the latter the intestinal stalk (*dn*) or vitelline duct, ductus vitello-intestinalis. The place of attachment of the dermal stalk in the middle of the ventral surface of the embryo is called the dermal navel (*hn*); the corresponding place of attachment of the intestinal stalk to the wall of the intestine the intestinal navel (*dn*). The embryonic body-cavity opens out between the two, and is continuous with the fissure between dermal and intestinal yolk-sac—with the "extra-embryonic body-cavity" or the blastospheric cœlom (lh^2).

The ultimate fate of the yolk-sac in the Fishes is the same as in the Amphibia. It is still employed, even in the extreme case of the Selachians, for the formation of the wall of the intestine and that of the body. The more its contents are liquefied and absorbed, the more the yolk-sac shrivels. When the intestinal yolk-sac has become very small, it is drawn into the body-cavity and finally serves to close the intestinal navel, just as the dermal yolk-sac upon its disappearance closes up the dermal navel. With the lower Vertebrates a shedding of the embryonic parts has not yet come into existence. The next chapter will explain what becomes of the yolk-sac in the case of Reptiles and Birds.

SUMMARY.

1. In the case of Vertebrates whose eggs contain little yolk, the embryo after the development of the germ-layers takes on an elongated, fish-like form.

2. In eggs with abundant yolk the body of the vertebrated animal is produced by only a small region of the germ-layers (the embryonic fundament); the far greater extra-embryonic area is employed for the formation of a yolk-sac and of embryonic membranes (the latter only in Reptiles and Birds).

3. The separate layers of the embryonic fundament constrict themselves off from the extra-embryonic territory, and at the same time become folded into tubes—the somatopleure into the tubular body-wall, the splanchnopleure into the intestinal tube (head-fold, tail-fold, lateral folds, intestinal groove, intestinal fold).

4. The extra-embryonic territory of the germ-layers remains in continuity with the two tubes by means of a stalk-like connection.

5. In Fishes the extra-embryonic territory of the germ-layers becomes the yolk-sac, which is composed of two sacs, the intestinal and the dermal yolk-sacs, separated from each other by a prolongation of the embryonal body-cavity.

6. The place where the dermal yolk-sac is attached to the belly-wall of the embryo by a stalk-like prolongation is called the dermal navel or umbilicus; the corresponding place of attachment of the intestinal yolk-sac to the middle of the intestinal canal is the intestinal navel or umbilicus.

7. In Fishes the yolk-sac after resorption of the yolk-material, accompanied by the phenomena of shrivelling, is employed for the closure of the intestinal and dermal navels.

8. In Reptiles and Birds the extra-embryonic region furnishes, in addition to the yolk-sac, several other embryonic membranes, which complicate the development.

CHAPTER XI.

THE FŒTAL MEMBRANES OF REPTILES AND BIRDS.

As has already been stated, the course of development in all animals which do not deposit their eggs in water—in Reptiles, Birds, and Mammals—is unusually complicated, owing to the appearance of special egg-envelopes (embryonic or fœtal membranes). Some of them, according to their origin, are to be referred to the extra-embryonic area of the germ-layers, and indeed to that part which in Fishes is employed for the yolk-sac. They arise from folds, which grow around the embryo while it is still small, and furnish a double envelope for it.

The egg-envelopes (embryonic membranes) of Reptiles and Birds, which exhibit almost identical conditions, and the consideration of which we shall take up first, are more simply constituted than those of Mammals. In the case of the former there are associated with the yolk-sac, in the possession of which they agree with the Amphibia and Fishes, three additional embryonic appendages, the *amnion*, the *membrana serosa* (or briefly *serosa*), and the *allantois*. They are partly laid down at an early period, at the time when the embryonic body is converted into tubes by the infolding of the germ-layers and is thereby constricted off from the yolk-sac.

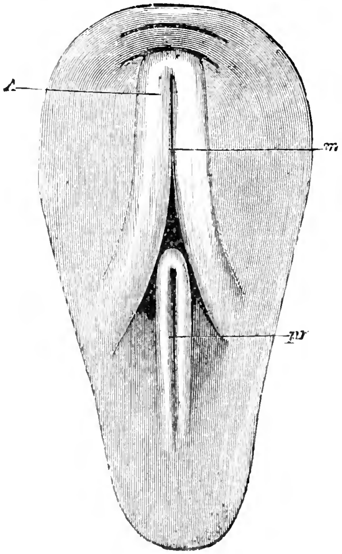

Fig. 124.—Surface-view of the pellucid area of a blastoderm of a Chick of 18 hours, after BALFOUR.

In front of the primitive groove, *pr*, lies the medullary furrow surrounded by the medullary folds. Immediately in front of these one sees a curved line, the head-fold, and in front of it a second curved line running concentric with it, the anterior fold of the amnion.

The Chick shall again serve as a basis for our description.

1. The Amnion, the Serosa, and the Yolk-Sac.

The *amnion* is a structure the appearance of which is recognisable remarkably early in the Chick. At the time when one recognises the semicircular head-fold at the anterior end of the incipient embryo (fig. 124), by the growth of which the head of the embryo is marked off, there is already present, at a short distance from it, a second fold running parallel to it. This is the *anterior fold of the amnion*, a product of the extra-embryonic part of the ectoderm and of the parietal mesoderm united with it.

The two infoldings, which lie near to each other, have opposite directions (fig. 125). While the head-fold (*F.So*) advances with its margin toward the yolk, the anterior fold of the amnion (*Am*), separated from it by the marginal groove, rises externally above the plane of the blastoderm. At the time when the head is being formed, the amnion enlarges rather rapidly (Plate I., fig. 11 *vaf*), and grows over and around the head in a cap-like fold, the rim of which is directed backwards. At the end of the second day of incubation it already

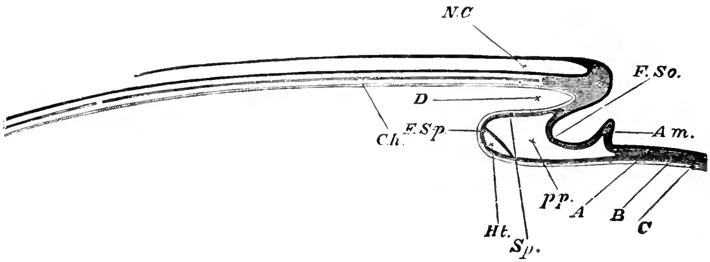

Fig. 125.—**Diagrammatic longitudinal section through the axis of an embryo Bird,** after Balfour.

The section represents the condition when the head-fold is already formed, but the tail-fold is still wanting.

F.So, Head-fold of the somatopleure; *F.Sp*, head-fold of the splanchnopleure, forming at *Sp* the floor of the anterior part of the intestine. For the remaining references see fig. 122, p. 201.

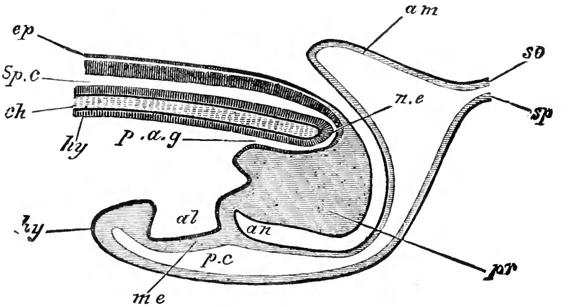

Fig. 126.—**Diagrammatic longitudinal section through the posterior end of an embryo Chick at the time of the formation of the allantois,** after Balfour.

ep, *me*, *hy*, Outer, middle, and inner germ-layers; *ch*, chorda; *Sp.c*, neural tube; *n.e*, neurenteric canal; *p.a.g*, post-anal gut; *pr*, remains of the primitive streak folded toward the ventral side; *al*, allantois; *an*, point where the anus will be formed; *p.c*, perivisceral cavity; *am*, amnion; *so*, somatopleure; *sp*, splanchnopleure.

covers the anterior part of the head like a thin transparent veil, and is therefore called the cephalic sheath.

In like manner, but at a somewhat later stage, there arise at the tail-end and at both sides of the embryo the *posterior* and *lateral folds* of the *amnion*. *The posterior fold* is still very inconspicuous even at the time when the head is covered with the veil-like pellicle (Plate I., fig. 11 *kaf*). It enlarges slowly, and under the name of caudal sheath covers over the posterior end of the body (fig. 126 *am*).

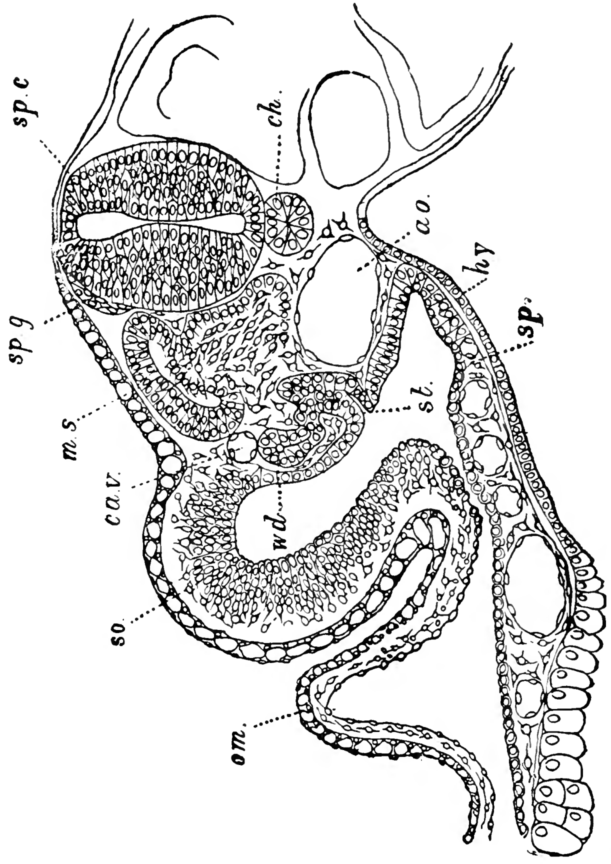

Fig. 127.—**Transverse section through the trunk of a Duck embryo with about 24 primitive segments, after** BALFOUR.
m, Amnion; *so*, somatopleure; *sp*, splanchnopleure; *wd*, Wolffian duct; *st*, segmental canal; *ca.v*, cardinal vein; *ms*, muscle-plate; *sp.g*, spinal ganglion; *sp.c*, spinal cord (neural tube); *ch*, chorda; *ao*, aorta; *hy*, hypoblast (entoblast).

The *lateral folds of the amnion* are elevated externally to the lateral marginal grooves (fig. 127 *om*), and project in the opposite direction from those lateral folds by the bending in of which the lateral and ventral walls of the embryo are produced. By this means the rim of the fold is carried farther and farther from the splanchnopleure (*sp*), which remains spread out flat over the yolk. In this way the extra-embryonic part of the body-cavity, or the cavity of the blastoderm (KÖLLIKER), increases in extent in the vicinity of the embryo. When the lateral folds of the amnion have grown up to the dorsal surface of the embryo (Plate I., fig. 9 *saf*), they begin, by the bending over of their edges medianwards, to form the so-called lateral sheaths.

Inasmuch as the folds of the amnion, which are called by special names, become, when they are in full development, continuous, and are only parts of a single *ring-like fold*, the embryo eventually becomes surrounded on all sides as though by a high wall. With further enlargement, the amniotic sheaths then bend together over the back of the embryo from in front and behind, and from the right and the left (Plate I., figs. 2, 3, and 10, *af*, *vaf*, *haf*), come together with their edges in the median plane, and then fuse with each other along a line, the amniotic suture, which closes from in front backwards (Plate I., fig. 10), except that at one very small place near the tail-end the closing is interrupted for a considerable time, and a small opening is preserved.

The fusion of the amniotic folds takes place in the same manner as the fusion of the medullary folds described on page 79. Each fold (Plate I., figs. 3 and 10) consists of two layers, an inner and an outer one, which are continuous at the margins of the folds, and are separated by a fissure, which is a portion of the extra-embryonic body-cavity. At the amniotic suture the corresponding layers of the folds of both sides fuse, and hand in hand with this a separation of the inner from the outer layers takes place (Plate I., fig. 4). As a result of this *there have now arisen two envelopes* over the back of the embryo, *an inner and an outer one, the amnion* (*A*) *and the serosa* (*S*).

The amnion is the product of the inner layer of the folds (Plate I., fig. 10 *ifb*). It forms a sac which immediately after its origin is closely applied about the embryo, and which encloses a very small amniotic cavity filled with fluid.

The serous membrane (serosa), which is derived from the outer layer of the folds (*afb*, Plate I., fig. 10), lies as a very delicate transparent membrane closely applied to the amnion, and thus encloses the embryo in still another envelope.

If we now glance back at the conditions described in the previous chapter, and compare the development of Fishes with that of Reptiles and Birds, it is to be seen that a considerable complication has arisen in the case of the latter. Whereas in Fishes the extra-embryonic area of the somatopleure becomes exclusively the dermal yolk-sac, in Reptiles and Birds two sacs have arisen out of it by a process of folding. The influences producing this folding appear to be clear.

Since the egg is enclosed in firmly applied envelopes, the embryonic body, when it is formed by the folding together of the germ-layers, cannot rise from the yolk-sac ; it therefore comes to lie in a depression of the latter. There is the more reason for the occurrence of this because the embryo at the beginning of development is excessively small in comparison with the yolk, and because the yolk-layers immediately underlying it become liquefied and absorbed. With the sinking of the body into the yolk (Plate I., figs. 2 and 3), the parts which in Fishes become the simple dermal yolk-sac (Plate I., figs. 6 and 7) fold in around it on all sides as amniotic folds, and enclose it the more completely the deeper it sinks into the yolk.

The preceding account of the development of the amnion is made somewhat schematic in a single point. That is to say, the anterior fold of the amnion is developed so early, that the middle germ-layer has not yet been able to spread out as far as the anterior part of the embryonic area. The infolding, therefore, in this region involves only the outer and inner germ-layers, which are still closely united. This condition is changed somewhat later, when the middle germ-layer has grown into the region of the anterior fold of the amnion, and has there split into a visceral and a parietal layer. The process has not yet been followed out in detail in series of longitudinal sections. But at all events we must assume that the entoblast, which is united with the visceral middle layer, retracts from the anterior fold of the amnion and again spreads out flat, as is represented in diagrammatic figure 11 (Plate I.). In this manner the anterior amniotic fold, which in the meantime has become greatly enlarged, now consists of the outer germ-layer and the parietal middle layer, as is the case from the beginning with the subsequently arising posterior and lateral folds of the amnion.

We now have to enter still more particularly upon the further relations of amnion and serosa.

Up to the end of embryonic development the *amniotic sac* remains in continuity with a small region on the ventral side of the embryo, which is called the dermal umbilicus. In figs. 3, 4, 5, and 10 (Plate I.) this place is indicated by means of a circular line (*hn*). Here the primitive layers of the body-wall are continuous with the corresponding layers of the amnion, as, for instance, the epidermis of the body with an epithelial layer lining the amniotic cavity. The dermal umbilicus of Reptiles and Birds corresponds therefore with the structure of the same name in embryo Fishes (Plate I., fig. 7 *hn*), for it is at this point that the dermal yolk-sac is continuous by means of its stem-like elongation with the walls of the belly. As in the Fishes, it surrounds an opening (Plate I., figs. 7 and 5 *hn*) which unites the portion of the body-cavity lying within the embryo (lh^1) with the extra-embryonic part lying between the embryonic membranes (lh^2). Furthermore, the stalk of the yolk-sac or vitelline duct, which is continuous with the embryonic intestine, and which is indicated in the above-mentioned figures of Plate I. by the small circle *dn*, passes through the opening.

The amniotic sac affords an additional special advantage to the embryos of Reptiles and Birds in that an albuminous saline fluid, the liquor amnii, collects in its cavity. In it the delicate, easily injured embryo composed of plastic cells floats, as it were, and is able to move.

The amniotic sac is small at the beginning of its development, but enlarges with each day of incubation, since it keeps pace with the growth of the embryo and encloses a larger and larger amount of amniotic fluid.

At the same time its wall becomes contractile. Certain cells in its somatic mesoderm develop into contractile fibres, which in the Chick give rise to rhythmic movements from the fifth day of incubation onward. One can observe these while the egg-shell remains intact, if one holds the egg toward a source of bright light, and for this purpose makes use of the oöscope constructed by PREYER. In this manner it can be determined that the amnion executes about ten contractions in a minute, which, beginning at one pole, proceed to the opposite end, like the contractions of a worm. Thus the amniotic fluid is set in motion, and the embryo oscillates or rocks regularly from one end to the other. The rocking of the embryo, as PREYER expresses it, becomes more and more obvious in the later days of incubation, since the contractions of the amnion become more energetic.

The *serosa* (*S*) is a wholly transparent, easily ruptured membrane, which is closely applied to the vitelline membrane. It consists of two thin cell-layers, which take their origin from the outer germ-layer and the parietal middle layer, and like them are distinguished by blue and red lines in the diagram. The serous membrane is originally present as a separate structure only in the region of the amnion and of the embryo (Plate I., fig. 4), as far as the body-cavity is formed in the middle germ-layer. It then enlarges to the same extent as the

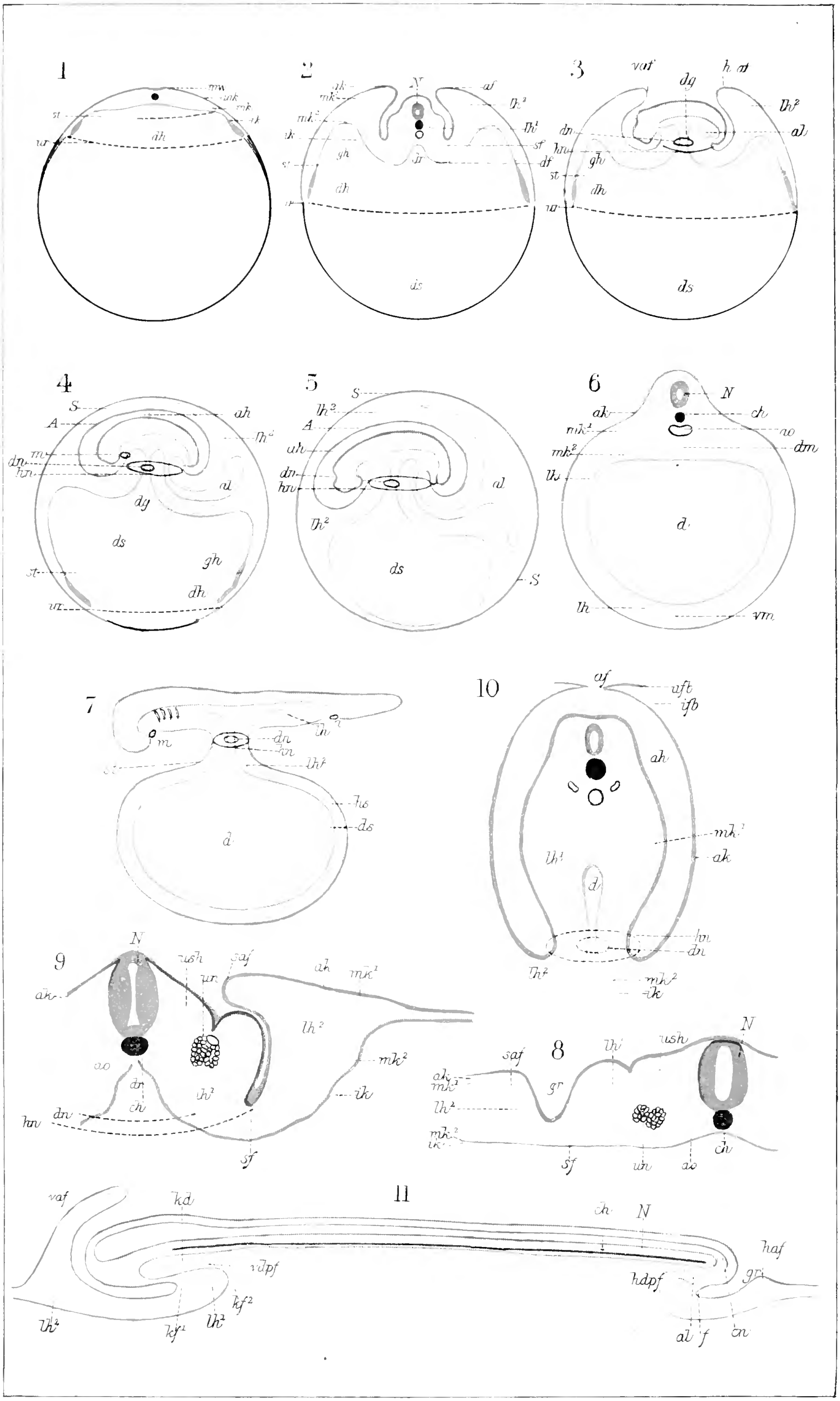

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PLATE I.

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yolk becomes overgrown and as the vascular area extends farther downwards. Parietal and visceral middle layers separate more and more from each other, until finally (in the Chick toward the end of incubation) a separation results over the entire periphery of the yolk-sphere. Figs. 3, 4, and 5, Plate I., show stages in this process. In the last figure, which represents the condition on about the seventh day of incubation, the extra-embryonic part of the body-cavity has already become very considerable; the serous envelope is, with the exception of a small place at the vegetative pole of the yolk, everywhere formed as a separate structure.

In connection with this the wall of the yolk-sac also becomes changed. Whereas at the beginning of the overgrowth it embraces for a considerable distance all the germ-layers, after the separation of the serosa it is composed exclusively of entoderm and the visceral middle layer.

Explanation of the Figures on Plate I.

Figs. 1-5 are diagrammatic representations of cross and longitudinal sections through the Hen's egg at different stages of incubation. They are intended to illustrate how the body of the Chick is developed out of the embryonic fundament, and how the yolk-sac, the amnion, the serosa, and the allantois arise out of the extra-embryonic area of the germ-layers.

For the sake of clearness the embryonic fundament, and later the embryo, are represented much too large in relation to the yolk.

In order more easily to distinguish the different parts from one another different colors have been selected for them. The yolk is represented in yellow, the entoderm green, the outer germ-layer blue, and the middle germ-layer, together with the mesenchyme, red. The black dots indicate the limit to which the outer and inner germ-layers have grown over the yolk in the different stages; the red dots mark the boundary for the time being of the middle germ-layer, which after the development of the blood-vessels ends in the sinus terminalis.

The references apply to all of the figures.

ak, *Outer germ-layer* (blue).
mw, Medullary ridges or folds.
N, Neural tube.
af, Amniotic fold.
vaf, *haf*, *saf*, Anterior, posterior, and lateral amniotic folds.
A, Amnion.
ah, Amniotic cavity.
S, Serous membrane (Serosa).
hn, Dermal umbilicus.
sf, Lateral folds. kf^1, kf^2, Head-fold; *afb*, *ifb*, outer and inner limbs of fold.
ik, *Inner germ-layer* (green).
ur, Its margin of overgrowth.
dr, Intestinal groove.
dg, Vitelline duct.
al, Allantois.
ds, Intestinal sac.
dn, Intestinal umbilicus.
mk, *Middle germ-layer* (red).
mk^1, Parietal lamella of the same or parietal middle layer.
mk^2, Visceral lamella of the same or visceral middle layer.
st, Lateral limit of the same, sinus terminalis, marginal vein.
dm, *vm*, Dorsal and ventral mesenteries.
lh, Body-cavity. lh^1, Embryonic, lh^2, extra-embryonic part of the same.

Fig. 1.—*Cross section through a Hen's egg on the second day of incubation.*

The germ-layers are spread out flat over the yolk; the middle one is less extensive than the other two. The first blood-vessels have developed, and terminate with the marginal vein (*st*) at the edge of the middle germ-layer. One now distinguishes therefore the vascular area, which extends to the red dotted line (*st*), and external to it the yolk-area (*dh*), which terminates with the black dotted line (*ur*), the edge of overgrowth of the outer and inner germ-layers.

Fig. 2.—*Cross section through a Hen's egg on the third day of incubation.*

The outer and inner germ-layers are spread out over half of the yolk. The yolk-area (*dh*) terminates with the black dotted line (*ur*), the edge of overgrowth.

The middle germ-layer, with the vascular area, which is now well developed, has also grown over the yolk as far as the line *st* (the sinus terminalis). In the middle germ-layer the body-cavity has become distinct in the embryonic region (lh^1) and in its immediate vicinity (lh^2), the parietal (mk^1) and visceral middle layers (mk^2) having separated from each other.

The embryonic fundament begins to be constricted off from the extra-embryonic part by a process of folding and to constitute the trunk. The lateral folds (*sf*) have grown downwards for a certain distance, thus giving rise to the lateral walls of the trunk, whereas ventrally the body is still open. Corresponding to these lateral folds (*sf*), the lateral intestinal folds (*df*) have arisen on the splanchnopleure, and bound the intestinal groove (*dr*).

The embryo in process of being constricted off has sunk into a depression of the more and more liquefied yolk, and becomes partly enveloped by the somatopleure of the extra-embryonic area of the germ-layers, the lateral folds of the amnion (*af*) having already encircled the sides of the embryonic body.

Fig. 3 *shows a longitudinal section through the stage represented in cross section in fig.* 2. (*Third day of incubation.*)

The head-end of the body is entirely constricted off from the blastoderm. It encloses the cephalic portion of the intestine (Kopfdarmhöhle). The tail-end is only slightly differentiated. The anterior fold of the amnion (*vaf*) has invested the head, the posterior fold (*haf*) the tail (cephalic sheath, caudal sheath).

The middle of the trunk is still wide open ventrally. The place where the body-wall passes over into the folds of the amnion, and which is indicated in the diagram by the ring *hn*, is called the dermal umbilicus.

The splanchnopleure has become closed into a tube anteriorly and posteriorly (the cephalic and pelvic portions of the intestinal cavity); in the middle the tube is still open ventrally, and by means of the vitelline duct (*dg*) is continuous with the yolk-sac (*ds*). The place of transition indicated by the ring *dn* is the intestinal umbilicus. The allantois (*al*) grows out as a small vesicle from the ventral wall of the pelvic portion of the intestinal cavity into the body-cavity of the embryo.

Fig. 4.—*Longitudinal section through a Hen's egg at the beginning of the fifth day.*

After the fusion of the amniotic folds, the embryo, together with the amniotic cavity (*ah*), is enveloped in the amniotic sac. The serous membrane (*S*) has been developed from the outer layer of the amniotic folds. By further separation of the middle germ-layers the extra-embryonic part of the body-cavity (lh^2) has enlarged, and the allantois (*al*) has grown into it.

With the exception of a third of its surface, the yolk has become overgrown by the outer and inner germ-layers, as far as the line *ur*. The vascular area has extended to the line *st*. The cephalic portion of the intestinal cavity has opened into the amniotic cavity by means of the newly arisen mouth (*m*).

Fig. 5.—*Longitudinal section through a Hen's egg on the seventh day of incubation.*

By the enlargement of the extra-embryonic body-cavity the serous membrane (serosa) has entirely separated from the yolk-sac, with the exception of a small area. The outer and the inner germ-layers have now grown over the yolk on all sides; the middle germ-layer with the vascular area has extended farther downwards. The amniotic cavity, in which the embryo floats, has become much extended by the increase of the amniotic fluid. The allantois has enlarged considerably, and forms a sac, which connects with the hind gut by means of a narrow stalk (urachus). The sac extends out into the extra-embryonic body-cavity between amnion, yolk-sac, and serous membrane, more particularly on the right side of the embryo.

Fig. 6 *represents a diagrammatic cross section through an embryo Fish.*

The dorsal part is already far advanced in development and encloses the neural tube (*N*), the chorda (*ch*), the aorta (*ao*), and the primitive segments. The ventral side is greatly distended by the considerable yolk-mass (*d*). The latter lies in an enlargement of the intestinal canal, the intestinal yolk-sac; this is separated from the enlarged dermal yolk-sac by means of a narrow fissure, the body-cavity (*lh*).

Fig. 7.—*Diagrammatic longitudinal section through a Selachian embryo.*

The yolk-sac has been partly constricted off from the body of the embryo; it still remains united to its ventral side, but only by means of a narrow stalk (*st*), which consists of two tubes, one within the other, the intestinal stalk (vitelline duct) and the dermal stalk. The yolk-sac communicates with the embryonic intestinal canal by means of the vitelline duct. The point of transition is called the intestinal umbilicus (*dn*). The point of attachment of the dermal stalk to the belly of the embryo is the dermal umbilicus (*hn*). The space between dermal and intestinal umbilicus (*hn* and *dn*) serves to put the body cavity of the embryo (lh^1) in communication with the body-space (lh^2) between the dermal and intestinal yolk-sacs.

Figs. 8, 9, 10, 11.—*Diagrammatic cross and longitudinal sections through embryo Chicks of different ages.*

Fig. 8.—*Half of a cross section through an embryo Chick of two days*, after KÖLLIKER.

The embryonic body, in which the neural tube (*N*), chorda (*ch*), primitive segment with its cavity (*ush*), primitive aorta (*ao*), and the fundament of the primitive kidney (*un*) are to be seen, is marked off from the extra-embryonic region of the germ-layers by the marginal groove (*gr*). The body-wall begins to be developed, owing to the somatopleure having given rise to the lateral fold (*sf*), the ridge of which is directed toward the yolk. External to it the lateral fold of the amnion (*saf*) rises in an opposite direction.

Fig. 9.—*Cross section of an embryo Chick at the beginning of the third day*, after KÖLLIKER.

The lateral folds (*sf*) have grown farther downward, and have completed the body-wall. The lateral folds of the amnion (*saf*) likewise have risen up farther toward the back of the embryo. The splanchnopleure has folded in to form the groove *dr*. The dotted line *hn* indicates the still broad dermal umbilicus, the line *dn* that of the intestinal umbilicus.

Fig. 10.—*Cross section through the trunk of a five-days embryo Chick in the region of the umbilicus*, after REMAK.

By an approximation of the lateral folds, the body-wall has been completely formed up to the region enclosed by the line *hn*, in which the body-cavity still possesses an opening, and communicates with the extra-embryonic portion of the body-cavity. At the line *hn*, the dermal umbilicus, the body-wall bends over into the folds of the amnion (*af*), which have grown over the back of the embryo, and are about to fuse along their edges. At the dermal umbilicus (*dn*) the intestinal tube (*d*) passes over into the yolk-sac, which is not represented.

Fig. 11.—*Diagrammatic longitudinal section through an embryo Chick.*

The head is already fully differentiated from the blastoderm by the process of folding, the tail-portion is less completely separated; the former encloses the cephalic portion of the intestinal cavity (*kd*), which is in connection with the yolk-sac by means of the anterior intestinal portal (*v.dpf*). The pelvic portion of the intestinal cavity, which shows the first traces of the allantois (*al*), communicates backwards and above with the neural tube by means of the neurenteric canal (*cn*), and toward the yolk-sac by means of the posterior intestinal portal (*h.dpf*). The head-end is already partly ensheathed by the anterior amniotic fold (*vaf*), whereas at the tail-end the posterior amniotic fold (*haf*) is just beginning to be elevated.

2. The Allantois.

While the development of the amnion is still going on, there is formed in Reptiles and Birds an embryonic organ of no less importance, the *allantois*, or urinary sac. It has two different functions to perform at the same time. In the first place it serves, as its name implies, for the reception of the excretory products which are furnished during embryonic life by the kidney and primitive kidney; and secondly, by virtue of the abundance of blood-vessels and the superficial position that it acquires, it is the most important organ of respiration.

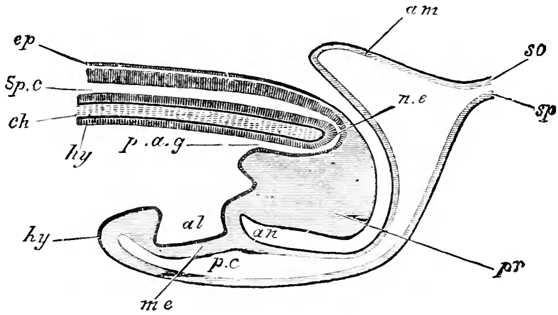

Fig. 128.—Diagrammatic longitudinal section through the posterior end of an embryo Chick at the time of the formation of the allantois, after Balfour.

The section shows that the neural tube, *Sp.c*, is continuous at its posterior end with the hind gut, *p.a.g*, by means of the neurenteric canal, *n.e*. The latter passes through the remains of the primitive streak, *pr*, which is folded over toward the ventral side. *ep*, Outer germ-layer; *ch*, chorda; *hy*, entoderm (hypoblast); *al*, allantois; *me*, middle germ-layer; *an*, the point where the anus will arise; *am*, amnion; *so*, somatopleure; *sp*, splanchnopleure.

The allantois takes its origin from the posterior portion of the hind gut, which is afterwards designated as the cloaca, and in the Chick the first traces of it can be recognised even at the end of the second day, at a time when the walls of the hind gut are still in the process of formation. It appears in this instance as a small cæcal evagination (*al*) on the anterior wall of the splanchnopleure (*hy*) (fig. 128; Plate I., fig. 3 *al*).

The evagination is lined by the entoderm, and is covered externally by a growth of the splanchnic mesoderm. It enlarges rapidly into a vesicle, which grows out into the body-cavity (Plate I., fig. 4 *al*). At the same time the blind end enlarges, whereas the proximal part, where it passes over into the hind gut, becomes narrow and elongated into a hollow stalk, the urinary duct or urachus.

On the fourth day the urinary sac is so enlarged that it can no longer find room in the embryonic part of the body-cavity, and therefore forces itself into the extra-embryonic portion of it between the intestinal and dermal portions of the umbilical stalk (Plate I., fig. 5 *al*). Here it comes into the space between the yolk-sac (*ds*) and amnion (*A*); then it comes in contact with the inner surface of the serosa (*S*), and spreads out under it for a considerable distance over the right side of the embryonic body.

In regard to the *subsequent fate of the embryonic membranes in the Chick,* it is to be noticed that up to the middle of incubation, *i.e.*, up to about the eleventh day, they continue to develop in a progressive direction, but that from this time onward certain regressive processes commence, which later become more and more apparent.

In the first period (fifth to eleventh day) the following changes are effected in the yolk-sac, the amnion, the allantois, etc. The vascular area spreads out, in the manner before described, over a greater area in the wall of the yolk-sac, which still retains a considerable size. On the seventh day it covers about two-thirds (Plate I., fig. 5), and on the tenth three-fourths of the yolk-sac. At the same time the marginal vein becomes indistinct, and the sharp separation from the non-vascular portion ceases.

The contents of the yolk-sac have become fluid by chemical changes of the yolk-mass. The serosa (*S*) is raised from its surface as far as the vascular area has extended, owing to the enlargement of the extra-embryonic body-cavity. At the same time the *allantois* (Plate I., fig. 5 *al*) has grown into the intermediate space. This has enlarged so much by the tenth day that it leaves uncovered only a small portion of the yolk-sac and amnion. It has lost still more of its sac-like character; for between its outer layer, which almost everywhere is closely applied to the inner surface of the serosa, and its inner layer, adjoining the amnion and yolk-sac, there is found only an insignificant intermediate space filled with urine.

The allantois, moreover, has by this time become a very vascular organ and is nourished by the umbilical vessels, which will engage our attention in a subsequent chapter devoted to the vascular system. The network of blood-vessels is densest in its outer layer, which spreads out at the surface of the egg; it serves to maintain here the processes of embryonic respiration, since carbonic acid is given off from the superficially circulating blood and oxygen is taken up. The latter is acquired in part directly through the egg-shell and in part out of the air chamber (fig. 8 *a.ch*) situated at the blunt pole of the egg, which is in contact with a large part of the allantois.

Finally, in addition to respiration, the allantois serves for the *resorption of the albumen*, which becomes more and more thickened during incubation, and compressed into a lump at the pointed pole of the egg. It grows over the albumen and envelops it in a sac, the epithelial surface of which arose from the serosa, which was evaginated at the same time with the growing allantois. There are developed on the inner surface of the sac highly vascular villi, which sink into the albumen, and have been described as a placenta by DUVAL, who has called attention to these conditions.

The *air chamber* also has undergone modifications during incubation, and, at the same time with the acquisition of air, has increased in size by the separation of the two layers of the shell-membrane in which it is enclosed (fig. 8, p. 17).

Finally, the *amnion*, which at the beginning of its development is rather closely applied to the embryo, has enlarged and become a sac (Plate I., fig. 5 *A*) entirely filled with amniotic fluid. Its rhythmical contractions already described become most active and powerful on the eighth day, and from that time forward to the end of incubation diminish in frequency and in force.

As a result of all these processes of growth, the embryo with its appendages now demands a much larger space than at the beginning of incubation. It acquires this in the following manner. The albumen which surrounds the yolk diminishes considerably, since it disappears, especially its fluid portion, partly by evaporation to the exterior, partly also by resorption on the part of the embryo. The vitelline membrane has become ruptured by the enlargement.

In the second period, which we have reckoned from the eleventh to the twenty-first day, or to the hatching of the Chick, *retrogressive metamorphoses* are most prominent.

These assert themselves first of all on the *yolk-sac*. As the result of the vigorous sucking up of its contents it becomes more and more flaccid, so that its wall begins to lie in folds. It now becomes entirely separated from the serosa, since the extra-embryonic body-cavity has extended all around it, and thereupon it is drawn closer to the wall of the belly by the shortening of the umbilical stalk. On the nineteenth day of incubation it begins to slip into the peritoneal cavity through the dermal umbilicus, which has now become very narrow, whereby it takes on an hour-glass shape during its passage through the ventral wall. It is here employed to help in the closure of the intestinal wall.

The amnion undergoes regression, inasmuch as the fluid diminishes and almost entirely disappears, until the membrane is again closely applied to the body of the embryo. The albumen, too, is almost entirely consumed. The allantois alone continues to increase, and finally grows around so completely on the entire inner surface of the serosa that its edges come together and fuse with one another into a sac entirely enclosing the embryo and the amnion. It adheres so firmly to the serosa that a separation is no longer possible.

The *urine* likewise diminishes toward the end of incubation, and finally, like the amniotic fluid, has entirely disappeared. As the result of this, there are found in the allantois precipitates of uric salts, which become more and more abundant.

Amnion and allantois finally undergo complete retrogressive metamorphoses. Inasmuch as the Chick, shortly before hatching, breaks through the surrounding membranes with its bill, it begins to take in directly the air contained in the air chamber, which has become larger. A result of this is that the circulation in the allantois is retarded and finally ceases altogether. The afferent umbilical vessels disappear. Amnion and allantois die away, dry up, and then separate from the dermal umbilicus, which closes on the last day before hatching, and when the Chick leaves the egg-shell they are stripped off with it as useless remains.

SUMMARY.

1. In Reptiles and Birds the embryo during its development sinks into the underlying yolk, which has become liquefied, and becomes enveloped by folds of the extra-embryonic area of the somatopleure, the anterior, posterior, and lateral folds of the amnion (cephalic sheath, caudal sheath, lateral sheaths).
2. As the result of the folding processes two sacs arise around the embryonic body, the amnion and the serous membrane (serosa).
3. The amnion is united at the dermal umbilicus with the belly of the embryo.
4. The dermal umbilicus encloses an opening through which the embryonic and extra-embryonic portions of the body-cavity are in connection.
5. The stalk of the yolk-sac passes through the dermal umbilicus in order to attach itself to the intestine at the intestinal umbilicus.

6. The allantois is evaginated from the ventral wall of the posterior tract of the hind gut (cloaca), grows as a pedunculated sac (1) into the body-cavity, and (2) through the dermal umbilicus into the extra-embryonic part of the same, extends out from here on all sides between the amnion and serosa, and by virtue of its great vascularity functions as an organ of respiration.

7. At the end of embryonic development the constantly diminishing yolk-sac, after the consumption of the yolk, slips through the open dermal umbilicus into the body-cavity, and is employed in the closure of the intestinal umbilicus.

8. Amnion, serosa, and that part of the allantois which has grown out beyond the embryonic body, are cast off as useless structures at the dermal umbilicus, which becomes closed.

CHAPTER XII.

THE FŒTAL MEMBRANES OF MAMMALS.

In their early stages of development the fœtal membranes of Mammals present an extraordinary correspondence with those of Reptiles and Birds (fig. 129). We find a yolk-sac (*UV*) with abundant capillaries, an amnion (*am*), a serous membrane or serosa (*sz*), and an allantois (*ALC*); we find that, in the same way as before, the embryo is developed out of a small region of the blastula, and is constricted off in the same way from the extra-embryonic area, with which it remains united only by means of a dermal and intestinal yolk-stalk.

The correspondence becomes a striking one and stimulates to further reflection, when we take into consideration that the developmental processes enumerated are primarily evoked by means of the accumulation of yolk-material in the eggs of Reptiles and Birds, and that the eggs of most Mammals lack almost entirely the yolk, are of very small size, undergo total segmentation, and in all these respects resemble more the eggs of Amphioxus.

Why, then, does the mammalian germ nevertheless undergo metamorphoses which in other cases are only the result of the accumulation of yolk? Why is there developed a yolk-sac that contains no yolk, with a system of blood-vessels that is designed for the resorption of yolk?

For the explanation of these conditions we must have recourse to an hypothesis which can be formulated about as follows:—

The Mammalia must have descended from animals which possessed large eggs with abundant yolk, which were oviparous, and in which consequently the embryonic membranes were developed in the same way as in Reptiles and Birds. The loss of the yolk-contents from the eggs of these animals must have been a supplementary event, which began at the time when the eggs were no longer deposited outside, but were developed in the uterus. For by this change there was found a new and more productive, because unlimited, source of nourishment for the developing germ in substances which were secreted by the walls of the uterus from the maternal blood. There was therefore no more need of a dower of yolk. But the enveloping structures, which were originally called into existence by the presence of yolk-contents in the eggs, were retained, because they were still of use in many other relations, and because, through a change of function, they became subservient to *uterine nourishment* and correspondingly underwent changes.

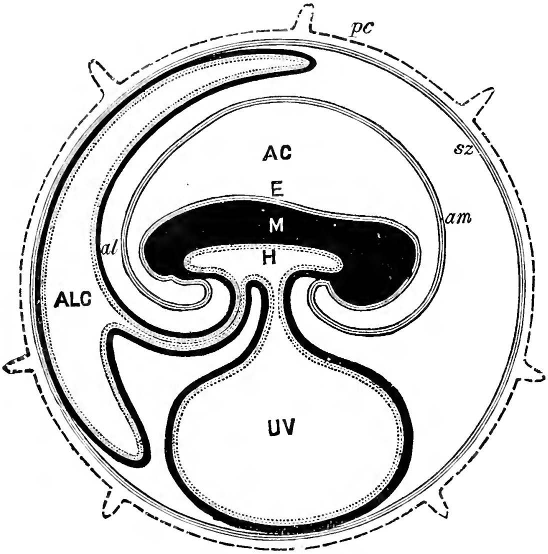

Fig. 129.—Diagram of the fœtal membranes of a Mammal, after TURNER.
pc, Zona pellucida with villi (prochorion); *sz,* serous membrane; *E,* outer germ-layer of the embryo; *am,* amnion; *AC,* amniotic cavity; *M,* middle germ-layer of the embryo; *H,* inner germ-layer of the same; *UV,* yolk-sac (vesica umbilicalis); *ALC,* allantoic cavity; *al,* allantois.

Three facts can be cited in favour of this hypothesis.

In the first place, in the lowest classes of Mammals, as in the Monotremes and Marsupials, the eggs are larger than in placental animals. They are characterised by a large quantity of yolk, which, as in Ornithorhynchus for instance, is deposited in closely compacted spheres of varying size and fat-like lustre. In this particular they form a transition to the eggs of Reptiles and Birds.

Secondly, it has been observed that the Monotremes, the lowest division of the Mammalia, are oviparous, like Birds and Reptiles. Quite recently two investigators, HAACKE and CALDWELL, have made the interesting discovery that Echidna and Ornithorhynchus, instead of giving birth to living young, as was hitherto assumed, lay eggs which are nearly two centimetres in diameter, and enveloped in a parchment-like shell, and which they carry about with them in their brood-pouch or mammary pocket.

Thirdly, the fœtal membranes of Marsupials, which next to the Monotremes are to be considered as the lowest Mammals, remain permanently in a condition which corresponds to that of Reptiles and Birds, although the development takes place in the uterus. As we know through OWEN, the embryo, which is enclosed in a capacious amnion, possesses a very large vascular yolk-sac, which extends out to the serosa, and in addition a small allantois and a serosa. The latter lies closely applied to the walls of the uterus, but without being intimately united with it. Probably, therefore, after resorption of the yolk, substances which have been secreted by the uterus are taken up by the blood-capillaries of the yolk-sac. Thus a kind of intra-uterine nutrition begins to be established in the Marsupials; but otherwise the embryo with its envelopes lies in the cavity of the uterus, like the Avian or Reptilian embryo with its membranes in the firm egg-shell.

Having established the hypothesis, already expressed by various authors, that the eggs of Mammals must originally have contained more yolk, let us turn to a more exact description of the fœtal membranes. As regards the first stages of development, let us begin with the Rabbit, because its embryology has been the most thoroughly investigated; then, in order to facilitate our understanding of the structure of the human placenta, we shall show in a brief sketch how, in the class of Mammalia, in various ways more intimate anatomical and physiological relations are developed between the mucous membrane of the uterus and the embryonic membranes. We shall treat of the fœtal membranes of Man in a special chapter.

When, in the Rabbit, the ovum, which has reached the uterus, has here become metamorphosed into the blastula already described, it is still enveloped by the zona pellucida. This in the meanwhile has been distended into a thin pellicle (prochorion), which is subsequently destroyed.

The blastula, or blastodermic vesicle, expands rapidly, and from the fifth to the seventh day grows from 1·5 mm. to 5 mm. in diameter. In consequence of this increase in size the prochorion on the seventh and eighth days is so closely applied to the inner surface of the uterus that it becomes more and more difficult, and finally impossible, to detach the eggs without injury. For by the rupturing of the prochorion, which adheres to the walls of the uterus, the delicate blastula, which is in close contact with it, generally becomes injured and torn open, and thereupon collapses, owing to the escape of its contents. The latter have also suffered changes which make the investigation more difficult, having increased in consistency until they equal in density the albumen of the Hen's egg.

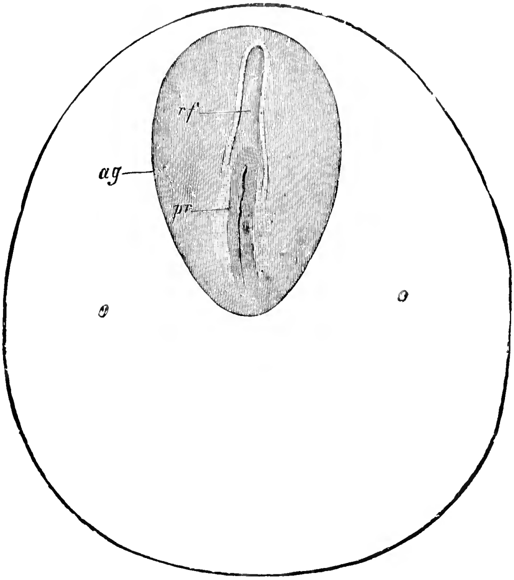

Fig. 130.—Embryonic fundament of the ovum of a Rabbit of seven days, from Kölliker.

o, Vascular area (area opaca) ; *ag*, embryonic fundament ; *pr*, primitive streak ; *rf*, dorsal furrow.

During the process of attaching itself, the embryonic fundament, which at first is round, increases in size and takes on a more elongated form. On the seventh day it becomes oval (fig. 130 *ag*), then pear-shaped, and on the eighth day acquires a more and more marked sole-like form; meanwhile it grows to a length of about 3·5 mm. (fig. 131).

As has been already described in the previous chapter, at this time the middle germ-layer spreads out in the embryonic fundament, the medullary groove (figs. 130 and 131 *rf*), the chorda, and a number of primitive segments are formed, and, on the eighth day, the first trace of the vessels and blood appears in the vascular area (*o*). On the ninth and tenth days the embryonic fundament is by a process of folding converted into the body of the embryo, and is constricted off from the remaining part of the blastodermic vesicle, out of which at the same time various fœtal membranes begin to be developed. The initial stages of all these processes are the same in Mammals as in Birds and Reptiles, so that we can express ourselves very briefly in describing them. We shall connect the description with the diagrammatic drawings which KÖLLIKER has made, and which have found a place in many text-books (fig. 132, 1-5).

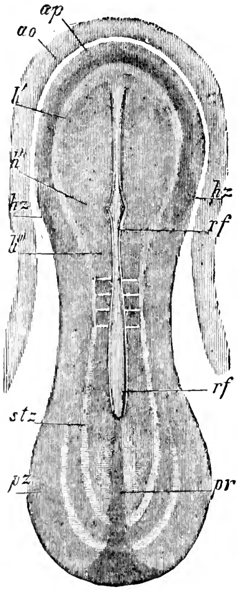

Fig. 131.—Embryonic fundament of a Rabbit of nine days with a portion of the area pellucida, from KÖLLIKER.

Ap, Area pellucida; *ao*, area opaca; *h'*, *h''*, *h'''*, medullary plate in the region of the first, second, and third cerebral vesicles; *stz*, stem-zone (Stammzone); *pz*, parietal zone; *rf*, dorsal furrow; *pr*, primitive streak.

Diagram 1 shows a blastodermic vesicle which in the Rabbit would correspond to about the seventh or eighth day. It is still enclosed from without by the very much attenuated vitelline membrane (*d*), which is now also called prochorion, since in many Mammals flakes and shreds of albumen have been precipitated on its outer surface out of the fluid secreted by the mucous membrane of the uterus. The inner germ-layer (*i*)—which in a slightly younger blastula, such as is represented in figure 62 *B*, reaches only to the line *ge*, and still leaves uncovered a third of the inner surface of the sphere—has now entirely grown around to the vegetative pole. The middle germ-layer (*m*) is in full process of development, and embraces about a fourth part of the surface of the sphere. A small portion of this three-layered region contains the embryonic fundament, which would be in about that stage of development which we have

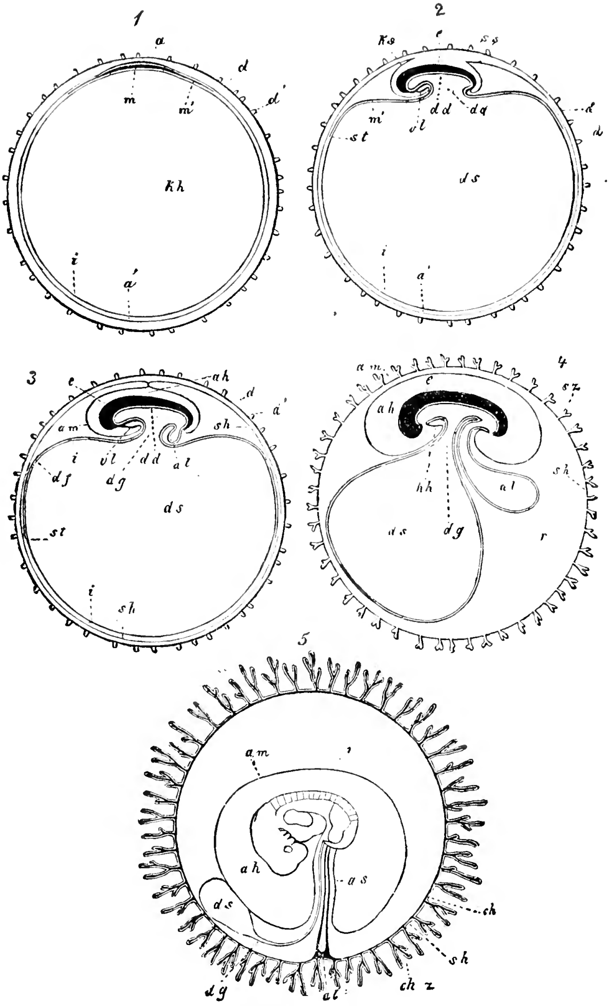

Fig 132.—Five diagrammatic figures illustrating the development of the fœtal egg-membranes of a Mammal, after Kölliker.

In figures 1 to 4 the embryo is represented in longitudinal section.

(1) Ovum with zona pellucida, blastula, embryonic area, and embryonic fundament.

(2) Ovum in which the yolk-sac and the amnion are beginning to develop.

(3) Ovum in which, by the fusion of the amniotic folds, the amniotic sac and the serous membrane are formed, and the allantois makes its appearance.

(4) Ovum with serous membrane, which has developed villi, with a large allantois and an embryo, in which the oral and anal openings have arisen.

(5) Diagrammatic representation of a young human ovum, in which the vascular layer of the allantois has become applied to the serous membrane on all sides, and has grown into its villi. The serous membrane from this time forward takes the name of chorion. The cavity

before us in the surface-view in figure 130. It is ovate, and shows the primitive streak (*pr*) in the posterior half, and in front of it a deep dorsal furrow (*rf*); the extra-embryonic part of the middle germ-layer can be designated as the vascular area (*o*), since the first traces of the formation of the vessels and the blood are noticeable in it.

In the much further developed embryo figured in diagram 2 (at about the ninth day in the Rabbit) the middle germ-layer has spread out over about the third part of the blastula, and now encloses an easily distinguishable body-cavity, since the parietal and visceral middle layers have separated from each other in the embryonic as well as extra-embryonic regions. It extends as far as the place marked *st*, where the sinus terminalis is found as the outer limit of the now clearly defined vascular area.

The embryonic fundament is in the act of being constricted off from the blastodermic vesicle. The head- and tail-ends of the embryo, by foldings of the separate layers, have been elevated from the area pellucida in the same way as in the Chick. As there, a cephalic and pelvic part of the intestinal tract (fore and hind gut) have arisen, with an anterior and posterior intestinal portal, which open toward the cavity of the blastodermic vesicle.

At the same time occurs the development of the amnion, which was first recognised in the Mammalia by BAER and BISCHOFF. On the diagrammatic section one sees that the extra-embryonic body-cavity has become very capacious, in that the outer germ-layer with the closely applied parietal middle layer has risen up in the vicinity of the embryo and formed itself into the folds *ks* and *ss*. The anterior fold of the amnion (*ks*) has bent over the head, and the posterior fold (*ss*) over the tail. The two sheaths lie so close to the embryo in the Mammalia, that in looking from the surface they are not easily recognised, especially as they are extraordinarily transparent.

On the third diagram the amniotic folds have greatly enlarged, and have grown toward each other over the back of the embryo till their

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of the allantois has diminished and the yolk-sac has become very small, but the amniotic cavity is in the act of increasing.

d, Vitelline membrane (zona pellucida); *d'*, villi of the same; *sh*, serous membrane [serosa]; *ch*, chorion; *ch.z*, villi of the chorion; *am*, amnion; *ks*, *ss*, cephalic and caudal folds of the amnion; *a*, outer germ-layer; *a'*, the same in the extra-embryonic region of the blastula; *m*, middle germ-layer; *m'*, the same in the extra-embryonic region; *dd*, inner germ-layer; *i*, the same in the extra-embryonic region; *df*, vascular area; *st*, sinus terminalis; *kh*, cavity of the blastula, which later on becomes the cavity of the yolk-sac (*ds*); *dg*, stalk of the yolk-sac (vitelline duct); *al*, allantois; *e*, embryo; *r*, space between chorion and amnion, extra-embryonic part of the body-cavity, filled with albuminous fluid; *vl*, ventral body-wall; *hh*, pericardial cavity.

edges are in mutual contact. The closure of the sac takes place in a somewhat different manner from that of the Chick. Instead of meeting in a longitudinal suture, the edges of the amniotic folds meet, in the Rabbit at least, approximately in the middle of the back in a small spot, where for a considerable time a circular opening in the sac is retained. The outer layer of the amniotic fold, which in diagram 3 is still in connection with the amniotic sac at the point of fusion, but which later entirely separates from it, represents, as in the Chick, the serosa. It first appears as an independent structure in the vicinity of the embryo, whereas farther downwards it is still firmly united with the entoblast, and together with it constitutes the wall of the original blastula, which is here only two-layered.

In the third diagram, furthermore, we can recognise the first trace of the allantois (*al*), which grows out from the anterior wall of the hind gut in the manner already described (p. 217), and which in the Rabbit is seen as early as the ninth day in the form of a small, pedunculated, exceedingly vascular sac.

The fourth diagram shows the development of the fœtal membranes much further advanced. The prochorion has become ruptured by the distension of the entire blastodermic vesicle, and is no longer recognisable as a separate membrane. What we see on the outside is the serosa, which has been changed in a striking manner. In the first place, it has become completely detached from the amnion; however, it should be remarked in this connection that in certain Mammals, and especially in Man, a stalk uniting the two membranes is retained for a considerable time at the amniotic suture. Secondly, the serosa is everywhere separated from the yolk-sac, and loosely surrounds the embryo and its remaining membranes as a thin sac. This condition has been brought about in the following manner: the middle germ-layer, which in diagram 3 had grown over only one half of the original blastula, has now spread over the other half also, and has become divided into its two layers. By this means the extra-embryonic part of the blastula is now completely split, as in the Chick, into an outer sac, the serosa, and the yolk-sac, separated from it only by the body-cavity.

Moreover, there exist in this respect differences among the Mammalia, since in some the serosa remains to a greater or less extent permanently united with the yolk-sac. This is the case, for example, in the Rabbit.

In the Rabbit, in which the yolk-sac at first fills the greater part of the blastodermic vesicle, the middle germ-layer spreads out over that half of the yolk-sac only which is turned toward the embryo. There is developed in it a system of capillaries, which ends abruptly in a marginal vein. The other half of the yolk-sac is without vessels, and is everywhere firmly united with the serosa. When, after the resorption of its contents, the yolk-sac commences to shrivel, it begins to take on a mushroom-like form (fig. 133 *ds*), owing to the folding in of the vascular half (*fd*) against the non-vascular part (*ed″*), which is fused with the serosa (*sh*). It remains united with the umbilicus of the embryo by means of an elongated intestinal stalk (or vitelline duct), which is comparable to the stalk of the mushroom.

The space (*r*) which is produced in the blastodermic vesicle by the shrinking of the yolk-sac does not become filled out by compensating growths of the amnion (*a*) and allantois (*al*), both of which remain small. Therefore a large amount of fluid collects between the separate fœtal membranes. The space filled with fluid is none other than the extra-embryonic part of the body-cavity, which in the Rabbit, as in no other Mammal, is highly developed. The allantois (*al*) hangs freely in this space as a stalked vesicle, a part of its surface having applied itself to that portion of the serosa (*sh*) which is not united with the yolk-sac, and which is circumscribed by the sinus terminalis (*st*). It is gradually metamorphosed into an organ of nutrition for the embryo, the placenta (*pl*), inasmuch as it receives a rich supply of blood through the vessels of the allantois, the umbilical vessels.

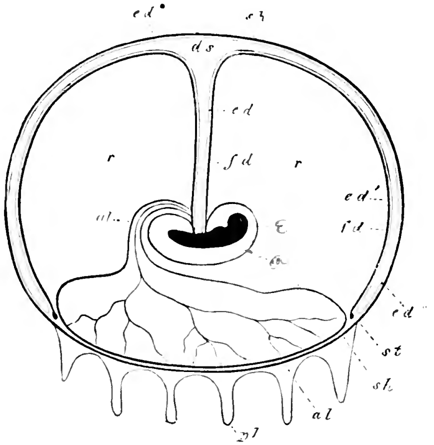

Fig. 133.—Diagrammatic longitudinal section through the ovum of a Rabbit at an advanced stage of pregnancy, after BISCHOFF.

e, Embryo; *a*, amnion; *u*, urachus; *al*, allantois with blood-vessels; *sh*, subzonal membrane; *pl*, villi of the placenta; *fd*, vascular layer of the yolk-sac; *ed*, entoblast of the yolk-sac; *ed′*, *ed″*, inner and outer lamellæ of the entoblast which lines the flattened cavity of the yolk-sac; *ds*, cavity of the yolk-sac; *st*, sinus terminalis; *r*, the space between amnion, allantois, and yolk-sac that is filled with fluid.

Subsequently the remaining surface of the blastodermic vesicle, over which the umbilical vessels do not extend, also becomes vascular. This is due to the fact that the albuminous fluid still contained in the mushroom-like yolk-sac becomes entirely absorbed, and that consequently its outer non-vascular and inner, invaginated vascular walls come to lie on each other and to fuse into a single membrane. In this manner the blastodermic vesicle in the Rabbit becomes provided with blood on its entire surface, but from two different sides—the placental portion from the vessels of the allantois, and the larger part of the surface from the degenerating vitelline vessels.

In regard to the formation of the amnion in the Rabbit, upon which VAN BENEDEN ET JULIN have made very thorough investigations, it is to be added that the middle germ-layer is wanting in the region of the anterior amniotic fold to a greater degree in this case than in the Chick. The anterior amniotic fold therefore consists during a considerable period of only the two primitive germ-layers, closely joined together. VAN BENEDEN has therefore given to the cephalic sheath, as long as the inner germ-layer takes part in its formation, the name of proamnion. Later on, however, a separation of the amnion from the entoblast takes place also in the head-region in the Rabbit.

Finally, in our fourth diagram, still a third change has appeared in the serosa. By rapid growth of the epithelium large numbers of small evaginations or villi have arisen on its outer surface. On this account the name of *chorion or villous layer* has been applied to it when these changes have been completed. It should also be added here that in the development of the villi uniformity among all Mammals by no means prevails. In the lowest orders (Monotremes, Marsupials) the surface of the blastodermic vesicle remains almost smooth, as in Reptiles and Birds. In them, therefore, the serosa is permanently retained during embryonic life, whereas in other Mammalia it is transformed into a villous membrane. By reason of these differences KÖLLIKER has divided Mammals into Mammalia achoria and Mammalia choriata.

On the other embryonic membranes of fig. 132, 4, it is principally changes in size only that have been effected. The yolk-sac (*ds*), over the entire surface of which the vitelline vessels now spread, has become considerably smaller, and is continuous with the embryonic intestine by means of a long slender stalk, the vitelline duct (*dg*). The amniotic sac (*am*) has already enlarged and is filled with fluid, the liquor amnii. Its walls are continuous at the umbilicus with the ventral wall of the embryo. The allantois (*al*) has become a vascular pear-shaped sac, which has grown out between the dermal stalk and umbilicus into the extra-embryonic part of the body-cavity, and soon after reaches the serosa.

The accurate representation of an embryo Dog of twenty-five days (fig. 134) affords us, better than the diagram (fig. 132, 4), a view of the connection of the two vascular sacs, the allantois and yolk-sac, with the intestinal canal.

The embryo is removed from the chorion and amnion. The ventral belly-wall is partly removed, and thereby the dermal umbilicus, which about this time has become rather narrow, has been destroyed. The intestinal canal, now to be seen in its entire length, is already converted throughout into a tube (*d*); near its middle it is continuous, by means of a short vitelline duct, with the yolk-sac (*ds*), which was cut open in the process of preparation. The allantois (*al*) is attached to the very end of the intestinal canal by means of the attenuated stalk-like urachus.

Up to this stage the correspondence in the development of the embryonic membranes in Mammals, Birds, and Reptiles is clear. But from now on the course of development in the Mammalia becomes more and more divergent, since *one portion of the embryonic membranes enters into closer relations with the mucous membrane of the uterus, and is thus converted into an organ of nutrition for the embryo.* In this manner a compensation is provided for the loss of the yolk.

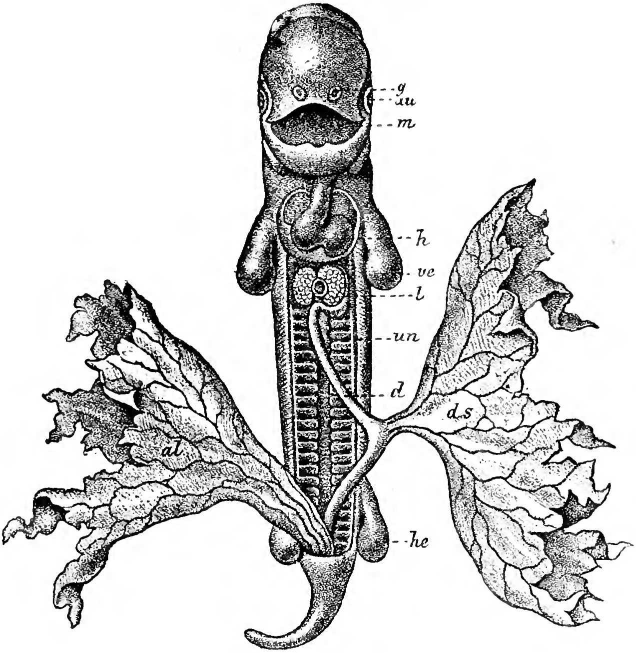

Fig. 134.—Embryo Dog of 25 days, extended and seen from in front. Magnified 25 diameters. After Bischoff.

d, Intestine ; *ds*, yolk-sac ; *al*, allantois, urinary sac ; *un*, primitive kidney ; *l*, the two lobes of the liver, with the lumen of the omphalomesenteric vein between them ; *ve*, *he*, anterior and posterior appendages ; *h*, heart ; *m*, mouth ; *au*, eye ; *g*, olfactory pit.

The interesting adaptations for intra-uterine nutrition—they have been studied especially by the English anatomist Turner in a series of profound comparative-embryological works—present very great differences in the separate orders of Mammalia : sometimes they are of a simple kind, at other times they are more complicated organs, which have been designated as the *after-birth*, or *placenta*. Since a knowledge of them will facilitate our comprehension of the human placenta, we shall consider them somewhat at length.

It is most expedient to distinguish three different modifications in the way in which the surface of the blastodermic vesicle comes into relation with the mucous membrane of the uterus, and accordingly to divide the Mammals into three groups.

In one the serosa is retained nearly in its simple primitive condition,

In the second it is transformed into a villous layer or chorion, and

In the third a placenta arises out of one or more portions of the chorion.

To the *first group* belong, among the Mammalia, only the Monotremes and the Marsupials, whose embryonic membranes are in the main constituted like those of Birds and Reptiles. Ordinarily in the Marsupials the serosa retains its smooth surface. Inasmuch as it lies in close contact with the vascular mucous membrane of the uterus, it can absorb nourishment from the latter and transmit it to the deeper-lying embryonic parts.

In the *second group* of Mammals an improvement in the intra-uterine nourishment is effected by important changes in the organisation of the serosa, which is converted into a villous layer or chorion.

In the first place, it is provided with blood-vessels by the allantois, which grows out into contact with it, and whose connective-tissue layer, containing the ramifications of the umbilical vessels, grows over its entire inner surface.

Secondly, the epithelial membrane begins to grow out into folds and villi, into which there soon penetrate vascular outgrowths of the connective-tissue layer. By this process a larger resorbing surface is provided.

Thirdly, the mucous membrane of the uterus and the chorion unite more intimately and firmly with each other, while the former also increases its surface and acquires pits and depressions into which the processes of the latter penetrate.

All these changes have simply the purpose of facilitating and rendering more perfect the interchange of materials between the tissues of the mother and those of the offspring.

We meet with membranes thus constituted in the Suidæ, the Perissodactyla, Hippopotamidæ, Tylopoda, Tragulidæ, Sirenia, and Cetacea. In the Pig, which shall serve as an example, the blastodermic vesicle, in adaptation to the form of the uterus, is transformed into a spindle-shaped sac. The inner embryonic appendages, the yolk-sac and allantois, are also drawn out in the same manner into two long tapering ends.

On the entire surface of the chorion, with the exception of the two ends of the sac, there have arisen rows of very vascular pads, which radiate from separate smooth round spots of the membrane, and are covered at their edges with small simple papillæ. The mucous membrane of the uterus is exactly fitted into the elevations and depressions of the chorion. There are also found on it circular smooth places similar to those of the chorion, which are further noteworthy from the fact that it is only on them that the tubular uterine glands open out. At birth the interlocking surfaces of contact separate from each other without any loss of substance on the part of the mucous membrane of the uterus; for the pads and small papillæ are easily withdrawn from the depressions which serve for their reception.

In the *third group* a special organ, the placenta, or after-birth, has been developed for the purpose of intra-uterine nutrition. Its origin was brought about by separate portions of the chorion having assumed different characters, owing to the unequal size and distribution of the villi.

One part exhibits a condition in which the villi are entirely gone or much stunted, so that the surface of the membrane feels smooth; moreover, it possesses few blood-vessels or is entirely destitute of them.

Another part of the chorion contains, closely packed together, villi which are extremely long and covered with many ramifying lateral branches; furthermore, it receives large blood-vessels, which approach the tufts of villi and distribute their terminal capillaries to the finest lateral ramifications of the latter; finally, it has entered into the most intimate relations with the mucous membrane of the uterus. Wherever the latter comes in contact with the tufts of villi it is much thickened, very vascular, and in a state of active growth. It encloses numerous branched cavities of varying size, into which the villi of the chorion exactly fit.

The entire structure is called a placenta, in which *the part of the chorion which is covered with villi is distinguished as the placenta fœtalis, and the part of the mucous membrane of the uterus which is united with and adapted to the latter as the placenta uterina.* Both parts together constitute an organ for the nutrition of the embryo.

The term placenta has often been extended to the kind of chorion which is evenly covered with small villi, such as exists in the Suidæ, etc., and the designation of diffuse placenta has been created for it. But in the interest of a more precise definition it is advisable to use the name only in the restricted sense in which it has been employed in this chapter, and in other cases to speak of a villous membrane or chorion only.

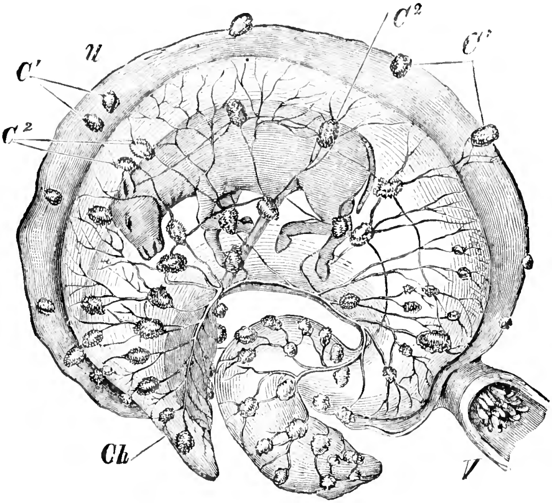

Fig. 135a.—Uterus of a Cow laid open, in the middle of the period of gestation. From BALFOUR, after COLIN.
V, Vagina; U, uterus; Ch, chorion; C^1, cotyledons of the uterus; C^2, fœtal cotyledons.

The formation of the placenta presents in its details important modifications.

The *Ruminants*, in which the blastodermic vesicle is drawn out into two tips, as in the Pig, present a special type (fig. 135a). On their chorion (*Ch*) have been developed very many small fœtal placentæ (C^2), which here are also called cotyledons. The number of the latter is exceedingly variable in the different species, from sixty to one hundred in the Sheep and Cow, and only from five to six in the Doe. They are united with

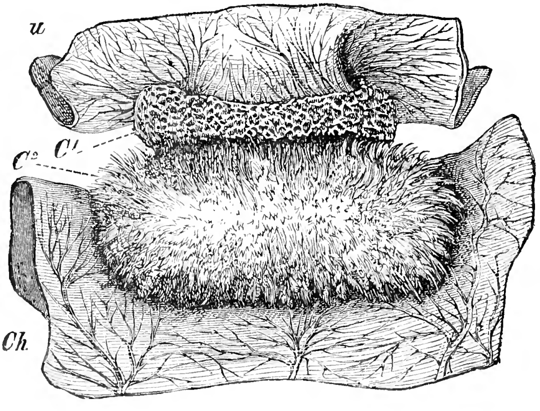

Fig. 135b.—Cotyledon of a Cow, the fœtal and maternal parts half detached from each other. After COLIN, from BALFOUR.
u, Uterus; C^1, maternal part of the cotyledon (placenta uterina); Ch, chorion of the embryo; C^2, fœtal part of the cotyledon (chorion frondosum or placenta fœtalis).

corresponding thickenings of the uterine mucous membrane, the placentæ uterinæ (C^1), though only in a loose manner, so that a little pulling is sufficient to produce a separation, and to draw the chorionic villi out of the depressions which serve for their reception, as one draws the hand out of a glove. In fact, in the preparation which serves as the basis of our figure 135a the cotyledons of offspring and mother (C^2 and C^1) are separated from each other, since the uterus (U) has been opened by means of an incision and drawn back from the chorion (Ch) for a little distance.

Figure 135b shows a single cotyledon of figure 135a somewhat larger than the natural size. The wall of the uterus (u) is drawn back a little from the chorion (Ch). As a result of this, the maternal (C^1) and fœtal parts (C^2) of the cotyledon are partially separated from each other. On the placenta uterina (C^1) one perceives many small pits, on the placenta fœtalis (C^2) the closely packed dendritically branching chorionic villi, which have been withdrawn from the pits.

As the diagrammatic section figure 136 teaches, the fœtal and maternal tissues abut immediately on each other. The villi are covered with flattened cells, and the depressions of the mucous membrane are lined with cylindrical cells; the latter develop within them granules of fat and albumen; they disintegrate in part, and thereby contribute to the formation of a milky fluid, the so-called uterine milk, which can be pressed out of the placenta uterina and serves for the nutrition of the fœtus. It is to be noticed also that in the Ruminants the uterine glands have openings on the mucous membrane only between the cotyledons.

In all other Mammals that are provided with a placenta the intergrowth of the fœtal and maternal tissue is still more intimate. At the same time there is formed in this way such a close union, that *a separation of the chorion without injury to the mucous membrane of the uterus is now no longer possible. At birth therefore a more or less considerable superficial layer of the mucous membrane of the uterus is cast off with the fœtal placenta.* The part that is cast off is called *the caducous membrane, or the decidua.*

In accordance with HUXLEY's proposal, all Mammals in which, in consequence of the special growth of the placenta, such a membrane is formed are now grouped together as Mammalia deciduata, or briefly Deciduata, in contradistinction to the remaining Mammals—the Indeciduata, the formation of whose placentæ has just been discussed.

In the Mammalia with a decidua we must distinguish *two sub-types of placenta, a ring-like and a disc-like*, a *placenta zonaria* and a *placenta discoidea*.

The *placenta zonaria* is characteristic of the Carnivora. The blastodermic vesicle in this case generally has the shape of a cask. With the exception of both poles, which retain a smooth surface, the chorion is covered with numerous villi arranged in a girdle-shaped zone; the villi are furnished with lateral branches, like a tree.

The branched villi of the chorion sink into the thickened mucous membrane of the uterus in various directions, so that in sections there arises the appearance of an *irregular interlacing* (fig. 137). However, according to the concurrent accounts of Turner and Ercolani, there is no penetration into the uterine glands in this case, any more than in the case of the Indeciduata.

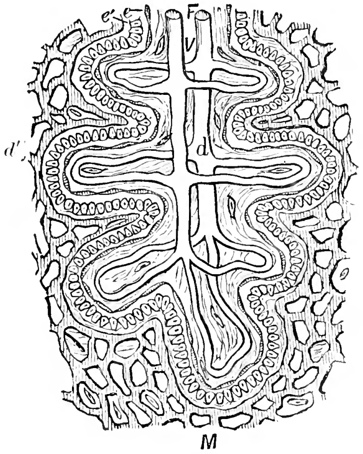

Fig. 136.

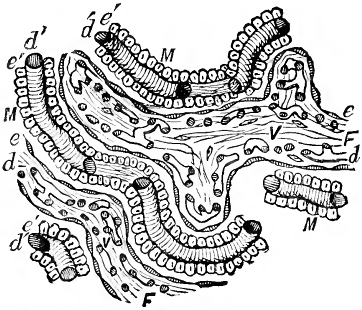

Fig. 137.

Fig. 136.—Diagrammatic representation of the finer structure of the placenta of a Cow, after Turner.

F, Fœtal, *M*, maternal placenta; *V*, villus; *e*, epithelium of the chorionic villus; *e'*, epithelium of the maternal placenta; *d*, fœtal, *d'*, maternal blood-vessels.

Fig. 137.—Diagrammatic representation of the finer structure of the placenta of a Cat, after Turner. Explanation of letters as in fig. 136.

The epithelium (*e'*) of the maternal mucous membrane (*M*) persists and forms a boundary between the villi (*V*) and the *maternal blood-vessels* (*d'*), *which latter have enlarged to cavities from three to four times as wide as the fœtal capillaries* (*d*). This enlargement of the maternal blood-passages is full of significance for the formation of the placenta in the Deciduata as opposed to that of the Indeciduata.

The second form, the *discoid placenta*, is characteristic of the Rodentia, the Insectivora, the Chiroptera and Prosimiæ, the Apes and Man. Here the portion of the chorion devoted to the formation of the placenta is small; but in compensation for this the tufts of villi (fig. 138 *V*) are very highly developed; the union between placenta uterina (*M*) and placenta fœtalis (*F*) is most intimate; the maternal blood-spaces (*d'*), in the case of the Apes and Man at least, are, as nowhere else, enormously distended, so that the villi of the chorion (*V*) appear to sink directly into them and to be bathed immediately by the maternal blood.

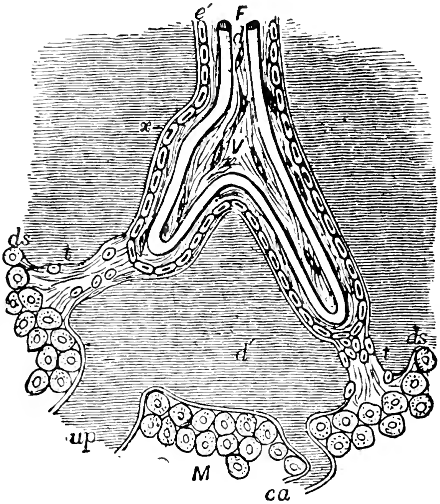

Fig. 138.—Diagrammatic representation of the finer structure of the human placenta according to the hypothesis of Turner.

F, Fœtal, *M*, maternal placenta; *e'*, epithelium of the maternal placenta; *d*, fœtal, *d'*, maternal blood-vessels; *V*, villus; *ds*, decidua serotina of the human placenta; *t*, *t*, trabeculæ of the serotina running to the fœtal villi; *ca*, convoluted artery which sinks into the blood-space *d'*; *up*, one of the utero-placental veins conveying blood from the latter; *x*, a continuation over the villus of maternal tissue—lying outside the epithelial layer *e'*—which represents either the endothelium of the maternal blood-vessels or a delicate connective tissue pertaining to the serotina, or both together. The layer *e'* consists, at all events, of maternal cells derived from the serotina. The fœtal epithelial layer is no longer to be seen on the villi of the completely formed human placenta.

Since we shall occupy ourselves more at length in the next chapter with the human placenta, which belongs to this type, these few remarks may suffice for the time being.

I close this section with a reference to the high systematic significance of the embryonic accessory organs of Vertebrates. They present, as we have seen, such great and striking differences in the separate classes, that the utilisation of them for systematic purposes which has been made by Milne-Edwards, Owen, and Huxley was natural.

All lower Vertebrates, Amphioxus, Cyclostomes, Fishes, Dipnoi, and Amphibia, either possess no accessory organs at all, or only an evagination of the intestinal tube, the yolk-sac. The embryos of Reptiles, Birds, and Mammals, on the contrary, are further enclosed in two fugitive membranes characteristic of embryonic life, the amnion and serosa. They have therefore been grouped together as *amniotic* animals or *Amniota*, and the classes first mentioned have been contrasted with them as non-amniotic animals or *Anamnia*.

Among the amniotic animals a further separation into two groups can be made: on the one side are the egg-laying Reptiles and Birds, which HUXLEY unites into the Sauropsida; on the other side Mammals, in which (with the exception of the Monotremes) the eggs develop in the uterus, and the young are further nourished after birth by the secretions of milk-glands.

In the Mammalia the fœtal membranes, inasmuch as they unite with the mucous membrane of the uterus to form an organ of nutrition, take on a still more complicated character, and present modifications which in turn can readily be utilised for systematic purposes.

In Monotremes and Marsupials the outer embryonic membrane retains an almost smooth surface, as in Reptiles and Birds; in all other Mammals there arise on the surface of the chorion villi, which grow into the maternal mucous membrane. OWEN has designated the one as Implacentalia, the other as Placentalia. The terms Achoria and Choriata introduced for these by KOLLIKER are better.

In the Choriata the union of the villi with the mucous membrane is either loose or firm; corresponding to this there is either no detachable layer of the mucous membrane of the uterus formed, no decidua, or such a structure arises as the result of close intergrowth of the placenta uterina and placenta fœtalis. Thus we have the Mammalia indeciduata and the Mammalia deciduata. In each division there are again two sub-types in the formation of villi. In the Indeciduata the villi are either evenly distributed over the surface, or they are united into more or less numerous groups (placentæ or cotyledons), which are separated from one another by smooth tracts of the chorion. In a part of the Deciduata the placenta is girdle-shaped, in another part disc-shaped.

SUMMARY.

1. In the Mammalia there is developed, in the same way as in Reptiles and Birds, a yolk-sac, an amnion, a serosa, and an allantois.
2. Excepting in the Monotremes and Marsupials, the serosa is metamorphosed into a chorion, in that it puts forth villi, and in that

the connective-tissue layer of the allantois, which is provided with the umbilical blood-vessels, spreads out on its inner surface and penetrates into the villi.

3. In a part of the Mammalia certain regions of the serous membrane, where the villi grow more vigorously and put forth lateral branches, and sink into corresponding depressions of the mucous membrane of the uterus, are converted into a placenta (when many of them have arisen on one chorion they are called cotyledons).

4. On the placenta one distinguishes:—

(*a*) A placenta fœtalis, *i.e.*, that part of the chorion which has developed the tufts of villi.

(*b*) A placenta uterina, *i.e.*, that part of the mucous membrane of the uterus which has proliferated and is provided with depressions for the reception of the placenta fœtalis.

5. Fœtal and maternal parts of the placenta can become more firmly united with each other; the result is that at birth a larger or smaller tract of the mucous membrane of the uterus is also cast off, and is known as the caducous membrane, or the decidua.

6. According to the character of the embryonic membranes, the following divisions of Vertebrates may be established:—

I. Anamnia, animals without an amnion.
(Amphioxus, Cyclostomes, Fishes, Amphibia.)

II. Amniota, animals with an amnion (with yolk-sac, amnion, serosa, and allantois).

A. *Sauropsida.* Egg-laying, amniotic animals.
(Reptiles and Birds.)

B. *Mammalia.* In all of them, except the Monotremes, the eggs are developed in the uterus.

(*a*) Achoria. The serosa develops no villi, or only a few.
(Monotremes, Marsupials.)

(*b*) Choriata. The serosa becomes the villous membrane (chorion).

Mammalia non-deciduata.
(1) With evenly distributed villi.
(Perissodactyla, Suidæ, Hippopotamidæ, Tylopoda, Tragulidæ, Cetacea, etc.)
(2) Placentalia. The serosa is at intervals metamorphosed into a placenta.
α. Numerous cotyledons. (Ruminantia.)

Mammalia deciduata.
β. Placenta zonaria. (Carnivora.)
γ. Placenta discoidea. ([Man,] Apes, Rodents, Insectivores, Bats.)

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CHAPTER XIII.

THE FŒTAL MEMBRANES OF MAN.

The investigation of the first stages in the development of man, which are accomplished during the first four weeks of pregnancy, is coupled with extraordinary difficulties. Only very exceptionally does the embryologist come into possession of young human ova, whether found in the uterus at the time of dissection, or coming into the hands of a physician as the result of miscarriage. In the latter case the ova have often been dead for a long time in the uterus, and consequently are in process of decomposition. Finally, a good preservation and an accurate investigation of such small and delicate objects demand no slight degree of skill.

This accounts for the fact that we do not possess in the case of Man a single observation upon the process of fertilisation or that of cleavage, upon the formation of the germ-layers, or upon the first establishment of the form of the body, the fœtal membranes, and a large number of other organs. Concerning this whole period we are dependent upon the conclusions which are furnished by the development of other Mammals. Thus we assume that fertilisation normally takes place in the enlarged beginning of the oviduct (Fallopian tube); that the seminal elements, which remain alive in the female sexual organs perhaps for days or weeks, here await the ovum as it emerges from the ovary; that the ovum already segmented enters into the cavity of the uterus, attaches itself in the mucous membrane, and during the first weeks of pregnancy gives rise to the germ-layers, the outer form of the body, and the fœtal membranes, according to the well-known rules for other Mammals.

A little, although very scanty, information has been acquired, but this concerns only the second and subsequent week. A small number of ova have been described in the literature, which for the most part come from miscarriages, and the age of which has been estimated at from twelve to fifteen days. The blastodermic vesicles measured 5 to 6 mm. in diameter. Here belong two ova described by **Allen Thomson**, and those by **Schröder v. d. Kolk**, **Hennig**, **Reichert**, **Breuss**, **Beigel und Löwe**, as well as the cases published by **Ahlfeld**, **Kollmann**, **Fol**, and **Graf Spee**.

Upon critical comparison of the discoveries, there are two facts which we can regard as established.

First. At the end of the second week the blastodermic vesicle (blastula) no longer lies free in the cavity of the uterus, but is enclosed in a special capsule produced by the growth of the mucous membrane. Hitherto no one has had the opportunity to make observations concerning the formation of this capsule. Following an hypothesis of Sharpey, which has been somewhat modified by Reichert, it is now generally assumed that the ovum upon its entrance into the uterus imbeds itself in a depression of the mucous membrane, which is thrown into ridges and is in process of being metamorphosed into the decidua. The margins of the depression soon grow around the blastula on all sides, and fuse together to form a closed fœtal capsule. The fusion takes place at a point diametrically

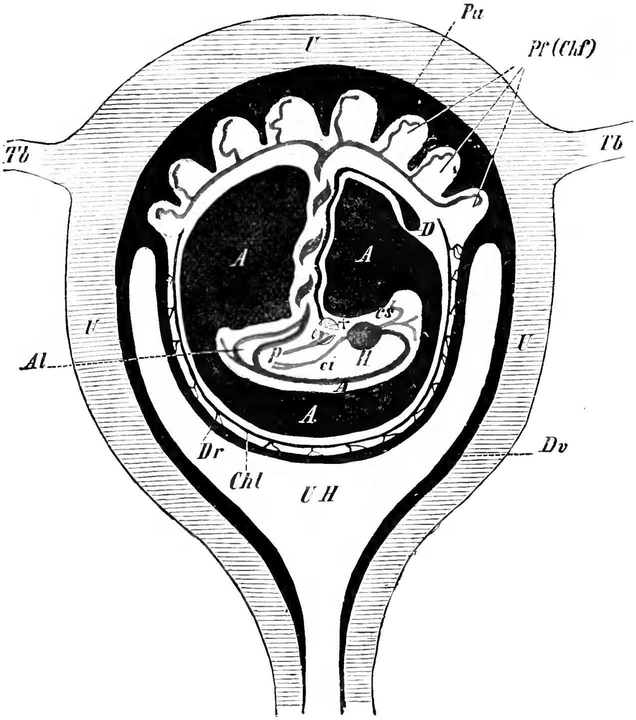

Fig. 139.—Diagrammatic section through the gravid human uterus, from Wiedersheim.
U, Uterus ; *UH*, cavity of the same ; *Tb*, Fallopian tube ; *Dv*, decidua vera ; *Dr*, decidua reflexa ; *Pv*, placenta uterina (decidua serotina) ; *Pf*, placenta fœtalis or chorion frondosum (*Chf*) ; *Chl*, chorion læve ; *A* (on black background), cavity of the amnion filled with amniotic fluid ; *D*, yolk- (umbilical) vesicle ; in the embryo one sees the umbilical vessels (*Al*) ; † the liver traversed by the vena umbilicalis ; *H*, the heart ; *A*, the aorta ; *ci* and *cs*, the vena cava inferior and superior ; *p*, vena portarum.

opposite the attachment, and is described as resembling a cicatrix. It is destitute of blood-vessels, whereas these, as well as uteirne glands, are present in the remaining portion of the overgrowing mucous membrane. The blastula lies in this receptacle now, and even into the beginning of the second month, loosely enclosed ; after opening the capsule the blastula can be removed easily and without injury.

Whereas in other Mammals only that part of the uterine mucous membrane which contributes to the formation of the placenta is cast off, in the case of Man there occurs a much more extensive ecdysis of the most superficial layer, namely, over the whole inner surface of the uterine cavity. Here, too, the part which is cast off is designated as *deciduous membrane* or *decidua*, and three regions are distinguishable (fig. 139)—the part which is thrown around the blastula as *decidua reflexa* (*Dr*), the part which forms the floor of the depression in which the ovum has established itself as *decidua serotina* (*Pu*), and the remaining portion as *decidua vera* (*Dv*).

In the reflexa we become acquainted with a structure which in this complete form occurs only in the case of Man and the Apes, whereas beginnings of such a structure are also found in other groups, as, *e.g.*, in the Carnivores. Since the fœtal capsule does not at first completely fill the uterus, there remains between reflexa and vera a space filled with mucus.

A *second* and in many respects astonishing result is, that even in very young and small blastodermic vesicles, as all discoveries agree in showing, a *well-developed chorion* with *abundant villi* is begun.

The villi are either distributed over the whole surface of the ovum, or, as in REICHERT's case (fig. 140 *A* and *B*), they leave two opposite poles of the blastula free. They attain a length of one millimetre, and in part have the form of simple cylindrical elevations; in part they already possess lateral branches. At no place have they fused with the decidua. Like the chorion itself, they consist of two layers —of a superficial epithelial layer, derived from the serosa, concerning which AHLFELD and KOLLMANN have made very definite and reliable statements, and of a layer of embryonic gelatinous tissue, which extends into the axis of the villi and already appears to bear here and there blood-vessels.

Unfortunately we have learned nothing from investigations of these youngest of all human embryos concerning the structures within the chorion,—the remaining fœtal membranes and the fundament of the embryo itself. Either the ova were already more or less pathologically altered, or the contents were considerably damaged in consequence of the method of preservation and by the preparation. At all events with other investigators one, I think, may conclude from the condition of the chorion that the embryo must have been in an advanced stage, in which germ-layers, yolk-sac, and amnion were already formed.

This assumption is all the more reasonable, since well-developed embryos from blastodermic vesicles which were only a few millimetres larger have been described by Coste, Allen Thomson, His, and others. In these cases the head-end of the embryo only is rather sharply differentiated from the yolk-sac, which is continuous with the fundament of the intestine throughout nearly its entire length. The neural canal is not yet closed, but the amnion nevertheless is completely developed, and in fact lies almost in contact with the embryonal body; at its posterior end it is connected with the chorion by means of a short cord, which is connected with the fundament of the allantois and has been named the *belly-stalk* (Bauchstiel) by His.

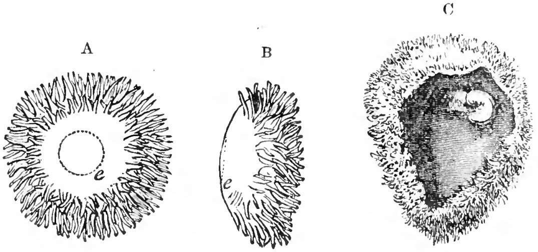

Fig. 140.—The human ovum at an early stage of development.

A and *B*, Front and side views of a human ovum of 12 to 13 days, figured by Reichert. *e*, The part designated by Reichert as embryonic spot. From Quain's "Anatomy."

C, An ovum of 4 to 5 weeks, showing the general character of the villous membrane before the formation of the placenta. A part of the wall of the ovum is removed in order to show the embryo in situ. After Allen Thomson, from Kölliker's "Entwicklungsgeschichte des Menschen, etc."

Also in the only slightly older embryo of Coste (fig. 141)—in which the neural tube is closed, the body distinctly segmented (*us*), the head provided with visceral arches (*vb*), behind the latter the heart (*h*) recognisable, and the yolk-sac (*ds*) further constricted off—a short belly-stalk (*bst*) is present. It is composed of the amnion (am^1) drawn out to a point and of a connective-tissue cord, which arises from the ventral surface of the embryo out of the intestinal cavity of the pelvic region, encloses at its attached end a small cavity (the allantois), and conducts the allantoic blood-vessels from the pelvic portion of the intestine to the chorion.

This cord is a characteristic structure for the human embryo, the significance of which is still in dispute. Kölliker and His have given somewhat different explanations of it. Kölliker brings the cord into relation with the development of the allantois. He makes the fundament of this important embryonic appendage arise, as in other Mammals, from the hind gut of the embryo, and approach the serosa as a thick vascular connective-tissue growth lined with a narrow, short epithelial tube, without previously developing inside itself a large epithelial sac. He also maintains that the connective-tissue part of the short allantoic cord, or belly-stalk, grows around on the whole inner side of the serosa, and into the epithelial villi.

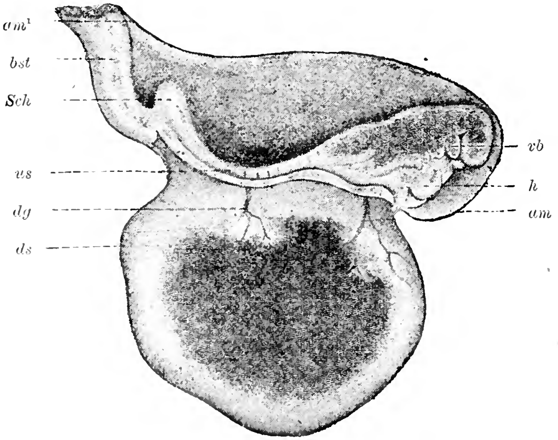

Fig. 141.—Human embryo with yolk-sac, amnion, and belly-stalk of 15 to 18 days, after Coste, from His ("Menschliche Embryonen"). His has untwisted somewhat the posterior end of the body in comparison with the original figure, in order to bring into view the right side of the end of the body, the left side being represented in Coste's fig. 4. The chorion is detached at am^1. *am*, Amnion; am^1, the point of attachment of the amnion to the chorion drawn out to a tip; *bst*, belly-stalk; *Sch*, tail-end; *us*, primitive segment; *dg*, vitelline blood-vessels; *ds*, yolk-sac; *h*, heart; *vb*, visceral arch.

His regards as unwarranted "the assumption, in opposition to the actual state of affairs, that the human embryo at first separates itself from the part of the blastodermic vesicle which is employed for the chorion, and subsequently unites with it again by means of the fundament of the allantois." He does not admit that the fundament of the embryo in Man is ever wholly constricted off from the chorion, as in the remaining Mammals, and he recognises in the belly-stalk "the bridge of connection between the fundament of the embryo and the chorionic part of the original blastodermic vesicle, which has never been severed." According to him the allantois in the human embryo has nothing to do with the development of the belly-stalk.

Neither of these two explanations seems to me entirely satisfactory. According to my view, the structure under consideration may be explained in a manner which is not only in complete harmony with the facts of the case, but also reconciles the views of KÖLLIKER and HIS.

As COSTE's embryo appears to show, *the origin of the belly-stalk is connected in the first place with a somewhat irregular formation of the amnion.* It follows from the fact that the latter is drawn out posteriorly to a point (fig. 141 am^1), the apex of which reaches to the chorion, that its closure in the human embryo takes place at the extreme posterior end of the body, and that at the same time a union with the chorion is retained at the place of closure. The fundament of the embryo therefore remains in connection with the chorion, *not directly*, as HIS maintains, but only *indirectly by means of the amnion.*

In the second place, the allantois, the somewhat eccentric development of which in the case of Man is perhaps intimately connected with the above-mentioned peculiarity in the formation of the amnion, takes part in the formation of the belly-stalk. It is therefore proper in this connection to enter somewhat more fully into the *allantois-question* in Man, so actively discussed during the last decade.

Since in other Mammals the allantois (fig. 142 *al*) has the form of a large stalked sac, which grows out from the navel till it comes in contact with the serosa (*sz*), and carries to it, along with connective tissue, the umbilical vessels, attempts have been made ever and anon to discover such a structure in the case of human embryos also. The proof of its existence in Man appeared to be furnished by a premature embryo, on which KRAUSE described a spherical, sac-like allantois.

The embryo of KRAUSE presented, however, in many respects such deviations from other known human embryos of the corresponding stage as to cause the statements to be accepted on the part of many persons with great reservation, and to permit the suggestion of HIS, that in this case it was not after all a human embryo.

Upon critical examination of the facts relating to the question, I am likewise of the opinion that *in the case of Man a stage of development with a free allantoic sac protruding out of the body-cavity is not reached.*

As results from the fine investigations of human embryos by HIS, the belly-stalk is found upon cross section to be composed of :—

(1) The pennant-like prolongation of the amnion;

(2) Beneath this, abundantly developed embryonic connective tissue;

(3) The fundament of the allantois, which has the form of a very narrow passage with epithelial lining;

(4) The umbilical blood-vessels, of which the arteries lie close upon the allantoic duct, while the veins run nearer to the amnion.

To the question, How have these parts arisen? that appears to me the most natural answer which permits of being harmonised with the known conditions in other Mammals. Now, such an agreement is possible upon the following assumption.

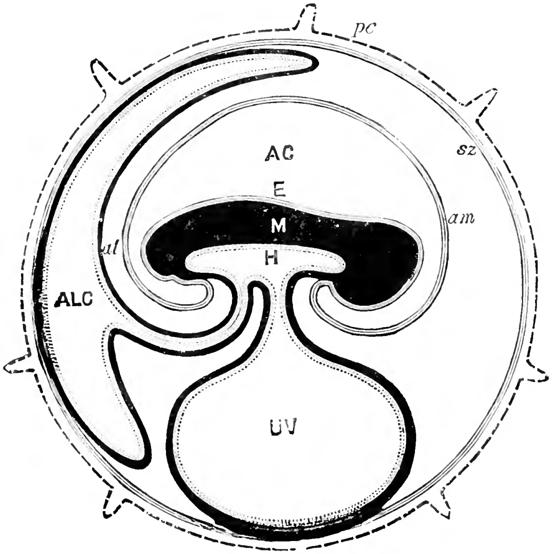

Fig. 142.—Diagram of the fœtal membranes of a Mammal, after Turner.
pc, Zona pellucida with villi (prochorion); *sz*, serous membrane; *am*, amnion *AC*, amniotic cavity; *E*, outer germ-layer; *M*, middle germ-layer; *H*, inner germ-layer; *UV*, yolk-sac (vesica umbilicalis); *al*, allantois; *ALC*, allantoic cavity.

Very early, when the hind gut begins to be formed, there arises on its ventral side as a fundament of the allantois a knob composed of many cells, and containing only a small evagination of the entodermic layer. The allantoic knob does not, however, grow free into the body-cavity, as in the remaining Mammals (fig. 142 *al*), but extends along the ventral wall of the embryo, and, from the place where this is reflected off to form the amnion, along the ventral wall of the latter (fig. 141 *am*^{1}) up to its place of attachment to the chorion. The evagination of the entodermic layer meantime becomes elongated into the narrow allantoic duct; the more voluminous connective-tissue growth carries with it the umbilical blood-vessels to the chorion, then spreads itself out on the inner surface of the latter in the well-known manner, and penetrates into the villi of the serosa.

The allantois, therefore, in its development, instead of growing out *free* to the serosa, makes use of the already existing connection between the latter and the embryo established by the pennant-like elongation of the amnion (*am*^{1}). But this mode of development perhaps results from the fact that the posterior end of the embryo in Man, as fig. 141 shows, is closely attached to the serosa at the place of the amniotic suture, whereby the allantois has only a short distance to grow in order to reach the serosa.

Finally, the early appearance of the allantois will become intelligible to us, if we remind ourselves that organs of great physiological importance have in general the tendency to an accelerated development, and that in the series of Mammals the provisions for the nutrition of the embryo by means of a placenta have become more and more complete.

While there is still much obscurity about the first stages of Man's development, we possess more satisfactory insight into the changes which the embryonic membranes in Man undergo from the third week onward.

From this point forward we shall examine each separate embryonic membrane by itself: first the structures that are developed from the blastodermic vesicle—(1) the chorion, (2) the amnion, (3) the yolk-sac; then (4) the deciduæ which are produced by the mucous membrane of the uterus; and finally (5) the after-birth (placenta) and (6) the umbilical cord.

1. The Chorion.

During the first weeks of pregnancy the whole surface of the *chorion* is covered with villi (fig. 132^5, p. 226, and fig. 140), and provided with terminal branches of the umbilical blood-vessels. After its growth has proceeded for a time uniformly, there begin to appear—from the beginning of the third month onward—differences between the part which lies directly against the wall of the uterus that is destined to become the decidua serotina and the remaining greater part, which has become overgrown by the decidua reflexa (fig. 143). While on the latter the villi (z') cease to grow, on the former they increase enormously in size and take the form of long, and at the base thick, tree-like, branching structures (z), which, united into tufts, project far beyond the surface of the membrane that bears them, and grow into pits of the maternal mucous membrane (*ds*). This part, to which we shall give more particular attention at the time of investigating the mature placenta, is therefore distinguished as *chorion frondosum* from the remaining larger part, the *chorion læve* or the *smooth chorion*.

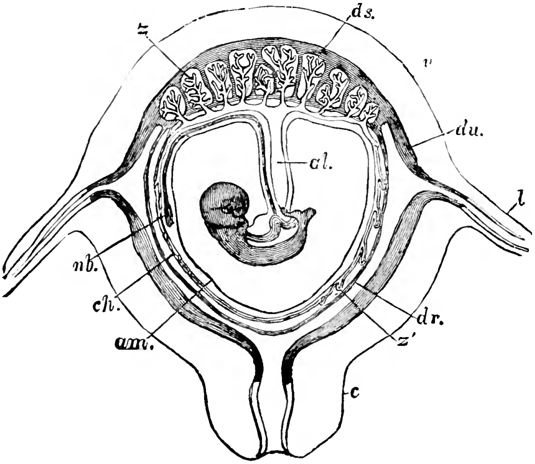

Fig. 143.—Diagrammatic section through the gravid human uterus with contained embryo, after LONGET, from BALFOUR.

al, Stalk of the allantois; *nb*, umbilical vesicle; *am*, amnion; *ch*. chorion; *ds*, decidua serotina; *du*, decidua vera; *dr*, decidua reflexa; *l*, Fallopian tube; *c*, cervix uteri; *u*, uterus; *z*, villi of the fœtal placenta; *z'*, villi of the chorion læve.

The expression "smooth chorion" is, strictly speaking, not quite applicable. Of the villi which are at first everywhere developed, some afterwards remain preserved on the chorion læve, especially in the vicinity of the placenta. They grow into the decidua reflexa, effecting a firm union with it (fig. 143 z').

At the same time a second distinction between chorion frondosum and chorion læve is developing. In the territory of the latter the blood-vessels arising from the umbilical arteries begin to dwindle, whereas the former becomes more and more abundantly supplied with blood-vessels, and finally alone receives the terminal distribution of the umbilical arteries. Thus the one region becomes destitute of vessels, while the other becomes extraordinarily vascular, and the nutritive organ for the embryo.

Histologically the chorion læve, which upon examination from the surface appears thin and translucent, consists of (1) a connective-tissue membrane, and (2) an epithelial covering, which is identical with the original serosa.

The *connective-tissue membrane* possesses at first the character of embryonic mucous tissue, and exhibits therefore branched stellate cells in a homogeneous matrix. Subsequently the mucous tissue is converted, as at other places in the body, into fibrous connective tissue.

The epithelium of the chorion consists in the first months, according to the statements of KASTSCHENKO and SEDGWICK MINOT, of two layers—a superficial one, in which no cell-boundaries are visible (protoplasmic layer), and a deeper one, in which the individual cells are distinctly separated. Additional particulars are given in the description of the placenta.

The embryonic adjuncts enclosed within the chorion—the amnion and yolk-sac—undergo in Man during pregnancy the following changes.

2. The Amnion.

The *amnion* (*am*) immediately after its origin lies close on the surface of the embryo (fig. 144), but soon becomes distended by the accumulation of fluid, the liquor amnii, in its cavity (fig. 132^5). It increases to a much greater extent than in other Mammals, in which it is often found to be smaller than the allantoic sac (compare the fœtal membranes of the Rabbit, fig. 133). *Finally, in Man it fills out the entire blastodermic vesicle, since it everywhere applies itself* (fig. 143 *am*) *closely to the inner wall of the chorion* (*ch*).

Its wall is rather thin and translucent, and also consists, like the chorion, of an epithelial and a connective-tissue layer.

The epithelium, derived from the outer germ-layer of the embryonic fundament, lines the amniotic cavity within, and is continuous with the epidermis of the embryo at the dermal navel ; at the place of transition it is composed of layers ; but elsewhere it is a single sheet of pavement cells. The connective-tissue layer is thin and at the navel continuous with the corium.

The *amniotic* or *fœtal water* is slightly alkaline, and contains about 1% solid constituents, among which are found albumen, urea, and grape-sugar. Its volume is greatest in the sixth month of pregnancy, and it often attains a weight of not less than a kilo [2·2 lbs. avoirdupois]; then it diminishes to about one-half that amount at the time of birth, and in the same ratio as the embryo by its increased growth demands for itself more room. Under abnormal circumstances the secretion of amniotic water can become much greater, and can, by a considerable distension of the amnion, lead to conditions which have been called dropsy of the amnion, or hydramnion.

3. The Yolk-Sac.

The *yolk-sac* or the *umbilical vesicle* (vesicula umbilicalis) in Man pursues the opposite course of development from that of the ever-increasing amnion, and shrivels to a structure that easily escapes observation.

In human fœtuses of the second and third week (fig. 144) the yolk-sac (*ds*) fills somewhat more than half of the blastodermic vesicle and is not constricted off from the intestine, which still has the form of a groove.

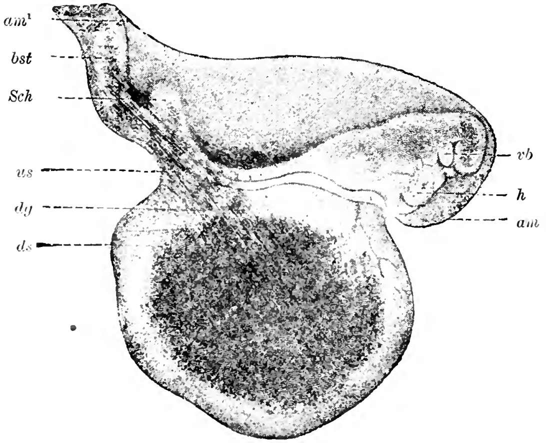

Fig. 144.—Human embryo with yolk-sac, amnion, and belly-stalk of 15 to 18 days, after Coste, from His ("Menschliche Embryonen"). His has untwisted somewhat the posterior end of the body in comparison with the original figure, in order to bring into view the right side of the end of the body, the left side being represented in Coste's fig. 4. The chorion is detached at am^1. *am*, Amnion; am^1, the point of attachment of the amnion to the chorion drawn out to a tip; *bst*, belly-stalk; *Sch*, tail-end; *us*, primitive segment; *dg*, vitelline blood-vessels; *ds*, yolk-sac; *h*, heart; *vb*, visceral arch.

In somewhat older embryos it is seen to be connected by means of a thick *stalk* or *vitelline duct* with the middle of the rudimentary intestine, now converted into a tube. It is supplied with blood by the vasa omphalomesenterica.

During the sixth week the vitelline duct or ductus omphalomesentericus has grown out into a long, narrow tube, which sooner or later loses its cavity and is converted into a solid epithelial cord. It terminates in the small egg-shaped umbilical vesicle (figs. 139 *D* and 143 *nb*). Since the amnion, in consequence of a greater accumulation of fluid, now fills the whole blastodermic vesicle (fig. 143), it has enveloped both the vitelline duct and the neck of the allantois (*al*), and, as it were, surrounded them with a sheath (amniotic sheath). The structure thus produced, the umbilical cord, funiculus umbilicalis, is now the only means of connection between the embryo, which floats free in the amniotic fluid, and the wall of the blastodermic vesicle. Its attachment to the latter always coincides with the place where the placenta is developed.

By the enlargement of the amnion the umbilical vesicle is crowded out to the surface of the blastodermic vesicle, where it is enclosed between amnion (*am*) and chorion (*ch*), at some distance from the place where the umbilical cord is attached. It continues to exist here up to the time of birth, although in a very rudimentary condition. It is only by painstaking examination that it is to be found, usually several inches away from the margin of the placenta. Its longest diameter measures only from 3 to 10 millimetres. It was on this account that the older text-books of anatomy, physiology, and embryology contained the statement that in Man the vesicula umbilicalis disappeared as a useless structure; this idea prevailed until the constancy of its presence was demonstrated by B. Schultze.

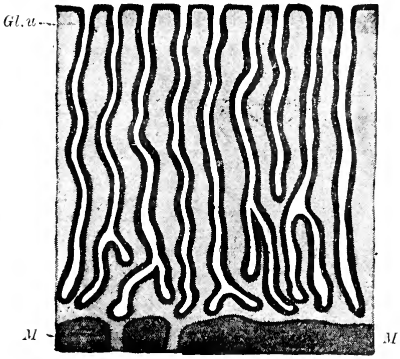

Fig. 145.—Cross section through the mucous membrane of the uterus, after Kundrat und Engelmann.

Gl.u, Uterine glands; *M*, muscular layer of the uterus.

4. The Deciduæ.

The deciduæ or caducous fœtal membranes take their origin from the mucous membrane of the uterus, the structure of which is greatly altered during pregnancy.

In the unmodified condition the mucous membrane is a soft layer about a millimetre thick, which reposes *directly* and *immovably* upon the musculature (*M*) of the uterus, which does not possess a submucosa in this region (fig. 145). It is traversed by numerous *tubular uterine glands* (glandulæ utriculares, *Gl.u*), which begin at the surface with small orifices and pass directly downward in a sinuous course close to one another until they reach the musculature (*M*), where they terminate, often after dichotomous division.

Mucous membrane and glands are lined with ciliate cylindrical cells. The connective tissue that separates the glands embraces an extraordinary abundance of cells, some of which are spindle-shaped, others roundish.

From the beginning of pregnancy the mucous membrane undergoes very profound changes, which affect all parts. Concerning these we possess accurate observations, which relate to every month of pregnancy, by Kundrat und Engelmann, as well as by Leopold and Sedgwick Minot.

We take up in succession (1) the decidua vera, (2) the decidua reflexa, and (3) the decidua serotina or placentalis, the part which enters into the formation of the placenta.

(1) *Decidua vera.* As Leopold remarks, with the beginning of pregnancy the mucous membrane constantly increases in thickness, until it becomes 1 cm. or more thick, up to the time, indeed, when the growing ovum attaches itself completely to the walls of the uterus, therefore approximately up to the end of the fifth month. From that time forward there begins, as it were, a *second stage*, in which, under the pressure of the growing fœtus, it again becomes thin and finally is only 1 to 2 mm. thick. Meanwhile both the glands and the tissue between them undergo changes.

During the first stage the uterine glands, which at the beginning are tubes of uniform calibre, *increase in size*, especially in their middle and deeper parts (fig. 146); whereas at their open ends they are rectilinear and drawn out lengthwise, deeper down they take a spiral course and are covered with evaginations and pocketings.

Upon sections therefore one can now distinguish two layers in the decidua vera :—

(1) An outer more compact layer (*C*), possessing more abundant cells, and

(2) A deeper ampullar or spongy layer (*Sp*).

In the *former* one sees the glands as elongated, parallel canals. In consequence of a great growth of the inter-tubular tissue they are separated from one another farther than at first; they begin at the surface with *enlarged funnel-shaped pits* (*tr*). The surface of a mucous membrane stripped off from the musculature has, as Kölliker states, a sieve-like appearance, due to the enlarged orifices of the glands.

In the *spongy layer* (*Sp*) one encounters irregular, lobed cavities (*dh*) one above another, the capacity of which continually increases up to the middle of pregnancy, and which are finally separated from one another by thin septa and cords of the matrix-tissue only. The appearance is explained by the fact that in the middle of their course the glands are highly tortuous and have enlarged and become pocketed.

The *ciliate cylindrical epithelium* at the surface of the mucous membrane of the uterus gradually disappears entirely; it is destroyed as early as the end of the first month of pregnancy (MINOT). In the glands it undergoes fundamental changes. In the first months all the cavities are still lined with it, a condition which, on account of the increase in the size of the cavities, presupposes an active cell-growth. Meanwhile the originally elongate cylindrical cells are in part converted into small cubical, in part into small flat structures, except in the portions of the glands which adjoin the muscular membrane. The cells here preserve more or less their normal form up to the end of pregnancy, and subsequently serve for the regeneration of the epithelial lining of the mucous membrane of the uterus.

In the fourth and fifth

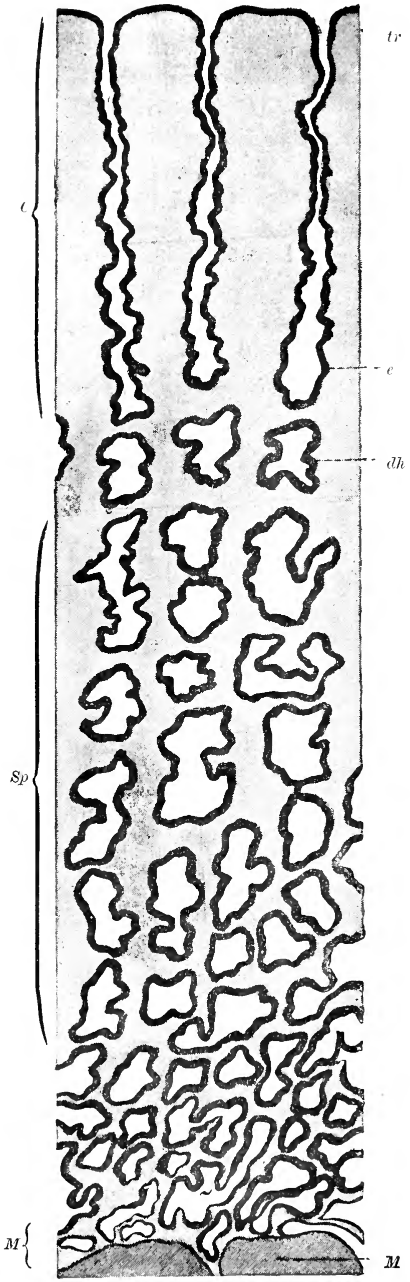

Fig. 146.—Cross section through the mucous membrane of a uterus at the beginning of pregnancy, after KUNDRAT UND ENGELMANN.

C, Compact layer; *Sp*, spongy layer; *M*, musculature of the uterus; *tr*, funnel-shaped mouths of the uterine glands; *e*, enlarged region; *dh*, ampullæ produced by the windings and evaginations of the growing glands.

months one still finds all cavities up to the mouth of the glands lined with a thin layer of cubical or flat epithelial cells.

Likewise in the first stage there occurs in the inter-glandular

Fig. 147.—Cross section through the fœtal membranes and the uterus at the margin of the placenta at the sixth month of pregnancy, after Leopold.
M, Musculature of the uterus; *Dc*, decidua vera; *C*, compact, *Sp*, spongy layer of the same; *Dr*, decidua reflexa; *ch*, chorion; *am*, amnion; *bl*, blood-vessels of the compact layer; *dh*, enlarged gland cavities; *de*, glandular epithelium undergoing degeneration; *rz*, giant cells in the compact layer.

tissue an active process of growth, especially in the upper compact layer. In this there are formed spheroidal structures, 30 to 40 μ in diameter, which have been called *decidual* cells by Friedländer. In many places they lie so close together that, as a consequence and because of their form, they appear very similar to an epithelium.

They are also found in the spongy layer, but in the cords and septa they are more elongated and spindle-shaped.

In the second stage, from the sixth month forward, in which the decidua vera becomes much thinner, and under the pressure of the growing fœtus gradually diminishes from 1 *cm. to* 2 *mm. in thickness, many regressive processes take place in the individual parts that have just been described* (fig. 147).

The *mouths of the glands,* which caused the sieve-like condition of the inner surface of the decidua, become more and more difficult to see and finally disappear altogether.

The *inner compact layer* (*C*) assumes a uniform, compact, lamellar condition, since by the pressure the cavities of the glands occupying it become wholly obliterated, and then by disappearance of the epithelium their walls become fused.

In the *spongy layer* (*Sp*) the cavities of the glands (*dh*) persist, but, in consequence of the pressure, are converted into fissures, which are parallel to the wall of the uterus, and are separated by partitions which in comparison to earlier months of pregnancy have become very much thinner. The glandular cavities which are adjacent to the compact layer *have lost their epithelium* or exhibit cellular debris (*de*), swollen bodies, and a slimy mass permeated with fine granules; toward the uterine musculature, on the contrary, they possess a well-preserved epithelium of short cylindrical or cubical cells.

(2) *The decidua reflexa* (fig. 148 *Dr*) *exhibits close agreement in its structure with the decidua vera.* That it has arisen from the latter by a *process of folding* may be inferred, as Kundrat has rightly maintained, especially from the circumstance that during the first months of pregnancy the mouths of uterine glands (*glu*), at least at the place of transition to the vera, are found upon both its surfaces. The mouths lead into fissures (*glu*) which are parallel to the surface of the reflexa and are lined with cuboidal epithelium. In the inter-glandular tissue there appear the same large, round *decidual* cells as in the vera.

From the fifth month forward the space between vera and reflexa begins to disappear; both membranes now, after loss of their epithelium, become firmly pressed together, and finally completely fused with each other (fig. 147). By this process the reflexa, from which the glandular spaces disappear except in the transitional region, becomes so extraordinarily thinned that it constitutes [in sections] only a narrow band, occasionally $\frac{1}{2}$ mm. broad.

A separation of the two membranes at the close of pregnancy is very difficult, but occasionally it may still be accomplished to some extent.

Moreover in later months the inside of the decidua reflexa is firmly fused with the chorion, and since the chorion in its turn is in contact with the amnion (fig. 147 *ch* and *am*), one now comes, by

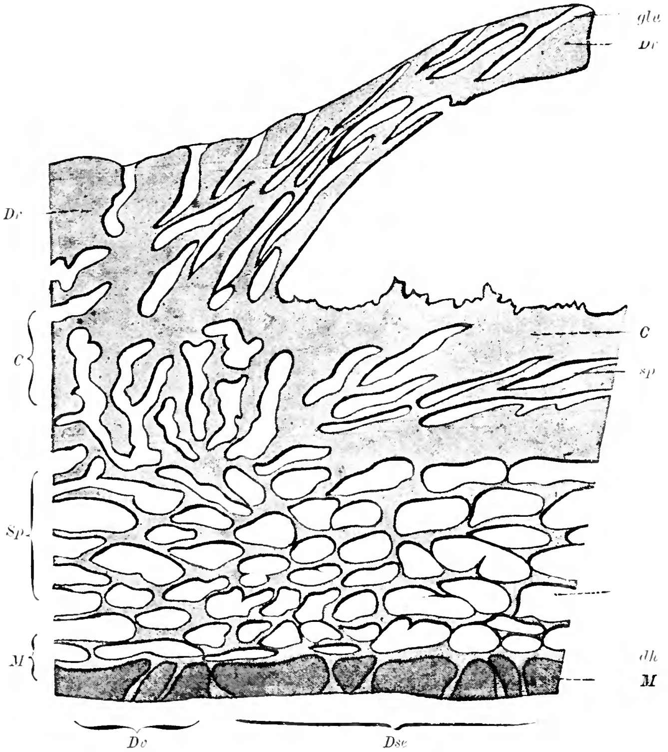

Fig. 148.—**Section through decidua serotina** (*Dse*) **at the transition into decidua vera** (*Dv*) **and reflexa** (*Dr*), after KUNDRAT UND ENGELMANN.

M, Musculature of the uterus; *Sp*, spongy layer of the decidua vera and serotina; *C*, compact layer of the same; *glu*, uterine glands; *sp*, fissures in the serotina resulting from growth of the glands; *dh*, ampullarial spaces in the spongy layer produced by growth of the glands.

cutting through the muscular wall of the uterus, and then opening the fœtal membranes, which are thus pressed together, directly into the amniotic cavity, in which the embryo lies bathed in the amniotic fluid.

(3) The third region of the uterine mucous membrane, or the *decidua serotina* (fig. 148 *Dse*), is that part which joins with the

chorion frondosum to form a nutritive organ for the embryo,—the after-birth, or placenta.

According to the statements of KUNDRAT and LEOPOLD it undergoes changes similar to those of the decidua vera. Here also the uterine glands grow rapidly in its deeper portions (fig. 148) and are converted into irregular spaces (*dh*), which are from the beginning, however, most extended in breadth. Subsequently they are crowded together still more by the pressure and the growth of the placenta until they become narrow fissures which lie parallel to the surface of the uterus.

The glandular epithelia disintegrate to a still greater extent than in the vera, and by disintegrating and swelling up become detached from the connective-tissue walls; only those regions of the glands which are adjacent to the muscular layer (*M*) retain their cylindrical cells.

In this presentation KUNDRAT and LEOPOLD disagree with KÖLLIKER and with TURNER, who likewise, it is true, find great spaces in the deeper layer of the serotina, but interpret them for the most part as greatly enlarged blood-vessels, an assumption according to which there would exist an important difference between the serotina and the vera.

In the superficial layer the outlets of the glands must disappear early, since they become pressed together. Besides, more active cell-proliferation takes place in the inter-glandular tissue.

Therefore the decidua serotina (fig. 148 *Dse*) is also converted into two readily distinguishable layers :—

(1) A deeper spongy layer (*Sp*), in which the detachment of the placenta subsequently takes place, and

(2) A superficial, more compact layer (*C*). The latter alone shares in the formation of the placenta, and is accordingly called the *placenta uterina* (or materna). It undergoes from the second month forward more profound alterations.

We shall become acquainted with these in the description of the placenta, to which we now pass.

5. The Placenta.

The *placenta* is a very vascular, and when filled a spongy or doughy, disc-shaped structure, which at the height of its development measures 15 to 20 cm. in diameter and is 3 to 4 cm. thick. Its weight reaches somewhat more than a pound (500 grammes). The surface which is turned toward the embryo is concave (figs. 139 and 143) and altogether smooth, since it possesses a covering of the amnion (*am*); the surface which reposes on the wall of the uterus is convex, after its detachment at birth feels uneven, and is divided by deep furrows into separate lobes or cotyledons.

The normal position of the placenta is, in the majority of cases, at the fundus uteri, where it is sometimes developed more to the left side, sometimes more to the right. Consequently the opening of one or the other of the Fallopian tubes may be covered and sealed by it.

In rare cases the placenta, instead of being attached to the fundus, is united to the wall of the uterus nearer its mouth [os uteri]. This results from the fact that the fertilised egg, when it passes from the Fallopian tube into the cavity of the uterus, sinks down farther owing to abnormal conditions, instead of attaching itself at once to the mucous membrane.

Occasionally the attachment takes place quite low, in the immediate vicinity of the inner mouth of the uterus. In this case, as the placenta with the growth of the fœtus extends itself, it grows either partly or wholly over the mouth of the uterus, and closes it more or less completely. This anomaly is known as *placenta prævia* (lateralis or centralis) and presents a dangerous condition, because the regular progress of birth is disturbed.

In consequence of the low position of the placenta perilous bleeding is produced, either during pregnancy, or at least at the beginning of labor pains, because the placenta detaches itself from the wall of the uterus prematurely, whereby large blood-vessels are ruptured and laid open.

In the investigation of the finer structure of the placenta serious obstacles are encountered, since it is a very soft organ traversed by numerous capacious blood-vessels. Therefore very contradictory views still prevail concerning many points which are of the greatest importance in judging of the structure. It does not appear to me possible to give at present a final opinion upon these points.

In the description it is best for us to start with the fact that the placenta, as was previously stated, is composed of two parts,—of one part which is furnished by the embryo, and another part which is produced by the mother,—the placenta fœtalis and the placenta uterina (Plate II.).

The *placenta fœtalis* is the part of the chorion (chorion frondosum) which is thickly covered with much-branched villi. The villi (*z*), united into great tufts or cotyledons, elevate themselves from a firm membrane, the *membrana chorii* (m), in which the chief branches of the umbilical arteries and veins take their course. They consist of (1) large main stems (z), which grow straight out from the membrana chorii, and the ends of which (h^1) sink into and firmly unite with the placenta uterina, which faces them, and (2) numerous lateral branches (f) which arise on all sides at right angles or obliquely, and which are in turn covered with fine twigs. A small part of these (h^2) also fuse, by means of their tips, with the tissue of the placenta uterina (LANGHANS), so that a separation of the fœtal and the maternal portions can be accomplished only by forcible detachment. KÖLLIKER has therefore appropriately divided the branches of the chorionic villi into *roots of attachment* (h^1, h^2) and *free processes* (f).

To each arborescent chorionic villus there goes a large branch of an umbilical artery, which, corresponding to the ramifications of the former, is divided up into branches; the capillary networks which arise from this are situated quite superficially immediately under the epithelium of the villi. From this network the blood is collected into vessels, leading from the villi, which are again united into a single chief stem that emerges from the chorionic tuft.

Consequently *the vascular system of the placenta fœtalis is entirely closed.* A direct mingling of the fœtal and maternal blood cannot take place in any manner; on the other hand the prerequisite for an easy exchange of fluid and gaseous components of the blood is furnished by the very superficial position of the thin-walled capillaries.

PLATE II.

Diagrammatic section through the human placenta at the middle of the fifth month, after LEOPOLD.

The musculature of the uterus is followed by the spongy layer of the decidua serotina (sp), in which the separation of the placenta takes place at birth along the line of separation indicated by two heavy marks; this is followed by the compact layer (CS), which is thrown off at birth as the placenta uterina, and which consists of the (WINKLER'S) basal plate (BP), closing plate (Schlussplatte) (SP), cavernous blood-spaces (c), the arteria advehentes (a), and the marginal sinus. The placenta fœtalis has grown into the placenta uterina; it consists of the membrana chorii (m) and the villi (z) arising from it; on the latter are to be distinguished the roots of attachment (h^1, h^2) and the free processes (f). [ep, Fœtal epithelium derived from the serosa.] The chorion is still covered internally by the amnion. [The fœtal part of the placenta is reproduced in blue, the maternal part in black and brown; pink indicates the blood-spaces.]

Placenta and Uterus, Middle of the Fifth Month.

face p. 260.

PLATE II.

Swan, Sonnenschein & Co.

The *connective substance of the chorionic villi* is gelatinous tissue with stellate and spindle-shaped cells in the finer branches; in the larger stems it takes on a more fibrillar condition.

The views of investigators are still at variance upon the important point whether the *epithelium of the membrana chorii and the villi* is of fœtal or maternal origin. KÖLLIKER, LANGHANS, LEOPOLD, and others derive it from the cells of the serosa, whereas ERCOLANI and TURNER, whom BALFOUR has followed in his text-book, state more or less explicitly that, although originally the cells of the serosa cover the villi as an epithelium, during the mutual intergrowth of the placenta fœtalis and the placenta uterina they perish, and are replaced by proliferating cells of the decidua serotina.

The recent investigations of KASTSCHENKO and SEDGWICK MINOT, as well as the observations of WALDEYER, KUPFFER, GRAF SPEE, and KEIBEL, afford much enlightenment on this controversial subject.

KASTSCHENKO, who has most carefully investigated the epithelium of the chorion frondosum in the different months of pregnancy, and with whom recently S. MINOT essentially agrees, can readily distinguish two layers: (1) a cell-layer (LANGHANS), which lies immediately upon the gelatinous substance of the villi and the connective-tissue membrana chorii, and in which the limits of some of the cell-territories may be made out, and (2) a multinuclear protoplasmic layer, in which separate cells cannot be demonstrated in any manner. These layers are rather sharply contrasted from each other.

The double-layered chorionic epithelium is already distinctly present in eggs four weeks old, as is confirmed by KUPFFER, GRAF SPEE, and KEIBEL. The deeper layer consists of a single sheet of well-marked cubical cells; the outer layer discloses at the free surface a striated border, the significance of which is obscure.

In the following months the chorionic epithelium undergoes noteworthy alterations. The deeper layer becomes thickened in many places into special cell-patches, in which the elements are much superposed. The outer, protoplasmic layer changes still more; it is converted into a hyaline, peculiarly lustrous substance, which is traversed by numerous fissures and spaces, and has therefore received from LANGHANS the name "canalised fibrin."

There is one conclusion that in my opinion results from these investigations: the view of TURNER, according to which the chorionic epithelium is replaced in the course of pregnancy by uterine epithelium, must be abandoned. The chorionic epithelium, which is derived from the serosa, is preserved; it constitutes in any event the deeper layer, composed of epithelial cells, which lies immediately on the membrana chorii or the gelatinous tissue of the villi. Perhaps there belongs to it in addition the so-called protoplasmic layer and the canalised fibrin. However, the source and significance of these structures, especially the latter substance, appear to me to be less satisfactorily explained, and to be in need of still further investigations, in which the question of its origin from the maternal mucosa is not to be overlooked. For even if TURNER has erred in regard to the degeneration of the chorionic epithelium, he is probably in the right in the second point, that the whole surface of the chorion frondosum is directly invested by a layer of maternal tissue.

The connective-tissue framework of the chorion frondosum, then, is provided, as I think must be assumed, with a double investment: (1) with a fœtal epithelium, derived from the serosa, and (2) with a layer, however thin it may be, of maternal tissue.

I shall endeavor to establish this view in now turning to the discussion of the placenta uterina, the structure of which likewise presents great difficulties, and is therefore interpreted in very different ways.

The *placenta uterina* is developed out of the part of the uterine mucosa designated as decidua serotina (fig. 148 *Dse*). At birth it detaches itself, like the corresponding part of the decidua vera, from the inner surface of the womb at the line of separation shown on Plate II., by the breaking down of the thin connective-tissue septa of the underlying spongy layer. It then forms a thin membrane of only 0·5 to 1 mm. thickness, the basal plate of WINKLER (Plate II. *BP*), and forms a complete investment over the placenta fœtalis, which it covers up at the time of the detachment of the fœtal membranes. At the margin it is directly continuous with the vera and reflexa (fig. 148).

The surface turned toward the wall of the uterus is divided by deep furrows into separate divisions. Larger and smaller partitions, the *septa placentæ* (figs. 139 and 143), corresponding in position to the furrows, arise from the opposite surface of the membrane and penetrate in between the chorionic villi (fig. 143 *z*); they always unite a small number of these into a tuft or a *cotyledon.* If we imagine the cotyledons wholly removed, there would be formed in the placenta uterina a corresponding number of irregular compartments. These are in turn subdivided into smaller and more shallow compartments by finer connective-tissue outgrowths from the membrane and the septa.

The edges of the septa do not reach to the roots of the villi in the middle of the placenta, but only in a narrow peripheral region, where they come into immediate contact with the membrana chorii (Plate II. *m*), and are joined together underneath it into a thin, closely applied membrane, which is pierced by the roots of the villi. This has been called by WINKLER *closing plate* (Schlussplatte, *SP*), by KÖLLIKER decidua placentalis subchorialis. Still more appropriate is the term employed by WALDEYER, subchorial terminal ring (Schlussring), because it is thereby stated that the membrane in question is present only at the margin of the placenta, leaving the middle area of the chorion free.

The connective-tissue framework of the placenta uterina possesses in general the properties of the compact, abundantly cellular layer of the decidua vera and reflexa, but exhibits one peculiarity in the presence of a very special form of cells, the so-called *giant cells.* These are large masses of protoplasm appearing yellowish grey, and with from ten to forty nuclei; they begin to develop in the fifth month, and are found in the after-birth in great numbers; they lie partly in the basal plate, partly in the septa, ordinarily in the immediate vicinity of large blood-vessels; but they are also found isolated in the spongy layer of the decidua serotina and even between the adjacent muscle-bundles of the uterus.

The greatest difficulties in the investigation of the placenta uterina are caused by its blood-courses. Numerous spirally twisted arterial stems (Plate II. *a*) penetrate through the muscular layer of the womb, and, passing through the spongy layer, reach the basal plate of the placenta uterina, where their structure undergoes important changes. For they here lose their muscular layer, and now appear as large tubes, lined with endothelium only. From the basal plate they penetrate in part into the septa placentæ. From here they are not to be followed further as closed vessels; *a transition to capillaries does not take place anywhere.* On the contrary, it can be proved that through openings in the basal plate and the septa they pour their blood into a system of cavities between the chorionic villi, *i.e.*, into the *intervillous* or *intraplacental spaces* (*c*). The latter are bounded on the one side by the membrana chorii (*m*) with its villi (*z*), on the the other side by the basal plate (*BP*) with its septa.

The blood is collected from this system of cavernous spaces into large veins, which are likewise simply tubes lined with endothelium.

These are distributed as a network in the septa, as well as in the basal and closing plates of WINKLER, and they begin with narrow openings, which connect with the intervillous spaces. At the margin of the placenta they are joined together, and thereby produce the *marginal sinus* (Plate II.), or the *ring-like sinus* of the placenta. This, however, is not to be regarded as a vessel of uniform calibre, but as a system of irregular spaces joined together.

In virtue of the conditions described, the chorionic villi are directly bathed by the maternal blood. At the same time, from what has already been said, it is to be seen that the motion of the blood is retarded, owing to the great enlargement of the blood-courses, and that it is irregular, corresponding to the form of the intervillous spaces. In general the motion of the blood is from the middle and from the convex side of the placenta, where the arteries chiefly enter, toward its concave surface and its margin.

The question as to the significance and the *origin of the intervillous blood-spaces* constitutes the key to the comprehension of the structure of the placenta.

According to *one view*, which for a long time was the dominant one in Germany, and is defended by KÖLLIKER, LANGHANS, and others, the intervillous spaces originally have no connection with the maternal blood-system. Developmentally they are nothing but spaces between chorion and uterine mucosa, and owe their existence to the fact that the two structures have not everywhere come in contact, but have acquired firm connection only by means of the tips of the villi. The spaces in the earliest stage would be bounded by the epithelium of the villi and the maternal mucosa. LANGHANS therefore designates them as *placental spaces*. According to this view they would acquire their blood-contents later only, and in this way, as KÖLLIKER expresses it: "The proliferating chorionic villi everywhere corrode, and in part destroy the maternal placental tissue, and thus produce an opening of their vessels, which must naturally lead to a gradual penetration of the maternal blood into the intervillous spaces."

This view has been modified by other observers (BRAXTON HICKS, AHLFELD, RUGE, and others) to this extent, that the intervillous spaces, even in the mature placenta, do not normally contain blood nor have connection with the maternal blood-vessels. The almost universally received views concerning placental nutrition are thus called in question. The denial of a regulated blood-circulation has induced the further hypothesis, that a *uterine milk*, as in the Ruminants, is secreted by the cells of the decidua serotina into the intervillous spaces, and is taken up by the fœtal villi.

According to *the second diametrically opposite view*, which finds its defenders in Virchow, Turner, Ercolani, Leopold, Waldeyer, and others, *the intervillous spaces are nothing else than the enormously enlarged capillary blood-vessels of the maternal mucosa.* Chorion and decidua serotina early unite very intimately by means of their surfaces, so that no fissures are left between them. The villi grow into the mucous tissue, the superficial capillaries of which enlarge to capacious spaces.

If this view is correct, the chorionic villi will necessarily be surrounded on all sides by thin coverings of maternal tissue, or, since a partial degeneration of the covering would certainly be possible, there will of necessity be at least a stage in the development in which such a covering will be demonstrable.

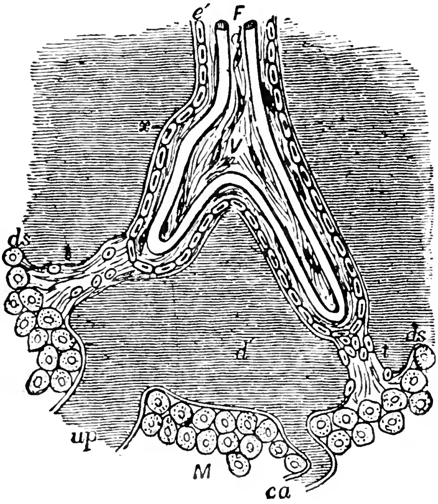

Fig. 149.—Diagrammatic representation of the finer structure of the human placenta, after Turner.

F, Placenta fœtalis; *M*, placenta uterina; *ca*, tortuous artery; *up*, vein which conducts the blood away from the intervillous maternal blood-sinus (*d′*); *x*, a continuation of the maternal tissue over the villi: this lies outside the layer *e′* (the metamorphosed epithelium of the uterine mucosa), and is probably a connective-tissue membrane with vascular endothelium; *t*, cords of the placenta uterina, which unite with the tips of some of the fœtal villi (Haftwurzeln); *ds*, decidua serotina of the placenta.

Ercolani, Romiti, and Turner have in fact, as has been previously stated, expressed themselves to the effect that probably the epithelial layer resting upon the connective-tissue axis of the villi is not the original chorionic epithelium derived from the serosa, but a covering which arises from the decidua placentalis—a view the untenableness of which has already been shown.

In the diagram which Turner has sketched to illustrate his view of the structure of the human placenta (fig. 149) the real original villous epithelium is degenerated.

The cell-layer *e′* is the epithelium of the uterine mucosa, into which the villous tufts (F) have grown, and with which the most intimate contact everywhere prevails. Outside the epithelium TURNER describes in addition a thin membrane (x), which he interprets as an exceedingly thin connective-tissue layer, upon which is probably to be found an endothelial covering which lines the blood-spaces. The cords indicated by t are connective-tissue strands of the maternal mucosa, which join the tips of certain fœtal villi with the septa placentæ (ds), by which the origin of the so-called attachment-roots (Haftwurzeln) is explained. The great blood-spaces d' are simply enormously enlarged, superficially located capillaries of the mucosa.

The exact determination of the true state of affairs is coupled with great difficulties.

However, it seems to me that the second of the two hypotheses cited, according to which the intervillous spaces are the enlarged maternal capillaries, is the more probable because the more natural, and the following facts especially appear to me to favor it :—

(1) From a comparative-anatomical point of view it can be maintained that in all Mammals where a special adaptation to intra-uterine nutrition is developed, the epithelial surfaces of the chorion and the mucous membrane of the uterus lie directly on each other, and with the increase of surface produced by the formation of folds effect mutual ingrowth. An intra-placental fissure, such as LANGHANS and KÖLLIKER assume for Man, is found nowhere else among Mammals. We also see in some instances how the capillaries of the uterine mucosa become enlarged and acquire attenuated walls (Rodents, Carnivora, etc.), so that the fœtal villi are almost directly bathed in maternal blood. *The enlargement of the blood-courses in Man may therefore be regarded as a further elaboration of an already existing arrangement.*

(2) That capillaries become metamorphosed into a cavernous system is also realised in other parts of the human body (corpora cavernosa of the sexual organs), whereas *the employment of spaces lying outside the blood-courses as component parts of the vascular system would be a phenomenon without analogy.*

(3) In the placenta uterina the capillaries originally present are wanting between the arteries and veins, whereas they ought to be demonstrable, if they have not been converted into the intervillous spaces.

(4) The exposition which LEOPOLD has given of the development of the placenta in the second month of pregnancy favors the

second of the hypotheses cited. "Villi and the tissue of the decidua," he says, "become shoved into each other, as one can interlock the outspread fingers of the two hands. If now the blood-vessels of the serotina be followed, one will recognise here the greatly enlarged capillary network of the surface, upon which the egg comes to lie when it lodges. But its innumerable vessels apparently continue with the sprouts of the decidua to grow toward the villi, and become distended and more voluminous; on the other hand the villi increase rapidly in size, and thus it is intelligible that the new branches of the villi, whose stems have, as it were, sucked themselves fast in the decidua by means of their tips, at once encounter the enlarged capillaries of the surface, and press forward against these and break into them."

The weightiest objection that can be brought against this interpretation is the assertion of many investigators that the chorionic villi are not covered with a mantle of maternal tissue, and that the intervillous spaces are not lined with vascular endothelium. However, it is precisely upon this point that more exhaustive and especially ontological investigations are desirable. For one is not at liberty to draw conclusions from the conditions of "delivered" placentæ, since degeneration may have taken place. Moreover TURNER and LEOPOLD claim to have demonstrated endothelia at certain places of the intervillous spaces. But especially decisive here appear to me to be, first, the important investigations which WALDEYER has recently published upon the placental circulation in Man, and, secondly, KEIBEL's very noteworthy preliminary communication upon the embryology of the human placenta.

WALDEYER has injected the maternal blood-vessels of placentæ which still possessed their normal attachment to the uterus, and has prepared sections through the hardened organ. He finds that the intervillous spaces are nothing else than the enormously enlarged maternal blood-vessels, and that at many places there is still present outside the villous epithelium a layer of flat cells, which he is inclined to interpret as vascular endothelium. He appropriately compares the intrusion of the chorionic villi into the intervillous blood-spaces with the ingrowth of the arachnoideal villi into the blood-sinus of the dura mater, carrying before them invaginations of the endothelial covering of the latter.

KEIBEL has investigated by means of sections a well preserved and prepared human embryo, which was in about the middle of the fourth week. He saw the villi (fig. 150 *Z*), which were provided with numerous secondary sprouts and were clothed in a two-layered chorionic epithelium, already attached by their tips in the maternal tissue (attachment villi), and also *the intervillous spaces filled with maternal blood. But this was distinctly separated from the chorionic epithelium by a special thin cellular membrane* (*E*). This membrane consisted of very thin endothelial cells, and was frequently elevated more or less from the chorionic villi, probably owing to the method of preparation. Keibel justly concludes from the establishment of the existence of an endothelial membrane that the *intervillous spaces are the enormously dilated maternal capillaries.*

Between the chorionic epithelium and the walls of the maternal capillaries Keibel finds no further remnant of maternal tissue in the very young ovum. This would indicate an early and complete disappearance of the uterine epithelium, and would make it probable that the protoplasmic layer and the canalised fibrin described at p. 261 are to be derived from the cell-layers of the chorion, a mooted point concerning which I have been unable to form a definite opinion.

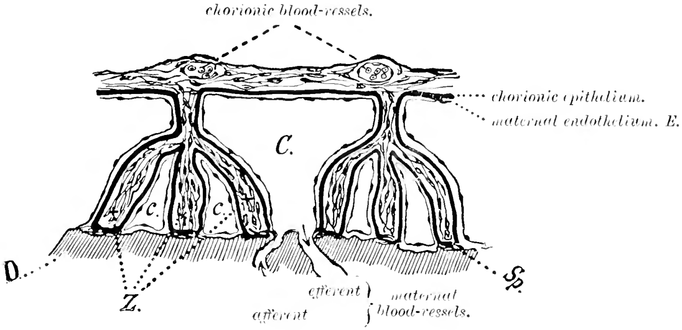

Fig. 150.—Diagram of the structure of the human placenta from an embryo four weeks old, after Keibel.

Z, Chorionic villi ; *Sp*, attachment of the tips of the same in the maternal decidua (*D*) ; *C*, enlarged maternal blood-capillaries.

Thus the observations are increasing which favor a special limitation of the intervillous spaces and the existence of a thin layer of maternal tissue, a vascular endothelium, upon the villi.

6. The Umbilical Cord.

The *umbilical cord* (funiculus umbilicalis) constitutes the union between the placenta and the embryonic body (fig. 143). It is a cord about as thick as the little finger (11-13 mm. or 0·5 inch), and attains the considerable length of 50 to 60 cm. (20-24 inches). It almost always exhibits a very pronounced *spiral twist*, which, regarded from the embryo, runs usually from left to right.

There are often knot-like thickenings of the umbilical cord, which may be due to either of two causes. For the most part they are due to an increased growth here and there in the connective-tissue matrix of the cord (false knots). More rarely they are formed by a knotting of the cord, which results from the fact that the embryo, in the motions which it executes in the amniotic fluid, accidentally slips through a loop of the cord and then gradually tightens it into a knot. The thickening then presents, in distinction from the other, a *true* knot.

The attachment of the umbilical cord to the placenta ordinarily takes place in or near its middle (*insertio centralis*). However, exceptions to the rule are not rare. Thus one distinguishes in addition an *insertio marginalis* and an *insertio velamentosa*. In the first case the umbilical cord unites with the margin of the placenta; in the second place it does not reach the placenta at all, but attaches itself at a lesser or greater distance from the margin of the latter, to the fœtal membranes themselves, and sends out from that point the outspreading large branches of its vessels to the placenta.

Man is distinguished from almost all of the remaining Mammals by the possession of a long slender umbilical cord. Its condition in Man results from the great distension of the amniotic sac. Whereas this at first lies close upon the body of the embryo, it subsequently becomes so distended (compare fig. 144 with fig. 143) that it fills the whole cavity of the blastodermic vesicle and everywhere clings closely to the inner surface of the chorion. Owing to this, the remaining structures—the yolk-sac with its blood-vessels, the slender canal of the allantois with its connective-tissue envelope, and the umbilical blood-vessels—which emerge through the dermal navel of the embryo into the extra-embryonic body-cavity and betake themselves to the chorion, become more and more hemmed in by the amnion, and finally are crowded together into a small cord.

At first the umbilical cord is short, since it pursues a straight course in uniting the navel of the embryo to the fœtal membranes; afterwards it becomes greatly elongated and folded in the amniotic fluid.

Its structure varies at different times during pregnancy corresponding to the changes which the yolk-sac and the allantois with their blood-vessels undergo.

I shall give a detailed description of its finer structure for the end of pregnancy only, and shall consider especially the following parts: (1) the gelatin of WHARTON, (2) the umbilical vessels, (3) the remnant of the allantois, of the vitelline duct, and of the vasa omphalomesenterica, (4) the amniotic sheath.

(1) The gelatin of WHARTON forms the common matrix in which the remaining parts are imbedded. It is a gelatinous or mucous tissue. In this soft gelatinous substance there run strands of connective-tissue fibrillæ and elastic fibres, which are the scantier the younger the umbilical cord. They are joined together into a network, the meshes of which are narrower at some places than at others. In this way there are formed in the gelatin numerous firm peculiarly differentiated strands. The cells of the gelatinous connective tissue are partly spindle-shaped, partly stellate elements, the latter with widely branching processes.

(2) The umbilical blood-vessels consist of two large arteries (art. umbilicales), which conduct the blood from the embryo to the placenta, and a capacious vena umbilicalis, in which the blood flows back to the embryo after having traversed the placental circulation. The two arteries are wound spirally, like the umbilical cord itself, and are joined to each other by an anastomosis near their entrance into the placenta. They are very contractile, and exhibit a thick muscular membrane (tunica muscularis), consisting of circular and longitudinal fibres.

(3) The canal of the allantois and the vitelline duct, which are essential components of the umbilical cord during the first months of pregnancy, subsequently undergo reduction, and are present at the end of embryonic life only in the form of insignificant remnants, as has been shown by KÖLLIKER, AHLFELD, and RUGE. The canals lose their lumens; there then exist in the gelatin of WHARTON solid cords of epithelial cells; finally, these also disappear in part, so that only here and there strands and nests of epithelial cells have been preserved. The vitelline blood-vessels (vasa omphalomesenterica), which have a rôle to perform at the beginning of development, soon become inconsiderable, and diminish more and more in comparison with the enlarging umbilical blood-vessels. In the mature umbilical cord they are very rarely to be demonstrated (AHLFELD); usually they have wholly degenerated.

(4) At the beginning of development the amnion forms around the allantoic canal and the vitelline duct a sheath, which can be removed. Afterwards the sheath is firmly fused with the gelatin

of Wharton, except at the attachment at the navel, where for a short distance it may be peeled off as a special thin membrane.

Condition of the Fœtal Membranes during and after Birth.

As a conclusion to the account of the fœtal membranes some further remarks may be in place regarding their history at birth.

At the end of pregnancy, with the beginning of labor pains, the fœtal membranes, which form a fluid-filled sac surrounding the embryo, are ruptured as soon as the contractions of the musculature of the uterus have reached a certain degree of intensity. The rupture ordinarily arises at the place where the wall of the sac is pressed out through the mouth of the uterus (rupture of the amnion). In consequence the amniotic water now flows away.

With the continuation and increase of the pains, the child is next forced out of the uterus through the rupture in the fœtal membranes —it is born, whereas the placenta and embryonic membranes usually still remain behind for a short time in the cavity of the uterus. Immediately after birth the union between child and fœtal membranes has to be artificially interrupted, by the tying and cutting off of the umbilical cord at a little distance from the navel.

Finally, the fœtal membranes with the placenta are detached from the inner surface of the uterus, and with renewed pains are discharged to the outside as the *after-birth*.

The separation takes place in the spongy layer of the decidua vera, approximately in the region which is designated as the line of separation in the diagram given by Leopold (Plate II.). The after-birth is composed of both fœtal and maternal membranes, which are quite firmly grown together: (1) the amnion, (2) the chorion, (3) the decidua reflexa, (4) the decidua vera, (5) the placenta (placenta uterina and placenta fœtalis). Notwithstanding the growing together, a partial separation of the individual membranes from each other is still possible.

After birth the inner surface of the uterus is one great surface-wound, since by the detachment of the placenta and the deciduæ numerous blood-vessels are ruptured. Also during the first days of childbed fragments of the spongy layer of the decidua vera and serotina, which remained behind at birth, continue to be detached from it. Only the deepest layer of the mucosa, that immediately in contact with the musculature of the uterus, is retained. This still contains remnants of the cylindrical epithelium of the uterine glands, as has been already stated. In the course of several weeks it is again converted, by an active process of growth, into a normal mucous membrane, whereby its superficial epithelium probably arises from the preserved remnants of the glandular epithelium.

SUMMARY.

1. The human ovum establishes itself ordinarily at the base of the uterus (fundus uteri), between the mouths of the two Fallopian tubes, and becomes overgrown by folds of the mucosa and enclosed in a capsule.

2. The mucous membrane of the uterus is developed into the maternal envelopes of the ovum, the deciduæ, which are distinguished as decidua serotina, reflexa, and vera.
   - (*a*) The decidua serotina is that part of the mucous membrane upon which the ovum immediately lies after its entrance into the uterus and on which the placenta is afterwards developed.
   - (*b*) The decidua reflexa is the part that grows around the ovum.
   - (*c*) The decidua vera arises from the remaining portions of the mucous membrane lining the uterus.

3. In the formation of the deciduæ or deciduous fœtal membranes the uterine mucosa undergoes profound alterations of structure, and, accompanied by a rapid growth of the uterine glands and a partial disappearance of its epithelium, becomes differentiated into an inner compact and an outer spongy layer.

4. Out of the wall of the blastodermic vesicle, so far as it is not employed in the formation of the embryo itself, are developed the fœtal envelopes of the offspring, which in the main agree with the fœtal envelopes of the remaining Mammals in number and the method of their development, but which present in detail important modifications, which are essentially as follows :—
   - (*a*) The amnion is closed from before backward, remains united at the hinder end of the embryo with the serosa (subsequently the chorion) by means of a short pointed prolongation, and thus contributes to the formation of the so-called belly-stalk of human embryos.
   - (*b*) The allantois does not grow as a free sac into the extra-embryonic part of the body-cavity, but, in the form of a narrow canal, shoves itself along the under surface of the pointed amniotic prolongation to the chorion, and thus furnishes the chief component of the belly-stalk.

(*c*) The yolk-sac (umbilical vesicle) is reduced to an exceedingly small vesicle, and is connected with the embryonic intestine by means of a long thread-like stalk, the vitelline duct.

(*d*) By the enlargement of the amnion, which at length fills the entire blastodermic vesicle (increase of amniotic fluid), the canal of the allantois and the vitelline duct, together with the umbilical and vitelline blood-vessels, become completely enveloped by the amniotic sheath; in this way is formed the umbilical cord (funiculus umbilicalis), a cord-like connection between the inner surface of the egg-membrane and the navel of the embryo.

(*e*) The serosa at a remarkably early period (second week) develops villi over its whole surface, and by the ingrowth of the connective tissue of the allantois into the latter it becomes the villous membrane (chorion).

(*f*) The villous membrane is differentiated into a chorion læve and a chorion frondosum:—

(*α*) The part which lies in contact with the decidua reflexa and is firmly united with it by means of villi which lag behind in growth becomes the chorion læve.

(*β*) The region which abuts upon the decidua serotina, and in which the villi grow out into large, much-branched tufts, is converted into the chorion frondosum.

5. By the penetration of the villous tufts of the chorion frondosum into the decidua serotina and their firm union with it, there is formed an especial organ of nutrition for the embryo, the after-birth, or placenta.

6. One distinguishes a fœtal and a maternal part of the placenta: (1) the placenta fœtalis or the chorion frondosum, and (2) the placenta uterina or the original decidua serotina.

(*a*) The placenta fœtalis consists—

First, of the membrana chorii, in which the chief branches of the umbilical blood-vessels spread themselves out, and to which the umbilical cord is attached, ordinarily in the middle (insertio centralis), rarely at the margin (insertio marginalis), still more rarely at a distance from the margin (insertio velamentosa);

Secondly, of bundles of chorionic villi, the "attachment-roots" of which are firmly grown together with the uterine mucosa by means of their tips, whereas the free processes project into the cavernous blood-spaces of the placenta uterina.

(*b*) The placenta uterina, like the decidua vera, is composed of a compact layer, which becomes detached at birth (pars caduca), and a spongy layer, in which the separation takes place, a part remaining behind on the musculature (pars fixa).

The compact layer (basal plate of WINKLER) sends partition-walls (septæ placentæ) between the chorionic tufts, and thereby divides them into separate bundles, the cotyledons.

There are interpolated between the arteries and veins—which run in the basal plate and the septæ—enormously enlarged vascular spaces, in which the villi appear to hang free.

The vascular spaces are probably extraordinarily distended maternal capillaries, in which case one may expect to find the chorionic villi invested by a very thin layer of maternal tissue (endothelial membrane), as is maintained by some investigators.

7. At birth the deciduæ or caducous membranes become detached from the uterus along the spongy layer, and together with the fœtal envelopes and the placenta constitute the after-birth.

8. In the first weeks after birth a normal mucosa is developed out of the remnants of the spongy layer left upon the musculature and the remnants of the uterine glands, from the epithelium of which the epithelium of the mucous membrane is probably regenerated.

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PART SECOND.

INTRODUCTION TO PART II.

In the first part of the text-book, which treated of the fundamental processes of the beginning of development, it was shown how there were formed from the embryonic cells, the descendants of the cleavage-process, several cell-layers: the outer, the middle, and the inner germ-layers, and the intermediate layer which inserts itself into all the interstices between the former. In the further progress of development each of these chief layers, which Carl Ernst v. Baer has called the fundamental organs of the animal body, undergoes a series of manifold changes, and is in consequence gradually converted into the separate organs of the adult body.

The study of the development of the organs constitutes the theme of the second part of this text-book.

A division of the extensive material to be presented here is best undertaken with reference to the separate germ-layers from which the various organs are derived, as was first attempted by Remak in his pioneer work "Untersuchung über die Entwicklung der Wirbelthiere."

But it must be observed at the very outset that the *principle of the classification of organs according to the germ-layers* can be carried out only with certain limitations. For the completed organs of the adult are ordinarily compound structures, which are not formed out of a single embryonic layer, but out of two or even out of three. Thus, for example, a muscle is developed from the middle germ-layer and the intermediate layer. The teeth arise from the latter and the outer germ-layer; the alimentary canal with its glands contains elements from three layers, from the inner and the middle germ-layers, as well as from the intermediate layer. When, notwithstanding, these organs are cited as descendants of one germ-layer, it is for the reason that the various tissues are of unequal value in the construction and function of an organ, the important components being furnished preëminently by *one* germ-layer. Thus the structure and the function of the liver or the pancreas are primarily determined by the glandular cells which are derived from the inner germ-layer, whereas connective tissue, blood-vessels, nerves, and serous covering, although they also belong to these glands as a whole, are of less significance, because the characteristic properties of liver or pancreas do not depend upon them. In the anatomy and physiology of a muscle the muscular tissue is the more significant part, in the sensory organs the sensory epithelium.

Guided by such considerations one has a perfect right to designate the intestinal glands as organs of the inner germ-layer, the muscles, the sexual and urinary organs as belonging to the middle germ-layer, and the nervous system together with the sensory organs as products of the outer germ-layer.

Thus the science of the embryology of organs is divisible into four main sections—into the science of the morphological products of

(1) the inner germ-layer,
(2) the middle germ-layer,
(3) the outer germ-layer,
(4) the intermediate layer.

CHAPTER XIV.

THE ORGANS OF THE INNER GERM-LAYER.

The Alimentary Tube with its Appended Organs.

After completion of the formation of the germ-layers and the first processes of differentiation described in the tenth chapter, the body of the vertebrated animal consists of two simple tubes, one within the other (Plate I., figs. 7 and 10),—the inner, smaller alimentary tube, and the body-tube separated from the former by the body-cavity (*lh'*),—each of which is composed of more than one of the primitive cell-layers of the germ.

The *alimentary tube*, the further development of which will first engage our attention, is composed of two epithelial layers,—the entoderm and the visceral portion of the middle layer, which furnishes the epithelial lining of the body-cavity,—separated from each other by the intermediate layer, which is at this time little developed. Of the three layers the entoderm is unquestionably the most important, since the further processes of differentiation primarily proceed from it, and since the physiological capabilities of the alimentary canal are determined by the activity of its cells.

The changes which occur in the further course of development are best divided into three groups. First, the alimentary tube comes into communication with the surface of the body by means of a large number of openings, the visceral clefts, the mouth, and the anus. Secondly, it grows enormously in length, and is at the same time differentiated into œsophagus, stomach, small intestine and large intestine, with their peculiarly modified mesenteries and omenta. Thirdly, numerous organs, which are for the most part concerned in the duties of digestion, take their origin from the walls of the alimentary tube.

I. The Formation of the Mouth, the Throat- or Gill-Clefts, and the Anus.

At the beginning of development the alimentary tube opens out to the surface of the germ by means of the *primitive mouth* (primitive groove), which marks the place at which, during the stage of the blastula, the inner and middle germ-layers have been invaginated (Chapters V. and VI., figs. 44, 47, 54, 55, 78 *u*). *But this opening is only a transitory structure.*

Located at the future hind end of the embryonic fundament, it is at first overgrown by the medullary ridges, and establishes a temporary union between the intestinal and neural tubes, the canalis neurentericus (figs. 68 *cn*, 80, 88 *ne*). Afterwards it becomes entirely closed by the growing together of the edges of the primitive mouth.

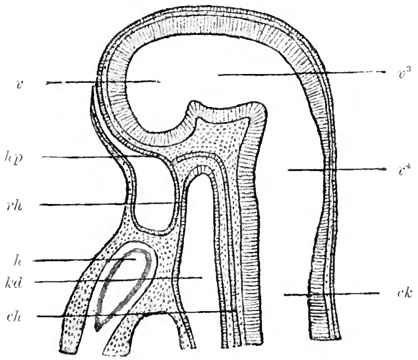

Fig. 151.—Median section through the head of an embryo Rabbit 6 mm. long, after MIHALKOVICS.
rh, Membrane between stomodæum and fore gut, pharyngeal membrane (Rachenhaut); *hp*, place from which the hypophysis is developed; *h*, heart; *kd*, lumen of fore gut; *ch*, chorda; *v*, ventricle of the cerebrum; v^3, third ventricle, that of the between-brain [thalamencephalon]; v^4, fourth ventricle, that of the hind-brain and after-brain [epencephalon and metencephalon,* or medulla oblongata]; *ck*, central canal of the spinal cord.

It is affirmed by some that in certain Vertebrates (Petromyzon, several Amphibia) the primitive mouth persists, and becomes the anus of the adult animal.

There arise, however, on the permanent alimentary tube, both at its anterior and posterior ends, *new openings, part of which are unpaired, part paired*; for the wall of the alimentary tube at several places fuses with the wall of the body, then becomes thinner, and finally breaks through to the outside. The *unpaired openings are mouth and anus; the paired ones are the throat-, gill-, or visceral clefts.* The first to be established are the mouth and the gill-clefts, in the regions of head and neck. These are of the greatest importance in the external morphology of the

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* [Huxley has employed metencephalon and myelencephalon instead of epencephalon and metencephalon for the fourth and fifth regions of the brain respectively.]

embryo, because with their appearance the head- and neck-regions become distinguishable.

A. The Development of the Mouth.

In all vertebrated animals the epidermis forms on the under side of the rudimentary head, which at first has the appearance of a rounded knob, a small shallow pit (Plate I., fig. 11, and fig. 151), which meets the blind end of the fore gut (*kd*). In the region of this pit the middle germ-layer is from the beginning absent (Keibel, Carius). Outer and inner germ-layers meet to form a thin membrane (fig. 151 *rh*), which separates oral sinus or oral pit [stomodæum] and fore gut, and which has been described since the time of Remak as *pharyngeal membrane* (Rachenhaut). By its rupture and the degeneration of the shreds of it known as the *primitive palatal velum* communication with the outside is established (Plate I., figs. 4 and 7 *m*).

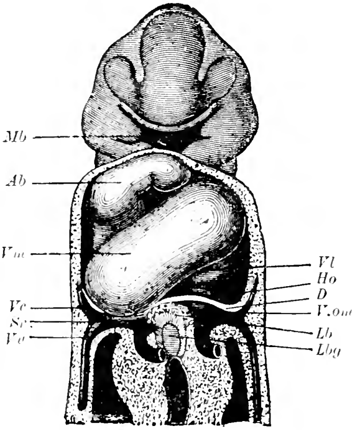

Fig. 152.—Human embryo (*Lg* of His) 2·15 mm. long, neck measurement.* Drawing from a reconstruction, after His ("Menschliche Embryonen"). Magnified 40 diameters.

Mb, Oral pit (or sinus); *Ab*, aortic bulbus; *Vm*, middle part of the ventricle of heart; *Vc*, vena cava superior or ductus Cuvieri; *Sr*, sinus reuniens; *Vu*, vena umbilicalis; *Vl*, left part of the ventricle; *Ho*, auricle of heart; *D*, diaphragm; *V.om*, vena omphalo-mesenterica; *Lb*, solid fundament of the liver; *Lbg*, hepatic duct.

In the case of the Chick the oral pit is observable on the second day of incubation, the front end of the embryonic fundament having a short time previously elevated itself as a cephalic knob above the extra-embryonic part of the germ-layers. The rupture of the pharyngeal membrane takes place on the fourth day. In the case of an embryo Rabbit of nine days the pharyngeal membrane is not yet ruptured. His has studied in detail this early stage in Man on his embryo "*Lg*," the age of which he estimates at twelve days.

In all amniotic Vertebrates the entrance to the oral pit (fig. 152 *Mb*) presents a very uniform condition and appears as a large five-

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* [It will be seen by an inspection of figure 158 that the longest straight line which can be drawn through the embryo connects the neck- and rump-regions. It is this distance which is designated as the neck, or neck-rump, measurement.]

sided opening, which is surrounded by *five ridges.* A knowledge of these is of great importance in studying the history of the formation of the face.

Of the five ridges one is unpaired, the *frontal* or *naso-frontal process,* a broad, rounded projection which bounds the oral pit above. Its origin is connected with the development of the central nervous system, which reaches up to the anterior end of the embryonic fundament, where it is developed into the cerebral vesicles (fig. 153 *gh, zh, mh*). Examined by means of a longitudinal section, the frontal process at this stage, therefore, encloses a large cavity belonging to the neural tube, and has the form of a vesicle, which is composed of three layers, the epidermis, a layer of mesenchyma, and the thickened epithelial wall of the neural tube. The primary oral cavity and the fundament of the brain are closely apposed at the beginning of development; they are separated by only a thin sheet of tissue, within whose territory there is *subsequently formed, among other things, the floor of the cranium.*

The four remaining ridges are paired structures which surround the oral sinus upon its sides and below. These are produced by growths of the embryonic connective tissue, through which large blood-vessels take their course. They are distinguished according to their positions as *upper-jaw* (*maxillary*) and *lower-jaw* (*mandibular*) *processes.* The former are on either side in immediate contact with the frontal process, from which they are separated by a groove only, the naso-optic furrow, which will be discussed in a subsequent chapter, and which runs obliquely upward and outward to that region of the face in which the eye begins its development. The maxillary process is separated from the mandibular process by an incision which corresponds to the place of the future angle of the mouth. The two processes of either side together form the pharyngeal arches, or the membranous jaw-arches.

Before the rupture of the pharyngeal membrane the oral sinus has become still deeper, but only in its upper part, whereas toward the mandibular arch it becomes shallow. This condition is connected with curvatures which in all amniotic Vertebrates as well as Selachians affect that part of the head which encloses the brain-vesicles and lies above the alimentary tube. For the front end of the head is bent down toward the ventral side of the embryo, and finally makes a right angle with the posterior half of the head (fig. 153). Consequently the place at which the so-called *anterior cephalic curvature* has occurred, and at which the posterior and anterior halves of the head bend into each other, has become an elevation, the *parietal* [or *mid-brain*] *elevation* (Scheitelhöcker), *SH.* The latter encloses the middle brain-vesicle (*mh*), the future mid-brain. Furthermore the frontal process, in consequence of the curvature, covers in the oral sinus more and more from above and in front, and thereby contributes to its depth.

As His has shown for the human embryo, the pharyngeal membrane before rupturing extends obliquely backward and upward from the mandibular arch, and becomes firmly attached at the point of curvature *hp*, where, as a result of the bending, the anterior and posterior halves of the head meet each other at right angles. Even after the rupture of the pharyngeal membrane there is retained, in front of its attachment, a small pit, which constitutes RATHKE'S pocket (fig. 153 *hp*).

It is to be noted that the oral sinus, in front of the pharyngeal membrane, and the fore gut, which lies behind it, do not correspond respectively to the cavities designated in the anatomy of the adult as oral cavity and pharynx. But the region of RATHKE'S pocket, which belongs to the embryonic oral sinus, is in the adult referred to the pharynx.

In consequence of the early and complete disappearance of the pharyngeal membrane, it is no longer possible to say at what place in the adult is to be sought the transition from the primitive, epidermis-lined oral sinus to the epithelial layer of the alimentary tube.

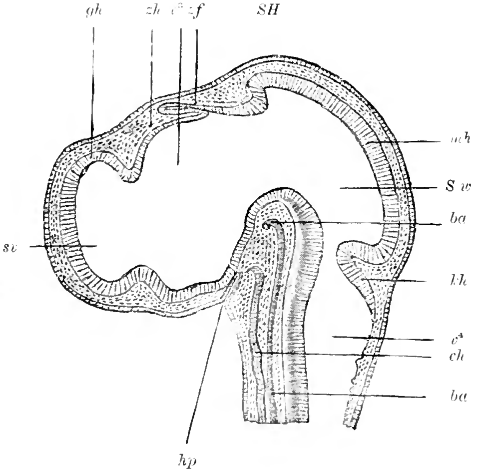

Fig. 153.—Median sagittal section through the head of a Chick incubated 4½ days, after MIHALKOVICS.

SH, Parietal [mid-brain] elevation ; *sc*, lateral ventricle of the brain ; c^3, third ventricle ; v^4, fourth ventricle ; *Sw*, aqueductus SYLVII ; *gh*, cerebral vesicle ; *zh*, between-brain [thalamencephalon] ; *mh*, mid-brain ; *kh*, cerebellum ; ***zf***, pineal process ; *hp*, hypophysial (or RATHKE'S) pocket ; *ch*, chorda ; *ba*, basilar artery.

B. The Development of the Visceral Clefts.

While the changes described take place in the vicinity of the oral sinus, several *visceral clefts* make their appearance immediately behind the jaw-arches upon either side of the body. They are developed in the case of Selachians, Teleosts, Ganoids, and Amphibia, as well as Amniota, in a rather uniform manner (figs. 154, 155). From the epithelium of the fore gut there are formed deep outpocketings (*sch*^{1}—*sch*^{6}), which run from above downward on the lateral wall of the throat parallel to the jaw-arches. They crowd aside the middle germ-layers, which extend into this region, and thus grow outward to the surface, where they unite with the epidermis. The latter now become depressed into furrows along the regions of contact (fig. 154), so that one can distinguish *inner, deeper throat-pockets, and outer, shallower throat- or gill-furrows.* The two are separated from each other for a time by a very thin *closing membrane*, which consists of two epithelial layers, the epidermis and the epithelium lining the fore gut.

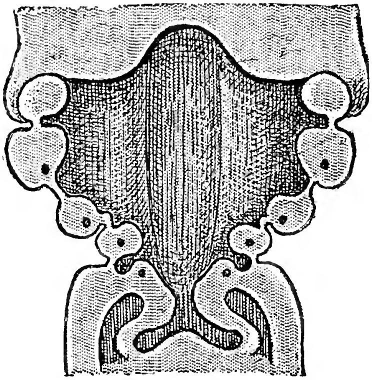

Fig. 154.—**Frontal (reconstruction) section of the oro-pharyngeal cavity of a human embryo** (*Bl* of His) **4·5 mm. long, neck measurement,** from His "Menschliche Embryonen." Magnified 30 diameters.

The figure shows four outer and four inner visceral furrows, with the closing plates at the bottom of them. In the visceral arches separated by furrows one sees the cross sections of the second to the fifth aortic arches. By reason of the greater development of the anterior visceral arches the posterior ones are already somewhat pressed inwards.

The bands of substance which lie between the successive throat-pockets (figs. 154 and 157) are the membranous *branchial, throat-,* or *visceral arches.* They consist of an axis, which is derived from the middle germ-layer and the mesenchyma, and of an epithelial covering, which on the side toward the pharynx is furnished by the inner germ-layer, on the outside by the outer germ-layer. They are designated according to their sequence as the second, third, fourth, etc., visceral arches, inasmuch as the ridge which surrounds the mouth constitutes the first visceral arch.

In all water-inhabiting Vertebrates which breathe by means of gills the thin epithelial closing plates break through between the visceral arches, and indeed in the same sequence as that in which they arose. Currents of water therefore can now pass from the outside through the open clefts into the cavity of the fore gut and be employed for respiration, since they flow over the surface of the mucous membrane. There is now developed in the mucous membrane, upon both sides of the visceral clefts, a *superficial, close* network of blood-capillaries, the contents of which effect an exchange of gases with the passing water. Moreover the mucous membrane becomes folded, for the increase of its respiratory surface, into numerous, close-set, parallel branchial leaflets, which are provided with the greatest abundance of capillary blood-vessels. In this manner the most anterior section of the alimentary canal, which lies immediately behind the head, has become converted into an organ of respiration adapted to life in water.

The important differentiation of the alimentary canal into an anterior respiratory chamber and a following nutritive region is possessed by Vertebrates and Amphioxus in common with certain Invertebrates (Tunicates and Balanoglossus).

Likewise in the case of the higher (amniotic) Vertebrates both inner and outer visceral furrows, together with the visceral arches separating them, are, as has already been stated, formed; but here they are never developed into an actually functioning respiratory apparatus; they belong consequently in the category of rudimentary organs. Upon the mucous membrane there arise no branchial leaflets; indeed the formation of open clefts is not always and everywhere achieved, since the thin epithelial closing membranes between the separate visceral arches are preserved at the bottom of the externally visible furrows. Upon this point, however, the opinions of the investigators who have been engaged in the study of the throat-region in late years are very dissimilar. Whereas HIS, BORN, and KÖLLIKER maintain that the closing plate does not as a rule rupture, FOL, DE MEURON, KASTSCHENKO, LIESSNER, and others find that at least the first two or three visceral clefts are temporarily open. The opening takes place to a greater extent in Reptiles than in Birds and Mammals, where it remains limited to a small territory. In the most posterior visceral pockets there can be no breaking through, because they are not as deep, and the closing plate is therefore thicker and contains also a layer of connective tissue. The conditions in Reptiles and Mammals, as well as the differences in the number of visceral arches, to be mentioned directly, express separate stages in the process of regressive metamorphosis, to which the whole visceral apparatus in the vertebrate series has been subjected.

The number of visceral clefts which actually appear in the separate classes of Vertebrates is variable. The greatest number is encountered among the Selachians, where there may be as many as six (fig. 155), in a few species indeed seven or eight. In Teleosts, Amphibia, and Reptiles the number sinks to five. In Birds, Mammals, and Man (figs. 154 and 157) only four arise. *We can therefore say in general that from the lower to the higher Vertebrates a reduction has taken place in the number of visceral clefts which* *make their appearance.* In view of these phenomena, and guided by other comparative-anatomical considerations, many investigators have advanced the hypothesis that in the case of the ancestors of Vertebrates the fore gut has been pierced by a greater number of clefts than is now to be observed even in the Selachians, and further that *degraded or metamorphosed remnants* of them are still to be found in the head- and neck-regions.

VAN BEMMELEN has observed in embryos of various Sharks and Skates out-pocketings of the lateral wall of the throat behind the last visceral arch, and has interpreted them as rudimentary visceral clefts, which no longer succeed in breaking through (fig. 155 *nsd*). Subsequently there are developed out of them, by growth of the epithelium, glandular organs, the supra-pericardial bodies (BEMMELEN), which are similar in their structure to the thyroid gland. Also in the head-region, which lies in front of the first visceral arch, a reduction and a metamorphosis of clefts has, according to the opinion of various observers, taken place. DOHRN especially has propounded several hypotheses of this kind, for which, however, I do not find valid grounds: (1) that the mouth has arisen by the fusion of a pair of visceral clefts, (2) that the olfactory organs are to be referred to the metamorphosis of another pair of clefts, —a view which is also shared by M. MARSHALL and several others,—(3) that a disappearance of gill-clefts in the region of the sockets of the eye is to be assumed, and that the eye-muscles are to be interpreted as remnants of gill-muscles.

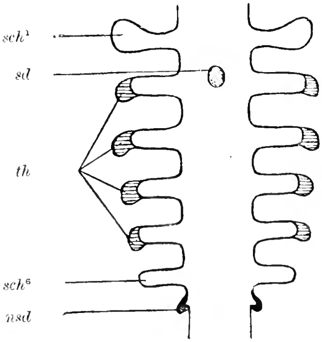

Fig. 155.—Diagram of the development of the thymus, the thyroid gland, and the accessory thyroid glands, and their relations to the visceral pockets in an embryo Shark, after DE MEURON. *sch*¹, *sch*⁶, First and sixth visceral pockets; *th*, fundament of the thymus; *sd*, thyroid gland; *nsd*, accessory thyroid gland.

In the Chick the visceral furrows become visible in the course of the third day of incubation, only three pairs at first, but, at the end of the same day, a fourth pair is added.

In human embryos the visceral furrows are to be seen most distinctly (figs. 157, 154) when the embryo has attained a length of three or four millimetres (HIS). Outer and inner furrows are in this case deeply excavated and separated from each other by only a thin epithelial closing plate; they diminish in length from before backward. Of the visceral arches which separate them, the first is the largest, the last the smallest; seen in frontal section they form two rows converging below, so that the oro-pharyngeal cavity tapers funnel-like into the intestinal tube.

From the fourth week of development onward the visceral arches begin to be displaced in relation to one another, owing to a more rapid growth of the first two than of the following ones (fig. 156). "They glide over one another," as His remarks, "like the tubes of a telescope, in such a way that, viewed from the outside, first the fourth arch is surrounded and covered in by the third, and this in turn by the second, whereas on the inner surface, that which is turned toward the pharynx, the fourth arch lies over the third, the third over the second." As a result the length of the oro-pharyngeal cavity is relatively less in the older than in the younger embryos. In consequence of this unequal growth, which moreover takes place in an entirely similar way in the embryos of Birds and Mammals, there is formed a deep depression of the surface at the posterior margin of the cephalo-cervical region, the *neck-sinus, sinus cervicalis* (Rabl) or *sinus præcervicalis* (His) (figs. 156 and 158 *hb*). In the depths of this depression and on its front wall lie the third and fourth visceral arches, which are now no longer visible from without. The entrance to the sinus is bounded in front by the second visceral, or the hyoid, arch (*zb*). The latter gradually develops a small process backward, which covers over the cervical sinus and has been justly compared by Rathke with the operculum of Fishes and Amphibia. *The opercular process at last fuses with the lateral wall of the body. Thereby the sinus cervicalis, which corresponds to the cavity beneath the operculum which in Fishes and Amphibia covers in the real gill-arches, is closed up.*

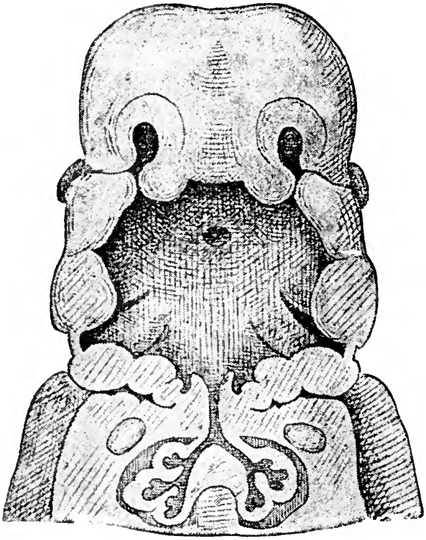

Fig. 156.—Frontal reconstruction of the oro-pharyngeal cavity of a human embryo (*Rg* of His) 11·5 mm. long, neck measurement. From His, "Menschliche Embryonen." Magnified 12 diameters.

The upper jaw is seen in perspective, the lower jaw in section. The last visceral arches are no longer visible externally, since they have moved into the depths of the cervical sinus.

One easily gets an accurate conception of these important processes of growth by comparing fig. 154 with fig. 156 and fig. 157 with fig. 158.

The development of the visceral clefts and the cervical sinus has also a practical interest. Sometimes there occur in the neck-region in Man fistulæ, which penetrate variable distances from without inward, and may even open into the pharyngeal cavity. They result from embryonic conditions, the cervical sinus having remained partly open. From this sinus a passage may lead, even in the adult, into the pharyngeal cavity, if abnormally the second visceral cleft has not closed.

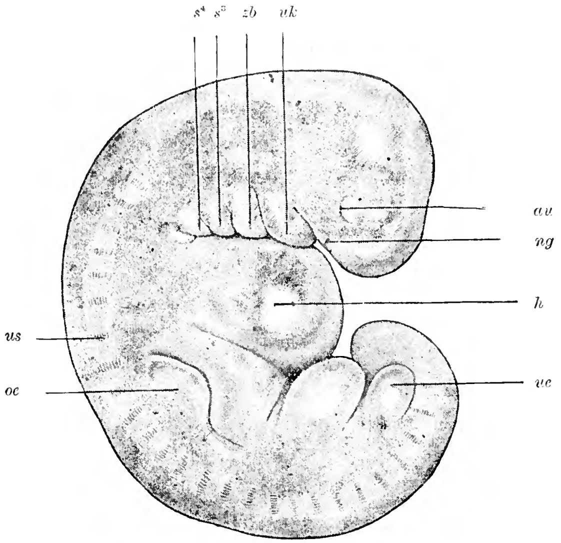

Fig. 157.—Very young human embryo of the fourth week 4 mm. long, neck-rump measurement; taken from the uterus of a suicide 8 hours after her death, after Rabl.

au, Eye; *ng*, nasal pit; *uk*, lower jaw; *zb*, hyoid arch; s^3, s^4, third and fourth visceral arches; *h*, protrusion of the wall of the trunk produced by the growth of the heart; *us*, boundary between two primitive segments; *oe*, *ue*, anterior and posterior limbs.

C. The Development of the Anus and the Post-anal Gut.

The question concerning the fate of the primitive mouth [blastopore] and the development of the anus is not yet settled. Many disclosures are still to be expected from a comparative study of these structures in the different classes of Vertebrates. According to the common representation, which appears to me to correspond on the whole with the real state of affairs, the primitive mouth is a transitory structure without permanent existence. In all Vertebrates it is surrounded, as in Amphioxus, by the growth of the medullary folds, and when these are closed, it no longer leads directly to the outside, but into the posterior end of the neural tube. It has thereby become the familiar canalis neurentericus (fig. 159 *ne*). Neural tube and intestinal canal together form a U-shaped tube, at the bend of which the rudiment of the primitive mouth, or primitive groove, is to be sought.

The anus is a new structure. It arises on the ventral side of the body (fig. 159 *an*) at some distance in front of the place where the neural tube bends around into the intestine. Over a small area the entoderm and the epidermis here grow toward each other, and, by crowding aside the middle germ-layer, come into contact and form a thin septum, the anal membrane. Externally this place is characterised in many animals by a depression of the epidermis, the anal pit (fig. 159 *an*). The opening of the intestine to the outside takes place in most cases at a rather advanced stage of development by the rupture of the thin anal membrane, which consists of only two epithelial layers. The process is therefore similar to that by which the mouth is formed. In one important point, however, there exists a difference between the opening at the anterior and that at

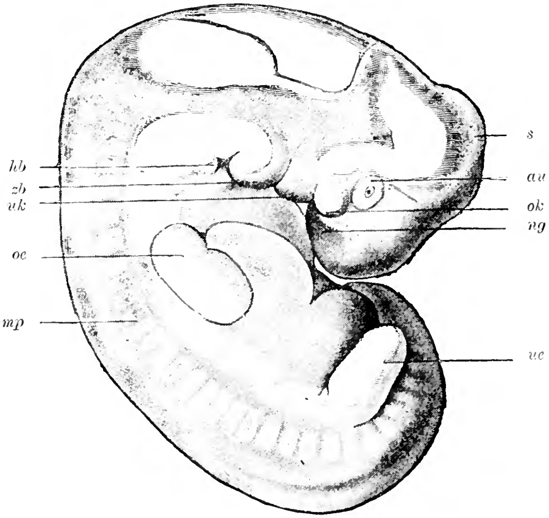

Fig. 158.- Human embryo of the middle of the fifth week 9 mm. long, neck-rump measurement, after Rabl.
s, Mid-brain [parietal] elevation ; *au*, eye ; *ok*, upper jaw ; *uk*, lower jaw ; *zb*, hyoid arch ; *hb*, sinus cervicalis ; *ng*, nasal pit ; *oe*, anterior, *ue*, posterior limb ; *mp*, muscle-plates (trunk-segments).

the posterior end of the body. Whereas the oral sinus comes in contact with the *anterior end* of the fore gut, the formation of the anus does not take place at the posterior end of the embryonic intestine, which is occupied by the primitive mouth [blastopore], but at some distance in front of it. (Compare also fig. 126, that of the Chick, in which the region where the anal pit is to be formed is designated by the letters *an*.) Consequently in the embryos of Vertebrates, when the anus has broken through, the embryonic intestinal tube is still continued for some distance back of the anus to the primitive mouth. This portion is designated as the *post-anal* or *caudal gut* (fig. 126 *p.a.g.*). The latter designation is appropriate, because the part of the body which lies behind the anus, in which is enclosed the part of the intestine under consideration, becomes the tail-end of the embryo.

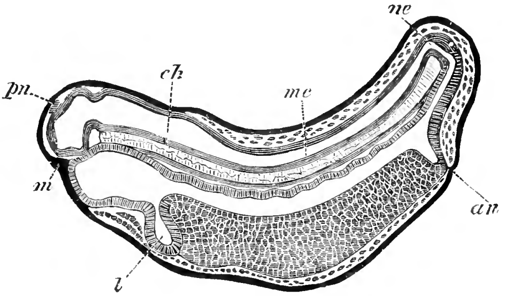

Fig. 159. — Sagittal section through an advanced embryo of Bombinator, after Goette.
m, Mouth ; *an*, anus ; *l*, liver ; *ne*, neurenteric canal ; *me*, medullary tube ; *ch*, chorda ; *pn*, pineal gland.

The post-anal gut appears to be established as a shorter or longer tract in all Vertebrates ; it has already been observed in the most widely different animals by several investigators : first by Kowalevsky in Amphioxus, the Acipenseridæ, Selachians, and Teleosts ; then by Goette, Bobretzky, Balfour, His, Kölliker, Gasser, Braun, Bonnet, and others in the Amphibia, Selachians, Birds (fig. 126 *p.a.g.*), and Mammals. In the Selachians (Scyllium) the post-anal section at the time of its greatest development attains about one-third the length of the whole alimentary canal. It exhibits at its end a small vesicular enlargement, which communicates with the neural tube by means of a narrow opening. In an advanced embryo of Bombinator it is also to be seen well developed, as shown in the sagittal section fig. 159. It begins at the place marked by *an*, at which the epidermis has sunk down to form the anal pit (*an*) and at which it has united with the intestine, immediately behind the mass of yolk-cells collected in the ventral wall of the latter. From this point it runs backward as a narrow but open tube, and bends around dorsally into the neural tube as the neurenteric canal. The primitive mouth, now closed, formerly lay at the place of bending.

The post-anal gut, sooner or later, undergoes regressive metamorphosis in all Vertebrates; it loses its cavity, becomes a solid epithelial cord, afterwards detaches itself from the anal part of the intestine and from the neural tube, and then disappears altogether. Thereby the neurenteric canal, the last remnant of the primitive mouth, has ceased to exist.

A few still more specific statements, in accordance with the representations of Strahl, Kölliker, Bonnet, Keibel, and Giacomini, concerning the formation of the anus in Mammals, may be mentioned in this connection. The first fundament of the anus is demonstrable even in embryos with few primitive segments. At the posterior end of the primitive streak—at the anterior end of which the neurenteric canal is situated—the anal membrane is formed by the disappearance of the middle germ-layer over a small area and the close contact of entoderm and epidermis. This, however, takes place so that the two latter layers always remain separated from each other by a sharp contour (fig. 160 *afm*). One might be inclined to regard this position, at the hindermost end of the primitive streak (*pr*), as deviating from the representation just given, according to which the anus arises on the ventral side of the body somewhat in front of the neurenteric canal. That is not the case, however, as the further course of development teaches; for in meroblastic eggs, in consequence

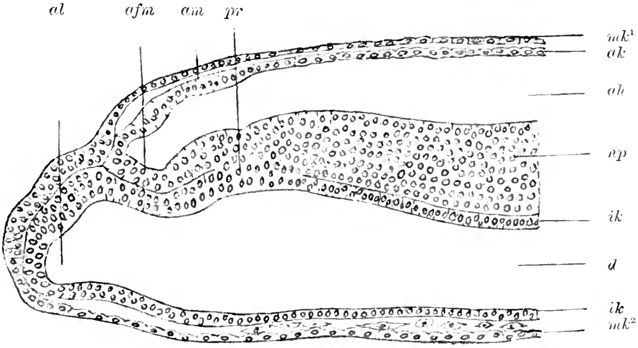

Fig. 160.—Sagittal section through the posterior end of an embryo Sheep 16 days old and with 5 pairs of primitive segments, after Bonnet.

al, Allantois; *afm*, anal membrane; *am*, amnion; *ah*, amniotic cavity; *ak*, outer germ-layer, and *mk*¹, middle germ-layer, which share in the formation of the amnion; *np*, neural plate as it merges into the primitive streak; *pr*, primitive groove in the region of the neurenteric canal; *ik*, inner germ-layer; *mk*², splanchnic portion of the middle germ-layer; *d*, alimentary tube.

of the previously described process of folding,—by means of which the body is formed from the flattened-out germ-layers,—the region which originally lies behind the primitive groove comes to lie ventral to and in front of the tail-end. At a somewhat later stage than that shown in fig. 160, the primitive streak in front of the anal membrane grows outward as a small ridge and subsequently enlarges into the tail of the Mammal. The neurenteric canal, located in the ridge, is overgrown by the medullary folds, and upon the complete closure of the latter is incorporated in the neural tube, as in the case of the remaining Vertebrates. In the case of Mammals also there is formed a small caudal gut, which subsequently degenerates. The more the caudal bud protrudes outward (fig. 161 *sch*), the more it projects over and beyond the anal membrane (*afm*), which constantly moves farther toward the ventral side of the body and is now found between the base of the tail (*sch*) and the fundament of the allantois (*al*). The rupture of the anal membrane takes place relatively late; in the case of Ruminants, for example, in embryos that are more than twenty-four days old.

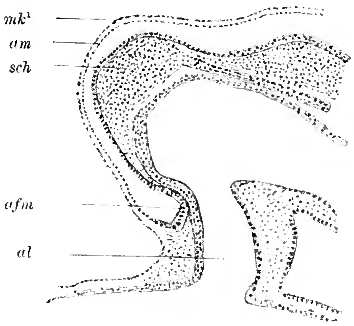

Fig. 161.—Sagittal section through the tail-end of an embryo Sheep 18 days old and with 23 pairs of primitive segments, after Bonnet.

sch, Tail-bud or terminal ridge; *am*, amnion; *mk*¹, its mesodermal (somatic) layer; *afm*, anal membrane lying ventral to and in front of the tail-bud; *al*, allantois.

Apparently the anus in Birds arises in a manner similar to that in Mammals. According to the statements of Gasser and Kölliker its opening, produced by the rupture of the anal membrane, occurs on the fifteenth day.

It is asserted for many Vertebrates (Petromyzon, Triton, Salamandra, Rana temporaria, Alytes) that the primitive mouth is converted directly into the anus (Gasser, Johnson, Sedgwick, Spencer, Kupffer, Goette). But since the development of the posterior part of the body proceeds from the margins of the primitive mouth (formation of the chorda and of the middle germ-layer), it would be difficult to understand how, in these cases, the tail-end of the body and a tail-gut could still be formed. Other investigators (Schanz and Bonnet) find that the primitive mouth is divided into two openings—an anterior, which is incorporated in the hind end of the neural canal (canalis neurentericus, chorda-blastopore), and a posterior, which becomes the anus (anal blastopore, anal canal). The statements, which are still contradictory, must be cleared up by means of comparative investigations.

II. Differentiation of the Alimentary Tube into Separate Regions and Formation of the Mesenteries.

At first the alimentary tube is broadly in contact (fig. 116) with the dorsal wall of the trunk; it is united to the chorda (*ch*), the neural tube, and the primitive segments by means of a broad tract of embryonic connective tissue, in which the fundaments of two large blood-vessels, the primitive aortæ (*ao*), are enclosed. The right and left portions of the body-cavity are therefore still separated from each other on the dorsal side by a considerable distance. The older the embryo is, the less this distance becomes, until there results a *mesentery*, a structure which is established along the whole length of the intestinal tube, with exception of the anterior portion, in the following manner (compare, Plate I., figs. 8 and 9 with fig. 10). The alimentary tube recedes from the chorda; at the same time the broad tract of connective tissue previously mentioned becomes narrower from right to left, but elongated dorso-ventrally (fig. 10, Plate I.); the two aortæ embraced in it move nearer and nearer together and finally fuse into a single trunk, which lies in the median plane between chorda and intestine. After the further advance of this process the alimentary tube and chorda remain united by means of only a thin band, which stretches from the front to the hind end of the embryo. This proceeds from the connective tissue enveloping the chorda, encloses along its line of origin the aorta, and is composed of three layers: a connective-tissue lamella, in which blood-vessels run to the intestine, and two epithelial coverings, which are derived from the middle germ-layer and are now composed of greatly flattened cells.

The differentiation of the alimentary tube into separate non-equivalent regions lying one behind the other begins with the development of the stomach. This first becomes distinguishable, at some distance behind the respiratory tract, as a small spindle-shaped enlargement, the long axis of which corresponds with that of the body (figs. 162 and 163 *Mg*). Such a condition is attained by the human embryo of the fourth week. Five successive regions may now be distinguished in the whole embryonic alimentary tube: the oral cavity, the throat-cavity with its visceral clefts, which is narrowed into the shape of a funnel where it merges into [the third region,] the gullet. This is followed by the spindle-shaped enlargement, the stomach, and the latter by the remaining portion of the alimentary tube, which still is more or less broadly connected (*Ds*) with the yolk-sac. Excepting the first three regions, the whole alimentary tube possesses a mesentery (mesenterium), the part which is attached to the stomach being designated by the special name *mesogastrium*.

In many Fishes and Amphibia this condition is permanent. Even in the adult the alimentary tube takes only a slightly sinuous course through the body-cavity. The stomach appears as a spindle-shaped enlargement of it.

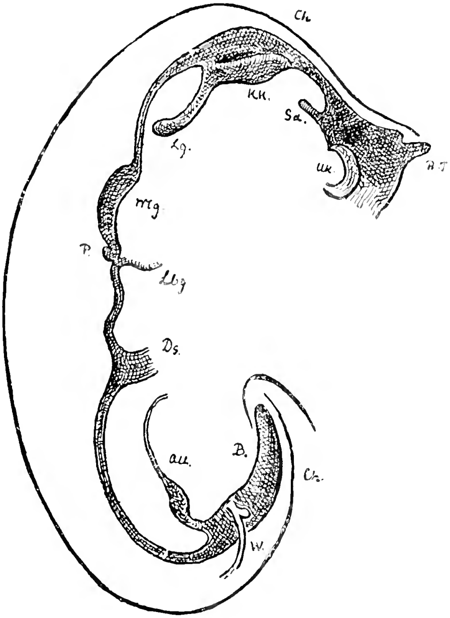

Fig. 162.

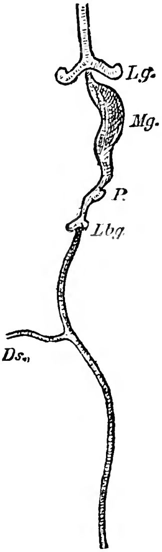

Fig. 163.

Fig. 162.—Alimentary tube of a human embryo (*R* of His) 5 mm. long, neck measurement. From His, "Menschliche Embryonen." Magnified 20 diameters.
RT, Rathke's pocket; *Uk*, lower jaw; *Sd*, thyroid gland; *Ch*, Chorda dorsalis; *Kk*, entrance to larynx; *Lg*, lung; *Mg*, stomach; *P*, pancreas; *Lbg*, hepatic duct; *Ds*, vitelline duct (stalk of the intestine); *All*, allantoic duct; *W*, Wolffian duct, with budding kidney-duct (ureter); *B*, bursa pelvis.

Fig. 163.—Alimentary tube of a human embryo (*Bl* of His) 4·25 mm. long, neck measurement. From His, "Menschliche Embryonen." Magnified 30 diameters.
The abbreviations mean the same as in fig. 162.

An alteration is brought about in all higher Vertebrates by a more or less considerable increase in the length of the tube, which eventually far exceeds that of the trunk. Consequently the alimentary tube, in order to find room for itself in the body-cavity, is compelled to take a tortuous course. In this way certain parts remain near the vertebral column, whereas others, as a result of the folding, are more distant. The former are attached by means of a narrow mesentery and are consequently less movable, the latter by their change in position have drawn out their suspensorial band into a thin lamella, which sometimes attains a remarkable breadth and allows a correspondingly increased freedom of motion.

The processes of development, which are in part very complicated, are satisfactorily explained by the excellent works of Meckel, Johannes Müller, Toldt, and His, even in the case of human embryos, so that these may serve as a foundation for the description.

In human embryos of the fifth and sixth weeks the posterior surface of the stomach, that which is turned toward the vertebral column (fig. 164 *gc*), is greatly distended; the anterior wall (*kc*) on the contrary, which upon opening the body-cavity is found to be covered by the already voluminous liver, is somewhat depressed. Consequently a line running along the posterior surface from the entrance of the stomach (cardia) to its outlet (pylorus) is much longer than the corresponding line along the anterior surface. The latter becomes the future lesser curvature (*kc*); the former, along which the mesogastrium is attached, is the greater curvature (*gc*).

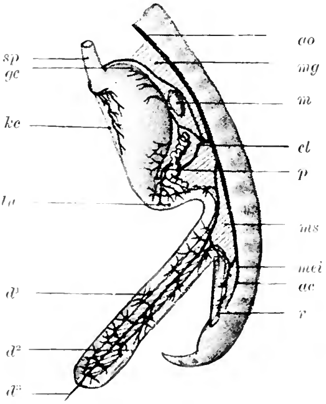

Fig. 164.—Diagrammatic representation of the alimentary canal of a six-weeks embryo of Man, after Toldt.

sp, Œsophagus; *kc*, lesser curvature; *gc*, greater curvature of the stomach; *du*, duodenum; d^1, part of the loop that will become the small intestine; d^2, part of the loop that will become the large intestine and begins with the cœcum; d^3, place of connection with the vitelline duct; *mg*, mesogastrium; *ms*, mesenterium; *m*, spleen; *p*, pancreas; *r*, rectum; *ao*, aorta; *cl*, cœliaca; *mei*, mesenterica inferior; *ac*, aorta caudalis.

The portion of the tube which follows the stomach has become folded, in consequence of its great increase in length. From the pylorus the intestinal tube (*du*) at first runs backward [dorsad] for a short distance until it is close to the vertebral column, makes a sharp bend here, and then describes a large loop, the convexity of which is directed forward [ventrad] and downward [caudad] toward the navel. The loop consists of two nearly parallel arms (d^1 and d^2)

running near each other, between which is stretched the mesentery (*ms*), which is likewise drawn out with the loop. One arm (d^1) lies in front and is directed backward, the other (d^2) lies behind it and runs upward, to be again bent near the vertebral column; thence, supported by a narrow mesentery, it pursues a straight course (r) backward to the anus. The transition from the first to the second arm, or the apex of the loop, is imbedded in an excavation in the fœtal end of the umbilical cord, and it is there in communication with the umbilical vesicle by means of the vitelline duct (d^3), now in process of degeneration. At some distance from the origin of the vitelline duct there is to be seen in the second arm of the loop a small enlargement and evagination (d^2). This is afterwards developed into the cœcum, and it therefore indicates the important boundary between the small and large intestine.

In consequence of these first foldings four regions of the intestine can be distinguished even now; these are more sharply separated later. The short portion, running from the stomach to the backbone and provided with a small mesentery, becomes the duodenum (*du*); the anterior [ventral], descending arm (d^1), together with the bend in the loop, furnishes the small intestine; the posterior [dorsal], ascending arm is developed into the colon (d^2), and the terminal part, embracing the last bend, into the sigmoid flexure and the rectum (r).

In embryos of the third and following months there occur, in connection with a further increase in length, important changes in the position of the stomach and the intestinal loops.

The stomach undergoes a double twisting, about two different axes, and thereby early acquires a form and position (figs. 165 *A* and *B*) which correspond approximately to the permanent condition. First its longitudinal axis, which unites cardia and pylorus and is in the beginning parallel with the vertebral column, takes an oblique and finally an almost transverse position, in consequence of a rotation around the dorso-ventral axis. Thereby the cardia moves to the left half of the body and downwards, but the pylorus more to the right side and somewhat higher. Secondly, at the same time the stomach experiences a torsion around its longitudinal axis, by which the originally left side becomes the front [ventral] and the right the back [dorsal]. Consequently the greater curvature comes to lie below [posterior], the lesser above [anterior]. The terminal part of the œsophagus is also affected by the torsion; it undergoes a spiral twisting, by which its left side becomes the front.

The embryonic processes of growth in the case of the alimentary tube shed light on the asymmetrical position of the two nervi vagi, which pass through the diaphragm, the left on the front side of the œsophagus to be distributed to the front side of the stomach, the right on the back side of the œsophagus to the corresponding surface of the stomach. If we imagine the process of torsion in case of the œsophagus and stomach to be reversed, the symmetry in the course and distribution of the vagi will be completely restored.

The torsion of the stomach naturally exercises a great influence on the mesogastrium, and, as Joh. Müller was the first to show clearly, initiates the development of the *greater omentum* (omentum majus). As long as the stomach has a vertical position, its mesentery is a vertical lamella, which stretches from the vertebral column (fig. 164) directly to the greater curvature, that is still directed backward [dorsad]. But in consequence of the torsion it becomes greatly stretched and enlarged, because its attachment to the stomach must follow all the displacements of that organ. From its origin at the vertebral column, it therefore now betakes itself to the left and downward to become attached to the greater curvature of the stomach; it assumes a shape and position of which the reader will easily form a correct idea if he mentally combines the diagram of

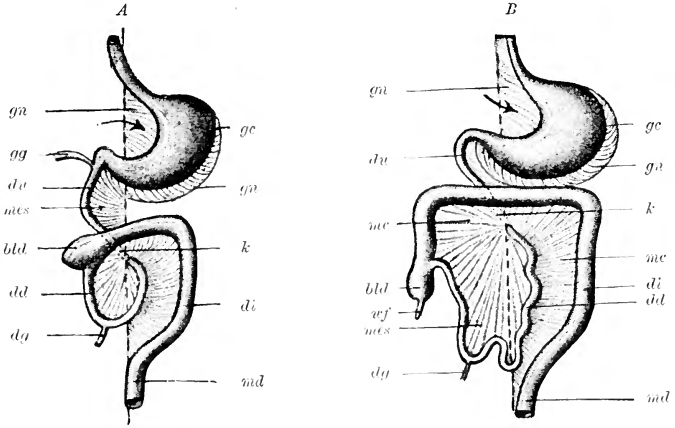

Fig. 165.—Diagram of the development of the human alimentary canal and its mesentery. *A*, earlier, *B*, later stage.

gn, Greater omentum, which is developed from the mesogastrium (fig. 164 *mg*). The arrow indicates the entrance to the omentum (bursa omentalis). *gc*, Greater curvature of the stomach; *gg*, ductus choledochus; *du*, duodenum; *mes*, mesenterium; *mc*, mesocolon; *dd*, small intestine; *di*, large intestine (colon); *md*, rectum; *dg*, vitelline duct; *bld*, cœcum; *wf*, appendix vermiformis; *k*, place where the loops of the intestine cross each other. The colon with its mesocolon crosses the duodenum.

fig. 165 with the cross section shown in fig. 166. In this way there is formed a cavity (*bursa omentalis*, fig. 166 **), separated from the rest of the body-cavity, which has its opening turned toward the right, whose front wall is formed by the stomach and whose back and lower wall is formed by the mesogastrium (gn^1, gn^2). In the diagrammatic figures 165 *A* and *B* the entrance to the bursa is indicated by the direction of the arrows.

The bursa omentalis (fig. 166 **) moreover acquires a still greater extension from the fact that the liver (*l*) has by this time grown into a large gland, and is united to the lesser curvature of the stomach by means of the lesser omentum (*kn*), the development of which we shall treat of later. Therefore the bursa does not open, as in the diagram (fig. 165), in which the liver with its ligaments is omitted, at once into the common body-cavity at the lesser curvature of the stomach, but first into an *ante-chamber* (the *atrium bursæ omentalis*), or the *lesser omental pocket*, which lies behind the lesser omentum (*kn*) and the liver (*l*).

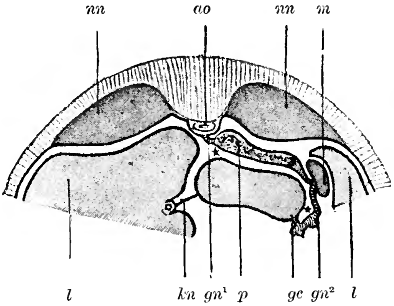

Fig. 166.—Diagrammatic cross section through the trunk of a human embryo in the region of the stomach and mesogastrium, to show the formation of the omentum, at the beginning of the third month, after Toldt.

nn, Suprarenal bodies ; *ao*, aorta ; *l*, liver ; *m*, spleen ; *p*, pancreas ; gn^1, origin of the greater omentum (mesogastrium) at the vertebral column ; gn^2, the part of the mesogastrium which is attached to the greater curvature (*gc*) of the stomach ; *kn*, lesser omentum ; *gc*, greater curvature of the stomach. * Atrium and cavity of the greater omentum.

The intestinal loop with its mesentery passes through a no less fundamental twisting around its place of attachment in the lumbar region than the stomach does. The descending and the ascending arms at first lie side by side. Then the latter, which becomes the colon (fig. 165), lays itself obliquely *over* [ventral to] the former, and *crosses the beginning of the small intestine* (*k*) *transversely.* Both parts, but especially the small intestine, continue from the end of the second month to increase rapidly in length and to take on a folded condition. Meanwhile the initial part of the colon, or the cœcum (fig. 165 *A bld*), which exhibits even in the third month a curved, sickle-shaped, vermiform appendage, comes to lie wholly on the right side of the body up under the liver; from here it runs in a transverse direction across [ventral to] the duodenum under [caudad of] the stomach to the region of the spleen, then bends sharply about (flexura coli lienalis) and descends to the left pelvic region, where it is continued into the sigmoid flexure and rectum. Therefore there are distinguishable in the colon, even in the third month, the cœcum, the transverse and the descending colon. An ascending colon is still wanting. It is formed in the succeeding months (fig. 165 *B*) by the gradual sinking down of the cœcum, which was at first under the liver, until in the seventh month it is below the right kidney, and from the eighth month onward descends past the crest of the ilium.

Meanwhile the *cœcum* has increased in length and toward the end of pregnancy is a rather large appendage at the place of transition from the small to the large intestine. It early exhibits a want of uniformity in development (fig. 165 *B bld*). The terminal part, which often embraces more than half its length, does not keep pace in its growth with the more rapidly enlarging proximal portion; the former is designated as the *appendix vermiformis*, the latter as the *cœcum*. At the time of birth the vermiform appendage is still not so sharply differentiated from the cœcum as it is a few years later, when it has been converted into an appendage of the size of a goose-quill and 6 to 8 cm. long.

Within the region embraced by the bends of the large intestine, the small intestine, which is derived from the descending arm of the loop, is disposed in more and more numerous folds owing to its extensive growth in length (fig. 165 *B*).

At first all regions of the intestine from the stomach onward are so united to the lumbar region of the vertebral column by means of a *common mesentery* (mesenterium commune) that they can move freely (fig. 165 *A* and *B*). The mesentery is naturally influenced by the increase in the length of the intestine, inasmuch as its line of insertion on the intestine exceeds in length many times the line of origin at the vertebral column (radix mesenterii), and is thereby laid into folds like a frill. Such an arrangement of the mesentery is found to be the permanent condition in many Mammals, as in the Dog, the Cat, etc.

But in the case of Man, from the fourth month onward, the arrangement of the mesentery is much more complicated. There occur changes which may be briefly characterised as *processes of fusion and concrescence of certain portions of the mesenterial lamella with contiguous parts of the peritoneum*, either of the posterior wall of the body-cavity, or of neighboring organs. They affect the mesentery of the duodenum and colon, which is always present in the first half of embryonic development.

The *duodenum*, describing the well-known horseshoe-shaped curve, applies its mesentery, in which the beginning of the pancreas is enclosed, broadly to the posterior wall of the body, and fuses throughout its whole extent with the peritoneum of the latter; from being a movable it has become an immovable portion of the intestine (fig. 167 *du*).

The *large intestine* (figs. 165 and 167 *A* and *B ct*) still possesses in the third month a very broad suspensorium arising from the vertebral column, which is nothing else than a part of the common mesentery of the intestine, but which has received the special designation of *mesocolon* (*msc*). In consequence of the previously described twisting of the primitive loop of the intestine, not only the colon transversum, but also the considerable mesocolon belonging to it, has been drawn transversely across the end of the duodenum; for a certain distance it fuses with the latter and with the posterior wall of the body, thereby acquires a new secondary line of attachment (fig. 167 *msc*) running from right to left, and thus appears as a part that has become detached from the common mesentery. The colon transversum (*ct*) with its mesocolon (*msc*) now divides the body-cavity into an

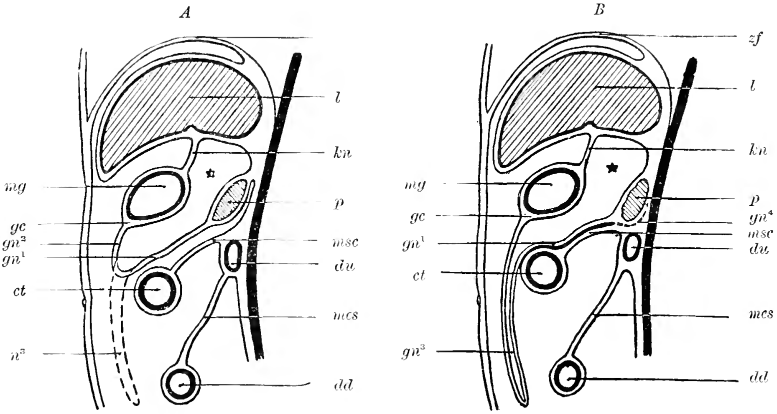

Fig. 167 A B.—Two diagrams to illustrate the development of the bursa omentalis. *A*, earlier, *B*, later stage.

zf, Diaphragm; *l*, liver; *p*, pancreas; *mg*, stomach; *gc*, its greater curvature; *du*, duodenum; *dd*, small intestine; *ct*, colon transversum; *, bursa omentalis; *kn*, lesser omentum; *gn*¹, posterior [dorsal] lamella of the greater omentum, arising from the vertebral column; *gn*², anterior [ventral] lamella of the same, attached to the greater curvature of the stomach (*gc*); *gn*³, the part of the omentum which has grown over the small intestine; *gn*⁴, the part of the omentum which encloses the pancreas; *mes*, mesentery of the small intestine *msc*, mesocolon of the transverse colon.

upper [anterior] part, which contains the stomach, liver, duodenum, and pancreas, and a lower part, holding the small intestine.

Thus embryology explains the striking condition of the duodenum, which, in order to pass from the upper to the lower space and to become continuous with the small intestine, passes underneath [dorsal to] the transversely outstretched mesocolon (figs. 165 and 167 *du*).

Also in the case of the suspensorium of the cœcum, and of the ascending and descending arms of the colon, there occurs a more or less extensive concrescence with the peritoneum of the wall of the trunk. Therefore in the adult the parts of the intestine named sometimes lie with their posterior wall broadly in contact with the body-wall; sometimes they are supported by a broader or narrower mesentery.

There still remain to be described the important changes of the *bursa omentalis*, the development of which during the first months of embryonic life we have already (p. 299) become acquainted with. The bursa is distinguished, first, by a very considerable growth, and, secondly, by the fact that it fuses with neighboring organs at various places. In the beginning it reaches only to the greater curvature of the stomach (figs. 165, 166), to which it is attached; but even from the third month onward it enlarges and lays itself over [ventral to] the viscera which lie below the stomach, at first over the transverse colon (fig. 167 *A* gn^1, gn^2), then over the whole of the small intestine (fig. 167 *A* gn^3). The bursa consists, as far as it has extended downwards, of two lamellæ, which lie close to each other, separated by only a very narrow space, and are continuous at their lower margin. Of these the more superficial, the one which is nearer to the ventral wall of the belly, is attached to the greater curvature of the stomach (*gc*); the posterior [dorsal] lamella, which lies upon the intestines, is originally attached to the vertebral column and here encloses the main part of the pancreas (figs. 167 *A* *p* and 166 *p*). In the case of many Mammals (Dog) the bursa omentalis remains in this condition. In Man it begins as early as the fourth month to undergo fusions (fig. 167 *B*). On the left side of the body the posterior lamella reposes on the posterior wall of the body over a large extent of surface, and fuses with it (gn^4), so that its line of attachment to the vertebral column moves laterad up to the origin of the diaphragm (lig. phrenico-lienale). Farther down it glides over the upper [anterior] surface of the mesocolon (*msc*) and over the transverse colon (*ct*); it becomes fused with both of them, with the former as early as the fourth embryonic month. At the time of birth the two lamellæ of the portion of the bursa which has grown over the intestines are, as in many Mammals, separated by a narrow fissure (fig. 167 *B* gn^3); during the first and second years after birth they ordinarily fuse into a single lamella in which fat is deposited.

III. Development of the Separate Organs of the Alimentary Tube.

The simple growth in length, to which is to be referred the formation of the convolutions just described, is only *one* and certainly not the chief means by which the inner surface of the intestine is increased. The latter acquires a much greater addition from the fact that the inner, originally smooth epithelial layer, which is derived from the entoblast of the germ, forms evaginations and invaginations. By invaginations toward the cavity of the intestine there arise numerous folds, small papillæ and villi, which give to the mucous membrane at most places a velvety structure; by evaginations toward the outer surface of the tube there are developed various kinds of larger and smaller glands.

By this simple device, the formation of folds,—the great importance of which in the determination of form in animals was particularly set forth in Chapter IV. of Part I.,—the mucous membrane acquires to a much greater extent the ability: (1) to secrete digestive fluids, and (2) to absorb the nutritive substances that are mechanically and chemically prepared in the intestine, and to transfer them into the body-fluids.

I discuss the numerous organs which are produced by the process of folding according to the regions into which the intestinal tube is divided, beginning with the organs of the oral cavity.

A. The Organs of the Oral Cavity: Tongue, Salivary Glands, and Teeth.

(1) The **Tongue** arises, according to the investigations of His upon human embryos, out of an *anterior* and a *posterior fundament* (fig. 168).

The *anterior fundament* appears very early as an *unpaired* elevation (tuberculum impar, His) on the floor of the oral cavity in the space surrounded by the mandibular ridges. It grows a good deal in width, and its anterior margin projects free over the mandible, thus forming the body and tip of the tongue. Even as early as the beginning of the third month some papillæ make their appearance on it (His, Kölliker).

The *posterior fundament* produces the root of the tongue, which, although free from papillæ, is richly provided with follicular glands. It is developed out of two ridges in the region where the second and third visceral arches come together in the median plane. The anterior and posterior fundaments unite in a V-shaped furrow, the arms of which diverge in front. The circumvallate papillæ are formed on the body of the tongue along this furrow, which persists for a long time. Where the two arms of the V meet there is a deep pit, the foramen cœcum, which His has brought into connection with the origin of the thyroid glands, which will soon be discussed.

(2) The **Salivary Glands** are demonstrable even in the second month. The fundament of the submaxillary appears first in human embryos at the sixth week (Chievitz), afterwards the parotid in the eighth week, and finally the sublingual.

(3) From a morphological point of view, the **Teeth** can well be designated as the most interesting structures of the oral cavity. Their development in Man and Mammals is accomplished in a manner which is neither simple nor easily intelligible; in the lower Vertebrates, on the contrary, it is simpler, and for that reason I shall make use of the latter as the starting-point of the description.

Fig. 168.—Tongue of a human embryo about 20 mm. long, neck measurement. After His, "Menschliche Embryonen."

The teeth, which in Mammals are attached to the edges of the jaws and only bound the entrance to the alimentary tube, possess in the lower Vertebrates a very wide distribution. For in many species they not only cover the roof and the floor of the oral cavity and the inner surface of the branchial arches in immense numbers, as palatal, lingual, and pharyngeal teeth, but they are also distributed in close-set rows over the whole surface of the skin, and produce, as in the Selachians, a strong and at the same time flexible coat of mail.

The *teeth are originally nothing else than ossified papillæ of the skin and the mucous membrane*, upon the contiguous surfaces of which they are formed. The *development of the dermal teeth* in Selachians shows this in a very convincing manner.

In young Shark embryos, by a proliferation on the part of the subepithelial cells, there are developed on the otherwise smooth surface of the dermis, which comes from the embryonic mesenchyme, small papillæ composed of numerous cells (fig. 169 *zp*), and these penetrate into the thick overlying epidermis. The latter also undergoes changes on its part, which are directed toward the formation of the tooth; for those of its cells which immediately cover the papilla grow out into very long cylindrical forms, and produce an organ the function of which is to secrete enamel, the so-called *enamel-membrane* (fig. 169 *sm*). By means of further growth the whole fundament next assumes a form which corresponds to the future hard structure (fig. 170).

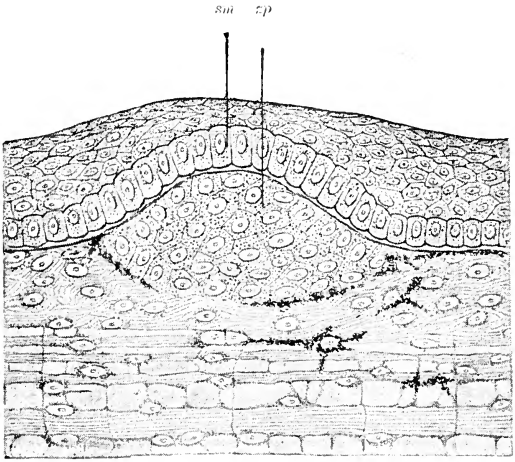

Fig. 169.—Very young fundament of a dermal tooth (a placoid scale) of a Selachian embryo. *zp*, Dental papilla; *sm*, enamel-membrane.

Then the process of ossification begins. There is secreted by the most superficial cells of the papilla (*o*), the *odontoblast-layer* (membrana eboris), a thin layer of dentine (*zb*), which rests upon the papilla like a cap. At the same time the enamel-membrane (*sm*) begins its secretive activity, and coats the outer surface of the dentinal cap (*zb*) with a firm, thin layer of *enamel* (*s*). The body of the tooth is developed and becomes ever firmer and larger by the subsequent continual deposition of new layers on the first-formed ones,—on the dentinal cap new dentine from within through the activity of the odontoblasts; on the coating of enamel new layers of enamel from without, through the action of the enamel-membrane. Thus the structure projects more and more above the level of the skin, and the tip of the tooth finally breaks through the epidermal covering. The tooth then acquires a still firmer attachment in the dermis from the fact that, at the surface where the lower margin of the dentine occurs, salts of lime are deposited in the superficial layers of the connective tissue (lh^2), and thus a kind of connective-tissue bone, the *cementum of the tooth*, is produced.

The finished tooth therefore is constructed out of three calcified tissues, which arise from three separate fundaments. *The dentine takes its origin from the odontoblast-layer of the dental papilla (mesenchyme), the enamel from the epithelial enamel-membrane (outer germ-layer), and the cementum from connective tissue in the vicinity by means of direct ossification.* The finished tooth has, moreover, within it a cavity, which is filled with a vascular connective tissue (*pulp*), the remnant of the papilla. When the enamel-membrane has fulfilled its office it perishes, for in the process of secretion its cells become shorter and shorter, and are finally reduced to flat scales, which are afterwards thrown off.

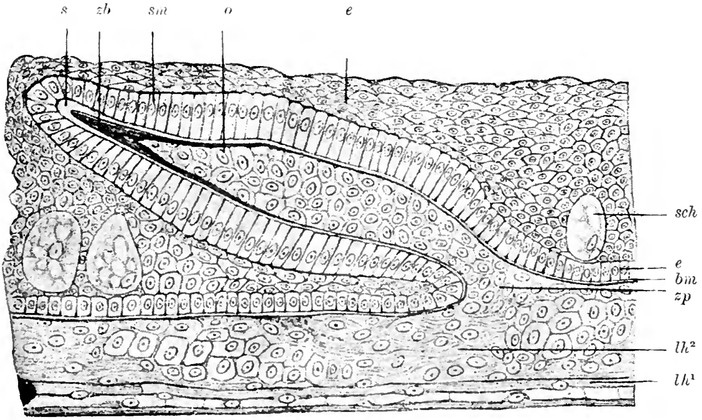

Fig. 170.—Longitudinal section through an older fundament of a dermal tooth of a Selachian embryo.

e, Epidermis; e^1, the deepest layer of epidermal cells, which are cubical; *sch*, mucous cells; lh^1, the part of the dermis which is composed of connective-tissue lamellæ; lh^2, superficial layer of the dermis; *zp*, dental papilla; *o*, odontoblasts; *zb*, dentine; *s*, enamel; *sm*, enamel-membrane.

In Selachians the formation of the teeth which occupy the edges of the jaws and serve for the comminution of the food differs from this simple process in one important point; they take their origin, not on the free surface of the mucous membrane, but in its depths (fig. 171). *The epithelial tract of the oral mucous membrane* *which shares in the formation of teeth has sunk deep down in the form of a ridge (zl) on the inner surface of the jaw-arches, into the underlying loose connective tissue, and now represents a special organ, distinguishable from its surroundings.* This important difference is produced by the fact that in the development of the teeth of the jaws more active processes of growth take place, first because these teeth are much larger than the dermal teeth, and, secondly, because they are more rapidly worn out and must consequently be more rapidly replaced by supplementary teeth. As we have often had the opportunity of observing in the study of the production of morphological conditions in animals generally, portions of epithelial membranes that grow more rapidly than their surroundings emerge from the latter and become folded either outward or inward.

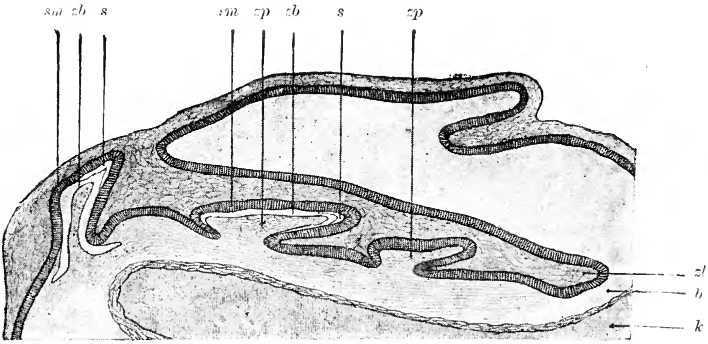

Fig. 171.—Cross section through the lower jaw of a Selachian embryo with fundaments of teeth. *k*, Mandibular cartilage ; *zl*, dental ridge ; *zp*, dental papilla ; *zb*, dentine ; *s*, enamel ; *sm*, enamel-membrane ; *b*, connective-tissue part of the mucous membrane.

The process of the formation of teeth is the same on the dental ridge itself as upon the free surface of the skin. There are developed on its outer side, which is turned toward the cartilage of the jaw (*k*), numerous papillæ (*zp*), lying alongside of and behind one another, which grow into the invaginated epithelium just as the dermal papillæ grow into the epidermis. Thus there arise in the depths of the mucous membrane several rows of teeth, of which the most superficial anticipate in development those which lie deeper ; the former are the first to break through the mucous membrane, to become functional, and, after having been worn out, to be cast off ; they are also the first to be supplanted by reserve teeth, which lie behind them, and, developing somewhat later, are consequently younger.

Whereas in the Selachians, as well as in the lower Vertebrates generally, *the replacement of teeth by new ones* is throughout life an *unlimited* process, since new papillæ are continually being formed in the depths of the dental ridge (polyphyodont), it is in the higher Vertebrates more limited, and in most Mammals occurs *only once. There are formed on the ridge two fundaments* (diphyodont), *one behind the other, one for the milk-teeth and a second for the permanent teeth.*

In the case of Man the development of the teeth begins as early as the second month of embryonic life. A ridge (*zl*) (the *enamel-germ* of older authors) grows from the epithelium of the oral cavity both on the maxillary and mandibular arches—as it also does in other mammalian embryos (fig. 290)—into the richly cellular embryonic connective tissue. The region from which this growth into the depths takes place (fig. 172 *A* and *B*) is marked exteriorly by a groove, which runs parallel to the arch of the jaw, the so-called *dental groove* (*zf*). The head of the human embryo represented in figure 289 shows this groove at a little distance behind the fundament of the upper lip.

At first the dental ridge is uniformly thin and separated from its surroundings by a smooth surface. There is nothing to be seen as yet of the separate fundaments of the teeth. Then the epithelial cells on the side of the ridge which is directed outwards begin at certain places to grow and to produce at regular intervals from one another as many thickenings as there are to be teeth (fig. 172 *A*). In Man, who has twenty milk-teeth, the number of these is ten in each jaw. The thickenings now assume a flask-shaped form (fig. 172 *B*), and gradually detach themselves from the outer surface of the epithelial ridge (*zl*), except at the neck of the flask, which remains in connection with it at a little distance from its deep edge. Because these epithelial growths have relation to the secretion of enamel, they have received the name of *enamel-organs.*

In the meantime the connective tissue has taken its first steps toward the formation of the tooth (fig. 172 *A* and *B*). At the bottom of each flask the connective-tissue cells exhibit active growth, and give rise to a papilla (*zp*) corresponding in form to the future tooth. As the papillæ of the dermal teeth grow into the epidermis, so this papilla grows into the enamel-organ, which is thereby made to take the form of a cap.

Then the special layers from which the formation of dentine and enamel proceed are differentiated in both fundaments so far as these are in mutual contact. At the surface of the papilla (fig. 172 *B sp*) the cells assume spindle-shaped forms and group themselves into a kind of epithelial layer, the layer of the dentine-forming cells (membrana eboris). On the part of the cap-like enamel-organ the cells of the deepest layer, which is in immediate contact with the papilla, are converted into very long cylinders and constitute the enamel-membrane (*sm*, membrana adamantinæ). The latter becomes gradually thinner toward the base of the papilla, where it is continued as a layer of more cubical elements (*se*), which forms the boundary at the surface of the cap separating it from the surrounding connective tissue. Between these two cell-layers (the inner and the outer epithelium of Kölliker) the remaining epithelial cells of the enamel-organ undergo a peculiar metamorphosis, and produce a kind of gelatinous tissue, the *enamel-pulp* (*sp*) ; they secrete between them a fluid rich in mucus and albumen, and become themselves converted into stellate cells, which are united to one another by their processes, and thus form a fine network. The enamel-pulp is most highly developed in the fifth or sixth month, and then diminishes up to the time of birth in the same ratio as the teeth increase in size.

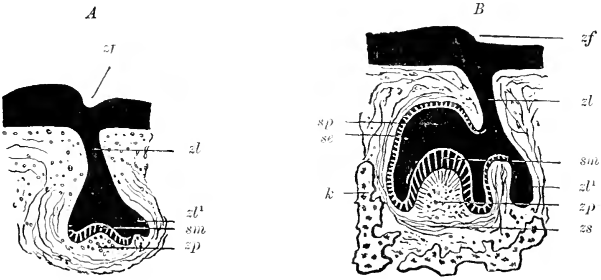

Fig. 172 A B.—Two stages in the development of the teeth of Mammals. Diagrammatic sections. *zf*, Dental groove ; *zl*, dental ridge ; zl^1, deepest part of the dental ridge, on which are formed the fundaments of the supplementary teeth ; *zp*, dental papilla ; *sm*, enamel-membrane ; *sp*, enamel-pulp ; *se*, outer epithelium of the enamel-organ ; *zs*, dental sac ; *k*, bony alveolus.

The connective tissue immediately enveloping the whole fundament acquires numerous blood-vessels, from which branches also make their way into the papilla ; it becomes somewhat differentiated from the surrounding tissue, and is distinguished as *dental sac* (fig. 172 *B zs*).

The soft fundaments of the teeth enlarge up to the fifth month of embryonic life, and at the same time acquire the particular forms of the teeth which are to arise from them—those of the incisors, the canines, and molars. Then the process of ossification begins (fig. 173) in the same manner as in the dermal teeth. A cap of dentine (*zb*) is formed by the odontoblasts (*o*), or dentinal cells; this cap at the same time acquires a coating of enamel (*s*) from the enamel-membrane (*sm*); then there are continually deposited on the first layers new ones, until the crown of the tooth is completed. Under pressure of the latter the enamel-pulp (*sp*) atrophies, and forms only a thin covering to the tooth at birth. The papilla (*zp*) is converted into a mass of connective tissue containing blood-vessels (*g*) and nerves, and fills the cavity of the tooth as the so-called pulp. The larger the whole structure becomes, the more it raises up the tissue of the gum, which covers the edge of the jaw, and causes it to become gradually thinner. Finally, it breaks through the gum soon after birth, and at the same time casts off from its surface the atrophied remnant of the enamel-organ.

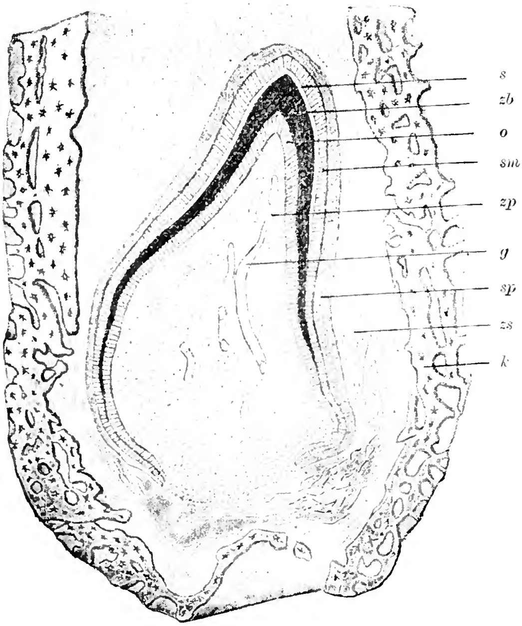

Fig. 173.—Section through the fundament of the tooth of a young Dog.

k, Bony alveolus of the tooth; *zp*, dental papilla; *g*, blood-vessel; *o*, odontoblast-layer (membrana eboris); *zb*, dentine; *s*, enamel; *sm*, enamel-membrane; *zs*, dental sac; *sp*, enamel-pulp.

The time has now come in which the third hard substance of the tooth is formed, the *cementum* that envelops the root. So far as the dentine has received no coating of enamel, the bounding connective tissue of the dental sac (*zs*) begins, after the eruption of the teeth, to ossify and to produce a genuine bone-tissue with numerous Sharpey's fibres; this bony tissue contributes to the firmer union of the root of the tooth with its connective-tissue surroundings.

The *eruption of the teeth* ordinarily takes place with a certain degree of uniformity in the second half of the first year after birth. First the inner incisors of the lower jaw break through in the sixth to the eighth months; then in the course of a few weeks those of the upper jaw follow. The outer [lateral] incisors appear during the period between the seventh and ninth months, those of the lower jaw, again, somewhat earlier than those of the upper jaw. The front molars usually appear at the beginning of the second year, those of the lower jaw first; then the gap thus left in the two rows of teeth is filled by the eruption of the canine or eye-teeth in the middle of the second year. Finally, the eruption of the back molars, which may be delayed into the third year, takes place.

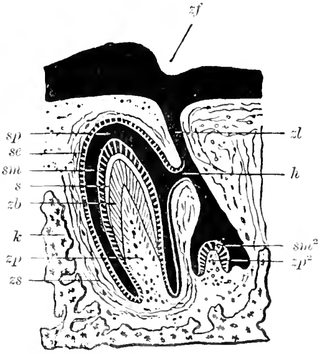

Fig. 174.—Diagrammatic section to show the development of the milk-teeth and permanent teeth in Mammals. Third stage in the series of which figs. 172 A and B are the first and second.

zf, Dental furrow; *zl*, dental ridge; *k*, bony alveolus of the tooth; *h*, neck, by means of which the enamel-organ of the milk-tooth is connected with the dental ridge, *zl*; *zp*, dental papilla; zp^2, dental papilla of the permanent tooth; *zb*, dentine; *s*, enamel; *sm*, enamel-membrane; sm^2, enamel-membrane of the permanent tooth; *sp*, enamel-pulp; *se*, outer epithelium of the enamel-organ; *zs*, dental sac.

The *fundaments of the reserve teeth make their appearance at the side of those of the milk-teeth* at an extraordinarily early period. They also take their origin from the epithelial ridge. As was previously (fig. 172 *A* and *B*) stated, the ridge extends still deeper (zl^1) into the underlying tissue from the place where the enamel-organs of the milk-teeth have been differentiated from it and where they remain united to it by means of an epithelial cord, the neck. Here in a short time there again appear near the edge of the ridge (fig. 174 sm^2, zp^2) flask-shaped epithelial growths and dental papillæ, which lie on the inner [median] side of the dental sacs of the milk-teeth. In addition there are developed at the ends of the epithelial ridges, in both the right and left halves of the jaw, the enamel-organs of the posterior grinders (the molar teeth of the permanent set), which are not subject to replacement, but are formed once for all. The ossification of the second generation of teeth begins a little time before birth with the first large molars, and is followed in the first and second years after birth by that of the incisors, canines, etc. As a result in the sixth year there are in both jaws forty-eight ossified teeth,—twenty milk-teeth and twenty-eight permanent crowns,—as well as four fundaments of wisdom teeth, which are still cellular.

The *shedding of the teeth* ordinarily begins in the seventh year. It is initiated by the disorganisation and absorption of the roots of the milk-teeth, under the pressure of the growing new generation. One finds here exactly the same appearances as in the atrophy of osseous tissue, concerning which we have the thorough investigations of KOLLIKER. There arise on the roots of the teeth the well-known pits of HOWSHIP, in which large, multinuclear cells, the *osteoclasts or bone-destroyers*, are imbedded. The crowns are loosened by surrendering their union with the deeper connective-tissue layers. Finally, when the permanent teeth, owing to the growth of their roots, push forth out of the alveoli, the crowns of the milk-teeth are thereby raised up and fall off.

The *permanent teeth generally appear in the following order* : at first, in the seventh year, the first [front] molars ; a year later the middle incisors of the lower jaw, which are followed a little later by those of the upper jaw ; in the ninth year the lateral incisors are cut, in the tenth year the first premolars, in the eleventh year the second premolars. Then in the twelfth and thirteenth years the canines and the second molars come through. The eruption of the third molars, or wisdom teeth, is subject to great variation : it may take place in the seventeenth year, but it may be delayed till the thirtieth. Occasionally the wisdom teeth never attain a complete development, so that they are never cut.

B. The Organs arising from the Pharynx : Thymus, Thyroid Gland, Larynx, and Lung.

Whereas in the water-breathing Vertebrates the visceral clefts remain throughout life and subserve respiration, they are completely closed in all Amniota as well as in a part of the Amphibia. The only exception is in the case of the first cleft, lying between the mandibular and the hyoid arches, which is converted into the drum of the ear (tympanum) and the EUSTACHIAN tube, and thus enters into the service of the organ of hearing, in connection with which it will subsequently engage our attention.

However, the remaining visceral clefts do not disappear without leaving any trace. From certain epithelial tracts of these there arises an organ of the neck-region which functionally is still problematic, the thymus, the morphology of which has been very essentially advanced during the last few years.

(1) *The Thymus*

has been for several years a favorite object of embryological investigation, since the time when KÖLLIKER made the interesting discovery that in mammalian embryos it takes its origin from the epithelium of a visceral cleft. This discovery has since then been corroborated, and at the same time extended; for also in such animals as persistently breathe by means of gills the thymus is developed out of epithelial tracts of the open and functionally active gill-clefts.

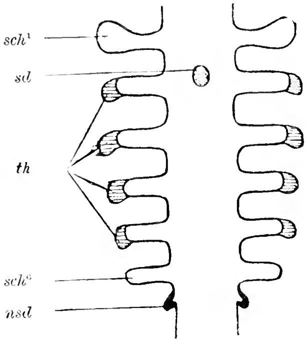

Fig. 175.—Diagram to show the development of the thymus, the thyroid gland, and the accessory thyroid glands, and their relations to the visceral pockets in a Shark embryo, after DE MEURON.
*sch*¹, *sch*⁶, First and sixth visceral pockets; *th*, fundaments of the thymus; *sd*, thyroid gland; *nsd*, accessory thyroid gland.

Let us first examine the original condition as exhibited by Fishes. As stated by DOHRN, MAURER, and DE MEURON, the thymus (*th*) of the Selachians (fig. 175) and the Bony Fishes has a multiple origin and is derived from separate solid epithelial growths, which take place at the dorsal ends of all the gill-clefts, and, indeed, to a greater extent on the anterior than on the posterior ones.

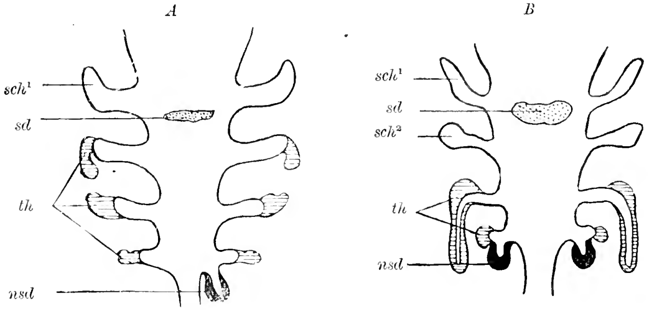

Fig. 176.—Two diagrams [ventral aspect] of the development of the thymus, the thyroid gland, and the accessory thyroid glands, and their relations to the visceral pockets in a Lizard embryo (*A*) and a Chick embryo (*B*), after DE MEURON.
*sch*¹, *sch*², First and second visceral pockets; *sd*, thyroid gland; *nsd*, accessory thyroid gland; *th*, fundament of thymus.

In the Bony Fishes the separate fundaments at an early period, even before they have detached themselves from their matrix, fuse together into a spindle-shaped organ lying above the insertion of the gill-arches, which subsequently becomes independent, just as it does in Selachians. The originally epithelial product acquires a peculiar histological character from being penetrated by ingrowths of connective-tissue elements. In the first place lymph-cells in great quantities migrate in between the epithelial cells, in a manner similar to that described by STÖHR as of frequent occurrence in the territory of mucous membranes. Secondly, the epithelial growth is traversed in all directions and cut up into small portions by connective tissue, in which lymph-follicles are formed. The thymus thereby acquires the appearance of a lymphoid organ, in which the epithelial remnants are still in part preserved, but only in the form of very small spherical portions, as the corpuscles of HASSALL. At a still later stage of development there arise in the organ irregular cavities filled with molecular granules. These are caused by the disintegration of lymph-cells and the melting down of the reticular connective tissue, which takes place here and there.

In the higher, air-breathing Vertebrates the thymus is derived either from the epithelium of two or three clefts or only from the epithelium of the third visceral cleft, which becomes closed. The former is the case with Reptiles (fig. 176 *A th*) and Birds (fig. 176 *B th*), the latter with Mammals. In Reptiles and

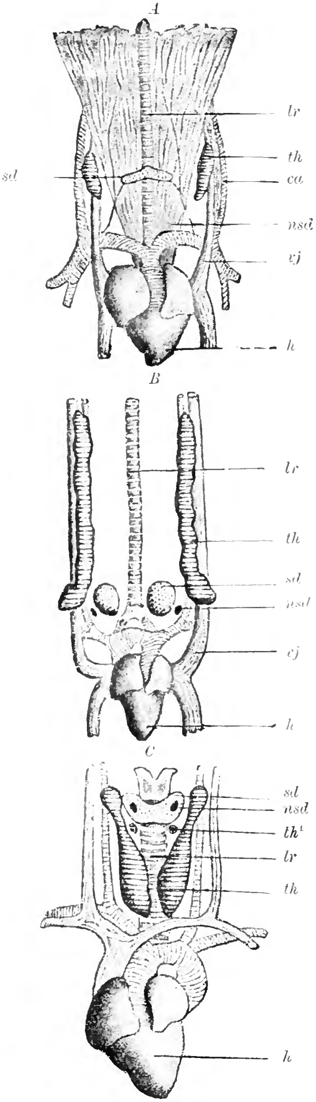

Fig. 177.—Semidiagrammatic illustrations to show the ultimate position of thymus, thyroid gland, and accessory thyroid gland on the neck of the Lizard (*A*), the Chick (*B*), and the Calf (*C*), after DE MEURON.

sd, Thyroid gland; *nsd*, accessory thyroid gland; *th*, thymus; *th*¹, accessory thymus; *lr*, trachea; *h*, heart; *vj* vena jugularis; *ca*, carotid vein.

Birds the two fundaments fuse early upon either side of the trachea into a longish tract of tissue, which in the former is shorter (fig. 177 *A*), but in the latter very much elongated (fig. 177 *B*).

In Mammals it is principally the third visceral cleft which contributes to the formation of the thymus. According to Kölliker, Born, and Rabl this is the only one which comes into consideration, whereas de Meuron, Kastschenko, and His give an account which differs from this, but only in minor details.

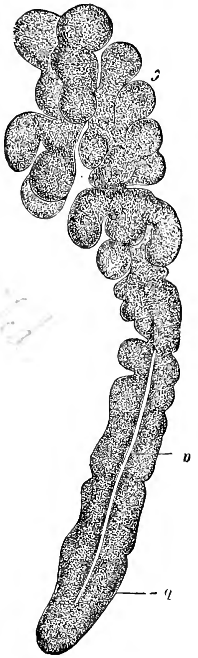

Fig. 178.—Thymus of an embryo Rabbit of 16 days, after Kölliker. Magnified.
a, Canal of the thymus; *b*, upper, *c*, lower end of the organ.

The further changes of the fundament of the thymus in Mammals and in Man may be briefly summarised as follows. The thymus-sac, which probably takes its origin from the third visceral pocket, encloses only a very narrow cavity, but possesses a thick wall composed of many elongated epithelial cells (fig. 178). It then grows downward toward the pericardium, and at the posterior end begins to form, like a botryoidal gland, numerous rounded lateral branches (*c*). (Kölliker.) These are from the beginning of their formation solid, whereas the sac-like part (*a*), which occupies the neck-region, always continues to exhibit a narrow cavity.

The budding continues for a long time, and meanwhile extends to the opposite end of the originally simple glandular sac, until the whole organ has assumed the lobed structure peculiar to it. At the same time an histological metamorphosis is also taking place. Lymphoid connective tissue and blood-vessels grow into the thick epithelial walls and gradually destroy the appearance which so resembles a botryoidal gland. With the increase in the size of the organ the lymphoid elements coming from the surrounding tissue predominate more and more; the epithelial remnants are finally to be found only in the concentric bodies of Hassall, as Maurer has shown for Bony Fishes and as His has undoubtedly rightly inferred for Man and Mammals. The cavity originally present and resulting from the invagination disappears, and instead of it there arise new irregular cavities, probably the result of a breaking down of the tissue.

The further history of the thymus in Man permits the recognition of two periods, one of progressive and one of regressive development.

The first period extends into the second year after birth. The thymus of the right side and that of the left move in their growth close together into the median plane and here fuse into an unpaired, lobed organ, whose double origin is to be recognised only by the fact that the organ is ordinarily composed of lateral halves separated by connective tissue. It lies in front of [ventral to] the pericardium and the large blood-vessels beneath the breastbone, and is often elongated into two horns which extend upwards to the thyroid gland.

The second period exhibits the organ undergoing regressive metamorphosis, which usually leads to its total disappearance, the particulars of which can be learned from the text-books of Histology.

(2) *The Thyroid Gland*

is found on the anterior surface of the neck, and appears to be developed in almost all classes of Vertebrates in a tolerably uniform, typical manner from an unpaired and a paired evagination of the pharyngeal epithelium. We must therefore distinguish unpaired and paired fundaments of the thyroid gland.

The *unpaired fundament* has been longest known. There is not a single class of Vertebrates in which it is wanting, as has been established especially by the investigations of W. Müller. It appears to be an organ of very ancient origin, which shows relationship to the hypobranchial furrow of Amphioxus and the Tunicates.

Dohrn has opposed this hypothesis and has expressed the view, which is also shared by others, but which lacks proof, that the thyroid gland is the remnant of a lost gill-cleft of the Vertebrates.

The unpaired thyroid gland arises as a small evagination of the epithelium of the front wall of the throat in the median plane and in the vicinity of the second visceral arch. Then it detaches itself completely from its place of origin, and is converted either into a solid spheroidal body (Selachians, Teleosts, Amphibia, etc.) or into an epithelial vesicle having a small cavity (Birds, Mammals, Man, etc.). The vesicle subsequently loses its cavity.

In Man the development of the unpaired part of the thyroid gland is related to the formation of the root of the tongue, as His states in his investigations of human embryos. The previously described ridges lying on the floor of the throat-cavity in the vicinity of the second and third visceral arches, which unite in the median plane to form the root of the tongue, surround a deep depression, which is the equivalent of the evagination of the pharyngeal epithelium in the remaining Vertebrates. By the further approximation of the ridges the depression becomes an epithelial sac, which remains for a long time in communication with the surface of the tongue by means of a narrow passage, the ductus thyreoglossus.

The *paired fundaments of the thyroid gland* were discovered a few years ago by STIEDA in mammalian embryos, but they have been more fully investigated by BORN, HIS, KASTSCHENKO, DE MEURON, and others in Mammals and other Vertebrates (excepting Cyclostomes). In the Amphibia, as well as in Birds and Mammals (fig. 176 *B*), there are formed, a little while after the appearance of the unpaired fundament, two hollow evaginations of the ventral epithelium of the throat behind the last visceral arch and in connection with the last visceral cleft. They come to lie immediately on either side of the entrance to the larynx. In many Reptiles (fig. 176 *A nsd*) there is an interesting deviation due to the fact that an evagination is developed only on the left side of the body, while on the right it has become rudimentary. Even in the Selachians (fig. 175), as DE MEURON appears rightly to maintain, paired fundaments of thyroid glands are present. They are the previously mentioned *supra-pericardial bodies* discovered by V. BEMMELEN. These arise as evaginations of the epithelium of the throat behind the last pair of gill-clefts near the anterior end of the heart. In all cases the evaginated portions of the epithelium become detached from their parent tissue and enclosed on all sides by connective tissue; they then undergo a metamorphosis similar to that of the unpaired fundament of the thyroid gland.

In regard to their ultimate position there exist considerable differences between the separate classes of Vertebrates. In the Selachians the supra-pericardial bodies remain far away from the unpaired thyroid gland, being located in the vicinity of the heart; but in the other Vertebrates they move more or less close to the gland, and have here acquired the name of accessory thyroid glands (fig. 177 *A* and *B nsd*). Finally, in Mammals and Man the approximation has led to a complete fusion of the unpaired and the lateral, paired fundaments (fig. 177 *C*). Together they constitute a horseshoe-shaped body that embraces the larynx. It is, however, to be observed, that at the time of their fusion the lateral fundaments, in comparison with the median one, are only very small nodules. Consequently KASTSCHENKO, who is probably in the right, ascribes to the former an inconsiderable importance for the development of the whole mass of the thyroid gland, whereas His maintains that they become in Man the voluminous lateral lobes, and that the unpaired fundament becomes the small middle part of the organ.

The further development of the thyroid gland is accomplished in a very similar manner in all Vertebrates. Two stages are distinguishable.

During the first stage the whole fundament grows out into numerous cylindrical cords, which in turn push out lateral buds (fig. 179). By the union of these with one another there is formed a network, into the interstices of which are distributed branches of the blood-vessels together with embryonic connective tissue. In the case of the Chick it is found that the thyroid gland has reached this stage of development on the ninth day of incubation, in the Rabbit embryo when it is about sixteen days old, in Man in the second month.

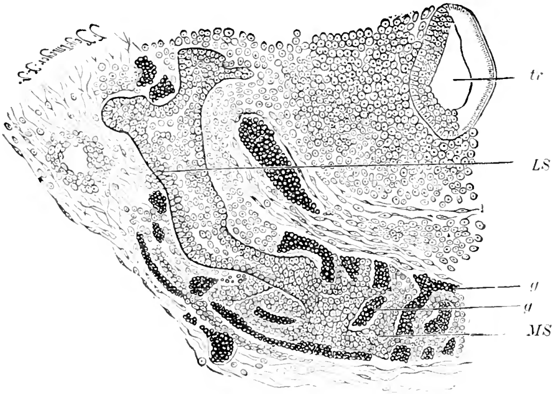

Fig. 179.—Right half of the thyroid gland of an embryo Pig 21·5 mm. long, crown-rump measurement,* after Born. Magnified 80 diameters.

The lateral (*LS*) and median (*MS*) thyroid glands are in process of fusion. *g*, Blood-vessels; *tr*, trachea.

During the second stage the network of epithelial cords is resolved into the characteristic follicles of the thyroid gland. The cords acquire a narrow lumen, around which the cylindrical cells are regularly arranged. Then there are formed on the cords at short intervals enlargements, which are separated by slight constrictions (fig. 180). By the deepening of the constrictions the whole network is finally subdivided into numerous, small, hollow epithelial vesicles or follicles, which are separated from one another

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* [The elevation caused by the mid-brain may be called the apex or crown (Scheitel). In later stages the distance between crown and rump is greater than that between neck and rump, hence the measurement is made from the crown. Compare foot-note, p. 283.]

by highly vascular embryonic tissue. Subsequently the follicles increase in size, especially in the case of Man; this results from the epithelial cells secreting a considerable quantity of colloid substance into the cavity.

A few further details concerning the thyroid gland of Man, for which we are indebted to His, may be of interest. First, it is to be noted that the lateral fundaments are considerably more voluminous than the middle part, and that the future fundamental form of the organ is thus from the beginning predetermined. Secondly, some rare anatomical conditions (His) are explained by the development, such as the ductus lingualis, the ductus thyroideus, and the glandula suprahyoidea and præhyoidea. As was previously stated, the unpaired fundament of the thyroid gland is connected with the root of the tongue by means of the ductus thyreoglossus. When the thyroid gland moves from its place of origin farther down, this duct becomes elongated into a narrow epithelial passage, whose external orifice remains permanently visible as the foramen cœcum at the base of the tongue. The remaining part usually undergoes degeneration, but occasionally some parts of it also persist. Thus the foramen cœcum is sometimes elongated into a canal (ductus lingualis) 2½ cm. long, that leads to the body of the hyoid bone. In other instances the middle part of the thyroid gland is prolonged upward in the form of a horn, which is continued as a tube (ductus thyroideus) to the hyoid bone. Finally, according to His, the glandular vesicles now and then to be observed in the vicinity of the hyoid bone—the accessory thyroid glands, as well as the glandula supra- and præ-hyoidea—are to be interpreted as remnants of the ductus thyreoglossus.

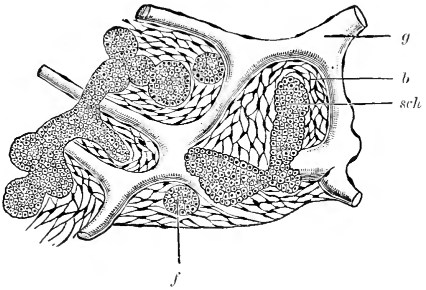

Fig. 180.—Section through the thyroid gland of an embryo Sheep 6 cm. long, after W. Müller.
sch, Sac-like fundaments of the gland; *f*, glandular follicles in process of formation; *b*, interstitial connective tissue with blood-vessels (*g*).

(3) *Lung and Larynx.*

The lung with its outlet (larynx and trachea) is developed, like a lobed gland, out of the œsophagus in a tolerably uniform manner, as it appears, for all amniotic Vertebrates. Immediately behind the unpaired fundament of the thyroid gland (fig. 181 *Sd*) there arises on the ventral side of the œsophagus a groove (*Kk*), which is slightly enlarged at its proximal end. It is to be seen in the Chick at the beginning of the third day, in the Rabbit on the tenth day after fertilisation, and in the human embryo when it is 3·2 mm. long.

Soon the groove-like evagination becomes separated from the overlying portion of the alimentary tube by two lateral ridges; this furnishes the first indication of a differentiation into œsophagus and trachea (fig. 181). Then there grow out from the enlarged posterior ends of the groove (figs. 181, 163) two small sacs (*Lg*) toward the two sides of the body (in the Chick in the middle of the third day), the fundaments of the right and left lung. Enveloped in a thick layer of embryonic connective tissue, they are in immediate contact behind with the fundament of the heart; laterally they project into the anterior fissure-like prolongation of the body-cavity. With this the essential parts of the respiratory apparatus are established; at this stage in amniotic Vertebrates they resemble the simple sac-like structures which the lungs of Amphibia present permanently.

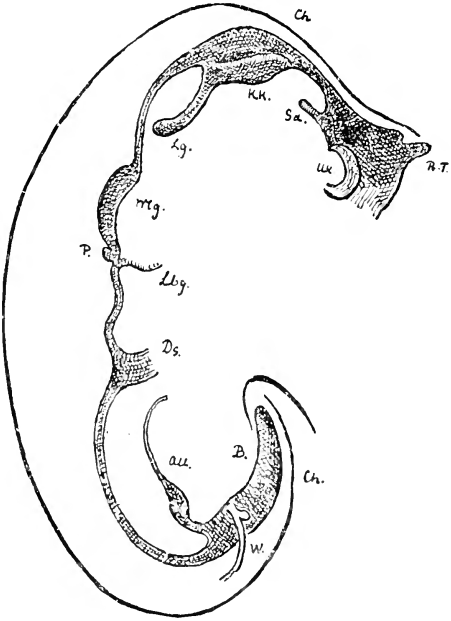

Fig. 181.—Alimentary tube of a human embryo (*R* of His) 5 mm. long, neck measurement. From His, "Menschliche Embryonen." Magnified 20 diameters.

RT, Rathke's pouch ; *Uk*, lower jaw ; *Sd*, thyroid gland ; *Ch*, chorda dorsalis ; *Kk*, entrance to the larynx ; *Lg*, lung ; *Mg*, stomach ; *P*, pancreas ; *Lbg*, primitive hepatic duct ; *Ds*, vitelline duct (stalk of the intestine) ; *All*, allantoic duct ; *W*, Wolffian duct, with kidney-duct (ureter) budding out of it ; *B*, bursa pelvis.

In the further course of development the fundaments of trachea and œsophagus, which communicate by means of a fissure, become separated by a constriction which begins behind, where the pulmonary sacs have budded out, and gradually moves forward. The constricting off is here interrupted at the place which becomes the entrance to the larynx. The latter is distinguishable in the case of Man at the end of the fifth week as an enlargement at the beginning of the fundament of the trachea. It acquires its cartilages in the eighth or ninth week. Of these the thyroid cartilage arises, according to the comparative-anatomical investigations of Dubois, from a fusion of the fourth and fifth visceral arches, whereas the cricoid and arytenoid cartilages, as well as the half-rings of the trachea, are independent chondrifications in the mucous membrane.

Two stages are recognisable in the metamorphosis of the primitive lung-sacs of Man and Mammals.

The *first stage* begins with the elongation of the sac, which is attenuated at its origin from the trachea, but is enlarged at its opposite or free end. At the same time—in Man from the end of the first month (His)—it pushes out, in the manner of an alveolar gland, hollow evaginations, which grow out into the thick connective-tissue envelope and enlarge at their ends into little sacs. The first bud-like outgrowths *on the two sides of the body are not symmetrical* (fig. 182), *because the left lung-sac produces two, the right three bud-like enlargements.* An important feature of the architecture of the lungs is thus established from the beginning, namely, the differentiation of the right lung into three chief lobes, and of the left into two.

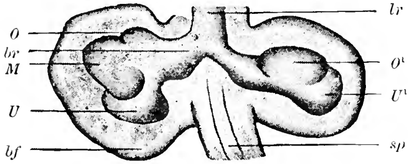

Fig. 182.—View of a reconstruction of the fundament of the lungs of a human embryo (*Pr* of His) 10 mm. long, neck measurement, after His.

lr, Trachea; *br*, right bronchus; *sp*, œsophagus; *bf*, connective-tissue envelope and serous membrane (pleura) into which the epithelial fundament of the lung grows; *O*, *M*, *U*, fundaments of the upper, middle, and lower lobes of the right lung; O^1, U^1, fundaments of the upper and lower lobes of the left lung.

The further budding is distinctly dichotomous (fig. 183). It takes place in the following way: each terminal vesicle (primitive lung-vesicle), which is at first spheroidal, becomes flattened and indented on the wall (*lb*) which lies opposite its attachment. Thus it becomes divided, as it were, into two new pulmonary vesicles, each of which is then differentiated into a long stalk (lateral bronchus) and a spherical enlargement. Inasmuch as such a process of budding is kept up for a long time,—in Man until the sixth month,—there arises a complicated system of canals, the bronchial tree, which opens into the trachea by means of a single main bronchial tube from either side of the body, and the ultimate branches of which, becoming finer and finer, terminate in flask-shaped enlargements, the primitive lung-vesicles. The latter are at first confined to the surface of the lung, while the system of canals occupies its interior.

During this budding the lungs as they increase in volume continue to grow downwards into the thoracic cavities, and thereby come to lie more and more at the right and left of the heart. With their ingrowth into the cavities of the chest (fig. 314 *brh*), they push before them the serous lining of the latter, and thus acquire their pleural covering (the pleura pulmonalis, or the visceral layer of the pleura).

During the *second stage* the organ, which up to this time has the typical structure of a botryoidal gland, assumes the characteristic pulmonary structure. The metamorphosis begins in Man, as Kölliker states, in the sixth month, and comes to a close in the last month of pregnancy. There now arise close together on the fine terminal tubules of the bronchial tree, on the alveolar passages, and on their terminal vesicular enlargements, very numerous small evaginations. But in distinction from the earlier ones, these are not constricted off from their source of origin, but communicate with the latter by means of wide orifices, and thus constitute the *air-cells* or *pulmonary alveoli*. Their size is only a third or fourth as great in the embryo as in the adult; from this Kölliker concludes that the increase in the volume of the lung from birth up to complete development of the body is to be attributed exclusively to the enlargement of the vesicular elements which exist in the embryo.

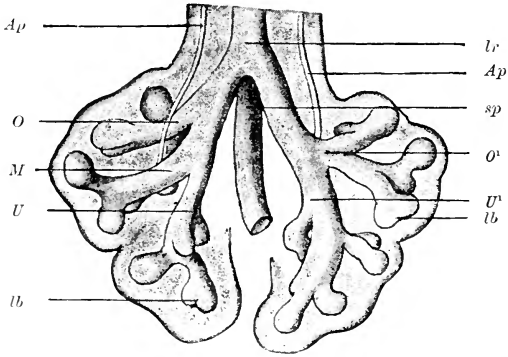

Fig. 183.—View of a reconstruction of the fundament of the lungs of a human embryo (N of His) older than that of fig. 182. After His. Magnified 50 diameters.

Ap, Arteria pulmonalis; *lr*, trachea; *sp*, œsophagus; *lb*, pulmonary vesicle in process of division; *O*, upper lobe of the right lung with an eparterial bronchus leading to it; *M*, *U*, middle and lower lobes of the right lung; O^1, upper lobe of the left lung with hyparterial bronchus leading to it; U^1, lower lobe of the left lung.

The *epithelial lining* of the lung is variously modified in different regions during development. In the whole bronchial tree the epithelial cells increase in height, acquire in part a cylindrical, in part a cubical form, and from the fourth month onward (Kölliker) have their free surfaces covered with cilia. In the air-sacs, on the contrary, the cells, which are arranged in a single layer, become more and more flattened, and in the adult become so thin that formerly the presence of an epithelial covering was wholly denied. Then they assume a condition similar to that of endothelial cells; as in the case of the latter, their boundaries are demonstrable only after treatment with a weak solution of silver nitrate.

C. The Glands of the Small Intestine: Liver and Pancreas.

(1) *The Liver.*

In the section which treats of the liver we must enter upon a discussion not only of the development of the parenchyma of the gland, but also of the various hepatic ligaments—the lesser omentum, the ligamentum suspensorium, etc.; in fact, we must begin with the latter because they are developed out of a structure—a *ventral mesentery*—which is ontogenetically older than the liver itself. In view of the manner in which the body-cavity arises, as a pair of cavities, such a structure ought to be found along the whole length of the ventral side of the alimentary canal in the same manner as on its dorsal side. Instead of that, it is found only at the anterior region of the alimentary canal, along a tract which extends from the throat to the end of the duodenum.

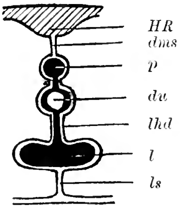

Fig. 184.—Diagram (view of a cross section) to show the original relations of duodenum, pancreas, and liver, and of the ligamentous structures belonging to them.
HR, Posterior wall of the trunk; *du*, duodenum; *p*, pancreas; *l*, liver; *dms*, dorsal mesentery; *lhd*, ligamentum hepato-duodenale; *ls*, ligamentum suspensorium hepatis.

This ventral mesentery acquires a special significance, because several important organs take their origin in it; in front, the heart, together with the vessels that bring the blood back to it—the terminal parts of the venæ omphalomesentericæ and of the vena umbilicalis; immediately behind the latter, the liver with its outlet and its blood-vessels.

The part which, during an early stage of development, encloses the heart is called *mesocardium anterius* and *posterius*; we shall return to it later in considering the development of that organ. The portion (fig. 184) which joins this behind [caudad] has been hitherto less regarded by embryologists. Since it stretches from the lesser curvature of the stomach and the duodenum (*du*) to the anterior [ventral] wall of the trunk, it may be especially designated as the *ventral gastric and duodenal mesentery*, or, under a more compre-

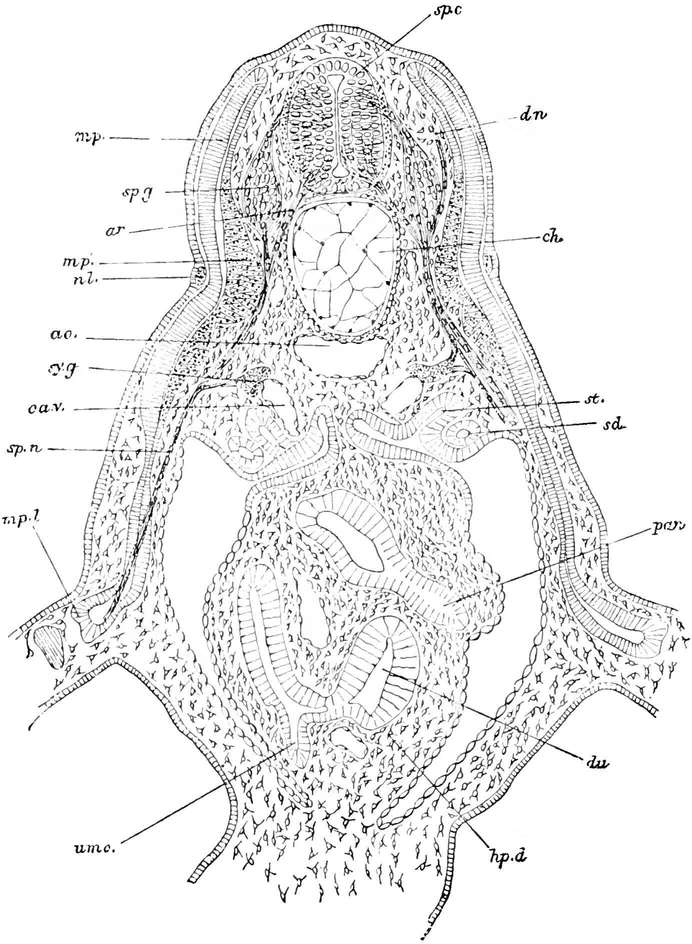

Fig. 185.—Cross section through the anterior part of the trunk of an embryo of Scyllium, after Balfour.

Between the dorsal and ventral walls of the body, where the attachment of the stalk of the yolk-sac is cut, there is stretched a broad mesentery which contains numerous cells and completely divides the body-cavity into a right and a left half. The duodenum (*du*), lying in the mesentery, is twice cut through; dorsally it gives rise to the fundament of the pancreas (*pan*), ventrally to that of the liver (*hp.d*). Further, the place where the vitelline duct (*umc*) emerges from the duodenum is to be seen. *sp.c*, Neural tube (spinal cord); *sp.g*, ganglion of posterior root; *ar*, anterior root; *dn*, dorsally directed nerve springing from the posterior root; *mp*, muscle-plate; mp^1, part of muscle-plate already converted into muscles; *mp.l*, part of muscle-plate which gives rise to the muscles of the limbs; *nl*, nervus lateralis; *ao*, aorta; *ch*, chorda; *sy.g*, sympathetic ganglion; *ca.v*, cardinal vein; *sp.n*, spinal nerve; *sd*, segmental duct (duct of primitive kidney); *st*, segmental tube (pronephric tubule).

hensive title, as *ventral alimentary mesentery* (*lhd* + *ls*). It has been described by Kölliker on sections of Rabbit embryos as *liver-ridge* (Leberwulst), and by His in his "Anatomie menschlicher Embryonen" as *prehepaticus* (Vorleber); it has the form of a mass of tissue rich in cells, which inserts itself between the wall of the belly and the regions of the intestine previously mentioned. In cross sections through human and mammalian embryos there are encountered in it the capacious venæ omphalomesentericæ. As far as a mesocardium and a mesogastrium anterius are developed in Vertebrates, *the body-cavity appears even subsequently as a paired structure.*

The cross section through a Selachian embryo (fig. 185) shows this distinctly. The duodenum (*du*) is enclosed in the connective-tissue mesentery, which reaches from the aorta (*ao*) to the front [ventral] wall of the trunk; dorsally the pancreas (*pan*) is budded forth from its wall, ventrally the liver (*hp.d*).

The liver begins to be developed very early in the ventral mesentery (liver-ridge or prehepaticus), and in this exhibits, as will appear later, two modifications, which are, however, unessential; for sometimes it appears in the form of a single, sometimes as a paired evagination of the epithelial lining of the ventral wall of the duodenum.

The first is the case, for example, in the Amphibia and Selachii. In Bombinator (fig. 159), as Goette has shown, the liver arises as a broad ventrally directed evagination of the intestine, which lies immediately in front of the accumulation of yolk-material. The liver remains permanently in this simplest form in the case of Amphioxus lanceolatus, in which it is located immediately behind the gill-region as an appendage of the intestinal canal.

In the case of Birds and Mammals, on the contrary, the fundament of the liver is from the beginning double. As has been known since the investigations of Remak, in the case of the Chick (fig. 186) on the third day of incubation, two sacs (*l*) grow out of the ventral wall of the duodenum immediately behind the spindle-shaped stomach (*St*). They grow into the broad cell-mass of the ventral mesogastrium (the Leberwulst), one passing forward to the left, the other backward to the right, and thereby embrace from above the vena omphalomesenterica on its way to the heart. The process in Mammals is somewhat different. According to the observations of Kölliker in the case of the Rabbit, the primitive hepatic tube of the left side is formed in the embryo of ten days, to which a right duct is added in the course of another day. Also in the case of human embryos 4 mm. long His demonstrated that at first there is only a single hepatic duct, and that some time afterwards a second appears (fig. 163 *Lbg*).

In the further course of development both the unpaired and the paired hepatic fundaments are metamorphosed quite rapidly into a tubular gland with numerous branches; this acquires a special character, differing from that of simple tubular glands, owing to the fact that the tubes early become joined together to form a fine network, since the primitive hepatic tubes send out numerous lateral buds, which in some Vertebrates (Amphibia, Selachii) are from the beginning hollow, in others (Birds, Mammals, Man) solid. Imbedded in the embryonic connective substance of the ventral mesogastrium, they grow out in the former case into hollow tubes, in the latter into solid cylinders. These in turn are soon covered with corresponding lateral processes, and so on. Inasmuch as these grow toward one another, and where they meet (fig. 187 *lc*) fuse, there arises a close network of hollow glandular canals or solid hepatic cylinders in the common connective-tissue matrix.

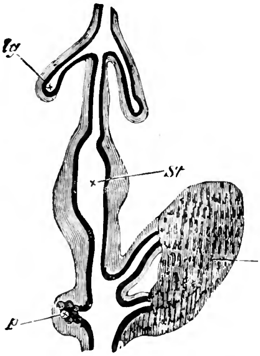

Fig. 186.—Diagrammatic view of the alimentary canal of a Chick on the fourth day, after Goette.
The heavy line indicates the inner germ-layer, the shaded portion surrounding it the splanchnic portion of the mesoblast. *lg*, Lung; *St*, stomach; *p*, pancreas; *l*, liver.

Simultaneously with the epithelial network there is formed in its meshes a network of blood-vessels (*g*). From the vena omphalomesenterica, which, as previously stated, is embraced by the two hepatic tubes, there grow out numerous shoots, and these by forming lateral branches unite with one another in a manner corresponding to that of the hepatic cylinders.

The liver of the Chick is found to be in this condition on the sixth day. It has become even now a rather voluminous organ, and is composed, as in the case of Mammals and Man, of two equally large lobes, each of which has arisen from one of the two primitive hepatic ducts by budding. The two lobes produce on the ventral mesentery two ridges, one of which projects into the left body-cavity and one into the right (fig. 184).

A further increase in the size of the liver is due to the fact that from the hepatic cylinders united into a network new lateral branches grow forth and undergo anastomosis, whereby new meshes are being continually formed.

Herewith the essential parts of the liver are present in the fundament: (1) the secretory liver-cells and the bile-ducts, (2) the peritoneal covering and the suspensory apparatus, both of which are derived from the ventral mesentery. The changes in these parts which lead to the permanent condition are now to be considered.

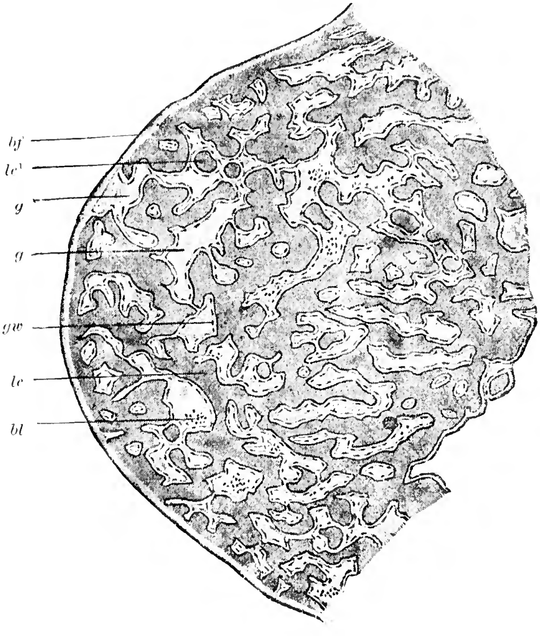

Fig. 187.—Section through the fundament of the liver of a Chick on the sixth day of incubation. Slightly enlarged.
lc, Network of hepatic cylinders; lc^1, hepatic cylinder cut crosswise; *g*, blood-vessels; *gw*, wall of the blood-vessel (endothelium); *bl*, blood-corpuscles; *bf*, peritoneal covering of the liver.

The epithelium of the ducts and the secretory liver-parenchyma are derived from the two hepatic tubes and from the network of hepatic cylinders,—products of the entoblast.

The parts of the two primitive liver-tubes first formed become the right and left ductus hepatici. In Birds and Mammals these open at first, as we have seen, into the duodenum close together; then at their place of entrance there is formed a small evagination of the duodenum, which receives the two ductus hepatici. The evagination gradually increases to a long single canal, the bile-duct or ductus choledochus, the result of which process is that the whole liver is farther removed from its source of origin.

By an evagination either of the ductus choledochus or of one of the two ductus hepatici, the *gall-bladder* with its ductus cysticus is established. In Man it arises from the ductus choledochus, and is present as early as the second month.

The network of hepatic cylinders, which are sometimes hollow, sometimes solid, is metamorphosed in two ways.

One part becomes the excretory ducts (the ductus biliferi). In the cases in which the hepatic cylinders are at first solid, they begin to become hollow and to arrange their cells into a cubical or cylindrical epithelium around the lumen. In this process some of the branches of the network must degenerate. For, whereas all hepatic cylinders at first communicate with one another by means of anastomoses, this is, as KÖLLIKER remarks, no longer the case in the adult, except at the outlet of the liver (Leberpforte), where the well-known network of bile-ducts exists.

The remaining part of the network furnishes the secretory parenchyma of liver-cells. The character of a netlike tubular gland, which becomes so evident during development, is to be recognised even in the fully developed organ in the case of the lower Vertebrates, the Amphibia and Reptiles. The tubules of the gland, which were from the beginning hollow, subsequently exhibit an exceedingly narrow lumen, which is demonstrable only by means of artificial injection, and which in cross section is surrounded by three to five liver-cells. Through their manifold anastomoses they produce an extraordinarily fine network, the small meshes of which are filled up by a network of capillary blood-vessels, together with a very small amount of connective substance.

In the higher Vertebrates (Birds, Mammals, Man) the tubular structure of the gland subsequently becomes very inconspicuous and the liver acquires a complicated structure, information concerning the details of which is given in the text-books of histology.

There are three things which, from a developmental point of view, are not to be lost sight of: first, the capillaries of the bile-duct have arisen by canalisation of the primitive hepatic cylinders; secondly, they are bounded by only two liver-cells, which are very large and flake-like; thirdly, they send out evaginations between and even into the liver-cells themselves. In this way a greater complication is brought about in the arrangement of the fine biliary capillaries and the hepatic cells, to which there also corresponds a greater complication in the distribution of the capillaries of the blood-vessels. By means of all this the original tubular structure of the gland becomes almost entirely obliterated in the fully developed organ. In the adult, as is well known, the parenchyma of the liver is divided by means of connective-tissue partitions into small lobes (acini or lobuli). At the beginning of development nothing is seen of the lobulated structure, because all the hepatic cylinders are united into a network. Detailed information concerning the development of the lobules is wanting.

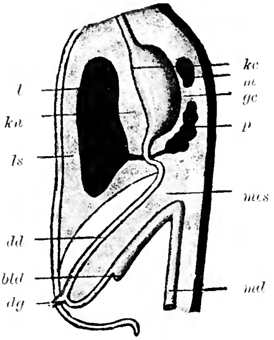

Fig. 188. — Diagram to show the original positions of the liver, stomach, duodenum, pancreas, and spleen, and the ligamentous apparatus pertaining to them. The organs are seen in longitudinal section.

l, Liver; *m*, spleen; *p*, pancreas; *dd*, small intestine; *dg*, vitelline duct; *bld*, cœcum; *md*, rectum; *kc*, lesser curvature, *gc*, greater curvature of the stomach; *mes*, mesentery; *kn*, lesser omentum (lig. hepato-gastricum and hepato-duodenale); *ls*, ligamentum suspensorium hepatis.

Now a few words concerning the ligaments and the conditions of form and size which the liver presents up to the time of birth.

The ligamentous apparatus, as was remarked in the beginning, is preformed in a ventral mesentery (the Vorleber). Owing to the fact that the two hepatic sacs grow out from the duodenum into this ventral mesentery, and by continual branching produce the right and the left lobes of the liver (figs. 184, 185, and 188), the ventral mesentery becomes divided into three portions: first, a middle part, which furnishes the peritoneal covering for both lobes of the liver; secondly, a ligament which proceeds from the front convex surface of the liver in a sagittal direction to the ventral wall of the body, extending as far as the navel and embracing in its free margin the subsequently disappearing umbilical vein (ligamentum suspensorium and teres hepatis, figs. 184, 188 *ls*); and thirdly, a ligament which proceeds from the opposite, concave or portal surface of the liver to the duodenum and the lesser curvature of the stomach, and which contains the ductus choledochus and the afferent hepatic blood-vessels (omentum minus, which is divided into the ligamentum hepato-gastricum and hepato-duodenale). (Figs. 184 *lhd* and 188 *kn*.)

The *lesser omentum* or *omentum minus* soon loses its original sagittal position and is stretched out into a thin membrane running from right to left (fig. 166 *kn*); this is due to the fact that the stomach undergoes the previously described displacement, and moves into the left half of the peritoneal cavity, whereas the liver grows out into the right half more than into the left. In consequence of the formation of the liver and the lesser omentum, the greater omentum, produced by the torsion of the stomach, receives an addition, which is designated as its antechamber (atrium bursæ omentalis). For there comes to be associated with the greater omentum that part of the body-cavity which lies behind the liver and lesser omentum, and which in the adult possesses, as is well known, only a narrow entrance (the foramen of WINSLOW) lying below the ligamentum hepato-duodenale.

Concerning the development of the coronary ligament, see a subsequent part which treats of the diaphragm.

As far as regards the conditions of form and size which the liver presents up to the time of birth, there are two points which are worthy of attention: first, the liver early acquires a very extraordinary size; secondly, its two lobes are developed at first quite symmetrically. In the third month it nearly fills the whole body-cavity; its free sharp margin—on which a deep incision between the two lobes is observable—reaches down almost to the inguinal region, leaving here only a small space free, in which, upon opening the body-cavity, loops of the small intestine are to be seen. It is a very vascular organ, for a great part of the blood returning from the placenta to the heart passes through it. At this time the secretion of bile begins, although only to a slight extent. This increases in the second half of pregnancy. In consequence of this the intestine gradually becomes filled with a brownish-black mass, the meconium. This is a mixture of bile with mucus and detached epithelial cells of the intestine, to which is added amniotic water with flakes of epidermis and hairs that have been swallowed. After birth the meconium is accumulated in the large intestine, from which it is soon afterwards eliminated.

In the second half of pregnancy the growth of the two lobes of the liver becomes unequal, and the left is surpassed more and more in size by the right. Before birth the lower margin of the liver projects downward for some distance beyond the costal cartilages, almost to the umbilicus. After birth it diminishes rapidly in size and weight, in consequence of the change in the circulation produced by the process of respiration. For the stream of blood which during embryonic life has branched off from the umbilical vein into the liver now ceases. During the growth of the body the liver also increases in size still further, but less than the body taken as a whole, so that its relative weight is constantly undergoing reduction.

(2) *The Pancreas.*

The pancreas is developed in all Vertebrates—with the exception of a few in which it is wanting (Bony Fishes)—as an evagination on the dorsal side of the duodenum, usually opposite to the origin of the liver (figs. 162, 163, 186 *p*). In the Chick (fig. 186) the first fundament is distinguishable as early as the fourth day; in Man it appears somewhat later than the primitive hepatic tube, and has been demonstrated by His in embryos 8 mm. long as a small evagination (figs. 162 and 163). The sac, usually hollow, grows into the dorsal mesentery (figs. 184, 188 *p*) by giving off hollow, branching, lateral outgrowths.

In the case of Man the pancreas is present as early as the sixth week in the form of an elongated gland (fig. 164 *p*), the free end of which has penetrated upward [cephalad] into the mesogastrium, and thus, midway between the greater curvature of the stomach and the vertebral column, it can move freely. It is therefore compelled to share in the alteration of position which the stomach together with its mesentery undergoes. In embryos of the sixth week its long axis still corresponds approximately with the longitudinal axis of the body. The free end then moves into the left half of the body-cavity, the whole organ being turned (fig. 166) until finally its long axis comes to lie in the transverse axis of the body, as in the adult. In this position its head is imbedded in the horseshoe-shaped curvature of the duodenum, whereas its tail reaches to the spleen and left kidney.

Inasmuch as the pancreas in its development has grown into the mesogastrium (figs. 164, 166, 188), it possesses in the first half of embryonic life, as Toldt has shown, a mesentery, on which it accomplishes the turning previously described. But at the fifth month this disappears. (Compare the diagrams fig. 167 *A* and *B p.*) For as soon as the gland has taken its transverse position, it attaches itself firmly to the posterior wall of the trunk and soon loses its freedom of motion, because its peritoneal covering and its mesentery become fused with the adjacent parts of the peritoneum (fig. 167 *B* gn^4). In this manner the pancreas of Man, which was developed, like the liver, as an intraperitoneal organ, has become a so-called extraperitoneal organ, owing to a process of fusion between the serous surfaces that come in contact with each other. By means of this also the attachment of the mesogastrium is displaced from the vertebral column farther to the left.

It still remains to be mentioned, in regard to the outlet of the pancreas, that during development it is continually moving nearer to the ductus choledochus, and that finally it opens in common with the latter into the duodenum at the diverticulum of Vater.

Summary.

A. Orifices of the Alimentary Canal.

1. The original orifice of the alimentary canal (resulting from the invagination of the inner germ-layer), the primitive mouth (blastopore), becomes closed later, owing to the circumcrescence of the medullary ridges, and furnishes temporarily an open communication with the neural tube, the canalis neurentericus.

2. The neurenteric canal likewise disappears subsequently by the fusion of its walls.

3. The alimentary tube acquires new openings to the outside (visceral clefts, mouth, anus) by the fusion of its walls with the body-wall at certain places, and by the regions of fusion then becoming thinner and rupturing.

4. The visceral clefts arise on both sides of the future neck-region of the body, usually five or six pairs in the lower Vertebrates, four pairs in Birds, Mammals, and Man. (Formation of outer and inner throat-furrows; breaking through of the closing plate.)

5. In water-inhabiting Vertebrates the visceral clefts serve for branchial respiration (development of branchial lamellæ by the formation of folds of the mucous membrane); in Reptiles, Birds, and Mammals they become closed and disappear, with the exception of the upper part of the first fissure, which is employed in the development of the organ of hearing (external ear, tympanum, Eustachian tube).

6. The mouth is developed at the head-end of the embryo by an unpaired invagination of the epidermis, which, as oral sinus, grows toward the blindly ending fore gut, and by the breaking through of the primitive pharyngeal membrane. (Primitive palatal velum.)

7. The anus arises, in a manner similar to that of the mouth, on the ventral side at some distance in front of the posterior end of the body, so that the intestinal tube is continued for a certain distance beyond the anus toward the tail.

8. The post-anal or caudal intestine, which at first stretches from the anus to the posterior end of the body (tail-part of the body), becomes rudimentary afterwards and wholly disappears, so that the

anus then marks the termination, as the mouth does the beginning, of the alimentary canal.

B. Separation of the Alimentary Tube and its Mesentery into Distinct Regions.

1. The alimentary canal is originally a tube running straight from mouth to anus, near the middle of which the yolk-sac (umbilical vesicle) is attached by means of the vitelline duct (stalk of the intestine).

2. The alimentary tube is attached throughout its whole length to the vertebral column by means of a narrow dorsal mesentery; it is also connected with the anterior wall of the trunk, as far back as the umbilicus, by means of a ventral mesentery (mesocardium anterius and posterius, anterior [ventral] gastric and duodenal mesentery). (Vorleber.)

3. At some distance behind the visceral clefts, the stomach arises as a spindle-shaped enlargement of the alimentary tube; its dorsal mesentery is designated as mesogastrium.

4. The portion which follows the stomach grows more rapidly in length than the trunk, and therefore forms in the body-cavity a loop with an upper [anterior], descending narrower arm, which becomes the small intestine, and a lower [posterior], ascending more capacious arm, which produces the large intestine.

5. The stomach takes on the form of a sac, and becomes so turned that its long axis coincides with the transverse axis of the body, and that the line of attachment of the mesogastrium, or its greater curvature, which was at first dorsal, comes to lie below, or caudad.

6. The intestinal loop undergoes such a twisting that its lower, ascending arm (large intestine) is laid over [ventral to] the upper, descending arm (small intestine) from right to left, and crosses it near its origin from the stomach.

7. The twisting of the intestinal loop explains why in the adult the duodenum, as it merges into the jejunum, passes under the transverse colon and through its mesocolon. (Crossing and crossed parts of the intestine.)

8. The lower arm of the loop, during and after its twisting and crossing of the upper arm, assumes the form of a horseshoe and permits one to distinguish the cœcum, the colon ascendens, c. transversum, and c. descendens.

9. Within the space bounded by the horseshoe, the upper arm

of the loop becomes folded to form the convolutions of the small intestine.

10. The mesentery, which is at first uniform and common to the whole alimentary tube, becomes differentiated into separate regions, for it adapts itself to the folds and to the elongations of the alimentary tube. It is elongated and here and there undergoes fusion with the peritoneum of the body-cavity, by means of which it either acquires new points of attachment or in certain tracts wholly disappears; some portions of the intestine are thus deprived of their mesentery.

11. The mesentery of the duodenum, and in part also that of the colon ascendens and c. descendens, fuses with the wall of the body (extraperitoneal parts of the intestine).

12. The mesentery of the colon transversum acquires a new line of attachment running from right to left, and becomes differentiated from the common mesentery as mesocolon.

13. The mesogastrium of the stomach follows the torsions of the latter and is converted into the greater omentum, which grows out from the greater curvature of the stomach to cover over all the viscera lying below.

14. Fusions of the walls of the omentum with adjacent serous membranes take place: (1) on the posterior wall of the body, in consequence of which the line of origin from the vertebral column is displaced to the left side of the body; (2) with the mesocolon and colon transversum; (3) on the part of the sac which has overgrown the intestines, where its anterior and posterior walls come into close contact and fuse into an omental plate.

C. Development of Special Organs out of the Walls of the Alimentary Tube.

1. The surface of the alimentary tube increases in extent inward by means of folds and villi, and by glandular evaginations outward.

2. There are developed, as organs of the oral cavity, the tongue, the salivary glands, and the teeth.

3. The teeth, which in the higher Vertebrates are found only at the entrance of the mouth, are distributed in the lower Vertebrates (Selachians, etc.) over the whole of the cavity of the mouth and throat, and indeed as dermal teeth over the whole surface of the body.

4. The dermal teeth are dermal papillæ ossified in a peculiar

manner, in the development of which both the superficial layer of the corium and also the deepest cell-layer of the epidermis investing the latter are concerned.

(*a*) The corium [dermis] produces the abundantly cellular dental papilla, which secretes the dentine at its surface, where a layer of odontoblasts is formed.

(*b*) The epidermis furnishes a layer of tall cylindrical cells, the enamel-membrane, which covers the dentine-cap with a thin layer of enamel.

(*c*) The base of the dentine-cap acquires a better attachment in the dermis from the fact that the latter becomes ossified in its vicinity and furnishes the cementum.

5. At the margins of the jaws the tooth-forming tract of the mucous membrane sinks down into the underlying tissue; there is first developed by a proliferation on the part of the epithelium a dental ridge, on which the teeth of the jaws arise in the same way that the dermal teeth do on the surface of the body.

6. The development of a tooth takes place on the ridge in the following way: the epithelium grows more rapidly at one point, and a papilla of the connective-tissue part of the mucous membrane grows into this proliferated part or enamel-organ. The dental papilla forms the dentine, but the enamel-organ, developing an enamel-membrane, secretes the enamel; finally, the connective-tissue dental sac becomes ossified and furnishes the cementum.

7. Beneath the milk-teeth there are early formed in Mammals and Man, at the deep edge of the dental ridge, the fundaments of supplementary teeth.

8. From the throat-region of the intestine there are developed thymus, thyroid gland, accessory thyroid gland, and lungs.

9. The thymus arises by the thickening and peculiar metamorphosis of the epithelium of several pairs (Selachii, Teleostei, Amphibia, Reptilia), or of only one pair, of visceral clefts.

(*a*) In Selachians and Teleosts there is a proliferation of epithelium at the dorsal ends of all the visceral clefts, which are penetrated by growths of connective tissue and blood-vessels.

(*b*) In Mammals and Man there is formed from the third pair of visceral clefts a pair of epithelial thymus-sacs, which send out lateral buds and become peculiarly altered histologically.

(*c*) In Man the two thymus-sacs are joined in the median plane to an unpaired body, which begins to degenerate in the first years after birth.

10. The thyroid gland is an unpaired organ, which arises in the region of the body of the hyoid bone from either a hollow or a solid outgrowth of the epithelium in the floor of the pharyngeal cavity.

(*a*) The epithelial rod detaches itself from its parental tissue and forms lateral rods.

(*b*) At a later stage these epithelial cords become separated into small epithelial spheres, which secrete in their interiors colloid substance and are converted into wholly closed glandular sacs enveloped in highly vascular capsules of connective tissue.

11. The accessory thyroid glands are paired and arise from evaginations of the epithelium of the last pair of visceral clefts, which undergo metamorphoses similar to those of the unpaired thyroid gland.

12. The accessory thyroid glands in most Vertebrates remain separated from the unpaired thyroid gland by a greater (Reptiles) or less (Birds) space, whereas in Mammals they appear to fuse with it to form a *single* body.

13. The lung is developed out of the floor of the alimentary canae in the throat-region, behind the fundament of the unpaired thyroid gland.

(*a*) A groove-like evagination, which is constricted off from the alimentary canal as far forward as its anterior end,—the entrance to the larynx,—becomes larynx and windpipe.

(*b*) From the posterior end of the groove there grow out two sacs, which acquire at their ends vesicular enlargements and constitute the fundaments of the right and left bronchus, together with the corresponding lung.

(*c*) The want of symmetry between the right and left lung is early exhibited, since the right sac provides itself with three vesicular lateral buds, the fundaments of the three lobes, whereas the left sac forms only two buds.

(*d*) The further development of the lungs allows one to distinguish two stages, of which the first exhibits a great similarity to the development of an acinous gland. In the first stages the primitive pulmonary sacs increase in number by constrictions and at the same time become differentiated into a narrower conducting part, the bronchial tubes, and a broader vesicular terminal part. In the second stage the air-cells or pulmonary alveoli are formed.

14. From the intestinal canal proper there are formed only two glands, which are large and developed from the duodenum—the liver and the pancreas.

15. The liver is developed as a branched tubular gland which becomes a network.

(*a*) There grow out from the duodenum into the ventral mesentery or prehepaticus (Vorleber) two liver-tubes, the fundaments of the left and right lobes of the liver.

(*b*) The tubes form hollow or solid lateral branches, the hepatic cylinders, which are united into a network and become in part bile-ducts, in part the secretory parenchyma of the liver and biliary capillaries.

(*c*) The ductus choledochus arises as an evagination of the wall of the duodenum which receives the two hepatic tubes, and it forms at one place an evagination which becomes the gall-bladder and the cystic duct.

16. From the ventral mesentery, into which the hepatic tubes grow, are derived the serous investment and a part of the ligamentous apparatus of the liver, namely, the lesser omentum (ligamentum hepato-gastricum and hepato-duodenale) and the ligamentum suspensorium hepatis.

17. The pancreas grows from the duodenum into the dorsal mesentery and into the mesogastrium.

18. The mesentery which the pancreas originally possesses subsequently disappears by becoming fused with the posterior wall of the trunk; at the same time, in consequence of the twisting of the stomach, the long axis of the pancreatic gland comes to lie in the transverse axis of the body.

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CHAPTER XV.

THE ORGANS OF THE MIDDLE GERM-LAYER.

VOLUNTARY MUSCULATURE, URINARY AND SEXUAL ORGANS.

THE organs which take their origin from the middle germ-layer stand in the closest genetic relation to the morphological products of the entoblast. For, as was stated in the first part of this work, the middle germ-layer is developed by a process of evagination from the inner germ-layer, and is therefore, like the latter, an epithelial membrane, which serves as the boundary of a cavity. In view of its origin, is it remarkable that the organs arising from it are of a glandular nature, and such as produce excretions by means of genuine epithelial glandular cells?

In earlier times this phenomenon was the cause of a good deal of difficulty, because since the time of REMAK there had been an endeavor to bring the middle germ-layer as a non-epithelial structure into contrast with the other germ-layers. Attempts were also made to explain this supposed contradiction by assuming that the glandular organs in question were derived, sometimes in one way, sometimes in another, from the outer germ-layer. With the acceptance of the cœlom-theory, however, the theoretical objections to the production of glands by the middle germ-layer have ceased to have any foundation.

Out of the middle germ-layer, or, otherwise expressed, out of the epithelial wall of the embryonic body-sacs, are developed—aside from the mesenchyme, concerning the source of which an extended account was given in the ninth chapter—three very different products: first the whole voluntary musculature, secondly the urinary and sexual organs, thirdly the epithelial or endothelial linings of the large serous cavities of the body.

I. The Development of the Voluntary Musculature.

The total, transversely striped, voluntary musculature, aside from a part of the muscles of the head, arises from those parts of the middle germ-layer which have been differentiated as primitive segments, and with their appearance have effected the first primitive and most important segmentation of the vertebrate body. As has been previously stated, the segmentation affects the head as well as the trunk, so that trunk-segments and head-segments must be distinguished. Since the latter are in many points distinguished in their origin and metamorphosis from the former, a separate description of the two is fitting. I begin with the history of the metamorphosis of the primitive segments of the trunk, and treat of the same first in Amphioxus and the Cyclostomes, which furnish the simplest and most easily interpreted conditions, and then in the Amphibia, and finally in the higher Vertebrates.

A. Primitive Segments of the Trunk.

In Amphioxus the primitive segments (fig. 103 *ush*) are sacs, which are provided with a large cavity, and the walls of which are composed of a single layer of epithelial cells. The latter are further developed in two ways, for an accurate knowledge of which we are indebted to HATSCHEK. Only the cells (fig. 189) which abut upon the chorda (*ch*) and the neural tube (*n*) are destined to form muscle-fibres; they increase considerably in size, project far into the cavity of the primitive segment, and assume the form of plates; these lie parallel to one another and to the longitudinal axis of the body; and one margin, which I shall designate as the base, is placed perpendicularly upon the surface of the chorda. Very early (in the stage with ten primitive segments) the cell-plates begin at their bases to be differentiated into transversely striped muscle-fibrillæ, with which the embryos are already able to execute feeble contractions. By the continual addition of new fibrillæ to those which are formed at the surface of the chorda, and by an extension of the differentiation to both the surfaces of the cell-plates which are in contact with each other, there arise the transversely striped *muscle-layers* (Muskelblätter) which are characteristic of the musculature of Amphioxus. These are attached to the chorda on the right and left like the leaves of a book. The more the fibrillæ increase in number, the more the protoplasm of the formative cells between them diminishes in amount and the more is the nucleus with a remnant of protoplasm forced toward that edge of the cell which faces the cavity of the primitive segment.

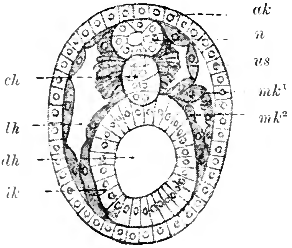


Fig. 189.—Cross section through the middle of the body of an Amphioxus embryo with 11 primitive segments, after HATSCHEK.

ak, *ik*, Outer, inner germ-layer; mk^1, mk^2, parietal, visceral lamella of the middle germ-layer; *us*, primitive segment; *n*, neural tube; *ch*, chorda; *lh*, body-cavity; *dh*, intestinal cavity.

The remaining cells of the primitive segment are converted into a low pavement-epithelium, which neither now nor later takes part in the formation of muscles. (Cutis-layer of HATSCHEK.)

Having arisen in the vicinity of the chorda, the muscle-layer in older animals spreads out both dorsally and ventrally, and thus furnishes the total voluminous musculature of the trunk, which, like the cellular primitive segments from which it is derived, is separated into successive portions (the myomeres).

In general the Cyclostomes (fig. 190) agree in the development of their muscles with Amphioxus. Here, as there, one must distinguish between an inner muscle-forming epithelial layer (*mf*), which bounds the chorda (*Ch*) and the neural tube (*N*), and an outer indifferent epithelial layer (*ae*), which occupies the side toward the epidermis. The latter (*ae*) consists of low flat cells, the former of very broad and elongated plates (*mk*), which as in Amphioxus are arranged perpendicularly to the surface of the chorda and neural tube. Since in Petromyzon the primitive segments are destitute of cavities, the two epithelial layers lie immediately in contact, and are continuous with each other, both dorsally and ventrally, by means of transitional cells (*WZ*), in the same way that in the fundament of the lens its epithelium is continuous with the lens-fibres. Muscle-fibrillæ (*mf*) are now differentiated on both the broad surfaces of the cell-plates. Thus arise muscle-layers (Muskelblätter) which are perpendicular to the chorda. These layers are each composed of two sheets of the finest fibrillæ, running parallel to one another. The two sheets are separated from each other by a delicate film of cementing substance; one of them owes its existence to one formative cell, the other to an adjacent cell.

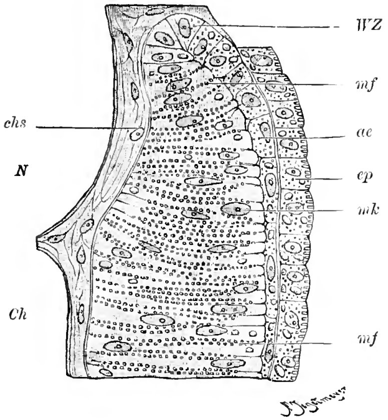


Fig. 190.—Cross section through the trunk-musculature of a larva of Petromyzon Planeri 14 days old. Magnified 500 diameters.

N and *Ch*, the part of the cross section which is adjacent to the neural tube and the chorda; *chs*, skeletogenous sheath of the chorda; *ep*, epidermis; *ae*, outer epithelial layer of the primitive segment; *mk*, nuclei of muscle-cells; *mf*, muscle-fibrillæ in cross section; *WZ*, zone of growth—transition from the outer cell-layer to the muscle-forming layer of the primitive segment.

In older larvæ the primitive segments spread out both above and below; accompanying this process there is a continual formation of new muscle-layers from the previously mentioned cells (*WZ*). The upper and lower margins of the primitive segments therefore constitute a *zone of proliferation*, by means of which the musculature of the trunk is continually growing further dorsad and ventrad.

At a later stage of development, in larvæ six weeks old (fig. 191), the muscle-layers are converted into *Muskelkästchen* (*k*), as Schneider has named these peculiar definite structural elements of the Cyclostomes. The facing fibrillæ-sheets of two adjacent layers (Blätter) unite with each other along their margins. Since these sheets have been produced on the two sides of one cell-plate, each formative cell is now surrounded on all sides, as though with a mantle, by the fibrillæ which it has generated.

Finally, three alterations of the Muskelkästchen take place. The homogeneous cementing substance, which was indicated during the first stage by only a fine line between the two fibrillæ-sheets of a muscle-layer, increases and produces the partition by means of which the individual Muskelkästchen are separated from each other, and in which afterwards connective-tissue cells and blood-vessels are also to be found. Secondly, the protoplasmic matrix of the formative cells is almost completely consumed in the continued production of numerous fine fibrillæ, which finally fill the whole interior of the Kästchen. One can now distinguish two different kinds of fibrillæ—those that are centrally located, and those that are firmly attached to the partitions. Thirdly, there are to be found scattered between the fibrillæ numerous small nuclei, which probably are descended from the original single nucleus of the formative cell by frequently repeated division.

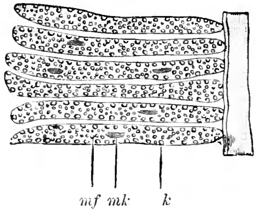


Fig. 191.—Cross section through the trunk-musculature of a larva of Petromyzon Planeri 6 weeks old. Magnified 500 diameters.

k, Muskelkästchen; *mk*, nuclei of muscle-cells; *mf*, muscle-fibrillæ cut crosswise.

The development of the muscle-segments takes place in the remaining Vertebrates in a somewhat different manner from that of Amphioxus and the Cyclostomes. For the study of this process the tailed Amphibia furnish the most instructive objects. In Triton (figs. 106, 105 *ush*) each of the primitive segments contains a considerable cavity, which is bounded on all sides by large cylindrical epithelial cells. In somewhat older embryos active cell-multiplication takes place in the part of the epithelium which is adjacent to the chorda and neural tube, and which, therefore, corresponds to the previously described muscle-forming layer of Amphioxus and the Cyclostomes. By this growth the cavity of a primitive segment becomes entirely filled. At the same time the cells lose their original arrangement and form; they are converted into longitudinally arranged cylinders, which correspond in length to a primitive segment and are located by the side of and above one another on both sides of, and parallel to, the spinal cord and chorda dorsalis (fig. 192). Each cylinder, which in the beginning exhibits only a single nucleus (*mk*), becomes surrounded with a mantle of the finest transversely striped fibrillæ (*mf*); it is now comparable with a Muskelkästchen of the Cyclostomes (fig. 191). A series of further alterations also takes place in this instance as in the former. In older larvæ there are continually being formed more fibrillæ (fig. 193), which gradually fill the interior portion of the cylinder. Only in the axis of the latter are there places left free, in which the small nuclei (*mk*) come to lie; these, formed by division of the single mother-nucleus, increase considerably in number. Moreover, connective tissue with blood-vessels now penetrates between the muscle-fibres or the primitive bundles (*pb*), as the finished elements are subsequently called.

If we consider from a general point of view the facts here presented, —which have been acquired in the study of the lower Vertebrates,— we arrive at two propositions of importance concerning the origin of the musculature:—

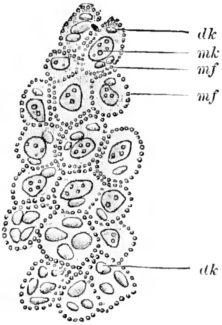


Fig. 192.

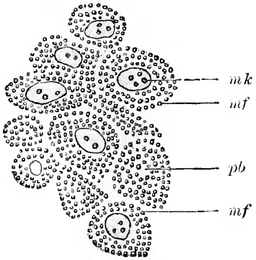


Fig. 193.

Fig. 192.—Cross section through the musculature of the trunk of a larva of Triton tæniatus 5 days old. Magnified 500 diameters.
mk, Nuclei of muscle-cells; *mf*, muscle-fibrillæ cut crosswise; *dk*, yolk-granules.

Fig. 193.—Cross section through the musculature of the trunk of a larva of Triton tæniatus 10 days old. Magnified 500 diameters.
pb, Primitive bundle of muscle-fibrillæ (Muskelprimitivbündel); *mf*, muscle-fibrillæ cut crosswise; *mk*, nuclei of muscle-cells.

(1) *In Vertebrates the elements of the musculature of the trunk are developed out of epithelial cells which are derived from a circumscribed territory of the epithelium of the body-cavity,—a territory that is constricted off from the latter to form the primitive segments.*

(2) *The epithelial products become surrounded and enveloped on all sides by connective tissue, just as do the glands and gland-ducts that bud forth from an epithelium.*

A comparison with the condition and development of the musculature of some classes of Invertebrates leads to a still better comprehension of the above propositions. In most of the Cœlenterates the muscular elements are components of the epithelium, not only during their development, but also in the adult animal, so that the designation *epithelio-muscular cells* is suitable for them.

The characteristic feature of these consists in their being simple—sometimes cubical, sometimes cylindrical, sometimes thread-like—epithelial cells, the outer ends of which ordinarily reach the surface of the epithelium and are here provided with cilia, whereas their basal ends lie upon the sustentative lamella (Stützlamelle) of the body and are there differentiated into one or several either smooth or transversely striped muscle-fibrillæ. Inasmuch as the fibrillæ of numerous cells lie parallel and close to one another, *muscle-lamellæ* arise, by the activity of which the changes in the form of the body are produced. *In Cœlenterates both the outer and the inner germ-layers can develop muscle-cells.*

When one turns to the Vermes it is seen, in those groups in which a body-cavity (an enterocœl) is formed by an infolding of the inner germ-layer, that the parietal wall of the body-cavity, or the parietal lamella of the middle germ-layer, has assumed the production of the entire musculature of the trunk. Here also, for example in the Chætognatha, etc., the epithelial cells differentiate at their basal ends, which are directed toward the surface of the body, a lamella of muscle-fibrillæ, whereas their other ends bound the body-cavity. *Thus from the lower to the higher animals the capability of producing muscles is, with the progressive differentiation of the body, more and more restricted to a limited special territory of the total epithelial investment of the body.*

This process has proceeded furthest in the Vertebrates, for in them the musculature of the trunk is no longer furnished by the whole parietal lamella of the middle germ-layer, but by only a small detached part of it, the primitive segments. Consequently in Vertebrates the musculature spreads out from a small region where it originates, distributes itself first in the trunk, and then from the latter grows out into the extremities.

In the Vertebrates we recognised two different forms of voluntary musculature, the muscle-layer (and the Muskelkästchen derivable from it) and the primitive bundle (Muskelprimitivbündel). Parallels to this are found in the Invertebrates, both in Cœlenterates and in Worms. In Cœlenterates both forms are derived from the primitive smoothly outspread muscle-lamella by the formation of folds, and are to be explained in the same way as the formation of those folds which in epithelial lamellæ play such an important part in the origin of the most various organs. When certain tracts of a muscle-lamella are called upon to execute additional labor, this can be effected only by an increase in the number of the fibrillæ lying parallel to one another. But a greater number of fibrillæ can be brought into a circumscribed territory only in one or the other of two ways: either by their coming to lie in several layers one above another, or—if the more simple arrangement of lying side by side is to be retained—by the folding of the muscle-lamella. The folding exhibits two modifications. Sometimes there are produced parallel daughter-lamellæ placed side by side and perpendicular to the mother-lamellæ; sometimes the folded lamellæ become wholly detached from the parent-layer and converted into muscle-cylinders, which imbed themselves in the underlying sustentative lamella.

With the conception here presented of the origin of the transversely striped muscle-fibres of Vertebrates, it must be assumed as very probable that subsequently an increase in their number will take place as a result of constriction and detachment into two parts, as was first maintained by WEISMANN.

In Amphioxus, the Cyclostomes, and the Amphibia the most important function of the primitive segments is the production of the fundament of the transversely striped and voluntary musculature. On the other hand it is not very evident that the primitive segments also share, in the manner previously (p. 172) described, in the development of the mesenchyme; this is correlated with the fact that in general the connective and sustentative substances play a slight rôle in the construction of the bodies of the lower Vertebrates, and especially during larval life are developed to only a very insignificant amount.

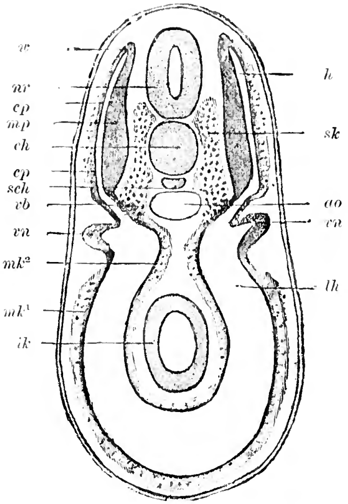


Fig. 194.– Cross section through the region of the pronephros of a Selachian embryo, in which the muscle-segments [myotomes] (*mp*) are in process of being constricted off. Diagram after WIJHE.

nr, Neural tube; *ch*, chorda; *ao*, aorta; *sch*, subnotochordal rod; *mp*, muscle-plate of the primitive segment; *w*, zone of growth, where the muscle-plate bends around into the cutis-plate (*cp*); *vb*, tract connecting the primitive segment with the body-cavity, out of which are developed, among other things, the mesonephric tubules (fig. 205 *uk*); *sk*, skeletogenous tissue, which arises by a proliferation from the median wall of the connecting tract *vb*; *vn*, pronephros; *mk*¹, *mk*², parietal and visceral middle layer, from whose walls mesenchyme is developed; *lh*, body-cavity; *ik*, entoblast.

This is altered in the Selachians and the three higher classes of Vertebrates. Not only does the mesenchyme in the adult bodies of these attain a more voluminous development and a degree of differentiation that is in all directions more advanced, but it is also established earlier and likewise in greater abundance. Therefore the primitive segments here exhibit in their metamorphosis somewhat modified phenomena. At the same time with the differentiation of the muscular tissue, and in part even before that event, the development of mesenchyme is observable. The primitive segment (fig. 194) in this case is differentiated from the start into two equally distinct fundaments, of which the one is designated as *sclerotome* or skeletogenous layer (*sk*), the other as muscle-plate (*mp*). While referring the reader to the ninth chapter, I add to the presentation given there a few further statements.

In the Selachians the skeletogenous layer, the origin of which has already been described, grows upward at the side of the chorda (fig. 195 *Vr*). Outside of this layer one finds the part of the primitive segment which serves for the formation of muscle. This consists of an inner layer (*mp'*) and an outer layer (*mp*), which are separated from each other by the remnant of the cavity of the primitive segment (fig. 194 *h*). The inner layer (fig. 195 *mp'*) is in contact with the skeletogenous tissue (*Vr*), and is composed of numerous, superposed, spindle-shaped cells, which are arranged longitudinally and give rise to transversely striped muscle-fibrillæ; they correspond to the inner wall of the primitive segment in the larvæ of Amphioxus (fig. 189) and Cyclostomes, which is in direct contact with the chorda. The outer layer lies in contact with the epidermis, and remains for a long time composed of cubical epithelial cells. Dorsally and ventrally it bends around into the muscle-forming layer, and here contributes to the enlargement of the latter, as in Amphioxus and the Cyclostomes, by its cells becoming longer and being metamorphosed into muscle-fibres (fig. 185). The muscle-plate then spreads out farther into the wall of the trunk both above and below (figs. 185 and 205). At the same time its cavity (myocœl) gradually disappears. The muscle-forming layer (fig. 185 *mp'*) continues to increase in thickness, since the number of muscle-fibres becomes greater; the outer layer also loses, rather late it is true, its epithelial character, and is concerned on the one hand in the development of the corium (fig. 205 *cp*), while on the other it furnishes an additional outer, thin muscle-lamella. This observation, made by BALFOUR, has often been called in question, but has recently been confirmed by VAN WIJHE.

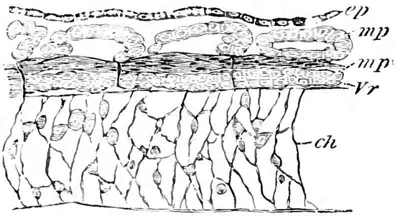


Fig. 195.—Horizontal longitudinal section through the trunk of an embryo of Scyllium, after BALFOUR.
The section is made at the height of the chorda, and shows the separation from the muscle-plates of the cells which form the bodies of the vertebræ.
ch, Chorda; *ep*, epidermis; *Vr*, fundament of the bodies of the vertebræ; *mp*, outer cell-layer of the primitive segment; *mp'*, portion of the primitive segment which has already been differentiated into longitudinal muscles (muscle-plate).

In Reptiles, Birds, and Mammals the proliferation of the primitive segments which furnishes the skeletogenous tissue is still more extensive than in Selachians. Thereby the muscle-plate, or the dorsal plate, as it is also called, is crowded farther away from the chorda. The differentiation of muscle-fibres follows at a much later stage of development, in comparison with Amphioxus and the Cyclostomes. The inner layer of the muscle-plate is converted into longitudinal muscle-fibres, the outer contributes to the formation of the corium (fig. 202).

Let us now consider somewhat more in detail the *original condition of the musculature.* It shows at the beginning complete uniformity in all classes of Vertebrates. Everywhere there appears as its foundation a very simple system of longitudinal contractile fibres, which first appear near the chorda and neural tube and spread themselves out thence dorsally toward the back and ventrally in the wall of the belly. The muscle-mass is divided in a very uniform manner into separate segments or myomeres by means of connective-tissue partitions (ligamenta intermuscularia), which run transversely or obliquely to the vertebral column. In the lower Vertebrates this condition persists, in the higher ones it gives place to a more complicated arrangement.

We cannot recount more precisely the details of the manner in which the groups of muscles of the higher Vertebrates, so various in form and position, are derived from the original system, especially since this field of embryology has been as yet little cultivated; let attention be here called to only two points, which come in question in the differentiation of the groups of muscles.

First, a very important factor is furnished in the development of the skeleton, which with its processes affords points of attachment for muscle-fibres. Some of these find in this way opportunity to detach themselves from the remaining mass.

Secondly, the development of the limbs, which arise as protuberances at the side of the trunk (figs. 157 and 158), operates toward a greater differentiation of the musculature. The limbs likewise acquire their musculature, which in the higher Vertebrates has a very complicated arrangement, from the primitive segments, as has been learned through the investigations of Kleinenberg and Balfour, as well as recently through the very convincing accounts of Dohrn.

In the Selachians, in which the processes are most clearly recognisable, *cell-buds sprout forth out of the still hollow primitive segments and grow into the paired and median fins, in which they become metamorphosed into muscle-fibres.* The fact that always from a large number of primitive segments buds are given off to a fin is *worthy of attention,* because it demonstrates that the extremity is a structure that belongs to several somites.

B. The Segments of the Head.

Important works on the development of the head have appeared in late years by Goette, Balfour, Marshall, Wijhe, Froriep, Rabl, and others. They have led to the important conclusion that the head is made up of a large number of segments, in the same manner as the trunk. These conditions are most evident in the Selachians.

When in these animals the middle germ-layers have grown into the fundament of the head, they here, as in the trunk, early separate from each other, and thus embrace on either side a narrow, fissure-like space, the head-cavity. This is continuous posteriorly with the general body-cavity. It follows from this that *the two primitive body-sacs (cœlom-sacs) possess a greater extent in the embryo than they do subsequently, since they reach into the most anterior part of the embryonic fundament, the head.*

In the further course of development the walls of the head-cavity are differentiated, in the same manner as the walls of the body-cavity, into a ventral portion and a dorsal portion, the latter producing primitive segments. Then there arises, however, an important difference between head and trunk; in the trunk only the dorsal portion is segmented, but in the head both ventral and dorsal portions are segmented, each in a manner peculiar to itself.

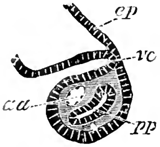


Fig. 196.—Cross section through the next to the last visceral arch of an embryo of Pristiurus, after Balfour. *ep*, Epidermis; *vc*, inner visceral pouch; *pp*, segment of the body-[head-] cavity in the visceral arch; *aa*, blood-vessel of the visceral arch (aortic arch).

The ventral part of the head-cavity is divided, in consequence of the development of the visceral clefts, into separate segments (branchiomeres Ahlborn), the first of which is situated in front of the first cleft, each of the remaining ones between two clefts. Each segment (fig. 196) consists of a wall composed of cylindrical cells and encloses a narrow cavity. With its enveloping connective tissue it constitutes the visceral arches, which are separated from one another by the visceral clefts; for this reason the fissures arising from the head-cavity have been designated by Wijhe as visceral-arch cavities. The latter communicate for a time under the gill-pouches with the pericardial chamber surrounding the heart. But then they begin to be closed; their walls come into contact; and out of the cylindrical epithelial cells are developed the transversely striped muscle-fibres *which produce the muscles of the jaws and gills.*

Consequently there results for the head-region of Vertebrates this important proposition: *the head-musculature is developed not only out of the primitive segments, but also out of a part of the epithelium of the head-cavity which corresponds to the lateral plates of the trunk; whereas the latter do not contribute to the formation of muscles.*

So far as regards the dorsal part of the middle germ-layer in the head-region, it is divided, as in the trunk, into primitive segments, which in the Selachians are nine in number and embrace each a cavity, with the exception of the first, which is solid. They arise first in the posterior region of the head, and increase from there forward. *The segmentation of the whole body is therefore accomplished in the Selachians—and the same is likewise true for all the remaining Vertebrates—in such a manner that it begins in the neck-region, and proceeds thence on the one hand backward to the tail, on the other forward.*

The walls of the primitive segments of the head in part furnish muscles, in part degenerate. Out of the first three pairs arise the eye-muscles, as MARSHALL and WIJHE have demonstrated in detail. The first segment envelops the primitive eye-vesicle like a cup, and is differentiated into musculus rectus superior, rectus inferior, and obliquus inferior. The second pair gives origin to the obliquus superior, and the third pair to the rectus externus. The segments from the fourth to the sixth inclusive disappear, while out of the last three are developed muscles which extend from the skull to the pectoral girdle.

In the remaining Vertebrates the metamorphosis of the middle germ-layer in the head has not been investigated in so exhaustive a manner as in the case of the Selachians. There do not appear to be any head-cavities developed, because the middle germ-layers remain at all times pressed together. However, we know that primitive segments are demonstrable even here. GOETTE describes four pairs of them in Bombinator; FRORIEP finds in Mammals in the occipital region alone on either side four muscle-segments, of which the two most anterior are believed subsequently to degenerate. In individual cases there still remains much to be elucidated by more exhaustive investigations.

RABL has recently expressed dissent in some points from the exposition of the head-segments as given by WIJHE. He divides the head-segments into two groups—four anterior or proximal, and five posterior or distal. Only the latter are according to RABL to be compared with the trunk-segments; whereas the first, owing to their method of origin, must take a separate position.

II. The Development of the Urinary and Sexual Organs.

The development of the urinary and sexual organs cannot be discussed separately in two chapters, because these systems of organs are most intimately connected with each other, both anatomically and genetically.

First, both take their origin at one and the same place on the epithelial investment of the body-cavity; secondly, parts of the urinary system subsequently enter into the service of the sexual apparatus, for they furnish the passages or canals which are entrusted with the evacuation of the eggs and semen. In anatomy also one therefore properly embraces the two genetically united systems of organs under the common name of urogenital system or apparatus.

Again in this subject we turn to one of the most interesting portions of embryology. The urogenital system claims an interest particularly from a morphological point of view, because a great number of important metamorphoses are effected in it during embryonic life. In the higher Vertebrates the pronephros and the mesonephros are formed first; they are organs of an evanescent nature, which in some cases disappear and are replaced by the permanent kidney, in other cases their ducts alone are preserved. But these transitory structures correspond to organs which are permanently functional in the lower Vertebrates.

In late years, the attention of investigators having been directed to a series of entirely new and unexpected phenomena, by the excellent researches of Waldeyer and Semper, the topic "urogenital organs" has been carefully worked out by very many different observers through the investigation of each separate class of Vertebrates. There has arisen a voluminous literature, and many important facts have been brought to light. Nevertheless it is not to be denied that conceptions concerning many fundamental questions are still very divergent.

As in several previous chapters, I shall also here give to the discussion a broader foundation by treating somewhat more exhaustively of the lower Vertebrates in certain questions.

(*a*) *The Pronephros and the Mesonephric Duct.*

The first thing that becomes noticeable in the origin of the urogenital apparatus is the fundament of the pronephros [head-kidney]. This is a structure which has now been demonstrated in the embryos of all Vertebrates, but which plays in some a greater part, in others a lesser one. In some Vertebrates (Myxine, Bdellostoma, Bony Fishes) it is retained permanently; in others, as the Amphibia, it grows during larval life to an important organ, which disappears after the animal's metamorphosis; finally, in the Selachians and Amniota its fundament is from the beginning very rudimentary. In the latter case it was held to be the front end of the mesonephric duct, until through comparative embryology the right view had been attained.

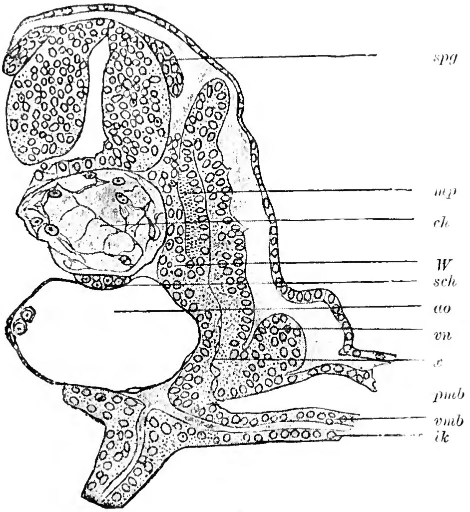


Fig. 197.

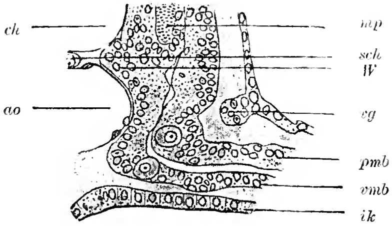


Fig. 198.

Figs. 197 and 198.—Two cross sections through an embryo of Pristiurus, after Rabl. Cross section fig. 198 lies a little farther back than section fig. 197.

ch, Chorda; *spg*, spinal ganglion; *mp*, muscle-plate of primitive segment; *W*, skeletogenous tissue which has grown forth from the median wall of the primitive segment; *sch*, subnotochordal rod; *ao*, aorta; *ik*, inner germ-layer; *pmb*, *vmb*, parietal, visceral middle layer; *vn*, pronephros; *cg*, pronephric duct; *x*, fissure in the primitive segment, which is still in communication with the body-cavity.

I select as types of the development of the pronephros the Selachians, Amphibia, and Birds.

In Selachians of about twenty-seven somites the pronephros begins with the third or fourth trunk-segment and is developed from there backwards. At the place where the segmented portion of the middle germ-layer is continuous with the lateral unsegmented portion, there grow out of its parietal lamella a number of cell-cords (fig. 197 *vn*) segmentally arranged one behind another, in Torpedo six, in Pristiurus four, which bend backwards and become united into a longitudinal cord. Soon afterwards the fundaments acquire small cavities through disassociation of the cells. In this manner there has now arisen between epidermis and parietal middle layer a longitudinal canal, which stretches over several segments of the trunk and communicates with the body-cavity by means of several successive openings, the pronephric funnels (fig. 194 *vn*). At one place the pronephric duct comes close up to the epidermis and fuses with it (fig. 198 *vg*). Although an actual opening is never formed here, still, supported by this fact, one may express the conjecture that originally the pronephros in Vertebrates opened out at a point far forward on the body (VAN WIJHE, RÜCKERT).

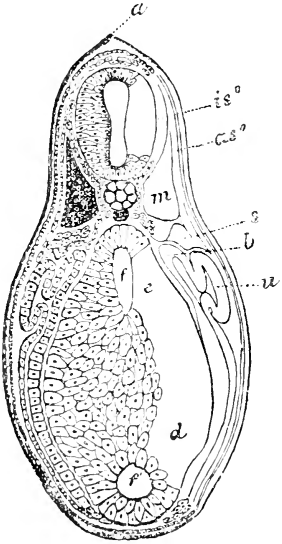


Fig. 199.—Cross section through a very young Tadpole of Bombinator in the region of the anterior end of the yolk-sac, after GOETTE.

a, Fold of the outer germ-layer that is continued into the dorsal fin; *is**, spinal cord; *m*, lateral muscle; *as**, outer cell-layer of the muscle-plate; *s*, mesenchymatic cells; *b*, transition of the parietal into the visceral middle layer; *u*, pronephros; *f*, intestinal cavity; *e*, entoblast, which is continuous with the mass of yolk-cells (*d*); *f'*, ventral cœcal pouch of the intestine, which becomes the liver.

A short time after its formation the fundament undergoes in its anterior half a complete degeneration; the posterior half, on the contrary, is further developed and enlarges, but remains in connection with the body-cavity by means of a single funnel only (fig. 194 *vn*), either because, as VAN WIJHE asserts, the several funnels are fused into a single one, or because, in accordance with the account of RÜCKERT, all the funnels except a single one become closed and degenerate.

In the Amphibia, with which the Bony Fishes exactly agree in this point, the pronephros is established in the most anterior part of the trunk as an organ that is from the beginning hollow (fig. 199). Below the primitive segments, which have already been differentiated into muscle-fibres (*m*), there appears a groove-like evagination (*u*) of the parietal layer of the peritoneum, which stretches from in front backward over several somites. By detaching itself from its parent-tissue at several places, and remaining in connection with it at others, it is converted into a longitudinal canal, which in Rana and Bombinator communicates with the body-cavity by means of three pronephric funnels, in Triton and Salamander by means of two. The whole fundament soon after, during the larval life, acquires ample proportions, owing to the fact that the nephridial funnels grow out into long and very tortuous tubes (pronephric canals). (Fürbringer, Goette.)

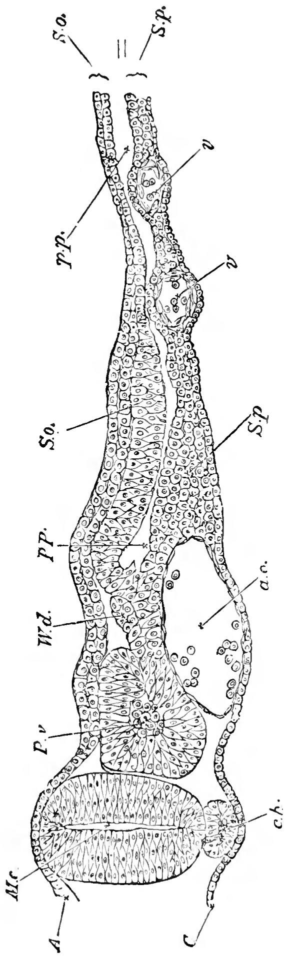


Fig. 200.– **Cross section through the dorsal region of an embryo Chick of 45 hours**, after Balfour.
The section shows the middle germ-layer partially separated into the primitive segment (*P.v*) and the lateral plate, which embraces between its lamellæ the body-cavity (*p.p*).
M.c, Medullary (neural) tube; *P.v*, primitive segment; *S.o*, somatopleure; *S.p*, splanchnopleure; *p.p*, body-cavity; *c.h*, chorda; *A*, outer; *C*, inner germ-layer; *a.o*, aorta; *v*, blood-vessel; *W.d*, Wolffian duct.

In Birds, with which Reptiles and Mammals agree, the pronephros appears, much as in Selachians, in a more or less rudimentary form (Sedgwick, Gasser, Renson, Siemerling, Weldon, Mihalkovics). It is first observable in embryo Chicks having eight primitive segments and in the region of the seventh somite; in older embryos it is developed from this place backward into the region of the twelfth somite. At the place where the primitive segments (fig. 200 *P.v*) are constricted off from the lateral plate (*S.o*), but still remain for some time in continuity with it by means of a connecting region (the middle plate), there grows out from the parietal lamella of the middle germ-layer (somatopleure) a ridge of cells (*W.d*), which is directed toward the overlying epidermis. Later, like the corresponding furrow in the Amphibia, it becomes detached in places from its parent-tissue, and when, meanwhile, the primitive segments have likewise wholly detached themselves from the lateral plates, it is converted into a longitudinal cord, which is united with the epithelium of the body-cavity by means of short transverse branches. Similar conditions exist in Reptiles and Mammals.

Finally, the pronephros subsequently acquires a peculiar condition from the fact that there are developed out of the wall of the body-cavity, in the vicinity of the openings of its tubules, one or several vascular glomeruli. In the Chick for example (fig. 201), in the region from the eleventh to the fifteenth somites, there is a proliferation of connective tissue on either side of the mesentery (*me*),—by means of which the right and left pronephridia are separated from each other,—which grows into the body-cavity as a spheroidal body (*gl*).

A blood-vessel from the aorta penetrates into each proliferation and is here resolved into a tuft of capillaries, which are then united again into an efferent vessel. Only in those Vertebrates in which the pronephros is functional, as in the larvæ of the Amphibia, in the Cyclostomes and the Teleosts, does the glomerulus attain to a considerable development, whereas in the Selachians and Amniota it remains rudimentary. In the first case fluid or urine is probably secreted by this apparatus, and then taken up by the openings of the pronephric tubules and conducted outside the body by means of the pronephric duct, which is to be discussed directly. There is one point in this connection that is noteworthy and characteristic of the structure of the pronephros: the glomerulus is developed, not in the wall of the pronephric tubule itself, as is the case in the tubules of the mesonephros, but in the wall of the body-cavity, so that the urine can be evacuated only through the agency of the latter.

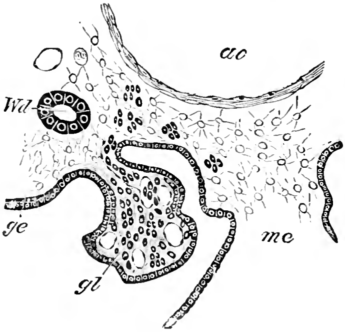


Fig. 201.—Cross section through the external glomerulus of a pronephric tubule of an embryo Chick of about 100 hours, after Balfour.

gl, Glomerulus; *ge*, peritoneal epithelium; *Wd*, mesonephric (Wolffian) duct; *ao*, aorta; *me*, mesentery. The pronephric tubule and its connection with the glomerulus are not shown in this figure.

But in what manner does the pronephros communicate with the outside?

This communication takes place by means of a longitudinal canal, which is developed in immediate continuation with the pronephros, and, beginning in front, gradually grows backwards until it reaches the proctodæum and opens into the cloaca. It is found in all Vertebrates in the region where the primitive segments abut upon the lateral plates. At the time of its origin it is always close under the epidermis, later it is farther and farther removed from the latter by the ingrowth of embryonic connective tissue, and comes to lie very deep (fig. 202 *wd* and fig. 205 *ug*). This canal has acquired a number of different names, and is cited in the literature as *pronephric*, *mesonephric*, *Wolffian*, or *segmental duct*. The different designations are explainable from the fact that the canal alters its function in the course of the development of the nephridial system, serving at first as an outlet for the pronephros only, afterwards for the mesonephros.

Views concerning the origin of the canal were for a time conflicting. According to one supposition, which a few years ago almost all investigators entertained, the longitudinal canal of the pronephros, when it had been constricted off from the parietal wall of the body-cavity, protruded with its posterior end as a free knob into the space between outer and middle germ-layers, and gradually grew out independently, by multiplication of its own cells, as far as the hind gut (proctodæum). It was said, therefore, to be constricted off from neither the outer nor the middle germ-layers, nor yet to derive from them cell-material for its increase.

This interpretation has recently become untenable. As is reported in an entirely trustworthy manner concerning several different classes of Vertebrates,—for Selachians (Wijhe, Rabl, Beard), for Amphibia (Perenyi), for Reptiles (Mitsukuri), and for Mammals (Hensen, Flemming, Graf Spee),—the posterior end of the pronephric duct in process of growth is in these cases by no means an entirely isolated structure, but is in close union with the outer germ-layer. Attention has already been called to this fact apropos of the development of the pronephros. In a Selachian embryo the condition which is represented in fig. 197 is soon followed by a condition (fig. 198) in which, in a series of cross sections, the pronephric duct now appears as a ridge-like thickening of the outer germ-layer. By a study of various older embryos it can be further established, that the ridge-like thickening of the outer germ-layer is prolonged backwards by means of cell-proliferation in that layer, while in front it is being constricted off from the parent-tissue. The pronephric duct therefore grows at the expense of the outer germ-layer, and moves as it were along the latter, with its terminal opening behind, as far as to the hind gut.

When Hensen, Flemming, and Graf Spee made their observations on Mammals, they were thereby led to adopt the view that the mesonephric duct, as well as the whole urinary system, was derivable from the outer germ-layer. The union with the middle germ-layer they regarded as one that had arisen secondarily. But their conception cannot be brought into unison with the conditions of the pronephros which have been found in the remaining and especially in the lower Vertebrates (Selachians, Teleosts, Amphibia, Birds); on the other hand allowance is made for all observations, if we summarise them as follows: that the pronephros is developed from the "middle plate," and that then its posterior end comes into union with the outer germ-layer and in conjunction with the latter grows farther backward as the pronephric duct.

If this explanation, which has also been expressed by **Wijhe** and **Rückert**, is correct, then one can designate the pronephric duct at its first appearance as a short canal-like perforation of the wall of the body, which begins in the body-cavity with one or several inner ostia and opens out upon the skin by a single external orifice. Originally the outer and inner openings lay near together, later they moved so far apart that the outer opening of the canal united with the hind gut. It may be said, in favor of the view here presented, that in the Cyclostomes the more primitive condition, that is to say, the union with the skin, has been preserved. For in them the mesonephric duct opens to the outside at the abdominal pore.

That openings should arise between the cavities of the body and its outer surface is in no way remarkable. I call to mind the intestinal tube, at various places in the territory of which there are formed openings, as mouth, anus, and branchial clefts. Still more frequent are passages through the body-wall of Invertebrates. As such, arise the openings at the tips of the hollow tentacles of the Actinia, on the ring-canal of the Medusæ, and the canals (segmental organs) which in Worms lead out from the body-cavity and serve for the elimination of the sexual products and the excretions.

(*b*) *The Mesonephros.* (Wolffian Body.)

Following upon the origin of the pronephric system there is developed in all Vertebrates, after the lapse of a longer or shorter interval of time, a still more voluminous gland, serving for the secretion of urine, the primitive kidney (mesonephros) or Wolffian body. It is developed earlier in those cases in which the fundament of the pronephros is from the beginning only rudimentary, as in the Selachians and Amniota; it appears relatively late, on the contrary, in those Vertebrates in which the pronephros attains to a temporary functional activity, as in the Amphibia and Teleosts.

The mesonephros is established on the portion of the pronephric duct immediately behind the pronephric tubules. The duct consequently serves from this time forward as an outlet for the newly formed glandular organ also, and can therefore be designated as mesonephric or Wolffian duct.

When it is stated that a gland is developed on the mesonephric duct, one at first thinks that lateral buds grow out from its wall and give forth branches, as occurs in the fundaments of glands formed from the outer or the inner germ-layers. Nothing of the kind takes place here. All observers—with the exception of a few earlier investigators—agree rather that the glandular tubules of the mesonephros arise independently of the mesonephric duct. The source

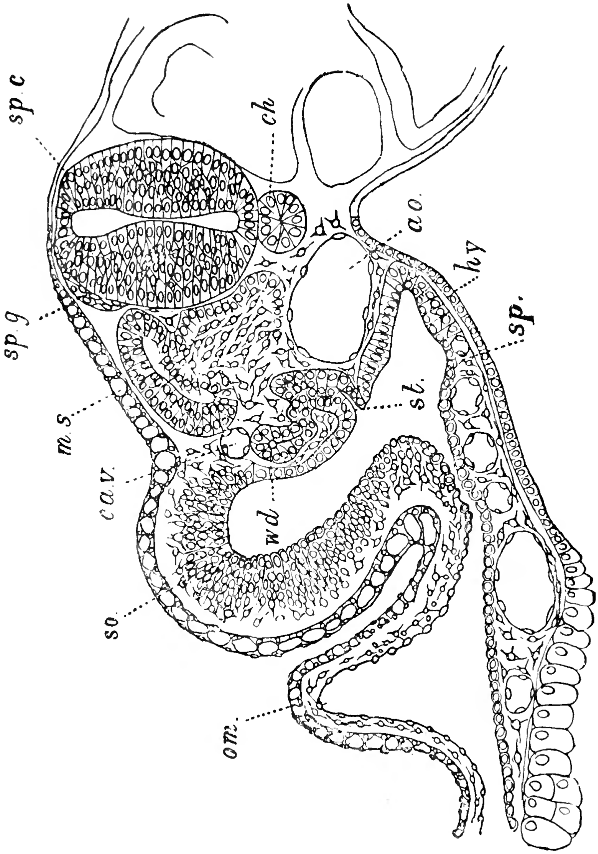


Fig. 202.—Cross section through the trunk of an embryo Duck with about 24 mesoblastic somites, after BALFOUR. One sees the four original germ-layers and the organs derived from them separated from one another by a small amount of connective substance containing embryonic stellate cells, and embracing, at the same time, the fundaments of the blood-vessels.

om, Amnion; *so*, somatopleuric, *sp*, splanchnopleuric mesoderm; *wd*, Wolffian duct; *st*, mesonephric tubules; *ca.v*, cardinal vein; *ms*, muscle-plate; *sp.g*, spinal ganglion; *sp.c*, spinal cord; *ch*, chorda dorsalis; *ao*, aorta *hy*, inner germ-layer.

of its material is either directly or indirectly the epithelium of the body-cavity, as it has been possible to prove in many cases—in Cyclostomes, Selachians, Amphibia, and Amniota.

There are formed, following one another in immediate succession, short transverse tubules (fig. 202 *st*), which are at one end continuous with the epithelium of the body-cavity, and at the other end, which remains for a long time closed, are joined to the mesonephric duct (*wd*), which runs close to them, but somewhat more laterad. The mesonephros elongates from before backward and attains a great length on both sides of the mesentery, for it reaches back from the region of the liver nearly to the posterior end of the body-cavity; it acquires a very delicate, regular condition, as the figure of an embryo Dog twenty-five days old shows (fig. 203 *un*), and can be designated as a *comb-shaped* gland, composed of a lateral collecting tube, running lengthwise of the body at a little distance from the mesentery, and,

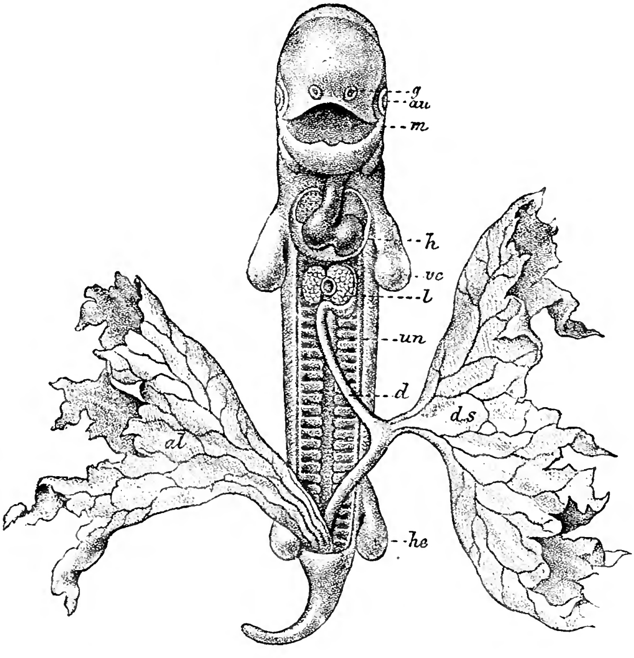


Fig. 203.—Embryo of a Dog of 25 days, straightened out and seen from in front, after Bischoff. Magnified 5 diameters.

d, Intestinal tube; *ds*, yolk-sac; *al*, allantois; *un*, mesonephros; *l*, the two lobes of the liver, with the lumen of the vena omphalomesenterica between them; *ve*, *he*, anterior and posterior extremities; *h*, heart; *m*, mouth; *au*, eye; *g*, olfactory pit.

attached to the median side of it, short transverse branches, which we shall designate as mesonephric tubules.

Whereas there can no longer exist any doubt about the origin of the mesonephric tubules from the middle germ-layer, the statements concerning the method of their formation are still at variance with one another. In accordance with the fundamental investigations of SEMPER, it was generally believed that the mesonephric tubules either were evaginated in metameric sequence along the dorsal wall of the body-cavity out of its epithelial lining, or grew forth as originally solid buds, as glandular sacs do from the outer or inner germ-layer.

This view, according to the more recent investigations of SEDGWICK, WIJHE, and RÜCKERT for the Selachians and the three higher classes of Vertebrates, is no longer adequate. In these cases the development of the mesonephric tubules is intimately connected with that of the primitive segments. When the latter begin to be more sharply separated from the lateral plates, there arises at the place of constriction a narrow stalk, which maintains for a time a connection between the two parts (fig. 204 *vb*). In the Selachians it possesses a small cavity, which unites the cavity of the primitive segment with the body-cavity. In the Amniota it is solid (fig. 200). Inasmuch as the successive cords (stalks) are here closely pressed together, they appear like a continuous cell-mass interpolated between primitive segment and lateral plate, and have been previously mentioned under the name of the *middle plate.* On account of its relation to the mesonephric tubules, the middle plate is also designated as mesonephric blastema. The mesonephric duct, split off from the outer germ-layer, is to be seen taking its way on the lateral side of and close to the connecting stalks of the primitive segments. Each of the connecting stalks, which RÜCKERT names at once *nephrotome,*—in contradistinction to the remaining parts of the primitive segment, which produce the muscle-plate (myotome) and the cell-material for the skeletogenous tissue (sclerotome),—is afterwards metamorphosed into a mesonephric tubule. Whereas one of its ends remains connected with the body-cavity, the other becomes separated from the primitive segment (fig. 205 *uk^1*), then applies itself closely to the mesonephric duct, fuses with the wall of the latter, and opens into it. In the diagram (fig. 205) the detachment of the connecting stalk from the primitive segment is shown on the right, the fusion of the detached end with the mesonephric duct on the left. According to this whole process of development the mesonephros is from the very beginning a segmentally formed organ, as can be best followed in the Selachians; for each mesonephric canal is developed in a single segment.

In Reptiles, Birds, and Mammals the connecting stalks are solid cords of cells (mesonephric cords). It is only when they have detached themselves from the primitive segment, and their blind ends have united with the mesonephric duct, that they acquire a small cavity (fig. 202 *st*). Now they also become more readily distinguishable as separate canals, since they become farther removed from

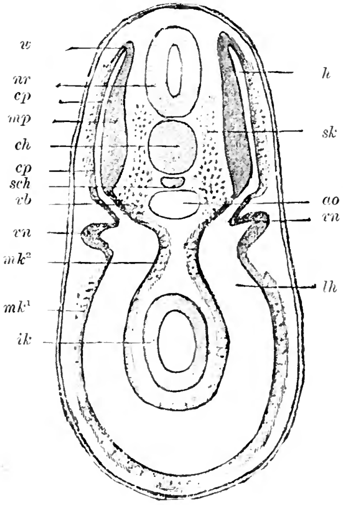


Fig. 204.

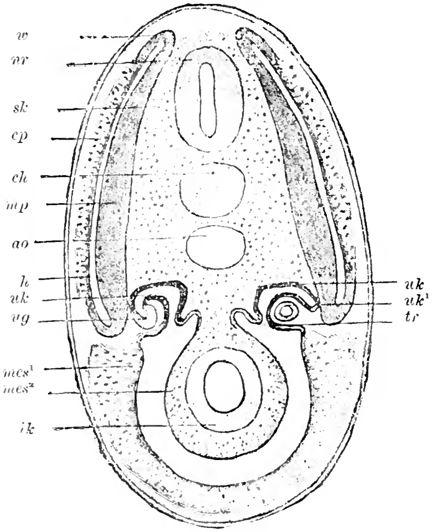


Fig. 205.

Figs. 204 and 205.—Diagrams of cross sections through a younger and an older embryo Selachian to show the development of the principal products of the middle germ-layer. After Wijhe, with some alterations.

Fig. 204.—Cross section through the region of the pronephros of an embryo in which the muscle-segments (*mp*) are in process of being constricted off.

Fig. 205.—Cross section through a somewhat older embryo, in which the muscle-segments have just been constricted off.

nr, Neural tube; *ch*, chorda; *ao*, aorta; *sch*, subnotochordal rod; *mp*, muscle-plate of the primitive segment; *w*, zone of growth where the muscle-plate bends around into the cutis-plate (*cp*); *vb*, the connecting piece which unites the primitive segment to the walls of the body-cavity, and from which are developed, among other things, the mesonephric tubules (fig. 205 *uk*); *sk*, skeletogenous tissue, which arises by a proliferation of the median wall of the connecting piece *vb*; *vn*, pronephros; *mk*¹, *mk*², parietal and visceral middle layer, out of which mesenchyma is developed; *lh*, body-cavity; *ik*, entoblast; *h*, cavity of the primitive segment; *uk*, mesonephric tubules, which have arisen from the connecting piece *vb* of the diagram fig. 204; *uk*¹, the place where the mesonephric tubule has been detached from the primitive segment; *ug*, mesonephric duct, with which, on the left side of the figure, the mesonephric tubule has united; *tr*, union of the mesonephric tubule with the body-cavity (nephridial funnel); *mes*¹, *mes*², mesenchyma that has arisen from the parietal and visceral middle layers.

one another and are marked off from the surrounding tissue by sharper contours.

Although it is often stated that in the Amniota the mesonephric tubules "*are differentiated out of*" the middle plate or the mesonephric blastema, it is nevertheless to be observed that this is not a case of new formation out of undifferentiated cell-material. The so-called middle plate at the time of its origin, in the manner previously described, is at once separated into segmentally arranged cords, which are afterwards metamorphosed into the mesonephric tubules. The differentiation out of a blastema is therefore here, as in most cases, to be conceived of as an increase in the distinctness of already established structures, which constitute a cell-mass that appears undifferentiated, but only on account of our limited means of discrimination.

In the Amphibia, Teleosts, and Ganoids the origin of the mesonephros deserves to be subjected to renewed investigation from the recently acquired points of view.

Soon after their union with the mesonephric duct the individual mesonephric tubules begin to grow somewhat in length, to take on S-shaped curves, and to be differentiated into three regions. The middle region undergoes a vesicular enlargement and is converted into a BOWMAN's capsule. Individual transverse branches from the primitive aortæ, which pass along close to the mesonephros, make their way to the capsules, and are there resolved into a tuft of capillaries. The knot of blood-vessels, or glomerulus, now grows into the epithelial vesicle, the median wall of which is pushed before it and invaginated into the interior. During this process the epithelial cells of the invaginated part of the wall become greatly flattened, whereas upon the opposite uninvaginated side they remain tall and cuboidal. Such a structure, consisting of a vascular glomerulus and the enveloping BOWMAN's *capsule*, is called a *Malpighian corpuscle*, an organ that is exceedingly characteristic of the primitive kidney (mesonephros) and the permanent kidney (metanephros) of Vertebrates.

In addition to the enlarged middle part, there is to be distinguished on each mesonephric tubule a narrow connecting portion, which continues to increase in length, running to the mesonephric duct, and, secondly, a short portion connecting with the body-cavity. The latter is metamorphosed in different ways in the separate classes of Vertebrates. In some, as in many of the Selachians, it retains its original connection with the body-cavity even in the adult animals; it begins at the peritoneum with an opening, surrounded with ciliate cells, which was discovered by SEMPER and has been designated *nephridial funnel* or *nephrostome*, and which in many respects recalls the similar structures of the excretory organs of segmented Worms. In the most of the Vertebrates, however, special nephridial funnels are no longer developed, inasmuch as the mesonephric tubules soon after their origin completely detach themselves from the epithelium of the body-cavity as well as from the primitive segments, and thereby lose all relation to the body cavity.

A mesonephros in the simple form in which it is at first produced developmentally is retained permanently only in Bdellostoma, a representative of the Cyclostomes. It here consists, as JOHANNES MÜLLER has shown, of an elongated canal (fig. 206 *A* and *B* *a*) and short transverse tubules (*b*), which open into it at short intervals. The latter are no longer connected with the body-cavity by means of a nephridial funnel, but they enclose a vascular glomerulus at their blind end (fig. 206 *B* *c*), which is somewhat set off by a constriction.

In all remaining Vertebrates the mesonephros is metamorphosed into a more voluminous and more complicated organ. For the originally short tubules, which run transversely into the mesonephric duct, begin to grow in length, and at the same time to be thrown into numerous folds (fig. 207 *s.t*). Moreover there are formed mesonephric tubules of a second and third order. These again are also formed independently of the mesonephric duct dorsal to the first-formed transverse tubules; their blind ends approach the primary urinary tubule and join its terminal part, which is thereby converted into a collecting tube. At the same time a Malpighian body is formed on each of them also.

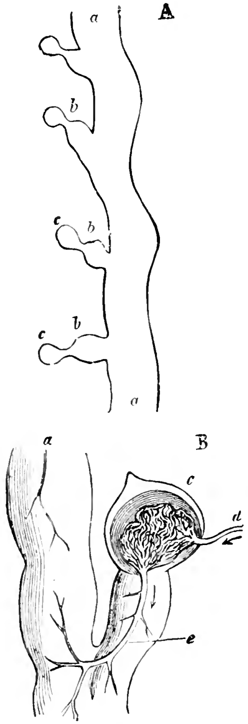


Fig. 206.—Parts of the mesonephros of Myxine, after J. MÜLLER.

a, Mesonephric duct; *b*, mesonephric tubules; *c*, glomerulus; *d*, afferent artery; *e*, efferent artery.

B a part of *A* more highly magnified.

Still more exhaustive investigations concerning the formation of the secondary and tertiary mesonephric tubules, especially for the higher Vertebrates, appear to me to be desirable. In the Selachians, according to the statements of Balfour, which are also confirmed by others, the epithelium of the already existing Malpighian glomeruli is the starting-point of a proliferation. Cell-buds grow out from the latter and toward the urinary tubules lying in front of them, with which their blind ends fuse. After this union has been effected they detach their other ends from the parent-tissue.

Through the development of *compound urinary tubules*, each of the branches of which is provided with a Malpighian corpuscle, the primitive kidney (mesonephros) acquires a complicated structure. But this is not uniform in all its parts; ordinarily the condition realised in the most of the Vertebrates is this: the anterior part, which afterwards enters into relation with the sexual glands, retains simple tubules, and only the posterior part passes into a more complicated form by the production of secondary and tertiary fundaments.

The more the mesonephros, with its tortuous tubules and its further differentiation, increases in volume, the more it becomes delimited from its surroundings and emerges from the wall of the body into the body-cavity as a distinctly differentiated organ, where it forms a protruding band on either side of the mesentery (fig. 210 *WK*).

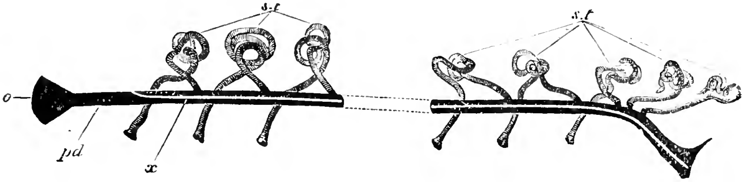


Fig. 207.—Diagram of the original condition of the kidney in an embryo Selachian, after Balfour. *pd*, Mesonephric duct, which opens into the body-cavity at *o*, and into the cloaca at the other end; *x*, line along which the Müllerian duct (lying below in the diagram) is divided off from the mesonephric (Wolffian) duct; *s.t*, mesonephric (segmental) tubules, which on the one hand open into the body-cavity, on the other into the mesonephric duct.

On a cross section one can recognise in the human embryo also (Nagel) two distinctly separated regions on each urinary tubule—(1) a larger one, which begins with the Bowman's capsule and is lined with large epithelial cells containing abundant protoplasm, and (2) a narrower region with small cubical elements. The latter is the collecting tube, which unites with other collecting tubes before it opens into the mesonephric duct; on the other hand, probably the former region alone has the secretory function, as also it is best developed at the time of the greatest prominence of the Wolffian body. The Malpighian glomeruli, likewise, attain at this time in human embryos a remarkable size (Nagel).

The further fate of the primitive kidney is very different in the separate classes of Vertebrates. In the Anamnia, *i.e.*, in Fishes and Amphibia, it becomes the permanent urinary organ, through which the excretions of the body are eliminated; but besides that, it also acquires relations to the sexual apparatus, upon which, however, I shall not enter until later. In Birds and Mammals, on the contrary, the primitive kidney is functional only a short time during embryonic life; soon after its establishment it undergoes profound regressive changes, and at last is preserved only in part, in so far as it enters into the service of the sexual apparatus, and, as we shall likewise see later, participates in conducting away the sexual products.

(*c*) *The Kidney.* (Metanephros.)

The secretion of urine is assumed in the higher Vertebrates by a third gland, which is established at the posterior end of the mesonephric duct—*the permanent kidney.* The method of its formation, which appears to differ at first from that of the mesonephros, presents great obstacles to its investigation. It is most accurately known from studies on the development of the Chick through the works of SEDGWICK. At the beginning of the third day of incubation in the Chick there grows out of the [posterior] end of the mesonephric duct, from its dorsal wall, an evagination—*the excretory duct of the kidney or ureter.*

There are two conflicting views relative to its connection with the development of the kidney. According to the older view, which is still shared by many, the kidney is formed from the ureter in the manner of an ordinary glandular growth. It is maintained that evaginations take place which give rise to other evaginations, and thus produce the whole parenchyma of the kidney. According to the second view, which has been formulated especially by the more recent embryologists,—by SEMPER, BRAUN, FÜRBRINGER, SEDGWICK, and BALFOUR,—the permanent kidney is, on the contrary, developed out of two different fundaments, which come into relation with each other only secondarily: the medullary substance with its collecting tubules out of the ureter, the cortical substance with the tortuous tubules and the loops of HENLE, on the other hand, out of a special fundament. According to this view there would be an agreement between the development of the kidney and primitive kidney, in as far as in the latter the mesonephric duct and the mesonephric tubules also arise separately, and only secondarily enter into relation with each other by means of fusion. The agreement here indicated is a not unimportant ground for my giving preference to the second rather than the first view.

As far as regards the details of the conditions, they are in the Chick—according to the investigations of SEDGWICK, which BALFOUR has confirmed—as follows: the ureter, which has arisen by an evagination from the end of the mesonephric duct, grows into that part of the middle plate which is located at the end of the Wolffian body in the region of the thirty-first to the thirty-fourth primitive segment. The fundament, however, is not at once and at this place converted into a kidney, but first undergoes, after the ureter has penetrated into it, a very considerable change in position; together with the ureter it grows forward on the dorsal side of the mesonephric duct farther; it meanwhile gradually enlarges, and begins to show internal differentiation only when it has come into this new position. One then sees that tortuous tubules become more and more distinct in the small-celled mass and that in their walls Malpighian corpuscles are established. One finds, in addition, that there are evaginated from the end of the ureter separate sacs, which grow out into collecting tubes, and probably later — certainty in regard to this has not yet been established—join the tortuous tublues which have arisen in the cortical portion of the kidney.

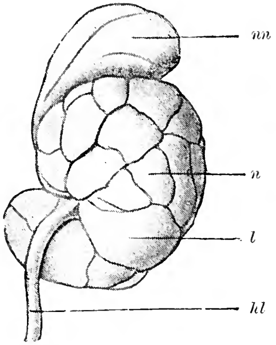


Fig. 208.—Kidney and suprarenal body of a human embryo at the end of pregnancy.

nn, Suprarenal body; *n*, kidney; *l*, lobes of the kidney; *hl*, ureter.

This voluminous organ, which has soon outstripped the mesonephros in size, is originally composed of individual lobes separated by deep furrows (fig. 208). The lobation is retained permanently in Reptiles, Birds, and some of the Mammals (Cetacea). In most Mammals, however, it disappears, in Man soon after birth. The surface of the kidney acquires an entirely smooth condition; the internal structure (Malpighian pyramids) alone points to its composition out of individual portions, originally also separated externally.

For the sake of clearness the development of the three regions, pro-, meso-, and metanephros, has been treated as a whole up to this point. Consequently there have been left out of consideration for the time being other processes which are taking place in the vicinity of the fundament of the mesonephros at the same time. These have to do with the evolution of the Müllerian duct and the sexual organs.

(*d*) *The Müllerian Duct.*

The Müllerian duct is a canal which is found lying at first parallel and close to the mesonephric duct in the embryos of most Vertebrates (Selachians, Amphibia, Reptiles, Birds, Mammals). It is a canal that is established in both sexes in the same manner, but subsequently acquires in each a different function. It takes its origin in the lower Vertebrates from the mesonephric duct, as can be most easily followed in the Selachians (Semper, Balfour, Hoffmann). In this case the mesonephric duct becomes enlarged, acquires in cross section (fig. 209^4) an oval form, and presents a different condition in its dorsal (*sd*) and ventral (*od*) halves, the latter being at the same time in immediate contact with the peritoneal epithelium. The mesonephric tubules open into the dorsal half, while ventrally the wall is considerably thickened. Then a separation of the two parts takes place, which begins at a little distance from the anterior end (cross sections 3-1) and proceeds backward to the point of opening into the hind gut. Of the parts which result from the fission, that which lies dorsally is the permanent mesonephric duct (*wd*); it exhibits at first a broad lumen and receives the urinary tubules (fig. 207 *st*). Ventrally, between it and the epithelium of the body-cavity, lies the Müllerian duct (fig. 209 *od* and fig. 207), which is at first only a narrow passage, but later a much enlarged one. In the process of fission the anterior initial part of the primary canal (fig. 207 *pd*), which was described at p. 353 as pronephros and which opens into the body-cavity by means of a ciliate funnel (*o*), becomes a part of the latter duct, and the ciliate funnel becomes the ostium abdominale tubæ.

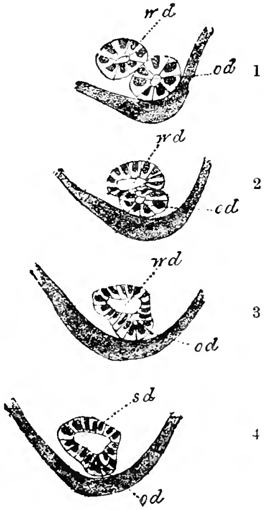


Fig. 209.—Four cross sections through the anterior region of the mesonephric duct of a female embryo of Scyllium canicula, after Balfour.
The figure shows how the Müllerian duct (*od*) is split off from the mesonephric duct (*sd* and *wd*).

Also in the case of the Amphibia the Müllerian duct is developed by being split off (Fürbringer, Hoffmann) from the mesonephric duct, with the exception of the anterior end, which bears the orifices leading into the body-cavity. A small territory of the epithelium of the body-cavity immediately adjacent to the pronephros serves for the construction of this portion. The epithelium becomes thickened, owing to the fact that its cells take on a cylindrical shape; it sinks in to constitute a groove, and then becomes constricted off from the surrounding tissue in the form of a short funnel, which in front remains in connection with the body-cavity by means of a broad opening, but posteriorly becomes continuous with the part of the Müllerian duct that is produced by fission. The pronephric tubules and the glomerulus degenerate.

The fission of the single mesonephric duct into two canals lying close together is a peculiar process, which is intelligible only upon the assumption that the mesonephric duct has possessed a double function. Probably it originally served as an outlet for the secretions of the mesonephric tubules, and also by means of its pronephric funnel took up out of the body-cavity the sexual products (eggs or seminal filaments) eliminated into it at their maturity, and conducted them to the outside. Similar conditions are often observed in Invertebrates, *e.g.*, in various divisions of the Worms, in which also the segmental canals, which break through the body-wall, transmit to the outside both secretions from the body and sexual products. In Vertebrates each of the two functions is assigned to a special canal, one of which loses its communication with the body-cavity, but remains in connection with the transverse mesonephric tubules, while the other retains as its part the ciliate funnel of the pronephros, and thus is adapted to conducting away the sexual products (eggs).

In Reptiles, Birds, and Mammals the manner of the development of the Müllerian duct is still a subject of scientific controversy. Most observers (WALDEYER, BRAUN, GASSER, JANOSIK, and others) state that at no time was a process of fission observed. According to their representation the Müllerian duct arises in Birds and Mammals quite independently as a new structure, at a time when the mesonephros is already well developed and has the form of a band-like body (the mesonephric fold) projecting into the body-cavity (fig. 210). One then sees on the lateral face of the anterior region of this body that the epithelium of the body-cavity over a limited area (a') is thickened in a remarkable manner and composed of cylindrical cells, whereas elsewhere the cells are flattened. The thickened portion of the epithelium sinks down in the form of a funnel and applies itself closely to the mesonephric duct (y), which is near at hand. The blind end of the funnel grows from this point backwards *independently*, as is usually asserted, by means of the proliferation of its own cells, and gives rise to a solid cord, which lies directly between the mesonephric duct and the peritoneal epithelium, which is here somewhat thickened. The funnel produced by the invagination now becomes the ostium abdominale tubæ, but the solid cord of cells, which is soon hollowed out and finally opens behind into the cloaca, becomes the Müllerian duct.

If the representation just given is correct in all particulars, the Müllerian ducts in the Anamnia and the Amniota, although possessing the same location, form, and function, would still be non-homologous organs, because their development is different. For the one is split off from the mesonephric duct, the other is formed independently by a new invagination of the epithelium.

Such a surprising result appears to us, however, upon grounds of comparative anatomy, to be very improbable, and therefore the attempt made by some investigators to refer back the conditions found in the Amniota to such as exist in the Anamnia deserves every attention. This would be possible if the statements of Balfour and Sedgwick, which have however been called in question by others (Janosik), should be confirmed. As we have previously seen, there are two different regions to be distinguished on the Müllerian duct—an anterior, which is the degenerated pronephros and bears the orifice of the tuba,

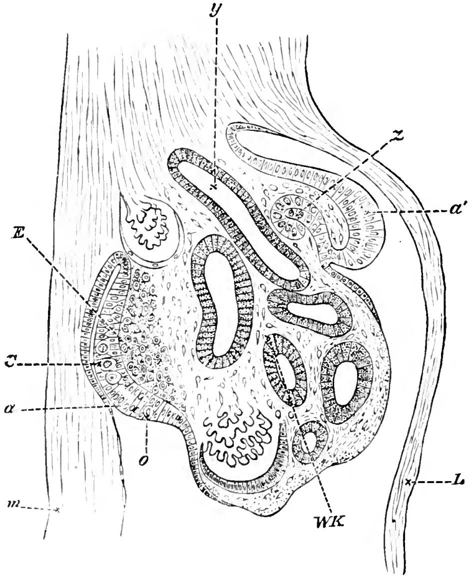


Fig. 210.—Cross section through the mesonephros, the fundament of the Müllerian duct, and the sexual gland of a Chick of the fourth day, after Waldeyer. Magnified 160 diameters.

m, Mesentery ; *L*, somatopleure ; *a'*, the region of the germinal epithelium from which the Müllerian duct (*z*) has been invaginated ; *a*, thickened part of the germinal epithelium, in which the primary sexual cells, *C* and *o*, lie ; *E*, modified mesenchyme out of which the stroma of the sexual gland is formed ; *WK*, mesonephros ; *y*, mesonephric duct.

and a posterior, which is formed by being split off from the mesonephric duct. Such a double origin BALFOUR AND SEDGWICK endeavor to establish for the Müllerian duct in the Chick also. The part produced by invagination of the peritoneum (fig. 210 *z*) they interpret as pronephros. A similarity with the latter they find in the fact that this part does not, according to their investigations, consist of a single invagination of the peritoneal epithelium, but of three open invaginations lying one behind the other, which are joined together by ridge-like epithelial thickenings which afterwards become hollow (fig. 211 *gr* 2, *gr* 3, *r* 2). From this ridge is formed a slightly curved, short duct, which communicates with the body-cavity through three openings.

If this explanation is right, the most anterior fundament of the excretory system of the Chick, which was described on page 356 as pronephros, must have undergone a change in position, and, with the appearance of the Wolffian body, have slipped backward somewhat along this organ. As long as this alteration of position is not demonstrated by the study of intermediate stages, the interpretation, however probable it may seem to us, still lacks actual proof.

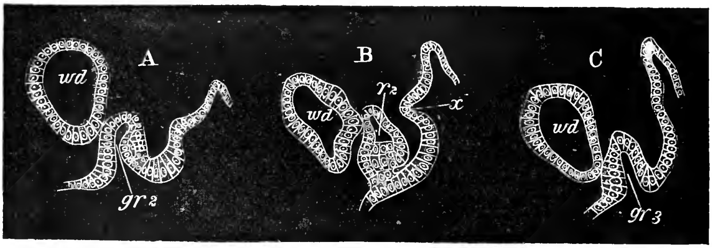


Fig. 211.—Cross sections through two peritoneal invaginations out of which is formed the anterior region of the Müllerian duct (the pronephros) of the Chick, after BALFOUR AND SEDGWICK.
A is the 11th, *B* the 15th, *C* the 18th section of the whole series.
gr 2, 3, Second and third furrows; *r 2*, second ridge; *wd*, Wolffian duct.

As far as regards the posterior, longer region of the Müllerian duct, SEDGWICK maintains that it arises by being split off from the mesonephric duct. One always finds, according to his researches, the pronephric part of the Müllerian duct in union at its posterior end with the ventral wall of the mesonephric duct. He maintains that it is enlarged at the expense of the latter in somewhat the same manner as the mesonephric duct grows from in front backwards by a proliferation of the outer germ-layer. The cross sections *A* and *B* of figure 212 exhibit this condition. Figure *B* shows the place where the ventral wall of the mesonephric duct is thickened into a ridge (*md*) by an increase of the epithelial cells; upon a cross section (*A*) made farther forward the thickened part has become detached as a cord (*md*), which subsequently becomes still more isolated and acquires a cavity of its own. The condition recalls very clearly the appearances which the cross sections through embryo Selachians (fig. 209) gave.

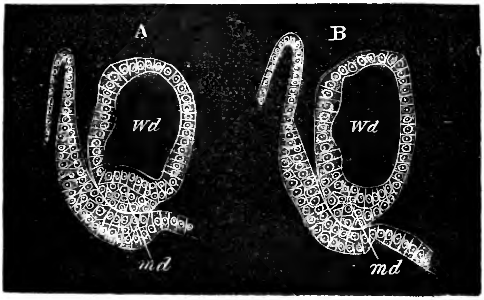


Fig. 212.—Two sections to show the union of the solid terminal part of the Müllerian duct with the mesonephric duct in the Chick, after BALFOUR AND SEDGWICK.
In *A* the terminal part of the duct is still quite distinctly separate; in *B* it has united with the wall of the mesonephric duct.
md, Müllerian duct; *Wd*, Wolffian duct.

According to the observations of SEDGWICK, therefore, the anterior end of the Müllerian duct would be derived from the pronephros, but the posterior end by a splitting off of cells from the mesonephric duct. Thus an agreement with the conditions in the non-amniotic Vertebrates would be established.

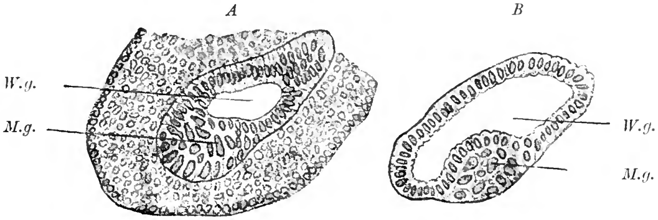


Fig. 213.—Cross sections through the Wolffian and Müllerian ducts of two human embryos, after NAGEL.
A, A female embryo 21 mm. long.
B, A male embryo 22 mm. long.
W.g., Wolffian duct; *M.g.*, end of the Müllerian duct in process of development.

It still deserves to be especially mentioned that in human embryos also the Müllerian ducts (fig. 213 *A* and *B M.g.*) during their development have their posterior ends fused for a short distance with the mesonephric duct (*W.g.*). NAGEL, to whom we are indebted for this fine observation, expresses himself, it is true, against a splitting off; however, the similarity with the conditions found in the Chick and the non-amniotic Vertebrates is not to be denied, and has indeed been emphasised by NAGEL.

(e) *The Germinal Epithelium.*

In Vertebrates, at the time when the Müllerian duct is established, the first traces of the sexual glands are also to be recognised. The parent-tissue of these is likewise the epithelium of the body-cavity. This acquires—for example in the Chick, which is to serve as the foundation for our description—a different appearance in the various regions of the body-cavity (fig. 210). In most places the epithelia become extraordinarily flattened and assume the condition of the permanent "endothelium." Also on the mesonephros, which projects into the body-cavity as a thick, vascular fold, the epithelium is for the most part greatly flattened, but retains its original condition (1) on its lateral surface along a tract (*a'*) from which, as we have previously seen, the Müllerian duct is formed, and (2) along a tract (*a*) which stretches from in front backward along the median side of the mesonephros; the signification of the latter has been correctly estimated by BORNHAUPT and by WALDEYER, who have characterised it as *germinal epithelium. From it are derived the germ-cells: in the female the primitive ova, in the male the primitive seminal cells.* It is only in the very earliest stages that it is impossible to distinguish whether the germinal epithelium will be developed into testis or ovary. Differences soon appear, which allow a positive determination. We shall take up first the development of the ovary, then that of the testis.

(*f*) *The Ovary.*

The development of the ovary is tolerably well known both in the lower and the higher Vertebrates, except for a few controversial points. I can therefore limit myself simply to the presentation of the results which have been acquired in the case of the Chick and Mammals.

At about the fifth day of incubation the germinal epithelium in the Chick increases a good deal in thickness, becoming two to three layers of cells deep. Certain elements in this thickening are prominent; they are distinguishable (fig. 210 *C* and *o*) by their richness in protoplasm and by their large round nuclei. Because they stand in the closest relation to the development of eggs, they have been designated as *primitive eggs* by WALDEYER, who was the first to study them in detail.

Beneath the germinal epithelium there is to be found, even at that time, embryonic connective tissue with stellate cells (E), which are in an active state of proliferation. In this way there arises on the median side of the mesonephros the ovarian ridge, which is separated from the urinary tubules by a small quantity of embryonic connective substance.

Changes similar to those of the Chick occur in Mammals, with this difference, that the germinal epithelium appears to attain a much greater thickness.

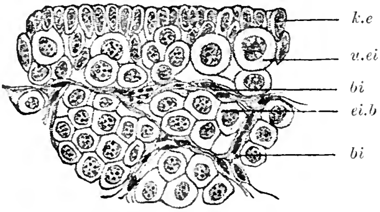


Fig. 214.—Cross section through the ovary of a Rabbit 5 days old, after Balfour. Highly magnified.

k.e, Germinal epithelium ; *u.ei*, primitive (or primordial) ova ; *ei.b*, egg-nests ; *bi*, connective tissue.

In older stages of development the boundaries between the germinal epithelium, which is in process of rapid proliferation and therefore exhibits numerous figures of nuclear division, and the underlying connective tissue become less and less distinct. This results from the simple fact that *a process of mutual ingrowth now occurs between the epithelium and the embryonic connective tissue* (fig. 214). I purposely say a process of mutual ingrowth, for I leave it undetermined whether the germinal epithelium in consequence of its development grows into the embryonic connective tissue in the form of cords and distinct groups of cells, or whether the connective tissue penetrates with its projections into the epithelium. Probably both tissues are actively engaged in the process.

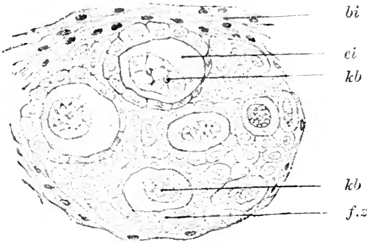


Fig. 215.—Section through an egg-nest of a Rabbit 7 days old, after Balfour.

ei, Ovum, the germinative vesicle (*kb*) of which exhibits a filar network ; *bi*, connective-tissue stroma ; *f.z*, follicular cells.

In the phenomenon of intergrowth, which continues for a long time during development, two chief stages can be distinguished.

At first there arise from the germinal epithelium both slender and stout cords and balls of cells (figs. 214 and 215), which have received from the name of their discoverer the designation Pflüger's *egg-tubes.* Occasionally these are joined to one another by means of lateral branches. Together with the connective tissue separating them, they form the foundation for the cortex of the ovary. Afterwards they are covered over on the side toward the body-cavity with a thick continuous layer of connective tissue, which becomes the albuginea of the ovary; they are thereby more sharply separated from the germinal epithelium (fig. 216 *k.e*), which is still preserved, even after this, as a layer of cubical cells upon the albuginea.

There are two kinds of cells to be found in the Pflügerian egg-tubes: *follicular cells* and *primitive ova* (fig. 215 *f.z* and *ei*). Concerning the source of the former opinions are still contradictory (compare p. 382); according to my view both arise from the germinal epithelium.

Whereas the follicular cells become by means of an uninterrupted process of division more numerous and smaller, the primitive ova increase in size continually, and their nuclei become very large and vesicular and acquire a distinctly developed filar network (*kb*). They rarely lie singly in the cords and balls of follicular cells, but ordinarily in groups, which are designated as *egg-nests*. One frequently observes in the nests, as has been announced by BALFOUR and VAN BENEDEN, that several primitive ova become fused into a common, multinuclear mass of protoplasm—a syncytium. From this there is afterwards developed usually only a single egg. One of the numerous nuclei soon outstrips the others in size and becomes the germinative vesicle, whereas the remaining ones undergo degeneration and are dissolved. It is not to be concluded from these processes that the egg, as is occasionally asserted, corresponds to a multiple of cells; the condition is more properly to be interpreted as follows: of the eggs contained in a nest, *one* outstrips the others in its growth and thereby represses them and employs them, in a certain sense as nutritive material, for its own growth.

This is a process that occurs very frequently in Invertebrates, and in the phylum of the Arthropods has been studied with the greatest detail by WEISMANN. In these cases—the lower Crustacea and Insects—one can see how, step by step, out of numerous primitive ova which are originally contained in a germinal chamber of an ovariole, only one becomes the egg, whereas the others from an early period lag behind in development, then undergo degeneration, and in the form of products of degeneration are taken up as yolk-material into the persisting egg-cell.

During the enlargement of the egg-cell the second stage of the process of intergrowth of epithelium and connective tissue is introduced: the *stage of the formation of the follicle* (fig. 216). At the boundary between the medullary and cortical zones of the ovary the surrounding connective tissue, carrying with it the blood-vessels, grows into the egg-tubes of PFLÜGER (*e.sch*) and the nests (*ei.b*), and divides them all into spheroidal bodies, the individual follicles (*f*). Each such structure contains a single ovum, that is enveloped on all sides by a layer of follicular cells. The vascular connective tissue that grows around it becomes the follicular membrane or *theca folliculi.*

The resolution into follicles continually advances from the medullary substance toward the germinal epithelium ; however, there are preserved under it for a long time Pflügerian tubes, which remain in connection with it by means of narrow epithelial cords (*e.sch*) and contain eggs in process of development.

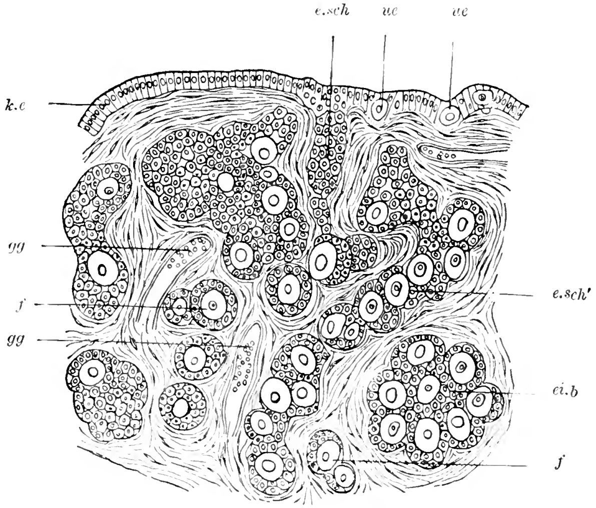


Fig. 216.—Part of a sagittal section of an ovary of a Child just born, after WALDEYER. Highly magnified.

k.e, Germinal epithelium ; *e.sch*, PFLÜGER'S egg-tubes ; *ue*, primitive ova lying in the germinal epithelium ; *e.sch'*, long PFLÜGER'S tubes, in process of being converted into follicles ; *ei.b*, egg-balls [nests], likewise in process of being resolved into follicles ; *f*, youngest follicle already isolated ; *gg*, blood-vessels.

In the tubes and egg-nests the primordial eggs are distinguishable from the smaller epithelial cells, the future follicular epithelium.

The formation of new Pflügerian tubes and young ova is a process which continues in the lower Vertebrates throughout life, but in the higher appears to be limited to the period of embryonic development, or to the first years of life. In the first case, there being an unlimited capacity for the formation of new structures, egg-germs are found, even in the adult animal, sometimes in the most widely separated parts of the ovary, sometimes limited to definite regions of the gland. In the second case the period of forming primitive ova in the germinal epithelium bears a direct ratio to the total number of ova eliminated during the life of the individual. Thus WALDEYER states concerning Man that in the second year after birth the formation of new ova can no longer be shown.

Nevertheless in Man the number of ova contained in a single ovary is very great. They have been estimated to number in a sexually mature girl 36,000. In other Mammals the production of new ova appears to last longer. PFLÜGER's tubes which were still connected with the germinal epithelium and contained small primordial ova have been observed even in young animals (Dog, Rabbit, etc.). However, it has been questioned whether we here have really new structures or only primitive ova that in their development have remained stationary. It is maintained by VAN BENEDEN with certainty for a few Mammals, *e.g.*, the Bat, that in the sexually mature animal PFLÜGER's tubes and primitive ova still continue to be produced from the germinal epithelium.

In connection with the first formation of the follicle I will here add some statements about its further metamorphosis. This is very similar in the different Vertebrates, excepting Mammals.

In most Vertebrates the follicle (fig. 216 *f*) consists at first of a small, centrally located egg-cell and a single layer of small follicular cells enveloping it. Soon both are more sharply separated from each other by means of a vitelline membrane. In older follicles both parts have increased in size. The follicular cells ordinarily grow out into long cylinders, and appear to play an important part in the nutrition of the egg. In many animals, *e.g.*, in Sharks and Dipnoi, yolk-granules have been found in them, as in the egg itself, and it has been concluded from this, as well as from other phenomena, that the follicular cells take up nutritive substance from the vascular follicular capsule, and pass it along to the egg. Such a method of nutrition is made easier by the fact that the vitelline membrane (fig. 5 *z.p*) is traversed by tubules, through which the follicular cells (*f.z*) send protoplasmic filaments to the egg. When the egg has attained its full size, the follicular cells lose their significance as nutritive organs and become more and more flattened.

In the lower Vertebrates the mature ova are generally eliminated in great numbers all at once, frequently in the course of a few days or even hours. The discharge takes place by the rupture of the connective-tissue envelope, which causes the eggs to escape into the body-cavity, as in the Fishes and most of the Amphibia. After the elimination, the ovary, which up to this time was extraordinarily large and took up most of the space in the body-cavity, shrivels into a very small cord and now encloses only the young germs of ova, part of which are destined to mature during the next year.

The formation of the follicle takes place in a somewhat different way in Mammals. The follicle originally contains, as in the remaining Vertebrates, only a single egg and a single layer of follicular cells, which are at first flat, then cubical, then cylindrical (fig. 216 *f*). For a long time these cells envelop the egg as a single layer, but they then grow, undergo division, and are converted into a thick envelope of many layers. But the difference from the course of development described above becomes still greater, owing to the fact that a fluid, the liquor folliculi, is secreted by the proliferated follicular cells, and collects in a small cavity at the side of the egg (fig. 217 *A ff*).

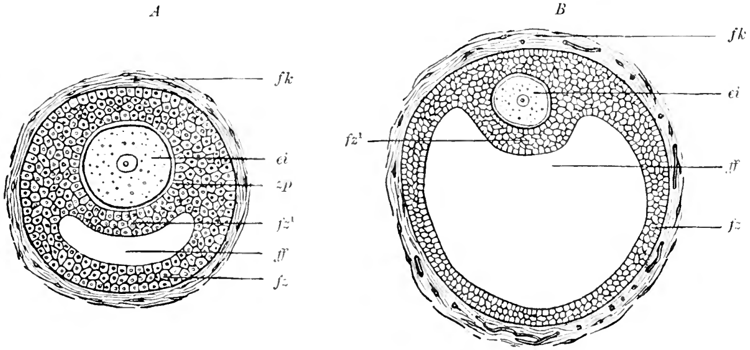


Fig. 217 A and B.—Two stages in the development of the Graafian follicle. *A* with the follicular fluid beginning to be formed; *B* with a greater accumulation of it.
ei, Egg; *fz*, follicular cells; *fz*¹, follicular cells which envelop the ovum and constitute the discus proligerus; *ff*, follicular fluid (liquor folliculi); *fk*, follicular capsule (theca folliculi); *zp*, zona pellucida.

In consequence of a considerable increase of the fluid, the originally solid follicle becomes converted finally into a large or small vesicle (fig. 217 *B*), which was discovered more than two hundred years ago by the Hollander Regnier de Graaf and was held to be the human ovum. The structure has also been named after him the *Graafian follicle*. Such a follicle (fig. 217 *B*) now consists of (1) an outer connective-tissue, vascular envelope (*fk*), the theca folliculi;

(2) lying on its inner surface, an epithelium composed of many layers of small follicular cells (*fz*), the membrana granulosa; (3) the liquor folliculi (*ff*); and (4) the ovum (*ei*), which originally lay in the centre of the follicle, but which has now been crowded to the periphery. Here, enveloped in a great mass of follicular cells (fz^1), it causes an elevation of the wall,—the *discus proligerus*,—which protrudes into the cavity.

When the egg has reached complete maturity its elimination occurs by a collapse of the Graafian follicle, which has then attained in Man a diameter of about 5 mm. and causes an elevation at the surface of the ovary. The liquid of the follicle flows out through the rupture and at the same time carries away with it from the discus proligerus the egg, which comes first into the body-cavity, being surrounded by a small number of follicular cells, which still cling to the zona pellucida (fig. 5). The egg is then taken up by the oviduct.

Into the cavity of the follicle produced by the flowing out of the liquid an effusion of blood takes place from the ruptured blood-vessels in the vicinity. The blood coagulates, and, accompanied by a proliferation of the adjacent tissue, is converted into the *yellow body*, or corpus luteum, which is a characteristic structure of the ovary of Vertebrates. Both the follicular cells (membrana granulosa) which are left behind and the connective-tissue follicular capsule participate in this proliferation. The follicular cells continue to multiply, penetrate into the interior of the coagulum, and after a time begin to undergo degeneration and to be dissolved into a granular mass. Vascular outgrowths from the capsule penetrate into the yellow body, and at the same time there is an extensive emigration of white blood-corpuscles or leucocytes, which likewise undergo fatty and granular degeneration at a later period.

It is of great importance for the further development of the yellow body whether the egg set free is fertilised or remains unfertilised. For according as the one or the other event supervenes, the corpus luteum is distinguished as true or false. In the first case it acquires a much greater size, the maximum of which is reached in the fourth month of pregnancy. It then appears as a fleshy reddish mass. After the fourth month a process of degeneration begins. The products of degeneration, which have resulted from the granular metamorphosis of the follicular cells and leucocytes, as well as from the coagulum of blood, are absorbed by the blood-vessels. Out of the decomposed coloring matter of the blood there have arisen hæmatoidin crystals, which now give to the body an orange-red color. The connective tissue, originally with an abundance of cells, begins to shrivel, as in the formation of a scar; as a result of these various processes of degeneration the yellow body, which projects beyond the surface of the ovary, begins to become considerably smaller, and is finally converted into a firm connective-tissue callus, which causes a drawing in at the surface of the organ.

When fertilisation has not occurred, the same metamorphosis and processes of growth it is true take place, but the false corpus luteum remains very much smaller. This is probably due to the fact that the afflux of blood to the sexual organs is very much less when there is no fertilisation than in case pregnancy takes place.

In addition to the tubes of PFLÜGER,—which arise from the germinal epithelium and produce the primitive ova,—in most classes of Vertebrates *epithelial cords of another kind and another origin enter into the composition of the ovary.* As has been observed by various persons in Amphibia, Reptiles, Birds, and Mammals, there grow out from the Wolffian body, which lies in the immediate vicinity, epithelial shoots, the "*sexual cords of the primitive kidney,*" and these penetrate toward the developing ovary even as early as the beginning of the intergrowth between germinal epithelium and connective tissue. They arise from the epithelium of the Malpighian corpuscles, as BRAUN has shown for Reptiles, HOFFMANN for Amphibia, and SEMON for Birds. In Mammals, in which at present their subsequent fate has been most accurately traced out, they then unite with one another into a network at the base of the fundament of the ovary, which protrudes as a ridge into the body-cavity, and, pursuing tortuous courses, grow into contact with the tubes of PFLÜGER. Whereas in Mammals the cortex of the ovary is developed out of the latter, the former share in the composition of the future medullary substance, and are on that account designated as *medullary cords.* In the vicinity of the follicle they remain solid, whereas the part near the primitive kidney acquires a cavity which is surrounded by cylindrical cells.

The medullary cords exhibit in different species of Mammals different degrees of development, as the comparative investigations of HARZ have established. In some animals, *e.g.*, in the Pig and Sheep, they reach only to the base of the ovary, and therefore remain separated from the tubes of PFLÜGER by a wide space; in others they grow out into the vicinity of the latter, and in part apply themselves closely to them (Cat, Guinea-pig, Mouse, etc.), and take a very prominent part in the composition of the medullary substance.

There are two antagonistic views *relative to the significance of the sexual cords of the primitive kidney, or the medullary cords, in the formation of ova.* According to Kölliker and Rouget the medullary cords early fuse with the tubes of Pflüger and furnish to them the cells which become the follicular epithelium. The cells contained in a follicle would, according to this, come from two sources—the follicular cells would arise from the primitive kidney, the eggs from the germinal epithelium. Most embryologists dispute this. According to their observations the medullary cords only exceptionally extend close up to a follicle, in many Mammals they do not reach it at all; consequently not only the primitive ova but also the accompanying follicular cells must be furnished by the germinal epithelium. I also favor the latter view, which appears to me to be best supported by the facts. But what significance the medullary cords have will be better understood when we have become acquainted with the development of the testis, to which we shall now proceed.

(*g*) *The Testis.*

I will at once state that our knowledge of the development of the testis is less complete than that of the development of the ovary.

The conditions appear to me to be the clearest in the *non-amniotic Vertebrata.* We possess here the pioneer researches of Semper and Balfour on the Selachians, and of Hoffmann on Amphibia. All these investigators have, with one accord, come to the conclusion that the male sexual products, as well as the female, arise from the germinal epithelium of the body-cavity. In males also there is to be recognised in the region of the primitive kidney a special thickened band of tall epithelial cells, in which are imbedded larger cells with vesicular nuclei, the *primitive spermatic cells.* In the Sharks, the conditions of which I shall make the basis of the further description, they form irregular cords of cells, the "Vorkeimketten" of Semper (fig. 218 *A*). Out of these are developed small, spherical, follicular-like bodies (fig. 218 *B*), by the ingrowth of surrounding connective tissue into the cords, which are thereby divided up.

Thus far, therefore, complete agreement exists in the development of both kinds of sexual products. But whereas in the case of the ovary one cell in each follicle increases in size and is converted into the ovum, a like process does not take place in the male; here the follicle-like structures become hollow and thus converted into *seminal ampullæ*, whose epithelial cells gradually grow out into long cylinders. The greater part of these become seminal mother-cells, which by many repeated divisions are converted into sixty seminal cells, each of which is metamorphosed into a seminal filament. Since the filaments derived from each seminal mother-cell always arrange themselves parallel to one another, it is easily understood why before the attainment of complete maturity the seminal filaments are found united in great numbers into bundles.

Fig. 218 A.—Pregerminal chain of cells (Vorkeimketten) from the pregerminal ridge of an embryo Acanthias 17 cm. long, after SEMPER. Magnified 330 diameters.

There are to be seen cells with small nuclei and also primitive seminal cells which resemble primitive ova.

B.—Seminal ampulla from the pregerminal ridge of an embryo Acanthias 25 cm. long, after SEMPER. Magnified 330 diameters.

us, Primitive seminal cell; *sc*, collecting tubule, which has attached itself with its blind end to the ampulla.

Whereas the testis, like the ovary, draws its specific histological components directly from the germinal epithelium, it acquires its efferent ducts from the primitive kidney. As in the female, so also in the male, epithelial shoots, the sexual cords (genital canals of HOFFMANN), grow from the primitive kidney toward the testis; in the Amphibia they arise as proliferations from the cells of the wall of certain Malpighian corpuscles; in the Selachians, on the contrary, they sprout out in a somewhat different manner from the ciliate funnels. Arrived at the base of the testicular ridge, they are joined together into a longitudinal canal, from which fine tubules are sent still farther into the substance of the testis, where they unite with the structures that take their origin in the germinal epithelium. As figure 218 *B* shows, the efferent tubules (*sc*) in Selachians at first apply their blind ends to the ampullæ, and enter into open communication with them, but only after the maturation of the seminal filaments begins.

Many differences of opinion still prevail concerning the development of the testis in the higher Vertebrates. It is true that the presence of a germinal epithelium upon the surface of the mesonephros has also been established in this case by WALDEYER for the male, but its participation in the fundament of the testis has been called in question. According to the original account of WALDEYER, which is still defended by many investigators, especially by KÖLLIKER, the seminal tubules are morphological products of the primitive kidney. However, more recent researches, which it must be admitted do not yet harmonise with one another in all points, indicate that the development of the testis of Reptiles, Birds, and Mammals agrees with that of non-amniotic Vertebrates in the main outlines. In continuation of the work of BORNHAUPT and EGLI, who it is true worked with incomplete methods of investigation, BRAUN has recently maintained for Reptiles, SEMON for the Chick, MIHALKOVICS and JANOSIK for the latter and for Mammals, that in the male also the germinal epithelium begins to proliferate, penetrates into the depths of the testis, and furnishes the primitive seminal cells. The tubules, which according to KÖLLIKER and WALDEYER grow into the fundament of the testis from the primitive kidney,—the sexual cords,—serve only for *carrying away* the semen. As stated by BRAUN for Reptiles, and by SEMON for the Chick, they sprout out from the epithelium of Malpighian corpuscles, as in the case of the Amphibia.

Although according to these accounts the *double origin of the substance of the testis, on the one hand from the germinal epithelium, on the other from the primitive kidney*, can no longer be well called in question, nevertheless in the details many conditions, which are still differently described in the higher Vertebrates, demand renewed investigation. Before all else this point should be still further explained: In what proportion do the epithelial cells furnished by the germinal epithelium and those by the primitive kidney share in the formation of the testicular substance? Are the tubules which produce the semen formed exclusively from germinal epithelium, or is it only the seminal mother-cells which have this origin, while there are associated with the latter indifferent cells from the "sexual cords of the primitive kidney"?

I hold it to be the more probable that *the tubules producing the semen, the tubuli seminiferi, are derived from the germinal epithelium; the tubuli recti and the rete testis, on the contrary, from the primitive kidney.*

Nagel has studied the development of the testis in human embryos. According to his description also, there arise from the actively proliferating germinal epithelium numerous cords, in which large primitive seminal cells are imbedded. The cords afterwards become the seminal tubules. In Man there prevails from the beginning, as Nagel remarks, such a great difference between the two sexes, both in the form of the original germinal ridge and in the whole process of its differentiation, that one can recognise in the anatomical structure of the sexual glands from a very early stage whether one has before him a male or a female.

(*h*) *Metamorphosis of the Different Fundaments of the Urogenital System into the Adult Condition.*

We have become acquainted in the preceding pages with the first development of the various parts which constitute the foundations of the urogenital system. These are (fig. 219) three pairs of canals —the mesonephric ducts (*ug*), the Müllerian ducts (*mg*), and the ureters (*hl*)—and in addition a great number of glandular structures —pronephros, mesonephros (*un*), metanephros (*n*), and the sexual glands (*kd*), ovary and testis.

It will be my task in what follows to indicate how the ultimate condition is derived from these embryonic fundaments. In this I shall limit myself, in the main, to Man, because we now have to do with more easily investigated, and in general well-known conditions.

In a human embryo eight weeks old (fig. 220) the fundaments, if we neglect differences which are recognisable only by the aid of the microscope, are so similar in male and female as to be indistinguishable.

All the glands lie at the sides of the lumbar vertebræ: farthest forward the kidney (*n*), which is a small bean-shaped body; upon this lies the suprarenal body (*nn*), that at this time is disproportionately large and is to be seen only on the left half of the figure.

Somewhat lateral to the kidney one sees the primitive kidney (*un*) as an elongated, narrow tract of tissue. It is attached to the wall of the trunk by a connective-tissue lamella, a fold of the peritoneum, the so-called mesentery of the primitive kidney. In the middle of the gland it is rather broad, but above, toward the diaphragm, it is elongated into a narrow band, which Kölliker has described as the *diaphragmatic ligament* of the primitive kidney. Upon careful examination one also observes at the lower end of the primitive kidney a second fold of the peritoneum, which runs from it to the inguinal region (figs. 219 and 220 *gh*). It encloses a firm strand of connective tissue, a kind of ligament, that is destined to play a part in the development of the female and male sexual organs—*the inguinal ligament of the primitive kidney.* It subsequently becomes in man the *gubernaculum Hunteri*, in woman the *round ligament of the uterus* (*ligamentum teres uteri*).

On the median side of the primitive kidney is found either the testis or the ovary (*kd*), according to the sex of the embryo, both sexual organs still being at this time small oval bodies. They also possess mesenteries of their own, a *mesorchium* or *mesovarium*, by means of which they are connected with the root of the primitive kidney. As long as the sexual organs retain their positions on each side of the lumbar vertebræ, the blood-vessels that supply them run in an exactly transverse direction: the arteria spermatica from the aorta to the ovary or the testis, the vena spermatica from the gland to the vena cava inferior.

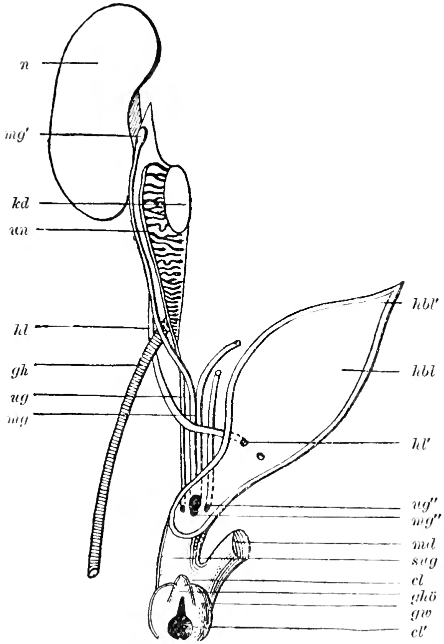


Fig. 219.—Diagram of the indifferent fundament of the urogenital system of a Mammal at an early stage.

n, Kidney; *kd*, sexual gland; *un*, primitive kidney; *ug*, mesonephric duct; *mg*, Müllerian duct; *mg'*, its anterior end; *gh*, gubernaculum Hunteri (mesonephric inguinal ligament); *hl*, ureter; *hl'*, its opening into the urinary bladder; *ug''*, *mg''*, openings of the mesonephric and Müllerian ducts into the sinus urogenitalis (*sug*); *md*, rectum; *cl*, cloaca; *ghö*, sexual eminence; *gw*, sexual ridges; *cl'*, external orifice of the cloaca; *hbl*, urinary bladder; *hbl'*, its elongation into the urachus (the future lig. vesico-umbilicale).

The various efferent ducts lie at this time close together at the margin of the mesonephric fold (fig. 219), the most anterior [ventral] being the Müllerian duct (*mg*). Farther backwards toward the pelvis the ducts of both sides approach the median plane (fig. 219), whereby the Müllerian duct (*mg*) comes to lie for a certain distance on the median side of and then behind [dorsal of] the mesonephric duct (*ug*), so that altogether it describes around the latter a kind of spiral course. When they reach the lesser pelvis, the four ducts are united behind the bladder (*hbl*) into a fascicle, the *genital cord*; this union is due to their becoming surrounded by the umbilical arteries—which have at this time attained a large size, and which run from the aorta on both sides of the bladder up to the umbilicus—and to their being, as it were, tied up into a bundle by them. In a cross section through the genital cord (fig. 228) we find the mesonephric ducts (*ug*) somewhat more anterior [ventral] and at the same time farther apart than the Müllerian ducts (*mg*), which are a little behind them and pressed quite close together in the median plane.

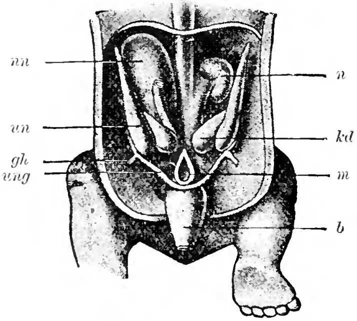


Fig. 220.—Urinary and sexual organs of a human embryo 8 weeks old, after Kölliker. Magnified about 3 diameters, and seen from the ventral side.

nn, Right suprarenal body; *un*, primitive kidney; *n*, kidney; *ung*, mesonephric duct; *gh*, Hunter's directive or inguinal ligament (gubernaculum Hunteri or ligamentum uteri rotundum); *m*, rectum; *b*, bladder; *kd*, sexual gland.

In older embryos there arise in the evolution of the urogenital system differences between the two sexes which are visible even externally and which become more distinct from month to month. These result from fundamental metamorphoses, which the whole apparatus continually undergoes in its separate parts. In connection with this some originally quite large fundaments undergo almost complete degeneration; of those which remain some are serviceable only in the female, others only in the male; when not employed, they disappear. Moreover the conditions which were referred to at the beginning of the description are extensively altered by the fact that the sexual organs surrender their original position, on either side of the lumbar vertebræ, and move farther downward into the pelvic cavity.

I describe first the changes in the male, then those in the female.

(A) *The Metamorphosis in the Male. Descensus testiculorum.*

Whereas the testis (figs. 221 and 222) by conglomeration of the seminal tubules becomes a bulky organ (*h*), the mesonephros (*nh*+*pa*) is retarded in its development more and more, and is at the same time differently metamorphosed in its anterior and its posterior portions. The anterior or *sexual part of the primitive kidney* (*nh*), which has come into communication with the seminal tubules by means of individual canals, in the manner previously described, and has thereby furnished the rete testis and the tubuli recti, is converted into the head of the epididymis. It exhibits in the tenth to the twelfth week from ten to twenty short transverse canals, which are now to be designated as vasa efferentia testis. They unite in the mesonephric duct (fig. 222), which continues to have a straight course, and has now become the seminal duct (*sl*, vas deferens). During the fourth and fifth months the individual canals begin to grow in length and thereby to become tortuous. The vasa efferentia in this way produce the coni vasculosi, which are at once the initial part of the vas deferens and the tail of the epididymis.

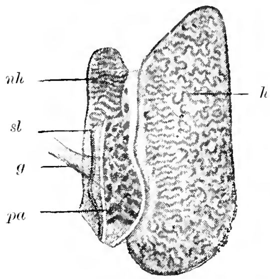


Fig. 221.—The internal sexual organs of a male human embryo 9 cm. long, after WALDEYER. Magnified 8 diameters.
h, Testis; *nh*, epididymis (sexual part of the primitive kidney); *pa*, paradidymis (remnant of the primitive kidney); *sl*, vas deferens (duct of the primitive kidney); *g*, vascular bundle of connective tissue.

Incidentally let it be stated that near the external opening of the vas deferens, as it passes along the posterior surface of the bladder, there arises in the third month a small evagination, which becomes the seminal vesicle (*sbl*).

The posterior region of the primitive kidney (*pa*) degenerates into very insignificant remnants. In older embryos one still finds for a time, between vas deferens and testis, small, tortuous canals, usually blind at both ends, between which degenerated Malpighian corpuscles also occur. The whole forms a small yellow body. In the adult these remnants are still further reduced; they produce on the one hand the *vasa aberrantia of the epididymis*, and on the other the organ discovered by GIRALDÈS, the *paradidymis*. The latter consists, according to HENLE's description, of a small number of flat, white bodies, lying in contact with the blood-vessels of the seminal cord, each of which is a knotted tubule blind at both ends; each tubule is lined with an epithelium containing fat, and is enlarged at its blind ends into irregularly lobed vesicles.

The Müllerian ducts (fig. 222 *mg*) do not acquire in the male any function, and therefore, as useless structures, undergo degeneration; the middle region in fact usually disappears without leaving a trace although it has been for a time during embryonic life demonstrable as an epithelial cord. Gasser indeed observed a rudimentary canal of considerable extent at the side of the vas deferens in a recently born male child. Certain rudiments of the terminal portions, on the contrary, are preserved even in the adult individual, and in descriptive anatomies are called *uterus masculinus* (*um*) and *non-stalked hydatids of the epididymis* (*hy*).

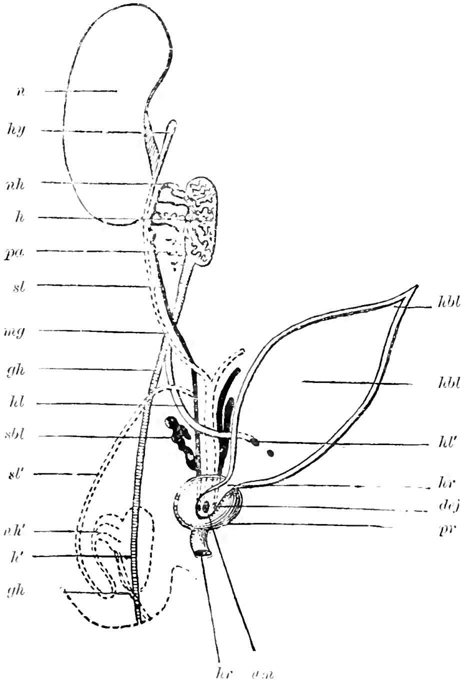


Fig. 222.—Diagram to illustrate the development of the male sexual organs of a Mammal from the indifferent fundament of the urogenital system, which is diagrammatically represented in fig. 219.

The persistent parts of the original fundament are indicated by continuous lines, the parts which undergo degeneration by dotted lines. Dotted lines are also employed to show the position which the male sexual organs take after the completion of the descensus testiculorum.

n, Kidney; *h*, testis; *nh*, epididymis; *pa*, paradidymis; *hy*, hydatid of the epididymis; *sl*, vas deferens; *mg*, degenerated Müllerian duct; *um*, uterus masculinus, remnant of the Müllerian ducts; *gh*, gubernaculum Hunteri; *hl*, ureter; *hl'*, its opening into the bladder; *sbl*, vesiculæ seminales; *hbl*, urinary bladder; *hbl'*, its upper tip, which is continuous with the ligamentum vesico-umbilicale medium (urachus); *hr*, urethra; *pr*, prostata; *dej*, external orifice of the ductus ejaculatorii.

The letters *nh'*, *h'*, *sl'* indicate the position of the several organs after the descent has taken place.

The posterior terminal parts of the two Müllerian ducts, which lie close together enclosed in the genital cord, are modified into the *uterus masculinus* (*um*). Owing to the disappearance of the partition separating them, they are united into a single small sac, which is situated between the openings of the two vasa deferentia at the prostata and therefore still bears the name of sinus prostaticus. Extraordinarily inconspicuous in Man, it acquires in many Mammals, in Carnivores and Ruminants (Weber), a considerable size, and is differentiated, as in the female, into a vaginal and a uterine part. In Man it corresponds chiefly to the vagina (Tourneux).

The *non-stalked hydatid* (*hy*) is developed out of the other end of the Müllerian duct. It is a small vesicle that rests upon the epididymis, is lined with ciliate cylindrical epithelium, and is continued into a small, likewise ciliate canal. At one place it possesses a funnel-shaped opening, which has been compared by Waldeyer to the pavilion of a Fallopian tube in miniature.

In order to complete the account of the development of the sexual organs, there still remain to be mentioned the *important changes of position* which the testis together with the attached rudiments undergoes. Since early times, these have been embraced under the name of *descensus testiculorum.*

Originally the testes (fig. 222 *h*) lie, as previously stated, in the peritoneal cavity at the side of the lumbar vertebræ. In the third month we find them already in the greater (false) pelvis, in the fifth and sixth on the inner side of the anterior wall of the abdomen close to the inner abdominal ring (fig. 223). In consequence of these changes the nourishing blood-vessels, which at first ran transversely, have altered their direction and now pass obliquely from below upward, because their original place of attachment to the abdominal aorta and the inferior vena cava remains the same. How is the migration to be explained?

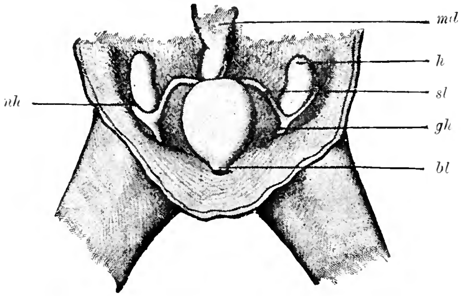


Fig. 223.—Human embryo of the fifth month, after Bramann. Natural size.
md, Rectum; *h*, testis; *nh*, epididymis; *sl*, vas deferens; *gh*, gubernaculum Hunteri with processus vaginalis peritonei; *bl*, bladder with lig. vesico-umbilicale medium.

I have already mentioned the inguinal ligament, or the gubernaculum Hunteri (fig. 222 and 223 *gh*), which puts the primitive kidney, or, when this has disappeared, the testis, into connection with the inguinal region. This ligament has in the meantime become a strong connective-tissue cord, in which non-striate muscles also lie. Its upper end is attached to the head of the epididymis (*nh*); its lower end traverses the abdominal wall to be inserted into the corium of the inguinal region. Apparently this gubernaculum plays a part in the migration of the sexual organs. Formerly it was believed that it exercised a traction upon the testis, in which connection attention was directed to the non-striate muscle-fibres contained in it, or a shortening of the connective-tissue cord by gradual shrinkage was assumed. But it is impossible for this very important change in position to have taken place in that manner. One therefore rightly seeks to explain the agency of the ligament in another way, without assuming an active shortening or a traction exercised by muscular action. We have to do here simply with processes of unequal growth. When, out of several organs originally lying beside one another in the same region of the body, certain ones in later months of embryonic life increase in size less, while others, on the contrary, grow extraordinarily in length, the natural consequence is that the more rapidly growing parts are shoved past those that grow more slowly. If, now, in the present case the skeletal parts and their accompanying muscles in the lumbar and pelvic regions become elongated, while the Hunterian ligament does not grow and therefore remains short, the latter necessarily—because one of its ends is attached to the skin of the inguinal region and the other to the testis—draws down the testis as the movable part; it draws the testis at first gradually into the cavity of the false pelvis, and finally, when the other parts have become still larger, when at the same time the abdominal wall has become much thicker, into the vicinity of the inner abdominal ring (fig. 223).

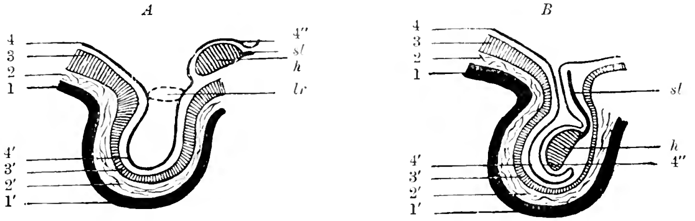


Fig. 224.—Two diagrams to illustrate the descensus and the formation of the envelopes of the testis.

A, The testis lies in the vicinity of the inner abdominal ring. *B*, The testis has entered the scrotum.

1, Skin of the abdomen; 1′, scrotum with tunica dartos; 2, superficial abdominal fascia; 2′, Cooper's fascia; 3, muscle-layer and fascia transversa abdominis; 3′, tunica vaginalis communis with cremaster; 4, peritoneum; 4′, parietal layer of the tunica vaginalis propria; 4″, peritoneal investment of the testis or visceral layer of the tunica vaginalis propria.

lr, Inguinal or abdominal ring; *h*, testis; *sl*, vas deferens.

The testis migrates still farther in consequence of a second process, which begins even in the second month. For there is formed at the place where Hunter's ligament traverses the wall of the abdomen an evagination of the peritoneum, the *processus vaginalis peritonei* (fig. 224 *A*). This gradually penetrates the abdominal wall and enters into a fold of the skin, which is developed in the pubic region, as will be shown in a subsequent section (see fig. 231 *gw*). The opening of the hernia-like evagination, which leads into the body-cavity, is called the *inner inguinal* [*abdominal*] *ring* (*lr*); the portion which traverses the musculature of the abdominal wall, the *inguinal canal*; and the blind end which is expanded within the dermal fold, the *scrotum*.

In its migration the testis (fig. 224 *B*) also sinks down into this peritoneal fold, whereby it remains undetermined whether HUNTER's ligament exercises an influence on it or not. The entrance into the inguinal canal usually takes place in the eighth month, into the scrotum in the ninth month, so that at the end of embryonic life the descent is, as a rule, completed. The canal then closes by fusion of its walls, and thereby the testis comes to lie in a sac constricted off from the abdominal cavity and enclosed on all sides.

The various *enveloping structures of the testis* also become intelligible from the sketch of the development just given. Since the cavity which shelters it is simply a detached portion of the body-cavity, it is, as a matter of course, lined by peritoneum (fig. 224 $_4{}'$). This is the so-called *tunica vaginalis propria*, on which, as on other regions of the peritoneum, we have to distinguish a parietal layer ($_4{}'$) lining the wall of the sac and a visceral layer ($_4{}''$) investing the testis. Outside of this follows the *tunica vaginalis communis* ($_3{}'$); it is the evaginated, and at the same time extraordinarily attenuated, layer of muscles and fasciæ ($_3$) of the abdominal wall. Consequently it also contains some muscle-fibres enclosed in it, which are derived from the musculus obliquus abdominis internus, and constitute the suspensory muscle of the testis or cremaster.

In the descensus testiculorum, which should normally be completed in Man at the end of embryonic life, interruptions may, under certain circumstances, occur and produce an abnormal location of the testis, which is known under the name of *cryptorchism*. The descent remains incomplete. Then the testes of the recently born child are either found to be located in the body-cavity, or they still stick fast in the wall of the abdomen, in the inguinal canal. In consequence the scrotum feels small, flabby, and flaccid.

Such anomalies are designated as *inhibition-malformations*, because they are explained by the fact that the processes of development have not reached their normal termination.

(B) *The Metamorphosis in the Female. Descensus ovariorum.*

The metamorphosis of the primitive embryonic fundaments in the female is in many particulars the opposite of that in the male, inasmuch as parts which are made use of in the latter become rudimentary in the former, and *vice versâ* (compare with one another the diagrams shown in figs. 219, 222, and 225). Whereas in man the mesonephric duct becomes the vas deferens, in woman the Müllerian duct (fig. 225 *t*, *ut*, *sch*) assumes the function of conducting away the ova, while the mesonephric duct (*ug*) and the primitive kidney (*ep*, *pa*) become rudimentary.

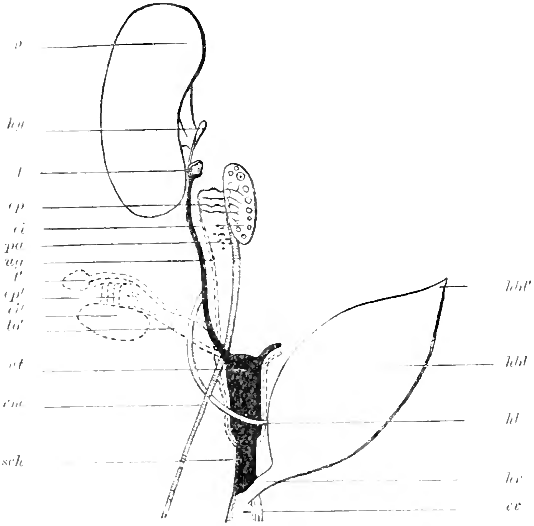


Fig. 225.—Diagram to illustrate the development of the female sexual organs of a Mammal from the indifferent fundament of the uro-genital system, which is diagrammatically represented in fig. 219.

The persistent parts of the original fundament are indicated by continuous lines, the parts which undergo degeneration by dotted lines. Dotted lines are also employed to show the position which the female sexual organs take after the completion of the descensus.

n, Kidney ; *ei*, ovary ; *ep*, epoöphoron ; *pa*, paroöphoron ; *hy*, hydatid ; *t*, Fallopian tube (oviduct) ; *ug*, mesonephric duct ; *ut*, uterus ; *sch*, vagina ; *hl*, ureter ; *hbl*, urinary bladder ; *hbl'*, its upper tip, which is continuous with the ligamentum vesico-umbilicale medium ; *hr*, urethra ; *ve*, vestibulum vaginæ ; *rm*, round ligament (inguinal ligament of the primitive kidney) ; *lo'*, ligamentum ovarii.

The letters *t'*, *ep'*, *ei'*, *lo'* indicate the positions of the organs after the descent.

The *pronephric duct* in advanced human embryos of the female sex is still demonstrable as an inconspicuous structure in the broad ligament and at the side of the uterus; in the adult it has, as a rule, entirely disappeared, except the terminal portion, which is enclosed in the substance of the neck of the uterus, where it is distinguishable, but only by means of cross sections, as an extraordinarily narrow tubule (Beigel, H. Dohrn). In many Mammals, as in Ruminants and Swine, the mesonephric ducts persist even later in a rudimentary condition, and are here known under the name of GARTNER's canals.

There are to be distinguished on the degenerating primitive kidney, as in Man, an anterior and a posterior region (WALDEYER).

The anterior region (figs. 225 *ep*, 226 *ep*), *or the sexual part of the primitive kidney*, which in the male becomes the epididymis, is also retained by the female as an organ without function and here becomes the *parovarium* (*ep*), which was first accurately described by KOBELT (the parovarium or epoöphoron of WALDEYER). It lies in the broad ligament (fig. 226) between ovary (*ei*) and Müllerian duct (*t*), and consists of a longitudinal canal (*ug*), the remnant of the upper end of the mesonephric duct, and of ten to fifteen transverse tubules (*ep*). The latter have at first a straight course, but afterwards become tortuous (fig. 227 *ep*), in much the same way as the canals which in the male are converted into the coni vasculosi. The comparison between parovarium and epididymis may be carried still further. As in the male tubules grow out from the latter into the cortex of the testis and are there differentiated into the rete testis and the tubuli recti, so there are also canals found in the female which proceed from the parovarium, enter the medullary substance of the ovary itself, and form here the previously (p. 381) described medullary cords, which are highly developed in many Mammals.

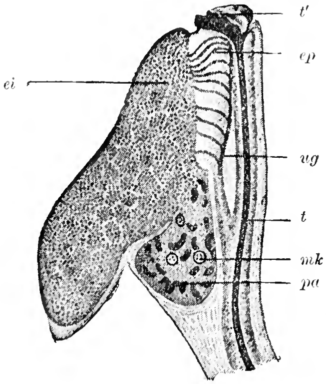


Fig. 226.—The internal sexual parts of a female human embryo 9 cm. long, after WALDEYER. Magnified 10 diameters.
ei, Ovary ; *t*, Müllerian duct or oviduct (Fallopian tube) ; *t'*, ostium abdominale tubæ ; *ep*, epoöphoron (= epididymis of the male —sexual part of the primitive kidney) ; *ug*, mesonephric duct (vas deferens of the male) ; *pa*, paroöphoron (paradidymis of the male—rudiment of the primitive kidney) ; *mk*, Malpighian corpuscles.

The posterior portion of the primitive kidney, which in the male (figs. 221 and 222 *pa*) furnishes the paradidymis and the vasa aberrantia, degenerates in the female (fig. 225 *pa*) in a similar manner into the paroöphoron, and is still to be recognised for a long time in the human embryo as a yellowish body (fig. 226 *pa*), which lies medianwards of the epoöphoron (*ep*) in the broad ligament, and is composed of small, tortuous, ciliate tubules (*pa*) and a few degenerating vascular glomeruli (*mk*). Certain canals and cyst-like structures, which are often found in the broad ligament of the adult close to the uterus, are to be referred to it.

The two *Müllerian ducts* (fig. 219 *mg*), which from the beginning lie in the margin of the peritoneal fold that serves for the reception of the ovary and subsequently becomes the broad ligament, undergo a very profound metamorphosis. It has already been mentioned that as they enter the lesser or true pelvis they approach the median plane, and are joined to the genital cord. We can therefore distinguish in them two different regions, one enclosed in the genital cord, the other lying in the margin of the broad ligament. The latter becomes the oviduct (the tuba Fallopiæ) with its funnel-shaped beginning (figs. 225 *t*, 226, 227 *t*, *t'*). The anterior end of the Müllerian duct, which in the embryo reaches far forward and is here enclosed in the diaphragmatic ligament of the primitive kidney, appears in the meantime to degenerate, whereas the permanent opening (figs. 225 *t* and 226 *t'*) is probably an entirely new formation. Morgagni's *hydatid* (fig. 225 *hy*) is perhaps to be referred to the anterior rudimentary part—the conditions here have not yet been made entirely clear. This structure is a small vesicle, which is joined, by means of a longer or shorter stalk, with one of the fimbriæ of the funnel-shaped end of the oviduct.

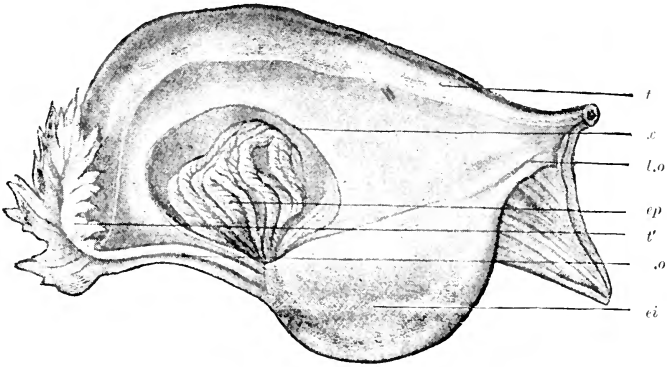


Fig. 227.—Broad ligament with ovary and oviduct in the adult condition, seen from behind. *ei*, Ovary ; *t*, oviduct ; *t'*, ostium abdominale tubæ with fimbriæ ; *f.o*, fimbriæ ovarii ; *l.o*, ligamentum ovarii ; *x*, a portion of the peritoneal investment is dissected away, in order to see the epoöphoron (parovarium), *ep*.

Out of the part of the Müllerian ducts enclosed in the genital cord (fig. 219 *mg*) are formed the *uterus* and the *vagina* (fig. 225 *ut* and *sch*), as **Thiersch** and **Kölliker** have shown for Mammals, and as **Dohrn** and **Tourneux et Legay** afterwards showed for Man. Their formation is accomplished by a process of fusion, which in Man is effected in the second month. When the Müllerian ducts (fig. 228 *mg*) are closely pressed together, the partition between them becomes thin and breaks through—at first in the middle of the genital cord. Thus there is developed out of them by an extension of this process a single sac (the sinus genitalis), which is also established in the male as a rudimentary organ, the previously mentioned sinus prostaticus or uterus masculinus (fig. 222 *um*). In woman it begins to be differentiated in the sixth month into uterus and vagina. The upper portion, which receives the oviducts, acquires very thick, muscular walls and a narrow lumen, and is limited below by a re-entering ring-like ridge—that becomes the vaginal portion [of the uterus]—from the lower portion, the vagina, which remains spacious and possesses a thinner wall.

Similarly to the testis, the ovaries also have to pass through a considerable change in position: the *descensus ovariorum* (fig. 225 *ei'*, *t'*), which corresponds to the descent of the testes. In the third month of embryonic life, at the time when the primitive kidney begins to disappear, the ovaries move from the region of the lumbar vertebræ down into the false pelvis, where they are found medianwards from the musculus psoas. Probably the above-described *inguinal ligament* of the primitive kidney (fig. 225 *rm*), which is not wanting in the female, participates in the change of position in this case also. As **Wieger** has recently shown, the ligament is differentiated into three distinct regions by the fact that it acquires a firm union with the Müllerian ducts at the place where they meet to form the sexual cord. The uppermost region becomes a strand of non-striate muscle-fibres, which, arising from the parovarium, is imbedded in the hilus of the ovary. This is continuous with the second region, or the ligamentum ovarii (*lo'*), and the latter with the round ligament (*rm*) (ligamentum teres uteri). The round ligament, produced from the third and most developed region of the inguinal ligament, extends from the upper end of the genital cord to the inguinal region. Here there is usually, as in the male, a small evagination of the peritoneum, the processus vaginalis peritonei, which occasionally persists even in the adult as the diverticulum Nuckii, and then may likewise be the cause of the formation of an inguinal hernia in the female. At this place the round ligament passes through the wall of the abdomen and ends in the external skin of the labia majora.

In its last stages the descent in the female is accomplished in a manner different from that in the male. For instead of advancing like the testes toward the inguinal region, the ovaries, when the development is normal, sink down instead into the true pelvis. Here they are enclosed between bladder and rectum in the broad ligament, which is developed out of the peritoneal folds, and in which originally the primitive kidneys, the ovaries, and the Müllerian ducts are imbedded.

Naturally the round ligament cannot be of influence during this last stage of the descent in the female, because it can exercise a traction only in the direction of the inguinal region, where it is attached. The descent into the true pelvis seems rather to be due to the conversion of the lower region of the Müllerian ducts into the uterus. At any rate, the ovaries are joined to the uterus by means of a firm cord of connective tissue, the ligamentum ovarii.

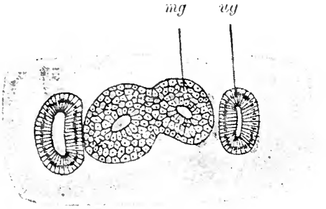


Fig. 228.—Cross section through the genital cord, after Tourneux et Legay. The cross section shows the fusion of the Müllerian ducts (*mg*); *ug*, mesonephric ducts.

In rare cases in the female the ovaries can continue to change their position in a manner corresponding to that in the male. They migrate then toward the inguinal region up to the entrance into the processus vaginalis (diverticulum Nuckii); occasionally they here cease to advance, but sometimes they enter farther into the abdominal wall through the inguinal canal; indeed, as has been observed in several instances, they can pass quite through the wall of the abdomen and at last imbed themselves in the labia majora. The latter then acquire a great similarity to the scrotum of the male.

(*i*) *The Development of the External Sexual Organs.*

The section which deals with the urinary and sexual organs is really the most suitable place at which to introduce the development of the external sexual organs, notwithstanding they do not arise from the middle germ-layer, but in part from the outer and in part from the inner germ-layer. In order to give an exhaustive account of them, we must go back to rather early stages of development—to the time when in the embryo the Wolffian and Müllerian ducts are established. Having first arisen in the most anterior part of the embryo, they grow backwards to the terminal part of the intestine, and there implant themselves in the allantois. This is, as we have seen in the first part of this text-book (fig. 132, 3 and 4 *al*), an organ which is produced by evagination of the anterior [ventral] wall of the hind gut. In most Mammals (figs. 134 *al* and 142 *ALC*) it attains during embryonic life a quite extraordinary development, for it grows out of the body-cavity, penetrates between the other fœtal membranes, and is distended into a large vesicle, which receives the urinary fluid secreted by the embryo. The part of it which lies in the body-cavity remains, on the contrary, narrow. The terminal part of it which receives the Wolffian and Müllerian ducts is called *sinus urogenitalis* (fig. 219 *sug* and 229 *ug*), a structure which will often demand our attention in considering the development of the external sexual organs.

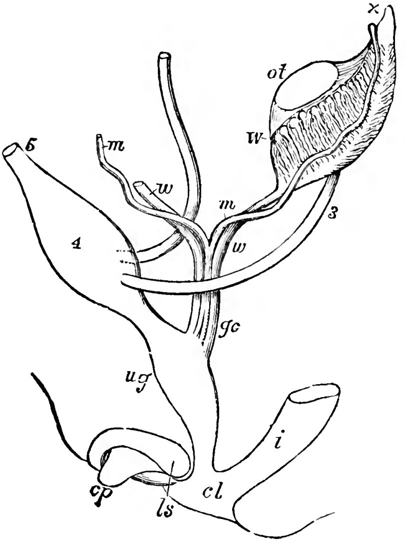


Fig. 229.—Diagram of the urogenital organs of a Mammal at an early stage, after ALLEN THOMSON; from BALFOUR.

The parts are seen chiefly in profile, but the Müllerian and Wolffian ducts are seen from the front.

3, Ureter; *4*, urinary bladder; *5*, urachus; *ot*, genital gland (ovary or testis); *W*, left Wolffian body (primitive kidney); *x*, its diaphragmatic ligament; *w*, Wolffian (mesonephric) duct; *m*, Müllerian duct; *gc*, genital cord consisting of Wolffian and Müllerian ducts enveloped in a common sheath; *i*, rectum; *ug*, urogenital sinus; *cp*, genital eminence, which becomes the clitoris or penis; *ls*, genital ridges from which the labia majora or the scrotum are developed.

The sinus urogenitalis and the hind gut unite to form a short, unpaired region, the cloaca (fig. 229 *cl*), a small depression which opens out at the surface of the body and in very many Vertebrates—in the Amphibia, Reptiles, Birds, and the lowest Mammals, the Monotremes—persists throughout life. In the remaining Mammals, however, these structures have only an embryonic existence. In the first case all the elimination-products of the body are conducted to the outside through the cloaca,—out of the hind intestine the fæcal masses, out of the sinus urogenitalis the urinary fluid and the male or female sexual products.

As far as regards the special conditions in Man, the allantois remains in his case very small (fig. 132, 5 *al*) and possesses a lumen in the region of the body-cavity *only*, whereas in the umbilical cord and between the remaining fœtal membranes only its connective-tissue part, together with the blood-vessels, which shares largely in the development of the placenta, grows further. In the second month its hollow part, lying on the front wall of the abdomen, becomes a spindle-shaped body (fig. 229 $_4$). Its middle enlargement becomes the urinary bladder ($_4$), its upward prolongation, which reaches to the navel, is called urachus ($_5$), the other end (*ug*) is the sinus urogenitalis. The urachus degenerates during embryonic life and furnishes a connective-tissue cord, the ligamentum vesico-umbilicale medium, which extends from the apex of the bladder (fig. 219 *hbl′*) to the navel, and often in the first years after birth still contains an epithelial cord, a remnant of the original epithelial canal.

As is well known, the ureters (figs. 229 $_3$ and 219 *hl′*) in the adult open close together at the posterior surface of the urinary bladder (229 $_4$). In very young embryos this is not the case at first, for the two ureters arise from the posterior part of the mesonephric duct, and this opens into the sinus urogenitalis. But this condition is soon altered. The ureter splits off from the mesonephric duct, and comes to open independently into the posterior wall of the sinus urogenitalis, from which it afterwards becomes gradually removed, since its orifice, as it were, creeps higher up on the posterior wall of the bladder. Like the change in the position of the sexual glands, we must also conceive of this shifting as produced by processes of growth in such a way that especially the tract between mesonephric duct and ureter, which is at first small, increases in size, and thereby produces the apparent upward migration of the opening of the ureter.

In the sixth week the cloaca in Man undergoes alterations which are connected with the development of the external sexual organs. The cloacal depression, which in earlier stages (fig. 230 *A*) appears fissure-like, afterwards becomes (fig. 230 *B*) surrounded by a ring-like fold, the genital ridge (*gw*), and there also arises in its anterior portion a growth of connective tissue, which produces the externally protruding genital eminence (*gh*). Along the lower surface of the latter there is formed at the same time a groove (*gr*), which extends downward to the cloaca, of which it is, as it were, the continuation.

In the following weeks of development the eminence protrudes still more, and thereby becomes converted into the genital member, which is at first possessed by both sexes in the same condition; meanwhile the groove (*gr*) on its under surface becomes deeper, and surrounded, at the right and left, by projecting folds of the skin, the genital folds (*gf*). (Compare also the diagrams fig. 219 *ghö*, *gw*, *cl′* and fig. 229 *cp*, *ls*, *cl*.)

Alterations follow (fig. 231 *M* and *W*) by which the cloaca is differentiated into two openings, one lying behind the other, the anus (*a*) and the separate urogenital opening (*ug*). The deep partition (fig. 229) by which the sinus urogenitalis and the rectum are separated from each other begins to grow outward, and at the same time folds also arise on the lateral walls of the cloaca and unite with it. Thus a membrane (fig. 231 *d*) is developed which separates a posterior opening (*a*), the anus, from an anterior opening, the entrance to the sinus urogenitalis (*ug*). Inasmuch as this partition continues to become thicker up to the end of embryonic life, it finally crowds the two openings far apart and forms between them the perinæum (fig. 231 *M** and *W* d*). In this way the anus (*a*) moves entirely out of the territory of the previously mentioned genital ridge (fig. 230 *gw*).

From the fourth month onward great differences arise in the development of the external sexual parts in male and female embryos.

In the female (fig. 231 *W* and *W**) the metamorphoses of the originally common embryonic foundations are on the whole only slight; the genital eminence grows only slowly and becomes the female member, the *clitoris* (*cl*). Its anterior end begins to thicken and to be marked off from the remaining part of the body as the *glans*. By a process of folding in the integument there is developed around it (fig. 231 *W* vh*) a kind of foreskin (the præputium clitoridis). The two genital folds (*W gf*), which have bounded the groove on the under surface of the genital knob, take on a more vigorous development in the female than in the male, and are converted into the *labia minora* (*W* ksch*). The space between them (*W ug*), or the sinus urogenitalis, which receives the outlet of the urinary bladder and the vagina developed by the fusion of the Müllerian ducts, is called the *vestibulum vaginæ* (*W* vv*). In the female the genital ridges (*W gw*), owing to the deposition of fatty tissue, become very voluminous, and are thus converted into the *labia majora* (*W* gsch*).

The corresponding fundaments pass through much more essential metamorphoses in the *male* (fig. 231 *M* and *M**). By an extraordinarily vigorous growth in length the genital eminence is

Fig. 230.

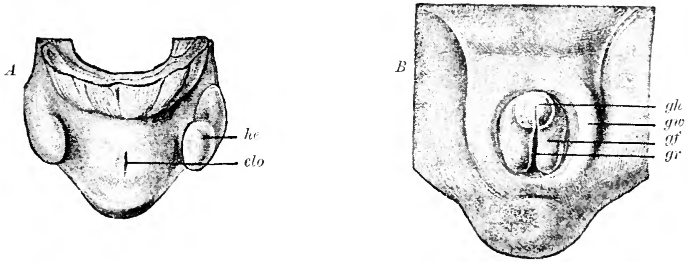
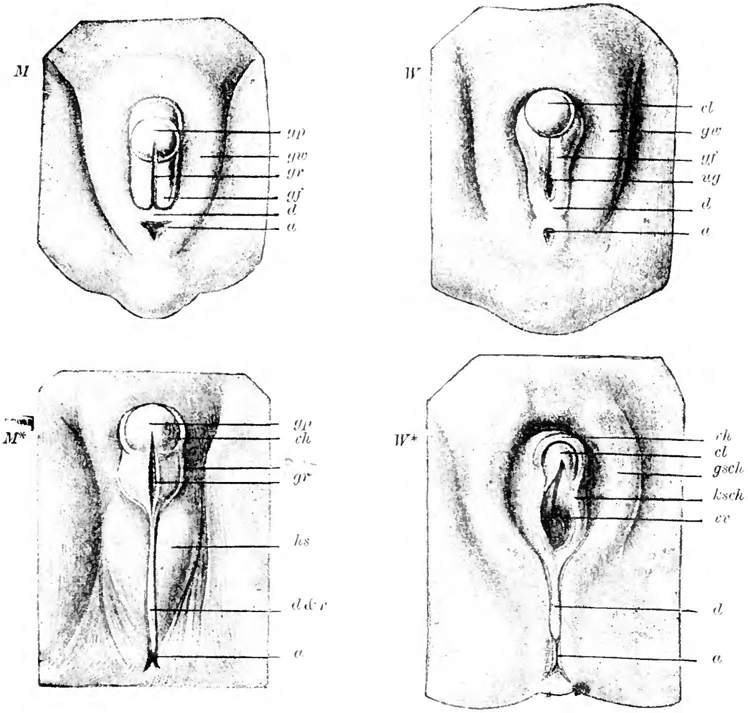


Fig. 231.



Figs. 230 and 231.—Six stages in the development of the external sexual organs in the male and the female, after the Ecker-Ziegler wax models.

Fig. 230 *A* and *B*.—Two stages in which a difference of the sexes is not yet to be recognised, *B* from an embryo 8 weeks old.

Fig. 231.—The two stages *M* and *M** exhibit the metamorphosis of the original fundament in the male in embryos 2½ and 3 months old respectively. The stages *W* and *W** present the metamorphosis in the female (2½ and 4½ months).

The same designations are used for all of the figures.

he, Posterior paired extremity; *clo*, cloaca; *gh*, genital eminence; *gf*, genital fold; *gr*, genital groove; *gw*, genital ridges; *gp*, glans penis; *cl*, clitoris; *d*, perinæum; *a*, anus; *ug*, entrance to sinus urogenitalis or vestibulum vaginæ; *vv*, vestibulum vaginæ; *ch*, foreskin (prepuce); *hs*, scrotum; *d & r*, raphe perinei and scroti; *gsch*, labia majora; *ksch*, labia minora.

converted into the *male member*, or the *penis*, which corresponds to the clitoris of the female. Like the latter, it possesses an anterior knob-like enlargement, the glans (*M gp*), which is embraced by a fold of the skin, the præputium (*M* vh*). The sinus urogenitalis, which in the female remains short and broad as the vestibulum vaginæ, is in the male converted by a process of fusion into a long narrow canal, the urinary tube or *urethra*. This results from the fact that the furrow on the under surface of the genital protuberance (*M gr*) becomes elongated during the development of the latter and at the same time deeper, and that the sexual folds (*gf*) bordering it protrude farther, coming into immediate contact along their edges (*M**) as early as the fourth month, and begin to fuse together.

The posterior end of the urethra early (second month) undergoes changes by which the *prostata* (fig. 222 *pr*) is formed. The walls become greatly thickened, acquire non-striate muscular tissue, and constitute a ring-like ridge, into which evaginations from the epithelium of the tube penetrate, and by their branchings furnish the glandular portions of the organ. On its posterior wall are found, as is well known, the openings (*dej*) of the vasa deferentia, and between them the sinus prostaticus or uterus masculinus (*um*), produced by the fusion of the Müllerian ducts.

The genital ridges (fig. 231 *M gw*), which in woman become the labia majora, also undergo a fusion in man. They surround the root of the penis and then fuse in the median plane, where the place of union is indicated afterwards by the so-called raphe scroti (*M* r*). Into the *scrotum* (*M* hs*) thus formed the testes, toward the end of embryonic life, migrate, as previously described.

From the fact that originally the external sexual parts are constituted exactly alike in both sexes, it is evident why, with a derangement of the normal course of development, forms come into existence in which it is sometimes extremely difficult to determine whether one has to do with male or female external parts. These are cases which in earlier times were erroneously designated as *hermaphroditism*. There are two ways in which they may arise. They are either to be referred to the fact that in a female the process of development has proceeded further than normally (*i.e.*, as in the male), or that in a male the process of development has suffered an early interruption, and thereby led to formations which are similar to the female genital parts.

As far as regards the first kind of malformations, the genital eminence in the female occasionally assumes such a size and form that it resembles in every particular the male organ. The resemblance may become even greater, when the ovaries migrate into the inguinal region instead of the true pelvis, pass through the wall of the abdomen, and become imbedded in the labia majora. In consequence of this the latter lie upon the root of the large clitoris and simulate a kind of scrotum.

The malformations which have given occasion for the assumption of hermaphroditism are of more frequent occurrence in the male. They are attributable to the fact that the processes of fusion which normally take place are interrupted. We then have a genital member, which ordinarily is rudimentary, along the under side of which there runs only a furrow instead of the urethra, a malformation which is designated as *hypospadias*. With this morphological deficiency may be united, secondly, an arrest of the normal descent of the testes. The latter remain in the body-cavity, and the genital ridges thus acquire a great similarity to the labia majora of the female.

III. The Development of the Suprarenal Bodies.

The discussion of the suprarenal bodies best follows that of the urogenital system. For, aside from the fact that the suprarenal bodies and the genito-urinary organs are in all Vertebrates very closely connected spatially, they also appear to stand in very close relation to each other in the history of their development. At least the recent investigations of WELDON, JANOSIK, and MIHALKOVICS point that way, and are perhaps also sufficient to suggest the direction of the physiological research by which one can acquire an explanation concerning the ever problematic function of these bodies.

As is well known, there are to be distinguished in the suprarenal bodies two different substances, which in Mammals are described, according to their mutual relations, as medulla and cortex. Most investigators ascribe to them a double origin. BALFOUR, BRAUN, KÖLLIKER, and MITSUKURI make the medulla arise from the ganglionic fundaments of the sympathetic nerve-trunk (Grenzsträng),—it is for this reason that in many text-books the suprarenal bodies are treated of in connection with the sympathetic,—but GOTTSCHAU and JANOSIK controvert this; they maintain that only certain ganglionic cells and nerve-fibres grow in from the sympathetic, but that the real medullary cells arise by a metamorphosis of cortical cells. It appears to me from the existing investigations that the question is not ready for discussion.

There are also two different interpretations concerning the development of the cortical substance. Balfour, Braun, Brunn, and Mitsukuri derive it from accumulations of connective-tissue cells, which are formed at the anterior portion of the primitive kidney along the course of the inferior vena cava and the cardinal veins. According to Janosik, Weldon, and Mihalkovics, on the contrary, the cell-accumulations are either directly or indirectly formative products of the epithelium of the body-cavity. I say "direct or indirect" because in details the results of the three investigators named differ somewhat. According to Janosik and Mihalkovics, it is the germinal epithelium in the anterior portion of the genital ridge that furnishes by its proliferation the material for the suprarenal body. Mihalkovics therefore calls it "a detached part of the sexually undifferentiated genital gland, which consequently remains at a primitive stage of development." Weldon, on the contrary, brings the suprarenal body into relation with the most anterior part of the primitive kidney. According to his representation, which appears to me to deserve especial consideration, and from which indeed other researches will have to begin, *the sexual cords of the primitive kidney are concerned in the formation of the suprarenal bodies.* When, at the head-end of the kidney, they sprout out of the epithelium of the Malpighian glomerulus in the manner previously (p. 383) described, they divide into two branches. One of these grows ventrally into the fundament of the sexual gland, the other turns dorsally and spreads out in the vicinity of the vena cava.

Moreover, even Mihalkovics describes a connection of the sexual cords with the fundament of the suprarenal body at certain places, but makes both arise from proliferations of the epithelium of the body-cavity. The connection is subsequently destroyed by the interpolation of blood-vessels.

For the solution of the still pending questions most is to be expected from the investigation of non-amniotic animals.

During its development the suprarenal body is for a time of very considerable size. In Mammals it temporarily covers the much smaller kidney, as in the human embryo of the eighth week represented in fig. 220, in which at the left the suprarenal body (*nn*) is to be seen in its normal position, whereas on the right it has been removed to disclose the kidney (*n*). Afterwards its growth does not keep pace with that of the kidney; however at birth (fig. 208), when it already rests upon the latter (*n*) as a crescentic body (*nn*), it still is larger in comparison with the kidney than it is in the adult.

During its development some small portions of the fundament of the suprarenal cortex appear sometimes to detach themselves and to remain in the vicinity of the sexual organs, in whose migrations they participate. Thus, indeed, are to be explained the *accessory suprarenal bodies* observed by Marchand at the margin of the broad ligament.

Summary.

1. The following structures are to be interpreted as formative products of the middle germ-layer : the epithelium of the body-cavity (of the pericardium, of the thoracic and abdominal cavities, of the cavity of the scrotum), the whole of the transversely striped, voluntary musculature, the seminal cells and ova, the epithelium of the sexual glands, of the kidneys and their outlets, and the cortical cords of the suprarenal bodies.

The Development of the Musculature.

2. The musculature of the trunk is developed exclusively from the cell-layer of the primitive segments that abuts upon the chorda and neural tube, which by the formation of muscle-fibrillæ is converted into a muscle-plate.

3. The muscle-plate enlarges dorsally and ventrally, where it becomes continuous (zone of growth) with the outer (lateral) epithelial layer of the primitive segment, and spreads itself out over the neural tube above and into the walls of the abdomen below.

4. The original musculature consists of segments of longitudinal fibres (myomeres), which are separated from one another by connective-tissue partitions (ligamenta intermuscularia).

5. The musculature causes the first segmentation of the body of Vertebrates into equivalent successive parts or metamera.

6. Buds grow out from the muscle-plates (Selachians) into the fundaments of the limbs, and thus furnish the foundation for the whole musculature of the extremities.

7. In the head-region of Vertebrates the musculature is developed not only out of the primitive segments, the number of which in Selachians amounts to nine, but also out of that part of the middle germ-layer which corresponds to the lateral plates of the trunk, and which is divided up by the formation of the visceral clefts into separate visceral-arch cords, which in the Selachians are provided with cavities.

8. From the primitive segments of the head are formed the muscles of the eyes, and from the visceral-arch cords the masticatory muscles, the muscles of the hyoid arch and also those of the small bones of the ear (?).

The Development of the Urogenital System.

9. The first fundament of the urogenital system is the same in both sexes: it consists of (1) three pairs of canals—the mesonephric duct, the Müllerian duct, and the ureter; (2) four pairs of glands—the pro-, meso-, and metanephros and the sexual gland, which at first is indifferent.

10. The mesonephric duct arises in its most anterior part out of a groove-like evagination or a ridge-like thickening of the parietal middle layer; posteriorly it detaches itself from its parental tissues, fuses with the neighboring outer germ-layer, and thereby forms at first a short, tubular communication between the cœlom and the surface of the body.

11. The mesonephric duct is gradually converted into a long canal, inasmuch as it grows backward on the outer germ-layer, which forms a thickened ridge, until it opens out into the cloaca (terminal part of the hind intestine).

12. The pronephros (head-kidney) is developed at the anterior part of the mesonephric duct in the following manner: the duct, upon being constricted off from the parietal middle layer, remains in connection with the latter at several places, and the resulting cords of connection grow out into long pronephric tubules, at the inner openings of which an intraperitoneal vascular glomerulus is established out of the wall of the body-cavity.

13. Behind the pronephros the mesonephros (primitive kidney) arises thus: when the primitive segments are constricted off from the lateral plates, segmentally arranged cellular tubes or cords (nephrotome) are formed, which communicate at one of their ends with the body-cavity and at their other ends put themselves into connection with the laterally situated mesonephric duct and become the mesonephric tubules. (Development of Malpighian corpuscles, of secondary and tertiary mesonephric tubules and the glomeration of the latter.)

14. In the higher Vertebrates the development of the primitive kidney is to a certain extent abbreviated, in so far as the separate cords of cells which arise at the constricting off of the primitive segments lie very close together and constitute an apparently

undifferentiated cell-mass (the middle plate or the mesonephric blastema), out of which the mesonephric tubules subsequently—when they become clearly distinguishable—appear to have been differentiated.

15. In a part of the non-amniotic Vertebrates (some Selachians, Amphibians) the primitive kidney remains in open communication with the body-cavity by means of numerous ciliate funnels (nephrostomes), whereas in all Amniota the mesonephric tubules early surrender their genetically established connection with the body-cavity through the disappearance of the ciliate funnels.

16. The permanent kidney (metanephros) is the latest to be formed and takes its origin from two separate parts :—

(*a*) From an evagination of the end of the mesonephric duct, which furnishes the ureters, the pelvis of the kidney, and the straight urinary tubules (in other words, the efferent apparatus) ;

(*b*) From a renal blastema, which represents a backward prolongation of the mesonephric blastema, has the same origin as the latter, and is converted into the tortuous urinary tubules with the Malpighian corpuscles (therefore the secretory part of the kidney).

17. The fundaments of the kidney, which have arisen far back in the body, rapidly increase in size and undergo a change of position by moving farther forward by the side of the primitive kidneys, whereby the ureter becomes wholly detached from the mesonephric duct and moves to the posterior [dorsal] surface of the allantois, the future urinary bladder.

18. In the non-amniotic Vertebrates the mesonephros also gives rise by a process of fission to the Müllerian duct, which runs parallel with it.

19. In the Amniota the relation of the Müllerian duct to the mesonephric duct is still uncertain, because the front end of the former is established by a groove-like depression of the epithelial investment on the lateral face of the mesonephros, while concerning the remaining part it is still undetermined whether it grows backwards independently or is constricted off from the mesonephric duct.

20. The sexual glands proceed from two fundaments :—

(*a*) From a germinal epithelium, a modified part of the epithelium of the body-cavity, located on the median face of the primitive kidney ;

(*b*) From the sexual cords, which grow out toward the germinal epithelium from the adjacent part of the primitive kidney (in Reptiles and Birds from the epithelium of Malpighian glomeruli).

21. The specific components of the sexual glands, the eggs and seminal cells, arise from the germinal epithelium (with its primitive ova and primitive seminal cells).

22. In the female there arise, in consequence of a process of mutual intergrowth on the part of the germinal epithelium and the subjacent stroma, the tubes of PFLÜGER and egg-balls (or nests), and out of these finally egg-follicles, containing each a single ovum; in the male there are formed, in consequence of a similar process, seminal ampullæ (Selachians, some Amphibia) or seminal tubules (tubuli seminiferi) with their seminal mother-cells.

23. The sexual cords of the primitive kidney participate in the composition of the medullary substance of the ovary as medullary cords; in the testis they unite with the seminal ampullæ or seminal tubules and furnish the tubuli recti and the rete testis, consequently the initial part of the outlet for the semen.

24. The ovarian follicles are composed of a centrally located ovum, an envelope of follicular cells, and a vascular connective-tissue capsule (theca folliculi).

25. In Mammals the ovarian follicle is converted into a Graafian follicle by an increase in the number of follicular cells and by their secreting between them a follicular fluid. (Discus proligerus, membrana granulosa.)

26. The Graafian follicles, after the elimination of the mature ova into the abdominal cavity, become the so-called yellow bodies in the following manner: blood flows out of the ruptured blood-vessels into their cavities, and both the follicular cells left behind and the connective-tissue capsule undergo proliferation accompanied by an emigration of white blood-corpuscles (true and false corpora lutea).

27. The yellow bodies subsequently cause by their scar-like shrivelling the cicatriculæ and callosities on the surface of old ovaries.

28. The canals and glands of the urogenital system, which are at first established in the same form in both sexes, are afterwards differently employed in the male and female and undergo a partial degeneration.

29. In the male the mesonephric duct becomes the vas deferens, in the female it becomes rudimentary (GARTNER'S duct, in many Mammals).

30. The Müllerian duct assumes in the male no function, and

only inconspicuous remnants of it are left at its ends (hydatid of the epididymis and sinus prostaticus or uterus masculinus); in the female it becomes the efferent apparatus of the ovary,—the anterior part the oviduct, the posterior part the uterus and vagina, the latter resulting from the fusion of the ducts of the opposite sides of the body as far as they are enclosed in the genital cord.

31. In the male the anterior portion of the primitive kidney (mesonephros)—having united with the seminal tubules by means of the sexual cords—persists as the epididymis; the remainder degenerates into the paradidymis. In the female both parts degenerate into epoöphoron and paroöphoron, which correspond respectively to the epididymis and paradidymis of the male.

32. The sexual glands, which are originally established in the lumbar region, gradually move with their outlets downward toward the pelvic cavity. (Descensus testiculorum et ovariorum. Oblique course of the spermatic arteries and veins.)

33. In the migration of the sexual glands a rôle appears to be played by the inguinal ligament, which passes from the primitive kidney underneath the peritoneum to the inguinal region, penetrates through the wall of the abdomen, and ends in the skin of the genital ridges that surround the cloaca. (Gubernaculum Hunteri in the male; round ligament and ligamentum ovarii of the female.)

34. The testis is received some time before birth into the scrotum, an appendage of the body-cavity; the scrotum owes its origin to the fact that the peritoneum forms an evagination (processus vaginalis peritonei) through the wall of the abdomen into the genital ridges, and that afterwards the evagination is completely cut off from the body-cavity by the closure of the inguinal canal.

35. The layers of the scrotum or the envelopes of the testes correspond, in accordance with their development, to the separate layers of the body-wall, as is shown in the following comparative summary:—

Envelopes of the Testes.	*Wall of the Abdomen.*
Scrotum with tunica dartos.	Skin of the abdomen.
Cooper's fascia.	Superficial abdominal fascia.
Tunica vaginalis communis with cremaster.	Muscle-layer and fascia transversa abdominis.
Tunica vaginalis propria (parietal and visceral layers).	Peritoneum.

36. The external sexual organs are developed in man and woman from the same kinds of fundaments in the neighborhood of the cloaca.

37. The term cloaca is applied to a depression at the hinder end of the embryo, into which open the hind gut and the allantois, after the latter has received—on the posterior face of its attenuated terminal part, the sinus urogenitalis—the closely approximated Müllerian and mesonephric ducts.

38. The cloaca becomes divided by projecting folds, which unite to form the perinæum, into an anterior [ventral] and posterior [dorsal] portion, of which the former is the prolongation of the sinus urogenitalis, the latter the prolongation of the intestine (anus).

39. At the anterior margin of the cloaca, or, after completed separation, at the anterior rim of the sinus urogenitalis, there is found in both sexes the genital eminence, which bears along its under surface a groove flanked by the two genital folds ; the eminence, together with the opening lying under it (cloaca or sinus urogenitalis), is embraced by the genital ridges.

40. In the female the genital eminence remains small and becomes the clitoris, the genital folds become the labia minora, the genital ridges the labia majora; the sinus urogenitalis remains short and broad and represents the vestibulum, which receives the vagina (the end of the Müllerian ducts) and the external orifice of the allantois or urinary bladder, the female urethra.

41. In the male the genital eminence grows out to a great length as the male organ ; the genital folds close on their under surface to form a narrow canal, which appears as a prolongation of the narrow sinus urogenitalis, together with the latter is designated as the male urethra, and receives at its beginning the vas deferens and the uterus masculinus ; the two genital ridges, which increase in size for the reception of the testes, surround the roots of the male organ and unite to form the scrotum.

42. The following table gives a brief survey (1) of the comparable parts of the outer and inner sexual organs of the male and female, and (2) of their derivation from indifferent fundaments of the urogenital system in Mammals :—

Male sexual parts.	*The common form from which both arise.*	*Female sexual parts.*
Seminal ampullæ and seminal tubules.	Germinal epithelium.	Ovarian follicle, Graafian follicle.
	Primitive kidney.	
(*a*) Epididymis with rete testis and tubuli recti.	(*a*) Anterior part with the sexual cords (sexual part).	(*a*) Epoöphoron with medullary cords of the ovary.
(*b*) Paradidymis.	(*b*) Posterior part (the real mesonephric part).	(*b*) Paroöphoron.

Male sexual parts.	*The common form from which both arise.*	*Female sexual parts.*
Vas deferens with seminal vesicles.	Mesonephric duct.	GARTNER'S canal, in some Mammals.
Kidney and ureter.	Kidney and ureter.	Kidney and ureter.
Hydatid of epididymis. Sinus prostaticus. (Uterus masculinus.)	Müllerian duct.	Oviduct and fimbriæ. Uterus and vagina.
Gubernaculum Hunteri.	Inguinal ligament of primitive kidney.	Round ligament and lig. ovarii.
Male urethra (pars prostatica et membranacea).	Sinus urogenitalis.	Vestibulum vaginæ.
Penis.	Genital eminence.	Clitoris.
Pars cavernosa urethræ.	,, folds.	Labia minora.
Scrotum.	,, ridges.	,, majora.

The Development of the Suprarenal Bodies.

43. The most anterior part of the mesonephros appears to share in the development of the suprarenal bodies, since lateral branches sprout out from the sexual cords, become detached, and are converted into the peculiar cellular cords of the cortical substance.

44. The suprarenal bodies in the embryo for a time exceed in size the kidneys.

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CHAPTER XVI.

THE ORGANS OF THE OUTER GERM-LAYER.

The outer germ-layer has for a long time also borne the name dermo-sensory layer. By this its two most important functions are both indicated. For in the first place it forms the epidermis together with its various products, such as hair, nails, scales, horns, and feathers; and in addition various kinds of glands: the sebaceous, sweat- and milk-glands. Secondly, it is the matrix out of which the nervous system and the most important functional parts of the sensory organs, the optic, auditory, and olfactory cells, are derived.

I begin with the most important function of the outer germ-layer, the development of the nervous system, then proceed to the development of the organs of sense (eye, ear, and organ of smell), and finally discuss the development of the epidermis and its products.

I. The Development of the Nervous System.

A. The Development of the Central Nervous System.

The central nervous system of Vertebrates is one of the organs first established after the separation of the germ into the four primary germ-layers. As has already been stated, it is developed (fig. 41 *A*) out of a broad band of the outer germ-layer (*mp*), which stretches from the anterior to the posterior end of the embryonic fundament and lies in the median plane directly above the chorda dorsalis (*ch*). In this region the cells of the outer germ-layer grow out into long cylindrical or spindle-shaped structures, whereas the elements occurring in the surrounding parts (*ep*) flatten out and under certain conditions become altogether scale-like. Consequently the outer germ-layer is now divided into two regions—into the attenuated *primitive epidermis* (Hornblatt) (*ep*) and the thicker median *neural* or *medullary* plate (*mp*).

Both regions are soon sharply separated from each other, since the neural plate bends in a little (fig. 41 *B*) and its edges rise above the surface of the germ. In this way there arise the two medullary or *dorsal folds* (*mf*), which enclose between them the originally broad and shallow medullary or dorsal furrow. They are simply folds of the outer germ-layer, formed at the place where the neural plate is continuous with the primitive epidermis. They are therefore composed of an outer and an inner layer, of which the inner belongs to the marginal part of the neural plate, the outer, on the contrary, to the adjacent epidermis.

In all the classes of Vertebrates the medullary plate is transformed into a *neural tube* at a very early period. This process can be accomplished in three different ways. In most of the classes of Vertebrates, namely Reptiles, Birds, and Mammals, the tube is formed by a typical process of folding. The medullary folds rise still higher above the surface of the germ, then bend together toward the median plane, and grow toward each other until their edges meet, along which they then begin to fuse. The neural tube, thus formed, still continues to remain in connection with the overlying epidermis along the line of fusion, a connection which soon disappears, since the connecting cells become loosened and separated from one another (fig. 41 *C*). The closure begins in all Vertebrates at the place which corresponds approximately to the future mid-brain —in the Chick (fig. 87 hb^2) on the second and in the Rabbit on the ninth day of development—and from there proceeds slowly both backwards and forwards. There is retained for a long time, especially behind, a place where the neural tube is open to the exterior. A connection with the intestinal tube by means of the neurenteric canal also exists at the posterior end, as has been already mentioned (p. 126) in the discussion of the germ-layers. It is only at a later period that this connection is interrupted by the closing of the blastopore.

The *second type* in the development of the central nervous system is met with in Cyclostomes and Teleosts. In them the neural plate is transformed into a solid cord of cells instead of a tube. Instead of the folds rising up over the surface of the germ, the neural plate grows downward in the form of a wedge. In this way the right and left halves of the plate come to lie immediately in contact with each other, so that one cannot find the slightest trace of a space between them ; only after the cord of cells has been constricted off from the primitive epidermis do the halves separate and allow a small cavity, the central canal, to appear between them. Probably this modification in the Bony Fishes and Cyclostomes is connected with the fact that the egg with its abundant yolk is very closely enveloped by the vitelline membrane, as a result of which the medullary folds cannot rise toward the surface.

The *third modification* occurs only in Amphioxus lanceolatus. It has already been described briefly in another place (p. 109).

The neural tube retains an undifferentiated condition in Amphioxus lanceolatus only; in all other Vertebrates, on the contrary, it is differentiated into spinal cord and brain.

(*a*) *The Development of the Spinal Cord.*

The part of the neural tube which is converted into the spinal cord is oval in cross section (fig. 200). At an early period a separation into a right and left half can be recognised (fig. 232). For the lateral walls are greatly thickened and consist of several layers of long, cylindrical cells, whereas the upper and lower walls are thin and can be distinguished respectively as posterior [dorsal] and anterior *commissure* (*hc* and *vc*), or as *roof-plate* and *floor-plate.*

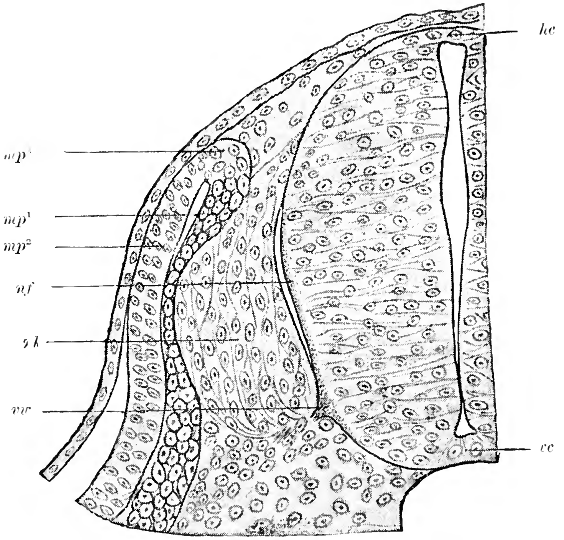

Fig. 232.—Cross section of an embryo Lizard with completely closed intestinal tube, after SAGEMEHL.

hc, Posterior, *vc*, anterior commissure of the spinal cord ; *vw*, anterior root of nerve ; *nf*, nerve-fibrillæ ; *spk*, spinal ganglion ; *mp*¹, muscle-plate, muscle-forming layer ; *mp*², outer layer of the muscle-plate ; *mp*³, transition of the outer into the muscle-forming layer.

The further development, of which I shall mention only the most important points, takes place in such a manner that the lateral halves become thicker and thicker (fig. 233). The cells continue to increase in number by division, and at the same time to be differentiated into two histological groups—(1) into elements which provide the sustentative framework, the epithelium surrounding the central canal and the spongiosa (spongioblasts of His), and (2) into elements which are transformed into ganglionic cells and nerve-fibres (neuroblasts of His). The thickening of the lateral walls depends partly upon the multiplication of cells, but mainly upon the fact that nerve-fibres apply themselves to the cell-mass from the outside. In time these fibres are separated into the anterior, lateral, and posterior columns of the spinal cord (fig. 233 *pcw*, *lcw*, *acw*). At their first appearance the nerve-fibres are non-medullated (fig. 232 *nf*), and only subsequently, sometimes earlier, sometimes later, acquire a medullary sheath. In this manner the already considerably thickened halves of the spinal cord become differentiated into the central gray substance containing the ganglionic cells, and into the white substance, which envelops the surface of the former like a mantle.

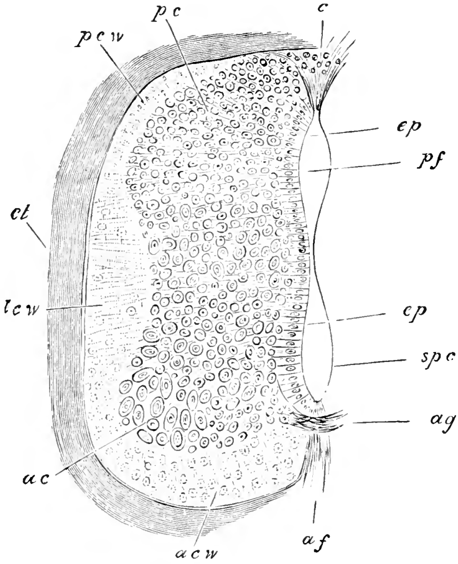

Fig. 233.—Cross section through the spinal cord of an embryo Chick of seven days, after Balfour.
pcw, Posterior white column; *lcw*, lateral white column; *acw*, anterior white column; *c*, dorsal tissue filling up the place where the dorsal fissure will be formed; *pc*, posterior horn of the gray substance; *ac*, anterior horn; *ep*, epithelial cells; *agc*, anterior gray commissure; *pf*, posterior [dorsal] part of the spinal canal; *spc*, anterior [ventral] part of the spinal canal; *af*, anterior fissure.

Since, meanwhile, the roof- and floor-plates grow only a little and are not differentiated into ganglionic cells, they come to lie deeper and deeper at the bottom of *anterior* and *posterior longitudinal furrows* (*c* and *af*). Finally, the completely formed spinal cord is composed of large lateral halves, which are separated from each other by deep anterior and posterior longitudinal fissures, being united only deep down by a thin transverse bridge. The latter is derived from the roof- and floor-plates, which have been retarded in their growth, and encloses in its middle the *central canal*, which has also remained small.

At the beginning—in Man up to the fourth month of embryonic development—the spinal cord occupies the entire length of the body. Therefore, at the time when the axial skeleton is divided up into separate vertebral regions, it reaches from the first cervical down to the last coccygeal vertebra. The end of the spinal cord, however, does not even begin to develop ganglionic cells and nerve-fibres, but remains throughout life as a small epithelial tube. It is united to the larger anterior portion, which has developed nerve-fibres and ganglionic cells, by means of a conically tapering region, which is spoken of in descriptive anatomy as the *conus medullaris.*

As long as the spinal cord keeps pace with the vertebral column in its growth, the pairs of nerves arising from it, in leaving the vertebral canal, pass out at right angles directly to the intervertebral foramina. In Man, beginning with the fourth month, this arrangement is changed; from that time forward the growth of the spinal cord does not equal that of the spinal column, and therefore the cord can no longer occupy the entire length of the vertebral canal. Since it is attached above to the medulla oblongata, and this together with the brain is firmly held in the cranial capsule, it must assume a higher and higher position in the vertebral canal. In the sixth month the conus medullaris is found in the upper end of the sacral canal, at birth in the region of the third lumbar vertebra, and some years later at the lower edge of the first lumbar vertebra, where it terminates even in the adult.

In the ascent (ascensus medullæ spinalis) the lower end of the spinal cord, the small epithelial tube which is attached to the coccyx, is drawn out into a long, fine filament, which persists even in the adult as the *filum terminale internum* and *externum.* At first it presents a small cavity, which is lined by ciliated cylindrical cells, and which forms a continuation of the central canal of the spinal cord. Further downward it is continued in the form of a cord of connective tissue as far as the coccyx.

A second consequence of the ascent of the spinal cord is a *change in the course of the roots of the peripheral nerve-stems.* Since, together with the spinal cord, their points of origin come to lie in the spinal canal relatively nearer and nearer the head, and since the places where they pass through the intervertebral foramina do not change, they are compelled to pass from a transverse to a more and more oblique course. The obliquity, moreover, is greater the farther down the nerve leaves the vertebral canal. In the neck-region their direction is still transverse, in the thoracic region it begins to be more and more oblique, and finally, in the lumbar region, and still more so in the sacral, it is more sharply downward. On this account the nerve-stems arising from the last part of the spinal cord come to lie for a considerable distance in the vertebral canal before they reach the sacral foramina serving for their exit; they therefore surround the conus medullaris and filum terminale, forming the structure known as the horse-tail or cauda equina.

Finally the spinal cord undergoes some changes in its form also. Even in the third and fourth months there appear differences of calibre in different regions. The places in the cervical and lumbar regions of the spinal cord at which the peripheral nerves depart to the anterior and posterior extremities, grow vigorously by the abundant formation of ganglionic cells; they become considerably thicker than the adjoining portions of the cord, on account of which they are distinguished as *cervical* and *lumbar enlargements* (intumescentia cervicalis et lumbalis).

(*b*) *The Development of the Brain.*

By the study of embryology knowledge of the anatomy of the brain has been greatly promoted. Justly, therefore, in all recent text books of human anatomy, the embryonic condition serves as the starting-point in the description of the intricate structure of the brain, the aim being to derive the complicated ultimate conditions from the more simple embryonic ones, and to explain them by means of the latter.

The initial form of the brain as well as of the spinal cord is a simple tube. At an early period, even before it is everywhere closed, it becomes metameric, on account of its growth being greater in some regions than in others. By means of two constrictions of its lateral walls it is divided into the *three primary brain-vesicles* (fig. 87 hb^1, hb^2, hb^3), which remain united with one another by means of wide openings, and are designated as the fore-, mid-, and hind-brain. The posterior of these divisions is the longest, gradually tapering and becoming continuous with the tubular spinal cord.

The first stage is quickly followed by a *second*, and that by a *third*, since the primary brain-vesicles soon separate into four, and finally five divisions.

During the *second stage* (fig. 234) the lateral walls of the primary fore-brain (*pvh*) begin to grow outward more vigorously and to evaginate to form the two optic vesicles (*au*). At the same time the lateral walls of the hind-brain, which from the beginning has been the longest portion, acquire a constriction which divides the hind-brain into two *vesicles*, that of the *cerebellum* (*kh*) and the *medulla* (*nh*), or *after-brain*.

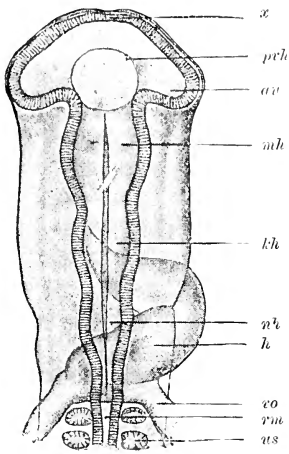

Fig. 234.- Dorsal aspect, by transmitted light, of the head of a Chick incubated 58 hours, after MIHALKOVICS. Magnified 40 diameters.

x, Anterior wall of the primary fore-brain vesicle, which afterwards evaginates to form the cerebrum; *prh*, primary fore-brain vesicle; *au*, optic vesicle; *mh*, mid-brain vesicle; *kh*, vesicle of the cerebellum; *nh*, after-brain vesicle; *h*, heart; *vo*, omphalomesenteric vein; *rm*, spinal cord; *us*, primitive segment.

The five-fold segmentation of the neural tube (fig. 235) soon succeeds the four-fold condition; by means of it the fore-brain vesicle undergoes fundamental transformations. First, the primary optic vesicles (*au*) begin to be constricted off from the fore-brain vesicle, until they remain attached by only slender, hollow stalks. Since the constriction takes place mainly from above downward, the stalks remain in connection with the base of the fore-brain vesicle. The front wall of the vesicle then begins to protrude anteriorly, and to be marked off by means of a lateral furrow, which runs from above and behind obliquely downward and forward. In this manner the primary vesicle of the fore-brain, like the hind-brain vesicle, is secondarily divided into two portions, which we can now distinguish as the *vesicles of the cerebrum* and *the between-brain* (*gh*, *zh*). The optic nerves remain united with the base of the latter.

The vesicle of the cerebrum is distinguished by a very rapid growth, and soon begins to surpass all the other parts of the brain in size. But it becomes divided before this into right and left halves. From the connective tissue enveloping the neural tube there grows down in the median plane a process, the future falx cerebri. This growth advances from above and in front against the cerebral vesicle and deeply infolds its upper wall. The halves (fig. 236 *hms*) that have thus arisen are united at their bases; they present a more flat median and a convex outer surface, and are called *the two vesicles of the hemispheres*, since they furnish the foundation for the cerebral hemispheres.

The separate regions of the brain-tube produced by constrictions and evaginations subsequently become still more sharply marked off from one another, owing to the alteration of their positions.

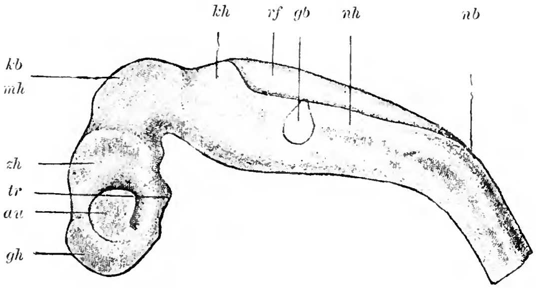

Fig. 235.—Brain of a human embryo of the third week (*Lg*). Profile reconstruction. After His. *gh*, Cerebral vesicle ; *zh*, between-brain vesicle ; *mh*, mid-brain vesicle ; *kh*, *nh*, vesicles of the cerebellum and medulla oblongata ; *au*, optic vesicle ; *gb*, auditory vesicle ; *tr*, infundibulum ; *rf*, area rhomboidalis ; *nb*, nuchal flexure ; *kb*, cephalic flexure.

At the beginning the three brain-vesicles formed by the first constrictions lie in a straight line one behind the other (fig. 87) and above the chorda dorsalis ; the latter extends only as far as to the anterior end of the mid-brain vesicle, where it tapers to a point. But from the moment when the optic vesicles begin to be constricted off, the three primary vesicles shift their positions in such a way that the longitudinal axis uniting them undergoes sharp, characteristic folds, which are distinguished as the *cephalic*, *pontal*, and *nuchal* flexures (fig. 235 *kb*, *nb*).

The cause of the formation of the curvatures, which are of fundamental importance in the anatomy of the brain, is to be sought principally in the more vigorous longitudinal growth which distinguishes the cerebral tube, and more especially its dorsal wall, from the surrounding parts. As His has established by means of measurements, the fundament of the brain more than doubles its length, while the spinal cord increases by only about one-sixth of its length.

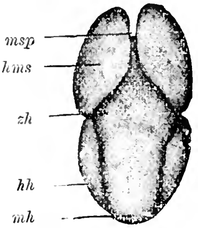

Fig. 236. — Brain of a human embryo seven weeks old, parietal (Scheitel) aspect, after Mihalkovics.
msp, Longitudinal or interpallial fissure (Mantelspalte), at the bottom of which is seen the embryonic lamina terminalis (Schlussplatte) ; *hms*, left hemisphere ; *zh*, between-brain ; *mh*, mid-brain ; *hh*, hind-brain and after-brain.

The *cephalic flexure* (fig. 235 *kb*) is developed first. The floor of the fore-brain sinks downward a little around the anterior end of the chorda dorsalis (fig. 237 *ch*), and forms at first a right angle with the part of the base of the brain lying behind it, but afterwards an acute angle (figs. 235, 238). In consequence of this, the vesicle of the mid-brain (fig. 235 *mh*) comes to lie highest, and forms a prominence, which causes a great protrusion of the surface of the embryo and is known as the parietal prominence (fig. 158 *s*).

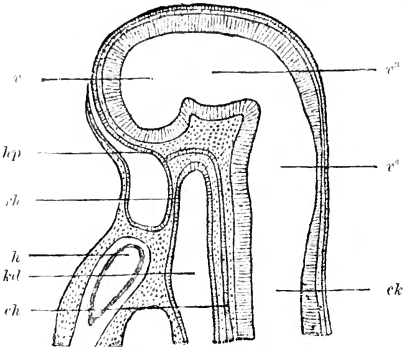

Fig. 237.—Median section through the head of a Rabbit embryo 6 mm. long, after Mihalkovics. *rh*, Pharyngeal membrane; *hp*, place whence the hypophysis develops; *h*, heart; *kd*, cavity of the head-gut; *ch*, chorda; *v*, ventricle of the cerebrum; v^3, third ventricle, that of the between-brain; v^4, fourth ventricle, that of the hind- and after-brain; *ck*, central canal of the spinal cord.

The *nuchal flexure*, which makes its appearance at the boundary between medulla oblongata and spinal cord, is less prominent (fig. 235 *nb*). It produces in the embryos of the higher Vertebrates a curvature which also projects outward, the so-called nuchal prominence (fig. 158).

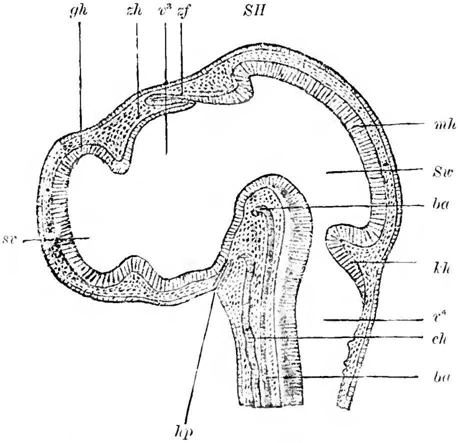

Fig. 238.—Median sagittal section through the head of a Chick incubated four and a-half days, after Mihalkovics. *SII*, Parietal prominence; *sv*, lateral ventricle; v^3, third ventricle; v^4, fourth ventricle; *Sw*, aqueduct of Sylvius; *gh*, vesicle of the cerebrum; *zh*, between-brain; *mh*, mid-brain; *kh*, cerebellum; *zf*, pineal process (epiphysis); *hp*, pocket of the hypophysis (pouch of Rathke); *ch*, chorda; *ba*, basilar artery.

The third curvature, which has been designated by Kölliker as the *pontal flexure* (fig. 239 *bb*), because it arises in the neighborhood of the future pons Varolii, is, on the contrary, very marked. It is further distinguished from the two other curvatures described, by the fact that its convexity is not directed toward the back of the embryo, but toward its ventral side. It is formed between the floor of the

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* [For terminology of the regions of the brain, see footnote, p. 282.]

vesicle of the cerebellum and that of the after-brain, and has the form of a ridge which projects ventrally for a considerable distance, where subsequently the transverse fibres of the pons Varolii are established.

The extent of these curvatures is very different in the various classes of Vertebrates. Thus the cephalic flexure is only slightly emphasised in the lower Vertebrates (Cyclostomes, Fishes, Amphibia); it is, on the contrary, much greater in Reptiles, Birds, and Mammals; but in Man especially, whose brain is the most voluminous, all of the flexures are developed to a very high degree.

The five brain-vesicles furnish the foundation for a natural subdivision of the brain, whose various chief divisions can be referred back to them. As the study of the further development teaches, there are formed from the after-brain vesicle the medulla oblongata, from the vesicle of the cerebellum the vermiform process with the hemispheres of the cerebellum and the pons Varolii, from the mid-brain vesicle the crura cerebri and corpora quadrigemina, from the between-brain vesicle the between-brain [thalamencephalon] with the infundibulum, the pineal gland, and the optic thalami, and finally from the vesicle of the cerebrum the cerebral hemispheres.

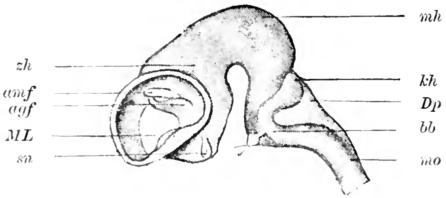

Fig. 239.—Brain of a Rabbit embryo 16 mm. long, viewed from the left side. The outer wall of the left cerebrum is removed. After MIHALKOVICS.

sn, Optic nerve; *ML*, foramen of MONRO; *agf*, fold of the choroid plexus; *amf*, fold of the cornu Ammonis; *zh*, between-brain; *mh*, mid-brain (cephalic or parietal flexure); *kh*, cerebellum; *Dp*, roof-plate of the fourth ventricle; *bb*, pontal flexure; *mo*, medulla oblongata.

In this metamorphosis the cavities of the primitive cerebral tube become the so-called *ventricles* of the brain: from the cavities of the fourth and fifth vesicles is derived the fourth ventricle or fossa rhomboidalis; from the cavity of the mid-brain vesicle, the aqueduct of SYLVIUS; from the between-brain, the third ventricle; and finally from the cavities of the hemispheres, the two lateral ventricles, which are also designated as the first and second ventricles.

A brief sketch will suffice to show in what manner the most important parts of the brain develop out of the five vesicular fundaments, and that at the same time histological and morphological differentiations are most intimately associated.

Histologically considered the walls of the vesicles originally consist everywhere of closely crowded spindle-shaped cells, just as in the spinal cord. These cells undergo in different places unlike modifications. In some places they retain their epithelial character, and furnish (1) the epithelial covering of the choroid plexus in the roof of the between-brain and after-brain, (2) the ependyma lining the ventricles of the brain, and (3) follicular structures such as the epiphysis (fig. 246). On the greater part of the wall of the five brain-vesicles the cells multiply to an extraordinary extent, and are transformed into more or less extensive layers of ganglionic cells and nerve-fibres. The distribution of the gray and white substances thus formed no longer presents in the brain-vesicles the same uniform condition that it does in the spinal cord. The only uniformity is found in the fact that in every part of the brain there occur gray "nuclei," which, like the anterior and posterior gray columns of the spinal cord, are enveloped with a mantle of white substance. However, there are added to the two parts of the brain that have attained the greatest development layers containing ganglionic cells, which furnish a superficial covering, the gray cortex of the cerebrum and cerebellum. By this means the white substance in certain parts of the brain becomes the core (nucleus medullaris), whereas the gray portion becomes the cortex, a condition differing in an important manner from the structure of the spinal cord.

The morphological differentiation of the brain depends upon the very unequal growth both of the five separate vesicles and of different tracts of their walls. For example, the other four vesicles remain in their development far behind that of the cerebral vesicle, in comparison with which they constitute only a small fraction of the entire mass of the brain (figs. 240, 241). They become overgrown by the cerebral vesicle from above and on the sides, and enveloped as by a mantle, so that they remain uncovered and visible only at the base of the brain. Therefore they, together with a small part of the basal portion of the cerebrum, are grouped together as the *stalk of the brain,* in contradistinction to the remaining chief part of the cerebrum, which constitutes the *cerebral mantle.*

The *unequal growth of the walls of the brain* manifests itself in the appearance of thickened and attenuated places, in the development of special nerve-columns (pedunculi cerebri, cerebelli, etc.), and in the formation of more or less extensive layers of ganglionic cells (thalamus opticus, corpus striatum). By these means the *principle of the formation of folds,* which was fully described in the fourth chapter, is shown to be carried out in a special manner on the hemispheres of the cerebrum and cerebellum inclusive of the vermiform process,—that is to say, on the two parts of the brain which are covered with a gray cortex. That the functional capacity of the cerebrum and cerebellum depends upon the extent of the gray cortex and the regularly arranged ganglionic cells in it, is to be concluded from a large number of phenomena. In this way is explained the very extensive increase of surface which is brought about in the cerebrum and cerebellum by means of somewhat different processes of folding. In the cerebrum *broad* ridges (gyri) arise from the medullary layer of the hemispheres (centrum semiovale), which, running in *meandering convolutions*, produce the characteristic relief of the surface (fig. 256). In the cerebellum the numerous ridges proceeding from the medullary nucleus are *narrow*, arranged *parallel* to one another, and provided with *smaller accessory* (secondary and tertiary) *ridges*, so that the cross section of the cerebellum presents an arborescent figure (arbor vitæ).

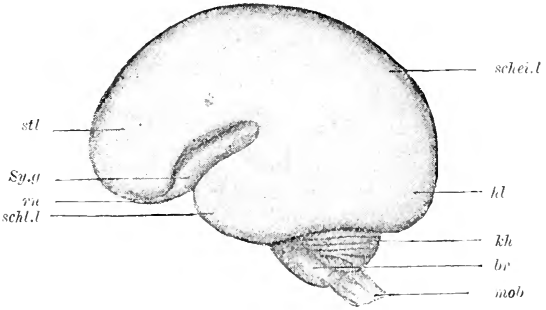

Fig. 240.—Lateral view of the brain of a human embryo from the first half of the fifth month, after MIHALKOVICS. Natural size.

stl, Frontal lobe ; *schei.l*, parietal lobe ; *hl*, occipital lobe ; *schl.l*, temporal lobe ; *Sy.g*, fissure of SYLVIUS ; *rn*, olfactory nerve ; *kh*, cerebellum ; *br*, pons ; *mob*, medulla oblongata.

If, after these preliminary remarks, we take under consideration the metamorphoses of the five vesicles, we may distinguish on each, as MIHALKOVICS has done in his monograph of the development of the brain, four regions : *floor, roof, and two lateral parts.* We shall begin our description with the fifth vesicle, because in its structure it approaches most closely to the spinal cord.

(1) *Metamorphosis of the Fifth Brain-Vesicle.*

The *fifth brain-vesicle* exhibits in different Vertebrates at the beginning of development (in the Chick on the second and third days) faint, regular infoldings of its lateral walls, by means of which it becomes separated into several smaller parts, lying one behind the other. Inasmuch as these afterward disappear without leaving any trace, no great importance was ascribed to them by the earlier investigators (REMAK). Recently, however, several persons have maintained for them a real significance. RABL and BÉRANECK recognise in them a segmentation of the brain-tube which is related to the exit of certain cranial nerves and is of importance in regard to the question of the metamerism of the entire head-region. The circumstance that the folds are so transitory appears to me to favor the older view.

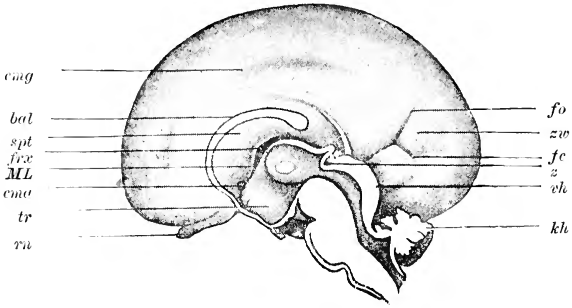

Fig. 241.—Brain of a human embryo from the first half of the fifth month, divided in the median plane; view of the median surface of the right half, after MIHALKOVICS. Natural size.
rn, Olfactory nerve; *tr*, infundibulum of the between-brain; *cma*, commissura anterior; *ML*, foramen of MONRO; *frx*, fornix; *spt*, septum pellucidum; *bal*, corpus callosum, which below, at the genu, is continuous with the embryonic lamina terminalis; *cmg*, sulcus calloso-marginalis; *fo*, fissura occipitalis; *zw*, cuneus; *fc*, fissura calcarina; *z*, epiphysis; *vh*, corpora quadrigemina; *kh*, cerebellum.

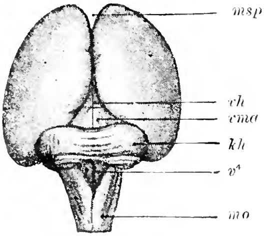

Fig. 242.—Brain of a human embryo from the second half of the third month, seen from behind, after MIHALKOVICS. Natural size.
msp, Longitudinal (interpallial) fissure; *vh*, corpora quadrigemina; *vma*, velum medullare anterius; *kh*, hemispheres of the cerebellum; v^4, fourth ventricle (fossa rhomboidalis); *mo*, medulla oblongata.

In the further development of the vesicle of the after-brain a distinction arises between the floor and side walls on the one hand

and the roof on the other. The former (figs. 241, 242) are considerably thickened by the addition of nervous substance and become separated on either side of the body (in Man in the third to the sixth months) into columns, which are recognisable from the outside because they are separated by grooves; these are the extensions with certain modifications of the three familiar columns of the spinal cord. The roof of the vesicle (fig. 235 *rf* and fig. 243 *Dp*), on the contrary, produces no nerve-substance, retains its epithelial structure, becomes still thinner, and in the adult consists of a single layer of flat cells. This forms the only covering to the cavity of the dorso-ventrally compressed vesicle of the after-brain—the fourth ventricle or fossa rhomboidalis. It is firmly applied to the under surface of the pia mater, and with it produces the *posterior choroid plexus* (tela choroidea inferior). The name choroid plexus has been chosen because the pia mater in this region becomes very vascular and in the form of two rows of branched villi grows into the cavity of the after-brain vesicle, always carrying before it, and thus infolding, the thin epithelial roof.

Laterally the roof-plate or the epithelium of the choroid plexus is continuous with the parts of the brain-vesicle that have been metamorphosed into nervous matter. The transition is effected by means of thin bands of white nervous substance, which, as obex, tænia sinus rhomboidalis, velum medullare posterius, and pedunculus flocculi, surround the edge of the fossa rhomboidalis. If with the pia mater one strips off from the medulla oblongata the posterior medullary velum, the epithelial covering of the fourth ventricle adhering to the latter will naturally be removed with it. In this way is produced the posterior brain-fissure of the older authors, through which one can penetrate into the system of cavities in the brain and spinal cord.

(2) *Metamorphosis of the Fourth Brain-Vesicle.*

The wall of the *fourth brain-vesicle* undergoes a considerable thickening in all its parts, and surrounds its cavity in the form of a *ring differentiated into several regions*; the cavity becomes the anterior part of the fossa rhomboidalis (figs. 243, 242, 241). The floor furnishes the *pons* (*bb*), the cross fibres of which become evident in the fourth month. From the lateral walls arise the pedunculi cerebelli ad pontem. *But it is the roof that grows to an extraordinary extent and gives to the cerebellum its characteristic stamp.* At first it appears as a thick *transverse ridge* (figs. 242, 243 *kh*), which overhangs the attenuated roof of the medulla. In the third month the middle portion of the ridge acquires four deep transverse folds by the sinking in of the pia mater (fig. 242), and in this way is distinguished as the *vermiform process* from the lateral parts, which still appear smooth (*kh*). From this time forward the lateral parts outstrip the middle part in growth, bulge out at the sides as two hemispheres, and, acquiring transverse folds, in the fourth month become the voluminous hemispheres of the cerebellum.

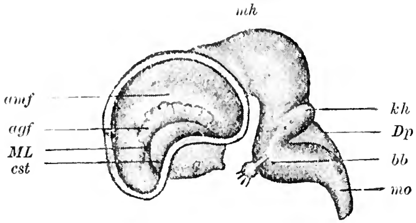

Fig. 243.—Brain of an embryo Calf 5 cm. long, seen from the side. The lateral wall of the hemisphere is removed. After Mihalkovics. Magnified 3 diameters.

cst, Corpus striatum; *ML*, foramen of Monro; *agf*, fold of the choroid plexus (plexus choroideus lateralis); *amf*, fold of the cornu Ammonis; *kh*, cerebellum; *Dp*, roof-plate of the fourth ventricle; *bb*, pontal flexure; *mo*, medulla oblongata; *mh*, mid-brain (cephalic flexure).

Only a little nerve-substance is developed where the roof of the fourth brain-vesicle, which has become thickened to constitute the vermiform process and hemispheres, is continuous with the roof of the third and fifth vesicles (fig. 241). Consequently there arise here thin medullary lamellæ, which serve as a transition on the one hand to the posterior choroid plexus, and on the other to the lamina quadrigemina (*vh*)—*the posterior and the anterior velum medullare.*

(3) *Metamorphosis of the Third or Mid-brain Vesicle.*

(Figs. 235, 243, 242, 241.)

The *mid-brain vesicle is the most conservative portion of the embryonic neural tube*, the part which is changed least of all; in Man a small portion only of the brain is derived from it. Its walls become rather uniformly thickened on all sides of the cavity, which is narrow and becomes the *aqueduct of* Sylvius. The base and lateral walls together supply the crura cerebri and substantia perforata posterior. The roof-plate (fig. 242 *vh*) becomes the corpora quadrigemina, owing to the appearance, in the third month, of a median furrow, and, in the fifth month, of a transverse one crossing it at right angles.

Whereas at the beginning of the development the mid-brain vesicle (figs. 235, 243 *mh*), as a consequence of the curvature of the neural tube, occupies the highest position and produces the *parietal prominence* of the head (fig. 158 *s*), it is afterwards covered in from above by the other parts of the brain, which are becoming more voluminous,—the cerebellum and cerebrum,—and is crowded down to the base of the brain (compare fig. 235 *mh* with fig. 241 *vh*).

(4) *Metamorphosis of the Second or Between-brain Vesicle.*

The *between-brain vesicle* also remains small, but undergoes a series of interesting changes, since, apart from the optic vesicles, which grow out from its walls, two other appendages, of problematical meaning, are developed from it—the pineal gland and the hypophysis.

In the case of the between-brain vesicle, it is only in the lateral walls that a considerable amount of nerve-substance is formed. By this means the walls thicken into the optic thalami with their ganglionic layers. Between them the cavity of the vesicle is retained as a narrow vertical fissure, known as the *third ventricle*; it is united with the fossa rhomboidalis by means of the aqueduct of Sylvius. The floor remains thin and at an early period becomes evaginated downwards; it thus acquires the form (figs. 235, 241 *tr*) of a short funnel (*infundibulum*), with the apex of which is united the hypophysis, soon to be fully described.

The roof presents in its metamorphosis a striking similarity to the corresponding part of the after-brain vesicle (fig. 241). It persists as a simple, thin epithelial layer, unites with the very vascular pia mater,—which sends out in this case also villous outgrowths with capillary loops which pass into the third ventricle,—and together with it constitutes the *anterior choroid plexus* (*tela choroidea anterior* or *superior*). When in withdrawing the pia mater the choroid plexus is also removed, the third ventricle is opened; thus is produced the anterior *great fissure of the brain* through which, as through the structure of the same name in the medulla oblongata, one can penetrate into the cavities of the brain.

The agreement with the medulla oblongata is expressed in still another point. As in the case of the latter the edges of the roof-plate develop into thin medullary bands, by means of which the attachment to the sides of the fossa rhomboidalis is accomplished, so here also the epithelium of the choroid plexus attaches itself to the surface of the optic thalamus by means of thin bands consisting of medullated nerve-fibres (tæniæ thalami optici).

Finally, out of the hindermost portion of the roof of the between-brain vesicle a peculiar organ, the *pineal gland* (fig. 241 *z*), takes its origin at a very early period, in Man in the course of the second month. Since in recent years numerous interesting works have appeared concerning it, and since many striking discoveries have been brought to light both in the case of the Selachians and more especially in that of the Reptiles, I will describe it at somewhat greater length.

The Development of the Pineal Gland (*Epiphysis cerebri*).

First it is to be mentioned that, with the exception of Amphioxus lanceolatus, the pineal gland (glandula pinealis s. conarium) is not wanting in any Vertebrate. It is in all cases formed in exactly the same way. On the roof of the between-brain, where it is continuous with the roof of the mid-brain or the lamina quadrigemina, there arises an evagination (figs. 238 and 241 *z*) which has the shape of the finger of a glove, the *processus pinealis* [*epiphysis cerebri*], the apex of which is at first directed forward, but subsequently backward. In its further metamorphosis there appear, as far as our knowledge at present extends, differences of considerable importance.

According to the investigations of Ehlers, the pineal process attains in adult *Selachians* an unusual length; its closed end swells into a vesicle, which penetrates the cranial capsule and extends out to the dermal surface. In many Selachians, such as Acanthias and Raja, the vesicular end is enclosed in a canal of the cranial capsule itself; in others it lies outside between the cranial capsule and the corium. The [proximal] end of the vesicle is united to the between-brain by means of a long slender canal.

Manifold conditions are met with in *Reptiles*, as the recent investigations of Spencer have taught. These conditions permit in part a direct comparison with the Selachians, but in part they are widely altered. Here, too, the pineal gland is a structure of considerable length, the peripheral end of which lies far away from the between-brain under the epidermis; it passes out through an opening in the roof of the skull which is situated in the parietal bone and is known as the *foramen parietale.* The position of the latter can easily be determined on the head of the living animal, because at this place the dermal scutes acquire a special condition and form, and, above all, are transparent.

In regard to the particular form of the organ, there are essentially *three types* to be distinguished.

In many Reptiles, *e.g.*, in Platydactylus, the pineal gland has the same structure as in Sharks: a small peripheral vesicle, which is enclosed in the parietal foramen, is lined with ciliated cylindrical cells, and is connected with the roof of the between-brain by means of a long, hollow stalk.

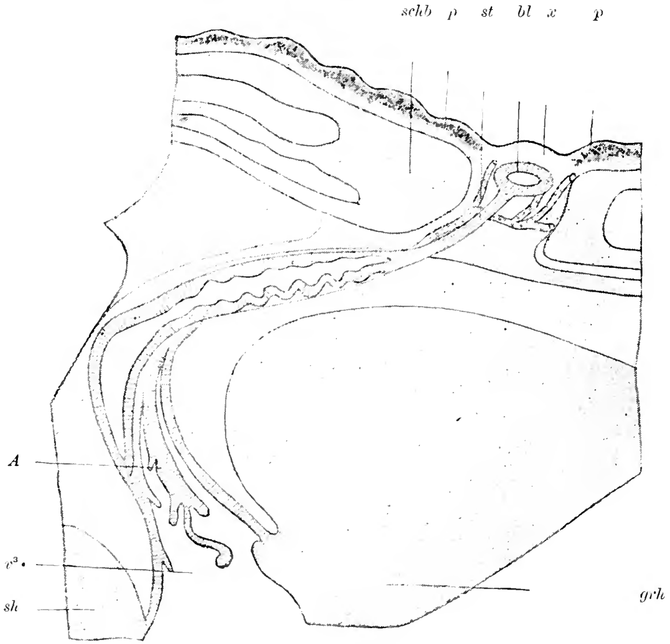

Fig. 244.—**Diagrammatic longitudinal section through the brain of Chameleo vulgaris with the pineal organ, which is separated into three portions, a vesicular, a cord-like, and a tube-like portion,** after BALDWIN SPENCER.

schb, Parietal bone with the foramen parietale; *p*, pigment of the integument; *st*, cord-like middle portion of the epiphysis; *bl*, its vesicular terminal portion; *x*, transparent region of the integument; *grh*, cerebrum; *sh*, optic thalamus; v^3, third ventricle, which is continued upwards into the tube-like initial portion (*A*) of the epiphysis.

In other Reptiles, as in the Chameleon, the organ is differentiated into three portions (fig. 244): first into a small closed vesicle (*bl*), which lies under a transparent scale (*x*) in the foramen parietale and is lined with ciliated epithelium; secondly into a solid cord (*st*), which consists of fibres and spindle-shaped cells, and bears a certain resemblance to the embryonic optic nerve; and thirdly into a hollow, funnel-shaped projection (*A*) of the roof of the between-brain, which still exhibits here and there sac-like enlargements.

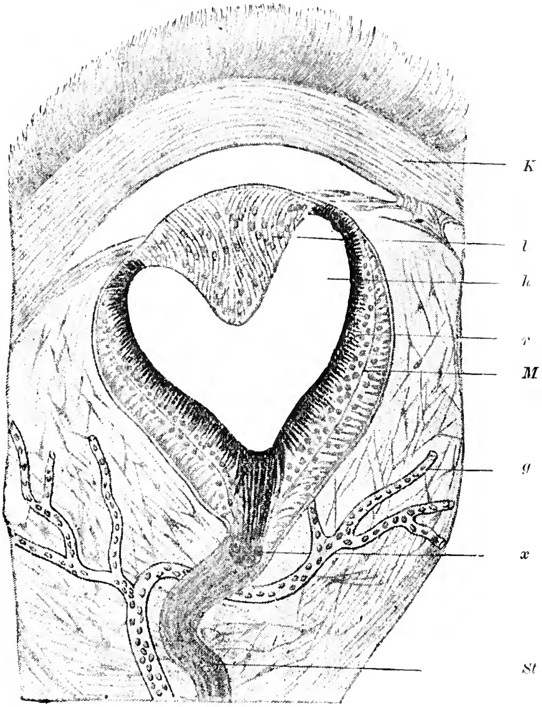

Fig. 245.—Longitudinal vertical section through the pineal eye of Hatteria punctata and its connective-tissue capsule, after BALDWIN SPENCER. Slightly enlarged.

The anterior part of the capsule fills up the parietal foramen.

K, Connective-tissue capsule; *l*, lens; *h*, cavity of the eye filled with fluid; *r*, retina-like portion of the optic vesicle; *M*, molecular layer of the retina; *g*, blood-vessels; *x*, cells in the stalk of the pineal eye; *St*, stalk of the pineal eye, comparable with the optic nerve.

In a third division of the Reptiles, in Hatteria, Monitor, the Blind-worms, and Lizards, the vesicular distal portion of the pineal gland undergoes a striking metamorphosis, by means of which it acquires a certain resemblance to the eye of many Invertebrates (fig. 245). The portion of its wall which lies next to the surface of the body has been transformed into a lens-like structure (*l*); the part of the wall lying opposite the latter and continuous with the fibrous cord (*St*) has, on the contrary, been converted into a retina-like structure (*r*). The formation of the lens (*l*) is due to the fact that the epithelial cells of the anterior wall of the vesicle have become elongated into cylindrical cells and uninucleate fibres, and have thereby produced an elevation, the convex surface of which projects into the cavity of the vesicle. In the posterior portion the epithelial cells are separated into different layers, the innermost of which is distinguished by the abundance of its pigment. Between the pigmented cells there are imbedded others, which can be compared to the rods of the visual cells in the paired eyes of Vertebrates, and which appear to be in connection below with nerve-fibres.

Those investigators who, like RABL-RÜCKHARD, AHLBORN, SPENCER, and others, have studied the pineal gland, are of opinion that *the pineal body must be considered as an unpaired parietal eye, which in many classes, for example in Reptiles, appears to be tolerably well preserved, but in most Vertebrates is in process of degeneration.*

That we have to do in Reptiles with an organ which reacts under the influence of light, does not appear improbable, when one takes into consideration that, owing to the transparency of the dermal scutes at the place in the skull where the parietal foramen is located, rays of light are here able to penetrate through the integument. The presence of a lens-like body and pigment is also favorable to this view. But whether the organ serves for sight, or only for the transmission of sensations of warmth,—whether, consequently, it is more an *organ for the perception of warmth* than an eye,—must for the present remain undecided. It is still more an open question whether this organ of warmth is a structure which has been developed as a special modification of the epiphysis of Reptiles alone,—as the auditory sac, for example, has been developed in the tail of the Crustacean Mysis,—or whether it represents a structure originally common to all Vertebrates. In the latter case processes of degeneration must be assumed to be widespread, for up to the present time nothing like the condition in Reptiles has been found in other Vertebrates.

In *Birds and Mammals* the pineal process undergoes metamorphoses which give rise to an *organ of a glandular, follicular structure.*

In Birds (fig. 246) it never attains such great length as in Selachians and Reptiles. At a certain stage it sends out from its surface into the surrounding vascular connective tissue cellular outgrowths, which increase in number by means of budding and finally break up into numerous small follicles (fig. 246 *f*). These consist of several layers of cells, the outermost being small, spherical elements, the innermost cylindrical ciliated cells. The proximal portion of the pineal process does not become involved in the follicular metamorphosis and persists as a funnel-shaped outfolding of the roof of the between-brain; the individual follicular vesicles constricted off from the parental tissue are united with its upper end by means of connective tissue.

In *Mammals* the development takes place in a manner similar to that of the Chick. In the Rabbit there also arise follicles, each of which at first encloses a small cavity, but later becomes solid. They are then entirely filled with spherical cells, which possess a certain resemblance to lymph-corpuscles. The opinion has therefore been expressed by many (Henle) that the pineal body is a lymphoid organ, an opinion, however, which is refuted by the study of the development, for genetically the follicles are exclusively epithelial structures.

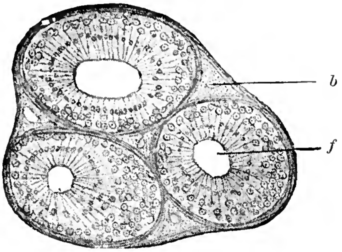

Fig. 246.—Section through the pineal gland of a Turkey, after Mihalkovics. Magnified 180 diameters.
f, Follicle of the pineal gland with its cavities; *b*, connective tissue with blood-vessels.

In the adult there are formed within the individual follicles concretions, the brain-sand (acervulus cerebri).

In Man the pineal body, which begins to appear in the sixth week (His), exhibits a peculiarity as regards its position. Whereas the free end of the epiphysis is at first directed forward, and in other Vertebrates is also retained in this position, it acquires in Man an opposite direction, inasmuch as it bends backward on to the surface of the lamina quadrigemina. Probably this is connected with the fact that the gland is crowded back by the excessive development of the corpus callosum.

As the signification of the pineal gland is still doubtful, so is that of the *pituitary body* or *hypophysis cerebri*, which, as has been previously mentioned, is united with the floor of the between-brain at the apex of the infundibular process.

The Development of the Hypophysis (Pituitary Body).

The hypophysis is an organ which has a double origin. This is expressed in its entire structure, since it is composed of a larger, anterior and a smaller, posterior lobe, which in their histological characters are fundamentally different from each other.

In order to observe the beginning of its formation, it is necessary to go back to a very early stage (fig. 237), in which the oral sinus has just arisen and is still separated from the cavity of the head-gut by means of the pharyngeal membrane (*rh*). At this time the cephalic flexure of the brain-vesicles has already appeared, and the anterior end of the chorda dorsalis (*ch*) terminates immediately behind the attachment of the pharyngeal membrane. In front of this is located the important place where the hypophysis is developed, as was first established by GOETTE and MIHALKOVICS. *The hypophysis is therefore a product of the outer germ-layer* and not a growth from the cavity of the head-gut, as had always been maintained previous to this time.

The first steps introductory to the formation of the hypophysis take place soon after the rupture of the pharyngeal membrane (figs. 238, 247), some unimportant remnants of which are retained at the base of the skull as the so-called *primitive velum palatinum.* Anterior to these there is now developed (in the Chick on the fourth day of incubation, in Man during the fourth week, HIS) a small evagination, *the pouch of* RATHKE *or the pocket of the hypophysis* (*hy*), which grows toward the base of the between-brain (*tr*). Then it becomes deeper, begins to be constricted off from its parent tissue, and to be metamorphosed into a small sac, whose wall is composed of several layers of cylindrical cells (fig. 248).

The sac of the hypophysis (*hy*) remains for a long time in connection with the oral cavity by means of a narrow duct (*hyg*). In later stages, however, the connection in the higher Vertebrates is interrupted, because the embryonic connective tissue, which supplies the foundation for the development of the skeleton of the head, becomes thickened and crowds the sac farther away from the oral cavity (figs. 248, 249). When, later on, the process of chondrification

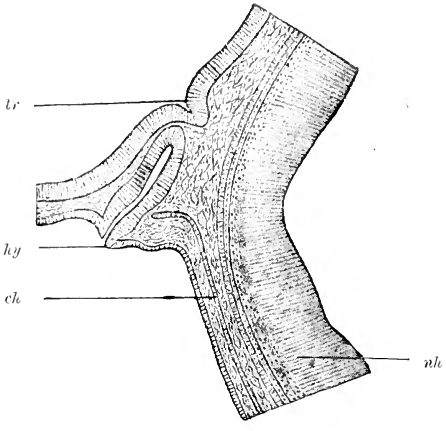

Fig. 247.—Median sagittal section through the hypophysis of a Rabbit embryo 12 mm. long, after MIHALKOVICS. Magnified 50 diameters.

tr, Floor of the between-brain with the infundibulum; *nh*, floor of the after-brain; *ch*, chorda; *hy*, pocket of the hypophysis.

takes place in the connective tissue, by means of which the cartilaginous base of the skull (*schb*) is established, the sac of the hypophysis (*hy*) comes to lie above the latter at the under surface of the between-brain (*tr*). At this time also the duct of the hypophysis (*hyg*), which meanwhile has lost its lumen, begins to shrivel and degenerate (fig. 249). In many Vertebrates, however, as in the Selachians, it is retained throughout life and forms a hollow canal, which perforates the cartilaginous base of the skull and is united with the epithelium of the mucous membrane of the mouth. In extremely rare cases there is retained in Man also a canal in the basi-sphenoid, which leads from the sella turcica to the base of the skull and receives a prolongation of the hypophysis (SUCHANNEK).

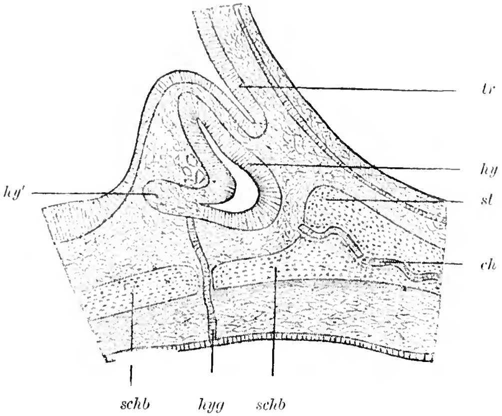

Fig. 248.—Sagittal section through the hypophysis of a Rabbit embryo 20 mm. long, after MIHALKOVICS. Magnified 55 diameters.

tr, Floor of the between-brain with infundibulum; *hy*, hypophysis; *hy'*, part of the hypophysis in which the formation of the glandular tubules begins; *hyg*, duct of the hypophysis; *schb*, base of the skull; *ch*, chorda; *sl*, dorsum sellæ.

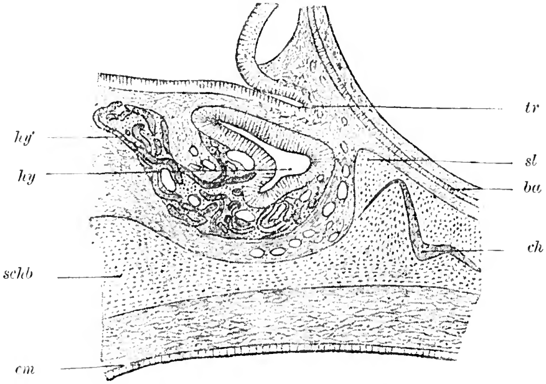

Fig. 249.—Sagittal section through the hypophysis of a Rabbit embryo 30 mm. long, after MIHALKOVICS. Magnified 40 diameters.

tr, Floor of the between-brain with infundibulum; *hy*, original pouch-like part of the hypophysis; *hy'*, the glandular tubules which have budded out from the sac of the hypophysis; *sl*, dorsum sellæ; *ba*, basilar artery; *ch*, chorda; *schb*, cartilaginous base of the skull; *em*, epithelium of oral cavity.

At an early period an evagination from the between-brain (figs. 247, 249), called the infundibulum (*tr*), has grown out toward the sac of the hypophysis and applied itself to the posterior wall of the latter, which it has folded in toward the anterior or opposite wall.

This first stage is followed by a second, in which the sac and the adjoining end of the infundibulum are metamorphosed into the two lobes of the complete organ already mentioned.

The sac begins (in Man in the second half of the second month, HIS) to send out from its surface into the surrounding very vascular connective tissue hollow tubules (the *tubules of the hypophysis*) (figs. 248, 249 *hy'*). These are then detached from the walls of the sac, by becoming enclosed on all sides by vascular connective tissue. In this respect the process of development agrees in the main with that of the thyroid gland, only that the spherical follicles are here represented by tubular structures. After the entire sac has been resolved into a large number of small, tortuous tubules provided with narrow lumina, the lobe thus produced applies itself closely to the lower end of the infundibulum, with which it becomes united by means of connective tissue.

The end of the infundibulum itself is transformed in the lower Vertebrates into a small *lobe of the brain*, in which, moreover, ganglionic cells and nerve-fibres can be identified. In the higher Vertebrates, on the contrary, no trace of such histological elements can be detected in the posterior lobe of the hypophysis, which in these forms consists of closely packed spindle-cells, and thus acquires a close resemblance to a spindle-cell sarcoma.

(5) *Development of the First or Fore-Brain Vesicle.*

The most important changes, the comprehension of which is in part attended with serious difficulties, take place in the vesicle of the fore-brain or cerebrum. It is divided (fig. 250), even at the time of its formation, as has already been mentioned, into a right and a left portion, owing to the fact that its wall becomes infolded from in front and from above by means of a vertical process of the connective-tissue envelope of the brain, the primitive falx. The two portions, the vesicles of the hemispheres (*hms*), come close together, being separated by only the narrow longitudinal or interpallial fissure (*msp*), which is filled up by the falx, so that their median surfaces become mutually flattened, whereas their lateral and under surfaces are convex. Where the plane and convex surfaces are continuous with each other there is a sharp *bend in the mantle* (Mantelkante).

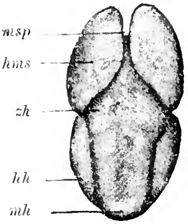

Fig. 250.—Brain of a human embryo seven weeks old, parietal (Scheitel) aspect, after Mihalkovics.
msp, Interpallial (longitudinal) fissure, at the bottom of which is seen the embryonic lamina terminalis (Schlussplatte); *hms*, left hemisphere; *zh*, between-brain; *mh*, mid-brain; *hh*, hind-brain and after-brain.

The vesicles of the hemispheres at first have thin walls formed of several layers of spindle-shaped cells (fig. 251, $_1$) and each encloses a large cavity, the *lateral ventricle* (fig. 251), which is derived from the central canal of the neural tube. Inasmuch as these have been reckoned by the earlier authors as the first and second ventricles, it is plain why the cavities of the between-brain and medulla oblongata are respectively designated as the third and fourth ventricles. In Man, during the earlier months, each lateral ventricle is in communication with the third ventricle by means of a wide opening, the *primitive foramen of* Monro (figs. 239 *ML* and 254 *m*).

Anterior to the foramen of Monro lies the part of the wall of the cerebrum which was infolded by the development of the great interpallial fissure: on the one hand it effects the anterior union of the walls of the two hemispheres; on the other it bounds the third ventricle in front, and is therefore called the anterior closing plate (lamina terminalis). It is continuous below with the anterior wall of the infundibulum of the between-brain.

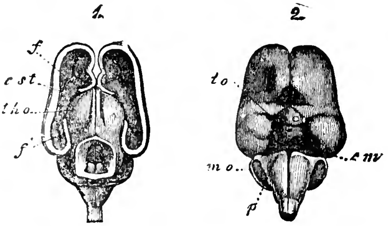

Fig. 251.—Brain of a human embryo of three months, after Kölliker. Natural size.
1. From above with the hemispheres removed and the mid-brain opened. 2. The same from below. *f*, Anterior part of the marginal arch (Randbogen) of the cerebrum cut through; *f'*, posterior part (hippocampus) of the marginal arch; *tho*, optic thalamus; *cst*, corpus striatum; *to*, tractus opticus; *cm*, corpora mammillaria; *p*, pons Varolii.

In the further development of each vesicle of the hemispheres four processes are intimately associated: (1) an extraordinary growth and an enlargement in all directions resulting from it; (2) an infolding of the wall of the vesicle, so that externally there arise deep clefts (the fissures), and internally projections into the lateral ventricles; (3) the development of a system of commissures, by means of which the right and left hemispheres are brought into closer union (corpus callosum and fornix); (4) the formation of furrows that cut into the cortex of the cerebrum more or less deeply from the outside, but cause no corresponding internal projections in the wall of the ventricle.

As regards its general features, the embryonic growth of the cerebral vesicles is especially characterised by an enlargement backward. In the third month the posterior lobe already completely overlies the optic thalamus (fig. 242); in the fifth month it begins to extend over the corpora quadrigemina (fig. 241), which it entirely covers up in the sixth month. From there it spreads over the cerebellum (fig. 256). The cerebrum is not characterised in all Mammals by such an extraordinary growth as in Man; comparative anatomy teaches rather that the stages of development of the human brain in different months here described, are met with in other Mammals as permanent conditions.

In some animals the posterior margins of the hemispheres extend as far as the corpora quadrigemina; in others they cover these more or less completely; in others, finally, they have grown over the cerebellum more or less. On the whole, the increase in the volume of the cerebrum, which is so varied in Mammals, goes hand in hand with an increase in intelligence.

The vesicles of the hemispheres undergo additional complication (in Man in the course of the second and third months), owing to *infoldings* of their thin walls, which still enclose a large cavity. As a result of this there arise on the outer surface deep furrows, which separate large areas from one another and which have been designated as *total furrows* or *fissures* by His, who has rightly estimated their importance in the architecture of the brain. Corresponding to the furrows which are visible on the outer surface, there are more or less prominent elevations on the inner surface of the lateral ventricles, by means of which the latter become narrowed and reduced in size. The total furrows of the cerebral hemispheres are the fissure of SYLVIUS (fossa Sylvii), the arcuate fissure, embracing the hippocampal fissure (fissura hippocampi), the fissura choroidea, the fissura calcarina, and the fissura parieto-occipitalis. The elevations produced by them are called the corpus striatum, fornix and pes hippocampi, tela choroidea and calcar avis. A prominence which in the embryo corresponds to the fissura parieto-occipitalis, becomes obliterated in the adult by a considerable thickening of the wall of the brain, so that no permanent structure results from it.

The *fissure of* SYLVIUS (fig. 252 *Sy.g*) is the first one formed. It appears as a shallow depression of the convex outer surface at about the middle of the lower margin of each hemisphere. The part of the wall which is thus depressed becomes considerably thickened (figs. 243, 251 *cst*, and 254 *st*), and forms an elevation on the floor of the cerebrum projecting into its cavity, the corpus striatum, in which several nuclei of gray matter are developed (the nucleus caudatus, the nucleus lentiformis, and the claustrum). Inasmuch as the elevation lies at the base of the brain and forms the direct forward and lateral continuation of the optic thalamus, it is regarded as belonging to the brain-stalk, and is distinguished as the *stalk part of the cerebral hemispheres* in distinction from the remaining portion or *mantle part.* The outer surface of the stalk part can be seen from the outside for a time,—as long as the Sylvian fissure is still shallow (fig. 252 *Sy.g*), —but it then becomes entirely overgrown and hidden by the edges of the gradually deepening fissure. Later this surface acquires in the embryo several cortical furrows and becomes the *island of* Reil (insula Reilii), or *the central lobe* (Stammlappen).

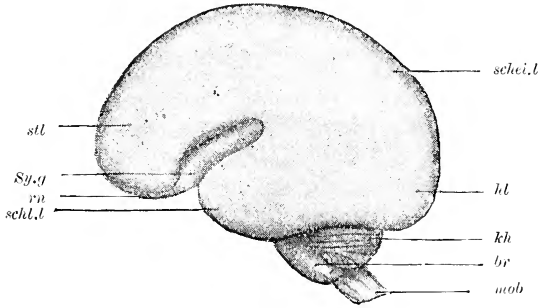

Fig. 252.—Lateral view of the brain of a human embryo during the first half of the fifth month, after Mihalkovics. Natural size.
stl, Frontal lobe ; *schei.l*, parietal lobe ; *hl*, occipital lobe ; *schl.l*, temporal lobe ; *Sy.g*, fissure of Sylvius ; *rn*, olfactory nerve ; *kh*, cerebellum ; *br*, pons ; *mob*, medulla oblongata.

The *mantle portion,* as it enlarges, spreads out uniformly around the island of Reil, as though about a fixed point, and surrounds it in the form of a half-ring open below (fig. 252) ; on this account it has received the name ring-lobe. Even now the regions of the four chief lobes into which the convex surface of each hemisphere is subsequently divided can readily be distinguished, although they are not yet sharply limited. The end of the half-ring which is directed forward and lies above the fissure of Sylvius (*Sy.g*) is the frontal lobe (*stl*) ; the opposite end, which embraces the fissure behind and below, is the temporal lobe (*schl.l*); the region lying above and connecting the two is the parietal lobe (*schei.l*). A prominence which is developed from the ring-lobe backward becomes the occipital lobe (*hl*).

The lateral ventricle has also become altered and corresponds to the external form of each hemisphere (fig. 253). It also assumes the shape of a half-ring, which lies above and surrounds the corpus striatum (*cst*)—that part of the wall of the vesicle which is forced inward by the fissure of SYLVIUS. Subsequently, when the individual lobes of the hemispheres are more sharply differentiated from one another, the lateral ventricle also undergoes a subdivision corresponding to the lobes. It becomes slightly enlarged at both ends, in front into the anterior cornu occupying the frontal lobe, behind and below into the inferior cornu of the temporal lobe. Finally, from the half-ring there is developed a small evagination, the posterior cornu, which extends backward into the occipital lobe. The region lying between the horns is narrowed and becomes the cella media.

All the fissures hitherto mentioned, except that of SYLVIUS, are developed on the plane [median] surface of the vesicle of the hemisphere.

At a very early stage—in Man in the fifth week (HIS)—there arise on this wall of the hemisphere two furrows running almost parallel with the edge or bend of the mantle, the arcuate or hippocampal fissure and the fissure of the choroid plexus (*fissura hippocampi* and *fissura choroidea*); both conform very closely in their direction to the ring-lobe, and, like it, with crescentic form embrace from above the stalk part of the cerebrum, the corpus striatum. They begin at the foramen of MONRO and extend from there to the tip of the temporal lobe, forming the boundaries of a region known as the *marginal arch* (Randbogen); this projects as a thickening on the median surface of the hemisphere, and takes part in the development of the commissural system. The invaginations of the median wall of the ventricle, caused by the fissures, the *hippocampal fold* and the *fold of the lateral choroid plexus*, are best understood by removing in an embryo the lateral wall of the hemisphere, so that one can survey the inner surface of the median wall of the still very spacious and ring-like lateral ventricle (fig. 253). The cavity is then seen to be partly filled with a reddish frilled fold (*agf*), which lies in the form of a crescent on the upper surface of the corpus striatum (*cst*). In the region of the fold the wall of the brain undergoes changes similar to those in the roof of the medulla oblongata and of the vesicle of the between-brain (figs. 254 *pl* and 255 *agf*). Instead of thickening and developing nerve-substance, it becomes attenuated, and is transformed into a single layer of flat epithelial cells, which are firmly united with the pia mater. The latter then becomes very vascular along the entire fold, and grows into the lateral ventricle in the form of tufts, which carry the epithelium before them. In this way the *lateral choroid plexus* arises (fig. 254 *pl*), which afterwards, in the adult, fills a part of the cella media and inferior cornu. It begins at the foramen of MONRO (fig. 253 *ML*), where it is continuous with the anterior unpaired choroid plexus which has arisen in the roof of the between-brain vesicle. If the delicate vascular pia mater is drawn out from the choroid fissure, the wall of the brain, which is reduced to a thin epithelium, is at the same time destroyed, and there is produced in the median wall of the hemisphere a gaping fissure, which extends from

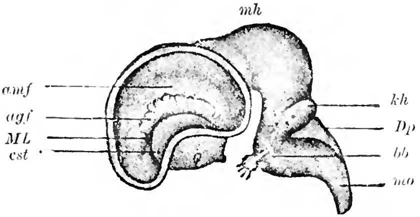

Fig. 253.—Lateral view of the brain of an embryo Calf 5 cm. long. The lateral wall of the hemisphere has been removed. After MIHALKOVICS. Magnified 3 diameters.

cst, Corpus striatum; *ML*, foramen of MONRO; *agf*, plexus choroideus lateralis; *amf*, hippocampal fold; *kh*, cerebellum; *Dp*, roof of the fourth ventricle; *bb*, pontal flexure; *mo*, medulla oblongata; *mh*, mid-brain (parietal flexure).

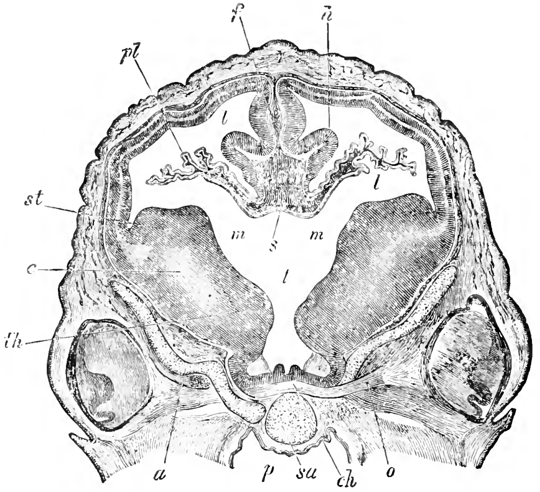

Fig. 254.—Transverse section through the brain of an embryo Sheep 2·7 cm. in length, after KÖLLIKER.

The section passes through the region of the foramen of MONRO.

st, Corpus striatum; *m*, foramen of MONRO; *t*, third ventricle; *pl*, plexus choroideus of the lateral ventricle; *f*, falx cerebri; *th*, deepest anterior part of the optic thalamus; *ch*, chiasma; *o*, optic nerve; *c*, fibres of the crus cerebri; *h*, hippocampal fold; *p*, pharynx; *sa*, presphenoid; *a*, orbito-sphenoid; *s*, part of the roof of the brain at the junction of the roof of the third ventricle with the lamina terminalis; *l*, lateral ventricle.

the foramen of MONRO to the tip of the temporal lobe and leads from the outside into the lateral ventricle. This is the *lateral cerebral fissure*, or the *great fissure of the hemispheres* (fissura cerebri transversa).

In a preparation made in the manner described the *hippocampal fold* is to be seen at a short distance from the choroid plexus and parallel to it (figs. 253 and 255 *amf* and fig. 254 *h*). This increases in size toward the apex of the inferior cornu, and in the completely formed brain produces the cornu Ammonis or pes hippocampi. Consequently that part of the lateral ventricle enclosed in the temporal lobe becomes (as the result of two infoldings of its median wall) restricted by two projections, the choroid plexus and the cornu Ammonis. As in the between-brain and medulla oblongata, the epithelial covering of the choroid plexus is continuous with the thicker nerve-substance of the cornu Ammonis. The transition is effected by means of a thin medullary plate, which in anatomy is described as the fimbria.

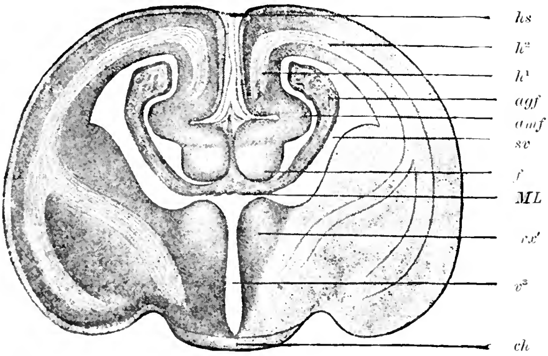

Fig. 255.—Transverse section through the brain of a Rabbit embryo 3·8 cm. in length, after MIHALKOVICS. Magnified 9 diameters.
The section passes through the foramina of MONRO.
hs, Great falx cerebri which fills up the interpallial fissure ; h^1, h^2, plane inner [median] and convex outer wall of the cerebral hemisphere ; *agf*, fold of the choroid plexus ; *amf*, hippocampal fold ; *f*, fornix ; *sv*, lateral ventricle ; *ML*, foramen of MONRO ; v^3, third ventricle ; *ch*, optic chiasma ; *fx'*, descending root of the fornix.

Inasmuch as the occipital lobe with its cavity develops as an evagination of the ring-lobe, the *fissura calcarina* belonging to it is therefore developed somewhat later than the arcuate fissure (fig. 241 *fc*). It appears at the end of the third month as a fissure branching off from the latter, and runs in a horizontal direction until near the apex of the occipital lobe. It invaginates the median wall of the lobe and produces the *calcar avis*, which invades the posterior cornu in the same way as the hippocampus major (cornu Ammonis) does the inferior cornu. At the beginning of the fourth month the *fissura occipitalis* (fig. 241 *fo*) is added to it. The latter rises from the anterior end of the fissura calcarina in a vertical direction to the bent rim of the mantle (Mantelkante), and sharply separates the occipital and parietal lobes from each other.

A *third factor* of great importance in the development of the cerebrum is the *formation of a system of commissures*, which supplements the connection of the two cerebral vesicles, at first effected by the embryonic lamina terminalis only. Those investigators who have occupied themselves with these difficult matters assert that in the third embryonic month fusions take place between the facing median walls of the hemispheres. These fusions begin in front of the foramen of MONRO within a triangular area. The fusions in this region occur only at the periphery, not in the middle of the area. Three parts of the brain of the adult are thus produced: in front, the genu of the corpus callosum, behind, the columns of the fornix, and between them, the septum pellucidum; the latter contains a fissure-like cavity, in the region of which the contiguous walls of the hemispheres, here very much attenuated, have remained separated from each other. Consequently the cavity just mentioned—the *ventriculus septi pellucidi* [or fifth ventricle]—ought not to be placed in the same category with the other cavities of the brain; for while the latter are derived from the central canal of the embryonic neural tube, the former is a new production, which has arisen by the enclosure of a portion of the space lying outside the brain between the two hemispheres—the narrow interpallial fissure.

A further enlargement of the commissural system is accomplished in the fifth and sixth months. The fusion now proceeds still farther, advancing from in front backwards, and involves that region of the median walls of the hemispheres which, situated between the arcuate fissure [above] and the fissure of the choroid plexus [below], has already been described as the marginal arch (Randbogen). By fusion of the anterior part of the marginal arch with its fellow of the opposite side,—which process takes place as far as the posterior limit of the between-brain,—there arise the body of the corpus callosum and the splenium, as well as the underlying fornix. The furrow bounding the corpus callosum above (sulcus corporis callosi) is therefore the anterior part of the arcuate furrow, whereas the posterior portion, that of the temporal lobe, is subsequently known as the fissura hippocampi.

The structure of the cerebrum is completed by *the appearance of numerous cortical furrows.* These differ in rank from the *total furrows* already described, because they are confined to the outer surface of the brain and do not cause corresponding projections into the ventricles. Their formation begins as soon as the wall of the brain becomes greatly increased in thickness by the development of white medullary substance, which occurs during and after the fifth month. This is due to the fact that the gray cortex with its ganglionic cells increases more rapidly in superficial extent than the white substance and is therefore raised into folds, the cerebral convolutions or gyri, into which only thin processes of white substance penetrate. At first, therefore, the furrows are quite shallow; they become deeper in proportion as the hemispheres become thicker and the cortical folds project farther outward.

Of the numerous furrows which the completely formed brain presents, some appear during the development earlier, others later. Thus they acquire different values in the architecture of the cerebral surface. For "*the earlier a furrow appears the deeper it becomes, the later it appears the shallower it is*" (Pansch). *The first are therefore the more important and constant ones, and are fittingly to be distinguished as chief or primary furrows from the subsequently formed and more variable secondary and tertiary furrows.* They begin to appear at the commencement of the sixth month. The first of them to appear is the central furrow (fig. 256 *cf*), which is one of the most important, since it separates the frontal and parietal lobes from each other. "In the ninth month all of the chief sulci and convolutions are formed, and since at this time the secondary sulci are still wanting, the brain during the ninth month presents a typical illustration of the sulci and convolutions" (Mihalkovics).

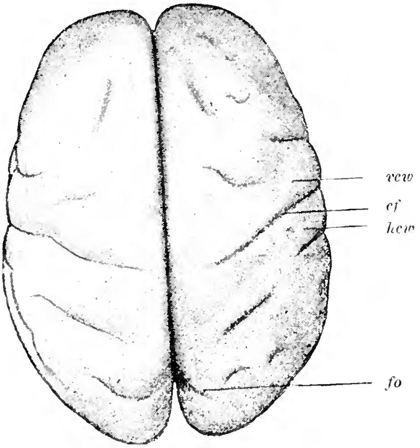

Fig. 256.—Brain of a human embryo at the beginning of the eighth month, after Mihalkovics. Three-fourths natural size.

cf, Central furrow; *vcw*, *hcw*, anterior and posterior central convolutions; *fo*, fissura occipitalis.

Very great differences exist between the different divisions of Mammals in the extent to which the sulci of the cerebrum are developed. On the one hand are the Monotremes, Insectivores, and many Rodents, whose cerebrum—also usually less developed in other features—possesses a smooth surface, and thus, as it were, remains permanently in the fœtal condition of the human brain. On the other hand the brains of the Carnivores and Primates, owing to the great number of their convolutions, approach more closely to the human brain.

Finally, in treating of the development of the cerebrum there is still to be considered an appendage to it, the *olfactory nerve.* This part, as well as the optic nerve, is distinguished from the peripheral nerves by its entire development, and must be considered as a specially modified portion of the cerebral vesicle. The older designation of nerve is therefore now more frequently replaced by the more appropriate name of *olfactory lobe* (lobus olfactorius, rhinencephalon). Even at an early stage—in the Chick on the seventh day of incubation, in Man during the fifth week (His)—there is formed on the floor of each frontal lobe at its anterior end a small evagination, which is directed forward (figs. 240, 241 *rn*). This gradually assumes the form of a club, the enlarged end of which, the part lying on the cribriform plate of the ethmoid bone, is designated as the *bulbus* olfactorius. The bulbus encloses a cavity which is in communication with the lateral ventricle.

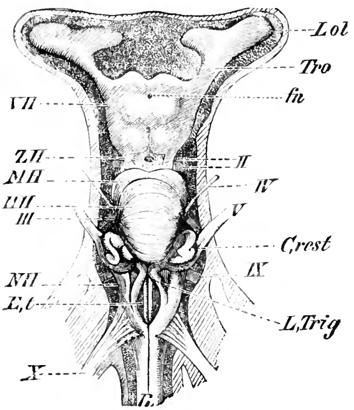

Fig. 257.—Brain of Galeus canis in situ, dorsal aspect, after Rohon.
Lol, Lobus olfactorius; *Tro,* tractus nervi olfactorii; *VH,* fore-brain, provided at *fn* with a vascular foramen (foramen nutritium); *ZH,* between-brain; *MH,* mid-brain; *HH,* hind-brain; *NH,* after-brain; *R,* spinal cord; *II,* n. opticus; *III,* n. oculomotorius; *IV,* n. trochlearis; *V,* n. trigeminus; *L,Trig,* lobus trigemini; *C,rest,* corpus restiforme; *IX,* glossopharyngeus; *X,* vagus; *E,t,* eminentiæ teretes.

During the first month of development the olfactory lobe, even in Man, is relatively large and provided with a central cavity. Later it begins to diminish somewhat, the sense of smell being only slightly developed in Man; its growth is arrested and at the same time its cavity also disappears. In most Mammals, on the contrary,—whose sense of smell, as is well known, is more acute than that of Man,—the olfactory lobe attains a greater size in the adult animal and exhibits more clearly the character of a part of the brain, for it permanently encloses in its bulb a cavity, which frequently (Horse) is even in connection with the anterior cornu by means of a narrow canal in the tractus olfactorius.

The olfactory lobe (*Lol*+*Tro*) attains an extraordinary development (fig. 257) in the Selachia, in which it exceeds in size the between-brain (*ZH*) and mid-brain (*MH* . In the Selachians two long hollow processes (tractus olfactorius, *Tro*) extend out from the anterior end of the little-developed cerebrum and terminate at a considerable distance from the fore-brain in two large hollow lobes, that are sometimes provided with furrows (*Lol*).

B. The Development of the Peripheral Nervous System.

Although it is easy to follow the development of the brain and spinal cord, the investigation of the origin of the peripheral nervous system is very difficult, for it requires the study of histological processes of the most subtle nature—the first appearance of non-medullated nerve-fibres and the method of their termination in embryos composed of more or less undifferentiated cells. One who knows how difficult it is even in the adult animal to follow non-medullated nerve-fibrillæ in epithelial layers or in non-striate muscle-tissue, and to get a clear idea of their method of termination, will understand that many, and indeed the most interesting, questions in regard to the development of the peripheral nerves are not yet ripe for discussion, because the observations necessary for their settlement are still wanting. There is only one point which is entirely clear. That concerns the development of the spinal ganglia, which HIS and BALFOUR independently of each other were the first to recognise, the one in the Chick, the other in Selachians. Since then numerous investigations embracing different groups of Vertebrates have been published on this subject by HENSEN, MILNES MARSHALL, KÖLLIKER, SAGEMEHL, VAN WIJHE, BEDOT, ONODI, BÉRANECK, RABL, BEARD, KASTSCHENKO, and others.

(*a*) *The Development of the Spinal Ganglia.*

The development of the spinal ganglia in the spinal cord is very easily followed. It begins just at the time the medullary groove closes to form a tube (fig. 258 *A* and *B*). At this time a thin ridge of cells (*spg′*, *spg*) one or two layers deep grows out of the neural tube on either side of the line of fusion, and, passing outward and downward, inserts itself between the tube and the closely investing primitive epidermis. In this way it reaches the dorsal angle of the primitive somites (*us*), which are by this time well developed. Then the *neural crest*, as Balfour names it, or the *ganglionic ridge*, as Sagemehl calls it, is divided up into successive regions. For the tracts which alternate with the primitive segments lag behind in their growth, while the parts lying opposite the middle of segments grow more vigorously, become thickened, and at the same time advance farther ventrad, penetrating between primitive segment and neural tube.

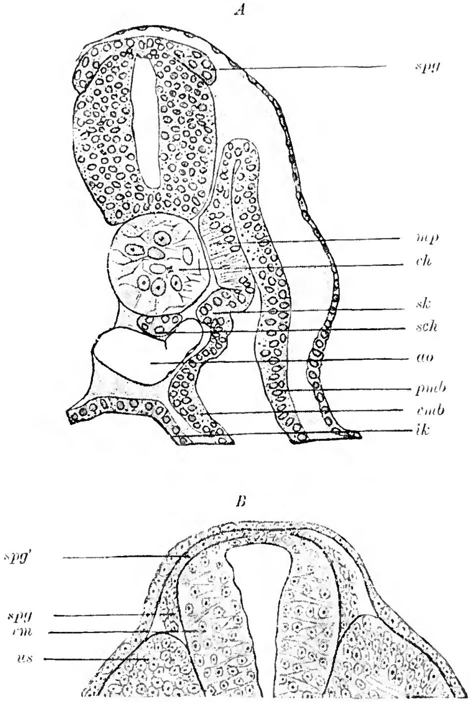

Fig. 258.—*A*, **Cross section through an embryo of Pristiurus,** after Rabl.

The primitive segments are still connected with the remaining portion of the middle germ-layer. At the region of transition there is to be seen an outfolding, *sk*, from which the skeletogenous tissue is developed. *ch*, Chorda; *spg*, spinal ganglion; *mp*, muscle-plate of the primitive segment; *sch*, subchordal rod; *ao*, aorta; *ik*, inner germ-layer; *pmb*, parietal, *vmb*, visceral middle layer.

B, **Cross section through a Lizard embryo,** after Sagemehl.

rm, Spinal cord; *spg*, lower thickened part of the neural ridge; *spg'*, its upper attenuated part, which is continuous with the roof of the neural tube; *us*, primitive segment.

Frontal sections furnish very instructive views of this stage. Fig. 259 exhibits such a section, taken from Sagemehl's work. Inasmuch as the longitudinal axis of the Lizard embryo employed for the sections was greatly curved, the five segments seen in the section are cut at different heights, the middle one deeper than the two preceding and the two following. In the middle segment the fundament of the ganglion (*spk*) is differentiated and it is bounded by blood-vessels in front and behind, whereas in the segments that are cut more dorsally, near the origin of the ganglia from the neural tube, the fundaments are still connected with one another. This connection appears to be most conspicuously developed and most persistent in the case of the Selachians; it has been called the longitudinal commissure by BALFOUR. Outside the ganglia are found the primitive segments (*mp*, *mp'*), each of which at this time still exhibits within it a narrow fissure.

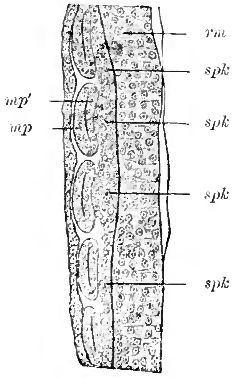

Fig. 259.—Frontal section of a Lizard embryo, after SAGEMEHL.

rm, Spinal cord; *spk*, neural ridge with thickenings that are converted into the spinal ganglia; *mp'*, the part of the primitive segment that produces the muscle-plate; *mp*, outer layer of the primitive segment.

In a monographic treatment of the peripheral nervous system BEARD differs from the preceding account, in which BALFOUR, KÖLLIKER, RABL, HENSEN, SAGEMEHL, KASTSCHENKO, and others agree. He believes that the fundaments of the ganglia arise, not out of the neural tube, but out of the deeper cell-layers of the adjacent part of the outer germ-layer. He finds that they are from the beginning separated from each other and segmentally arranged. According to him, moreover, they make their appearance earlier than is stated in the preceding account; for they are already recognisable as especially thickened places in the outer germ-layer at the right and left of the neural plate when the latter first begins to be bent inward. Subsequently, upon the closure of the neural tube, the ganglionic cells come to lie between the raphe and the primitive epidermis. From here they grow down ventrally at the sides of the brain and spinal cord.

BEARD approximates in his results the conception first expressed and subsequently maintained by HIS. For HIS derives the ganglionic ridge, not from the raphe of the neural tube, but from a neighboring part of the outer germ-layer, which he names intermediate cord (Zwischenstrang). The accuracy of BEARD'S description is, however, positively denied by RABL and KASTSCHENKO.

Different views are entertained concerning the further changes which take place in the fundaments of the spinal ganglia:—

According to HIS and SAGEMEHL the separate ganglionic fundaments are completely detached from the neural tube, and for a time lie at the side of it without any connection with it whatever. Secondarily a union is again established, through the development of the dorsal nerve-roots, by the formation of nerve-fibrillæ, which either grow out from the spinal cord into the ganglion, or from the ganglion into the spinal cord, or in both directions. SAGEMEHL favors the first view, His the last. All other investigators maintain that the fundaments of the ganglia, while they increase in size and become spindle-shaped, are permanently united with the neural tube by means of slender cords of cells which are metamorphosed into the dorsal roots. If the latter view is correct, the dorsal roots of the nerves must in time alter their place of attachment to the neural tube by moving from the raphe laterally and ventrally.

The discrepancy of these accounts is connected with the different interpretations which exist concerning the development of the peripheral nerves in general.

(*b*) *The Development of the Peripheral Nerves.*

When one reviews the various opinions which have been expressed concerning the development of the peripheral nerves, it is found that there are in the literature two chief opposing views. The greater number of investigators assume that the peripheral nervous system is developed out of the central,—that *the nerves grow forth from the brain and spinal cord uninterruptedly until they reach the periphery, where for the first time they effect a union with their specific terminal organs.* The outgrowth of the nerves from the spinal cord was first asserted for the ventral roots and conjectured for the dorsal ones by Bidder und Kupffer. Their conclusions have since been adopted by Kölliker, His, Balfour, Marshall, Sagemehl, and others. However, views concerning the method of the formation of the nerve-fibres are not in agreement.

According to Kupffer, His, Kölliker, Sagemehl, and others *the outgrowing nerve-fibres are processes of ganglionic cells located in the central organ*, which must grow out to an enormous length in order to reach their terminal apparatus. There are at first no cells or nuclei among them. These are furnished secondarily by the surrounding connective tissue. According to the accounts of Kölliker and His, cellular elements from the mesenchyme approach the bundles of nerve-fibrillæ, surround them, and then penetrate into the interior of the nervous stem, at first sparingly, afterwards more abundantly, and form around the axis-cylinders the sheaths of Schwann.

On the other hand, Balfour defends most positively the doctrine that cells which migrate out of the spinal cord along with the nerves share in the development. In his "Treatise on Comparative Embryology" [vol. ii., p. 372] he remarks upon this subject : "The cellular structure of embryonic nerves is a point on which I should have anticipated that a difference of opinion was impossible, had it not been for the fact that His and Kölliker, following Remak and other older embryologists, absolutely deny the fact. I feel quite sure that no one studying the development of the nerves in Elasmobranchii with well-preserved specimens could for a moment be doubtful on this point." Of the more recent investigators van Wijhe, Dohrn, and Beard side with Balfour.

Hensen has taken an entirely different view on the question of the origin of the peripheral nervous system, one which differs from that of Kupffer, His, and Kölliker, as well as from that of Balfour. He opposes the doctrine of the outgrowth of nerve-fibres chiefly from physiological considerations. He can think of no motive which is capable of conducting the nerves that grow out from the spinal cord to their proper terminations—which shall cause, for example, the ventral roots always to go to muscles, the dorsal roots to organs that are not muscular, and shall prevent confusion taking place between the nerves of the iris and those of the eye-muscles, between the branches of the trigeminus and the acusticus or facialis, etc. Therefore Hensen maintains on theoretical grounds that it is necessary to assume that "*the nerves never grow out to their terminations, but are always in connection with them.*" According to his view, which he endeavors to support by observations, the embryonic cells are for the most part united with one another by means of fine connecting filaments. He maintains that when a cell divides the connecting thread also splits, and in this manner there arises "an endless network of fibres." Out of these the nerve-tracts are developed, while other parts of the network degenerate.

The reasons given by Hensen are certainly worthy of great attention. With further reflection on the subject they are easily added to. If the nerves grow out to their terminal apparatus, why do they not take the most direct course to their destination, why are they often compelled to pursue circuitous paths, and why do they enter into the formation of complicated plexuses of the greatest variety? whence are the ganglionic cells that are found to be developed in considerable numbers even in the peripheral nervous system in different organs, especially in the sympathetic nerve? In order to make progress in this difficult field the **peripheral nervous system** *of Invertebrates* must be taken into account more than it is at present, and in the investigation of embryos not only series of sections but also other histological methods (surface-preparations of suitable objects together with staining of the nerve-fibrillæ, isolation of the elements preceded by maceration and staining) must be employed.

Having thus sketched out the various standpoints taken by numerous investigators on the question of the source of the peripheral nervous system, I give a number of observations that have been made upon the development of certain nerves. These relate to the development of :—

(1) The ventral and dorsal roots of the nerves ;
(2) Certain large peripheral nerve-trunks, as the nervus lateralis ; and
(3) The nerves of the head and their relation to the spinal nerves.

(1) Of the roots of the nerves the anterior [ventral] are demonstrable earlier. There may be distinguished three stages in their development.

The first stage has been observed by Dohrn and van Wijhe in Selachian embryos. At a time when the neural tube has not yet developed any mantle of nervous substance, and the muscle-segment still lies very close to it, there arises between the two a connection in the form of a very short protoplasmic cord. The fundament of the nerve is therefore, as van Wijhe remarks, ab origine near its muscle-complex, from which it never separates. Soon after this it is elongated by the removal of the muscle-segment farther from the neural tube ; it increases in thickness and now encloses numerous nuclei, and possesses therefore a cellular composition, a condition which I shall designate as second stage.

There is a difference of opinion as to the cells which make their appearance in the fundament of the nerve. Whereas Kölliker His, and Sagemehl recognise in them immigrated connective-tissue elements, which are destined to form simply the envelopes of the nerves, Balfour, Marshall, van Wijhe, Dohrn, and Beard maintain that they migrate out from the spinal cord and share in the development of the nerves themselves. Beard even derives the motor terminal plate from them. Soon after, as is asserted, connective-tissue cells from the surrounding mesenchyme become associated with the nerve-cells derived from the spinal cord and ordinarily become indistinguishable from them.

Finally, in the third stage the cellular fundament of the motor root acquires a fibrillar condition (fig. 260 *vw*), and it now becomes possible to trace the origin of the nerve-fibrillæ in the spinal cord from groups of embryonal ganglionic cells or neuroblasts (His).

The formation of the nerve-fibrillæ is also a subject of controversy, as has already been stated and as will be further explained in this connection. According to the view of most observers, the nerve-fibrillæ—the future axis-cylinders—are formed as processes of ganglionic cells of the spinal cord, the free ends of which grow out from the surface of the latter until they reach their terminal organs (KUPFFER UND BIDDER, KÖLLIKER, HIS, SAGEMEHL). Such accounts are given especially for the development of the motor roots in the higher Vertebrates.

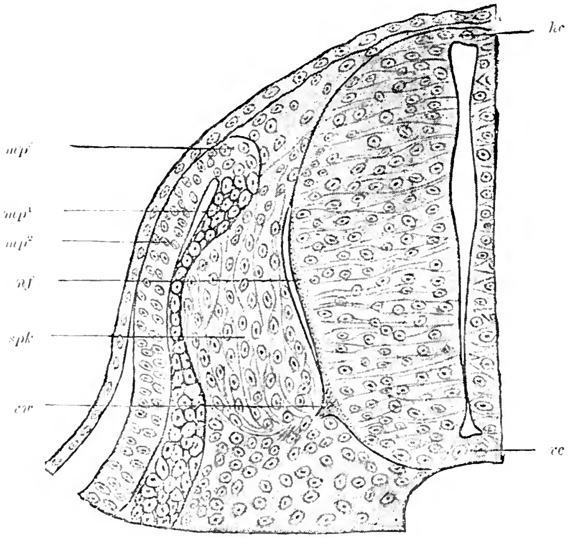

Fig. 260.—Cross section of a Lizard embryo with completely closed intestinal canal, after SAGEMEHL.

hc, Posterior [dorsal], *vc*, anterior commissure of the spinal cord; *vw*, ventral nerve-root; *nf*, nerve-fibrillæ; *spk*, spinal ganglion; mp^1, muscle-plate, muscle-producing layer; mp^2, outer layer of the muscle-plate; mp^3, transition from the outer to the muscle-forming layer.

According to the opinion of DOHRN and VAN WIJHE, on the contrary, the nerve-fibrillæ arise in situ, as products of differentiation, from the protoplasm of the cords of cells by means of which muscle-segment and spinal cord are already united. They do not need to seek out the terminal organ, since there exists already a protoplasmic union with it. They arise in a manner similar to that in which the muscle-fibrillæ do from the plasma of their muscle-cells.

I desire to lay particular stress upon the observations of **Dohrn** and **van Wijhe**, because they harmonise with the theoretical views which I have formed as the result of investigations on Invertebrates. As I have in several articles endeavored to establish, protoplasmic connections of the cells are the foundation out of which the nerve-fibrillæ are developed. The formation of a specific nervous system is preceded by a protoplasmic union of cells, which is effected at a time when the central and terminal nervous organs are still in the immediate vicinity of each other.

The dorsal roots become visible somewhat later than the ventral roots; there are formed fibrillæ which unite the upper [dorsal] end of the spinal ganglion with the side of the spinal cord.

(2) **Götte**, **Semper**, **Wijhe**, **Hoffmann**, and **Beard** have made concerning certain nerves the noteworthy statement—which has been called in question by some observers (**Balfour**, **Sagemehl**)—that the epidermis participates in their formation. In Amphibian larvæ and Selachian embryos *the posterior end of the nervus lateralis vagi in process of development is completely fused with the primitive epidermis, which is thickened in the lateral line* (fig. 262 *nl*). Somewhat farther forward the nerve is detached but still lies in close contact with the primitive epidermis, whereas in the vicinity of the head it is situated deeper and lies between the muscles. At the places where the nerve has become separated from the primitive epidermis, it remains in connection with the fundaments of the lateral organs by means of fine accessory branches only. Similar observations have also been made in the case of many of the branches of other cranial nerves in Selachian embryos. **Wijhe** sees, for example, a short branch of the n. facialis near its emergence from the brain so fused with a thickened portion of the epidermis composed of cylindrical cells, that it is impossible to say whether at the place of transition the cell-nuclei belong to the nerve or to its terminal organ. During a more advanced stage the older part of the nerve is detached from the terminal organ, sinks into the depths, becoming separated from the skin by ingrowing connective tissue, and remains united with the terminal organ only through fine accessory branches. The persistently growing younger end of the nerve still continues to be connected with the epidermis.

Also in the case of the higher Vertebrates similar conditions have been observed by **Beard**, **Froriep**, and **Kastschenko**. They find the ganglionic fundaments of the facialis, glossopharyngeus, and vagus at the dorsal margin of the corresponding visceral clefts for a long time broadly fused with the epithelium, which is thickened and has become depressed into a pit. In these connections they discern the fundaments of branchial sensory organs, which no longer attain to complete development. Also **Froriep**, on the strength of his own observations, holds as admissible the interpretation that at those places where fusion occurs *formative material* passes out of the epidermis into deeper parts to share in the formation of nervous tracts. **Beard** expresses himself still more precisely to the effect that the sensory nervous elements of the whole peripheral nervous system arise as differentiations from the outer germ-layer, independently of the central nervous system.

The accounts here given concerning a connection, in early stages of development, of certain nerve-trunks with the outer germ-layer, appear to me to afford an indication in favor of the hypothesis expressed by my brother and me, that the sensory nerves of the Vertebrates may have originally been formed out of a sub-epithelial nervous plexus, such as still exists in the epidermis of many Invertebrates.

(3) The investigations of the last few years, which have been carried out especially by **Balfour**, **Marshall**, **Kölliker**, **Wijhe**, **Froriep**, **Rabl**, and **Kastschenko**, have produced important results concerning the development of the cranial nerves, their relations to the head-segments and their value as compared with spinal nerves. On the brain, as well as on the spinal cord, there arise roots, some of which are dorsal, some ventral. Even at the time when the brain-plate is not yet fully closed into a tube (fig. 261), there is formed on either side, at the place of its bending over into the primitive epidermis, a neural ridge (*vg*), which begins rather far forward and may be traced on serial sections uninterruptedly in a posterior direction, where it is continuous with the neural ridge of the spinal cord. When, somewhat later, the closure and the detachment of the brain-vesicles from the primitive epidermis has taken place, the ridge lies on the roof of the vesicles and is fused with them in the median plane. The most of the cranial nerves—namely, the trigeminus with the Gasserian ganglion, the acusticus and facialis with the ganglion acusticum and probably also the ganglion geniculi, and the glossopharyngeus and vagus with the related ganglion jugulare and g. nodosum—are differentiated out of this fundament in the same manner as the dorsal roots of the spinal nerves. The nerves, which emerge dorsally, afterwards shift their origin downward along the lateral walls of the brain-vesicles toward the base of the latter.

All the remaining unenumerated cranial nerves—oculomotorius, trochlearis, abducens, hypoglossus, and accessorius—are developed independently of the neural ridge, as individual outgrowths of the brain-vesicles nearer their base, and are comparable with the ventral roots from the spinal cord.

FRORIEP finds that the hypoglossus in Mammals possesses dorsal roots, with small ganglionic fundaments, in addition to ventral roots. The latter subsequently undergo degeneration.

The agreement between cranial and spinal nerves which is expressed in this method of development, becomes still greater and acquires a further significance from the fact that *in the head also the nerves can be assigned to separate segments in much the same manner as in the trunk.* In this particular the conditions are clearest in the Selachians, where, in fact, the head-segments have been most thoroughly investigated, so that I limit myself to a statement of the results acquired in this field by WIJHE.

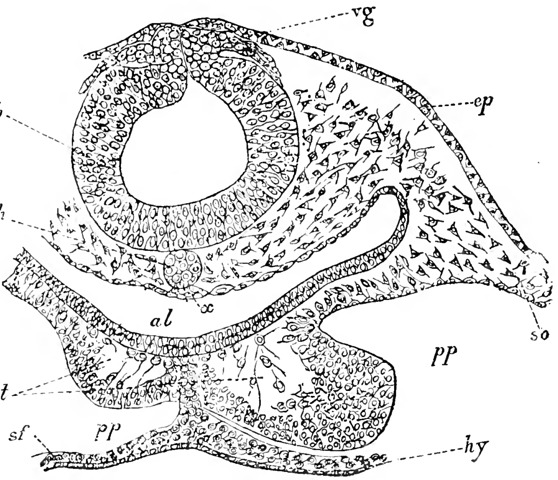

Fig. 261.—Cross section through the hind part of the head of a Chick embryo of 30 hours, after BALFOUR.

hb, Hind-brain; *vg*, vagus; *ep*, epiblast; *ch*, chorda; *x*, thickening of hypoblast (possibly a rudiment of the subchordal rod); *al*, throat; *ht*, heart; *pp*, body-cavity; *so*, somatic mesoblast; *sf*, splanchnic mesoblast (Darmseitenplatte); *hy*, hypoblast.

According to WIJHE nine * segments are distinguishable in the head of Selachians. To the first segment belongs the ramus

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* [Recent investigations indicate that the head-segments in Selachians are much more numerous.—TRANSLATOR.]

ophthalmicus of the trigeminus and, as motor root, the oculomotorius. The second segment is supplied by the remaining part of the trigeminus and the trochlearis, the latter having a ventral origin. The dorsal roots of the third (and fourth?) segments are represented by the acustico-facialis, the ventral roots by the abducens. The fifth segment possesses only the exclusively sensory glossopharyngeus, which arises from the neural ridge. The segments from the sixth to the ninth inclusive are innervated by the vagus and the hypoglossus, the former of which represents a series of dorsal roots, the latter a series of ventral ones.

According to WIJHE's account, notwithstanding the general agreement, there still exists a *considerable difference between the innervation of the cephalic segments and that of the trunk-segments.* For in the head the ventral, motor roots (oculomotorius, trochlearis, abducens, hypoglossus) supply only a part of the musculature—the eye-muscles and certain muscles that run from the skull to the pectoral girdle; that is to say, muscles which, as has already been stated, are developed out of the cephalic segments. Other groups of muscles, which arise from the lateral plates of the head, are innervated by the trigeminus and facialis, which have a dorsal origin. Thus the dorsal roots of the nerves in the head would be distinguished from those in the trunk by the important fact that they contain motor as well as sensory fibres. BELL's law would consequently possess a very limited application for the head-region of Vertebrates, and would have to be replaced by the following law, formulated by WIJHE:—

"The dorsal roots of the head-nerves are not exclusively sensory, but also innervate the muscles that arise from the lateral plates, not, however, those from the primitive segments (somites)."

"The ventral roots are motor, but innervate only the muscles of the primitive segments (somites), not those of the lateral plates."

In view of this fundamental difference, I desire to express a doubt whether there are not after all enclosed in the facialis and trigeminus parts which are established as ventral roots, but have hitherto been overlooked, as in the beginning all the ventral roots in the brain (see BALFOUR) were overlooked.

According to RABL the nerves of the posterior part of the head only—glossopharyngeus, vagus, accessorius, and hypoglossus—can be compared with the type of spinal nerves; the nerves of the anterior part of the head, on the contrary,—the olfactorius, opticus, trigeminus, together with those of the eye-muscles and the acustico-facialis,—belong in a separate category, just as the four most anterior head-segments do.

As is evident from this brief survey, there still exist many unsolved problems in the difficult subject of the development of the peripheral nervous system. Without permitting myself to enter upon a further discussion of the contradictory opinions entertained on this subject, I close this topic with a comparative-anatomical proposition, which appears to me sufficient *to furnish the morphological explanation of* BELL'S *law, or the separate origin of the sensory and motor nerve-roots.*

In Amphioxus and the Cyclostomes the motor and sensory nerve-fibres are completely separated, not only at their origin from the spinal cord, but also throughout their whole peripheral distribution. The former pass at once from their origin in the spinal cord to the muscle-segments; the latter ascend to the surface to be distributed to all parts of the skin to supply its sensory cells and sensory organs. *The separation of the peripheral nervous system into a sensory and a motor portion, which is rigorously carried out in Amphioxus and the Cyclostomes, is explained by the fact that the territories to which their ends are distributed are spatially distinct in their origin,* since the sensory cells arise from the outer germ-layer, the voluntary muscles from a tract of the middle germ-layer. Therefore the *sensory nerve-fibres have been developed from the spinal cord in connection with the outer germ-layer*, the motor fibres in relation with the muscle-segments.

I regard the sub-epithelial position of the sensory nerve-fibres as the original one, just as we find in many Invertebrates the whole peripheral sensory nervous system developed as a plexus in the deepest portion of the epidermis. The important conditions above described—according to which many dermal nerves (nervus lateralis, etc., fig. 262 *nl*) are fused with the epidermis at the time of their origin, and only subsequently become detached from it and sink deeper into the underlying mesenchyme—appear to me to indicate that such a position was the primitive one in the case of Vertebrates also.

I look upon the union of the sensory and motor nerve-fibres into mixed trunks (which occurs soon after their separate origin from the spinal cord, in the case of all Vertebrates except Amphioxus and the Cyclostomes) as a secondary condition, and maintain that it is caused especially by the following embryological influences: by the change in the position of the spinal cord and the muscular masses, and by the great increase in the amount of the connective substances.

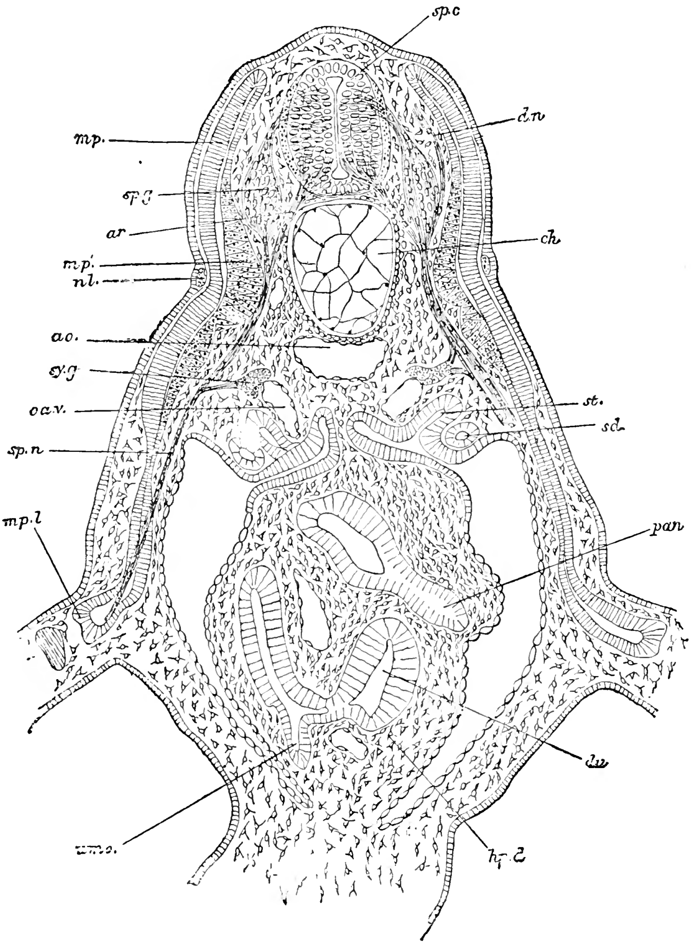

Fig. 262.—Cross section through the anterior part of the trunk of an embryo of Scyllium, after Balfour.

Between the dorsal wall of the trunk and its ventral wall, where the attachment of the stalk of the yolk-sac is cut, there is stretched a thick richly cellular mesentery, which completely divides the body-cavity into right and left halves. Within the mesentery the duodenum (*du*), from which the fundament of the pancreas (*pan*) is given off dorsally and the fundament of the liver (*hp.d*) ventrally, is twice cut through. In addition, the place where the vitelline duct [umbilical canal] (*umc*) joins the duodenum is visible.

sp.c, Spinal cord; *s.pg*, ganglion of posterior root; *ar*, anterior root; *dn*, dorsally directed nerve springing from the posterior root; *mp*, muscle-plate; *mp'*, part of the muscle-plate already converted into muscles; *mp.l*, part of the muscle-plate which gives rise to the muscles of the limbs; *nl*, nervus lateralis; *ao*, aorta; *ch*, chorda; *sy.g*, sympathetic ganglion; *ca.v*, cardinal vein; *sp.n*, spinal nerve; *sd*, segmental (archinephric) duct; *st*, segmental tube.

Since the spinal cord comes to lie in deeper layers of the body far away from its place of origin, the dermal nerves must follow it, and therefore their origins are correspondingly farther separated from their terminations. Since also, on the other hand, the muscle-plates grow around the neural tube, certain motor and sensory nerve-cords are brought near to each other in their passage to their peripheral distribution. And this will occur especially in all cases where the motor and sensory peripheral terminations lie at a great distance from the origin of the nerves out of the spinal cord, as, for example, in the case of the limbs. The mutual approximation of sensory and motor nerve-tracts thus brought about will finally lead to the formation of common tracts, according to the same principle of simplified organisation in accordance with which the blood-vessels also adapt themselves closely to the course of the nerves.

(*c*) *The Development of the Sympathetic System.*

The development of the sympathetic nervous system has as yet been investigated by only a few observers. Balfour first announced that it arose in connection with the cranial and spinal nerves, and therefore was, like the latter, really derived from the outer germ-layer. In the Selachians he found the sympathetic ganglia (fig. 262 *sy.g*) as small enlargements of the chief trunks of the spinal nerves (*sp.n*) a little below their ganglia (*sp.g*). In older embryos, according to Balfour's account, they recede from the spinal ganglia, and then at a later period unite with one another, by the development of a longitudinal commissure, into a continuous cord (Grenzstrang).

The origin of the sympathetic system has been the most thoroughly studied by Onodi in researches covering several classes of Vertebrates. According to him the sympathetic ganglia arise directly, as Balfour suggested and as Beard has also lately reiterated, from the spinal ganglia. The ventral ends of the spinal ganglia undergo proliferation, as is best seen in Fishes. The proliferated part detaches itself, and, as fundament of a sympathetic ganglion, moves ventrally. The fundaments of the individual segments are at first separate from one another. The cord (Grenzstrang) is a secondary product, produced by the growing out of the individual ganglia toward each other and the union of the outgrowths. Afterwards the sympathetic ganglia and plexuses of the body-cavity are derived from this part.

Summary.

Central Nervous System.

1. The central nervous system is developed out of the thickened region of the outer germ-layer which is designated as the medullary plate.

2. The medullary plate is folded together to form the medullary tube (medullary ridges, medullary groove).

3. The formation of the neural tube exhibits three principal modifications: (*a*) Amphioxus, (*b*) Petromyzon, Teleosts, (*c*) the remaining Vertebrates.

4. The lateral walls of the medullary tube become thickened, whereas the dorsal and ventral walls remain thin; the latter come to occupy the depths of the anterior and posterior longitudinal fissures, and constitute the commissures of the lateral halves of the spinal cord.

5. The spinal cord at first fills the whole length of the vertebral canal, but it grows more slowly than the latter, and finally terminates at the second lumbar vertebra (explanation of the oblique course of the lumbar and sacral nerves).

6. The part of the neural tube which forms the brain becomes segmented into the three primary cerebral vesicles (primary fore-brain vesicle, mid-brain vesicle, hind-brain vesicle).

7. The lateral walls of the fore-brain vesicle are evaginated to form the optic vesicles, the anterior wall to form the vesicles of the cerebrum.

8. The hind-brain vesicle is divided by constriction into the vesicles of the cerebellum and the medulla.

9. Thus from the three primary brain-vesicles there finally arise five secondary ones arranged in a single series one after the other —(*a*) cerebral vesicle (that of the hemispheres), (*b*) between-brain vesicle with the laterally attached optic vesicles, (*c*) mid-brain vesicle, (*d*) vesicle of the cerebellum, (*e*) vesicle of the medulla oblongata.

10. The originally straight axis uniting the brain-vesicles to one another later becomes at certain places sharply bent, in consequence of which the mutual relations of the vesicles are changed (cephalic flexure, pontal flexure, nuchal flexure). The cephalic or parietal protuberance at the surface of the embryo corresponds to the cephalic flexure, the nuchal protuberance to the nuchal flexure.

11. The separate parts of the brain are derivable from the five brain-vesicles; the accompanying table (MIHALKOVICS, SCHWALBE) gives a survey of the subject.

12. In the metamorphoses of the vesicles the following processes take place: (*a*) certain regions of the walls become more or less thickened, whereas other regions undergo a diminution in thickness and do not develop nervous substance (roof-plates of the third and fourth ventricles); (*b*) the walls of the vesicles are infolded; (*c*) some of the vesicles (first and fourth) greatly exceed in their growth the remaining ones (between-brain, mid-brain, after-brain, or medulla oblongata).

13. The four ventricles of the brain and the aqueductus Sylvii are derived from the cavities of the vesicles.

14. Of the five vesicles that of the mid-brain is the most conservative and undergoes the least metamorphosis.

15. The vesicles of the between-brain and after-brain exhibit similar alterations: their upper walls or roof-plates are reduced in thickness to a single layer of epithelial cells, and in conjunction with the growing pia mater produce the choroid plexuses (anterior, lateral, posterior choroid plexus; anterior, posterior brain-fissure).

16. The cerebral vesicle is divided by the development of the longitudinal (interpallial) fissure and the falx cerebri into lateral halves, the two vesicles of the cerebral hemispheres.

17. In Man the cerebral hemispheres finally exceed in volume all the remaining parts of the brain, and grow from above and from the sides as cerebral mantle over the other brain-vesicles (from the second to the fifth inclusive) or the brain-stalk.

18. In the folding of the walls of the hemispheres there are to be distinguished fissures and sulci.

19. The fissures (fossa Sylvii, fissura hippocampi, fissura choroidea, fissura calcarina, fissura occipitalis) are complete folds of the wall of the brain, by means of which there are produced deep incisions in the surface and corresponding projections into the lateral ventricles (corpus striatum, cornu Ammonis, fold of the choroid plexus, calcar avis).

20. The sulci are incisions limited to the cortical portion of the wall of the brain, and are deeper or shallower according to the time of their formation (primary, secondary, tertiary sulci).

21. In general the fissures appear earlier than the sulci.

22. The olfactory nerve is not equivalent to a peripheral nerve-trunk, but, like the optic vesicle and optic nerve, a special part of

NAMES OF THE BRAIN-VESICLES.		FLOOR.	ROOF.	LATERAL WALLS.	CAVITIES.	
I. Primary hind-brain vesicle.	(1) After-brain vesicle.	Medulla oblongata.	Membrana tectoria ventriculi quarti (obex, ligula).	Pedunculi cerebelli.	Ventriculus quartus.	A. Brain-stalk.
	(2) Cerebellar vesicle (secondary hind-brain).	Pons Varolii.	Velum medullare posterius cerebellum. Velum medullare anterius.	Crura cerebelli ad pontem. Processus cerebelli ad cerebrum.		
II. Mid-brain vesicle. (3)		Pedunculi cerebri. Lamina perforata posterior.	Corpora quadrigemina.	Laqueus. Brachia conjunctiva. Corpus geniculatum mediale.	Aqueductus Sylvii.	
III. Primary fore-brain vesicle.	(4) Between-brain vesicle.	Corpora candicantia. Tuber cinereum cum infundibulo. Chiasma nervorum opticorum.	Commissura posterior. Glandula pinealis. Membrana tectoria ventriculi tertii (tænia thalami).	Thalamus opticus.	Ventriculus tertius.	
	(5) Cerebral vesicle (secondary fore-brain).	Lamina perforata ant. Lobus alfactorius. Insula (with nucleus candatus and n. lentiformis) is comprised in brain-stalk.	Mantle-part of the cerebral hemispheres. Corpus callosum; commissura anterior. Fornix; septum pellucidum.		Ventriculi laterales.	B. Brain-mantle.

the brain produced by an evagination of the frontal lobe of the cerebral hemisphere (lobus or bulbus olfactorius with tractus olfactorius). (Enormous development of the olfactory lobes in lower Vertebrates,—Sharks,—degeneration in Man.)

Peripheral Nervous System.

23. The spinal ganglia are developed out of a neural ridge (crest), which grows outward and downward from the raphe of the neural tube on either side between the tube and the primitive epidermis, and becomes thickened in the middle of each primitive segment into a ganglion.

24. The spinal ganglia therefore arise, like the neural tube itself, from the outer germ-layer.

25. The sympathetic ganglia of the longitudinal cord (Grenzstrang) are probably detached parts of the spinal ganglia.

26. Concerning the development of the peripheral nerve-fibres there are different hypotheses:—

First hypothesis. The peripheral nerve-fibres grow out from the central nervous system and only secondarily unite with their peripheral terminal apparatus.

Second hypothesis. The fundaments of the peripheral terminal apparatus (muscles, sensory organs) and the central nervous system are connected from early stages of development by means of filaments which become nerve-fibres (HENSEN).

27. Anterior and posterior nerve-roots are developed on the spinal cord separately from each other, one ventrally, the other dorsally.

28. The cranial nerves arise in part like posterior, in part like anterior roots of spinal nerves.

29. The following cranial nerves with their ganglia, which are comparable with spinal ganglia, are developed out of a neural ridge which grows out from the raphe of the brain-vesicles: the trigeminus with the ganglion Gasseri, the acusticus and facialis with the ganglion acusticum and g. geniculi, the glossopharyngeus and vagus with the ganglion jugulare and g. nodosum.

30. The oculomotorius, trochlearis, abducens, hypoglossus, and accessorius are developed like ventral roots of spinal nerves.

31. The olfactory and optic nerves are metamorphosed parts of the brain.

II. The Development of the Sensory Organs, Eye, Ear, and Organ of Smell.

As the outer germ-layer is the parental tissue of the central nervous system, so also does it form the substratum for the higher sensory organs, the eye, the ear, and the organ of smell. For it furnishes the sensory epithelium, a component which, in comparison with the remaining parts, derived from the mesenchyma, is, it is true, of very small volume, but, notwithstanding, by far the most important both from a functional and a morphological point of view. Whether a sensory organ is adapted for seeing, hearing, smelling, or tasting depends primarily upon the character of its sensory epithelium, *i.e.*, upon whether it is composed of optic, auditory, olfactory, or gustatory cells. But also morphologically the epithelial part is preëminent, because it is chiefly this which determines the *fundamental form of the sensory organs* and affords the fixed centre around which the remaining accessory components are arranged. The genetic connection with the outer germ-layer may be most clearly recognised in many Invertebrates, inasmuch as here the sensory organs are permanently located in the epidermis, whereas in Vertebrates, as is well known, they are, for the sake of protection, embedded in deep-lying tissues. I begin with the eye, and then proceed to the organ of hearing and that of smell.

A. The Development of the Eye.

As has already been stated in the description of the brain, the lateral walls of the primary fore-brain (figs. 234, 263) are evaginated and produce the primary optic vesicles (*au*), which are constricted off more and more and remain in connection with the between-brain

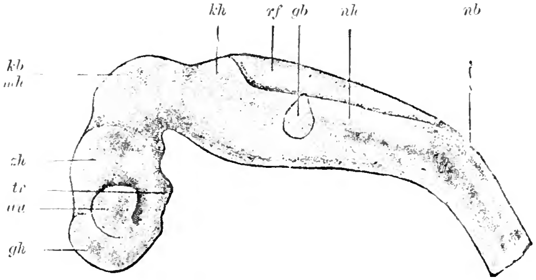

Fig. 263.—Brain of a human embryo of the third week (*Lg*). Profile reconstruction, after His. *gh*, Cerebral vesicle; *zh*, between-brain vesicle; *mh*, mid-brain vesicle; *kh*, *nh*, vesicles of cerebellum and medulla oblongata; *au*, optic vesicle; *gb*, auditory vesicle; *tr*, infundibulum; *rf*, area rhomboidalis; *nb*, nuchal flexure; *kb*, cephalic flexure.

by means of a slender stalk only (fig. 264 *A st*). They possess spacious cavities within, which are connected with the system of brain-ventricles through the narrow canal of the stalk of the optic vesicle. In many Vertebrates, in which the central nervous system is formed as a solid structure, as in the Cyclostomes and Teleosts, the optic vesicles are also without cavities; these do not make their appearance until the central nervous system becomes a tube.

Since the brain is for a long time separated from the primitive epidermis by only an exceedingly thin sheet of connective tissue, the primary optic vesicles at the time of their evagination either apply themselves directly to the epidermis, as in the case of the Chick, or are separated from it by only a very thin intervening layer, as in Mammals.

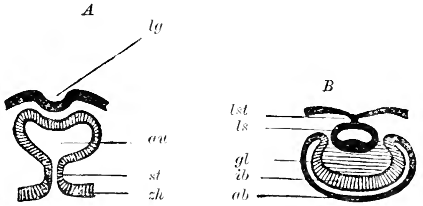

Fig. 264.—Two diagrams illustrating the development of the eye.

A, The primary optic vesicle (*au*), joined by a hollow stalk (*st*) to the between-brain (*zh*), is invaginated as a result of the development of the lens-pit (*lg*).

B, The lens-pit has become abstricted to form a lens-vesicle (*ls*). From the optic vesicle has arisen the optic cup with double walls, an inner (*ib*) and an outer (*ab*); *lst*, stalk of the lens; *gl*, vitreous body.

Upon each optic vesicle can be distinguished a lateral, a median, an upper and a lower wall. I designate as lateral that surface which reaches the epidermis at the surface of the body, as median the opposite wall joined with the stalk of the optic vesicle, and finally as lower the one which lies on a level with the floor of the between-brain. These designations will be useful in acquainting ourselves with the changes which the form of the optic vesicle undergoes during *its invagination, which occurs at two places, namely, at its lateral and lower surfaces. One of the invaginations is connected with the development of the lens, the other with the formation of the vitreous body.*

The first fundament of the lens appears in the Chick as early as the second day of incubation, in the Rabbit about ten days after the fertilisation of the egg. At the place where the epidermis passes over the surface of the primary optic vesicle (fig. 264 *A lg*), it becomes slightly thickened and invaginated into a small pit (lens-pit). The pit, by its deepening and by the approximation of its edges until they meet, is converted into a *lens-vesicle* (fig. 264 *B ls*), which for a time preserves its connection with its parental substratum, the epidermis, by means of a solid epithelial cord (*lst*). Upon being constricted off the lens-vesicle naturally pushes the adjacent lateral wall of the optic vesicle before it and folds the latter in against the median wall.

At the same time with the development of the lens, the primary optic vesicle is also invaginated from below along a line which stretches from the epidermis to the attachment of the stalk of the optic vesicle, and is even continued along the latter for some distance (fig. 265 *aus*). A loop of a blood-vessel from the enveloping connective tissue, embedded in soft, gelatinous substance (*gl*), here grows against the lower surface of the primary optic vesicle and its stalk, and pushes up before it the lower wall.

In consequence of the two invaginations the optic vesicle acquires the form of a beaker or cup, the foot of which is represented by its stalk (*Sn*). But the *optic cup*, as we can from this time forward designate the structure, exhibits two peculiarities. First, it has, as it were, a defect (fig. 265 *aus*) in its lower wall; for there runs along the latter from the margin of the broad opening which embraces the lens (*l*) to the attachment of the stalk (*Sn*) a fissure (*aus*), which is caused by the development of the vitreous body (*gl*) and bears the name *fœtal optic fissure* [or *choroid fissure*]. At first it is rather wide, but then becomes narrower and narrower by the approximation of its edges and finally closed altogether. Secondly, the optic cup, like the toy called the cup of Tantalus, is provided with double walls, which are continuous with each other along the edge of the front opening and also along the fissure. They will henceforth be designated as inner (figs. 264 *B* and 265 *ib*) and outer (*ab*) layers; the former is the invaginated, the latter the uninvaginated part of the primary optic vesicle.

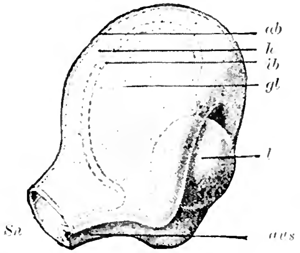

Fig. 265.—Plastic representation of the optic cup with lens and vitreous body.

ab, Outer wall of the cup; *ib*, its inner wall; *h*, cavity between the two walls, which later disappears entirely; *Sn*, fundament of the optic nerve. (Stalk of the optic vesicle with a furrow on its lower surface.) *aus*, Optic [choroid] fissure; *gl*, vitreous body; *l*, lens.

At the beginning of the infolding the two layers are separated by a broad space (*h*), which leads into the third ventricle through the stalk of the vesicle (*Sn*); but afterwards the space becomes reduced proportionally to the increase in the size of the vitreous body.

Finally outer and inner layers come to lie in close contact (fig. 266 *pi* and *r*). The fundaments of the lens (*le* and *lf*) and the vitreous body (*g*) constitute the contents of the cup. The vitreous body fills the bottom of the cup, the lens its opening.

In the process of invagination the stalk of the optic vesicle has also changed its form. Originally it is a small tube with an epithelial wall, but afterwards it becomes an inverted trough with double walls, inasmuch as its lower surface participates in the invagination caused by that growth of connective tissue which toward the periphery furnishes the vitreous body. Later the edges of the trough bend together and fuse with each other. In this way the connective-

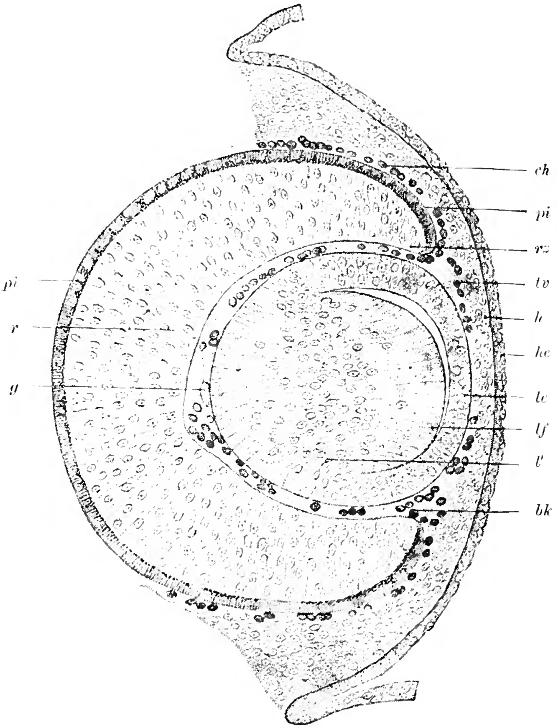

Fig. 266.—Section through the optic fundament of an embryo Mouse, after KESSLER.
pi, Pigmented epithelium of the eye (outer lamella of the optic cup, or secondary optic vesicle); *r*, retina (inner lamella of the optic cup); *rz*, marginal zone of the optic cup, which forms the pars ciliaris et iridis retinæ; *g*, vitreous body with blood-vessels; *tv*, tunica vasculosa lentis; *bk*, blood-corpuscles; *ch*, choroidea; *lf*, lens-fibres; *le*, lens-epithelium; *l'*, zone of the lens-fibre nuclei; *h*, fundament of the cornea; *hc*, external corneal epithelium.

tissue cord, with the arteria centralis retinæ, which traverses it, is enclosed within the stalk, which is now a quite compact structure.

Finally the tissue of the intermediate layer, apart from its producing the vitreous body, takes a further active share in the development of the whole eye, inasmuch as that portion of it which is adjacent to the optic cup is differentiated into the choroid membrane (fig. 266 *ch*) and the sclerotica of the eye.

After having thus delineated briefly the source of the most important components of the eye, it will be my purpose in what follows to pursue in detail the development of each part separately. I shall begin with the lens and vitreous body, then pass to the optic cup, and at that point add an account of the formation of the choroid membrane and the sclerotica, as well as the optic nerve; in a final section I shall treat of the organs that are accessory to the optic cup—the eye-lids, the lachrymal glands and their ducts.

(*a*) *The Development of the Lens.*

When the *lens-vesicle* has been completely constricted off from the primitive epidermis (fig. 264 *B ls*), it possesses a thick wall, which is composed of two or three layers of epithelial cells, and encloses a cavity that in Birds is partially filled with fluid, but in the case of Mammals by a mass of small cells. The mass of cells is the result of a proliferation of the most superficial flattened sheet of the primitive epidermis; it is without importance in the further development—a transient mass, that soon degenerates and is absorbed when the lens-fibres are developed. (ARNOLD, MIHALKOVICS, GOTTSCHAU, KORANYI.)

Externally the epithelial vesicle is sharply limited by a thin membrane, which is afterwards thickened into the *capsule of the lens* (capsula lentis). There are two opposing views in regard to its development. According to one, the capsule is a cuticular structure, that is to say, a structure secreted by the cells of the lens at their bases; according to the other view it is the product of a connective-tissue layer, to be described more fully hereafter, enveloping the lens-vesicle.

In later stages considerable differences arise in the development of the anterior and posterior walls (fig. 266). In the region of the anterior wall the epithelium (*le*) becomes more and more flattened; the cylindrical cells are converted into cubical elements, which are preserved throughout life in a single layer and constitute the so-called *lens-epithelium* in the lens of the adult (fig. 266 *le*). In the posterior wall, on the contrary, the cells increase greatly in length (fig. 266 *lf*) and grow out into long fibres, which form a protuberance projecting into the cavity of the vesicle. The fibres stand perpendicular to the posterior wall, are longest in its middle, become shorter towards the equator of the lens (figs. 266, 267 *l*), and finally appear as ordinary cylindrical cells; these in turn become still shorter and are continuous with the cubical cells (*le*) of the lens-epithelium. In this way there exists at the equator a zone of transition between the fibrous portion and the epithelial part of the lens.

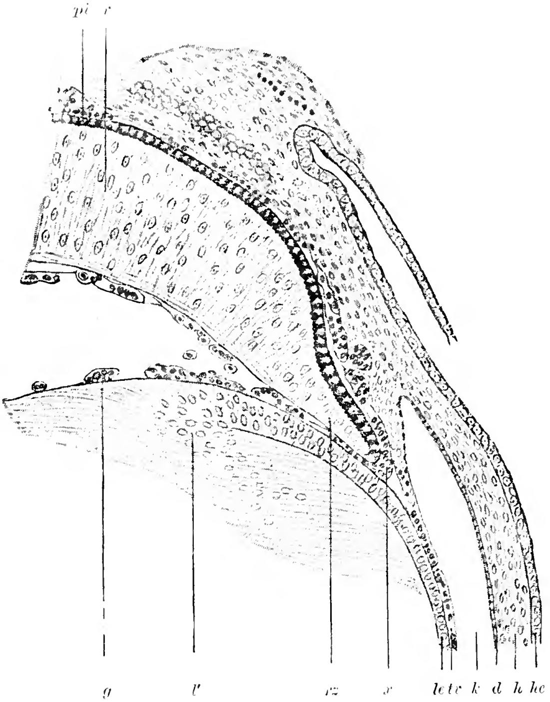

Fig. 267.—Part of a section through the fundament of the eye of an embryo Mouse. Somewhat older stage than that shown in fig. 266. After Kessler.

A part of the lens, the rim of the optic cup, the cornea, and the anterior chamber of the eye. *pi*, Pigmented epithelium of the eye; *r*, retina; *rz*, marginal zone of the optic cup; *g*, blood-vessels of the vitreous body in the vascular capsule of the lens; *tv*, tunica vasculosa lentis; *x*, connection of the latter with the choroid membrane of the eye; *l'*, transition of the lens-epithelium into the lens-fibres; *le*, lens-epithelium; *k*, anterior chamber of the eye; *d*, Descemet's membrane; *h*, cornea; *he*, corneal epithelium.

The next change consists in the elongation of the fibres until their anterior ends have reached the epithelium (fig. 267). Consequently the vesicle has now become a solid structure, which, as the lens-core, furnishes the foundation of the lens of the adult.

The further increase in the size of the lens is an appositional growth. Around the core first formed arise new lens-fibres, which are arranged parallel to the surface of the organ and are united into coats. These lie in layers one over another, which in macerated lenses may be detached like the coats of an onion. All fibres (fig. 268 *lf′*, *lf″*) extend from the anterior to the posterior surface, where their ends meet one another along regular lines, which in the embryo and the new-born animal have the form of two three-rayed figures, the so-called *stars of the lens* (fig. 268 *vst* and *hst*). These exhibit the peculiarity that the rays of the anterior face alternate with those of the posterior face, so that the three rays of one star halve the spaces between the three rays of the other.

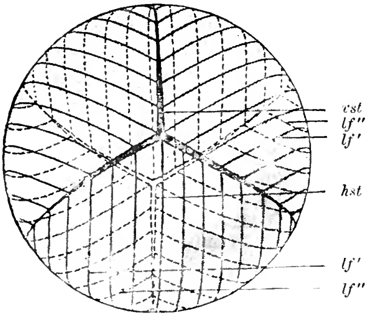

Fig. 268.—Diagram of the arrangement of the lens-fibres.

One sees the opposite positions of the anterior (*vst*) and the posterior (*hst*) stars of the lens. *lf′*, Course of the lens-fibres on the anterior surface of the lens and their termination at the anterior star of the lens; *lf″*, continuation of the same fibres to the posterior star on the posterior surface.

In the adult the figure becomes more complicated, because lateral rays arise on each of the three chief rays.

How have the newly deposited fibres been formed? Their origin is ultimately to be referred to the lens-epithelium of the front surface of the organ. In these cells figures of nuclear division can frequently be observed even in late stages of development. The cells which result from division serve to replace those which grow out into lens-fibres, and are placed upon the already formed layers. The new formation takes place only at the equator of the lens (fig. 267) in the zone of transition (*l′*) previously described, where, in the adult as well as in the recently born animal, the cubical epithelial cells gradually merge into cylindrical and fibrous elements, as one can convince himself from any properly directed section.

In the adult, as is well known, there exist no special *provisions for the nutrition of the lens,* which, after attaining full size, is not much altered, and certainly undergoes only a slight metastasis. With the embryo it is otherwise. Here a more active growth necessitates a special apparatus for nutrition. This is furnished in Mammals by the *tunica vasculosa lentis* (figs. 266, 267 *tv*). By this is understood a highly vascular connective-tissue membrane, which envelops the outer surface of the capsule of the lens on all sides. In Man it is already distinctly developed as early as the second month. Its vessels are derived from those of the vitreous body. Consequently on the posterior wall of the lens they are large. These, resolved into numerous fine branches, bend around the equator of the lens, and run toward the middle of the anterior surface, where they form terminal loops, and also unite with blood-vessels of the choroid membrane (fig. 267 *x*).

Separate parts of the nourishing membrane of the lens, having been discovered at different times by various investigators, have received special names, as membrana pupillaris, m. capsulo-pupillaris, m. capsularis. The first to be observed was the membrana pupillaris, the part of the vascular membrane which is situated behind the pupil on the anterior surface of the lens. It was the most easily found, because occasionally it persists even after birth as a fine membrane closing the pupil, and producing *atresia pupillæ congenita.* Later it was found that the membrana pupillaris is also continued laterally from the pupil on the anterior face of the lens, and this part was called membrana capsulo-pupillaris. Finally it was discovered that the blood-vessels are spread out on the posterior wall of the lens—the membrana capsularis. It is superfluous to retain all these names, and most suitable to speak of a *nutritive membrane of the lens*, or a membrana vasculosa lentis.

This vascular membrane attains its greatest development in the seventh month, after which it begins to degenerate. Ordinarily it has entirely disappeared before birth ; only in exceptional cases do some parts of it persist. Toward the end of embryonic life, moreover, the chief growth of the lens itself has ceased. For according to weighings carried on by the anatomist HUSCHKE, it has a weight of 123 milligrammes in the new-born child, and 190 milligrammes in the adult, so that the total increase which the organ undergoes during life amounts to only 67 milligrammes.

(*b*) *The Development of the Vitreous Body.*

The question of the development of the vascular membrane of the lens leads to that of the vitreous body. As was previously mentioned, there grows out from the embryonic connective tissue a process with a vascular loop, which makes its way into the primary optic vesicle and its stalk (fig. 265). The vascular loop then begins to send out new lateral branches; likewise the connective-tissue matrix, which is at first scanty, increases greatly and is characterised by its extraordinarily slight consistency and its large proportion of water (figs. 266, 267 *g*). There are also to be found in it here and there isolated stellate connective-tissue cells; but these disappear later, and in their place occur migratory cells (leucocytes), which are assumed to be immigrated white blood-corpuscles.

There are two opposing views regarding the nature and development of the vitreous body. According to KESSLER we have to do, not with a genuine connective substance, but with a transudation,—a fluid,—which has been secreted from the vascular loops; the cells are from the beginning simply immigrated white blood-corpuscles KÖLLIKER, SCHWALBE, and other investigators, on the contrary, regard the vitreous body as a genuine connective substance. According to SCHWALBE's definition, to which I adhere, it consists of an exceedingly watery connective tissue, whose fixed cells have early disappeared, but whose interfibrillar substance infiltrated with water is traversed by migratory cells. The vitreous body is afterwards surrounded by a structureless membrane, the *membrana hyaloidea*, which, according to some investigators, belongs to the retina, although, according to the researches of SCHWALBE, this view is not admissible.

The vitreous body, which in the adult is quite destitute of blood-vessels, is bountifully supplied with them in the embryo. They come from the *arteria centralis retinæ*, the branch of the ophthalmic artery that runs along the axis of the optic nerve.

The arteria centralis retinæ is prolonged from the papilla of the optic nerve as a branch which is designated as the arteria hyaloidea. This, resolved into several branches, runs forward through the vitreous body to the posterior surface of the lens, where its numerous terminal ramifications spread out in the tunica vasculosa, and at the equator pass over on to the anterior face of the lens. During the last months of embryonic life the vessels of the vitreous body, together with the nutritive membrane of the lens, undergo degeneration; they entirely disappear, with the exception of a rudiment of the chief stem, which runs forward from the entrance of the optic nerve to the anterior surface of the vitreous body, and during the degeneration is converted into a canal filled with fluid, the *canalis hyaloideus.*

(c) *The Development of the Secondary Optic Cup and the Coats of the Eye.*

The optic cup is further metamorphosed at the same time with the layer of mesenchyma which envelops it, and which furnishes the middle and outer tunics of the eye, so that it seems to be desirable to treat of both at the same time. I begin with the stage represented in figures 266 and 269. The optic cup still possesses at this time a broad opening, in which the lens (*le*) is embraced. The latter is either separated from the epidermis by only an exceedingly thin sheet of mesenchyma, as in the Mammals (fig. 266), or its anterior face is in immediate contact with the epidermis, as in the Chick (fig. 269). In the beginning, therefore, there is no separate fundament for the cornea between lens and epidermis; moreover, both the anterior chamber of the eye and the iris are wanting.

The *fundament of the cornea* is derived from the surrounding mesenchyma, which, as a richly cellular tissue, envelops the eyeball. In the Chick (fig. 269), as early as the fourth day, it grows in between the epidermis and the front surface of the lens as a thin sheet (*bi*). At first this *sheet is structureless*, then numerous mesenchymatic cells migrate into it from the margin and become the corneal corpuscles. These produce the corneal fibres in the same way that embryonic connective-tissue cells do the connective-tissue fibres, while the structureless sheet in part goes to form the cementing substance between them, and in part is preserved on the anterior and posterior walls as thin layers

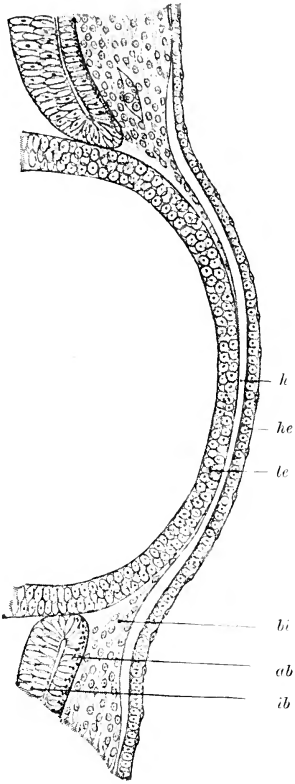

Fig. 269.—Section through the anterior portion of the fundament of the eye in an embryo Chick on the fifth day of incubation, after KESSLER.

he, Corneal epithelium; *le*, lens-epithelium; *h*, structureless sheet of the corneal fundament; *bi*, embryonic connective substance, which envelops the optic cup and, penetrating between lens-epithelium (*le*) and corneal epithelium (*he*), furnishes the fundament of the cornea; *ab*, outer, *ib*, inner layer of the secondary optic cup.

destitute of cells; these layers, undergoing chemical metamorphosis, become respectively the membrana elastica anterior and the membrane of DESCEMET.

The internal endothelium of the cornea is developed at an extraordinarily early epoch in the Chick. For as soon as the structureless sheet previously mentioned (fig. 269 *h*) has attained a certain thickness, mesenchymatic cells proceeding from the margin spread themselves out on its inner surface as a single-layered thin cell-membrane. With this begins also the *formation of the anterior chamber of the eye*. For the thin fundament of the cornea, which at first lay in immediate contact with the front surface of the lens, now becomes somewhat elevated from the latter, and separated from it by a fissure-like space filled with fluid (humor aqueus). The fissure is first observable at the margin of the secondary optic cup, and spreads out from this region toward the anterior pole of the lens. The anterior chamber of the eye does not, however, acquire a greater size and its definite form until the development of the iris.

Two opposing views exist concerning the origin of the structureless sheet which has been described as constituting the first fundament of the cornea in the Chick. According to KESSLER it is a product of the secretion of the epidermis, whereas the corneal corpuscles migrate in from the mesenchyma. In his opinion, therefore, the cornea is composed of two entirely different fundaments. According to KÖLLIKER, on the contrary, all its parts are developed out of the mesenchyma, and the homogeneous matrix simply outstrips the cells in its growth and extension.

In *Mammals* (fig. 266) the conditions differ somewhat from those of the Chick; for as soon as the lens-vesicle in Mammals is fully constricted off, it is already enveloped by a thin sheet of mesenchyma (*h*) with few cells, which separates it from the epidermis. The thin layer is rapidly thickened by the immigration of cells from the vicinity. Then it is separated into two layers (fig. 267), the pupillar membrane (*tv*) and the fundament of the cornea (*h*). The former is a thin, very vascular membrane lying on the anterior surface of the lens; its network of blood-vessels communicates on the one hand posteriorly with the vessels of the vitreous body, together with which it constitutes the tunica vasculosa lentis, and on the other anastomoses at the margin of the optic cup with the vascular network of the latter. The fundament of the cornea is first sharply delimited from the pupillary membrane at the time when the anterior chamber of the eye (*k*) is formed as a narrow fissure, which gradually increases in extent with the appearance of the iris.

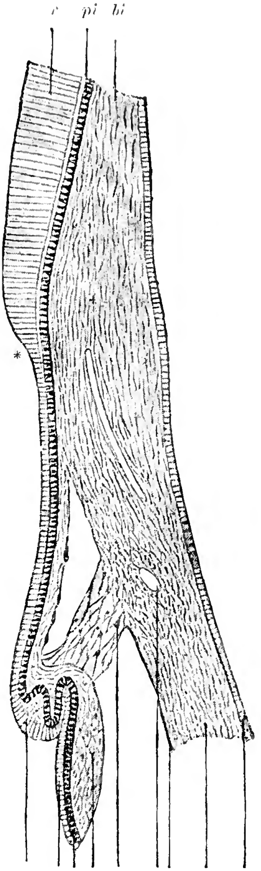

Fig. 270.—Section through the margin of the optic cup of an embryo Turdus musicus, after Kessler.

r, Retina; *pi*, pigmented epithelium of the retina (outer lamella of the optic cup); *bi*, connective-tissue envelope of the optic cup (choroidea and sclera); * ora serrata (boundary between the marginal zone and the fundus of the optic cup); *ck*, ciliary body; 1, 2, 3, iris; 1 and 2, inner and outer lamellæ of the pars iridis retinæ; 3, connective-tissue plate of the iris; *lp*, ligamentum pectinatum iridis; *sch*, canal of Schlemm; *D*, Descemet's membrane; *h*, cornea; *he*, corneal epithelium.

During these processes the condition of the optic cup itself has also changed. Its outer and inner lamellæ continually become more and more unlike. The former (figs. 266, 267 *pi*) remains thin and composed of a single layer of cubical epithelial cells. Black pigment granules are deposited in this in increasing abundance, until finally the whole lamella appears upon sections as a black streak. The inner layer (*r*), on the contrary, remains entirely free from pigment, with the exception of a part of the marginal zone; the cells, as in the wall of the brain-vesicles, become elongated and spindle-shaped, and lie in many superposed layers.

Moreover *the bottom of the cup* and its *rim* assume different conditions, and hasten to fulfil different destinies; the former is converted into the *retina*, the latter is principally concerned in the production of the *ciliary body* and the *iris.*

The *edge of the cup* (fig. 267 *rz*, fig. 270*, and fig. 271) becomes very much reduced in thickness by the cells of its inner layer arranging themselves in a single sheet, remaining for a time cylindrical, and then assuming a cubical form. But with its reduction in thickness there goes hand in hand an increase in its superficial extent. Consequently the margin of the optic cup now grows into the anterior chamber of the eye between cornea and the anterior surface of the lens, until it has nearly reached the middle of the latter. Then it at last bounds only a small orifice which leads into the cavity of the optic cup—the *pupil.* The *pigment layer of the iris* is derived from the marginal region of the cup, as Kessler first showed (fig. 270 [1] and [2]). Pigment granules are now deposited in the inner epithelial layer, just as in the outer lamella, so that at last the two are no longer distinguishable as separate layers.

The mesenchymatic layer which envelops the two epithelial lamellæ keeps pace with them in their superficial extension. It becomes thickened and furnishes the stroma of the iris with its abundant non-striated muscles and blood-vessels (fig. 270 [3]). In Mammals (fig. 267 *x*) this is for a time continuous with the tunica vasculosa lentis (*tv*), in consequence of which the pupil in embryos is closed by a thin vascular connective-tissue membrane, as has already been stated.

The part of the optic cup which is adjacent to the pigment layer of the iris and surrounds the equator of the lens, and which likewise belongs to the attenuated marginal zone of the cup (fig. 270 *ck*), undergoes an interesting alteration. In conjunction with the neighboring layer of connective substance, it is converted into the *ciliary body* of the eye. This process begins in the Chick on the ninth or tenth day of incubation (KESSLER), in Man at the end of the second or beginning of the third month (KÖLLIKER). The attenuated epithelial double lamella of the cup, in consequence of an especially vigorous growth in area, is laid into numerous, [nearly] parallel short folds, which are arranged radially around the equator of the lens. As in the iris, so here, the adjacent mesenchymatic layer participates in the growth and penetrates between the folds in the form of fine processes. A cross section through the folded part of the optic cup of a Cat embryo 10 cm. long (fig. 271) affords information concerning the original form of these processes in Mammals. It shows that the individual folds are very thin and enclose within them only a very small amount of embryonic connective tissue (*bi'*) with fine capillaries, and that, unlike the pigment epithelium of the iris, only the outer of the two epithelial layers (*ab*) is pigmented,

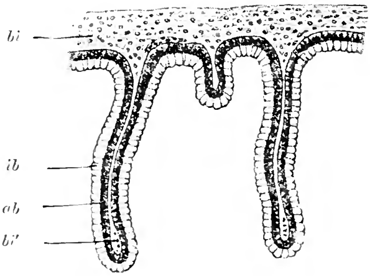

Fig. 271.—Cross section through the ciliary par of the eye of an embryo Cat 10 cm. long, after KESSLER.

Three ciliary processes formed by the folding of the optic cup are shown. *bi*, Connective-tissue part of the ciliary body; *ib*, inner layer, *ab*, outer pigmented layer of the optic cup *bi'*, sheet of connective tissue that has penetrated into the epithelial fold.

whereas the inner (*ib*) remains unpigmented even later and is composed of cylindrical cells.

Subsequently the ciliary processes become greatly thickened through increase of the very vascular connective-tissue framework, and acquire a firm union with the capsule of the lens through the formation of the *zonula Zinnii.* In Man the latter is formed, according to KÖLLIKER's account, during the fourth month, in a manner that here, as well as in other Mammals, is still incompletely explained.

LIEBERKÜKN remarks that the *zonula* is distinctly recognisable in eyes which have attained half their definite size. If one takes out of an eye the vitreous body together with the lens, and then removes the latter by opening the capsule on the front side, the margin of the capsule appears surrounded by blood-vessels which pass from the posterior over on to the anterior surface. "At the places where the processus ciliares are entirely removed, tufts of fine fibres are to be seen which correspond to, and fill up, the depressions between the ciliary processes; but between these tufts is also to be seen a thin layer of the same kind of finely striate masses, which must have lain at the same level as the ciliary processes." Furthermore LIEBERKÜKN states that "there lie within this striated tissue numerous cell-bodies of the same appearance as those that are found elsewhere in the embryonic vitreous body at a later period."

ANGELUCCI believes that the zonula arises from the anterior part of the vitreous body; at the time when iris and ciliary processes are developed he finds the vitreous body traversed by fine fibres, which extend from the ora serrata to the margin of the lens. He describes as lying between the fibres sparse migratory cells, which are maintained, however, to have no share in the formation of the fibres.

The fundus of the optic cup (figs. 266, 267, 270) furnishes the most important part of the eye—the *retina.* The inner lamelia of the cup (*r*) becomes greatly thickened, and, in consequence of its cells being elongated into spindles and overlapping one another in several layers, acquires an appearance similar to that of the wall of the embryonic brain. Subsequently it becomes marked off by an indented line, the ora serrata (at the place indicated by a star in fig. 270), from the adjoining attenuated part of the optic vesicle, which furnishes the ciliary folds. It also early acquires at its two surfaces a sharp limitation through the secretion of two delicate membranes: on the side toward the fundament of the vitreous body it is bounded by the membrana limitans interna; on that toward the outer lamella, which becomes pigmented epithelium, by the membrana limitans externa.

In the course of development its cells, all of which are at first alike, become specialised in very different ways, as a result of which there are produced the well-known layers distinguished by MAX SCHULTZE. I shall not go into the details of this histological differentiation, but shall mention some further points of general importance.

As WILHELM MÜLLER in his "Stammesentwicklung des Sehorgans der Wirbelthiere" has clearly shown, the development of the originally similar epithelial cells of the retina takes place in all Vertebrates in two chief directions: a part of them become sensory epithelium and the specific structures of the central nervous system—ganglionic cells and nerve-fibres; another part are metamorphosed into supporting and isolating elements—into MÜLLER's radial fibres and the granular [reticular or molecular] layers, which can be grouped together as epithelial sustentative tissue (fulcrum). Finally, with the descendants of the epithelium are associated connective-tissue elements, which grow from the surrounding connective tissue into the epithelial layer for its better nutrition, in the same manner as in the central nervous system. These ingrowths are branches of the arteria centralis retinæ with their extremely thin connective-tissue sheaths. The Lampreys alone form an exception, their retina remaining free from blood-vessels. In all other Vertebrates blood-vessels are present, but they are limited to the inner layers of the retina, leaving the outer granular (Körner) layer and that of the rods and cones free; the latter have been distinguished as sensory epithelium from the remaining portions with their nerve-fibres and ganglionic cells—the brain-part of the retina.

Of all the parts of the retina the *layer of rods and cones* is the last to be developed. According to the investigations of KÖLLIKER, BABUCHIN, MAX SCHULTZE, and W. MÜLLER, it arises as a product of the outer granular (Körner) layer, which, composed of fine spindle-shaped elements, is held to be, as has been stated, the essential sensory epithelium of the eye. In the Chick the development of the rods and cones can be made out on the tenth day of incubation. MAX SCHULTZE states concerning young Cats and Rabbits, which are born blind, that the fundament of the rods and cones can be distinguished for the first time in the early days after birth; in other Mammals and in Man, on the contrary, they are formed before birth.

In all Vertebrates, as long as rods and cones are not present, the inner layer of the optic cup is bounded on the side toward the outer layer by an entirely smooth contour, due to the membrana limitans externa. Then there appear upon the latter numerous, small, lustrous elevations, which have been secreted by the outer granules or visual cells. The elevations, which consist of a protoplasmic substance and are stained red in carmine, become elongated and acquire the form of the inner limb of the retinal element. Finally there is formed at their outer ends the outer limb, which MAX SCHULTZE and W. MÜLLER compare to a cuticular product, on account of its lamellate structure.

Inasmuch as the rods and cones of the retinal cells grow out in this way beyond the membrana limitans externa, they penetrate into the closely applied outer lamella of the optic cup, which becomes the pigmented epithelium of the retina (figs. 266, 267, 270 *pi*); their outer limbs come to lie in minute niches of the large, hexagonal pigment-cells, so that the individual elements are separated from one another by pigmented partitions.

A few additional words concerning the connective tissue enveloping the fundament of the optic cup. It acquires here, as on the ciliary body and the iris, a special, and for this region characteristic, stamp. It is differentiated into vascular [choroid] and fibrous [sclerotic] membranes, which in Man are distinguishable in the sixth week (KÖLLIKER). The former is characterised by its vascularity at an early period, and develops on the side toward the optic cup a special layer, provided with a fine network of capillary vessels, the membrana choriocapillaris, for the nourishment of the pigment-layer and the layer of rods and cones, which have no blood-vessels of their own. It further differs from the ciliary body in the fact that at the fundament of the optic cup the choroid membrane is easily separable from the adjoining membranes of the eye, whereas in the ciliary body a firm union exists between all the membranes.

If we now glance back at the processes of development last described, *one thing* will appear clear to us from this short sketch: that the changes in the form of the secondary optic cup are of preëminent importance for the origin of the individual regions of the eye. Through different processes of growth, which have received a general discussion in Chapter IV., there have been formed in the cup three distinct portions. By means of an increase in thickness and various differentiations of the numerous cell-layers, there is formed the retina; by an increase of surface, on the contrary, is produced an anterior, thinner part, which bounds the pupil and is subdivided into two regions by the formation of folds in the vicinity of the lens. From the folded part, which joins the retina at the ora serrata, is formed the epithelial lining of the ciliary body; from the thin portion which surrounds the pupil and which remains smooth, the pigmented epithelium (uvea) of the iris. Consequently there are now to be distinguished on the secondary optic cup three regions, as retinal, ciliary, and iridal parts. To each of these territories the contiguous connective tissue, and especially the part which becomes the middle tunic of the eye, is adapted in a particular manner; here it furnishes the connective-tissue plate of the iris with its non-striated musculature, there the connective-tissue framework of the ciliary body with the ciliary muscle, and in the third region the vascular choroidea with the choriocapillaris and lamina fusca.

In the development of the optic cup there arose on its lower wall a fissure (fig. 265 *aus*), which marks the place at which the fundament of the vitreous body grew into the interior of the cup. What is the ultimate fate of this fissure, which is usually referred to in the literature as *choroid fissure*?

It is for a time easily recognisable, after pigment has been deposited in the outer lamella of the optic cup. It then appears on the lower median side of the eyeball as a clear, unpigmented streak, which reaches forward from the entrance of the optic nerve to the margin of the pupil.

The name choroid fissure takes its origin from this phenomenon. It was given at a time when the formation of the optic cup was not adequately known, when the pigmented epithelium was still referred to the choroidea. Therefore in the absence of pigment along a clear streak on the under side of the eyeball it was supposed that a defect of the choroidea—a choroid fissure—had been observed.

The clear streak afterwards disappears. The fissure of the eye is closed by the fusion of its edges and the deposition of pigment in the raphe. In the Chick this takes place on the ninth day, in Man during the sixth or seventh week.

In still another respect is the choroid fissure noteworthy.

In many Vertebrates (Fishes, Reptiles, Birds) a highly vascular process of the choroidea grows through the fissure, before its closure, into the vitreous body and there forms a lamellar projection, which extends from the optic nerve to the lens. In Birds it has received the name "pecten," because it is folded into numerous parallel ridges. It consists almost entirely of the walls of blood-vessels, which are held together by a small amount of a black pigmented connective tissue.

In Mammals such a growth into the vitreous body is wanting.

The closure of the choroid fissure takes place at an early period and completely.

Occasionally in Man the normal course of development is interrupted, so that the margins of the choroid fissure remain apart. The usual consequence of this is a defective development of the vascular tunic of the eye at the corresponding place—an indication of the extent to which the development of the connective-tissue envelope is dependent on the formative processes of the two epithelial layers, as has already been stated. Both retinal and choroidal pigment are therefore wanting along a streak which begins at the optic nerve, so that the white sclera of the eye shows through to the inside and can be recognised in examinations with the ophthalmoscope. When the defect reaches forward to the margin of the pupil, a fissure is formed in the iris which is easily recognised upon external observation of the eye. The two structures resulting from this interrupted development are distinguished from each other as *choroidal* and *iridal fissures* (coloboma choroideæ and coloboma iridis).

(*d*) *The Development of the Optic Nerve.*

The *stalk of the optic vesicle* (fig. 272), by which the vesicle is united with the between-brain, is in direct connection with both lamellæ of the optic cup, the primary optic vesicle having been infolded from below by the fundament of the vitreous body to form the cup. Its dorsal wall is continuous with the outer lamella or pigment-epithelium of the retina; its ventral wall is prolonged into the inner lamella, which becomes the retina. *Thus, aside from the formation of the vitreous body, the development of a choroid fissure also has a significance in view of the persistence of the direct connection between retina and optic nerve.* For if we conceive the optic vesicle invaginated merely at its anterior face by the lens, the wall of the optic nerve would be continued into the outer, uninvaginated lamella only; direct connection with the retina itself, or the invaginated part, would be wanting.

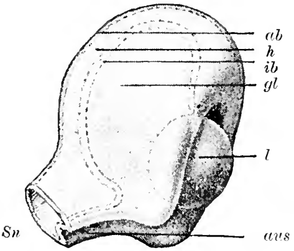

Fig. 272.—Plastic representation of the optic cup with lens and vitreous body.

ab, Outer wall of the cup; *ib*, its inner wall; *h*, space between the two walls, which afterwards entirely disappears; *Sn*, fundament of the optic nerve (stalk of the optic vesicle with groove-formation along its lower face); *aus*, choroid fissure; *gl*, vitreous body; *l*, lens.

Originally the optic nerve is a tube with a small lumen, which unites the cavity of the optic vesicle with the third ventricle (fig. 264 *A*). It is gradually converted into a solid cord. In the case of most Vertebrates this is produced simply by a thickening of the walls of the stalk, due to cell-proliferation, until the cavity is obliterated. In Mammals only the larger portion, that which adjoins the brain, is metamorphosed in this manner; the smaller part, that which is united with the optic vesicle, is, on the contrary, infolded by the prolongation of the choroid fissure backward for some distance, whereby the ventral wall is pressed in against the dorsal. Consequently the optic nerve here assumes the form of a groove, in which is imbedded a connective-tissue cord with a blood-vessel that becomes the arteria centralis retinæ. By the growing together of the edges of the groove, the cord afterwards becomes completely enclosed.

For a time the optic nerve consists exclusively of spindle-shaped, radially arranged cells in layers, and resembles in its finer structure the wall of the brain and the optic vesicle. Different views are held concerning its further metamorphoses, and especially concerning the origin of nerve-fibres in it. Differences similar to those concerning the origin of the peripheral nerve-fibres are maintained. Upon this point three theories have been brought forward.

According to the older view, which LIEBERKÜHN shares, the optic fibres are developed in loco by the elongation of the spindle-shaped cells. According to HIS, KÖLLIKER, and W. MÜLLER, on the contrary, the wall of the optic vesicle furnishes the sustentative tissue only, whereas the nerve-fibres grow into it from outside, *either from the brain toward the retina* (HIS, KOLLIKER), *or in the reverse direction* (MÜLLER). The stalk of the optic vesicle would constitute, according to this view, only a guiding structure as it were—would predetermine the way for its growth. When the ingrowth has taken place, the sustentative cells are, as KÖLLIKER describes them, arranged radially and so united with one another that they constitute a delicate framework with longitudinally elongated spaces. In the latter are lodged the small bundles of very fine non-nuclear nerve-fibres and numerous cells, arranged in longitudinal rows, which likewise belong to the epithelial sustentative tissue and help to complete the trestle-work.

The embryonic optic nerve is enveloped in a connective-tissue sheath, which is separated, as in the case of the brain and secondary optic cup, into an inner, soft, vascular and an outer compact fibrous layer. The former, or the pial sheath, unites the pia mater of the brain and the choroid membrane of the eye; the latter, or the dural sheath, is a continuation of the dura mater and at the eyeball becomes continuous with the sclerotica. Later the optic nerve acquires a still more complicated structure, owing to the fact that vascular processes of the pial sheath grow into it and provide the nerve-bundles and the epithelial sustentative cells belonging to them with connective-tissue investments.

As has been previously stated, the direction in which optic fibres grow into the stalk of the optic vesicle is still a subject of controversy. HIS, with whom KÖLLIKER is in agreement, maintains that they grow out from groups of ganglionic cells (thalamus opticus, corpora quadrigemina), and are only secondarily distributed in the retina. He supports his view on the one hand by the agreement in this particular which exists with the development of the remaining peripheral nerves, and on the other by the circumstance that the nerve-fibres are first distinctly recognisable in the vicinity of the brain.

W. MÜLLER, on the contrary, believes that the outgrowth takes place in the opposite direction; he maintains that the nerve-fibres arise as prolongations of the ganglionic cells located in the retina, and that they enter into union with the central nervous apparatus only secondarily. He is strengthened in his opinion by the conditions in Petromyzon, which he declares to be one of the most valuable objects for the solution of the controversy concerning the origin of the optic nerve. I refer, moreover, in connection with this controversy, to the section which treats of the development of the peripheral nervous system (p. 452).

(e) *The Development of the Accessory Apparatus of the Eye.*

There are associated with the eyeball auxiliary apparatus, which serve in different ways for the protection of the cornea: the eyelids with the Meibomian glands and the eyelashes, the lachrymal glands and the lachrymal ducts.

The *eyelids*, the upper and under, are developed at an early period by the formation, at some distance from the margin of the cornea, of two folds of the skin, which protrude beyond the surface. The folds grow over the cornea from above and below until their edges meet and thus produce in front of the eyeball the conjunctival sac, which opens out through the fissure between the lids. The sac derives its name from the fact that the innermost layer of the lid-fold, which is reflected on to the anterior surface of the eyeball at the fornix conjunctivæ, is of the nature of a mucous membrane, and is designated as the conjunctiva, or connecting membrane, of the eye.

In many Mammals and likewise in Man there is during embryonic life *a temporary closure of the conjunctival sac.* The edges of the lids become united throughout their whole extent, their epithelial investments fusing with each other. In Man the concrescence begins in the third month, and usually undergoes retrogression a short time before birth. But in many Reptiles (Snakes) the closure is permanent. Thus a thin transparent membrane is formed in front of the cornea.

In Man during the concrescence of the eyelids there are developed at their margins the Meibomian glands. The cells of the rete Malpighii begin to proliferate and to send into the middle connective-tissue plate of the eyelid solid rods, which afterwards become covered with lateral buds. The glands, at first entirely solid, acquire a lumen by the fatty degeneration and dissolution of the axial cells.

At about the time of the development of the Meibomian glands, the formation of the eyelashes takes place; this corresponds with the development of the ordinary hair, and therefore will be considered along with the latter in a subsequent section of this chapter.

In most of the Vertebrates there is associated with the upper and under lids still a third, the *nictitating membrane* or membrana nictitans, which is formed at the inner [median] side of the eye as a vertical fold of the conjunctiva. In Man it is present only in a rudimentary condition as plica semilunaris. A number of small glands which are developed in it produce a small reddish nodule, the caruncula lacrymalis.

The *lachrymal gland* is an additional auxiliary organ of the eye, which is destined to keep the sac of the conjunctiva moist and the anterior surface of the cornea clean. In Man it is developed in the third month through the formation of buds from the epithelium of the conjunctival sac on the outer side of the eye, at the place where the conjunctiva of the upper lid is continuous with that of the eyeball. The buds form numerous branches, and are at first solid, like the Meibomian glands, but gradually become hollow, the cavity beginning with the chief outlet and extending toward the finer branches.

A special *efferent lachrymal apparatus*, which leads from the inner angle of the eye into the nasal cavity, has been developed for the removal of the secretions of the various glands collected in the conjunctival sac, but particularly the lachrymal fluid. Such an apparatus is present in all classes of Vertebrates from the Amphibia upward; its development has been especially investigated by BORN in a series of researches.

In the Amphibia it begins to be formed at the time the process of chondrification becomes observable in the membranous nasal capsule. At that time the mucous layer of the epidermis, along a line that extends from the median side of the eye directly to the nasal cavity, undergoes proliferation and sinks into the underlying connective-tissue layer as a *solid ridge*. Then from the nose to the eye the ridge becomes constricted off, subsequently acquires a lumen, whereby it is converted into a canal lined with epithelium, and opens out into the nasal cavity. Toward the eye-end the canal is divided into two tubules, which at the time of detachment from the epidermis remain in connection with the conjunctival sac and suck up out of it the lachrymal fluid.

In Birds and Mammals, including Man (fig. 273), the place where the lachrymal duct is located is early marked externally by a furrow which runs from the inner angle of the eye to the nasal chamber. By means of this furrow two ridges, which play an important part in the formation of the face,—the maxillary process and the outer nasal process,—are sharply marked off from each other; these will engage our attention later. According to Coste and Kölliker the lachrymal duct arises by the simple approximation and concrescence of the edges of the *lachrymal groove*. These older conclusions have been contradicted by Born and Legal, one of whom has investigated Reptiles and Birds, the other Mammals. According to them there arises, in nearly the same manner as in Amphibia, through proliferation of the mucous epithelium, at the bottom of the lachrymal groove an epithelial ridge, which becomes detached but is not converted into a canal until a rather late period.

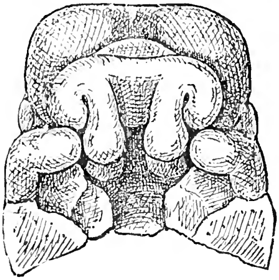

Fig. 273.—Head of a human embryo, from which the mandibular processes have been removed to allow a survey of the roof of the primitive oral cavity.

When we raise the question, how phylogenetically the lachrymal duct may have first originated, we shall doubtless find that it has been derived from a groove, by means of which the sac of the conjunctiva and the nasal chamber are first put into connection. When, therefore, we see the lachrymal duct established from the very beginning simply as a solid ridge, as for example in the Amphibia, we must call to mind how in other cases also originally groove-like fundaments, such as the medullary furrow, make their appearance, under special circumstances, as solid ridges.

Finally, as far as regards the development of the lachrymal tubules in Birds and Mammals, BORN and LEGAL refer the upper tubule to the proximal part of the epithelial ridge, and maintain that the lower one buds out from the upper. EWETSKY, on the contrary, declares that the proximal end of the epithelial ridge expands at the inner angle of the eye, and becomes divided by the ingrowth of underlying connective tissue, and metamorphosed into the two tubules, so that both arise from a common fundament.

SUMMARY.

1. The lateral walls of the primary fore-brain vesicle are evaginated to form the optic vesicles.

2. The optic vesicles remain united by means of a stalk, the future optic nerve, with that part of the primary fore-brain vesicle which becomes the between-brain.

3. The optic vesicle is converted into the optic cup through the invagination of its lateral and lower walls by the fundaments of the lens and vitreous body.

4. At the place where the lateral wall of the primary optic vesicle encounters the outer germ-layer, the latter becomes thickened, then depressed into a pit, and finally constricted off as a lens-vesicle.

5. The cells of the posterior wall of the lens-vesicle grow out into lens-fibres, those of the anterior wall become the lens-epithelium.

6. The fundament of the lens is enveloped at the time of its principal growth by a vascular capsule (tunica vasculosa lentis), which afterwards entirely disappears.

7. The membrana capsulo-pupillaris is the anterior part of the tunica vasculosa lentis and lies behind the pupil.

8. The development of the vitreous body causes the choroid fissure.

9. The optic cup has double walls; it consists of an inner and an outer epithelium, which are continuous with each other at the opening of the cup, which embraces the lens, and at the choroid fissure.

10. Mesenchymatic cells from the vicinity grow in between the lens and the somewhat closely applied epidermis to form the cornea and DESCEMET'S membrane, the latter being separated from the tunica vasculosa lentis by a fissure, the anterior chamber of the eye.

11. The optic cup is differentiated into a posterior portion, within the territory of which its inner layer becomes thickened and constitutes the retina, and an anterior portion, which begins at the ora

serrata, becomes very much reduced in thickness, and extends over the front surface of the lens, growing into the anterior chamber of the eye until the originally wide opening of the cup is reduced to the size of the pupil.

12. The anterior attenuated portion of the cup is, in turn, divided into two zones, of which the posterior becomes folded at the periphery of the equator of the lens to form the ciliary processes, whereas in front it remains smooth; so that in the whole cup three parts may now be distinguished, as retina, pars ciliaris, and pars iridis retinæ.

13. Corresponding to the three portions of the epithelial optic cup, the adjoining connective-tissue envelope takes on somewhat different conditions as the choroid proper, and as the connective-tissue framework of the ciliary body and that of the iris.

14. The skin surrounding the cornea becomes infolded to form the upper and lower eyelids and the nictitating membrane, of which the last is rudimentary in Man, persisting only as the plica semilunaris.

15. The epithelial layers of the edges of the two eyelids grow together in the last months of development, but become separated again before birth.

16. The lachrymal groove in Mammals passes from the inner angle of the eye, between the maxillary and outer nasal processes, to the nasal chamber.

17. The lachrymal duct for carrying away the lachrymal fluid is formed by the downgrowth and constricting off of an epithelial ridge from the bottom of the lachrymal groove, the ridge becoming hollow.

18. The two lachrymal tubules are developed by the division of the epithelial ridge at the angle of the eye.

B. The Development of the Organ of Hearing.

In the case of the ear numerous parts of quite different origin unite, in much the same manner as in the case of the eye, to form a single very complicated apparatus; of these, too, it is the portion to which the auditory nerve is distributed—the *membranous labyrinth* with its auditory epithelium—that is by far the most important, outstripping as it does all the remaining parts in its development: it must consequently be considered first.

(*a*) *The Development of the Otocyst into the Labyrinth.*

The membranous labyrinth is preëminently a product of the outer germ-layer. However great its complication in the adult is,—a complication that has given it the name labyrinth,—its earliest fundament is exceedingly simple. It arises on the dorsal surface of the embryo in the region of the medulla oblongata (fig. 263 *gb*), above the first visceral cleft and the attachment of the second visceral arch (fig. 274 above the numeral 3). Here over a circular territory the outer germ-layer becomes thickened and soon sinks down into an *auditory pit.* This process can be traced very easily in the embryo Chick on and after the end of the second day of incubation, and in the embryo Rabbit fifteen days old. The auditory nerve makes its way from the brain, near at hand, to the fundus of the pit, where it terminates in a ganglionic enlargement.

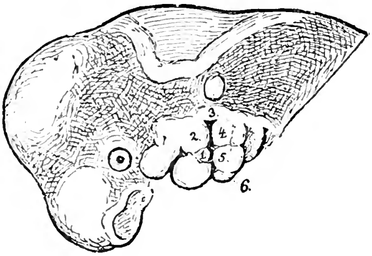

Fig. 274.—Head of a human embryo 7·5 mm. long, neck measurement. From His, "Menschliche Embryonen."
The auditory vesicle lies above the first visceral cleft. In the circumference of the visceral cleft there are to be seen six elevations, designated by numerals, from which the external ear is developed.

The Bony Fishes alone exhibit a deviation from these conditions. Just as the central nervous system was in their case formed not as a tube, but as a solid body, and the eye not as a vesicle, but as an epithelial ball, so we see here that instead of an auditory pit there is formed by means of the proliferation of the outer germ-layer a solid epithelial plug. This, like the brain-tube and the eye-vesicle, acquires an internal chamber at a later period only—namely, after being constricted off.

The next stage shows the pit converted into an auditory vesicle. In the Chick this takes place in the course of the third day. The invagination of the outer germ-layer grows deeper and deeper, and by the approximation of its margins becomes pear-shaped ; soon the connection with the outer germ-layer becomes entirely lost, as is shown by a section through the head of an embryo Sheep (fig. 275 *lb*).

In nearly all Vertebrates the auditory vesicle is constricted off from the ectoderm in the same manner. The Selachians are an exception : here the auditory vesicle which is metamorphosed into the labyrinth retains permanently its connection with the surface of the body in the form of a long narrow tube, which traverses the cartilaginous primordial cranium and is in union dorsally with the epidermis at the surface of the body, where it possesses an external opening.

In its first fundament the organ of hearing in Vertebrates resembles in the highest degree those structures which in the Invertebrates are interpreted as organs of hearing. These are lymph-filled vesicles lying under the skin, which are likewise developed out of the epidermis. Either they are wholly constricted off from the epidermis, or they remain connected with it by means of a long, ciliate, epithelial canal, as in the Cephalopods, even after they have become surrounded by connective tissue. In both cases the vesicles are lined with epithelium which consists of two kinds of cells: first of low, flat elements, which ordinarily exhibit ciliary movements and thereby put in motion the fluid within the vesicle, and secondly of longer cylindrical, or thread-like, auditory cells with stiff hairs, which project into the endolymph. The auditory cells are either distributed individually over the inner surface of the auditory vesicle or arranged in groups, or they are united at a particular place into an auditory epithelium,—the auditory patch (macula acustica) or the auditory ridge (crista acustica),—which may be either single or double. To all the auditory vesicles of the Invertebrates there is sent, moreover, a nerve which ends at the sensory cells in fine fibrillæ. Finally, there is present as a characteristic structure a firm, crystalline body, the otolith, which is suspended in the midst of the endolymph and is ordinarily set in vibration by the motion of the cilia. It consists of crystals of phosphate or carbonate of lime.

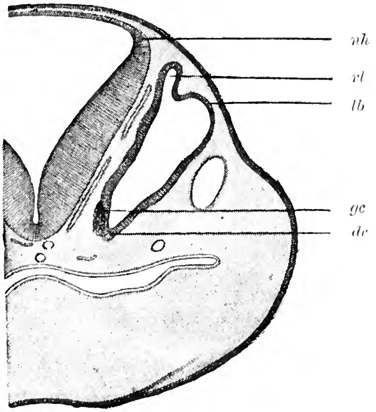

Fig. 275.—Vertical [cross] section through the vesicle of the labyrinth of an embryo Sheep 1·3 cm. long, after Boettcher. Magnified 30 diameters.

nh, Wall of the after-brain; *rl*, recessus labyrinthi; *lb*, vesicle of the labyrinth; *gc*, ganglion cochleare, which is in contact with a part of the labyrinth-vesicle (*dc*) that grows out into the ductus cochlearis.

Sometimes there is only a single large, in most cases concentrically laminated, spherical body, sometimes a number of small calcareous crystals, which are held together by means of a soft pulpy substance.

It is difficult to follow the formation of the otoliths within the otocyst. In one case, which Fol was able to follow, they were developed by an epithelial cell in the wall of the vesicle. The cell secretes small calcareous concretions in its protoplasm, becomes enlarged in consequence, and protrudes as an elevation into the endolymph. When it has become more heavily loaded with calcic salts, it is connected with the wall by means of a stalk only, and finally it becomes entirely detached from the wall and falls into the cavity of the vesicle, in which it is kept floating and rotating by the ciliate cells.

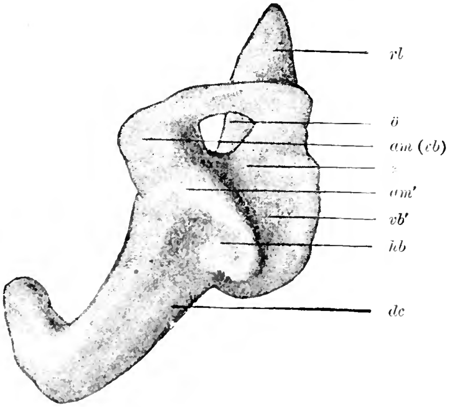

Fig. 276.—Membranous labyrinth of the left side of a [human] embryo, after a wax model by Krause.

rl, Recessus labyrinthi; *dc*, ductus cochlearis; *hb*, pocket from which the horizontal semicircular canal is formed; *am'*, enlargement of the pocket which becomes the ampulla of the horizontal canal; *am* (*vb*), *vb'*, * common pocket from which the two vertical semicircular canals are developed; *am* (*vb*), enlargement of the common pocket from which the ampulla of the anterior vertical canal arises. An opening (*ö*) has been formed in the pocket, through which one sees the recessus labyrinthi. * Region of the pocket which becomes the common arm of the two vertical canals (sinus superior); *vb'*, part of the common pocket which furnishes the posterior vertical canal.

In Vertebrates the otocyst, which, as we have seen, agrees in its first fundament with the organ of hearing in Invertebrates, is converted into a very complicated structure,—the membranous labyrinth,—the evolution of which in Mammals I shall describe in some detail. It undergoes metamorphoses, in which the *formation of folds and constrictions* plays the principal part (fig. 276).

The auditory sac detached from the epidermis, and lying at the side of the after-brain, soon exhibits a small, dorsally directed projection, the *recessus labyrinthi* or *ductus endolymphaticus* (fig. 275 *rl*). Probably we have to do in this with the remnant of the original stalk by means of which the auditory vesicle was connected with the epidermis. According to some investigators, on the contrary, the stalk disappears entirely and this evagination is a new structure. The first assumption is favored especially by the previously mentioned condition in the Selachians—the presence of a long tube, which maintains a permanent connection between labyrinth and epidermis.

Later this appendage of the labyrinth (figs. 276-9 *rl*) grows out dorsally to a great length, during which its walls come into close contact with each other, excepting at the blind end, which is enlarged into a small sac (fig. 279 *rl* *).

Meanwhile the auditory sac itself (figs. 275-7) begins to be elongated and to be formed into a ventrally directed conical process (*dc*), *the first fundament of the ductus cochlearis*, which is curved inward a little toward the brain (fig. 277 *nh*), and the concave side of which lies in close contact with the previously mentioned ganglionic enlargement (*gc*) of the auditory nerve (*hn*).

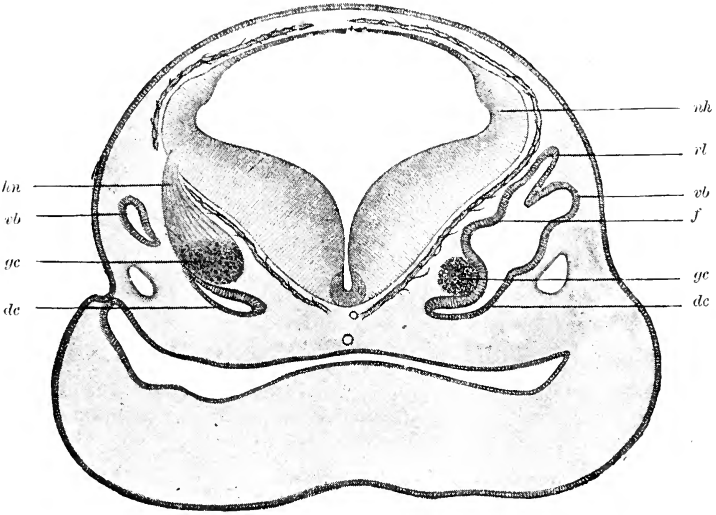

Fig. 277.—Cross section through the head of a Sheep embryo 1·6 cm. long, in the region of the labyrinth-sac. On the right side is represented a section which passes through the middle of the sac; on the left, one that is situated somewhat farther forward. After Boettcher. *hn*, Auditory nerve; *vb*, vertical semicircular canal; *gc*, ganglion cochleare (spirale); *dc*, ductus cochlearis; *f*, inward-projecting fold, whereby the sac of the labyrinth is divided into utriculus and sacculus; *rl*, recessus labyrinthi; *nh*, after-brain.

It will be serviceable in the following description if we now distinguish *an upper and a lower division of the labyrinth.* They are not yet, it is true, distinctly delimited from each other, but in later stages they become more sharply separated by an inward-projecting fold (figs. 277-9 *f*).

The upper part (*pars superior*) *furnishes the utriculus and the semicircular canals.* Of the latter the two vertical canals arise first, the horizontal canal being formed later. The method of their origin was early ascertained by the zoölogist RATHKE in the case of Coluber. Recently KRAUSE has still further elucidated the interesting processes by the construction of wax models of the conditions in mammalian embryos.

As is to be seen from the various sections (figs. 277, 278), but still better from the model (fig. 276) produced by reconstruction, the semicircular canals are developed by the protrusion of several evaginations of the wall of the sac, which have the form of thin pockets or discs (*hb*, *vb*) with a semicircular outline. The marginal part of each such evagination now becomes considerably enlarged, whereas the remaining portions of the two epithelial layers come into close contact and begin to fuse. As the result of this simple process—the enlargement at the margin and the fusion of the walls which takes place in the middle—there is formed a semicircular canal, which communicates at two places with the original cavity of the vesicle. At one of its openings the canal is early enlarged into an *ampulla* (fig. 276 *am* and *am'*). The middle part, in which the fusion has taken place, soon disappears, the epithelial membrane being broken through by a growth of the connective tissue (fig. 276 *ö*).

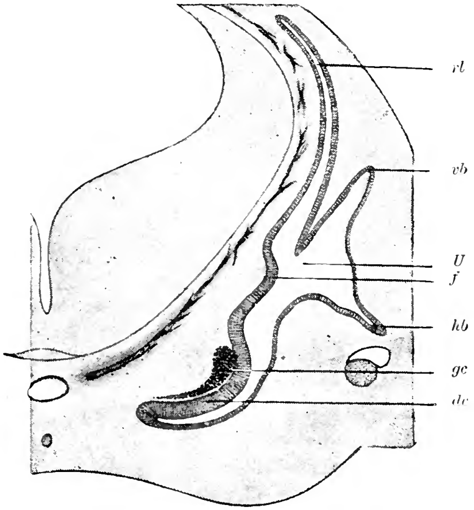

Fig. 278.—Cross section through half of the head of a fœtal Sheep 2 cm. long, in the region of the labyrinth, after BOETTCHER. Magnified 30 diameters.

rl, Recessus labyrinthi; *vb*, *hb*, vertical and horizontal semicircular canals; *U*, utriculus; *f*, inward-projecting fold, by which the labyrinth-sac is divided into utriculus and sacculus; *dc*, ductus cochlearis; *gc*, ganglion cochleare.

There exists an interesting difference between the development of the horizontal and the two vertical canals, which was discovered by KRAUSE. Whereas the horizontal canal is established as a small pocket by itself (fig. 276 *hb*), *the two vertical canals arise together from a single large pocket-like fundament* (fig. 276 *am* (*vb*), *, *vb'*).

The walls of this large pocket come into contact with each other and fuse at two different places. At one of them there has already been formed, in the preparation from which this model (fig. 276) was constructed, an opening (ö) by the resorption of the fused epithelial areas, whereas at the second place (*vb'*) the epithelial membrane is still preserved. Between the fused parts of the pocket there remains open a middle region, which is indicated in the model by an asterisk, and this becomes the common arm (sinus superior) of the two vertical canals. Thus embryology furnishes for this peculiarity, too, a simple satisfactory explanation.

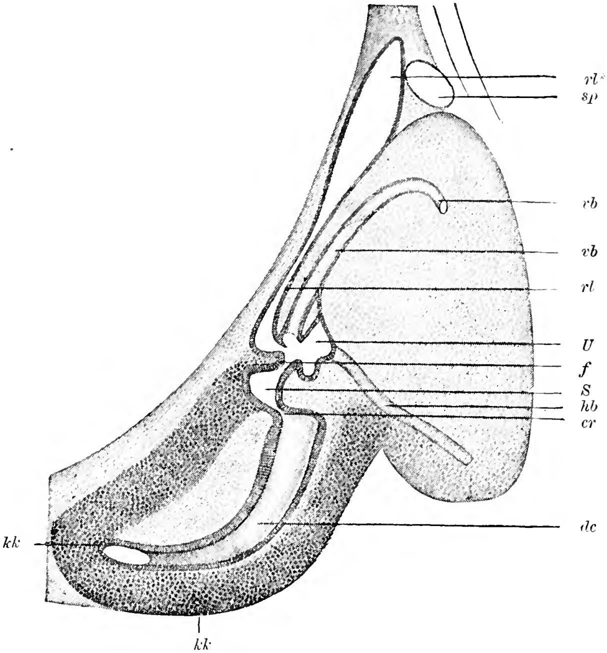

Fig. 279.—View produced by combination from two cross sections through the labyrinth of a Sheep embryo 2·8 cm. long, after Boettcher.

rl, Recessus labyrinthi; *rl**, its flask-like enlargement; *vb*, *hb*, vertical and horizontal canals; *U*, utriculus; *S*, sacculus; *f*, fold by means of which the labyrinth is divided into sacculus and utriculus; *cr*, canalis reuniens; *dc*, ductus cochlearis; *kk*, cartilaginous capsule of the cochlea; *sp*, sinus petrosus inferior.

That which remains of the upper portion of the auditory vesicle, after the semicircular canals have grown forth from its wall, is called the *utriculus* (figs. 278-80 *U*).

Meanwhile no less significant and fundamental *alterations take place in the lower part of the auditory sac* and lead to the formation of *sacculus* and *ductus cochlearis*.

By a continually deepening constriction (fig. 279 *f*) the lower portion (*S*) is delimited from the utriculus (*U*), and finally remains connected with it by a very narrow tubule only (canalis utriculo-saccularis—figs. 280 *R* and 282 $_2$). Since the constriction affects exactly that place of the labyrinth-sac from which the recessus labyrinthi arises, the opening of the latter subsequently comes to lie within the territory of the canalis utriculo-saccularis, at about its middle (figs. 280 *R* and 282 $_2$). In this manner there is produced an appearance as though the recessus labyrinthi were split at its beginning into two narrow tubules, one of which leads into the sacculus, the other into the utriculus.

By a second deep constriction (figs. 279, 280, 282) the sacculus (*S*) is separated from the developing ductus cochlearis (*dc*). Here also a connection is maintained by means of an extraordinarily fine connecting tubule only (*cr*), which Hensen discovered and has described as *canalis reuniens.* The ductus cochlearis itself increases greatly in length, and at the same time begins to be rolled up in spiral turns in the soft, enveloping, embryonic connective tissue, until in Man it describes two and a half turns (figs. 280 *C* and 282 *Con*). Since the first whorl is the largest, and the others are successively narrower, it acquires a great resemblance to a snail-shell.

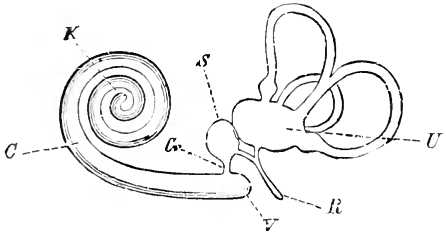

Fig. 280.—Diagram to illustrate the ultimate condition of the membranous labyrinth [after Waldeyer].
U, Utriculus; *S*, sacculus; *Cr*, canalis reuniens; *R*, recessus labyrinthi; *C*, cochlea; *K*, blind sac of the cupola; *V*, vestibular blind sac of the ductus cochlearis.

The alterations in the external form of the vesicle are accompanied by changes in the nature of its epithelium also. This is separated into the indifferent epithelial cells, which simply serve as a lining, and the real auditory cells. The former are flattened, becoming cubical or scale-like, and cover the greater part of the inner surface of the semicircular canals, the sacculus, the utriculus, the recessus labyrinthi, and the ductus cochlearis. The auditory cells, on the contrary, are elongated, become cylindrical or spindle-shaped, and acquire at the free surface hairs, which project into the endolymph. By the separation of the vesicle into its various divisions the auditory epithelium is distributed into an equal number of separate patches, to which then the auditory nerve is distributed. Accordingly the auditory epithelium is resolved into a macula acustica in the sacculus and another in the utriculus, into a crista acustica in each of the ampullæ of the semicircular canals, and into an especially complicated termination in the ductus cochlearis. Here the auditory epithelium grows out into a long spiral band, which is known under the name of Corti's organ.

Upon the separation of the auditory epithelium into maculæ, cristæ, and organ of Corti, the originally single auditory nerve distributed to the auditory vesicle is likewise resolved into separate branches. We distinguish in the case of the auditory nerve the *nervus vestibuli*, which is in turn divided into numerous branches distributed to the maculæ and cristæ, and the *nervus cochleæ*.

The originally single ganglion acusticum belonging to the auditory nerve also becomes differentiated into two separate portions. The portion belonging to the nervus vestibuli is in the adult located in the internal auditory meatus far from the terminal distribution, forming here the well-known intumescentia gangliformis Scarpæ; the portion belonging to the nervus cochleæ, on the contrary, adjoins the terminal distribution of the nerve. In the embryo it (figs. 277, 278 *gc*) is closely united with the fundament of the ductus cochlearis, and as the latter increases in size grows out to the same extent in the form of a thin band, which reaches to the blind end of the ductus and is known under the name of *ganglion spirale* (fig. 283 *gsp*).

(*b*) *Development of the Membranous Ear-Capsule into the Bony Labyrinth and the Perilymphatic Spaces.*

All of the changes which have been mentioned hitherto have proceeded from the epithelial vesicle which was constricted off from the outer germ-layer. It is now my purpose to direct attention to a series of processes which take place around the epithelial cavities, in the mesenchyme in which they are imbedded. The processes lead to the formation of the bony labyrinth, the perilymphatic spaces and soft connective-tissue layers, which are intimately joined to the purely epithelial structures hitherto treated of, and with the latter are embraced in descriptive anatomy under the name of membranous labyrinth. Changes take place here similar to those in the development of the neural tube and of the eye, in which cases also the connective-tissue surroundings are modified in a special manner and with reference to the epithelial parts. In the present instance there are produced structures which are comparable with those existing in the former cases, as has already been pointed out by **Kölliker**, **Schwalbe**, and others.

The comparison may be carried into details. The parts arising from the primitive auditory vesicle are at first surrounded by a soft, vascular connective-tissue layer, as the neural tube and the epithelial optic cup are. To the pia mater of the brain corresponds the vascular membrane of the eye and the soft ear-capsule, or the connective-tissue wall of the membranous labyrinth. Around all three organs a firm envelope has been developed for the purpose of protection; around the brain the dura mater with the cranial capsule, around the eye the sclerotica, and around the organ of hearing the bony labyrinth with its periosteum. To these is to be added still a third noteworthy agreement. In all three cases the soft and firm envelopes are separated by more or less considerable fissure-like spaces, which belong to the lymphatic system. Around the neural tube the subdural and the subarachnoid spaces are found, around the eye the perichoroid fissure, around the organ of hearing the perilymphatic spaces, which have received in the cochlea the special names of scalæ (fig. 283 *ST* and *SV*).

The details of the formation of the enveloping structures around the epithelial auditory vesicle are as follows:—

Soon after the auditory sac is constricted off from the epidermis it is enveloped on all sides by a richly cellular mesenchyme, the individual cells of which lie in an extremely scanty, soft, and homogeneous intercellular substance, and possess each a large nucleus with a thin protoplasmic covering having short processes. Gradually the envelope is differentiated into two layers (figs. 279, 281). In the vicinity of the epithelial canals the soft intercellular substance increases in amount; the cells become either stellate or spindle-shaped, in the former case sending out long processes in various directions. There is formed here that modification of connective substance known as *mucous or gelatinous tissue* (figs. 281 and 283 *g*), in which there are also blood-vessels. Outside of this the cells remain smaller and more closely crowded together, and are separated from one another by thin partitions of a firm intermediate substance. With an increase of the latter the tissue soon acquires the character of embryonic cartilage (*kk*).

The further changes must be followed separately in the semicircular canals, the utriculus and sacculus and the ductus cochlearis, The three semicircular canals do not lie exactly in the middle of the cavities of the embryonic cartilage containing the gelatinous tissue, but are so situated that their convex borders are in almost immediate contact with the cartilage, whereas their concave sides are separated from it by a thick layer of gelatinous tissue. The latter is differentiated into three layers: into a middle portion, in which the gelatinous intercellular substance is greatly increased in volume, and becomes at the same time more fluid, and into two limiting layers, which are converted into fibrous connective tissue. One of the two [the inner] is intimately united to the epithelial tube, for the nutrition of which it provides by means of a close network of blood-vessels distributed through it; the other [the outer] lies on the inner surface of the cartilaginous envelope and becomes its perichondrium.

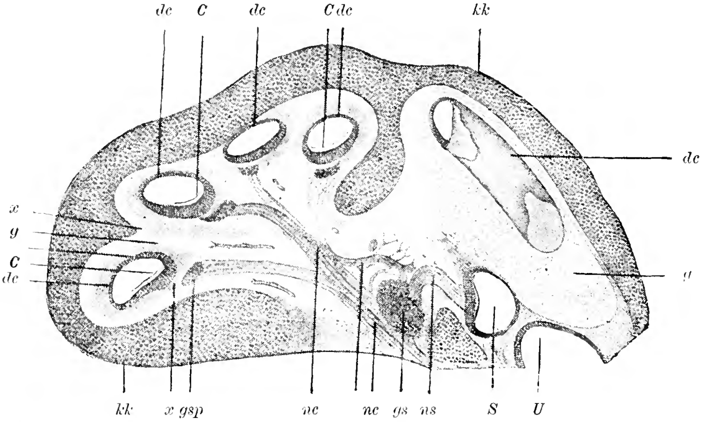

Fig. 281.—Section through the cochlea of a Sheep embryo 7 cm. long, after Boettcher. Magnified 20 diameters.

kk, Cartilaginous capsule of the cochlea; *S*, sacculus with the nerve (*ns*) distributed to it; *U*, utricle; *gs*, ganglion connected with the cochlear nerve (*nc*) and sending nerve-fibres (*ns*) to the sacculus; *gsp*, ganglion spirale; *dc*, ductus cochlearis; *C*, Corti's organ; *g*, gelatinous tissue in the periphery of the ductus cochlearis; *x*, more compact connective-tissue layers.

The gelatinous tissue of the middle layer is of only short duration. It soon shows signs of degeneration. The stellate cells become filled with fat granules in the vicinity of their nuclei and in their long processes; later they disintegrate. In the gelatinous matrix there are formed, by a continually advancing process of softening, cavities filled with fluid. These increase in size and then become confluent, until finally there has arisen between the connective-tissue membrane of the semicircular canals and the perichondrium, *in place of the* *gelatinous tissue, a large space filled with perilymph, which is indicated in the diagram, fig.* 282, *in black.* Here and there, however, connective-tissue cords remain running from one layer of connective tissue to the other, and serving as bridges for the nerves and blood-vessels which are distributed to the semicircular canals.

Finally, a last alteration takes place in the cartilaginous envelope by its becoming converted into bone-substance by endochondral ossification. Thus the membranous semicircular canals are enclosed in the bony semicircular canals (fig. 282 *a* and *b* *KL*), which are enlarged reproductions of the former.

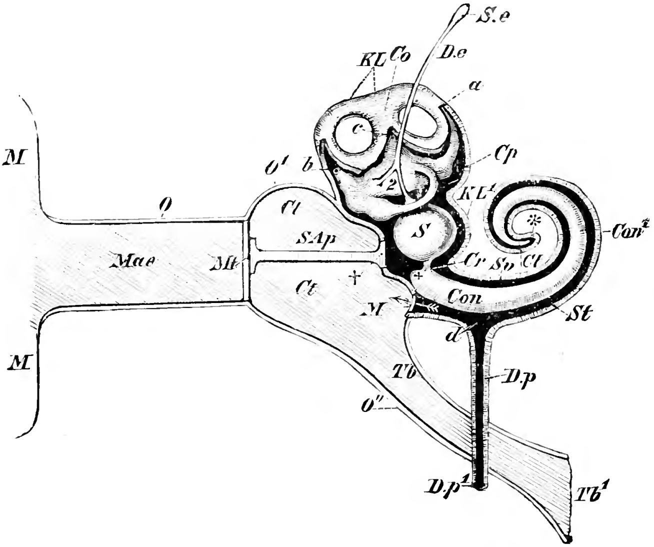

Fig. 282.—Diagrammatic representation of the whole organ of hearing in Man, from WIEDERSHEIM. *Outer ear:* *M*, *M*, auricle; *Mae*, meatus auditorius externus; *O*, its wall; *Mt*, membrana tympani. *Middle ear:* *Ct*, *Ct*, cavum tympani; O^1, its wall; *SAp*, sound-conducting apparatus, which is drawn as a simple rod-like body in place of the auditory ossicles; the place † corresponds to the stapedial plate, which closes the fenestra ovalis; *Tb*, tuba Eustachii; Tb^1, its opening into the pharynx; O'', its wall. *Inner ear:* the bony labyrinth (KL, KL^1) for the most part cut away; *S*, sacculus; *a*, *b*, the two vertical membranous and osseous semicircular canals; *S.e*, *D.e*, saccus and ductus endolymphaticus, of which the latter is divided at 2 into two arms; *Cp*, cavum perilymphaticum; *Cr*, canalis reuniens; *Con*, membranous cochlea, which produces at + the vestibular cœcum; Con^1, bony cochlea; *Sv* and *St*, scala vestibuli and scala tympani, which at * communicate with each other at the cupula terminalis (*Ct*); *D.p*, ductus perilymphaticus, which arises from the scala tympani at *d* and opens out at $D.p^1$. The horizontal semicircular canal is not specially designated, but is easily recognisable.

Corresponding changes (fig. 282) are also accomplished in the periphery of the utriculus and sacculus (*S*), and lead to the formation of (1) a perilymphatic space (*Cp*), which is in communication with the perilymphatic spaces of the semicircular canals, and (2) a bony envelope (*KL'*) of the atrium or vestibulum, which constitutes the middle region of the bony labyrinth.

The envelope of the epithelial cochlear duct, which becomes the bony cochlea with its scalæ, undergoes a more complicated alteration. It is already differentiated, at the time when the duct (fig. 279 *dc*) makes only half of a spiral turn, into an inner, soft and an outer, firm layer, the latter becoming cartilage (*kk*). The cartilaginous capsule (fig. 281 *kk*), which is continuous with the cartilaginous mass of the remaining parts of the labyrinth and together with them constitutes a part of the os petrosum, afterwards encloses a lenticular cavity and possesses below a broad opening, through which the cochlear nerve (*nc*) enters. The resemblance to a snail-shell is not yet observable; it takes place gradually and is produced by two changes: by the outgrowth of the epithelial duct and by the differentiation of the soft tissue surrounding it into parts which are fluid and such as become more firm.

In its outgrowth the epithelial ductus cochlearis describes within its capsule the previously mentioned spiral turns (*dc*), shown in cross section in fig. 283; at the same time it remains quite closely approximated to the inner surface of the capsule (*kk*). The cochlear nerve (*nc*) ascends from its place of entrance straight up through the centre of the turns, consequently in the axis of the capsule, and gives off numerous lateral branches to the concave side of the cochlear duct (*dc*), where they are enlarged into the ganglion (*gsp*), which has now also grown out into a spiral band. The nutritive blood-vessels have taken the same course as the nerves.

When the development has advanced as far as this, there still remains to be accomplished only an histological differentiation in the soft mesenchyme which fills the cartilaginous capsule in order to produce the parts of the finished cochlea that are still wanting—the modiolus, the lamina spiralis ossea, the bony cochlea, and the vestibular and tympanic scalæ (fig. 283). Here, as in the vicinity of the semicircular canals the utriculus and the sacculus, the mesenchyme is differentiated into a firmer connective substance, which becomes fibrous, and into a gelatinous tissue (*g*), which is continually becoming softer. Fibrous connective substance is developed first around the trunks of the nerves (*nc*) and blood-vessels that enter the cartilaginous capsule; furnishing the foundation of the future bony axis of the snail-shell (*M*), secondly it furnishes an envelope for nerve-fibres (*N*) that run from the axis to the epithelial cochlear duct, for the ganglionic cells (*gsp*), and for the blood-vessels, and constitutes a connective-tissue plate which is subsequently ossified to form the lamina spiralis ossea. Thirdly, it clothes with a thin layer the epithelial ductus, serving for the distribution of the blood-vessels on the latter, and together with it is designated as the membranous ductus cochlearis. Fourthly, it lines the inner surface of the cartilaginous capsule as perichondrium (*P*). Finally, fifthly, there is formed a connective tissue plate (*V*) extending between the cartilaginous ridge which, as previously described, projects inward from the capsule and the connective-tissue axis of the cochlea (*M*). It is stretched out between and separates the successive turns of the membranous cochlear duct, so that the latter now comes to lie in a large canal, the wall of which is in part cartilaginous, in part membranous. This canal is the foundation of the bony cochlea.

That portion of the mesenchyme which is not converted into fibrous connective tissue becomes gelatinous tissue (*g* and *g'*). It forms between the parts just mentioned two spiral tracts, one of which is located above and the other below the membranous ductus cochlearis and the membranous lamina spiralis. The tracts therefore occupy the place of the scala vestibuli (*SV*) and the scala tympani (*ST*). The latter arise, even before the process of ossification begins, in exactly the same way as the perilymphatic spaces in the case of the semicircular canals and the vestibule. In the gelatinous tissue the matrix becomes softer and more fluid, and the cells begin to undergo fatty degeneration. Small fluid-filled cavities make their appearance; these become joined to one another, and finally the whole space occupied by gelatinous tissue is filled with perilymph. The process of softening begins at the base of the cochlea in the region of the first spiral (*ST* and *SV*), and advances slowly toward the cupola. Here vestibular and tympanic scalæ finally unite, after the last remnant of the gelatinous tissue has been dissolved. Figure 283 exhibits a stage in which, at the base of the cochlea, the perilymphatic spaces (*SV* and *ST*) have been formed, and only small remnants of the gelatinous tissue (*g'*) are present, whereas at the apex of the cochlea the process of liquefaction of the gelatinous tissue (*g*) has not yet taken place.

With the development of the scalæ the membranous ductus cochlearis changes form. Whereas its cross section was formerly oval, it now assumes the form of a triangle (*dc*). For those portions of the wall which are adjacent to the vestibular and tympanic scalæ, and which have been named from them, gradually become flattened,

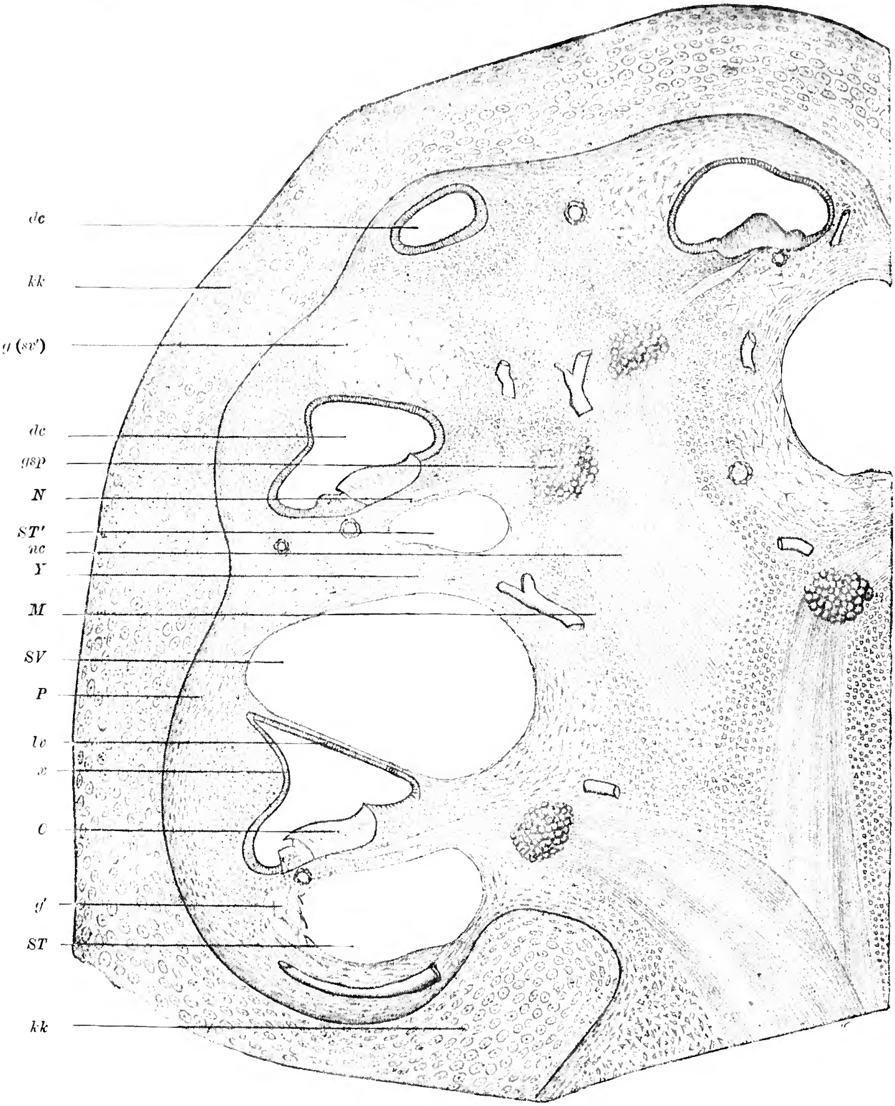

Fig. 283.—**Part of a section through the cochlea of an embryo Cat 9 cm. long,** after Boettcher. *kk*, Cartilaginous capsule, in which the cochlear duct describes ascending spiral turns; *dc*, ductus cochlearis; *C*, organ of Corti; *lv*, lamina vestibularis; *x*, outer wall of the membranous ductus cochlearis with ligamentum spirale; *SV*, scala vestibuli; *ST*, *ST'*, scala tympani; *g*, gelatinous tissue, which still fills the scala vestibuli (*sv'*) in its last turns; *g'*, remnant of the gelatinous tissue, which is not yet liquefied; *M*, firm connective tissue surrounding the cochlear nerve (*nc*); *gsp*, ganglion spirale; *N*, nerve which runs to Corti's organ in the future lamina spiralis ossea; *Y*, compact connective-tissue layer, which becomes ossified and shares in bounding the bony cochlear duct; *P*, perichondrium.

and are stretched out smoothly between the free margin of the lamina spiralis and the inner wall of the cartilaginous capsule. In this process the tympanic wall (*C*) comes to lie in the same plane as the lamina spiralis, the vestibular wall (*lv*) forms with the tympanic an acute angle, and the third wall (*x*) is everywhere in close contact with the perichondrium of the cartilaginous capsule.

The epithelial lining of the membranous ductus cochlearis assumes very different conditions in the three corresponding regions of its wall. Whereas the epithelial cells of the vestibular and the outer walls become in part cubical, in part quite flat, those of the tympanic wall become elongated, and are in connection with the terminal filaments of the cochlear nerve; they produce the complicated organ of CORTI (*C*), which, like the auditory ridges and auditory patches of the ampullæ, the sacculus and utriculus, contains the terminal ends of the auditory nerve.

The construction of the intricate cochlea approaches completion with the beginning of the process of ossification. The latter is accomplished by two methods. First, the cartilaginous capsule ossifies in the endochondral manner, as does the whole cartilaginous os petrosum, of which it constitutes a small part. The osseous tissue thus formed is for a long time spongy and provided with large medullary spaces. Secondly, the previously mentioned fibrous connective-tissue layers—the partitions between the cochlear canals, the connective-tissue axis or the modiolus and the lamina spiralis—undergo direct ossification. At the same time compact bone-lamellæ are laid down from within on the spongy bone-tissue formed from the cartilaginous capsule; these lamellæ are formed, as BOETTCHER has shown, by the original perichondrium, which becomes the periosteum. Consequently the bony cochlear capsule, since it is produced by periosteal secretion, may be easily detached from the loose osseous tissue of endochondral origin during early post-natal years.

(*c*) *Development of the Accessory Apparatus of the Organ of Hearing.* (*Middle and External Ear.*)

With the membranous and bony labyrinth, which are together called the inner ear, there is associated a subsidiary apparatus, in the same way that the eye-muscles, the lids, and the lachrymal glands and ducts are added to the eyeball. It is made up of structures which are wanting in the lower Vertebrates (Fishes), but, beginning to be developed in the Amphibia, become more and more complete in the higher forms. Their function is to transmit vibrations to the labyrinth, and consequently they are together called the conducting apparatus. From their position they are also known as middle and outer ear. The former consists in Mammals, where it attains its highest development (diagram, fig. 284), of the tympanic cavity (*Ct*), the Eustachian tube (*Tb*), and the three auditory ossicles (*SAp*); the latter, of the tympanic membrane (*Mt*), the external meatus (*Mae*), and the external ear or auricle (*M*). The statement just made, that these parts are wanting in Fishes, is to be taken cum grano salis: it is as a sound-conducting apparatus only that they are wanting, for they are present even in the case of Fishes, but only as structures of a *different function* and in a more simple condition. For *the various accessory apparatus of the organ of hearing are developed out of the first visceral cleft and certain parts which are located in its periphery.*

Here also it will be well to acquaint ourselves with the original—the initial condition, for which the Selachians may serve as an example.

In them the greater part of the first visceral cleft, which is situated between the mandibular and hyoid arches and between the nervus trigeminus and n. acustico-facialis, disappears; at the side of the throat it becomes closed, remaining open only at the origin, or base, of the two visceral arches. It then has the form of a short canal, which possesses a small round opening at its inner and another at its outer end, and which passes in very close proximity to the labyrinth-region of the skull, in which the organ of hearing is located. The canal, here called the spiracle, has no longer anything to do with respiration, since the branchial leaflets on its wall have undergone degeneration. Owing to its position in the immediate vicinity of the labyrinth, it presents, even in the Selachians, the best course for the propagation of the sound-waves to the inner ear, and this is the chief ground for its entering wholly into the service of the organ of hearing in the remaining Vertebrates, and for its being developed in a more serviceable manner for this particular function.

The structures in the higher Vertebrates corresponding to the spiracle of the Selachians are (fig. 284) the tympanic cavity (*Ct*), the Eustachian tube (*Tb*), and the external meatus (*Mae*). They likewise are developed out of the upper part of the first visceral cleft. Although it has recently been asserted by certain investigators (URBANTSCHITSCH) that they have nothing to do with the first visceral cleft, but are established independently by the evagination of the pharynx, this view is opposed not only to comparative-anatomical considerations, but also to statements of Kölliker, Moldenhauer, and Hoffmann, which relate to the development in Reptiles, Birds, and Mammals.

In the classes of Vertebrates just mentioned the first visceral cleft is closed in its upper part also, contrary to the condition in Selachians.*

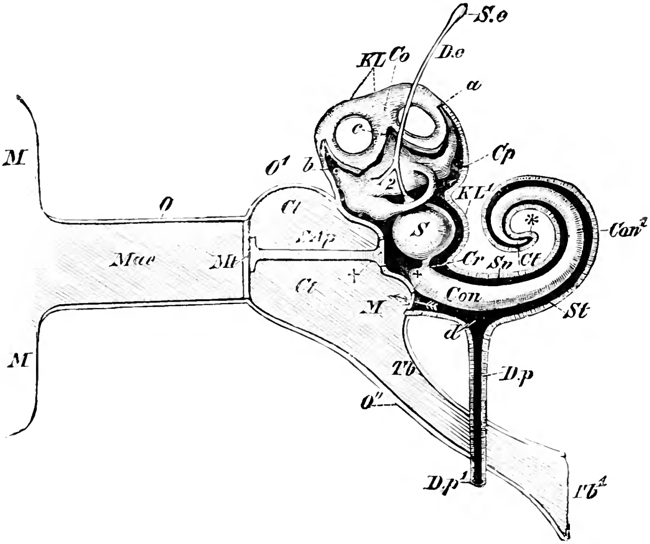

Fig. 284.—Diagrammatic representation of the whole organ of hearing in Man, from Wiedersheim. *Outer ear:* *M*, *M*, auricle; *Mac*, meatus auditorius externus; *O*, its wall; *Mt*, membrana tympani. *Middle ear:* *Ct*, *Ct*, cavum tympani; O^1, its wall; *SAp*, sound-conducting apparatus, which is drawn as a simple rod-like body in place of the auditory ossicles; the place † corresponds to the stapedial plate, which closes the fenestra ovalis; *Tb*, tuba Eustachii; Tb^1, its opening into the pharynx; O'', its wall. *Inner ear:* the bony labyrinth (KL, KL^1) for the most part cut away; *S*, sacculus; *a*, *b*, the two vertical membranous and osseous semicircular canals; *S.e*, *D.e*, saccus and ductus endolymphaticus, of which the latter is divided at 2 into two arms; *Cp*, cavum perilymphaticum; *Cr*, canalis reuniens; *Con*, membranous cochlea, which produces at + the vestibular cœcum; Con^1, bony cochlea; *Sv* and *St*, scala vestibuli and scala tympani, which at * communicate with each other at the cupula terminalis (*Ct*); *D.p*, ductus perilymphaticus, which arises from the scala tympani at *d* and opens out at $D.p^1$. The horizontal semicircular canal is not specially designated, but is easily recognisable.

The closure becomes more firm and complete owing to the ingrowth of a connective-tissue layer between the inner and outer epithelial plates. Remnants of the first visceral cleft are preserved

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* See the statements discussed in a previous chapter (p. 287), concerning the mooted question whether the visceral clefts remain closed by means of an epithelial membrane or are temporarily open.

on both sides of the closing membrane as depressions of greater or less depth; an inner one on the side toward the pharyngeal cavity, and an outer one which is surrounded by ridges of the first and second visceral arches.

The inner depression, which is called canalis or sulcus tubo-tympanicus (pharyngo-tympanicus), is located, like the spiracle, between trigeminus and acustico-facialis. It becomes the middle ear, and is enlarged by an evagination that is directed upward, outward, and backward. The evagination inserts itself between the labyrinth and the place of closure of the first visceral cleft, and takes the form of a laterally compressed space, which is now to be distinguished as tympanic cavity from the tubular remnant of the sulcus tympanicus, or Eustachian tube. Its lumen is very small, especially in the case of advanced embryos of Man and Mammals, its lateral and median walls being almost in immediate contact. This results chiefly from the fact that there is present beneath the epithelial lining of the middle ear a richly developed gelatinous tissue. The latter still encloses at this time structures,—the auditory ossicles and the chorda tympani,—which later come to lie, as it were, free in the tympanic cavity.

The tympanic membrane also is now in a condition very unlike that which it afterwards acquires. The history of its formation is by no means so simple as was formerly supposed. For it is not derived exclusively from the narrow closing membrane of the first visceral cleft; the neighboring parts of the first and second membranous visceral arches also participate in its production. The embryonic tympanic membrane is therefore at first a thick connective-tissue plate, and encloses at its margins the auditory ossicles, the tensor tympani, and the chorda tympani. The reduction in the thickness of the tympanic membrane takes place at a late period, simultaneously with an increasing enlargement of the tympanic cavity. Both are brought about by shrinkage of the gelatinous tissue, and by an accompanying growth of the mucous membrane lining the tympanic cavity. Wherever the gelatinous tissue disappears the mucous membrane takes its place, inserting itself between the individual ossicles and the chorda tympani, which thus come to lie apparently free in the tympanic cavity. In reality, however, they lie outside of it, for they continue to be clothed on all sides by the growing mucous membrane, and are connected with the wall of the tympanic cavity by means of folds of that membrane (malleus-fold, incus-fold, etc.), in much the same manner as the abdominal organs which grow into the body-cavity are invested by the peritoneum and supported from its walls by the mesenteries.

With a reduction in the thickness of the tympanic membrane there occurs a condensation of its connective-tissue substance, whereby it is enabled to fulfil its ultimate function as a vibrating membrane.

A more extended discussion of the development of the auditory ossicles will be deferred to a subsequent section, which deals with the origin of the skeleton. At present, only a few words further—concerning the *formation of the external ear*, which, as has already been stated, is derived from a depression on the outer side of the place of closure of the first visceral cleft. Its development has been minutely investigated in the Chick by Moldenhauer and in the human embryo by His. As the lateral view of a very young human embryo (fig. 274) shows, the first visceral cleft is surrounded by ridge-like margins, which belong to the first and second visceral arches, and are early divided into six elevations designated by Arabic numerals. From these is derived the auricle, which therefore involves a rather extensive tract of the embryonic head (the pars auricularis). The pocket between the ridges, at the bottom of which the tympanic membrane is met with, becomes the external meatus. This is continually growing deeper owing to the surrounding wall of the side of the face becoming greatly thickened; finally it is developed into a long canal, the wall of which is in part bony, in part cartilaginous. The six elevations mentioned, which surround the orifice of the external meatus, together constitute a bulky ring. The accompanying representation (fig. 285) shows clearly its metamorphosis into the external ear. It shows that out of the elevations 1 and 5 the tragus and antitragus are developed, out of 2 and 3 the helix, and out of 4 the antihelix. The lobule of the ear remains for a long time small; it is not until the fifth month that it becomes more distinct. It is derived from the hillock marked with the numeral 6. At the close of the second month all the essential parts of the external ear are easily

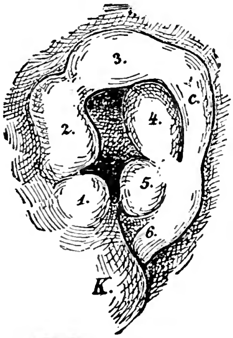

Fig. 285.—Fundament of the outer ear of a human embryo, after His.

The elevation marked 1 produces the tragus; 5, the antitragus. The elevations 2 and 3 produce the helix; 4, the antihelix. From the tract 6 is formed the lobule. *K*, Lower jaw.

recognisable; from the third month onward the upper and posterior part of the auricle grows out more from the surface of the head; and it acquires greater firmness upon the differentiation of the auricular cartilage, which had already begun at the end of the second month.

SUMMARY.

1. The most essential part of the organ of hearing, the membranous labyrinth, is developed at the side of the after-brain above the first visceral cleft from a pit-like depression of the outer germ-layer.

2. By closure the auditory pit becomes the auditory vesicle; it sinks down and becomes imbedded in embryonic connective tissue, from which the cranial capsule is subsequently developed.

3. The auditory vesicle acquires the complicated form of the membranous labyrinth by various evaginations of its wall, and becomes differentiated into the utriculus, with the three semicircular canals, into the sacculus with the canalis reuniens and the cochlea, as well as into the recessus vestibuli, by means of which sacculus and utriculus remain permanently connected with each other.

4. The auditory nerve and the auditory epithelium, which are at first single, are likewise divided—as soon as the vesicle is differentiated into a number of regions—into several nerve-branches (nervus vestibuli, n. cochleæ) and nerve-terminations (the cristæ acusticæ of the three ampullæ, a macula acustica for the utriculus and another for the sacculus, and the organ of CORTI).

5. The embryonic connective tissue, in which are enclosed the auditory vesicle and the products of its metamorphosis, is differentiated into three parts:—

(*a*) Into a thin connective-tissue layer, which is closely applied to the epithelial wall and together with it constitutes the membranous labyrinth;

(*b*) Into a gelatinous tissue, which becomes liquefied during embryonic life and furnishes the perilymphatic spaces (in the cochlea the scala vestibuli and the scala tympani);

(*c*) Into a cartilaginous capsule, from which there arises by a process of ossification the bony labyrinth.

6. The middle and outer ear are derived from the upper part of the first visceral cleft (the spiracle of Selachians) and its periphery.

7. The tympanic membrane, which at first is rather thick and only gradually becomes reduced to a thin, tense membrane, is developed out of the closing plate of the first visceral cleft and the adjacent parts of the visceral arches.

8. The tympanic cavity and the Eustachian tube are developed out of a depression on the median side of the tympanic membrane,—the sulcus tubo-tympanicus,—and out of an evagination from it extending upward, outward, and backward.

9. The tympanic cavity is at first extremely small, the connective tissue of the mucous membrane that surrounds it being gelatinous [and voluminous].

10. The auditory ossicles and the chorda tympani lie at first outside the tympanic cavity in the gelatinous tissue of its wall; it is only after shrivelling of the gelatinous tissue that they come to lie in folds of the mucous membrane, which project into the now more capacious tympanic cavity (incus-fold, malleus-fold).

11. The external meatus is developed from the periphery of the depression that lies on the lateral side of the tympanic membrane; the auricle arises from six elevations, which are converted into tragus, antitragus, helix, antihelix, and the lobule of the ear.

C. The Development of the Organ of Smell.

The organ of smell is, like the eye and ear, a product of the outer germ-layer, from which it is developed somewhat later than the two higher sensory organs. It first becomes noticeable, at either side of the broad frontal process (fig. 274) previously described, as a thickening of the outer germ-layer which His has designated in human embryos as *nasal area.* Both fundaments soon become more distinct owing to the fact that each nasal area becomes depressed into a kind of trough, the edges of which rise up as folds (fig. 286). An olfactory lobe, which has been formed meantime by an evagination of the cerebral vesicle, grows out on either side to the thickened epithelium of this area, where its nerve-fibrillæ terminate.

The two *olfactory pits,* which are formed in a similar manner in all Vertebrates with the exception of the Cyclostomes, in which only an unpaired pit arises, are separated from each other by a considerable distance. They therefore appear at first as distinctly paired structures, whereas in their ultimate condition in the higher Vertebrates they have approached each other toward the median plane and become an apparently unpaired organ, the nose.

The study of the development of the organ of smell acquires additional interest, when one takes into account the comparative-anatomical conditions. It is then found that the various stages through which the organ of smell passes during embryonic life, in Mammals for example, have been preserved as permanent conditions in lower classes of Vertebrates. Thus in the case of many groups of Fishes the organ of smell is preserved, as it were, in its initial stage in the form of a pair of pits. Upon closer histological investigation, however, this condition acquires a special interest, because it presents *points of comparison with simpler sensory organs which are distributed over the integument.* As Blaue especially has shown in a meritorious work, the olfactory nerve does not terminate in this case in a continuous olfactory epithelium, but in individual, sharply differentiated organs (fig. 287 *rk*), which, although closely crowded in an indifferent ciliate epithelium (*fe*), are nevertheless separated from each other.

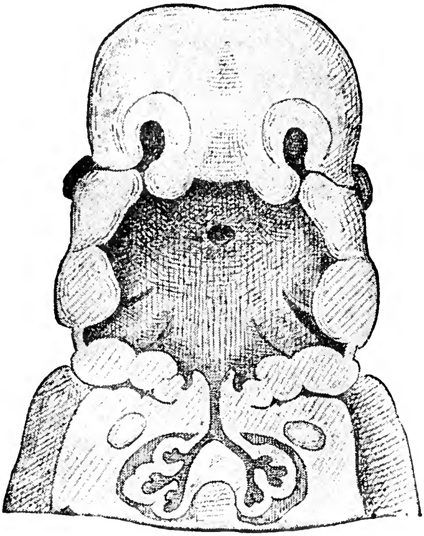

Fig. 286.—Frontal reconstruction of the oro-pharyngeal cavity of a human embryo (*Rg* of His) 11·5 mm. long, neck measurement. From His, "Menschliche Embryonen." Magnified 12 diameters.

The upper jaw is seen in perspective, the lower jaw in section. The posterior visceral arches are not visible from the outside, since they have moved into the depths of the cervical sinus.

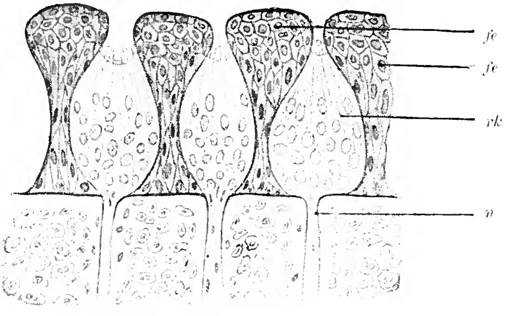

Fig. 287.—Longitudinal section through three olfactory buds from the regio olfactoria of Belone, after Blaue. Highly magnified. *rk*, Olfactory bud; *fe*, indifferent ciliate epithelium in several layers; *n*, branch of the olfactory nerve.

The organs (*rk*) consist of numerous fine, rod-like cells, which at their free ends bear fine bristles and are united into bundles that are distinctly delimited from the ordinary cells of the epidermis. They closely resemble the sensory nerve-terminations which are abundantly and widely distributed in the epidermis of Fishes and other lower Vertebrates—the *beaker-like organs* or the *nervous end-buds.* BLAUE has therefore named them *olfactory buds.* He proceeds from the conception that, like the similarly constructed gustatory buds of the oral cavity, they are descended from the sensory organs distributed over the whole integument. The organ of smell is simply a depressed patch of the skin richly provided with terminal nerve-buds, which, undergoing a change of function, has come to subserve a specific sense. The continuous olfactory epithelium of the higher Vertebrates has arisen from the originally scattered, isolated olfactory buds (fig. 287 *rk*) by a process of fusion, the indifferent epithelium (*fe*) having gradually disappeared. In certain species of Fishes and Amphibia such a transition can be demonstrated.

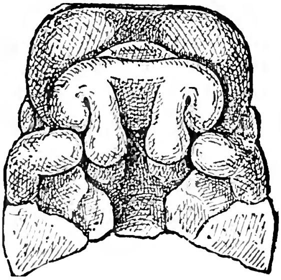

Fig. 288.—Fundament of the nose and the roof of the primitive mouth-cavity of a human embryo (C. II. of HIS), seen from below after removal of the lower jaw. From HIS, "Menschliche Embryonen." Magnified 12 diameters.

The further development of the organ of smell is especially characterised by the olfactory pits coming into relation with the oral cavity. Each of them (fig. 286) develops a furrow which runs downward to the upper margin of the mouth and receives on its outer side the previously described lachrymal groove, coming in an oblique direction from the eye. *Nasal pit* and *nasal furrow* become deeper in older embryos (fig. 288), owing to their margins protruding outward as ridges and forming the so-called *inner* and *outer nasal processes.* The two inner nasal processes are separated from each other by a shallow furrow running from above downward; they together produce a thick partition between the two olfactory pits that in the higher Vertebrates subsequently becomes more and more reduced in thickness. They also furnish the middle of the roof of the mouth. The outer nasal processes (also called the lateral frontal processes by HIS) form on either side a ridge protruding between the eye and the organ of smell, and furnish the material for the formation of the lateral walls of the nose and the alæ. Their lower margins meet the front end of the transversely located maxillary processes, from which they are delimited externally by the lachrymal grooves.

On the median wall of the nasal pit there exists a special small depression, which was first found by **Dursy** in mammalian embryos, and which is also observable in human embryos at a very early stage (**His**). It is the fundament of **Jacobson's** *organ*, which afterwards makes its way into the septum of the nose. It receives from the olfactory nerve a special branch, which is indeed of remarkable size in embryos.

The stage with the nasal groove exists as the permanent condition in many Selachians. In these cases the deep nasal pits, which are enclosed in a cartilaginous capsule, and the mucous membrane of which is raised up into numerous parallel folds, lie on the under surface of the elongated snout or rostrum. Deep grooves, which are bounded by folds of the skin containing muscles, and which can be closed as if by valves, lead to the front margin of the mouth at some distance from its angle.

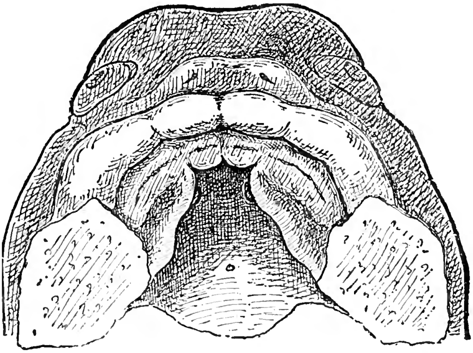

Fig. 289.—Roof of the oral cavity of a human embryo with the fundaments of the palatal processes, after His. Magnified 10 diameters.

The next stage, which in human embryos is reached in the second half of the second month, exhibits the organ of smell converted into two canals, which have been produced by the fusion of the margins of the two grooves, especially that of the inner nasal process with the maxillary process, which advances toward the median plane. The canals now possess two openings, the *external* and the *internal nasal orifice* (fig. 289) or the *nares*. The two external nares lie only a little above the border of the mouth-opening; the internal, in the roof of the primitive oral cavity, on account of which they have been named by **Dursy** the primitive palatal clefts. They are located far forward, only a little removed from the edge of the mouth, a position which they retain permanently in the case of the Dipnoi and Amphibia. At first round, they afterwards become elongated and assume the form of a fissure running from in front backward.

With the metamorphosis of the organ of smell into a canal leading into the oral cavity,—which has been effected in all Vertebrates that breathe by means of lungs,—*a second function* has been assumed. It is now not exclusively a sensory organ for the perception of odors, but serves at the same time to conduct currents of air both to and from the oral and pharyngeal cavities and the lungs. It has become a kind of *respiratory atrium for the apparatus of respiration.* The assumption of this accessory function gives a special stamp to the later stages of the development of the organ, and is to be taken into account in a proper estimate of it. For the course of the further development is most of all determined by the tendency to an extensive enlargement of the surface of the olfactory chamber. The *increase of surface,* however, does not affect the real olfactory mucous membrane or sensory epithelium, to which the olfactory nerve is distributed, but rather the ordinary ciliate mucous membrane. It is therefore less connected with an improvement of the sense of smell than with an accessory function in the process of respiration. By an increase of the surface of the soft, vascular mucous membrane the air that is swept over it becomes warmed and freed from particles of dust, which are caught by the moist surface. From this time forward therefore one must distinguish a *regio olfactoria* and a *regio respiratoria.* The former, which is derived from the sensory epithelium of the original olfactory pit, remains relatively small, receives the terminations of the olfactory nerve, and is limited in the case of Man to the region of the upper turbinal process and a part of the septum nasi. It is the respiratory function that causes the vast dimensions which the organ of smell attains in the higher Vertebrates.

The *increase in the surface of the nasal cavity* is produced by three different events: (1) by the formation of the hard and soft palate, (2) by the development of the turbinal bones, (3) by the appearance of the accessory cavities of the nose.

The first event begins in Man toward the end of the second month. There is then formed on the inner surface of the maxillary process (fig. 289) a ridge, which projects into the wide primitive oral cavity and grows out horizontally into a plate. The right and left **palatal plates** at first embrace between them a broad fissure, through which may be seen the original roof of the oral cavity and on this the inner nasal orifices, which become more and more slit-like and are separated by a bridge of substance which has arisen from the median frontal process and can now be designated as the nasal septum. In the third month the *embryonic palatal fissure* becomes gradually narrower.

The horizontal palatal processes of the upper jaw increase in size, and finally their free edges encounter in the median plane the still broad nasal septum, which has grown down yet farther into the oral cavity. Then the parts mentioned begin to fuse with one another from before backward.

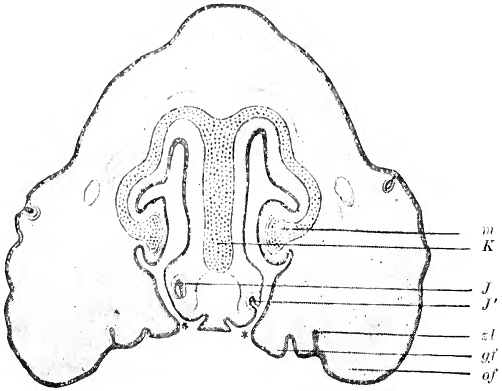

Fig. 290.—Cross section through the head of an embryo Pig 3 cm. long, crown-rump measurement.

The nasal cavities are seen to be in communication with the oral cavity at the places designated by a * ; *K*, cartilage of the nasal septum ; *m*, turbinal cartilage ; *J*, organ of Jacobson ; *J'*, the place where it opens into the nasal cavity ; *gf*, palatal process ; *of*, maxillary process ; *zl*, dental ridge.

Two stages of this process are illustrated by the accompanying figures (figs. 290, 291), in which cross sections through the anterior end of two embryo Pigs are represented. Figure 290 shows the stage at which the palatal plate (*gf*) of the maxillary process (*of*) has advanced close to the lower margin of the nasal septum. Oral and nasal cavities are still in communication by means of the very narrow palatal fissure indicated by an asterisk.

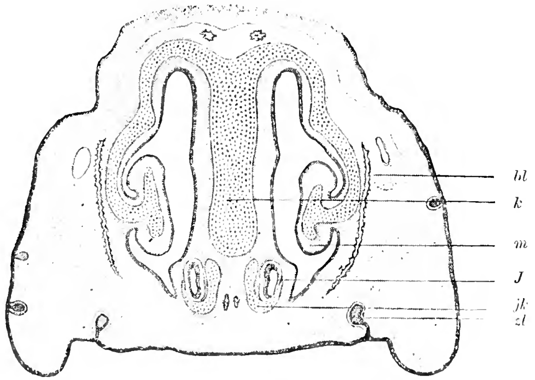

Fig. 291.—Cross section through the head of an embryo Pig 5 cm. long, crown-rump measurement.

k, Cartilaginous nasal septum ; *m*, nasal turbinal process ; *J*, Jacobson's organ with *jk*, Jacobson's cartilage ; *zl*, dental ridge ; *bl*, covering bone.

In figure 291 the fusion has taken place. In this manner the primitive oral cavity is divided into two storeys, one above the other. One, the upper part, becomes associated with the organ of smell, to the enlargement of which it contributes; it is distinguished from the space that arose from the original olfactory pit, or the olfactory labyrinth, as *naso-pharyngeal passage.* This opens behind into the pharynx by means of the posterior nares. The lower part becomes the secondary oral cavity. The partition that has been formed from the maxillary process is the *palate*, which later, when the development of the bones of the head can be traced, is differentiated into the *hard* and the *soft palate.*

A small portion of the palatal fissure, which in young embryos traverses the palate from in front backward and unites oral and nasal cavities (fig. 290 *), is preserved in most Vertebrates and constitutes the *ductus nasopalatinus* or STENSON'S *duct.* A probe may be passed through it from the nasal to the oral cavity. In Man the duct of STENSON is closed during embryonic life; there is preserved, however, in the palatal process of the bony maxilla at the corresponding place a vacuity, the *canalis incisivus*, occupied by connective tissue, blood-vessels, and nerves.

Where the ducts of STENSON are present, there are found in their vicinity the *organs* of JACOBSON, concerning which the statement has already been made that they are established very early as special depressions of the two olfactory pits. In Man this organ is converted into a narrow tube, which lies a little above the canalis incisivus and "pursues a straight course backward and slightly upward close to the cartilaginous partition, ending blindly" (SCHWALBE). In Mammals the organ is more highly developed (figs. 290, 291 *J*); it is enveloped in a special cartilaginous capsule (JACOBSON'S cartilage, *jk*) and receives a special branch of the olfactory nerve, which terminates in a sensory epithelium, which agrees with that of the regio olfactoria. Frequently (*e.g.*, in Ruminantia) it opens into the beginning of STENSON'S canal, which in this case remains open as a communication between nasal and oral cavities.

I cited the formation of folds as the second means of increasing the internal surface of the organ of smell. These are developed in Mammals (figs. 290, 291) and in Man on the lateral walls of the nasal chambers; they run parallel to one another from in front backward; their free margins grow downward, and in consequence of the forms which they assume are called the three *nasal turbinated processes*, while the spaces between them are designated as *upper*, *middle*, and *lower nasal passages.* From the cartilaginous cranial capsule they receive in Man as early as the second month a support, which subsequently ossifies. In many Mammals the turbinated processes acquire a complicated form owing to the production upon the first fold of numerous smaller secondary and tertiary folds, which become peculiarly bent and rolled up. On account of the complicated form resulting from the production of the turbinated processes the olfactory sac has received the name of *olfactory labyrinth.*

Thirdly and lastly, the mucous membrane of the nose is increased in extent by the formation of evaginations which grow out partly into the ethmoid region of the cranial capsule, which consists of cartilage during early stages of development, and partly into a number of the covering bones (Belegknochen).

In this manner are formed the numerous small *cribriform pits* in the cartilaginous cribriform plate. Somewhat later (in Man during the sixth month) an evagination into the upper jaw is developed into the *antrum of* HIGHMORE. Finally, after birth evaginations penetrate into the body of the sphenoid bone and into the frontal bone, producing the *sinus sphenoidales* and *sinus frontales*, which, however, attain their full development only at the time of sexual maturity. In many Mammals the enlargement of the nasal cavity takes place even farther backward into the body of the occipital bone (*sinus occipitales*). Inasmuch as the accessory cavities of the nose take the place of bone-substance, they naturally contribute to the diminution of the weight of the cranial skeleton.

In connection with the account of the organ of smell *the formation of the external nose* ought now to be briefly considered. It is developed out of the frontal process and the parts designated as nasal processes (figs. 286, 288, and 289), these becoming elevated more and more above the level of the surrounding parts. At first broad and bulky, the nose later becomes thinner and longer and acquires characteristic forms. The nostrils, which at their formation are far apart, come together in the median plane. Whereas the distance in an embryo five weeks old is, as HIS has shown by measurements, 1·7 mm., it has become reduced in an embryo seven weeks old to 1·2 mm., and in one somewhat older to 0·8 mm. The median frontal process is correspondingly reduced in thickness and furnishes the nasal septum.

SUMMARY.

1. The organ of smell is developed out of two pit-like depressions of the outer germ-layer, which are formed on the frontal process at a considerable distance from each other.

2. At a later stage the pits are united with the angle of the oral cavity by means of the nasal grooves.

3. The inner and outer margins of the olfactory pits and the nasal grooves project out as ridges and constitute the inner and outer nasal processes.

4. By fusion of the margins of the nasal grooves the organ of smell is converted into two nasal passages, which open out on the frontal process by means of the external nares and on the roof of the primitive oral cavity a little back of the upper lip by means of the internal nares.

5. The internal nares afterwards become fissure-like and move nearer together, owing to the nasal septum becoming thinner and growing downward somewhat into the primitive oral cavity.

6. The upper part of the primitive oral cavity shares in the formation of the organ of smell and serves for the increase of its respiratory region, since horizontal ridges (the palatal processes) grow inward from the maxillary processes toward the lower margin of the nasal septum, with which they fuse, and produce the hard and soft palate.

7. In the organ of smell a further enlargement of the spaces serving for respiratory purposes is produced by

- (*a*) The formation of folds of its mucous membrane, by which the turbinated processes arise;
- (*b*) Evaginations of its mucous membrane into the adjacent parts of the cartilaginous and bony cephalic skeleton (formation of the "cells" in the cribriform plate, the frontal and sphenoidal sinuses, and the antrum of HIGHMORE).

8. In human embryos there is early formed in the olfactory pit a special depression of the outer germ-layer as fundament of the organ of JACOBSON, which receives a special branch of the olfactory nerve.

9. JACOBSON'S organ comes to lie at the base of the nasal septum remote from the olfactory region.

10. The ducts of STENSON in many Mammals and the canales incisivi in Man are preserved as remnants of the so-called palatal fissures—the original fissure-like communications between nasal cavities and secondary oral cavity.

III. The Development of the Skin and its Accessory Organs.

Having now become acquainted with the physiologically more important functions of the outer germ-layer,—which consist in the production of the nervous system and the sensory organs,—I give a short survey of the changes which take place in the remaining part, which is now designated as primitive epidermis (Hornblatt). This furnishes the whole outer skin of the body or epidermis and the numerous and various organs that are differentiated out of it, such as the nails, the hair, and the sweat-, sebaceous, and milk-glands.

(*a*) *The Skin.*

The *epidermis* of Man is, according to the statements of KÖLLIKER, very thin during the first two months of development, and consists of only two single layers of epithelial cells. Of these the superficial layer exhibits flattened, transparent, hexagonal elements; the deeper one, on the contrary, consists of smaller cells; so that already there is indicated by this a differentiation into a corneous and a mucous layer. Even now, too, a detachment of epidermal cells begins to manifest itself. For the outer cell-layer is soon found to be in process of decay, with obliterated cell-contours and indistinct nuclei, while a supplementary layer arises beneath it. In many Mammals the dying layer of cells is detached as a continuous sheet and then constitutes for a time a kind of envelope around the whole embryo, to which WELCKER has given the name *epitrichium*, because the outgrowing hairs are developed beneath it.

From the middle of embryonic life onward both layers of the epidermis become thicker and the outermost of them contains cornified scales, the nuclei of which have degenerated. From this time onward a more extensive desquamation takes place at the surface, while the loss is made good by cell-divisions in the mucous layer and by the metamorphosis of these products of division into cornified cells. In consequence of this the surface of the embryo becomes up to the time of birth more and more covered with a yellowish-white, greasy mass—the *smegma embryonum* or *vernix caseosa*. This consists of a mixture of detached epidermal scales and of sebaceous secretions, which have been produced by the dermal glands that have arisen meantime. It forms a thick layer, especially on the flexor-side of the joints, on the sole of the foot, the palm of the hand, and on the head. Detached portions of it get into the amniotic fluid and make it turbid. Finally these, as well as some of the detached downy hairs, may be swallowed by the embryo with the amniotic fluid, and thus become a component of the meconium accumulated in the intestine.

The epidermis constitutes only one component of the skin of the adult or of the integument ; the other and more voluminous part—the *derma* or *corium*—is produced by the mesenchyme. The same thing takes place here as in the case of the other membranes and organs of the body. *The epithelial layers derived from the primary germ-layers enter into close relationship with the mesenchyme*, since they acquire from the latter a connective-tissue foundation that serves for their mechanical support and nutrition. Just as the inner germ-layer unites with the intermediate layer to form the mucous membrane of the alimentary canal, as the epithelium of the auditory vesicle with the adjacent connective substance to form the membranous labyrinth, and as the epithelial optic vesicle with the choroid and sclera to form the eyeball, so here also the epidermis unites with the corium to constitute the integument.

During the first months the corium forms in Man a layer of closely packed, spindle-shaped cells, and is delimited from the epidermis by a delicate, structureless, smooth-surfaced, bounding membrane (basement membrane), such as exists permanently in the case of the lower Vertebrates. In the third month it is differentiated into the corium proper and the looser subcutaneous tissue, in which there are soon developed clusters of fat cells. From the middle of pregnancy onward the latter so increase in number that the subcutaneous tissue soon becomes a layer of fat covering the whole body. At this time the smooth contour between epidermis and corium is lost, owing to the development on the surface of the latter of small papillæ, which grow into the mucous layer and produce the *corpus papillare of the skin.* The papillæ serve partly for the reception of loops of capillary blood-vessels, and thus effect a better nutrition of the mucous layer ; in part they receive the terminations of tactile nerves (tactile corpuscles), and thus are divided into vascular papillæ and nervous papillæ.

The skin of Vertebrates attains a higher degree of development in consequence of processes similar to those described for the intestinal canal. *The epidermis increases its surface outward by the formation of folds, inward by invaginations.* Because the evaginated and invaginated parts at the same time alter in many ways their histological peculiarities, there arises a large number of organs of different kinds, which are developed in different ways in the separate classes of Vertebrates and which preëminently determine the external appearance of the animals.

As external processes arise the dermal teeth, and scales, the feathers, hair, and nails. As invaginations of the epidermis are developed the sweat-, sebaceous, and milk-glands. We will begin with the former, and, not to go too far into details, will limit ourselves to the organs of the skin in Mammals.

(*b*) *The Hair.*

The most characteristic epidermoidal structures of Mammals and Man are the *hairs.* One can distinguish two modifications in the method of their development. The ordinary method of development is that which is known in Man. In this case, at the end of the third embryonic month, the mucous layer grows at certain places and forms small solid plugs, the *hair-germs*, which sink into the underlying corium (fig. 292 *B hk*). By afterwards elongating and becoming thickened at the deep end they assume the shape of a flask. Then there ensues a process similar to that which takes place upon the formation of the teeth. At the bottom of the epithelial plug the adjacent corium grows and forms a richly cellular nodule (*pa*), which grows into the epithelial tissue and is the fundament of the connective-tissue *hair-papillæ*, which is early provided with loops of blood-vessels. Around the whole ingrowing germ of the hair the surrounding parts of the corium are afterwards more and more distinctly arranged into special courses of fibres—some of which run lengthwise, others in a circular manner—and constitute a special, vascular, nutritive envelope, the *hair-follicle* (fig. 292 *C*, *D*, *hb*).

A somewhat different method of hair-formation has been observed by Reissner, Goette, and Feiertag in certain Mammals.

In these the first impulse to the formation of the fundament of a hair is produced by a limited cell-growth of the corium immediately below the epidermis. It produces a small elevation (fig. 292 *A*), which is simply the hair-papilla itself, projecting into the epidermis. Then the papilla is forced farther and farther away from the surface of the skin by the growth of the epidermal cells that cover it, and at last is found far removed from its place of origin and at the deep, somewhat thickened end of a long epithelial plug.

The final result is therefore the same in both cases, only the time of the formation of the first fundament of the papilla and of the epithelial plug is different. In the latter case the papilla arises at the surface of the skin and is forced down by a plug-like epithelial growth; in the former the epithelial plug first sinks into the underlying tissue and then at its deep end the hair-papilla is formed by a growth of the corium.

The question arises, Which of these two methods of development is to be considered the more primitive? In my opinion it is the *formation of the hair-papilla at the surface of the skin.* For this is unquestionably the simpler and less complete condition, from which the latter is derivable and through which it is explainable. The hairs sink into the underlying tissue for the purpose of better nourishment and attachment. A parallel is furnished by the development of the teeth. In the Selachians the latter arise (so far as they are developed as protective structures in the skin) from papillæ which grow from the corium into the epidermis; in Teleosts and Amphibia, on the contrary, the teeth, which are found distributed over extensive areas in the oral mucous membrane, are established deep down in that membrane, for epithelial growths in the form of plugs first sink down into the connective tissue, and it is only subsequently that the dental papillæ are formed by a process of growth in the connective tissue at the bottom of the epithelial downgrowth.

Let us return after this comparison to the further development of the hair; this takes place in the same manner in both the cases distinguished above. The epithelial cells which cover the papillæ multiply and are differentiated into two parts (fig. 292 *C*); first, into cells that are more remote from the papillæ, that become spindle-shaped and united into a small cone, and that by cornification produce the first point of the hair (*ha*), and secondly into cells which immediately invest the papilla, remain protoplasmic, and constitute the matrix—the hair-bulb (*hz*)—by means of which the further growth of the hair takes place. The cells of the hair-bulb, which rapidly increase by division, are added below to the first-formed part of the hair, and by cornification contribute to its elongation.

The hair in process of development on the papilla at first lies wholly concealed in the skin and is enveloped on all sides by cells of the epithelial plug, at the bottom of which the first trace of it was formed. From this investment are formed the *outer and the inner sheaths of the root* (fig. 292 *C* and *D aw* and *iw*). Of these the outer (*aw*) consists of small protoplasmic cells and is continuous externally with the mucous layer of the epidermis (*schl*), internally with the hair-bulb (*hz*). The cells in the inner sheath of the root (*iw*) assume a flattened form and become cornified.

In consequence of the growth which proceeds from the bulb the hairs are gradually shoved up toward the surface of the epidermis, and at the end of the fifth month in the case of Man begin to break forth to the outside (fig. 292 *D ha'*). They protrude more and more above the surface of the skin, even in the embryo, and constitute at many places of the skin, especially on the head, a rather thick covering. On account of their minute size and fineness, and because they fall out soon after birth, they are called the *downy hair or lanugo*.

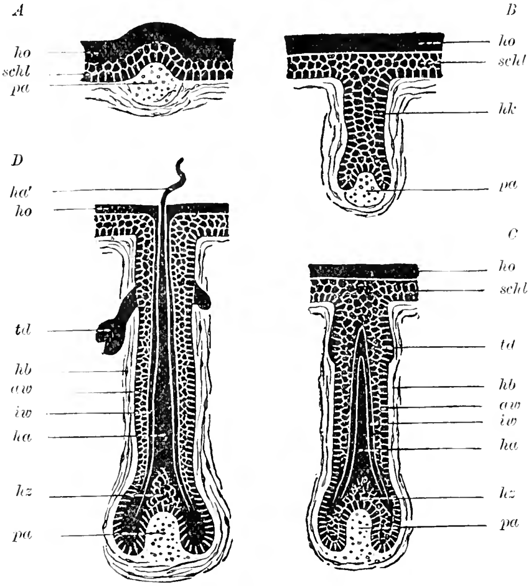

Fig. 292 *A*—*D*.—Four diagrams of the development of the hair. *A*, Development of the hair-papilla on the free surface of the skin, as it occurs, according to GOETTE, in many Mammals. *B*, *C*, *D*, Three different stages of the development of the hair in human embryos.

ho, Corneous layer of the epidermis; *schl*, mucous layer; *pa*, hair-papilla; *hk*, germ of hair; *hz*, bulb of hair; *ha*, young hair; *ha'*, tip of the hair protruding from the hair-follicle; *aw*, *iw*, outer and inner sheath of the root of the hair; *hb*, hair-follicle; *td*, sebaceous gland.

Each hair is a transitory structure of short duration. After a time it falls out and is replaced by a new one. This process begins even during embryonic life. The hairs that fall off get into the amniotic fluid, and since with this fluid they are swallowed by the embryo, they form one of the components of the meconium accumulated in the intestinal canal. A more extensive change takes place in Man soon after birth with the shedding of the downy hair, which is replaced on many parts of the body by a more vigorous growth of hair. In Mammals the shedding of the old and the formation of new hair exhibits a certain periodicity, which is dependent on the warmer and colder periods of the year. Thus they develop a summer and a winter coat. Even in Man the shedding of the hair is influenced, although less noticeably, by the time of year.

The falling off of the hair is initiated by changes in the part resting on the papilla and called the bulb. The cell-multiplication, by means of which the addition of new corneous substance takes place, ceases; the falling hair becomes detached from its matrix and its deep end looks as though it were split into shreds; but it is still retained in the hair-follicle by its closely investing sheath, until it is forcibly removed or is crowded out by the *supplementary hair* that takes its place.

The opinions of investigators still differ concerning the *manner in which the supplementary hairs are developed.* An especial subject of controversy is the point whether the young hair is formed from an entirely new papilla (STIEDA, FEIERTAG) or from the old one (LANGER, v. EBNER), or whether both methods occur (KÖLLIKER, UNNA). It seems to me that the first view is the correct one, and that the shedding of the hairs is due to the *atrophy of their papillæ.* During this slowly occurring process of degeneration, perhaps even before it begins, the substitution is initiated by the occurrence of an active cell-proliferation at a place in the outer sheath of the root—which indeed consists of cells rich in protoplasm—and by the formation of a new plug, which grows out deeper into the derma from the bottom of the fundament of the old hair. At the blind [deep] end of this *secondary hair-germ* there is then developed from the derma a new papilla, upon which is formed the new hair and its sheaths alongside of and below the old one, in the manner previously described. When it begins to increase in length, it presses against the old hair lying above it, crowds the latter out of its sheaths, until it falls off, and finally itself takes the place of it.

According to this account there would be a certain similarity between the shedding of the hair and that of the teeth, inasmuch as in both cases secondary epithelial processes, from which the new tooth- or hair-papilla begins, arise from the primary fundament, and inasmuch as the new structures by their growth displace the old.

In addition to the development of hairs from old fundaments, a second method of formation, which one might designate as direct or primary, is maintained by many writers (Goette, Kölliker). It is assumed that even after birth, both in the case of Man and other Mammals, hair-germs are formed directly from the mucous membrane of the epidermis, in the same manner as in the embryo. In how far, at what regions, and up to what age such a *direct formation of hair* takes place, demands still more detailed and exhaustive investigation.

(c) *The Nails.*

A second organ resulting from a cornification of the epidermis is the *nail*, which corresponds in a comparative-anatomical way to the claw- and hoof-like structures of other Mammals. In human embryos only seven weeks old there appear proliferations of the epidermis at the ends of the fingers, which are noticeably short and thick, and likewise at the ends of the toes, which are always less developed than the fingers. In consequence of the proliferations there arise from the loose epidermal cells complicated claw-like appendages, which have been described by Hensen as *predecessors of the nails* or *primitive nails.*

In somewhat older embryos, from the ninth to the twelfth week, Zander found the epidermal growth marked off from its surroundings by a ring-like depression. The growth consists of a single layer of cylindrical cells with large nuclei lying on the side toward the derma and corresponding to the rete Malpighii, of two or three layers of polygonal spinous cells, and of a corneous layer.

The territory thus distinguished by a depression and by an altered condition of the cells Zander calls the *primary basis of the nail* (Nagelgrund), and describes it as occupying a greater part of the dorsal, but also a smaller part of the ventral surface of the terminal segment. He infers from this that the nails in Man originally had, like the claws of the lower Vertebrates, a terminal position on the toes and fingers, and that they have secondarily migrated on to the dorsal surface. Thus he explains the fact that the region of the nail is supplied with the ventral nerves of the fingers.

Gegenbaur subscribes to Zander's view of the terminal position of the fundament of the nail, but, supported by the investigations of Boas, opposes Zander's assumption of a migration of the fundament of the nail dorsally. He distinguishes in the development of nails and claws two parts (fig. 293), the dorsally located firm *nail-*

plate (*np*) and the *plantar horn* (Sohlenhorn, *sh*) connected with it ventrally. Of these the latter arises from the smaller ventral surface of the primary basis of the nail. In unguiculate and ungulate Vertebrates it (fig. 294 *sh*) is developed to a great extent; in Man it atrophies, and is recognisable only in an exceedingly reduced condition as *nail-welt.* By this term is meant the welt-like thickening of the epidermis which forms the transition from the bed of the nail to the corrugated skin of the ball of the finger. The nail-plate, on the contrary, is from the beginning exclusively a product of the dorsal surface of the basis of the nail. There is therefore neither in Man nor in other Mammals a dorsal migration of the terminal fundament of the nail, but only a degeneration of its ventral portion, which otherwise furnishes a more complete plantar horn.

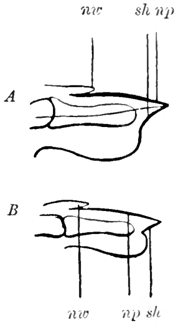

Fig. 293.

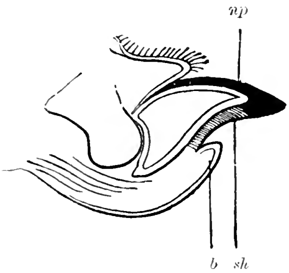

Fig. 294.

Fig. 293.—*A*, Longitudinal section through the toe of a Cercopithecus. *B*, Longitudinal section through the second finger of Macacus ater. After Gegenbaur.
np, Nail-plate; *sh*, plantar horn (Sohlenhorn); *nw*, nail-wall.

Fig. 294.—Section through a Dog's toe. After Gegenbaur.
np, Nail-plate; *sh*, plantar horn; *b*, ball of toe.

So far as regards the particular events in the development of the nail-plate, the structure is demonstrable in human embryos four months old as a thin flat layer of cornified, closely united cells on the dorsal surface of the primary basis of the nail or the bed of the nail. It is produced by the mucous layer upon which it immediately lies, but continues for a time to be covered by the thin corneous layer that is present at all points of the epidermis. This investment—Unna's *eponychium*—is not lost until the fifth month. However, notwithstanding their investment, the nails are easily recognisable some weeks before this from their whiteness, in distinction from the reddish or dark red color of the surrounding skin, Owing to the addition of new cells from the mucous membrane, both from below and from the posterior margin, the nail-plate grows—it becomes thickened and increased in surface extent. It is now pushed forward from behind over the bed of the nail, and at the seventh month its free margin begins to project beyond the latter.

With this the nail has acquired essentially the appearance and condition which it has in the adult. In new-born infants it possesses a margin which projects far over the ball of the finger, and which—because it was formed at an early embryonic period—is both much thinner and also narrower than the part formed later, which rests on the bed of the nail. This margin is therefore detached soon after birth.

(*d*) *The Glands of the Skin.*

The glandular structures of the epidermis, which are established by invagination, are of three kinds: sebaceous, sweat-, and milk-glands. They all arise as proliferations of the mucous layer which grow down as solid plugs into the derma, and then undergo further development either according to the tubular or the alveolar type.

The *sweat-glands* and the *ear-wax glands* are developed on the tubular plan. They begin in the fifth month to penetrate from the mucous membrane into the corium; in the seventh month they acquire a small lumen, take a winding course in consequence of increased growth in length, and become coiled especially at their deep ends, thereby giving rise to the first fundament of the glomerulus.

Sebaceous glands and *milk-glands are alveolar structures.* The former are either developed directly from the epidermis, as, for example, at the edges of the lips, on the prepuce and on the glans penis, or they are in close connection with the hairs, which is the ordinary condition. In the latter case they are formed as solid thickenings of the outer sheath of the root of the hair near the orifice of the follicle, even before the hairs are completely developed (fig. 292 *C*, *D*, *td*); at first they have the form of a flask, then they send out a few lateral buds, which develop club-shaped enlargements at their ends. The glands acquire cavities by the fatty degeneration and disintegration of the interior cells, which are eliminated as a secretion.

The *development of the milk-glands*, which are more voluminous organs entrusted with an important function and peculiar to the class Mammalia, is of greater interest. Of the numerous works that have appeared concerning them, the comparative-anatomical investigations of Gegenbaur especially have led to valuable results.

I present at the very beginning of the discussion the following proposition, which is of importance in interpreting the conditions found: *each milk-gland in Man is not a simple organ, like an ear-gland or a submaxillary salivary gland, with a simple outlet, but a great glandular complex.* Its earliest fundament has been observed in the human embryo at the end of the second month as a considerable thickening of the epidermis (fig. 295) upon the right and left sides of the breast. It has arisen as the result of a special proliferation of the mucous layer, which has sunk into the derma in the form of a hemispherical knob (*df*). But modifications arise afterwards in the corneous layer also, by its becoming thickened and projecting as a corneous plug into the proliferation of the mucous layer. Ordinarily there is found a small depression (*g*) at the middle of the whole epithelial fundament.

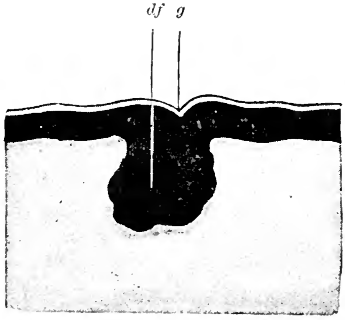

Fig. 295.—**Section through the fundament of the milk-gland of a female human embryo 10 cm. long,** after Huss.
df, Fundament of the glandular area ; *g*, small depression at its surface.

The proliferation of the epidermis that first appears is not precisely, as assumed by Rein, the first fundament of the glandular parenchyma ; it therefore does not correspond to the epithelial plugs which sink into the derma in the development of the sweat and sebaceous glands, because the further course of development and especially comparative-anatomical studies show, that by the thickening of the epidermis there is only an early delimitation of a tract of the skin, which is subsequently metamorphosed into the nipple-area and papilla, and from the floor of which the *separate* milk-producing glands at length sprout forth.

The correctness of this view is shown by the following changes : In older embryos the lens-shaped thickening produced by the proliferation of the epidermis has increased at the periphery and has thereby become flattened (fig. 296 *df*). At the same time it is more sharply defined at the surface, owing to the derma becoming thickened and elevated into a wall (*dw*)—the cutis-wall. Therefore the whole fundament now has the form of a shallow depression (*df*) of the skin, for which the name *glandular area* is very appropriate. For there early grow out from its mucous layer into the derma solid buds (*dg*), just as at other places the sebaceous glands arise from the epidermis. In the seventh month they are already well developed, and radiate out below and laterally from the pit-like depression. Their number increases up to the time of birth, and the larger ones become covered with solid lateral buds (*db*). Each sprout is the fundament of a milk-producing gland, which opens out on the glandular area (*df*) by means of a special orifice; each is morphologically comparable with a sebaceous gland, although its function has become different.

The name glandular area is also a happily selected one because it presents a point of comparison with the primitive conditions of the Monotremes. For in these animals one does not find, as in the higher Mammals, a sharply differentiated single complex of milk-glands, but instead a somewhat depressed area of the skin, even provided with small hairs, over which are distributed single small glands, the secretion of which is licked up with the tongue by the young, which are born in a very immature state.

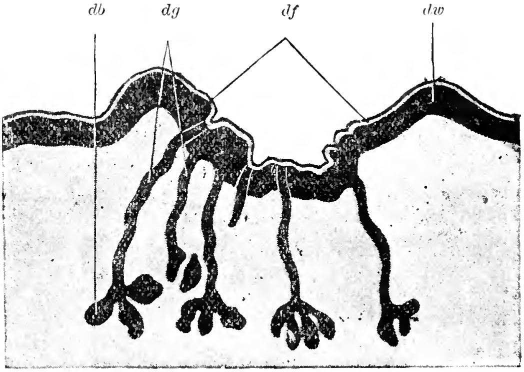

Fig. 296.—Section through the fundament of the milk-gland of a female human embryo 32 cm. long, after Huss.
df, Glandular area; *dw*, gland-wall; *dg*, duct of gland; *db*, vesicle of gland.

In the remaining Mammals the glands, in the former case opening separately upon the area, are united into a single organ, which better serves the young in sucking, namely a *papilla* [*nipple*] or *teat*, which encloses all the outlets of the glands and is grasped by the mouth of the suckling. In Man their development begins after birth. The glandular area, which is encircled by the cutis-wall and which before birth was depressed into a pit, now becomes flattened until it lies in the same niveau with the surrounding skin. It is distinguished from the latter by its redder color, which is due to its greater vascularity and the thinner condition of its epidermis. Then during the first years after birth the middle of the glandular area, together with the outlets (ductus lactiferi), which there open out close to one another, is raised up and becomes the nipple, in the derma of which non-striate muscle-fibres are formed in great numbers; the remaining part of the area as far as the cutis-wall becomes the areola mammæ. The metamorphosis takes place somewhat earlier in the female than in the male.

Soon after birth alterations take place in the still feebly developed glandular tissue. There occurs a transitory swelling of the pectoral glands accompanied with increased blood-pressure, and it becomes possible to press out of the gland a small quantity of a milky fluid, the so-called witches' milk. According to Kölliker its formation is due to the originally solid ducts of the glands acquiring at this time a lumen by the fatty degeneration of the central cells, which are dissolved, and, suspended in a fluid, are discharged from the ducts. According to the investigations of Barfurth, on the contrary, the so-called witches' milk of infants is the product of a genuine transitory secretion, and is like the real milk of the mother both in its morphological and chemical components.

After birth great differences arise between the two sexes in the condition of the milk-glands. Whereas in the male the glandular parenchyma remains stationary in its development, in the female it begins to increase, especially at the time of sexual maturity and still more after the beginning of pregnancy. From the first-formed ducts of the glands there grow out numerous lateral, hollow branches, which become covered with hollow vesicular glands (alveoli) lined with a single layer of cylindrical epithelium. At the same time there are developed in the connective tissue, between the separate lobules of the gland, numerous islands of fat-cells. In consequence the region at which the complex of milk-glands has been formed swells into a more or less prominent elevation, the mamma.

Summary.

1. The development of the hair is inaugurated in human embryos by the growing down of processes of the mucous layer of the epidermis—the hair-germs—into the underlying derma.

2. At the deep end of the hair-germ the vascular hair-papilla is begun by a growth of connective tissue.

3. The epithelial hair-germ is differentiated into :—
   (*a*) A young hair, by the cornification of a part of the cells;
   (*b*) An actively growing cell-layer situated between the shaft of the hair and the papilla,—the bulb,—which furnishes the material for the growth of the hair;
   (*c*) The outer and the inner sheaths of the root.

4. Around the epithelial part of the fundament of the hair there is formed from the surrounding connective tissue the hair-follicle.

5. The nails in Man and the claws in other Mammals are developed from a dorsal fundament—the nail-plate—and a ventral fundament—the plantar horn.

6. The plantar horn in Man is reduced to the nail-welt.

7. The thin nail-plate which is formed at first is for a time covered with a layer of cornified cells, the eponychium, which in Man is shed in the fifth month.

8. The milk-gland is a complex of alveolar glands.

9. At first there arises a thickening of the mucous layer of the epidermis, which is converted into the glandular area that is afterwards marked off from the surrounding parts by a wall and becomes somewhat depressed.

10. From the bottom of the glandular area there grow forth in great numbers the fundaments of alveolar glands.

11. After birth the glandular area, embracing the excretory ducts of the glands, is elevated above the surface of the skin, and converted into the nipple and the areola mammæ.

12. After birth there is a transitory secretion of a small quantity of milk-like fluid—the witches' milk.

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CHAPTER XVII.

THE ORGANS OF THE INTERMEDIATE LAYER OR MESENCHYME.

The grounds which made it appear necessary to distinguish in addition to the four epithelial germ-layers a special intermediate layer or mesenchyme have already been given in the first part of this text-book. This distinction is also warranted by the further progress of development. For all the various tissues and organs which are derived in many ways from the intermediate layer allow, even subsequently, a recognition of their close relationship. Histologically the various kinds of connective substance have been for a long time considered as constituting a *single family of tissues.*

It will be my endeavor to emphasise the relationship of the organs of the intermediate layer, and whatever is characteristic of them from a morphological point of view, more than has been hitherto customary in text-books, and to do the same in a formal way by embracing these organs in a chapter by themselves and discussing them apart from the organs of the inner, middle, and outer germ-layers.

It is the original province of the intermediate layer to form a packing and sustentative substance between the epithelial layers, a fact which stands out with the greatest distinctness particularly in the lower groups, as for example in the Cœlenterates. It is therefore closely dependent upon the epithelial layers in the matter of its distribution. When the germ-layers are raised up into folds, it penetrates between the layers of the fold as a sustentative lamella; when the germ-layers are folded inwards, it receives the parts that are being differentiated—as for example in the Vertebrates, the neural tube, the masses of the transversely striped muscles, the secretory parenchyma of glands, the optic cups, and the auditory vesicles—and provides them with a special envelopment that adjusts itself to them (the membranes of the brain, the perimysium, and the connective-tissue substance of the glands). In consequence of this the intermediate layer, in the same proportion as the germ-layers become more fully organised, becomes itself converted into an extraordinarily complicated framework, and resolved into the most divergent organs, by the formation of evaginations and invaginations and the constricting off of parts.

The form of the intermediate layer thus produced is of a secondary nature, for it is dependent upon the metamorphosis of the germ-layers, with which it is most intimately connected. But in addition, the intermediate layer, owing to its *own* great power of metamorphosis, acquires in all higher organisms, particularly in the Vertebrates, an intricate structure, especially *in the way of histological differentiation or metamorphosis.* In this way it gives rise to a long series of various organs—the cartilaginous and bony skeletal parts, the fasciæ, aponeuroses, and tendons, the blood-vessels and lymphatic glands, etc.

It is therefore fitting to enter here somewhat more particularly upon a discussion of the *principle of histological differentiation*, and especially to inquire in what manner it is concerned in the origin of organs differentiated in the mesenchyme.

The most primitive and simplest form of mesenchyme is gelatinous tissue. Not only does it predominate in the lower groups of animals, but it is also the first to be developed in all Vertebrates, out of the embryonic cells of the intermediate layer, and is here the forerunner and the foundation of all the remaining forms of sustentative substance.

In a homogeneous, soft, quite transparent matrix, which chemically considered contains mucous substance or mucin, and therefore does not swell in warm water or acetic acid, there lie at short and regular intervals from one another numerous cells, which send out in all directions abundantly branched protoplasmic processes and by means of these are joined to each other in a network.

In the lower Vertebrates the gelatinous tissue persists at many places, even when the animals are fully grown; in Man and other Mammals it early disappears, being converted into two higher forms of connective substance, either into *fibrillar connective tissue* or into *cartilaginous tissue.* The first-named arises in the gelatinous matrix by the differentiation of connective-tissue fibres on the part of the cells, which are sometimes close together, sometimes widely scattered. These fibres consist of collagen and upon boiling produce glue. At first sparsely represented, these glue-producing fibres continually increase in volume in older animals. Thus transitional forms, which are designated as fœtal or immature connective tissue, lead from gelatinous tissue to mature connective tissue, which consists almost exclusively of fibres and the cells which have produced them. This is capable of a great variety of uses in the organism, according as its fibres cross one another in various directions without order, or are arranged parallel to one another and grouped into special cords and strands. Thus, in connection with other parts derived from the germ-layers, it gives rise to a great variety of organs. In some places it forms the foundation for epithelial layers of great superficial extent; together with them it produces the integument, composed of epidermis, corium, and subcutaneous connective tissue, and the various mucous and serous membranes; in others it unites with masses of transversely striped muscle, and arranges itself under the influence of their traction into parallel bundles of tense fibres, furnishing tendons and aponeuroses. Again at other places it takes the form of firm sheets of connective tissue, which serve for the separation or enveloping of masses of muscle, the intermuscular ligaments and the fasciæ of muscles.

The second metamorphic product of the primary mesenchyme, cartilage, is developed in the following manner: At certain places the embryonic gelatinous tissue acquires as a result of proliferation a greater number of cells, and the cells secrete between them a cartilaginous matrix, chondrin. The parts which have resulted from the process of chondrification exceed in rigidity to a considerable extent the remaining kinds of sustentative substance, the gelatinous and the glue-producing intermediate tissue; they are sharply differentiated from their softer surroundings, and become adapted, in consequence of their peculiar physical properties, to the assumption of special functions. Cartilage serves in part to keep canals open (cartilage of the larynx and bronchial tree), in part for the protection of vital organs, around which they form a firm envelope (cartilaginous cranium, capsule of the labyrinth, vertebral canal, etc.), and in part for the support of structures projecting from the surface of the body (cartilage of the limbs, branchial rays, etc.). At the same time they afford firm points of attachment for the masses of muscle imbedded in the mesenchyme, neighboring parts of the muscles entering into firm union with them. In this manner there has arisen through histological metamorphosis a differentiated skeletal apparatus, which increases in complication in the same proportion as it acquires more manifold relations with the musculature.

Cartilaginous and connective tissues, finally, are capable of a further histological metamorphosis, since the last form of sustentative substance, *osseous tissue*, is developed from them in connection with the secretion of salts of lime. *There are therefore bones that have arisen from a cartilaginous matrix and others from one of connective tissue.* With the appearance of bone, the skeletal apparatus of Vertebrates has reached its highest perfection.

Even if the mesenchyme has by these processes experienced an extraordinarily high degree of differentiation and a great diversity of form, the histological processes of differentiation which take place in it are nevertheless not yet exhausted. In the gelatinous or connective-tissue matrix canals and spaces arise in which blood and lymph move in accomplishing their function of intermediating in the metastasis of the organism, not only conveying the nutritive fluids to the individual organs, but also conducting away both the substances which—owing to the chemical processes in the tissues—have become useless and the superfluous fluids. Out of these first beginnings arises a very complicated organic apparatus. The larger cavities constitute arteries and veins, and acquire peculiarly constructed thick walls, provided with non-striate muscle-cells and elastic fibres, in which three different layers can be distinguished as tunica intima, media, and adventitia. A small part of the blood-passages, especially distinguished by an abundance of muscle-cells, is converted into a propulsive apparatus for the fluid—the heart. The elementary corpuscles that circulate in the currents of the fluid, the blood-cells and lymph-cells, demand renewal the more frequently the more complex the metastasis becomes. This leads to the formation of special breeding places, as it were, for the lymph-corpuscles. In the course of the lymphatic vessels and spaces there takes place at certain points in the connective tissue an especially active proliferation of cells. The substance of the connective-tissue framework assumes here the special modification of reticular or adenoid tissue. The surplus of cells produced enters into the lymphatic current as it sweeps past. According as these lymphoid organs exhibit a simple or a complicated structure, they are distinguished as solitary or aggregated follicles, as lymphatic ganglia and spleen.

Finally there are formed at very many places in the intermediate layer, as especially in the whole course of the intestinal canal, organic [non-striate] muscles.

After this brief survey of the processes of differentiation in the intermediate layer, which are primarily of an histological nature, I turn to the special history of the development of the organs which arise from it, the blood-vessel and skeletal systems.

I. The Development of the Blood-vessel System.

The very first fundament of the blood-vessels and the blood has already been treated of in the first part of this text-book. We will therefore here concern ourselves with the special conditions of the vascular system, with the origin of the heart and chief blood-vessels, and with the special forms which the circulation presents in the various stages of development, and which are dependent on the formation of the fœtal membranes. In this I shall treat separately, both for the heart and for the rest of the vascular system, the first fundamental processes of development and the succeeding alterations, from which the ultimate condition is finally evolved.

A. The first Developmental Conditions of the Vascular System.

(a) Of the Heart.

The vascular system of Vertebrates can be referred back to a very simple fundamental form—namely, to two blood-vessel trunks—of which the one runs above and the other below the intestine in the direction of the longitudinal axis of the body. The dorsal trunk, the aorta, lies in the attachment of the dorsal mesentery, by means of which the intestine is connected to the vertebral column; the other trunk, on the contrary, is imbedded in the ventral mesentery, as far, at least, as such a structure is ever established in the Vertebrates; it is almost completely metamorphosed into the heart. The latter is therefore nothing else than a peculiarly developed part of a main blood-vessel provided with especially strong muscular walls.

In the first fundament of the heart there are two different types to be distinguished, one of which is present in Selachians, Ganoids, Amphibia, and Cyclostomes, the other in Bony Fishes and the higher Vertebrates—Reptiles, Birds, and Mammals.

In the description of the *first type* I select as an example the development of the heart in the Amphibia, concerning which a detailed account has very recently been published by Rabl.

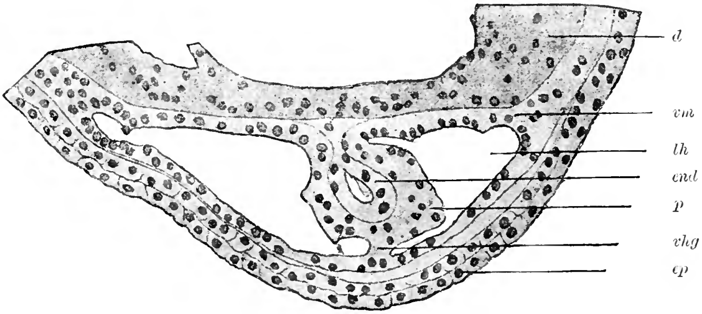

Fig. 297.—Cross section through the region of the heart of an embryo of Salamandra maculosa, in which the fourth visceral arch is indicated, after Rabl.

d, Epithelium of the intestine; *vm*, visceral middle layer; *ep*, epidermis; *lh*, anterior part of the body-cavity (pericardio-thoracic cavity); *end*, endocardium; *p*, pericardium; *vhg*, mesocardium anterius.

In Amphibia the heart is established very far forward in the embryonic body, underneath the pharynx or cavity of the head-gut (figs. 297, 298). The embryonic body-cavity (*lh*) reaches into this region, and in cross sections appears upon both sides of the median plane as a narrow fissure. The lateral halves of the body-cavity are separated from each other by a ventral mesentery (*vhg*), by means of which the under surface of the pharynx is united with the wall of the body. If we examine the ventral mesentery more closely, we observe that in its middle the two mesodermic layers from which it has been developed separate from each other and allow a small cavity (*h*) to appear, the primitive cardiac cavity. This is surrounded by a single layer of cells, which is afterwards developed into the endocardium (*end*).* Outside of the latter the adjacent cells of the middle germ-layer are thickened; they furnish the material out of which the cardiac musculature (the myocardium) and the superficial membrane of the heart (pericardium viscerale) arise. The fundament of the heart is attached above [dorsally] to the pharynx (*d*) and below to the body-wall by the remnant of the mesentery, which persists as a thin membrane. We designate these two parts as the suspensory ligaments of the heart, as back [dorsal] and front [ventral] cardiac mesenteries (*hhg*, *vhg*), or as mesocardium posterius and anterius. At this time there is nothing to be seen of a pericardial sac, unless we should designate as such the anterior [ventral] region of the body-cavity, from which, as the further course of development will show, the pericardium is chiefly derived.

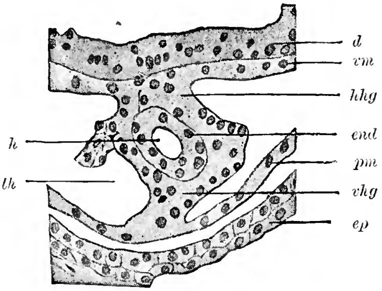

Fig. 298.—Cross section from the same series as that from which fig. 297 was drawn, after Rabl.

d, Epithelium of the intestine ; *vm*, visceral, *pm*, parietal middle layer ; *hhg*, posterior, *vhg*, anterior mesocardium ; *end*, endocardium ; *h*, cavity of the heart ; *lh*, ventral part of the body-cavity ; *ep*, epidermis.

In the second type the heart arises from distinct and widely separated halves, as the conditions in the Chick and the Rabbit most distinctly teach.

In the Chick the first traces of the fundament may be demonstrated at an early period, in embryos with four to six primitive segments. They appear here at a time when the various germ-layers are still spread out flat, at a time when the front part of the embryonic fundament first begins to be elevated as the small cephalic protuberance, and the cephalic portion of the intestine is still in the first phases of development. As has already been stated, the intestinal cavity in the Chick is developed by the folding together and fusion of the intestinal plates [splanchnopleure]. If one examines carefully the ridge of an intestinal fold in the very process of being formed (fig. 299 *A df*), one observes that its visceral middle layer is somewhat thickened, composed of large cells, and separated from the entoblast by a space filled with a jelly-like matrix. In the latter there lie a few isolated cells, which subsequently

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* Relative to the origin of the endothelial sac of the heart, compare the observations given on page 186.

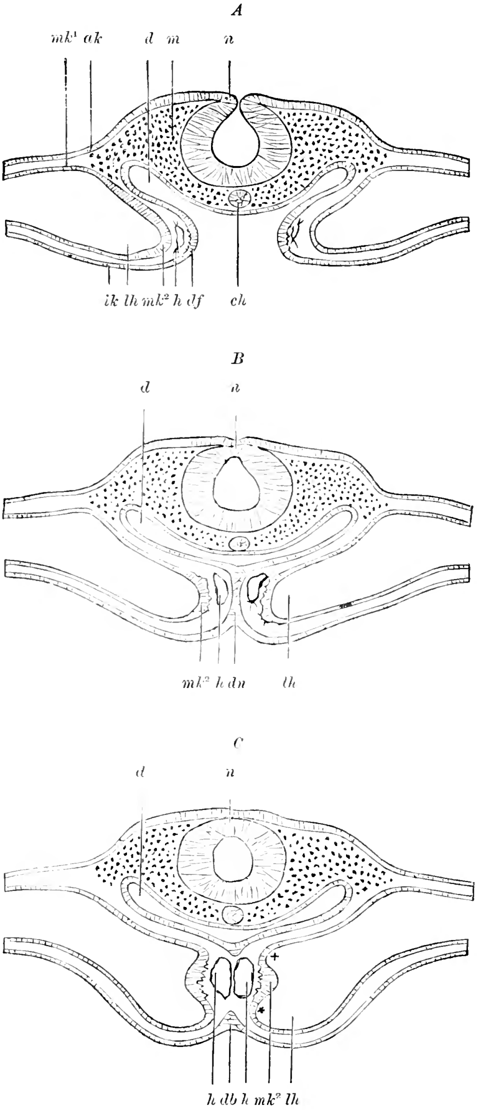

Fig. 299.—Three diagrams to illustrate the formation of the heart in the Chick.

n, Neural tube; *m*, mesenchyma of the head; *d*, intestinal cavity; *df*, folds of the intestinal plate [splanchnopleure], in which the endothelial sacs of the heart are established; *h*, endothelial sac of the heart; *ch*, chorda; *lh*, body-cavity; *ak*, outer, *ik*, inner germ-layer; mk^1, parietal middle layer; mk^2, visceral middle layer, from the thickened portion of which the musculature of the heart is developed; *dn*, intestinal suture, in which the two intestinal folds are fused; *db*, part of the entoblast which has become detached from the epithelium of the cephalic portion of the intestine at the intestinal suture and lies on the yolk; + dorsal mesocardium; * ventral mesocardium.

A, The youngest stage shows the infolding of the splanchnopleure, by means of which the cephalic part of the intestine is formed. In the angles of the intestinal folds the two endothelial sacs of the heart have been established between the inner germ-layer and the visceral middle layer.

B, Somewhat older stage. The two folds (*A df*) have met in the intestinal suture (*dn*), so that the two endothelial sacs of the heart lie close together in the median plane below the head-gut.

C, Oldest stage. The part of the entoblast which lines the head-gut (*d*) has become separated at the intestinal suture (*B dn*) from the remaining part of the entoblast, which (*db*) lies upon the yolk, so that the two endothelial sacs of the heart are in contact; they subsequently fuse. They lie in a cardiac suspensorium formed by the visceral middle layers, the mesocardium, on which one can distinguish an upper [dorsal] and an under part—mesocardium superius (+) and inferius (*). By means of this mesocardium the primitive body-cavity is temporarily divided into two portions.

surround a small cavity, the primitive cardiac cavity (*h*). These cells assume more of an endothelial character. While the intestinal folds grow toward each other, the two endothelial tubes become enlarged and push the thickened part of the visceral middle layer before them, so that the latter forms a low, ridge-like elevation into the primitive body-cavity. In the embryos of higher Vertebrates also, just as in the Amphibia, this stretches forward into the embryonic fundament as far as the last visceral arch, and has here received the special name of neck-cavity or parietal cavity.

In older embryos (fig. 299 *B*) the edges of the two folds have met in the median plane, and consequently the two cardiac tubes have moved close together. A process of fusion then takes place between the corresponding parts of the two intestinal folds.

First the entoblastic layers fuse, and in this way is produced (fig. 299 *B*) beneath the chorda dorsalis (*ch*) the cavity of the head-gut (*d*), which then detaches itself from the remaining part of the entoblast (fig. 299 *C db*); the latter is left lying on the yolk and becomes the yolk-sac. Under the cavity of the head-gut the two cardiac sacs have come close together, so that their cavities are separated from each other by their own endothelial walls only. By the breaking through of these there soon arises from them (*h*) a single cardiac tube. On the side toward the body-cavity this is covered by the visceral middle layer (mk^2), the cells of which are distinguished in the region of the fundament of the heart by their great length and furnish the material for the cardiac musculature, while the inner endothelial membrane becomes only the endocardium.

The whole fundament of the heart lies, as in the Amphibia, in a ventral mesentery, the upper [dorsal] part of which, extending from the heart to the head-gut (fig. 299 *C* +), can here also be called the dorsal suspensory of the heart or mesocardium posterius, and the lower [ventral] part (*) mesocardium anterius. In the Chick, when the cardiac tube begins to be elongated and bent into an S-shaped form, the mesocardium anterius quickly disappears.

Similar conditions are furnished by cross sections through *Rabbit embryos* 8 or 9 days old. In the latter the paired fundaments of the heart are indeed developed still earlier and more distinctly than in the Chick, even at a time when the entoderm is still spread out flat and has not yet begun to be infolded. Upon cross sections one sees (fig. 301), in a small region at some distance from the median plane, the splanchnopleure separated from the somatopleure by a small fissure (*ph*), which is the front end of the primitive body-cavity. At this place the visceral middle layer (*ahh*) is also raised up somewhat from the entoderm (*sw*), so that it causes a projection into the body-cavity (*ph*). Here there is developed between the two layers a small cavity, which is surrounded by an endothelial membrane (*ihh*), the primitive cardiac sac. At their first appearance the halves of the heart lie very far apart. They are to be seen both in the very slightly magnified cross section (fig. 300) and also in the surface view of an embryo Rabbit (fig. 302) at the place indicated by *h*. They afterwards move toward each other in the same manner as in the Chick by the infolding of the splanchnopleure, and come to lie on the under side of the head-gut, where they fuse and are temporarily attached above and below by means of a dorsal and ventral mesentery.

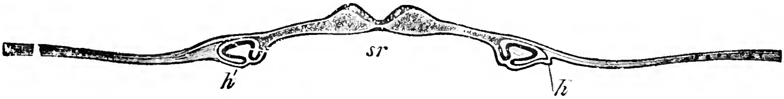

Fig. 300.

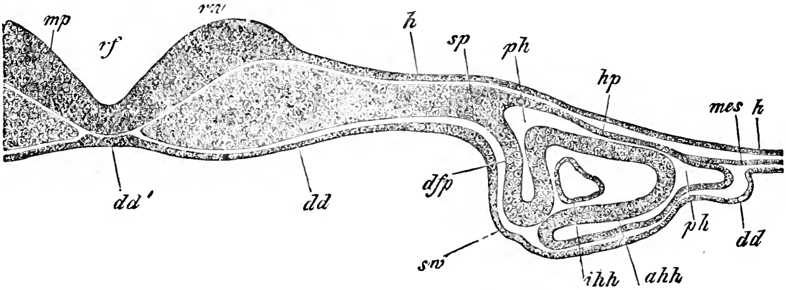

Fig. 301.

Figs. 300, 301.—Cross section through the head of an embryo Rabbit of the same age as that shown in fig. 302. From KÖLLIKER. Fig. 301 is a part of fig. 300 more highly magnified.
Fig. 300.—*h*, *h'*, Fundaments of the heart; *sr*, œsophageal groove.
Fig. 301.—*rf*, Dorsal groove; *mp*, medullary plate; *rw*, medullary ridge; *h*, outer germ-layer; *dd*, inner germ-layer; *dd'*, its chordal thickening; *sp*, undivided middle layer; *hp*, parietal, *dfp*, visceral middle layer; *ph*, pericardial part of the body-cavity; *ahh*, muscular wall of the heart; *ihh*, endothelial layer of the heart; *mes*, lateral undivided part of the middle layer; *sw*, intestinal fold, from which the ventral wall of the pharynx is formed.

Concerning the processes of development just sketched the question may be raised: What relation do the paired and the unpaired fundaments of the heart sustain to each other? It is to be answered to this, *that the unpaired fundament of the heart, which is present in the lower Vertebrates, is to be regarded as the original form. The double* *heart-formation, however aberrant it at first sight appears, can be easily referred back to this.*

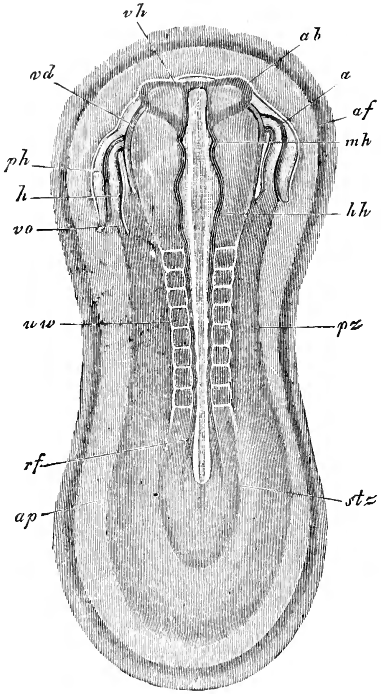

Fig. 302.—Embryo Rabbit of the ninth day, seen from the dorsal side, after Kölliker. Magnified 21 diameters.

The axial (stem-) zone (*stz*) and the parietal zone (*pz*) are to be distinguished. In the former 8 pairs of primitive segments have been formed at the side of the chorda and neural tube.

ap, Area pellucida; *rf*, dorsal groove; *vh*, fore brain; *ab*, optic vesicle; *mh*, mid-brain; *hh*, hind-brain; *uw*, primitive segment; *stz*, axial zone; *pz*, parietal zone; *h*, heart; *ph*, pericardial part of the body-cavity; *vd*, margin of the anterior intestinal portal showing through the overlying structures; *af*, fold of the amnion; *vo*, vena omphalomesenterica.

A single cardiac tube cannot be developed in the higher Vertebrates, because at the time of its formation a head-gut does not yet exist, but only the fundament of it is formed in the still flat entoderm. The parts which will subsequently form the ventral wall of the head-gut, and in which the heart is developed, are still two separated territories; they still lie at some distance from the median plane at the right and at the left. If therefore it is necessary for the heart to be formed at this early period, it must arise in the separated regions, which by the process of infolding are joined into a single ventral tract. The vessel must arise as two parts, which, like the two intestinal folds, subsequently fuse.

Whether the heart is formed in one way or the other, in either case it has for a time the form of a straight sac lying ventral to the head-gut and composed of two tubes one within the other, which are separated by a large space assumably filled with a gelatinous matrix. The inner, endothelial tube becomes the endocardium; the outer tube, which is derived from the visceral middle layer, furnishes the foundation for the myocardium and the pericardial membrane that immediately invests the surface of the heart.

(b) *The First Developmental Conditions of the Large Vessels. Vitelline Circulation, Allantoic and Placental Circulation.*

At both ends, in front and behind, the heart is continuous with the trunks of blood-vessels, which have been established at the same time with it. The anterior or arterial end of the cardiac tube is elongated into an unpaired vessel, the *truncus arteriosus*, which continues the forward course under the head-gut, and is divided in the region of the first visceral arch into two arms, which embrace the head-gut on the right and left and ascend within the arch to the dorsal surface of the embryo. Here they bend around and run backward in the longitudinal axis of the body to the tail-end. These two vessels are the *primitive aortæ* (figs. 107, 116 *ao*); they take their course on either side of the chorda dorsalis, above the entoderm and below the primitive segments. They give off lateral branches, among which the *arteriæ omphalomesentericæ* are in the Amniota distinguished by their great size. These betake themselves to the yolk-sac and conduct the greatest portion of the blood from the two primitive aortæ into the area vasculosa, where it goes through the *vitelline circulation.*

In the Chick, the conditions of which form the basis of the following account (fig. 303), the two vitelline arteries (*R.Of.A*, *L.Of.A*) quit the aortæ at some distance from their tail-ends, and pass out laterally from the embryonic fundament between entoderm and visceral middle layer into the area pellucida, traverse the latter, and distribute themselves in the vascular area. They are here resolved into a fine network of vessels, which lie, as a cross section (fig. 116) shows, in the mesenchyme between the entoderm and the visceral middle layer, and which are sharply bounded at their outer edge (toward the vitelline area) by a large marginal vessel (fig. 303 *S.T*), the sinus terminalis. The latter forms a ring which is everywhere closed, with the exception of a small region which lies in front, at the place where the anterior amniotic sheath has been developed.

From the vascular area the blood is collected into several large venous trunks, by means of which it is conducted back to the heart. From the front part of the marginal sinus it returns in the two *venæ vitellinæ anteriores*, which run in a straight line from in front backwards and also receive lateral branches from the vascular network. From the hind part of the sinus terminalis the blood is taken up by the venæ vitellinæ posteriores, of which the one of the left side is larger than the one of the right; the latter afterwards degenerates more and more. From the sides likewise there come still larger collecting vessels, the venæ vitellinæ laterales. All the vitelline veins of either side now unite in the middle of the embryonic body to form a single large trunk, the *vena omphalo-mesenterica* (*R.Of* and *L.Of*), which enters the posterior end of the heart (*H*).

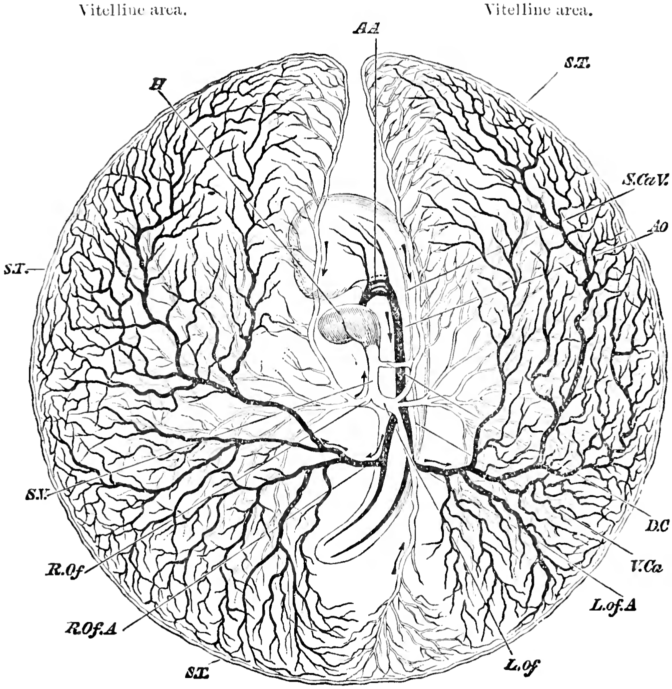

Fig. 303.—Diagram of the vascular system of the yolk-sac at the end of the third day of incubation, after Balfour.

The whole blastoderm has been removed from the egg and is represented as seen from below. Hence what is really at the right appears at the left, and *vice versâ*. The part of the area opaca in which the close vascular network has been formed is sharply terminated at its periphery by the sinus terminalis, and forms the vascular area; outside of the latter lies the vitelline area. The immediate neighborhood of the embryo is free from a vascular network, and now, as previously, is distinguished by the name area pellucida.

H, Heart; *AA*, aortic arches; *Ao*, dorsal aorta; *L.Of.A*, left, *R.Of.A*, right vitelline artery; *S.T*, sinus terminalis; *L.Of*, left, *R.Of*, right vitelline vein; *S.V*, sinus venosus; *D.C*, ductus Cuvieri; *S.Ca.V*, superior, *V.Ca*, inferior cardinal vein. The veins are left in outline; the arteries are black.

The *motion of the blood* begins to be visible in the case of the Chick as early as the second day of incubation. At this time the blood is still a clear fluid, which contains only few formed components. For the most of the blood-corpuscles still continue to lie in groups on the walls of the tubes, where they constitute the previously described *blood-islands* (fig. 114), which cause the red-besprinkled appearance of the vascular area. *The contractions of the heart*, by which the blood is set in motion, are at first slow and then become more and more rapid. On the average, according to PREYER, the strokes then amount to 130—150 per minute. However, the frequency of pulsations is largely dependent upon external influences; it increases with the elevation of the temperature of incubation and diminishes at every depression of it, as well as when the egg is opened for study. At the time when the heart begins to pulsate, no muscle-fibrillæ have been demonstrated in the myocardium; from this results the interesting fact that purely protoplasmic, still undifferentiated cells are in a condition to make strong rhythmical contractions.

At the end of the third or fourth day the vitelline circulation in the Chick is at its highest development; it has undergone some slight changes. We find instead of a single vascular network a double one, an arterial and a venous. The arterial network, which receives the blood from the vitelline arteries, lies deeper, nearer to the yolk, while the venous spreads itself out above the former and is adjacent to the visceral middle layer. The circulating blood is distinguished by the abundance of its blood-corpuscles, the blood-islands having entirely disappeared.

The *function of the vitelline circulation* is twofold. First it serves to provide the blood with oxygen, opportunity for acquiring which is afforded by the whole vascular network being spread out at the surface of the egg. Secondly it serves to bring nutritive substances to the embryo. The yolk-elements below the entoblast are disassociated, liquefied, and taken up into the blood-vessels, by which they are carried to the embryo, where they serve as nutrition for the rapidly dividing cells. Thus far the embryonic body increases in size at the expense of the yolk-material in the yolk-sac, which becomes liquefied and absorbed.

The system of vitelline blood-vessels in Mammals agrees in general with that of the Chick, and is distinguished from the latter only in some unimportant points, which do not need to be discussed. However, this question certainly arises· What signification has a vitelline circulation in Mammals (fig. 134 *ds*) in which the egg is furnished with only a small amount of yolk-material?

Two things are here to be kept in mind; first, that the eggs of

Mammals were originally provided with abundant yolk-material, like those of Reptiles (compare p. 222), and, secondly, that the blastodermic vesicle, which arises after the process of cleavage, becomes greatly distended by the accumulation within it of a fluid very rich in albumen, furnished by the walls of the uterus. Out of this vesicle likewise the vitelline blood-vessels undoubtedly take up nutritive material and convey it to the embryo, until a more ample nutrition is provided by means of the placenta.

In addition to the vitelline blood-vessels there arises in the higher Vertebrates *a second system of vessels, which is distributed in the fœtal membranes outside the embryo* and for a time is more developed than the remaining vessels of the embryo. It serves for the *allantoic circulation* of Birds and Reptiles and the *placental circulation* of Mammals.

When in the Chick the allantois (Pl. I., fig. 5 *al*) is evaginated from the front [ventral] wall of the hind-gut, and as an ever increasing sac soon grows out of the body-cavity through the dermal umbilicus into the cœlom of the blastodermic vesicle between the serosa and the yolk-sac, there appear in its walls two blood-vessels, which grow forth from the ends of the two primitive aortæ—*the umbilical vessels*, or *arteriæ umbilicales.* The blood is again collected from the fine capillary network, into which these vessels have been resolved, into the two *umbilical veins* (venæ umbilicales), which, after having arrived at the navel, pass on to the two Cuvierian ducts (see p. 577) and pour their blood into these near the entrance of the latter into the sinus venosus. The terminal part of the right vein soon atrophies, whereas the *left* receives the lateral branches of the right side and is correspondingly developed into a larger trunk. This now also loses its original connection with the ductus Cuvieri, since it effects with the left hepatic vein (vena hepatica revehens) an anastomosis, which continually becomes larger and finally carries the whole stream of blood. Together with the left hepatic vein the left umbilical vein then empties directly into the sinus venosus at the posterior margin of the liver (Hochstetter).

The umbilical and vitelline veins undergo opposite changes in calibre during development: while the vitelline circulation is well developed, the umbilical veins are inconspicuous stems; afterwards, however, with the increase in the size of the allantois they enlarge, whereas the venæ omphalomesentericæ undergo degeneration and in the same proportion as the yolk-sac by the absorption of the yolk becomes smaller and loses in significance.

So far as regards the *purpose of the umbilical circulation*, it subserves in Reptiles and Birds the *function of respiration*. For the allantois, when it has become larger, in the Chick for example, applies itself closely to the serosa and spreads itself out in the vicinity of the air-chamber and underneath the shell, so that the blood circulating in it can enter into an exchange of gases with the atmospheric air. It loses its importance for respiration in the egg only at the moment when the Chick with its beak breaks through the surrounding embryonic membranes, and breathes directly the air contained in the air-chamber. For the conditions of the circulation are now altered throughout the whole body, since with the beginning of the process of respiration the lungs are in a condition to take up a greater quantity of blood, resulting in a degeneration of the umbilical vessels (compare also p. 584).

The *umbilical* or *placental circulation in Mammals* (fig. 139 *Al*) plays a still more important rôle; for here the two umbilical arteries convey the blood to the placenta. After the blood has been laden in this organ with oxygen and nutritive substances, it flows back again to the heart, at first through two, afterwards through a single umbilical vein (p. 584).

B. The further Development of the Vascular System up to the Mature Condition.

(*a*) *The Metamorphosis of the Tubular Heart into a Heart with Chambers.*

As has been shown in a preceding section, the heart of a Vertebrate originally has for a short time the form of a straight sac, which sends off at its anterior end the two primitive aortic arches, while it receives at its posterior end the two omphalomesenteric veins. The sac lies far forward immediately behind the head on the ventral side of the neck (fig. 304 *h*), in a prolongation of the body-cavity (the parietal or cervical cavity). It is here attached by means of a mesentery of only brief duration, which stretches from the alimentary canal to the ventral wall of the throat, and which is divided by the cardiac sac itself into an upper [dorsal] and an under part, or mesocardium posterius and anterius.

During the first period of embryonic development the heart is distinguished by a very considerable growth, especially in the longitudinal direction; consequently it soon ceases to find the necessary room for itself as a straight sac, and is therefore compelled to bend itself into an *S-shaped loop* (fig. 304). It then takes such a position in the neck that one of the bends of the S, which receives the vitelline veins or, let us say briefly, the venous portion, comes to lie behind and at the left; the other or arterial portion, which sends off the aortic arches, in front and at the right (fig. 305).

But this initial position is soon altered (figs. 305, 313) by the two curves of the S assuming another relation to each other. The venous portion moves headwards, the arterial, on the contrary, in the opposite direction, until both lie approximately in the same transverse plane. At the same time they become turned around the longitudinal axis of the embryo, the venous loop moving dorsally, the arterial, on the contrary, ventrally. Seen from in front [ventral aspect] one hides the other, so that it is only in a side view that the S-shaped curvature of the cardiac sac is distinctly recognisable.

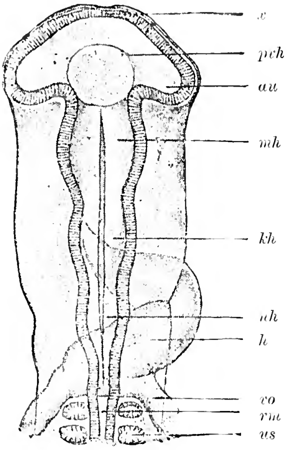

Fig. 304.—Head of a Chick incubated 58 hours, seen from the dorsal face, after MIHALKOVICS. Magnified 40 diameters.

The brain is divided into 4 vesicles: *pvh*, primary fore-brain vesicle; *mh*, mid-brain vesicle; *kh*, hind-brain vesicle; *nh*, after-brain vesicle; *au*, optic vesicle; *h*, heart (seen through the last brain-vesicle); *vo*, vena omphalomesenterica; *us*, primitive segment; *rm*, spinal cord; *x*, anterior wall of brain, which is evaginated to form the cerebrum.

By the increase in the size of this viscus the anterior part of the body-cavity is already greatly distended, and becomes still more so in later stages, when there is produced a very thin-walled elevation, that projects out to a great distance (figs. 157 *h*, 314). Inasmuch as the heart completely fills the cavity, and is covered in by only the thin, transparent, and closely applied wall of the trunk,—the membrana reuniens inferior of RATHKE,—it appears as though at this time the heart were located entirely outside of the body of the embryo.

After the completion of the twisting, there is effected a division of the S-shaped sac into several successive compartments (figs. 306, 308). The venous portion, which has become broader, and the arterial part are separated from each other by a deep constriction (*ok*) and can now be distinguished as *atrium* (*vh*) and *ventricle*, while the constricted region between the two may be indicated, by a designation introduced by Haller, as *auricular canal* (*ok*). The atrium thereby acquires a striking form, since its two lateral walls develop large out-pocketings (*ho*), the *auricles of the heart* (auriculæ cordis); the free edges of the latter, which in addition soon acquire notches, are turned forward, and subsequently enfold more and more the arterial part of the heart, the truncus arteriosus (*Ta*), and a part of the surface of the ventricle.

The auricular canal (fig. 308 *ok*) is in embryos a well-distinguished narrowed place in the cardiac tube. Owing to the great flattening of its endothelial tube in the sagittal direction,—its walls almost coming into contact,—the passage between atrium and ventricle is reduced to a narrow transverse fissure. It is here that the *atrio-ventricular valves* are afterwards developed.

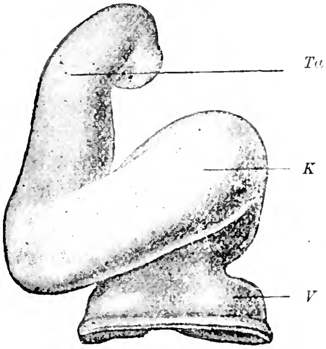

Fig. 305.

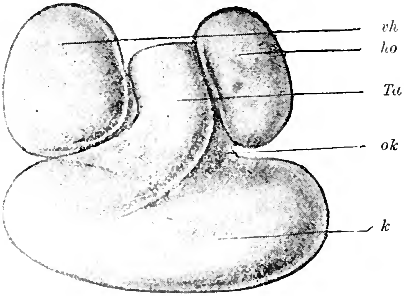

Fig. 306.

Fig. 305.—Heart of a human embryo, the body of which was 2·15 mm. long (embryo *Lg*), after His. [Compare fig. 313.]
K, Ventricle; *Ta*, truncus arteriosus; *V*, venous end of the S-shaped cardiac sac.

Fig. 306.—Heart of a human embryo that was 4·3 mm. long, neck measurement (embryo *Bl*), after His.
k, Ventricle; *Ta*, truncus arteriosus; *ok*, canalis auricularis; *vh*, atrium with the heart-auricles *ho* (auriculæ cordis).

The fundament of the ventricle at first presents the form of a curved tube (figs. 305, 306 *k*), which however soon changes its form. For at a very early period there is observable on its anterior [ventral] and posterior surfaces a shallow furrow running from above downward, the *sulcus interventricularis* (fig. 307 *si*), which allows a left and a right half of the ventricle to be distinguished externally. The latter is the narrower, and is continued upward into the truncus arteriosus (*Ta*), the beginning of which is somewhat enlarged and designated as bulbus. Between bulbus and ventricle lies a place that is only slightly constricted, called the *fretum Halleri*; it was recognised even by the older anatomists, then remained for a time little regarded, and now has been again described as noteworthy by His. For it marks the place at which subsequently the semilunar valves are established.

During the externally visible changes of form, some alterations are also progressing in the finer structure of the walls of the heart. As previously remarked, the fundament of the heart consists in the beginning of two sacs, one within the other—an inner endothelial tube lined with flat cells, and an outer muscular sac consisting of cells with abundant protoplasm and derived from the middle germ-layer. The two are completely separated from each other by a considerable space, which is probably filled with gelatinous substance.

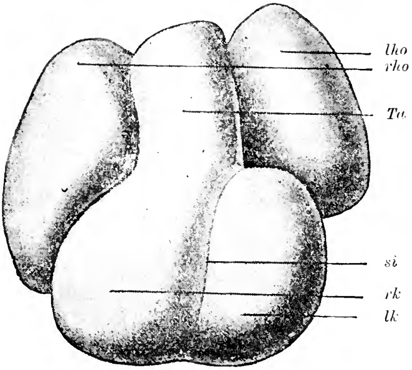

Fig. 307.—Heart of a human embryo of the fifth week, after His.
rk, Right, *lk*, left ventricle; *si*, sulcus interventricularis; *Ta*, truncus arteriosus; *lho*, left, *rho*, right auricle of the heart.

The *endothelial tube* is in general a tolerably faithful copy of the muscular sac, yet the narrower and wider regions are more sharply marked off from one another in the former than in the latter; "as regards its form, it sustains such a relation to the whole heart as it would if it were a greatly shrivelled, internal cast of it" (His).

In the *muscular sac* distinct traces of muscle-fibres can be recognised even at the time when the S-shaped curvature makes its appearance. At later stages in the development differences appear between atrium and ventricle. In the atrium the muscular wall is uniformly thickened into a compact plate, with the inside of which the endothelial tube is in immediate contact. In the ventricle, on the contrary, there occurs a loosening, as it were, of the muscular wall. There are formed numerous small trabeculæ of muscular cells, which project into the previously mentioned space between the two sacs and become united to one another, forming a large-meshed network (fig. 311 *A*). The endothelial tube of the heart, by forming out-pocketings, soon comes into intimate contact with the trabeculæ, and envelops each one of them with a special covering (His). Thus there arise in the spongy wall of the ventricle numerous spaces lined with endothelium, which toward the surface of the heart end blindly, but which communicate with the central cavity and like this receive into them the stream of blood.

The embryonic heart of Man and Mammals resembles in its first condition—that which has been described up to this point—the heart of the lowest Vertebrates, the Fishes. In the former as in the latter it consists of a region, the atrium, which receives the venous blood from the body, and of another, the ventricle, which drives the blood into the arterial vessels. Corresponding to this condition of the heart, *the whole circulation* in embryos of this stage and in Fishes *is still a simple and a single one.* This becomes changed in the evolution of Vertebrates, as in the embryonic life of the individual, *with the development of the lungs, upon the appearance of which a doubling of the heart and of the blood-circulation is introduced.*

The cause of such a change is clear, from the *topographical relation of the two lungs to the heart,* the former arising in the immediate vicinity of the heart by evagination of the fore-gut (fig. 314 *lg*). The lungs therefore receive their blood from an arterial stem lying very near the heart, from the fifth [sixth] pair of aortic arches that arise from the truncus arteriosus. Similarly they give back again the venous pulmonary blood directly to the heart through short stems, the pulmonary veins, which, originally united into a single collecting trunk (Born, Röse), open into the atrium at the left of the great venous trunks. *Therefore the blood that flows directly out of the heart into the lungs also flows directly back again to the heart. Herein is furnished the prerequisite for a double circulation. This comes into existence when the pulmonary and the body currents are separated from each other by means of partitions throughout the short course of the vascular system which both traverse in common* (viz., atrium, ventricle, and truncus arteriosus).

The process of separation begins in the vertebrate phylum with the Dipnoi and Amphibia, in which pulmonary respiration appears for the first time and supplants bronchial respiration. In the amniotic Vertebrates it is accomplished during their embryonic development. Therefore we now have to follow out further the manner in which, in the case of Mammals and especially of Man, according to the recent investigations of His, Born, and Röse, the partitions are formed—how atrium and ventricle are each divided into right and left compartments, and the truncus arteriosus into arteria pulmonalis and aorta, and how in this way the heart attains its definite form.

The partitions arise independently in each of the three divisions of the heart mentioned.

Let us first take into consideration the atrium, which is for a time the largest and most capacious region of the cardiac sac (fig. 308). In Man a separation into left and right halves (*lv* and *rv*) is observable even in the fourth week, since there is then formed on its hinder [dorsal] and upper wall a perpendicular projection inward, the first trace of the atrial partition (*vs*) or septum atriorum.

The halves are even now distinguished by the fact that they receive different venous trunks. The vitelline and umbilical veins, as well as the Cuvierian ducts to be discussed later, empty their blood into the right compartment, not directly, however, and by means of separate orifices, but after they have united with one another in the vicinity of the heart to form a large venous sinus (*sr*)—the sinus venosus or s. reuniens. This is immediately adjacent to the atrium and communicates with it by means of a large opening in its posterior [dorsal] wall, which is flanked on the right and on the left by a large venous valve (*). Only one small vessel, which traverses the musculature of the heart obliquely, opens, near the atrial partition, into the left compartment; it is the previously mentioned unpaired pulmonary vein, which is formed immediately outside the atrium by the union of four branches, two of which come from each of the two wings of the lung now being established.

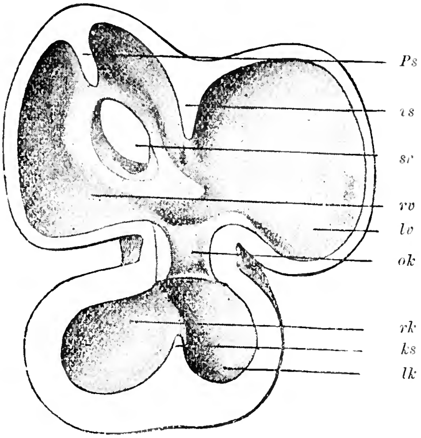

Fig. 308.—Heart of a human embryo 10 mm. long, neck measurement; posterior [dorsal] half of the heart, the front walls of which have been removed. After His.

ks, Partition of the ventricle; *lk*, left, *rk*, right ventricle; *ok*, auricular canal; *lv*, left, *rv*, right atrium; *sr*, mouth of the sinus reuniens; *vs*, partition of the atrium (atrial crescent, His; septum primum, Born); * Eustachian valve; *Ps*, septum spurium.

In the further course of development the atrial partition grows from above downward until it reaches the middle of the atrial canal (fig. 309 *si*). In this manner two completely separated atria would have come into existence at a very early period, if there had not been formed in the upper part of the partition, while it was still growing downward, an opening, the future foramen ovale, which maintains a connection between the two chambers (fig. 309) up to the time of birth. The opening has arisen either from the septum atriorum having become thin and having broken through at a certain region, or from its having been incomplete at this place from the very beginning, as is the case with the Chick for example, where it is traversed by numerous small orifices. Afterwards the foramen ovale, adapting itself to the conditions of the circulation existing at the time, becomes still larger.

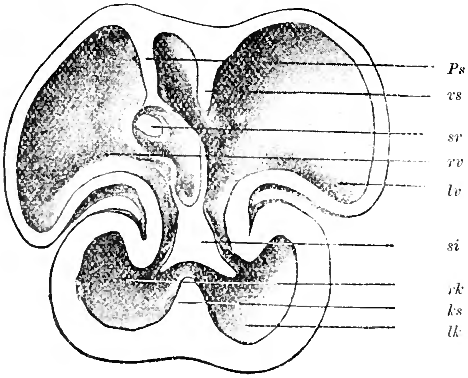

Fig. 309.—Posterior [dorsal] half of the heart of a human embryo of the fifth week, cut open, after His.

ks, Ventricular partition ; *lk*, left, *rk*, right ventricle ; *si*, lower [posterior] part of the atrial partition (septum intermedium, His) ; *lv*, left, *rv*, right atrium ; *sr*, mouth of the sinus reuniens ; *vs*, atrial partition (atrial crescent, His ; septum secundum, Born) ; *Ps*, septum spurium ; * Eustachian valve.

The downgrowth of the atrial partition has, moreover, the immediate result of separating the auricular canal into the left and right atrioventricular orifices (compare fig. 308 *ok* with fig. 309). The auricular canal, even very soon after its formation, undergoes important alterations both from without and within. At first visible from the outside (fig. 308 *ok*), it afterwards disappears from view (fig. 309) by being in a manner overgrown on all sides by the ventricle, and thereby incorporated in its walls, which enlarge upward and, in consequence of a vigorous growth of the musculature, acquire considerable thickness. The opening of the atrial canal into the ventricle, or the foramen atrioventriculare commune (fig. 310 *A F.av.c*), now has the form of a fissure extending from left to right, which is bounded on either side by two ridge-like lips (*o.ek* and *u.ek*)—the atrioventricular lips of Lindes, or the endothelial cushions of

SCHMIDT. The ridges have arisen from a growth of the endocardium, and consist of a gelatinous connective substance and an endothelial investment. The atrial partition, when it has grown down to the auricular canal, soon fuses along its free lower margin with these lips (fig. 309 *si*); the auricular canal is thereby divided into a left and a right atrioventricular opening,—ostium atrioventriculare sinistrum and dextrum (fig. 310 *B F.av.s* and *F.av.d*),—and at the same time both the dorsal and ventral endocardial ridges, which originally bound the opening, are divided in the middle (*o.ek* and *u.ek*). The dorsal components soon fuse with the corresponding pieces of the opposite [ventral] side, and thus there arise at the lower margin of the atrial partition (fig. 309 *si*) two new ridges,—one of which projects into the left, the other into the right atrioventricular opening,—which furnish the foundation of the median cuspidate valves.

The development of the atrial partition and the division of the auricular canal into the two atrioventricular openings are closely related processes, the former being the cause of the latter. This is clearly proved by pathological-anatomical conditions of arrested development of the heart. In all cases in which the formation of the atrial partition has been for any reason whatever interrupted and the lower part of it has been altogether wanting, there has always been only one atrioventricular opening (an ostium venosum commune) present (ARNOLD).

Before we progress further in the history of the development of the atrium, we must add an account of the metamorphoses which have taken place meanwhile in the territory of the ventricle and truncus arteriosus.

The ventricle begins to acquire its partition not much later than the atrium. By the end of the first month its musculature has become considerably thickened (fig. 311 *A*). Muscular trabeculæ have arisen, which project far into the interior of the chamber and are joined to one another, so as to constitute a spongy tissue, the numerous fissures in which are continuous with the narrowed cavity of the heart and likewise allow the current of the blood to pass through them. At one place the musculature is especially thickened and forms a crescent-shaped fold projecting inward, the fundament of the *ventricular partition* (septum ventriculorum) (figs. 308, 309, 310 *ks*). This takes its origin from the lower and posterior [dorsal] wall of the ventricle, in the region which is marked externally by the previously mentioned *sulcus interventricularis* (fig. 307 *si*). Its free edge is directed upwards and grows toward the bulbus arteriosus and the atrioventricular opening. The latter originally lies more in the left half of the ventricle (fig. 310 *A F.av.c*), but it gradually moves over more to the right, and finally assumes such a position that the ventricular partition by its growth upwards meets it exactly in the middle and fuses with its edges directly opposite the atrial partition (figs. 309, 310 *B*).

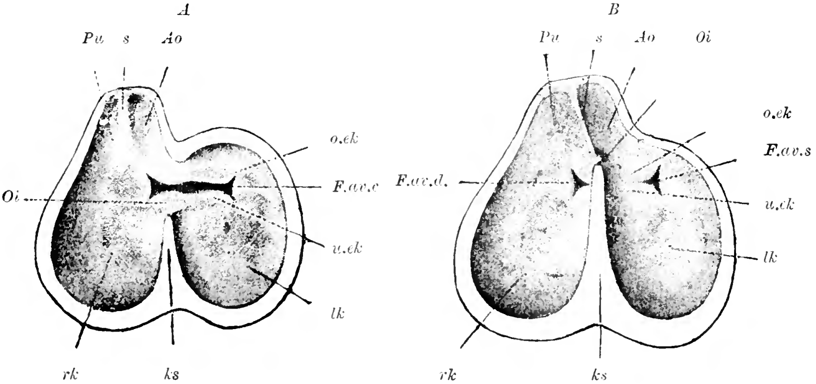

Fig. 310.—Two diagrams (after Born) **to elucidate the changes in the mutual relations of the ostium atrioventriculare and the ostium interventriculare, as well as the division of the ventricle and large arteries.** The ventricles are imagined to have been divided into halves; one looks into the posterior [dorsal] halves, in which, moreover, the cardiac trabeculæ, etc., have been omitted for the sake of simplifying the view.

A, **Heart of an embryo Rabbit, in which the head is 3·5—5·8 mm. long.** The ventricle is divided by the ventricular partition (*ks*) into a left and a right half as far as the ostium interventriculare (*Oi*). The right end of the foramen atrioventriculare commune (*F.av.c*) extends into the right ventricle; the endocardial cushions (*o.ek*, *u.ek*) are developed.

B, **Heart of an embryo Rabbit, head 7·5 mm. long.** The endocardial cushions (*o.ek*, *u.ek*) of the foramen atrioventriculare commune are fused, and thereby the for. atrioventr. com. is now separated into a for. atrioventr. dextrum (*F.av.d*) and sinistrum (*F.av.s*). The ventricular partition (*ks*) has likewise fused with the endocardial cushions, and has grown forward as far as the partition (*s*) of the truncus arteriosus. By the closure of the remnant of the ostium interventriculare (*Oi*) the septum membranaceum is formed.

rk, Right, *lk*, left ventricle; *ks*, ventricular partition; *Pu*, arteria pulmonalis; *Ao*, aorta; *s*, partition of the truncus arteriosus; *Oi*, ostium interventriculare; *F.av.c*, foramen atrioventriculare commune; *F.av.d* and *F.av.s*, foramen atrioventriculare dextrum and sinistrum; *o.ek*, *u.ek*, upper and lower endothelial or endocardial cushions.

The division of the ventricle in Man is completed as early as the seventh week. From the atrium, the two compartments of which are united by the foramen ovale, the blood is now conducted through a right and a left ostium atrioventriculare into completely separated right and left ventricles.

The two atrioventricular openings are narrow at the time of their origin; they are in part surrounded by the previously mentioned endocardial ridges that project from the partition, in part by corresponding growths of the endocardium at their lateral circumference. The membranous projections are comparable with primitive pocket-valves, such as are also established in the bulbus arteriosus (GEGENBAUR); they constitute the starting-point for the development of the large atrioventricular valves, but furnish, as GEGENBAUR and BERNAYS have shown, only a part—the membranous marginal thickening (mk^1)—which subsequently disappears almost completely, whereas the compact main part of the valve arises from that portion of the thickened muscular wall of the ventricle itself that surrounds the atrioventricular opening (fig. 311 *B mk*).

As was previously stated, in the case of Man the wall of the ventricle during the first months consists of a close spongy network of muscular trabeculæ, which are invested by the endocardium and the interstices of which communicate with the small central cavity (fig. 311 *A*). Such a spongy condition of the wall of the heart persists permanently in Fishes and Amphibia; in the higher Vertebrates and Man, on the contrary, metamorphoses occur. Toward its external surface the wall of the heart becomes more compact, in that the muscular trabeculæ become thicker and the spaces between them narrower, in some parts even disappearing entirely (fig. 311 *B tc*). The reverse of this process takes place toward the inside. In the vicinity of the atrioventricular opening the trabeculæ become thinner and the interstices larger. In this way a part of the thick wall of the ventricle, which looks toward the atrium and encloses the opening, is undermined, as it were, by the blood-current. In this part the muscle-fibres afterwards become entirely rudimentary;

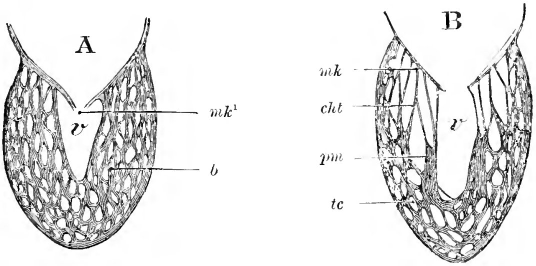

Fig. 311.—**Diagrammatic representation of the formation of the atrioventricular valves.** *A*, **Earlier,** *B*, **later condition.** After GEGENBAUR.
mk, Membranous valve; mk^1, the primitive part of the same; *cht*, chordæ tendineæ; *v*, cavity of the ventricle; *b*, trabecular network of cardiac musculature; *pm*, papillary muscles; *tc*, trabeculæ carneæ.

there are formed from the interstitial connective-tissue substance tendinous plates, which with the endocardial cushions attached to their margins become the permanent atrioventricular valves (fig. 311 *B mk*). The latter therefore arise from a part of the spongy wall of the ventricle.

The remnants of the shrivelled muscular trabeculæ (fig. 311 *B cht*), which are attached to the valve from below, become still more rudimentary in the immediate vicinity of the attachment: here also a part of the muscular fibres disappears entirely; the connective tissue, on the contrary, is preserved, and is converted into the tendinous cords which, known under the name of *chordæ tendineæ*, serve to hold in place the valves. At some distance from the latter the trabeculæ projecting into the ventricle preserve their fleshy condition and become the papillary muscles (*pm*), from the apices of which the chordæ tendineæ arise. "Whatever of the primitive trabecular network still persists on the inner surface of the ventricle forms a more or less stout meshwork of muscles, the fleshy pillars of the heart (*tc*), or trabeculæ carneæ."

In consequence of all these alterations the originally small cavity of the ventricle has become considerably enlarged at the expense of a part of its spongy wall. For the whole of the space which in fig. 311 *B* lies below the valves has been produced from the system of originally narrow spaces (fig. 311 *A*), and has been employed for the enlargement of the central cavity by the degeneration of the fleshy columns into slender tendinous cords.

It still remains for us to investigate the division of the truncus arteriosus and the final metamorphosis of the atrium.

At about the time when the formation of the partition in the ventricle takes place, the truncus arteriosus, which arises from it, becomes somewhat flattened, and thus acquires a fissure-like lumen. On the flat sides two ridge-like thickenings make their appearance (fig. 310 *A* and *B s*), grow toward each other, and by their fusion divide the cavity into two passages which are triangular in cross section. Now, too, the beginning of the internal separation makes itself visible externally as two longitudinal furrows, in the same way that the formation of a partition in the ventricle is indicated by the sulcus interventricularis. The two canals resulting from the division are the aorta and the pulmonary artery (*Ao* and *Pu*). For a time they continue to be surrounded by a common adventitia, then they become widely separated and also externally detached from each other. The whole process of separation in the truncus arteriosus takes place independently of the development of a partition in the ventricle, beginning as it does at first above and advancing from there downwards. Finally the aortic septum penetrates also into the cavity of the ventricle itself (fig. 310 *B s* and *ks*), there unites with the independently developed ventricular partition, furnishes the part known as pars membranacea (*Oi*), and thus completes the separation of the vessels leading out from the heart, the aorta falling to the lot of the left ventricle, the art. pulmonalis to the right.

The pars membranacea indicates therefore in the finished heart the place at which the separation between the right and left halves of the heart is completed (fig. 310 *B Oi*). "It is, as it were, the keystone in the final separation of the primitive simple cardiac sac into the four secondary cardiac cavities, as they are formed in Birds and Mammals" (RÖSE). From a comparative-anatomical point of view this place presents a special interest from the fact that in Reptiles there exists here a permanent opening between the two ventricles, the foramen Pannizzæ.

Even before the division of the truncus arteriosus, *the semilunar valves have become established as four ridges*, consisting of gelatinous tissue with a covering of endothelium, at the contracted place which is designated as the *fretum Halleri*. Two of them are halved at the time of the division of the truncus into aorta and art. pulmonalis. For each vessel, therefore, there are now three ridges, which, owing to a shrivelling of the gelatinous tissue, assume the form of pockets. Their arrangement, to which GEGENBAUR has called attention, is intelligible from their method of development, as the accompanying diagram (fig. 312) shows. "By the division of the originally single bulbus arteriosus (*A*) into two canals (*B*), the nodule-like fundaments of the four original valves are distributed in such a manner that the anterior [ventral] one and the anterior halves of the two lateral ones fall to the anterior arterial trunk (pulmonalis), the posterior and the posterior halves of the lateral ones to the posterior arterial trunk (aorta)."

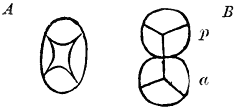

Fig. 312.—Diagram of the arrangement of the arterial valves. From GEGENBAUR.
A, Undivided truncus arteriosus with four fundaments of valves. *B*, Division into pulmonalis (*p*) and aorta (*a*), each of which possesses three valves.

Finally, as regards the atrium, it is to be said that the sinus venosus, mentioned at p. 558, the mouth of the pulmonary vein, and the foramen ovale undergo important alterations.

The sinus venosus disappears as an independent structure, since it is gradually merged into the wall of the atrium. In consequence of this the great venous trunks, which originally emptied their blood into it and which have meanwhile been converted into the superior and inferior venæ cavæ and into the sinus coronarius (the details of which are given in section *d*), empty directly into the right half of the atrium, and here gradually separate farther and farther from one another. Of the two valves which surround, as was previously stated, the mouth of the sinus venosus, the left becomes rudimentary (figs. 308, 309); the right (*), on the contrary, persists at the mouth of the inferior vena cava and of the sinus coronarius, and is divided, corresponding to these, into a larger and a smaller portion, of which the former becomes the valvula Eustachii, the latter the valvula Thebesii.

The four pulmonary veins are united for a time into a common short trunk, which empties into the left half of the atrium. Subsequently the common terminal portion becomes greatly enlarged and merged with the wall of the heart, in the same way as the sinus venosus does. In consequence the four pulmonary veins then open separately and directly into the atrium.

The foramen ovale, the formation of which was previously described, maintains a broad communication between the two sides of the atrium during the entire embryonic life. It is bounded behind and below by the atrial partition, a connective-tissue membrane that subsequently receives the name of valvula foraminis ovalis (fig. 309 *si*). Also from above and in front there is formed a sharp limitation, since a muscular ridge projects inward from the atrial partition, the anterior atrial crescent or the limbus Vieussenii (*vs*). Even in the third month all of these parts are distinctly developed; the valvula foraminis ovalis already reaches nearly to the thickened margin of the anterior muscular crescent, but is deflected obliquely into the left half of the atrium, so that a broad fissure remains open and permits the blood of the inferior vena cava to enter into the left part of the atrium. After birth the margins of the anterior and posterior folds come into contact, and, with occasional exceptions, fuse completely. The posterior fold furnishes the membranous partition of the foramen ovale; the anterior, with its thickened muscular margin, produces above and in front the limbus Vieussenii. With this the heart has attained its permanent structure.

While the cardiac sac undergoes these complicated differentiations, it changes its position in the body of the embryo and acquires at an early period a special investment, the pericardium. In connection with the latter the diaphragm is formed as a partition between the thoracic and abdominal cavities. This is consequently the most suitable place at which to acquaint ourselves better with these important processes, a part of which are not easily understood. The most of the discoveries in this field we owe to the investigations of Cadiat, His, Balfour, Uskow, and others.

(*b*) *The Development of the Pericardial Sac and the Diaphragm. The Differentiation of the Primary Body-cavity into Pericardial, Thoracic, and Abdominal Cavities.*

Originally the body-cavity is widely extended in the body of the embryo, for it can be traced in the lower Vertebrates into the fundament of the head, where it furnishes the cavities of the visceral arches. After the latter have become closed, during which muscles arise from the cells composing their walls, the body-cavity extends forward as far as the last visceral arch and constitutes a large space (fig. 313), in which the heart is developed within the ventral mesentery (mesocardium anterius and posterius). Remak and Kölliker named this space *throat-cavity*; His introduced the name *parietal cavity*. But it will be most appropriate if one designates it, after the permanent organs which are derived from it, as the *pericardio-thoracic cavity*. The more the cardiac tube is thrown into curves, the more extensive this cavity becomes, and it soon acquires in the embryo a comparatively enormous size. By this its front wall is protruded ventrally like a hernia between the head and the navel of the embryo (figs. 314, 157).

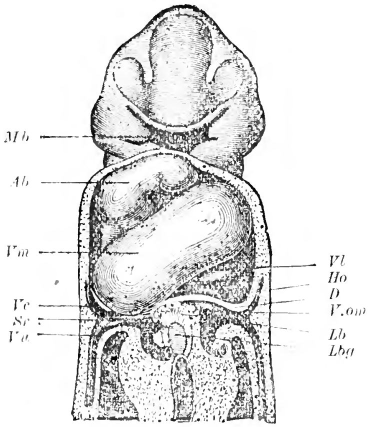

Fig. 313.—Human embryo (*Lg* of His) 2·15 mm. long, neck measurement. Reconstruction figure, after His ("Menschliche Embryonen"). Magnified 40 diameters.

Mb, Oral sinus; *Ab*, aortic bulb; *Vm*, middle part of the ventricle; *Vc*, vena cava superior or ductus Cuvieri; *Sr*, sinus reuniens; *Vu*, vena umbilicalis; *Vl*, left part of the ventricle; *Ho*, auricle of the heart; *D*, diaphragm; *V.om*, vena omphalomesenterica; *Lb*, solid fundament of the liver; *Lbg*, hepatic duct.

The pericardio-thoracic cavity begins very early to be sharply marked off from the future abdominal cavity by a *transverse fold* (figs. 313, 314 $z+l$), which begins at the front [ventral] and lateral walls of the trunk, and the free edge of which projects dorsalwards and medianwards (fig. 314 $z+l$) into the primitive body-cavity. It marks the course which the terminal part of the vena omphalo-mesenterica takes in order to reach the heart. Subsequently there are found imbedded in the fold *all of the venous trunks which empty into the atrial sinus of the heart* (figs. 313, 314),—the omphalo-mesenteric and umbilical veins and the Cuvierian ducts (*dc*), which collect the blood from the walls of the trunk. *Therefore the formation of the transverse fold is most intimately connected with the development of the veins.* It takes the name of *septum transversum* (massa transversa, USKOW), and has the form of a transverse bridge of substance uniting the two lateral walls of the trunk (fig. 313), which inserts itself between the sinus venosus and the stomach, and is united with both as well as with the ventral mesentery. Its posterior portion (fig. 314 $z+l$) contains abundant embryonic connective tissue and blood-vessels, and constitutes a mass described as *prehepaticus* (Vorleber), since the two liver-sacs (fig. 313 $Lb+Lbg$) grow out from the duodenum into it and produce the hepatic cylinders. In proportion as this takes place, and the hepatic cylinders spread out from the ventral mesentery laterally into the septum transversum, the latter increases in thickness and now embraces two different fundaments,—in front, a plate of substance in which the Cuvierian ducts and other veins run to the heart (*the primary diaphragm*); behind, the two lobes of the liver, which produce ridges that project into the body cavity.

By means of the septum transversum the pericardio-thoracic and the abdominal cavities are almost completely separated (fig. 314). There remain only two narrow canals (*brh*) (thoracic prolongations of the abdominal cavity, HIS), which establish a connection behind with the abdominal cavity at either side of the intestinal tube and its dorsal mesentery. The two canals (*brh*) receive the two fundaments of the lungs (*lg*) when they grow out from the ventral wall of the intestinal tube. They afterwards become the two thoracic or pleural cavities (*brh*), whereas the larger cavity communicating with them (*hh*), in which the heart has developed, becomes the pericardial chamber. The latter takes up the whole ventral side of the embryo; the thoracic cavities, on the contrary, lie quite dorsal next to the posterior wall of the trunk.

How does the closure of these three originally communicating spaces take place, and how do they attain their altered, final position in relation to one another?

The pericardial sac is the first to be separated off. The impulse to separation is furnished by the Cuvierian ducts (fig. 314 *dc*). One portion of the latter runs down from the dorsum, where it arises by the confluence of the jugular and cardinal veins, along the lateral walls of the trunk to the transverse septum (fig. 314 *dc*); it thereby crowds the pleura into the pericardio-thoracic cavity, and in this manner produces the pleuro-pericardial fold. Since the latter is carried farther and farther inward, it continues to narrow the communication between the pericardial cavity (*hh*) and the two pleural cavities (*brh*); finally, it cuts off the communication entirely, when its free edge has grown [medianwards] as far as, and has fused with, the mediastinum posterius, in which the œsophagus lies. By this migration of the Cuvierian ducts is also explained the position of the superior vena cava, which later opens into the atrium from above, for it is derived from the Cuvierian duct. Originally located in

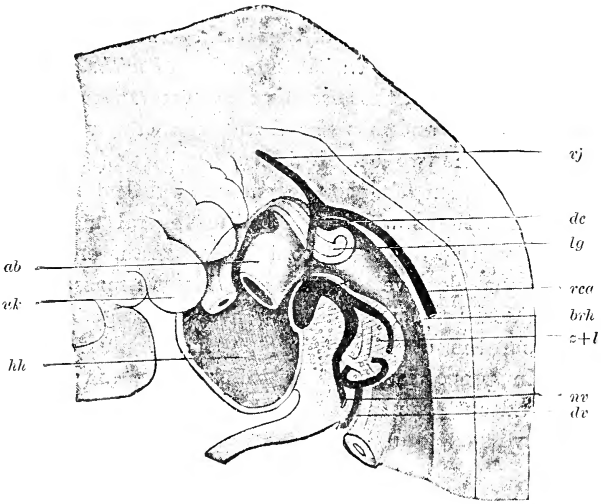

Fig. 314.— Sagittal reconstruction of a human embryo 5 mm. long, neck measurement (embryo *R*, His), **to elucidate the development of the pericardio-thoracic cavity and the diaphragm,** after His.

ab, Bulbus arteriosus; *brh*, thoracic cavity (recessus parietalis, His); *hh*, pericardial cavity; *dc*, ductus Cuvieri; *dv*, vena omphalomesenterica; *nv*, umbilical vein; *rca*, cardinal vein; *vj*, jugular vein; *lg*, lung; *z* + *l*, fundament of the diaphragm and liver; *uk*, mandible.

the lateral wall of the trunk, its terminal part is afterwards enclosed in the mediastinum.

After the closure of the pericardial sac, the narrow, tubular thoracic cavities (fig. 314 *brh*) continue for a time to remain in communication behind with the abdominal cavity. The fundaments of the lungs (*lg*) meantime grow farther into them, and their tips finally come in contact with the upper surface of the liver, which also has now become larger. Then a closure is effected at these places also. From the lateral and posterior walls of the trunk project folds (the pillars of USKOW), which fuse with the septum transversum, and thus form the *dorsal part of the diaphragm. One can therefore distinguish a ventral older part and a dorsal younger one.*

As GEGENBAUR points out, this explains the course of the phrenic nerve, which runs *in front of* [ventral to] the heart and lungs and approaches the diaphragm from in front.

Occasionally the fusion of the dorsal and ventral fundaments is interrupted on one side. The consequence of such arrested development is a *diaphragmatic hernia—i.e.*, a permanent connection between abdominal and thoracic cavities by means of a hernial orifice, through which loops of the intestine can pass into the thoracic chamber.

When the four large serous spaces of the body have been completely shut off from one another, the individual organs must still undergo extensive alterations of position, in order to attain their ultimate condition. The pericardial sac at first takes up the whole ventral side of the breast, and over a large area is connected with the anterior wall of the thorax and with the upper wall of the diaphragm. Moreover, the latter is united with the liver along its whole under surface. The lungs lie hidden in narrow tubes at the dorsal side of the embryo.

There are two factors that come into the account in this connection (fig. 315). With the increase in the extent of the lungs (*lg*), the thoracic cavities (*pl.p*) extend farther ventrally, and thereby detach the wall of the pericardial sac (*pc*), or the pericardium, on the one hand from the lateral and anterior walls of the thorax, and on the other from the surface of the diaphragm. Thus the heart (*ht*), with its pericardial sac, is displaced step by step toward the median plane, where, together with the large blood-vessels (*ao*), the œsophagus (*al*), and the bronchial tubes, it helps to form a partition—the mediastinum—between the greatly enlarged thoracic cavities. In front the pericardial sac then remains in contact with the wall of the thorax (*st*) and below with the diaphragm for a little distance only.

The second factor is the separation of the liver from the primary diaphragm, with which it was united to form the septum transversum. This takes place as follows: At the margin of the liver the peritoneum, which originally covered only its under surface, grows over on to its upper surface, separating it from the primary diaphragm. A connection is retained near the wall of the trunk only. Thus is explained the development of the *ligamentum coronarium hepatis,* which was disregarded in the section which treated of the ligamentous supports of the liver (p. 330).

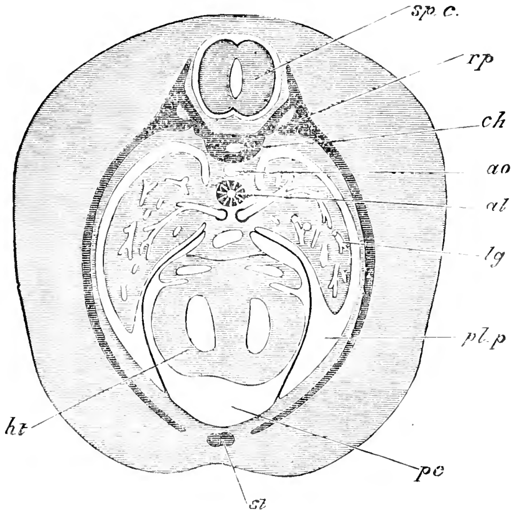

Fig. 315.—Cross section through an advanced embryo of a Rabbit, to show how the pericardial cavity becomes surrounded by the pleural cavities, from Balfour.
ht, Heart; *pc*, pericardial cavity; *pl.p*, thoracic or pleural cavity; *lg*, lung; *al*, alimentary canal; *ao*, dorsal aorta; *ch*, chorda; *rp*, rib; *st*, sternum; *sp.c*, spinal cord.

The diaphragm finally acquires its permanent condition by the ingrowth of muscles from the wall of the trunk into the connective-tissue lamella.

(c) *The Metamorphoses of the Arterial System.*

The development of the large arterial trunks lying in the vicinity of the heart is of great interest from a comparative-anatomical point of view. As in all Vertebrates at least five pairs of visceral arches are established on the two sides of the fore-gut (permanently in the gill-breathing Fishes, Dipnoi, and a part of the Amphibia, transitorily in the higher Vertebrates), so also there are developed at the corresponding places on the part of the vascular system five pairs of vascular arches* (fig. 316 $^{1\text{-}5}$). They take their origin from the truncus arteriosus (figs. 316, 317), which runs forward under the fore-gut, then follow along the visceral arches up to the dorsal surface of the embryo, and here unite on either side of the vertebral column into longitudinal vessels, the two primitive aortæ (fig. 317 *ad*). On this account they are called *aortic arches,* but they are more appropriately designated as *visceral-arch vessels.*

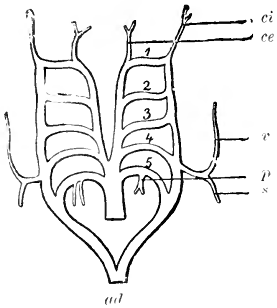

Fig. 316.—Diagram of the arrangement of the vessels of the visceral arches from an embryo of an amniotic Vertebrate.

1—5, First to fifth aortic arches ; *ad*, aorta dorsalis ; *ci*, carotis interna ; *ce*, carotis externa ; *v*, vertebralis ; *s*, subclavia ; *p*, pulmonalis.

In the Vertebrates that breathe by means of gills, the vessels of the visceral arches *become of importance in the process of respiration*, and early lose their simple structure. From their ventral initial portions there arise numerous lateral branches running to the branchial lamellæ, which have arisen in large numbers from the mucous membrane investing the visceral arches ; here they are resolved into fine capillary networks. From these the blood is re-collected into venous branches, which open into the upper end of the visceral-arch vessels. The larger the ventral and dorsal lateral branches, the more inconspicuous does the middle part of the vessel of the visceral arch become. At length it has separated into an initial part, the *branchial artery*, which is distributed to the branchial lamellæ in numerous branches, and an upper part, the *branchial vein*, into which the blood is re-collected. The two are connected with each other by means of the close network only, which, from its superficial position in the mucous membrane, presents a suitable condition for the removal of the gases from the blood.

Since in the Amniota there are no branchial lamellæ produced, branchial arteries and veins also fail to be developed, the vessels of

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* [The existence of *six* pairs of vascular arches has recently been shown to be the typical condition, the newly discovered pair, situated between the fourth and fifth pairs of RATHKE'S scheme (fig. 316), being of short duration in Amniota.]

the visceral arches retaining their original simple condition. But they are in part of only short duration; they soon suffer, by the complete degeneration of extensive portions, a profound metamorphosis, which is effected in a somewhat different manner in Reptiles, Birds, and Mammals. An exposition of the changes in the case of Man only will be given here.

In human embryos only a few millimetres long, the truncus arteriosus, which emerges from the still single cardiac tube, is divided in the vicinity of the first visceral arch into a left and a right branch, which surround the pharynx, and are continuous above with the two primitive aortæ. It is the first pair of aortic arches. In only slightly older embryos their number is rapidly increased by the formation of new connections between the ventral truncus arteriosus and the dorsal primitive aortæ. Soon a second, a third, a fourth, and, finally, a fifth pair make their appearance in the same sequence in which the visceral arches are established in the case of Man as well as the remaining Vertebrates.

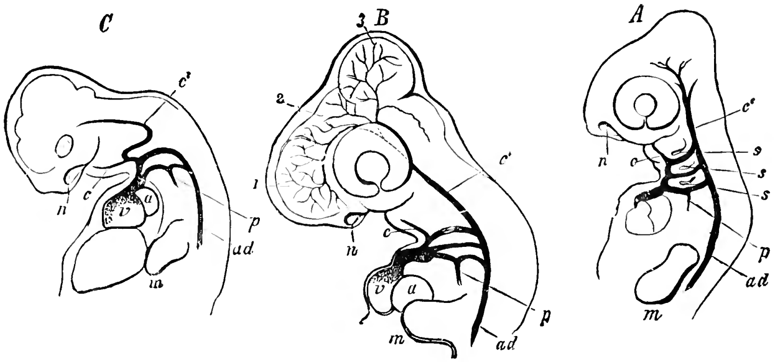

Fig. 317.—Development of the large arterial trunks, represented from embryos of a Lizard (*A*), the Chick (*B*), and the Pig (*C*), after Rathke.

The first two pairs of arterial arches have in all cases disappeared. In *A* and *B* the third, fourth, and fifth pairs are still fully preserved; in *C* only the two latter are still complete. *p*, Pulmonary artery arising from the fifth arch, but still joined to the dorsal aorta by means of a ductus Botalli; *c*, external, *c'*, internal carotid; *ad*, dorsal aorta; *a*, atrium; *v*, ventricle; *n*, nasal pit; *m*, fundament of the anterior limb.

The five pairs of vascular arches give off lateral branches to the neighboring organs at a very early period; of these several acquire a great importance and become carotis externa and interna, vertebralis and subclavia as well as pulmonalis. The carotis externa (fig. 316 *ce* and fig. 317 *c*) arises from the beginning of the first vascular arch, and is distributed to the region of the upper and lower jaws. The carotis interna (figs. 316 *ci*, 317 *c'*) likewise arises from the first arch, but farther dorsally, at the point where the arch bends around to become continuous with the root of the aorta; it conducts the blood to the embryonic brain and to the developing eye-ball (arteria ophthalmica). From the dorsal region of the fourth vascular arch (fig. 316 ^{4}) a branch is given off which is soon divided into two branches, one of which goes headwards to the medulla oblongata and the brain, the arteria vertebralis (*v*), whereas the other (*s*) supplies the upper limb (arteria subclavia). In the course of development these two arteries interchange relations in respect to calibre. In young embryos the vertebralis is by far the more important, while the subclavia is only a small inconspicuous lateral branch. But the more the upper extremity increases in size, the more the subclavia is elevated into the position of the main trunk, and the more the vertebralis sinks to the rank of an accessory branch. Finally, from the fifth [sixth] arch there bud forth branches to the developing lungs (figs. 316, 317 *p*).

As the simple diagram shows, the fundament of the arterial trunks which arise from the heart is originally *strictly symmetrical.* But at an early period there occur reductions of certain vascular tracts even to their complete disappearance; in this way the *symmetrical arrangement is gradually converted into an unsymmetrical one.*

The accompanying diagram (fig. 318)—in which the parts of the vascular course that degenerate are left free, and those which continue to be functional are marked by a heavy central line—will serve to illustrate this metamorphosis.

First, as early as the beginning of the nuchal flexure, the first and second vascular arches—with the exception of the connecting portions through which the blood flows to the carotis externa (*b*)—disappear.

The third arch (*c*) persists, but loses its connection with the dorsal end of the fourth, and therefore now conveys all its blood toward the head into the carotis interna (*a*), of which it has now become the initial part.

The chief rôle in the metamorphosis is assumed by the fourth and fifth arches (fig. 317 *C*). They soon exceed all other vessels in size, and as they lie nearest to the heart, they are converted into the two chief arteries which arise from it, the aortic arch and the arteria pulmonalis. An important modification is effected at the place of their origin from the truncus arteriosus when the latter is divided lengthwise by means of the development of the partition previously mentioned. The fourth arch (fig. 318 *e*) then remains in connection with the trunk (*d*) which arises from the left ventricle and receives blood exclusively from that source. The fifth arch (*n*), on the contrary, forms the continuation of that half (*m*) of the truncus arteriosus which emerges from the right ventricle. Thus the division of the blood into two separate currents initiated in the heart is also continued into the nearest vessels, but for a short distance only, since the fourth and fifth pairs of vascular arches (fig. 317) still empty their blood together into the aorta communis (*ad*), with the exception of a certain portion which runs through their accessory branches, in part to the head (*c.c′*) and upper limbs, in part to the still diminutive lungs. *Gradually, however, the process of separation thus introduced is continued still farther into the region of the peripheral vessels and finally leads to the establishment of the entirely distinct major and minor circulations. The final condition is attained by the degeneration of certain portions of the vessels and the enlargement of others.*

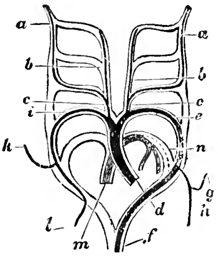

Fig. 318.—Diagrammatic representation of the metamorphosis of the blood-vessels of the visceral arches in a Mammal, after Rathke.

a, Carotis interna; *b*, carotis externa; *c*, carotis communis; *d*, body or systemic aorta; *e*, fourth arch of the left side; *f*, dorsal aorta; *g*, left, *k*, right vertebral artery; *h*, left subclavian artery; *i*, right subclavian (fourth arch of the right side); *l*, continuation of the right subclavian; *m*, pulmonary artery; *n*, its ductus Botalli.

A preponderance of the vascular arches of the left side over those of the right is soon recognisable (fig. 318). The former continually increase in size, while those of the right side become less and less apparent and finally in places disappear altogether. They are retained only in so far as they conduct the blood to the lateral branches which, arising from them, go to the head, the upper limbs, and the lungs. Consequently of the right aortic arch there remains only the tract which gives rise to the right carotis communis (*c*) and the right subclavia (*i*+*l*). We designate its initial part as the arteria anonyma brachiocephalica. With this the permanent condition is now established. The remnant of the right fourth vascular arch appears as a side branch only of the aorta (*e*), which forms an arch on the left side of the body, and here gives rise to the carotis communis sinistra (*c*) and the subclavia sin. (*h*) as additional lateral branches.

The right half of the fifth [sixth] pair of vascular arches likewise undergoes degeneration, except for the portion that conveys blood to the right lung. On the left side of the body, on the contrary, the pulmonary arch still persists for a long time and conducts blood into the left lung and also through the ductus arteriosus Botalli (*n*), into the aorta. After birth, in connection with pulmonary respiration, the duct of Botalli also degenerates. For the lungs, when they are expanded by the first act of inspiration, are in a condition to receive a greater quantity of blood. The consequence is that blood no longer flows into the ductus Botalli, and that the latter is converted into a connective-tissue cord, which extends between aorta and art. pulmonalis.

In addition to the regressive changes mentioned, there are effected meantime alterations of position in the large vascular trunks that arise from the heart. They move at the same time with the heart from the neck region into the thoracic cavity. In this fact lies the explanation of the peculiar course of the nervus laryngeus inf. or recurrens. At the time when the fourth vascular arch still lies forward in the region of its formation in the fourth visceral arch, the vagus sends to the larynx a small nerve branch, which, to reach its destination, passes below [caudad of] the vascular arch. When the latter migrates downwards, the nervus laryngeus must thereby be carried down with it into the thoracic cavity, and must form a loop, one portion of which, arising in the thoracic cavity from the vagus, bends around the arch of the aorta on the left side of the body (but around the subclavia on the right side of the body) to become continuous with the second portion, which takes the opposite or upward course to the region of its distribution.

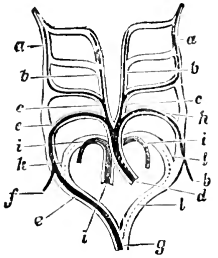

Fig. 319.—Diagrammatic representation of the metamorphosis of the arterial arches in Birds, after Rathke.

a, Internal, *b*, external, *c*, common carotid; *d*, systemic aorta; *e*, fourth arch of the right side (root of the aorta); *f*, right subclavian; *g*, dorsal aorta; *h*, left subclavian (fourth arch of the left side); *i*, pulmonary artery; *k* and *l*, right and left ductus Botalli of the pulmonary arteries.

The processes of development discussed also throw light on a series of abnormalities which are quite frequently observed in the large vascular trunks. I shall cite and explain two of the most important of these cases.

Occasionally in the territory of the vessels of the fourth visceral arches the original symmetrical condition is retained. The aorta is then divided in the adult into right and left vascular arches, which convey the blood into the unpaired aorta. From each of them there arises, as in the embryo, a separate carotis communis and subclavia.

Another abnormality is brought about by the development of the aortic arch of the right side of the body instead of that of the left, a condition which is met with in the class of Birds (fig. 319) as the normal state. This malformation is always connected with an altered position of the organs of the chest, a situs inversus viscerum. Of the other changes in the region of the arterial system the metamorphosis of the primitive aorta is to be mentioned before all others. As in the other Vertebrates (fig. 127 *ao*), so in Man, there are formed a right and a left aorta; but they subsequently move close together and fuse. This, again, explains an abnormality, which, it is true, has very rarely been observed in Man. The aorta is divided into right and left halves by means of a longitudinal partition; the process of fusion, therefore, has not been fully effected.

The aorta gives off at an early period as branches the unpaired mesenterica sup. and mesenterica inf. to the intestinal canal; furthermore, near its posterior end, the two voluminous navel vessels, arteriæ umbilicales (fig. 139 *Al*). These run from the dorsal wall of the trunk along the sides of the pelvic cavity ventrally to that part of the allantois which is subsequently differentiated into urinary bladder and urachus, here bend upward and pass on either side of the latter in the abdominal wall to the navel, enter the umbilical cord, and are resolved in the placenta into a capillary network, from which the blood is re-collected into the venæ umbilicales. During their passage through the pelvic cavity the umbilical arteries give off lateral branches that are at first inconspicuous, the iliacæ internæ, to the pelvic viscera, the iliacæ externæ to the posterior limbs now sprouting forth from the trunk as small knobs. The more the latter increase in size in older embryos, the larger do the iliacæ externæ and their continuations, the femorales, become.

After giving off the two umbilical arteries, the aorta becomes smaller and is continued to the end of the vertebral column as an inconspicuous vessel, the aorta caudalis or sacralis media.

At birth an important alteration occurs in this part of the arterial system also. With the detachment of the umbilical cord, the umbilical arteries can no longer receive blood; they therefore waste away with the exception of the proximal portion, which has given off as lateral branches the internal and external iliacs, and is now designated as the iliaca communis. However, two connective-tissue cords result from the degenerating vessels, the ligamenta vesico-umbilicalia lateralia, which run to the navel on the right and left of the bladder.

(*d*) *Metamorphoses of the Venous System.*

The older excellent works of **Rathke** and the more recent meritorious investigations of **His** and **Hochstetter** constitute the foundation of our knowledge in the difficult field with which we are now concerned. They show us that *originally all of the chief trunks of the venous system, with the exception of the inferior vena cava, are established in pairs and symmetrically.* This holds true not only for the vessels which collect the blood from the walls of the trunk and from the head, but also for the veins of the intestinal tube and the embryonic appendages which arise from it.

In the first place, so far as regards the veins of the body, the venous blood is collected from the head into the two *jugular veins* (fig. 320 *vj* and fig. 321 *A je, ji*), which run downwards along the dorsal side of the visceral clefts and unite in the vicinity of the heart with the *cardinal veins* (fig. 320 *vca* and fig. 321 *A ca*). The latter advance in the opposite direction, from below upwards, in the dorsal wall of the trunk, and collect the blood especially from the mesonephros. There arise from the confluence of the two veins the Cuvierian ducts (figs. 320, 321 *A dc*), from which are subsequently developed the two superior venæ cavæ. The veins of the trunk in Fishes exhibit a symmetrical arrangement like this throughout life.

In the earliest stages the Cuvierian ducts lie for some distance in the lateral wall of the pericardio-pleural cavity, where they run downwards from the dorsum to the front [ventral] wall of the trunk (fig. 320). On arriving at this point, they enter into the septum transversum, **Kölliker**'s mesocardium laterale, in order to reach the atrium of the heart. This important embryonic structure forms a point of collection for all the venous trunks emptying into the heart. In it there are joined to the Cuvierian ducts the veins from the viscera (fig. 313 *V.om* and *Vu*, fig. 320 *dv* and *uv*),—the paired yolk veins and umbilical veins,—all of which are joined into the common sinus venosus, which was previously (p. 558) mentioned apropos of the development of the heart, and which is situated directly between atrium and septum transversum.

The two vitelline veins (v. omphalomesentericæ) return the blood from the yolk-sac; they are the two oldest and largest venous trunks of the body, but they become inconspicuous in the same ratio as the yolk-sac shrinks to an umbilical vesicle. They run close together along the intestinal tube, and come to lie at the sides of the duodenum and stomach, where they are united to each other by transverse anastomoses even at a very early period.

The navel veins (venæ umbilicales) are also originally double. At first very small, they subsequently become, in contrast with the vitelline veins, more and more voluminous, as the placenta, from which they convey the blood back to the body of the embryo, is further developed. At the time of their first appearance the umbilical veins are found to be imbedded in the lateral wall of the abdomen (fig. 313 *Vu*), in which they make their way to the septum transversum and the sinus venosus (*sr*).

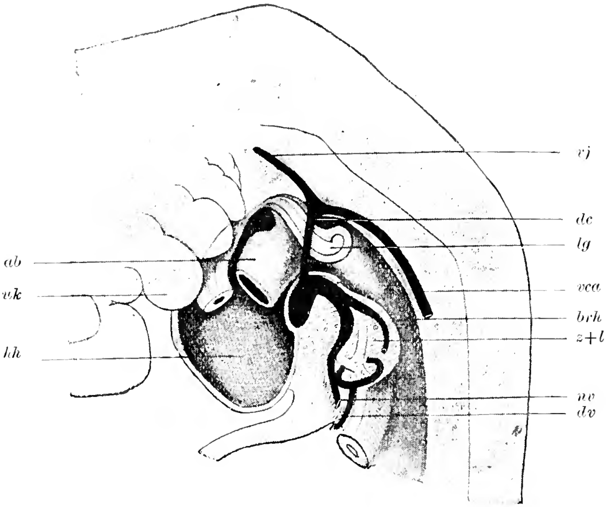

Fig. 320.—Sagittal reconstruction of a human embryo 5 mm. long, neck measurement (embryo *R*, HIS), **to illustrate the development of the pericardio-thoracic cavity and the diaphragm,** after HIS.

ab, Aortic bulb; *brh*, thoracic cavity (recessus parietalis, HIS); *hh*, pericardial cavity; *dc*, ductus Cuvieri; *dv*, vitelline vein (v. omphalomesenterica); *nv*, umbilical vein; *vca*, cardinal vein; *vj*, jugular vein; *lg*, lung; *z* + *l*, fundament of the diaphragm and the liver; *uk*, lower jaw.

The inferior vena cava (fig. 321 *A ci*) is established later than any of these paired trunks. It makes its appearance as an inconspicuous, from the beginning unpaired, vessel (in the Rabbit on the twelfth day, HOCHSTETTER) on the right side of the aorta in the tissue between the two primitive kidneys; caudalwards it is connected by lateral anastomoses with the cardinal veins. At the heart it opens into the sinus venosus.

From this primitive form of the venous system (fig. 321 *A*) is derived the ultimate condition in Man. There are three changes which are conspicuous in this connection. (1) The veins empty directly into the atrium instead of a venous sinus. (2) The symmetrical arrangement in the region of the Cuvierian ducts and the jugular and cardinal veins gives place to an unsymmetrical arrangement accompanied by a degeneration or stunting of some of the chief trunks. (3) With the development of the liver there is formed a special portal system.

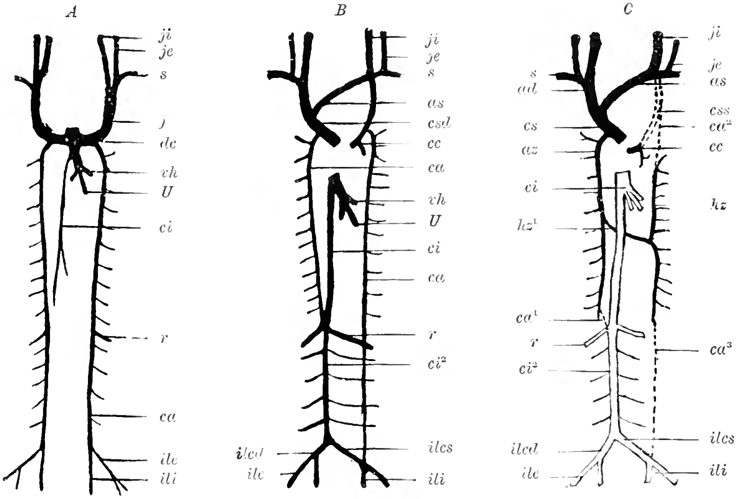

Fig. 321.—Diagram of the development of the venous system of the body.
dc, Ductus Cuvieri; *je*, *ji*, vena jugularis externa, interna; *s*, v. subclavia; *vh*, v. hepatica revehens; *U*, v. umbilicalis; *ci* (*ci*^{2}), v. cava inferior; *ca* (*ca*^{1}, *ca*^{2}, *ca*^{3}), v. cardinalis; *ilcd*, *ilcs*, v. iliaca communis dextra, sinistra; *ad*, *as*, v. anonyma brachiocephalica dextra, sinistra; *cs*, v. cava superior; *csd*, v. cava superior dextra; *css*, rudimentary portion of v. cava superior sinistra; *cc*, v. coronaria cordis; *az*, v. azygos; *hz* (*hz*^{1}), v. hemiazygos; *ile*, v. iliaca externa; *ili*, v. iliaca interna; *r*, v. renalis.

The alteration first mentioned is accomplished by the incorporation of the sinus venosus in the atrium. At first enclosed in the septum transversum, the sinus elevates itself above the upper surface of the latter, from which it detaches itself, and comes to lie as an appendage to the atrium in the anterior trunk-cavity. Finally it fuses completely with the heart and furnishes the smooth region of the atrial wall, which is destitute of the pectinate muscles (His).

There are in it separate openings for the two Cuvierian ducts—the future venæ cavæ superiores—and an opening distinct from them for the veins coming from the viscera below (the future cava inferior).

The metamorphoses in the region of the Cuvierian ducts begin with a change in their position. Their course from above downward becomes more direct. At the same time, like the sinus venosus, they emerge from the niveau of the transverse septum and lateral walls of the trunk into the body-cavity and carry before them the serous membrane, with which they are covered, as a crescent-shaped fold, which contributes to the formation of the pericardial sac, and has been already described as the *pleuro-pericardial fold.* By fusing with the mediastinum the Cuvierian ducts pass from the walls of the trunk into the latter and come to lie nearer together in the median plane. Of their affluents the jugular veins gradually predominate over the cardinal veins (fig. 322 *B*). There are three reasons for this. First, the anterior part of the body, and especially the brain, far outstrips in growth the posterior part; secondly, there arises in this region a competitor of the cardinal veins, the inferior vena cava, which assumes in place of them the function of returning the blood. Thirdly, when the anterior limbs are established, the venæ subclaviæ (*s*) empty into the jugulares. Consequently the lower portion of the jugular, from the entrance of the subclavia onward, now appears as the immediate continuation of the Cuvierian duct, and together with it is designated as superior vena cava (fig. 322 *B csd*).

There exists between the right and left sides a difference in the course of the superior venæ cavæ, which, as GEGENBAUR has pointed out, is the cause of the asymmetry that is developed in Man. While the right vena cava superior (fig. 322 *B csd*) descends more directly to the heart, the left (*css*) describes a somewhat longer course. Its terminal portion is bent from the right to the left around the posterior [dorsal] wall of the atrium, where it is imbedded in the coronal furrow and receives the blood from the coronal vein (*cc*) of the heart.

In Reptiles, Birds, and many Mammals a stage of this kind, with two venæ cavæ superiores, becomes permanent; in Man it exists only during the first months. Then there is a partial degeneration of the left vena cava superior. The degeneration is initiated by the formation of a transverse anastomosis (fig. 322 *B as*) between the right and left trunks. This conveys the blood from the left to the right side, where the conditions are more favorable for the return of the blood to the heart. In consequence of this the proximal end of the right cava becomes much larger, the left, on the contrary, proportionately smaller. Finally, there is a complete wasting away of the latter blood course (fig. 322 *C css*) as far as the terminal part (*cc*), which is lodged in the coronal groove. This part remains open, because the cardiac veins convey blood to it, and is now distinguished as sinus coronarius.

A process in many respects similar to this is repeated in the case of the cardinal veins (fig. 322 *A ca*). The latter collect the blood from the primitive kidneys and the posterior wall of the trunk, from the pelvic cavity and the posterior limbs. From the pelvic cavity they receive the venæ hypogastricæ (*ili*), and from the limbs the v. iliacæ externæ (*ile*) and their continuation, the v. crurales. In this way the cardinal veins are at first, as in Fishes, the chief collecting trunks of the lower half of the body. Subsequently, however, they diminish in importance, since the inferior vena cava becomes the main collecting trunk instead of them.

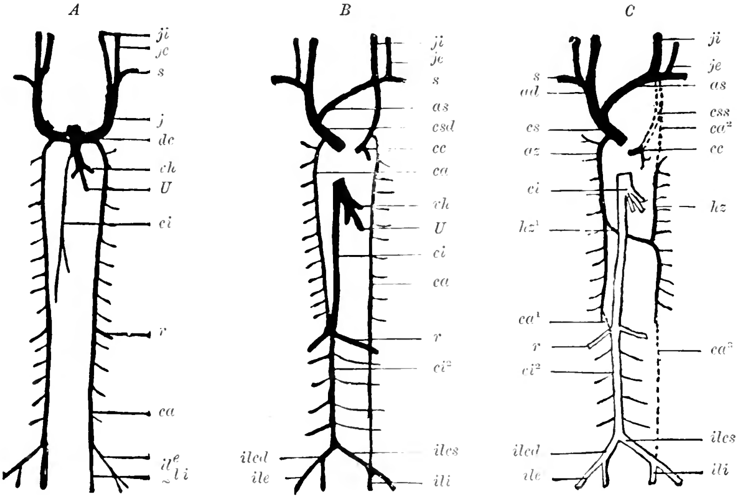

Fig. 322.—Diagram of the development of the venous system of the body.
dc, Ductus Cuvieri; *je*, *ji*, vena jugularis externa, interna; *s*, v. subclavia; *vh*, v. hepatica revehens; *U*, v. umbilicalis; *ci* (*ci*²), v. cava inferior; *ca* (*ca*¹, *ca*², *ca*³), v. cardinalis; *ilcd*, *ilcs*, v. iliaca communis dextra, sinistra; *ad*, *as*, v. anonyma brachiocephalica dextra, sinistra; *cs*, v. cava superior; *csd*, v. cava superior dextra; *css*, rudimentary portion of v. cava superior sinistra; *cc*, v. coronaria cordis; *az*, v. azygos; *hz* (*hz*¹), v. hemiazygos; *ile*, v. iliaca externa; *ili*, v. iliaca interna; *r*, v. renalis.

It is only within the last few years that the development of the inferior vena cava has been (by HOCHSTETTER) explained. According to his investigations there are to be distinguished two tracts which are of different origin, a shorter anterior and a longer posterior. The former, as previously mentioned, makes its appearance as an inconspicuous vessel on the right side of the aorta in the tissue between the two primitive kidneys (fig. 322 *A* and *B ci*); the latter, on the contrary, is developed subsequently out of the posterior region of the right cardinal vein (fig. 322 *B* ci^2). The anterior, independently arising part of the inferior vena cava, soon after its establishment, unites with the two cardinal veins by means of transverse branches in the vicinity of the vena renalis (*r*). In consequence of this increase of drainage territory, it soon increases considerably in calibre, and since it presents more favorable conditions for the conveyance of blood from the lower half of the body than the upper portion of the cardinal veins does, it finally becomes the chief conduit.

If the stage thus far described were to become the permanent condition (fig. 322 *B*), we should have an inferior vena cava, which forks in the region of the renal veins (*r*) into two parallel trunks, that descend at both sides of the aorta to the pelvis. Such cases, as is known, are found among the varieties of the venous system; they are derived from the previously described stages of development as malformations by arrested growth. However, they are only rarely observed, for in the normal course of development there is established at an early period an asymmetry between the lower portions of the two cardinal veins, from the moment, indeed, when they have united themselves to the lower part of the inferior vena cava by means of anastomoses. The right portion acquires a preponderance, becomes enlarged, and finally alone persists (fig. 322 *B*, *C*), whereas the left lags behind in growth and withers. This results from two conditions. First, the right cardinal vein (ci^2) lies more in the direct prolongation of the vena cava inferior than does the left, and thus occupies a more favorable situation; secondly, there is formed in the pelvic region an anastomosis (*ilcs*) between the two cardinal veins, which conducts the blood of the left hypogastrica and the left iliaca externa and cruralis to the right side. Owing to this anastomosis, which becomes the vena iliaca communis sinistra, the portion of the left cardinal vein lying between the renal veins and the pelvis (fig. 322 *C* ca^3) is rendered functionless, and with the degeneration of the primitive kidney disappears. The right cardinal vein has now become for a certain distance a direct continuation of the inferior vena cava; it furnishes that portion of the latter which is situated between the renal veins and the division into the two venæ iliacæ communis (fig. 322 *B* and *C* ci^2).

While the abdominal part of the left cardinal vein (fig. 322 *C* ca^3) succumbs and the corresponding region of the right cardinal vein produces the lower part of the inferior vena cava (ci^2), their thoracic portions persist in a reduced form, since they receive the blood from the intercostal spaces (fig. 322 *B* *ca*). In this region occurs still another and last metamorphosis, by which likewise an asymmetry is brought about between the halves of the body. In the thoracic part of the body the original conditions of the circulation are altered by the degeneration of the left cava superior (fig. 322 *C* *css*). The direct flow of the left cardinal vein to the atrium is thereby rendered more difficult, and finally ceases altogether, the tract designated by ca^2 undergoing complete degeneration. Meanwhile a transverse anastomosis (hz^1), which has been formed in front of the vertebral column and behind the aorta between the corresponding vessels of both sides, receives the blood of the left side of the body and transports it to the right side. In this manner the thoracic part of the left cardinal vein and its anastomosis become the left hemiazygos (*hz* and hz^1); the right and larger cardinal vein becomes the azygos (*az*).

Thus by many indirect ways is attained the permanent condition of the venous system of the trunk, with its asymmetry and its preponderance of the venous trunks in the right half of the body.

A third series of metamorphoses, which we shall now take into consideration, concerns the development of a *liver circulation.*

The liver receives its blood in different stages of the embryonic development from various sources: for a time from the vitelline veins; during a second period from the umbilical veins; after birth, finally, from the veins of the intestines—the portal vein. *This threefold alteration finds its explanation in the conditions of growth of the liver, the yolk-sac, and the placenta.* As long as the liver is small, the blood coming from the yolk-sac suffices for its nourishment. But when it increases greatly in size—the yolk-sac, on the contrary, growing smaller—other blood-vessels at this time, the umbilical veins, must supply the deficiency. When, finally, at birth the placental circulation ceases, the venous trunks of the intestinal canal, which meanwhile have become very large, can supply the needs.

These circumstances must be kept in mind, in order to comprehend the shifting conditions of circulation in the liver and the profound alterations to which the venous trunks connected with it—the vitelline, umbilical, and portal veins—are naturally subjected in the changing supply of blood.

When the hepatic ducts grow out from the duodenum into the ventral mesentery and septum transversum and send out shoots, they enclose the two vitelline veins accompanying the intestine, which are at this place connected with each other by ring-like anastomoses (sinus annularis, HIS) which surround the duodenum (fig. 320 *dv*). They are supplied with blood by lateral branches given off from these veins. The more the liver increases in size, the larger do the lateral branches (venæ hepaticæ advehentes) become. Between the network of hepatic cylinders (fig. 187 *lc*) they are resolved into a capillary network (*g*), from which at the dorsal margin of the liver large efferent vessels (venæ hepaticæ revehentes) re-collect the blood and convey it back into the terminal portion of the vitelline vein, which empties into the atrium. In consequence of this the portion of the vitelline vein which lies between the venæ hepaticæ advehentes and revehentes continually becomes smaller, and finally atrophies altogether, since all the blood from the yolk-sac is employed for the hepatic circulation. The same process in the main is accomplished here as in the vessels of the visceral arches of gill-breathing Vertebrates, which upon the formation of branchial lamellæ are converted into branchial arteries, branchial veins, and a capillary network interpolated between the two.

The two umbilical veins participate, even at an early period, in the hepatic circulation. Originally they run from the umbilical cord in the *front [ventral] wall of the abdomen* (fig. 313 *Vu*), from which they receive lateral branches, and then enter the sinus venosus (*Sr*) *above the fundament of the liver.* They pursue, therefore, an entirely different course from that which they do later, when the terminal part of the umbilical vein is situated *under the* liver. According to HIS, this change in their course takes place in the following manner: The right umbilical vein in part atrophies (as also in the Chick, p. 552) and becomes, as far as it persists, a vein of the ventral wall of the abdomen. The left umbilical vein, on the contrary, gives off anastomoses in the septum transversum to neighboring veins, one of which makes its way *under the liver* to the sinus annularis of the vitelline veins, and thereby conducts a part of the placental blood into the hepatic circulation. Since by its rapid growth the liver demands a large accession of blood, the anastomosis soon becomes the chief course, and finally with the degeneration of the original tract receives all the blood of the umbilical veins. This, mingled with the blood of the yolk-sac, circulates through the liver in the vessels which took their origin from the vitelline veins—in the venæ hepaticæ advehentes and revehentes. Then it flows into the atrium through the terminal part of the vitelline vein. The latter also receives the inferior vena cava, which at this time is still inconspicuous, and can therefore be designated even now, in view of the ultimate condition, as the cardiac end of the inferior vena cava.

During a brief period all of the placental blood must first traverse the hepatic circuit in order to reach the heart. A direct passage to the inferior vena cava through the ductus venosus Arantii does not yet exist. But such an outlet becomes necessary from the moment when, by the growth of the embryo and the placenta, the blood of the umbilical veins has so increased in amount that the hepatic circulation is no longer able to contain it. There is then developed on the under surface of the liver out of anastomoses a more direct connecting branch, the ductus venosus Arantii (fig. 323 *d.A*), between umbilical vein (*n.v*) and inferior vena cava (*c.i″*). Thus is established—and it persists until birth—a condition by which the placental blood (*n.v*) is divided at the porta into two currents: one passing through the ductus venosus Arantii (*d.A*) into the inferior vena cava (*c.i″*); the other pursuing a round-about way, passing through the venæ hepaticæ advehentes (*ha.s* and *ha.d*) into the liver, here mingling with the blood brought to the liver through the vitelline vein (*pf.a*) from the yolk-sac and from the intestinal canal, which has in the meantime become enlarged, and finally passing through the venæ hepaticæ revehentes (*h.r*), also to reach the inferior vena cava (*c.i″*).

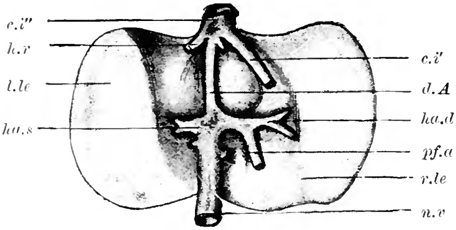

Fig. 323.—**Liver of an 8-months human embryo, seen from the under surface,** from GEGENBAUR.

l.le, Left lobe of the liver; *r.le*, right lobe; *n.v*, umbilical vein; *d.A*, ductus venosus Arantii; *pf.a*, portal vein; *ha.s*, *ha.d*, vena hepatica advehens sinistra and dextra; *h.r*, vena hepatica revehens; *c.i′*, cava inferior; *c.i″*, terminal part of the cava inferior, which receives the venæ hepaticæ revehentes (*h.r*).

There is still something to be added concerning *the development of* *the portal vein.* It is to be seen in fig. 323 as an unpaired vessel (*pf.a*). It empties into the right afferent hepatic vein, derives its roots from the region of the intestinal canal, and conveys the venous blood from the latter into the right lobe of the liver. It takes its origin from the two primitive vitelline veins.

According to the account of His, the two vitelline veins fuse along the tract where they run close together on the intestinal canal; on the contrary, in the region where they run to the liver and are connected with each other to form two ring-like anastomoses, each of which encircles the duodenum, an unpaired trunk is formed by the atrophy of the right half of the lower [posterior] ring and the left half of the upper one. The portal vein thus formed therefore runs first to the left and backward [dorsad] around the duodenum, and then emerges on the right side of it; it draws its blood partly from the yolk-sac and partly from the intestinal canal through the vena mesenterica. Afterwards the first source is exhausted with the regressive metamorphosis of the yolk-sac, but the other becomes more and more productive with the enlargement of the intestine, the pancreas, and the spleen, and during the last months of pregnancy conveys a large stream of blood to the liver.

The additional changes, which occur at birth, are easily comprehended (fig. 323). With the detachment of the after-birth the placental circulation ceases. The umbilical vein (*n.v*) conveys no more blood to the liver. That portion of its tract which extends from the umbilicus to the porta hepatis degenerates and becomes a fibrous ligament (the lig. hepato-umbilicale or lig. teres hepatis). Likewise the ductus Arantii (*d.A*) produces the well-known ligament enclosed in the left sagittal fissure (lig. venosum). The right and left venæ hepaticæ advehentes (*ha.d*, *ha.s*) again receive their blood, as in the beginning of the development, from the intestinal canal through the portal vein (*pf.a*).

Now that we have become acquainted with the details of the morphological changes, I close this section on the vascular system with a short *sketch of the fœtal circulation of the blood.* It is characteristic of this that no division into two separate circulations, into the major or systemic and the minor or pulmonary, has yet taken place; further, that in most of the vessels neither purely arterial nor purely venous blood circulates, but a mixture of the two. Purely arterial blood is contained only in the umbilical veins as they come from the placenta, whence we will follow the circulation.

Having arrived at the liver, the current of the umbilical veins is divided into two branches. One stream goes directly through the ductus Arantii into the inferior vena cava, and is here mingled with the venous blood which returns to the heart from the posterior limbs and the kidneys. The other stream passes through the liver, where there is added to it the venous blood of the portal vein coming from the intestine; by this circuitous course it also reaches, through the venæ hepaticæ revehentes, the inferior vena cava. From the latter the mixed blood flows into the right atrium, but, in consequence of the position of the Eustachian valve and because the foramen ovale is still open, the greater part of it passes through the latter into the left atrium. The other smaller part is again mingled with venous blood, which has been collected by the superior vena cava from the head, the upper limbs, and (through the azygos) from the walls of the trunk, and is propelled into the right ventricle and from there into the pulmonalis. The latter sends a part of its highly venous blood to the lungs, the other part through the ductus Botalli to the aorta, where it is added to the arterial current coming from the left ventricle.

The blood of the left ventricle comes principally from the inferior cava, only a small part of it from the lungs, which pour their blood, which at this time is venous, into the left atrium. It is driven into the aortic arch and part of it is given off through lateral branches to the head and upper limbs (carotis communis, subclavia); the rest is carried on downwards in the aorta descendens, where the venous current of blood from the right atrium by the way of the ductus Botalli is united with it. The mixed blood is distributed to the intestinal canal and the lower limbs, but the most of it reaches the placenta through the umbilical veins, where it is again made arterial.

In the distribution of the blood in the anterior and the posterior regions of the body a noteworthy difference is easily recognised. The former receives through the carotis and subclavia a more arterial blood, since to the stream in the aorta descendens is added the venous blood of the right ventricle through the ductus Botalli. Especially in the middle of pregnancy is this difference important. There has been an endeavor to refer to this fact the more rapid growth of the upper part of the body in comparison with the lower.

As this sketch has shown, there is everywhere a mingling of the different kinds of blood. This, it is true, is not uniform in the different months of embryonic life, because, indeed, the separate organs do not alter in size uniformly, and especially because the lungs during the later stages are in a condition to receive more blood, and finally because the foramen ovale and the ductus Botalli become narrower during the last months. On account of these facts, less blood passes, even before birth, from the inferior vena cava into the left atrium, and likewise less from the pulmonary artery into the descending aorta, than was the case in earlier months. Thus there is gradually introduced toward the end of pregnancy a separation into a right and a left heart, with their separate blood-currents (HASSE). But it is almost at a single stroke that this separation, in consequence of birth, becomes complete.

Great alterations are now brought about by the beginning of pulmonary respiration and by the cessation of the placental circulation. Both events coöperate to increase the blood-pressure in the left heart, and to diminish that in the right. The blood-pressure becomes reduced because no more blood runs into the right atrium from the umbilical vein and because the right ventricle must furnish more blood to the expanding lungs. In consequence of this the ductus Botalli (fig. 318 *n*) is closed and then converted into the ligamentum Botalli. Since, moreover, a greater quantity of blood now flows from the lungs into the left atrium, the pressure in the latter is increased, and since at the same time the pressure is diminished in the right atrium, the closure of the foramen ovale, owing to the peculiar valvular arrangements, is now effected. For the margin of the valvula foraminis ovalis applies itself firmly to the limbus Vieussenii and fuses with it.

By the closure of the oval foramen and the Botallian duct the division of the blood-current into a major, systemic circuit and a minor, pulmonary circuit, which was initiated before birth, is now completed.

SUMMARY.

Development of the Heart.

1. In the first fundament of the heart two different types can be distinguished in Vertebrates.

First Type. In Cyclostomes, Selachians, Ganoids, and Amphibia the heart is developed from the beginning as an unpaired structure on the under [ventral] surface of the cavity of the head-gut, in the ventral mesentery, which is thereby divided into a mesocardium anterius and posterius.

Second Type. In Birds and Mammals the heart is developed out of separate halves, which afterwards fuse with each other into a single tube, which then has the same position as in the first type.

2. The second type is to be derived from the first, and is explainable as an adaptation to the great size of the yolk, in that the heart is established at a time when the splanchnopleure is still spread out flat upon the yolk and is not yet folded together to form the head-gut.

3. The cells which are united to form the endothelium of the heart are split off from a proliferating, thickened place of the entoderm.

4. The heart is first established in all Vertebrates in the cervico-cephalic region behind the last visceral arch.

5. The posterior or venous end of the single cardiac tube receives the blood from the body through the omphalomesenteric veins; the anterior or arterial end gives off the blood to the body through the truncus arteriosus.

6. In the amniotic Vertebrates the single cardiac sac is converted by a series of metamorphoses—(1) by flexures, constrictions, and changes of position, and (2) by the formation of partitions inside of it—into a heart composed of two ventricles and two atria.

7. The straight sac assumes the form of a letter *S*.

8. The venous portion of the *S* comes to lie more dorsal, the arterial more ventral; the two are marked off from each other by a constriction, the auricular canal, and are now to be distinguished as atrium and ventricle.

9. The venous portion or the atrium forms lateral evaginations, the auricles of the heart, which surround from behind the truncus arteriosus.

10. The formation of partitions, by which atrium, ventricle, and truncus arteriosus are divided into right and left halves, begins at three different places.

  (*a*) First of all, the atrium is divided by an atrial partition into a right and a left half; but the separation is incomplete, since there exists a passage in the partition, the foramen ovale, which remains open up to the time of birth.

  (*b*) By its downward growth the atrial partition reaches the auricular canal (septum intermedium of HIS) and divides the opening in it into a right and left ostium atrioventriculare.

  (*c*) The ventricle is divided into right and left halves by a partition (septum ventriculi) beginning at the apex of the heart; the division is also indicated externally by the sulcus interventricularis.

(*d*) The truncus arteriosus is divided into pulmonary artery and aorta by the development of a special partition, which begins above, grows downward, and joins the ventricular partition.

(*e*) The complete separation of the atria first takes place after birth by the permanent closure of the foramen ovale.

11. At the ostium atrioventriculare and at the ostium arteriosum the first fundaments of the valves are formed as thickenings of the endocardium (endocardial cushions) projecting inward.

Development of the Chief Arterial Trunks of Man and Mammals.

12. From the truncus arteriosus there arise five pairs of visceral-arch vessels (aortic arches), which run along the visceral arches, embrace the head-gut laterally, and unite dorsally to form the two primitive aortæ.

13. The two vessels fuse at an early period to form the unpaired aorta lying under the vertebral column.

14. In Mammals, of the five pairs of visceral-arch vessels the first and second degenerate; the third furnishes the proximal part of the carotis interna; the fourth arch becomes on the left side the aortic arch, on the right side the arteria anonyma brachiocephalica and the proximal part of the subclavia; [the fifth early disappears;] the fifth [sixth] arch gives off branches to the lungs, and becomes the pulmonary artery, but on the left side remains until the time of birth in open communication with the aortic arch through the ductus Botalli, whereas the corresponding portion on the right side atrophies.

15. After birth the ductus Botalli is closed and converted into the ligament of the same name.

16. From the aorta two pairs of large arterial trunks go to the fœtal membranes—to the yolk-sac the vitelline arteries (arteriæ omphalomesentericæ), to the allantois and placenta the umbilical arteries.

17. The vitelline arteries subserve the vitelline circulation, and afterwards, with the reduction of the umbilical vesicle, degenerate.

18. The umbilical arteries, which continually become larger with the increasing development of the placenta, arise from the lumbar portion of the aorta, pass forward [ventral] in the lateral wall of the pelvis, then at the side of the bladder and along the inner surface of the abdominal wall to the umbilicus and umbilical cord.

19. The umbilical arteries give off the iliaca interna to the cavity of the pelvis, the iliaca externa to the lower limbs.

20. After birth the umbilical artery degenerates into the ligamentum vesico-umbilicale laterale, with the exception of its proximal part, which persists as the iliaca communis.

Development of the Chief Venous Trunks.

21. With the exception of the inferior vena cava, all venous trunks are established in pairs.

22. The two jugulars collect the blood from the head, the two cardinals from the trunk, but especially from the primitive kidneys.

23. The jugular and cardinal veins of either side unite to form the Cuvierian ducts, which pass transversely from the lateral wall of the trunk to the posterior end of the heart, imbedded in a transverse fold of the front wall of the trunk, the septum transversum.

24. The two vitelline veins collect the blood from the yolk-sac; from the navel onward they run in the ventral mesentery to the septum transversum.

25. The two umbilical veins collect the blood from the placenta; from the attachment of the umbilical cord they run at first in the abdominal wall to the transverse septum.

26. In the septum transversum the Cuvierian ducts and the vitelline and umbilical veins unite to form the sinus reuniens, which subsequently disappears as an independent structure and is incorporated in the atrium.

27. The cardinal veins diminish in importance (1) in consequence of the degeneration of the primitive kidneys, and (2) from the fact that the blood from the lower half of the body is conveyed back to the heart by the inferior vena cava.

28. The upper part of the inferior vena cava arises as an unpaired, independent vessel between the two cardinal veins, and then, at the place where the renal veins empty in, unites with the right cardinal vein. The latter is in this way converted into the lower portion of the inferior cava.

29. The Cuvierian ducts with the beginning of the jugular veins are designated as the venæ cavæ superiores.

30. An asymmetry in the embryonic venous trunks, which are established in pairs, is brought about by the fact that the two superior venæ cavæ, and also at their middle the remnants of the two cardinal veins, are joined together by transverse trunks:

31. Since through these cross anastomoses more and more of the blood, and finally the whole of it, is conveyed from the trunks of the left half of the body into those of the right half, the proximal part of the left superior vena cava, except a small portion, which lies in the coronary groove of the heart, degenerates, receives the cardiac veins, and becomes the sinus coronarius cordis. Likewise the cardiac end of the left cardinal vein disappears.

32. From the paired fundaments of the venous trunks are formed the single superior vena cava, the sinus coronarius cordis, and the vena azygos and hemiazygos.

33. The vitelline veins, which afterwards become unpaired, give rise, when the liver is developed, to the portal circulation (the venæ hepaticæ advehentes and revehentes).

34. The umbilical veins, of which the right early degenerates, originally run in the abdominal wall *above* the liver to the sinus reuniens; then the left forms an anastomosis with the vitelline vein *under* the liver, whereby its current shares in the portal circulation.

35. There arises out of an anastomosis between the umbilical vein and the cardiac end of the inferior vena cava on the under surface of the liver the ductus venosus Arantii, which results in the division of the blood of the umbilical vein into two currents.

36. After birth the umbilical vein degenerates into the ligamentum teres hepatis, and the ductus venosus Arantii is obliterated; the venæ hepaticæ advehentes now receive their blood from the terminal part of the original vitelline vein or the portal vein only, which collects the blood from the intestinal canal.

37. The septum transversum, in which run the venous trunks on their way to the heart, is the starting-point for the development of the diaphragm and the pericardial sac, and forms at first an incomplete partition between the abdominal cavity and pleuro-pericardial cavity, which still communicate with each other on either side of the vertebral column.

38. The pericardial sac is separated off from the thoracic cavity as follows: (1) the Cuvierian ducts or future superior venæ cavæ, instead of running transversely, run more and more obliquely from above downward, detach themselves from the septum transversum, and elevate the pleura into pericardial folds, which run from above downward and project inward; (2) the margin of the pericardial fold fuses with the mediastinum posterius, in which are enclosed œsophagus and aorta, whereby the superior venæ cavæ are transferred to the mediastinum.

39. The thoracic cavities have for a time the form of tubular spaces lying on the dorsal side of the heart and on either side of the spinal column; they receive the developing lungs, and still communicate caudad with the abdominal cavity.

40. The two thoracic cavities are separated from the abdominal cavity by the fusion of the dorsal rim of the septum transversum with peritoneal folds of the dorsal wall of the trunk (the pillars of Uskow).

41. The diaphragm is composed of two parts, the ventral septum transversum, and a dorsal part, the pillars.

42. Upon its first establishment the liver grows into the septum transversum, but subsequently detaches itself from the latter and remains united to the diaphragm by means of its peritoneal covering only, the coronal ligament.

II. The Development of the Skeleton.

With the exception of the chorda dorsalis, which takes its origin from the inner germ-layer, the skeleton of Vertebrates is a product of the intermediate layer, resulting from a series of histological differentiations, a general survey of which has already (p. 540) been given. There have appeared many articles treating on this very complicated apparatus in the higher Vertebrates from a developmental and also especially from a comparative-anatomical standpoint. By an exhaustive treatment of this subject this part of the work would attain to greater proportions than the plan of the present text-book permits. I shall therefore limit myself to the more important conditions of organisation and for what remains refer to the text-books of comparative anatomy.

Two chief parts are distinguishable in the skeleton of Vertebrates: (1) the axial skeleton, which is in turn divisible into that of the trunk and that of the head, and (2) the skeleton of the limbs. The former is the older and more primitive, being possessed by all Vertebrates; the latter has been developed later, and is entirely wanting in the lower groups (Amphioxus, Cyclostomes).

A. The Development of the Axial Skeleton.

The original foundation of the axial skeleton of all Vertebrates is the notochord or chorda dorsalis. By this is understood a flexible, rod-like structure, which is situated in the axis of the body below the neural tube and above the intestine and aorta. It reaches from the front end of the base of the mid-brain to the end of the tail.

For a time after its establishment the front end of the chorda remains in union at a small place with the epithelium of the fore-gut. This place is immediately behind the upper attachment of the primitive pharyngeal membrane (Rachenhaut). There is here found, a little behind the hypophysial pocket, a slight depression in the epithelial lining of the fore-gut—SEESSEL'S pocket or the palatal pocket of SELENKA. It is only some time after the rupture of the pharyngeal membrane that the chorda becomes detached from the intestinal epithelium and terminates free in the mesenchyma, often with a hook-like end (KEIBEL, KANN, CARIUS).

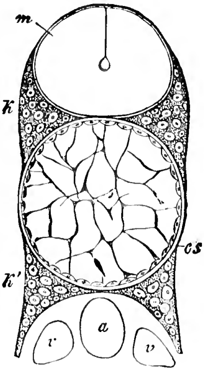

Fig. 324. — Cross section through the vertebral column of a young Salmon, after GEGENBAUR.
cs, Sheath of the chorda; *k*, neural arch; *k'*, haemal arch; *m*, spinal cord; *a*, dorsal aorta; *v*, cardinal veins.

In the case of Amphioxus the chorda is the only skeletal structure present in the whole of the soft body; in the lower Vertebrates (Cyclostomes, Fishes, Amphibia) it exists even in the adult animals as a more or less important organ; but in the Amniota it is reduced almost to obliteration, and only in the earliest stages of development plays a rôle as the forerunner, as it were, of the higher form of axial skeleton which finally takes its place. While reference is made to previous portions of the text-book for information about the first development of the chorda, its further metamorphosis may be treated of here more at length. This varies according as the chorda becomes a really functional organ or soon begins to degenerate.

In the first instance, when the band of chordal cells has been constricted off from the inner germ-layer, it becomes more sharply limited at its periphery by the secretion of a firm, homogeneous envelope, the sheath of the chorda (fig. 324 *cs*). Then the cells increase in size by the accumulation of fluid within their protoplasm, which finally exists in the form of a thin superficial layer only; the cells become enveloped in firm membranes, thus acquiring exactly the appearance of plant cells. But directly beneath the sheath of the chorda (fig. 324) the cells remain small and protoplasmic and constitute a special layer, the chordal epithelium, which by proliferation and metamorphosis of its elements causes an increase of the substance of the chorda.

Immediately after its formation the chorda is in contact above with the neural tube, below with the entoderm, and laterally with the primitive segments. This relation is altered as soon as the intermediate layer makes its appearance between the first embryonic fundaments. Then a layer of cells grows around the chorda (fig. 262), spreads itself out from here around the neural tube above, and furnishes the foundation from which are developed the segmented vertebral column and in front, in the region of the five brain-vesicles, the cranial capsule; it has therefore received the name of *membranous vertebral column* and of membranous cranial capsule (*membranous primordial cranium*); it is also appropriately designated as skeletogenous layer, the envelope which invests the chorda being called the skeletogenous sheath of the chorda. (Compare p. 172 for an account of the first formation of it.)

The mesenchyme also spreads out laterally in the embryo, penetrates into the spaces between primitive segments, and is converted into thin plates of connective tissue (ligamenta intermuscularia), by means of which the musculature of the trunk is parted into separate muscle segments (myomeres). The muscle-fibres find attachment and support upon both the anterior and posterior faces of these plates.

Such a condition is permanently preserved in Amphioxus lanceolatus. The chorda, with its sheath, is the only firm skeletal structure. Fibrous connective tissue (membranous vertebral column) envelops it and the neural tube, and sends out into the musculature of the trunk the intermuscular ligaments.

When the originally membranous tissue surrounding the chorda and neural tube is followed in its further development in the embryos of the higher Vertebrates, it is to be seen that it successively undergoes *two metamorphoses*: that at first it is partially chondrified, and that subsequently the cartilaginous pieces are converted into osseous tissue; or, in other words, *the first-established membranous vertebral column is soon converted into a cartilaginous, and this in turn is replaced by a bony one, and in the same manner the membranous primordial cranium is transformed into a cartilaginous, and this in turn into a bony cranial capsule.*

The three stages which succeed one another in the development of the higher Vertebrates are also encountered in a comparative-anatomical investigation of the axial skeleton in the series of Vertebrates, and in such a manner that the condition, which in many classes appears only as a transitory embryonic one, is retained permanently in the lower classes. As Amphioxus possesses a membranous axial skeleton, so the Selachians and certain of the Ganoids are representatives of the stage with cartilaginous vertebral column. The third stage in the evolution of the axial skeleton is more or less completely attained by all the higher Vertebrates.

This, again, is a very instructive example—of which the embryology of the skeleton presents many others—of the parallelism which exists between the development of the individual and that of the race; it teaches how embryological and comparative-anatomical investigations are mutually complemental. In the detailed description of the conditions which are observed in the development of the cartilaginous and bony axial skeleton, I shall limit myself to Man and Mammals, and since great differences exist between the posterior region, which encloses the spinal cord, and the anterior, which envelops the vesicles of the brain, I shall treat of them separately.

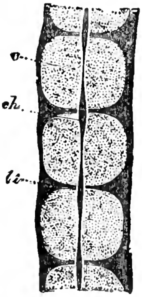

Fig. 325.—Longitudinal [frontal] section through the thoracic region of the vertebral column of a human embryo 8 weeks old, after Kölliker.
v, Cartilaginous body of vertebra; *li*, intervertebral ligament; *ch*, chorda.

(*a*) *Development of the Vertebral Column.*

The process of chondrification commences in Man at the beginning of the second month. At certain places in the tissue enveloping the chorda the cells secrete between themselves a cartilaginous matrix, and move farther apart, whereas at other intervening and narrower tracts the character of the tissue is not altered (fig. 325). In this manner the skeletogenous layer is differentiated into numerous vertebral bodies (*v*), which in longitudinal sections are the more translucent, and into the intervertebral discs (ligamenta intervertebralia) which separate them (*li*).

The process of chondrification, as Froriep has followed it in the case of the embryo calf, proceeds as follows: there arise on both sides of the chorda masses of cartilage which are united on the ventral side of it by a thinner layer. Somewhat later the cartilaginous half-cylinder is closed on the dorsal side also.

Upon the appearance of a segmented vertebral column the chorda loses its function of a supporting skeletal rod. From this time forward it therefore suffers a gradual obliteration. The parts enclosed in the bodies of the vertebræ are restricted in their growth, whereas the shorter portions lying in the soft intervertebral discs continue to enlarge (fig. 325 *ch*). Thus the chorda now acquires the appearance of a string of beads, since thickened spheroidal portions are joined to one another by small connecting thread-like portions. Subsequently it entirely disappears in the bodies of the vertebræ, especially when the latter begin to ossify (fig. 326); the intervertebral portion (*li*) alone persists, although indistinctly limited from the surrounding tissue, and produces by the proliferation of its cells the gelatinous core of the intervertebral disc.

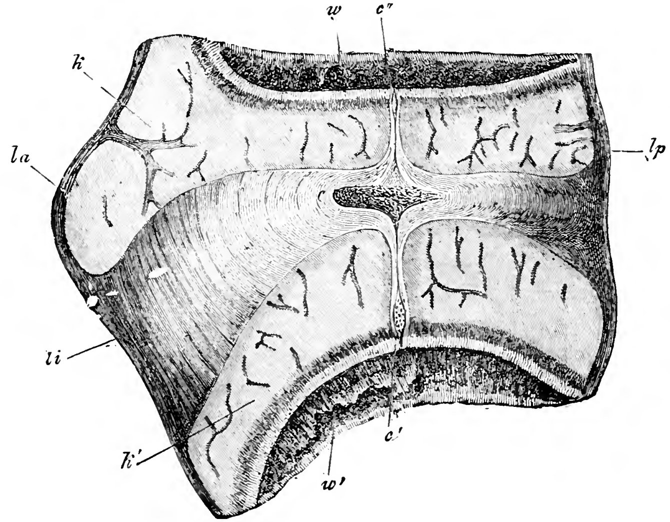

Fig. 326.—**Longitudinal [sagittal] section through the intervertebral ligament and the adjacent parts of two vertebræ from the thoracic region of an advanced embryo Sheep,** after Kölliker. *la*, Ligament longitudinale anterius ; *lp*, lig. long. posterius ; *li*, lig. intervertebrale ; *k*, *k′*, cartilaginous caps (epiphyses) of the vertebræ ; *w* and *w′*, anterior and posterior vertebræ ; *c*, intervertebral, *c′* and *c″*, vertebral enlargements of the chorda.

Soon after the appearance of the bodies of the vertebræ the fundaments of the corresponding arches are observable. According to Froriep's account, there arise small, independent pieces of cartilage in the membrane enveloping the spinal cord, in the immediate vicinity of the bodies of the vertebræ, with which they soon fuse. Their growth is rather slow. During the eighth week they still appear in Man as short processes from the bodies of the vertebræ, so that the spinal cord is still covered dorsally by the membranous skeleton. In the third month they grow into contact with each other at the dorsum; however, it is only in the following month that a complete fusion takes place, and that cartilaginous neural spines are formed. The part of the membrane which lies between the cartilaginous arches furnishes the ligamentous apparatus.

In the process of chondrification the nascent bodies of the vertebræ have a fixed position relative to the primitive or muscle-segments; it is such that on either side of the body they are adjacent to two of the latter, one half to a preceding segment, the other half to a following one; or, in other words, *the bodies of the vertebræ and the muscle-segments do not coincide, but in their positions alternate with each other.*

The necessity of such an arrangement follows from the very function which vertebral column and musculature together have to fulfil. The axial skeleton must possess two opposite properties united: it must be firm, but also flexible,—firm, in order to serve as a support for the trunk; flexible, so as not to impede the motions of the latter. Since a continuous cartilaginous rod would not have possessed sufficient flexibility, the process of chondrification could not take place throughout the whole extent of the skeletogenous layer, but there must be left more elastic tracts, which allow a movement of the cartilaginous pieces on one another. But a movement of the cartilaginous pieces would obviously be impossible if they should lie so that the muscle fibres had their origin and insertion on one and the same vertebral element. In order that the fibres of a muscle-segment may operate upon two vertebræ, the muscular and vertebral segments must alternate in position.

This process, which is easily intelligible in the way in which it has been outlined, has given occasion for the assumption of a "*resegmentation of the vertebral column.*" This conception originated with REMAK, and since then has been for a long time tenaciously held to in the literature.

REMAK, like other embryologists before him (BAER), perceived in the primitive segments of the Chick the material for the establishment of the vertebral column, and therefore gave them the name "protovertebræ." But inasmuch as he found that the cartilaginous vertebræ did not afterwards correspond in position with the protovertebræ, he announced the proposition that a new "segmentation of the vertebral column takes place, from which arise the secondary, permanent bodies of the vertebræ."

Both the name "protovertebra" and the assumption of a resegmentation of the vertebral column should be dropped, and for the following reasons:—

The signification of the primitive segments consists, if not exclusively, at least principally, in this, that they are the fundaments of the musculature of the body. *But in the arrangement of the musculature is expressed the original and oldest segmentation of the vertebrate body. It is present even in Amphioxus and the Cyclostomes. The segmentation of the vertebral column, on the contrary, was acquired much later, and has resulted, as was explained above, from a necessary dependence on the segmentation of the musculature.* A primary segmentation of the vertebral column as understood by Remak and his followers has never existed, for the cartilaginous vertebræ are formed from an *unsegmented* mass of tissue enveloping the chorda—from the skeletogenous layer. One cannot speak of a segmentation of the vertebral column until the beginning of the process of chondrification, by reason of which alone it became necessary.

Even before the cartilaginous vertebral column has been completely established, it enters in Mammals upon the *third stage*, which begins in Man at the end of the second month.

The *ossification* of every cartilage takes place in the main in a corresponding, typical manner. Blood-vessels at one or several places grow from the surface into its interior, dissolve the matrix of the cartilage of a limited region, so that there arises a small cavity filled with vascular capillaries and marrow-cells. In the vicinity of this salts of lime are deposited in the cartilage. By a portion of the proliferated medullary cells, which become osteoblasts, bone substance is then secreted (fig. 326 *w*). In this manner there arises in the midst of the cartilaginous tissue a so-called *bone nucleus* or *centre of ossification*, around which the destruction of the cartilage and its replacement by osseous tissue advance further and further.

The places where the separate bone nuclei are formed, as well as their number, are tolerably uniform for the different cartilages.

In general the ossification of each vertebra proceeds from three points. At first a centre of ossification is established in the base of each half of the vertebral arch, to which there is added somewhat later a third centre in the middle of the body of the vertebra. In the fifth month the ossification has advanced up to the surface of the cartilage. Each vertebra is now distinctly composed of three pieces of bone, which for a long time continue to be joined to one another by bridges of cartilage at the base of each half of the arch and at the union of the latter with the vertebral spines. The last remnants of cartilage do not ossify until after birth. During the first year with the development of a bony spinous process the halves of the arch are fused. Each vertebra is then separable after destruction of the soft parts into two pieces, into the body and the arch. These are united between the third and eighth years.

In addition to the pieces of bone just described, ***accessory centres of ossification*** appear on the vertebræ in subsequent years; it is in this way that there arise the epiphysial plates at the end-surfaces of the body and the small bony pieces at the ends of the vertebral processes (the spinous processes and the transverse processes). SCHWEGEL gives detailed information concerning the time of their appearance and their fusion.

Cartilaginous skeletal parts, which serve for the support of the lateral and ventral walls of the body, the *ribs* and *the breast bone*, contribute to the completion of the axial skeleton.

The *ribs* are developed independently of the vertebral column, in Man during the second month, by the chondrification of strips of tissue in the intermuscular ligaments between the successive muscle-segments. They are at first visible as small bent rods in the immediate vicinity of the body of the vertebra, and from here they rapidly extend ventrally.

In early stages of development ribs are established from the first to the last segment of the vertebral column (the coccyx in Man excepted), but only in the case of the lower Vertebrates (Fishes, many Amphibia, and Reptiles) are they developed into large bows supporting the wall of the trunk in a uniform manner in all regions, whereas in Mammals and in Man they exhibit in the separate regions of the vertebral column different conditions. In the neck, lumbar and sacral regions, they appear from the beginning in a rudimentary condition only, and undergo metamorphoses to be described later. It is exclusively in the thoracic region that they attain important dimensions, and here at the same time they give rise to a new skeletal part—the breast bone, or sternum.

The sternum, which is wanting in Fishes and Dipnoi, but is present in Amphibia, Reptiles, Birds, and Mammals, *is a formation derived from the thoracic ribs, and is originally established*, as RATHKE was the first to discover, *as a paired structure, which early fuses into an unpaired skeletal piece.*

RUGE has followed the development of the sternum in Man in a very thorough manner, and has found that in embryos 3 cm. long the first five to seven thoracic ribs have become prolonged into the ventral surface of the breast and by a broadening of their ends have united at some distance from the median plane to form a cartilaginous band, whereas the following ribs end free and at a greater distance from the median plane. The two *sternal bars* are separated from each other by membranous tissue; later they approach each other in the median plane, and commencing in front, begin to fuse together into an unpaired piece, from which the individual ribs which gave rise to them are afterwards separated by the formation of joints.

The paired origin of the sternum serves to explain some of its abnormalities. For example, in the adult there is sometimes seen a fissure, which, although closed by connective tissue, passes quite through the sternum (fissura sterni), or a few larger or smaller gaps are found in the body and xyphoid process of the sternum. All these abnormal cases are explained by the complete or partial failure of the two sternal bars to fuse in the usual way during embryonic life.

The ossification of ribs and sternum is in part accomplished by the development of special centres of ossification, that of the ribs beginning as early as the second month, the sternum somewhat late, in the sixth fœtal month.

Each rib contains at first one centre of ossification, through the enlargement of which the bony part is formed, while next to the sternum a portion remains cartilaginous throughout life. In the eighth to the fourteenth year there appear in the capitulum and tuberculum of the rib, according to SCHWEGEL and KÖLLIKER, accessory centres, which fuse with the main piece between the fourteenth and the twenty-fifth year.

The sternum (fig. 327) ossifies from numerous centres, of which one arises in the manubrium, and from six to twelve in its body. Between the sixth and twelfth years the latter begin to fuse together into the three or four large pieces of which the body of the sternum is composed. The xyphoid process remains partly cartilaginous, but acquires a centre of ossification during childhood.

Regarding the *episternal pieces* which appear on the manubrium, the text-books of comparative anatomy and the article by RUGE should be consulted.

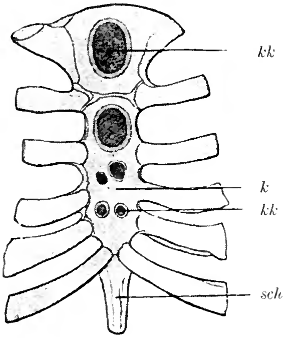

Fig. 327. — **Cartilaginous sternum, with portions of the ribs attached and with several centres of ossification (*kk*), from a child two years old.**

k, Cartilage; *kk*, centres of ossification; *sch*, xyphoid process.

Through inequalities in the development of the separate vertebral and costal fundaments and through the fusions which take place here and there are produced the different regions of the skeleton of the trunk: the cervical, dorsal, and lumbar regions of the vertebral column, the sacrum and coccyx. A correct understanding of these skeletal parts is to be acquired only through embryology.

The rudimentary fundaments of the cervical ribs at their first appearance fuse with the *cervical vertebræ*, at one end with the body of the vertebra, at the other with an outgrowth of the neural arch, and with the latter enclose an opening through which the vertebral artery runs—the foramen transversarium. The so-called transverse process of the cervical vertebra is therefore a compound structure, and were better designated *lateral process*, for the bony rod that lies dorsad of the foramen transversum is formed by an outgrowth from the vertebra and alone corresponds to the transverse process of a dorsal vertebra; the ventral rod, on the contrary, is a rudimentary rib, which possesses in fact a separate centre of ossification.

The fundament of the rib of the seventh cervical vertebra occasionally attains greater size, does not fuse with the vertebra—which consequently does not possess any foramen transversarium—and is described under the abnormalities of the skeleton as *free cervical rib.* Its presence is explained therefore as being the result of a more voluminous development of a part which in all cases exists as a fundament.

The *transverse process of the lumbar vertebræ* is also better designated as lateral process, because it encloses the rudiment of a rib. This explains the phenomenon of a thirteenth or small lumbar rib occasionally observed in Man.

The *sacral region* is the one that is most modified. A large number of vertebræ in this region by becoming firmly united with the pelvic girdle have lost the power of moving on one another, and are fused together into a large bone: the sacrum. This consists in human embryos of five separate cartilaginous vertebræ, the first three of which especially are characterised by very broad, well-developed lateral processes.

I say lateral processes because comparative-anatomical grounds and embryological evidence both indicate that there are included in them rudimentary *sacral ribs*, such as in lower Vertebrates make their appearance as independent structures. On the embryological side, the method of their ossification favors this view, for each sacral vertebra undergoes ossification from five centres. To the three typical centres, those of the body and the neural arches, are added in the lateral processes large bone-nuclei (centres), which are comparable with the centres of ossification of a rib. They produce the well-known lateral masses of the sacrum (massæ laterales), which bear the articular surfaces for union with the ilium.

The fusion of the five bony pieces of a sacral vertebra, at first separated by strips of cartilage, takes place later than in other parts of the vertebral column, namely, between the second and the sixth year after birth. For a long time the five sacral vertebræ remain separated from one another by their intervertebral discs, which begin to ossify in the eighteenth year; the process has usually come to an end by the twenty-fifth year.

Behind the sacrum there follow four or five rudimentary coccygeal vertebræ, which represent the caudal skeleton of Mammals and do not acquire centres of ossification until very late. In the thirtieth year or later they may fuse with one another, and sometimes with the sacrum.

Atlas and *epistropheus* (*axis*) now demand special mention. These vertebræ acquire their peculiarities of form by an early fusion of the cartilaginous body of the atlas (fig. 328*a*) with the epistropheus (*e*) to form the odontoid process of the latter. The one therefore contains less, the other more than a normally developed vertebra.

That the odontoid process is the real body of the atlas is recognisable even later by means of two facts. First, like every other vertebral body, it is traversed, as long as it remains cartilaginous, by the chorda, which at the tip of the process is continued into the ligamentum suspensorium and from this into the base of the cranium. Secondly, it acquires in the fifth month of development a separate centre of ossification (fig. 328 *a*), which is not completely fused with the body of the epistropheus until the seventh year.

Fig. 328.—Median section through the body and odontoid process of the epistropheus.
In the cartilage two centres of ossification (*e* and *a*) are to be seen.

The neural arches of the atlas, which have remained independent, are joined together on the ventral side of the odontoid process by a tract of tissue in which an independent piece of cartilage is formed (hypochordal cartilage-rod of FRORIEP)—a structure which, according to FRORIEP, is present in every vertebra in the case of Birds. This piece of cartilage develops in the first year after birth a special centre of ossification, fuses between the fifth and the sixth year with the lateral halves, and constitutes the anterior [ventral] arch (KÖLLIKER).

(*b*) *Development of the Head-Skeleton.*

From its position the skeleton of the head appears as the most anterior part of the axial skeleton, but it is on the whole very unlike the posterior part,—the vertebral column,—because it is adapted to peculiar purposes. For in the morphological plan of Vertebrates the head takes, in comparison with the trunk, a preëminent position; it is furnished with especially numerous and highly developed organs concentrated into a short space.

The neural tube has here become differentiated into the voluminous brain, with its dissimilar regions. In its immediate vicinity have arisen complicated sensory organs such as nose, eye, and ear. Likewise the part of the digestive tube enclosed within the head bears in many ways its peculiar stamp, since it contains the mouth opening and is provided with organs for the reception and trituration of the food, and is pierced by visceral clefts. All of these parts exercise a determining influence on the form of the skeleton, which adapts itself most accurately to the brain, to the sensory organs, and to the functions of the head-gut, and thereby becomes a very complicated apparatus, especially in the higher Vertebrates.

Embryology sheds a flood of light on the method of the origin of the cephalic skeleton of Vertebrates; it shows the relations to one another of widely different lower and higher forms, and also answers the question, What relation do the vertebral column and head-skeleton sustain to each other in the plan of organisation of Vertebrates? Consequently the development of the cephalic skeleton proves to be an especially interesting subject, which has always attracted morphologists, and which has incited to careful investigation.

During the account some comparative-anatomical digressions will be made, which will contribute to the better comprehension of certain facts, especially those treated of in the final section, in which the vertebral theory of the skull will be briefly discussed.

As in the case of the vertebral column, there are to be distinguished three stages of development according to the histological character of the sustentative substance: a membranous, a cartilaginous, and a bony.

The chorda serves as the foundation for the *membranous skeleton of the head*, and extends forward to the between-brain. At its anterior end there is formed in Amniota the cephalic flexure, by which the axis of the first two brain-vesicles makes an acute angle with the three following ones (fig. 153). Here also the mesenchyme early grows around the chorda and envelops it in a skeletogenous layer, which spreads out from this region laterad and dorsad, enveloping the five brain-vesicles, and is subsequently differentiated into the membranes of the brain and a layer of tissue, which becomes the foundation of the cranial capsule, and has received the name of *membranous primordial cranium.*

Thus far there is an agreement in the development of the vertebral column and of the cranium. With the beginning of the process of chondrification the conditions become more peculiar. Whereas in the region of the spinal cord the skeletogenous layer undergoes a regular differentiation into cartilaginous and connective-tissue parts—into vertebræ and vertebral ligaments—and is thereby divided into successive movable segments, such a segmentation does not take place in the head.

The layer of tissue called membranous primordial cranium undergoes continuous chondrification into a non-articulate capsule enveloping the brain-vesicles. If we go through the whole series of Vertebrates down to the lowest, in no one of them is there exhibited a separation into movable segments corresponding to vertebræ. *Therefore the anterior part and the remaining part of the axial skeleton pursue from an early period different directions in their development.*

The contrast is intelligible in view of the different duties to be fulfilled in the two regions, and especially in consideration of the different influences which the action of the muscles exercises upon the form of the skeleton.

In water-inhabiting animals the trunk-musculature is the most important organ of locomotion, for it bends the trunk now in this direction, now in that, and thereby propels it forwards through the water. If, however, the head region were likewise flexible and movable, it would be disadvantageous for forward motion, inasmuch as a rigid part operates as a cut-water. Moreover, the musculature developed on the head assumes a different function, inasmuch as in the grasping of food and in the process of respiration—which is accompanied by an enlargement and reduction of the respiratory tract of the alimentary tube—it now adducts and then abducts the ventrally situated parts of the axial skeleton. Besides, it is advantageous here to have the skeletal axis present firm points of attachment for the muscles. Finally, the voluminous development of the brain and the higher sensory organs is likewise a participating influence tending to make the part of the head that serves for their reception an inflexible region.

In view of these various factors working in the same direction, it becomes intelligible that *in the head a segmentation of the axial skeleton is wanting from the beginning.*

In other respects there prevails a great agreement with the vertebral column, especially in the manner in which the metamorphosis into cartilaginous tissue takes place in the membranous primordial cranium. In both the chondrification first begins at the surface of the chorda dorsalis (fig. 329 *A*).

As a foundation for the base of the skull there arise two pairs of elongated cartilages: behind, on either side of the chorda, the two *parachordal cartilages* (*PE*); in front, the two *trabeculæ cranii* (*Tr*) of Rathke, which begin at the tip of the chorda and from there run forward beneath the between- and the fore-brain.

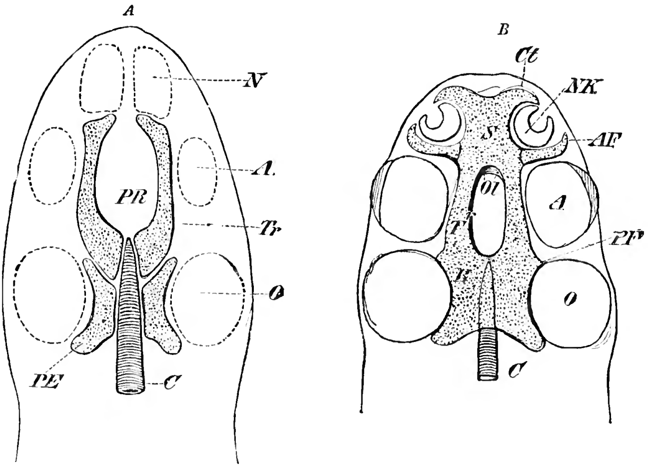

Fig. 329 *A* and *B*.—**First fundament of the cartilaginous primordial cranium,** from Wiedersheim.

A, *First stage*. *C*, Chorda; *PE*, parachordal cartilage; *Tr*, Rathke's trabeculæ cranii; *PR*, passage for the hypophysis; *N*, *A*, *O*, nasal pit, optic vesicle, otocyst.

B, *Second stage*. *C*, Chorda; *B*, basilar plate; *T*, trabeculæ cranii, which have become united in front to constitute the nasal septum (*S*) and the ethmoid plate; *Ct*, *AF*, processes of the ethmoid plate enclosing the nasal organ; *Ol*, foramina olfactoria for the passage of the olfactory nerves; *PF*, post-orbital process; *NK*, nasal pit; *A*, *O*, optic and labyrinthine vesicles.

The four pieces soon fuse with one another (fig. 329 *B*). The two parachordal elements grow around the chorda, first below, then above, thus enveloping it and producing the basilar plate (*B*). Its anterior margin rises far up into the angle of the flexure between mid-brain and between-brain and corresponds to the future dorsum sellæ. The *trabeculæ cranii* (*T*) spread out at their anterior ends, which become fused to constitute the ethmoid plate (*S*), the foundation of the anterior portion of the cranium, which acquires its particular stamp through its reception of the organ of smell. In the middle of their length they remain separate a long time, and enclose an opening, which corresponds to the sella turcica, and has been caused by the formation of the hypophysial pocket from the oral sinus and by its growing through the membranous basis of the cranium toward the infundibulum of the brain. Rather late there is also formed, as the floor of the sella turcica, beneath the hypophysis, a thin cartilaginous plate, which is pierced only by the holes for the internal carotids.

After the base of the cranium has been developed, the process of chondrification involves the side walls and at last the roof of the membranous primordial cranium, precisely as the halves of the neural arch grow out from the body of the vertebra and finally terminate in the dorsal spine.

In this manner there is developed around the brain in the case of the *lower* Vertebrates, in which the axial skeleton remains in the cartilaginous condition throughout life (fig. 330), a closed, tolerably thick-walled capsule, the *cartilaginous primordial cranium.*

In the *higher* Vertebrates, in which to a greater or less degree processes of ossification occur later, the primordial cranium attains a less complete development, as is shown by the fact that its walls remain thinner, and indeed acquire at some places openings, which are closed by connective-tissue membranes. In Mammals the latter condition occurs very extensively in the roof of the skull, which becomes cartilaginous only around the foramen magnum, whereas in the region in which afterwards the frontal and parietal bones are located the cranium remains membranous. The cartilage attains a greater thickness only at the base of the cranium and in the regions of the olfactory organ and the membranous labyrinth, where it gives rise to the nasal and ear capsules.

For the sake of better orientation, it is useful to distinguish in the primordial cranium different regions. There are two different principles of division that may be employed in this connection.

Following Gegenbaur, one can divide the primordial cranium, in accordance with its *relation to the chorda dorsalis,* into a posterior and an anterior portion.

The posterior region reaches up to the dorsum sillæ and encloses in its basal portion the chorda, which in Man enters into it from the odontoid process through the ligamentum suspensorium dentis. The anterior portion is developed in front of the pointed end of the chorda out of Rathke's cranial trabeculæ. Gegenbaur designates the two as *vertebral* and *evertebral regions* (for which Kölliker employs the names *chordal* and *prechordal*); he shows that the vertebral region must be, on account of its relation to the chorda, the older part and alone comparable with the remainder of the axial skeleton, that the non-vertebral part, on the contrary, is a later acquisition and constitutes a new structure, which has been caused by the forward extension of the fore-brain vesicle and by the development of the organ of smell, to the enclosing of which (nasal capsule) it contributes.

The second method of division is based upon the different appearance which the individual regions of the primordial cranium acquire through their *relations to the sense organs.* The anterior end of the cartilaginous capsule (fig. 330) receives the organ of smell; a following portion contains depressions for the eyeballs; in a third are imbedded the membranous auditory labyrinths; finally, a fourth effects a union with the vertebral column. Consequently one may distinguish an *ethmoidal*, an *orbital*, a *labyrinthine*, and an *occipital region.*

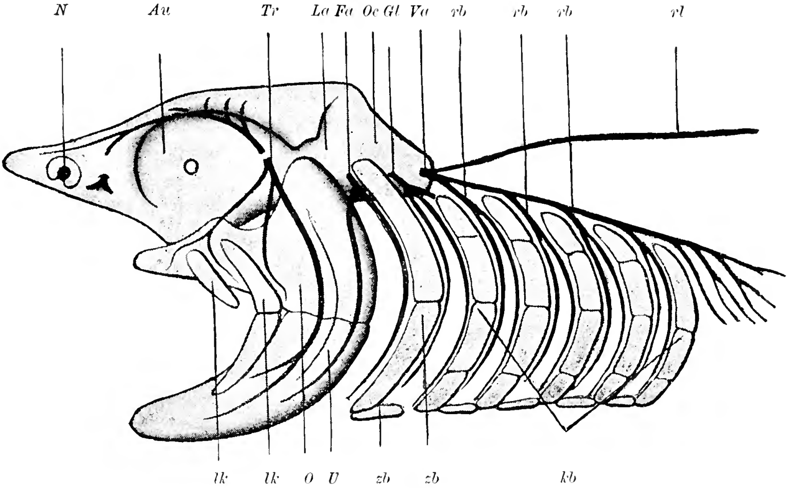

Fig. 330.—Diagrammatic representation of the cartilaginous cranial capsule and the cartilaginous visceral skeleton of a Selachian and of the larger nerve trunks of the head.

N, Nasal capsule (ethmoid region of the primordial cranium); *Au*, cavity for the eye (orbital region); *La*, region of the labyrinth; *Oc*, occipital region of the cranium; *O*, palato-quadratum; *U*, lower jaw (mandibulare); *lk*, labial cartilage; *zb*, hyoid arch; *kb*, first to fifth branchial arches; *Tr*, nervus trigeminus; *Fa*, facialis; *Gl*, glosso-pharyngeus; *Va*, vagus; *rl*, ramus lateralis of the vagus; *rb*, rami branchiales of the vagus.

In addition to the cartilaginous primordial cranium, there are developed in the head numerous cartilaginous pieces (which serve as supports to the walls of the head-gut) in a manner similar, although not directly comparable, to that in which the ribs (fig. 330) have arisen in the walls of the trunk in the region of the vertebral column. Together they constitute a skeletal apparatus which undergoes in the series of Vertebrates very profound and interesting metamorphoses. Whereas it attains in the lower Vertebrates a great development, it becomes in part rudimentary in Reptiles, Birds, and Mammals. The part, however, which remains furnishes the foundation for the *facial skeleton.* I begin with a short sketch of the original conditions in the lower Vertebrates, especially in the Selachians.

As has been described in a previous chapter, the lateral walls of the head-gut are traversed by the visceral clefts, of which there are ordinarily as many as six in Sharks (fig. 331). The bands of substance intervening between the clefts are called the *membranous throat-* or *visceral arches.* They consist of a connective-tissue foundation invested with epithelium, of transversely striped muscle-fibres, and of the visceral-arch blood-vessels (see p. 571). Inasmuch as they have different functions to fulfil, and consequently acquire different forms, they are distinguished as *jaw-*, *hyoid*, and *branchial arches.* The most anterior of them is the jaw-arch, which serves to bound the oral opening. Following this, and separated from it by only a rudimentary visceral cleft, the spiracle, is the hyoid arch, which is connected with the origin of the tongue. Ordinarily this is followed by five branchial arches.

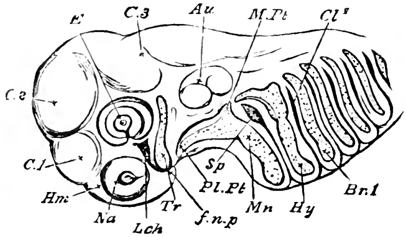

Fig. 331.—Head of a Shark embryo 11 lines long. From Parker and Bettany.
Tr, Rathke's trabeculæ cranii; *Pl.Pt*, pterygo-quadratum; *Mn*, mandibular cartilage; *Hy*, hyoid arch; *Br*.1, first branchial arch; *Sp*, spiracle; Cl^1, first branchial cleft; *Lch*, groove under the eye; *Na*, fundament of the nose; *E*, eyeball; *Au*, auditory vesicle; *C*.1, *C*.2, *C*.3, brain-vesicles; *Hm*, cerebral hemispheres; *f.n.p*, fronto-nasal process.

At the time when the membranous primordial cranium is converted into cartilage, chondrification also takes place in the connective tissue of the *membranous* visceral arches, thus producing the *cartilaginous visceral arches* (fig. 331). These exhibit a regular segmentation into several pieces, placed end to end and articulated with one another by connective tissue.

The jaw-arch is divided on either side into a cartilaginous palatoquadratum (fig. 330 *O*) and a lower jaw (mandibulare). These carry, in the mucous membrane investing them, the teeth of the jaws. The two mandibular elements are united to each other in the median plane by means of a mass of tense connective tissue. The following visceral arches, on the contrary, are alike in having their lateral halves, which are divided into several pieces, joined ventrally by means of an unpaired connecting piece, the copula, in a manner similar to that in which the ribs are united by the sternum. The pieces of the hyoid arch are designated, in sequence from the dorsal to the ventral side, hyomandibular, hyoid, and (the copula) os entoglossum.

In Mammals and Man (figs. 154, 157) structures similar to those of the Selachians are formed in the membranous stage, but subsequently they are only in part converted into cartilaginous pieces, which in turn never acquire a great size, having meantime lost their original function. They help to form the facial part of the head-skeleton, and have already been treated of partially in previous chapters—in the discussion of the head-gut and of the organ of smell. I am therefore compelled for the sake of continuity to repeat much that has already been presented concerning the visceral skeleton.

In very young human and mammalian embryos the mouth-opening is bounded on the sides and below by the paired maxillary and mandibular processes (fig. 156, compare p. 284). The former are widely separated from each other, because the unpaired frontal process, in the form of a broad, rounded projection, is at first inserted from above between them. Afterwards this projection becomes divided by the development, on its rounded surface, of the two nasal pits with the nasal grooves leading down to the upper margin of the mouth (compare p. 513); it is then divided into the outer and inner nasal processes. The former are separated from the maxillary process by a groove, which runs from the eye to the nasal furrow, and is the first fundament of the lachrymal duct.

Behind the first visceral arch comes the hyoid arch (figs. 157, 158 *zb*), the two being separated by a small visceral cleft, which becomes the tympanic cavity and Eustachian tube. This is followed by three additional visceral arches with three visceral furrows (or clefts), which are of only short duration.

During a later stage fusions take place between the processes that surround the oral opening (fig. 332).

The maxillary processes, by growing farther inward, meet the inner nasal processes, fuse with them, and produce a continuous upper boundary to the mouth. In this way each olfactory pit with its nasal groove is converted into a canal, which leads into the oral cavity through an inner opening close behind the margin of the upper jaw. The membranous margins of the upper and lower jaws also lose their superficial positions, because the skin that covers them is raised up into externally projecting folds, and forms the lips, which from this time forward constitute the boundary of the oral opening.

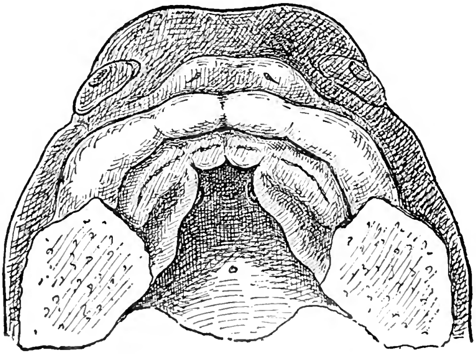

Fig. 332.—**Roof of the oral cavity of a human embryo with fundaments of the palatal processes,** after His. Magnified 10 diameters.

A third stage, with the *development of the palate*, practically completes the formation of the face. (Compare pp. 515-17.) From the membranous upper jaw there arise two ridges projecting into the mouth-cavity (fig. 290); these become enlarged into the *palatal plates*, which grow horizontally.

The plates meet in the median plane and fuse with each other and with the median part of the frontal process, which has meantime become reduced by the enlargement of the olfactory organ to the thin nasal septum. Thus there is cut off from the primary oral cavity an upper chamber, which contributes to the enlargement of the nasal cavity, and which opens into the pharynx through the posterior nares; at the same time [as the result of this growth] there has arisen a new roof of the mouth-cavity,—the palate,—which is afterwards differentiated into hard and soft palate.

A further differentiation of the face, which is now in the membranous stage of development, is brought about by the process of chondrification. This produces, however, in Mammals, as compared with Selachians, only small and unimportant skeletal structures. Some of these structures undergo degeneration (Meckel's cartilage), some are utilised as auditory ossicles in the function of hearing, and others are united to form the fundament of the hyoid bone. They arise from the soft tissue of the first, second, and third visceral arches; in the case of the fourth and fifth arches there is not even a process of chondrification in Mammals, so that with the closure of the fissures they are no longer recognisable as distinct parts, unless perhaps the thyroid cartilage is to be referred to them (Dubois).

I will describe the conditions in detail, first in the case of sheep embryos of different stages of development, and then in the case of a human embryo.

In a sheep embryo 2 cm. long there are to be found, according to the account of Salensky (fig. 333), two long and slender cylindrical cartilaginous rods, one in front, the other behind the first visceral cleft; their posterior (proximal) ends abut upon the labyrinth-region of the primordial cranium, and are here united to each other by means of embryonic connective tissue. In older embryos (fig. 334) the first visceral arch becomes at its upper [proximal] end more and more distinctly segmented, by means of constrictions, into two smaller pieces and a larger one. The first small piece, the one lying next to the wall of the labyrinth, gradually assumes the form of the incus (*am*) with its processes, the second becomes the malleus (*ha*); the two are joined by means of a mass of connective tissue. The third piece (*mk*) is of considerable length, and has the form of a cylindrical rod; it is enclosed in the membranous lower jaw, and is designated in honor of its discoverer as Meckel's *cartilage.* It remains for a long time in union with the fundament of the malleus by means of a narrow

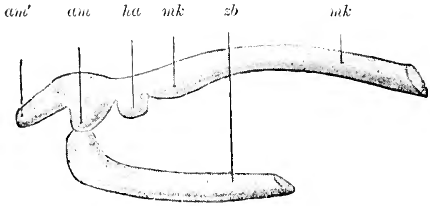

Fig. 333.

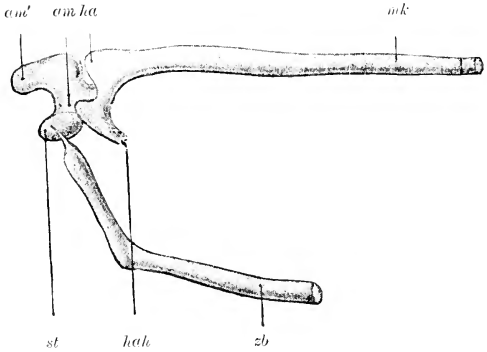

Fig. 334.

Figs. 333, 334.—The dissected-out cartilages of Meckel and Reichert with the fundament of the auditory ossicles, from a sheep embryo 2·7 cm. long. After Salensky.

Fig. 333.—*mk*, Meckel's cartilage; *ha*, hammer (malleus); *am*, anvil (incus) (long process); *am'*, its short process; *zb*, cartilaginous hyoid arch.

Fig. 334.—*am*, Anvil; *am'*, its short process; *ha*, hammer; *hah*, hammer-handle; *st*, stirrup (stapes); *mk*, Meckel's cartilage; *zb*, cartilaginous hyoid arch.

cartilaginous bridge, upon which the long process (pr. gracilis) of the malleus is afterwards developed by periosteal ossification. The second visceral arch (*zb*) becomes incorporated in the hyoid bone.

In a human embryo of the fifth month one observes structures similar to those just described, only somewhat further developed. Figure 335 exhibits the incus (*am*), easily recognised by its form, lying on the wall of the labyrinth; with it is articulated the malleus (*ha*), the long process of which is continuous with MECKEL's cartilage (*MK*). This extends ventrally as far as the median line, where it is united with the cartilage of the opposite side by means of connective tissue—a kind of symphysis.

The second visceral cartilage, called also REICHERT's cartilage, has become divided into three portions. The uppermost portion is fused with the labyrinth-region—the petrous portion of the temporal bone—and constitutes the fundament of the processus styloideus (*grf*); the middle portion has become fibrous tissue in Man, and forms a strong ligament, the lig. stylohyoideum (*lsth*), whereas in many Mammals it becomes a large cartilage; the third and lowest portion produces the lesser cornu (*kh*) of the hyoid bone. This sometimes becomes developed to a great length by the chondrification of the lower part of the ligamentum stylohyoideum, and reaches up very close to the lower end of the stylohyoid process.

In the third visceral arch chondrification takes place only in the ventral tracts, producing upon the sides of the neck the greater cornua of the hyoid bone (*gh*). Greater and lesser cornua are attached to an unpaired median piece of cartilage, which corresponds to a copula of the visceral skeleton of Selachians and becomes the body of the hyoid bone.

The third auditory ossicle, **the stapes** (fig. 335 *st*), also belongs to the visceral apparatus; it has been left unmentioned until now, because there is, even at present, a wide difference of opinion concerning its development. According to the original view of REICHERT, which GEGENBAUR is also inclined to adopt, the stapes arises from the uppermost end of the hyoid arch. KÖLLIKER refers it to the first visceral arch. According to GRUBER and PARKER, on the contrary, it arises in connection with the fenestra ovalis, as though it were cut directly out of the outer wall of the labyrinth.

According to the recent investigations of SALENSKY, GRADENIGO, and RABL, *it appears to me that the stapes has a double origin, arising from two different parts.*

The plate of the stapes, which is let into the fenestra ovalis, is differentiated in the manner first emphasised by GRUBER and PARKER, and now again by GRADENIGO, out of the cartilaginous capsule of the labyrinth. Its development therefore agrees with that of the operculum of the Amphibia, as described by STÖHR. The ring-like part of the stapes, on the contrary, comes from the upper end of the second visceral [hyoid] arch, which lies in contact with the capsule of the labyrinth (GRADENIGO, RABL). Its ring-like condition results from the fact that the tissue from which it is formed is traversed by a small branch of the carotis interna, the arteria mandibularis or perforans stapedia. In Man and certain of the Mammals this subsequently degenerates entirely, whereas in others (Rodents, Insectivores, etc.) it remains as a vessel of considerable size.

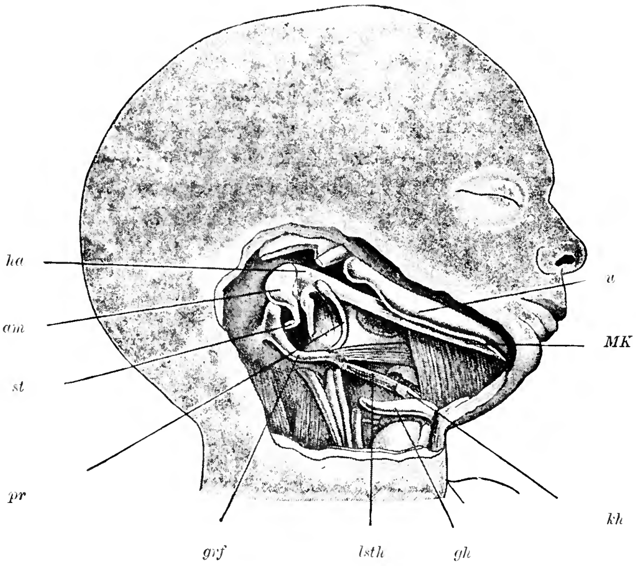

Fig. 335.—Head and neck of a human embryo 18 weeks old with the visceral skeleton exposed, after KÖLLIKER. Magnified.

The lower jaw is somewhat depressed in order to show MECKEL'S cartilage, which extends to the malleus. The tympanic membrane is removed and the annulus tympanicus is visible.

ha, Malleus, which passes uninterruptedly into MECKEL'S cartilage, *MK*; *uk*, bony lower jaw (dentale), with its condyloid process articulating with the temporal bone; *am*, incus; *st*, stapes; *pr*, annulus tympanicus; *grf*, processus styloideus; *lsth*, ligamentum stylohyoideum; *kh*, lesser cornu of the hyoid bone; *gh*, its greater cornu.

Both fundaments of the stapes fuse with each other very early and form a small cartilage, which on the one hand articulates with the incus by means of a lenticular connecting element (os lentiforme), and on the other reposes with its plate-like base in the fenestra ovalis.

The view here adopted—that the stapes belongs to the second, the malleus and incus to the first visceral arch—is supported by the *important relation of the nerves in their distribution to the musculus stapedius and to the tensor tympani*, as has recently been rightly pointed out by RABL. *The muscle of the stapes is supplied from the nerve of the second visceral arch, the nervus facialis;* it forms part of a group embracing the m. stylohyoideus, and the posterior belly of the digastric; *the muscle of the malleus receives a branch of the trigeminus, which is the nerve of the mandibular arch.*

The separation of the territories of innervation prevails, moreover, with the muscles of the palate, one of which—the tensor veli palatini—arises *in front* of the Eustachian tube—the remnant of the first visceral cleft—and is therefore supplied by the n. trigeminus, whereas the levator veli palatini and azygos uvulæ lie *behind* it, and, because belonging to the hyoid arch, receive branches from the n. facialis (RABL).

At first all the auditory ossicles lie imbedded in a soft gelatinous tissue outside the tympanic cavity, which still has the form of a narrow fissure. These conditions are not altered until after birth. The tympanic cavity, taking in air, then becomes enlarged, its mucous membrane is evaginated between the auditory ossicles, and the gelatinous tissue just mentioned undergoes a process of shrinkage. Auditory ossicles and chorda tympani thus come to lie apparently free in the tympanic cavity; accurately considered, however, they are only crowded out into it, for even in the adult they are enclosed in folds of the mucous membrane, and by means of these they preserve their original and genetically established connection with the wall of the tympanic cavity.——

Up to the present stage the construction of the head-skeleton is, on the whole, simple. In the third stage of development, on the contrary, upon the beginning of the process of ossification, it attains in a short time a high degree of complication, which is effected especially by the development of two entirely different kinds of bone, one of which has been called primordial bone, the other covering bone (Deck- oder Belegknochen).

Primordial bones are such as are developed out of the cartilaginous skeleton. Either there arise centres of ossification within the cartilage after softening and dissolution of its matrix, as was described in the ossification of the vertebral column, the ribs, and the sternum, or the perichondrium alters its formative activity, and secretes, in place of layers of cartilage, bony tissue upon the already formed cartilage. In the first instance one can speak of an endochondral, in the second instance of a perichondral ossification. The cartilaginous primordial skeleton can be crowded out and replaced by a bony one in both ways, remnants of cartilage of greater or less magnitude being preserved in the several classes of Vertebrates.

The covering bones, on the contrary, arise outside the primordial cranium in the connective tissue enveloping it, either in the skin which covers its surface or in the mucous membrane that lines the head-gut. They are therefore ossifications which do not occur on any other part of the axial skeleton and which are also at first foreign to the skeleton of the head. Consequently in early stages of development, and in many classes of Vertebrates even in the adult animal, they can be dissected off without in any way injuring the primordial cranium. It is otherwise with the primary bones, the removal of which always causes a partial destruction of the cartilaginous skeleton.

If, as just now stated, the covering bones are at first foreign to the skeleton of the head, there arises the question of their source. To answer this I must go back a little.

In lower Vertebrates there is developed, besides the internal cartilaginous axial skeleton, an external or *dermal skeleton,* which serves for the protection of the surface of the body, and is also continued at the mouth for some distance into the cavity of the head-gut, where it may be designated as mucous-membrane skeleton. In the simplest condition it consists, like the scaly armor of the Selachians, of small close-set denticles, the placoid scales, which have arisen from ossifications of dermal and mucous-membrane papillæ. In other groups of the Fishes the dermal armor is composed of larger or smaller bony plates, which bear upon their surfaces numerous denticles or simple spines. They are described according to their form and size as scales, scutes, plates, or dermal bones; they are explainable in a very simple manner as derivatives from the Selachian armor of placoid scales, by the fusion at their bases of larger or smaller groups of denticles, which thus produce larger or smaller skeletal pieces. The larger bony pieces arise principally in the region of the head, and especially at the places where cartilaginous parts of the cranial capsule or of the visceral arches approach close to the surface. Thus in many Ganoids and Teleosts the brain is found to be enveloped by a *double capsule*—an inner capsule, either purely cartilaginous or provided with centres of ossification, and a bony armor lying directly upon it.

In the higher Vertebrates the most of the dermal skeleton has completely degenerated, but on the head it is in large part preserved, and furnishes the previously mentioned covering bones, which serve to supplement and complete the internal skeleton.

An interesting insight into the original method of the development of covering bones can still be acquired in many of the Amphibians (fig. 336). For example, the vomer and the palatinum, which are covering bones, arise in very young Triton larvæ by the formation of small denticles (z') in the mucous membrane of the oral cavity, and by the fusion of their bases to form small tooth-bearing plates of bone (z, z). These plates increase in size for a time, owing to the establishment in the neighboring mucous membrane of additional dental spines, which become attached to their margins; afterwards they often lose the equipment of denticles, which are destroyed by being resorbed.

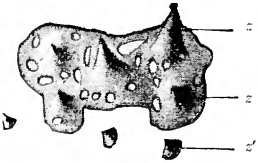

Fig. 336.—Vomer of an Axolotl larva 1·3 cm. long.
By the fusion of teeth (z, z) a tooth-bearing plate of bone has arisen in the mucous membrane. z', Apices of teeth in process of development, which are subsequently attached to the margin of the bony plate and contribute to its growth.

It may be said that the original process in the development of covering bones here described is abbreviated in most of the Amphibia. For at the places in the mucous membrane which the vomer and the palatinum occupy, the tips of denticles are not even begun; but in the layer of tissue in which otherwise the bases of the denticles would have been fused, a process of direct ossification takes place. In the same abbreviated way the covering bones arise in all Reptiles, Birds, and Mammals.

The skulls of many Amphibia (Frog, Axolotl) likewise afford the best explanation of the original relation of the covering bones to the primordial skeleton (fig. 337). The covering bones are found to be loosely superposed upon the primordial cranium, from which they can be easily removed. Thus upon the left side of the accompanying figure the premaxillaria (*Pmx*), maxillaria (*M*), vomer (*Vo*), palatinum (*Pal*), pterygoid (*Pt*), and parasphenoid (*Ps*) have been detached, whereas upon the right side they have been retained. After their detachment there is left the inner head-skeleton proper—a capsule still consisting in great part of the original cartilaginous tissue (*N*, N^1, *PP*, *Qu*), into which, however, there are introduced at some places bony pieces: the occipitalia (*Olat*), petrosa (*Pro*), sphenoidea [sphenethmoid] (*E*), etc.

In the higher Vertebrates, especially in Mammals, the primordial cranium, the primary ossifications, and the covering bones, which in Fishes and Amphibia are easily distinguishable from one another even in the adult animals, are to be recognised as separate parts only in very early stages of development; later it becomes more difficult to distinguish them, at last impossible. This is due to several things:—

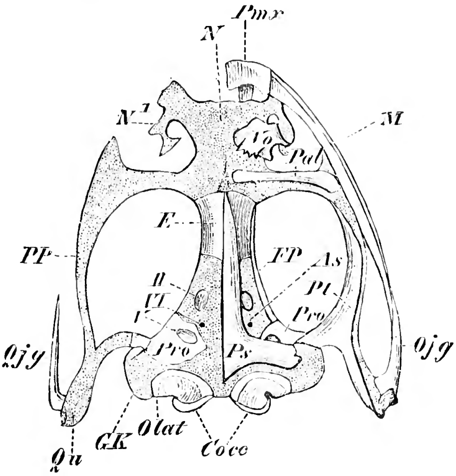

Fig. 337.—Skull of a Frog (Rana esculenta). View from beneath. After Ecker.

The lower jaw is removed. On the left side of the figure the covering bones have been removed from the cartilaginous part of the skull.

Cocc, Condyli occipitales; *Olat*, occipitale laterale; *GK*, auditory capsule; *Qu*, quadratum; *Qjg*, quadratojugale; *Pro*, proöticum; *Ps*, parasphenoid; *As*, alisphenoid; *Pt*, osseous pterygoid; *PP*, palato-quadratum; *FP*, fronto-parietale; *E*, ethmoid (os en ceinture); *Pal*, palatinum; *Vo*, vomer; *M*, maxilla; *Pmx*, premaxillare; *N*, *N*¹, cartilaginous nasal framework; *II*, *V*, *VI*, places of emergence of n. opticus, n. trigeminus, and n. abducens.

First, the cartilaginous primordial cranium is laid down from the beginning in a rudimentary condition: then, too, a large part of the roof is wanting, the opening being closed by a connective-tissue membrane.

Secondly, the cartilaginous primordial cranium subsequently disappears almost entirely, partly by being dissolved, partly by conversion into primordial bones. There persist *small remnants, which have been retained only in the cartilaginous septum narium and the cartilages of the outer nose connected with it.*

Thirdly, in the fully developed skull the primordial bones and the covering bones are no longer distinguishable; for the latter lose their superficial position, become intimately united to the bones derived from the primordial cranium, and with them, filling up the gaps, constitute a firm, closed, bony receptacle of *mixed origin.*

Fourthly, in the adult animal, bones which in the embryo are formed separately, and in lower Vertebrates always remain thus, are often fused. There is a fusion not only between bones of like origin, but also between primordial and covering bones, whereby it finally becomes altogether impossible to distinguish them. *Many of the bones of the human cranium are consequently bone-complexes.*

It may be stated as a general rule that the ossifications on the base and sides of the cranium are primordial, but that on the roof and in the face covering bones make their appearance.

The following parts of the human skull belong to the *primordial elements*: (1) occipitale, except the upper part of the squamous portion; (2) the sphenoidale, except the internal pterygoid plate; (3) ethmoidale and turbinatum; (4) petrosum and mastoid portions of the temporale; (5) the auditory ossicles—malleus, incus, and stapes; (6) the body of the hyoides, with its greater and lesser cornua.

The following are *covering bones*: (1) the upper part of the squamous portion of the occipitale; (2) the parietale; (3) the frontale; (4) the squamous portion of the temporale; (5) the internal pterygoid plate of the sphenoidale; (6) the annulus tympanicus; (7) palatinum; (8) vomer; (9) nasale; (10) lachrymale; (11) zygomaticum; (12) maxillæ sup.; (13) maxillæ inf.

I will now, after this survey, give a somewhat more detailed account of the development of the bones of the head enumerated above.

I. *Bones of the Cranial Capsule.*

(1) *The occipitale* is at first a cartilaginous ring surrounding the foramen magnum; it begins to ossify early in the third month at four points. One centre of ossification is formed below the foramen, another above, and two more at its sides. In this way there arise four bones, which are joined by broader or narrower bands of cartilage, according to the degree of their development. In the lower Vertebrates—Fishes, Amphibia (fig. 337 *Olat*)—they remain in this condition as separate bones, and are designated as occipitale basilare, oc. superius, and oc. laterale.

To these are added in Mammals and Man a covering bone, which arises from two centres of ossification in the connective tissue farther above the foramen—the *interparietale*. This begins, even in the third fœtal month, to fuse with the superior occipital bone to constitute the squama; however, up to the time of birth furrows running in from right and from left mark the boundary of the two genetically different parts. In the new-born child squama, occipitalia lateralia and oc. basilare are still separated from each other by thin remnants of cartilage. Then in the first year the squama fuses with the lateral parts (partes condyloideæ), and finally there is united with these, in the third or fourth year, the pars basilaris. The occipitale is therefore a complex that has originated from five separate bones.

(2) *The sphenoidale* also arises from numerous centres of ossification, which appear in the base of the primordial cranium, and which in the lower classes of Vertebrates represent parts of the cranial capsule that remain separate. In the anterior prolongation of the pars basilaris of the occipitale there appear in the vicinity of the sella turcica an anterior and a posterior pair of centres, which constitute the fundaments of the bodies of the anterior and posterior sphenoidea. At the sides of these there are developed special centres of ossification for the lesser and for the greater wings.

In most Mammals the lesser wings fuse with the anterior, the greater with the posterior body. Thus there are formed two sphenoidea, an anterior and a posterior, which are placed in front of the occipitale, and are separated from each other by a thin strip of cartilage. In Man these two bones become joined together, by the ossification of the cartilaginous strip mentioned, to constitute the unpaired single sphenoidale, with its many processes. The fusions of the numerous separate ossifications take place in the following order. In the sixth fœtal month the lesser wings of the sphenoid fuse with the anterior body; shortly before birth the latter unites with the posterior body, and in the first year after birth the greater wings are united with the rest. From the latter the outer pterygoid plates grow downward, whereas the *inner pterygoid plates are formed as covering bones.* For in the connective tissue of the lateral wall of the oral cavity there is developed a special region of ossification; this furnishes a thin bony lamella, which is preserved in many Mammals as a special skeletal element (os pterygoideum) lying on the pterygoid process of the sphenoidale. In Man it early fuses with the sphenoidale, notwithstanding it has an entirely different origin from the latter.

(3) *The temporale* is a complex of various bones, the greater part of which are still separate in the new-born infant. The os petrosum with the mastoid process is developed from numerous centres of ossification in that part of the primordial cranium which encloses the organ of hearing, and has therefore been designated as cartilaginous ear-capsule. With it is united after birth the styloid process, which in the embryo is a cartilaginous rod that is derived from the upper end of the second visceral arch and that ossifies from its own independent centre.

To the primordial bones there are added in Man two covering bones,—*squama* and *pars tympanicus*,—which are as foreign to the primordial cranium as the parietal or frontal bones. Of these the pars tympanicus (fig. 335 *pr*) is at first a narrow bony ring, which serves as a frame for the tympanic membrane. It is developed in connective tissue outside of the auditory ossicles, and, in particular, outside the malleus (*ha*) and the connected MECKEL's cartilage (*MK*). Thus is explained the position of the long process of the malleus in the fissura petrotympanica, when, soon after birth, the primordial and covering bones fuse with each other. For the annulus tympanicus gradually becomes broadened into a bony plate, which serves as a support for the external meatus. This plate then fuses with the petrosal bone, except along a narrow cleft,—the fissura petrotympanica or Glaseri,—which remains open, because here the chorda tympani and the long process of the malleus were in the embryo shoved in between the bones, while they were still separate.

In lower Vertebrates, and also in many Mammals, the pieces mentioned remain separate, and are distinguished in comparative anatomy as os petrosum, os tympanicum, and os squamosum.

(4) The *ethmoidale* and the *turbinatum* of the nose are primordial bones, which are developed out of the posterior part of the cartilaginous nasal capsule, whereas the anterior part remains cartilaginous and becomes the cartilaginous septum nasorum and the external nasal cartilages.

"The ossification begins in the lamina papyracea in the fifth month. Then follows the ossification of the lower and middle turbinals. At birth these are united by means of cartilaginous portions of the ethmoidale. After birth the vertical plate with the crista galli is the first to ossify; then follows the ossification of the upper turbinal and of the gradually developed labyrinth, from which the ossification advances to the corresponding halves of the cribriform plate. The union of the two lateral halves with the lamina perpendicularis does not take place until between the fifth and the seventh year." (GEGENBAUR.)

Of the covering bones of the primordial cranium, which in general begin to ossify at the beginning of the third month, the following remain separate: the parietale, frontale, nasale, lachrymale, and vomer. Of these the frontale is originally, like the others, a paired structure, and still continues in this condition into the second year after birth, when the closure of the frontal suture begins. Nasale and lachrymale are covering bones of the cartilaginous nasal capsule. The vomer arises as a paired structure at the sides of the cartilaginous septum of the nose in the third month. The two lamellæ afterwards fuse, the cartilage between them disappearing.

II. *Bones of the Visceral Skeleton.*

The remaining bones of the head, which have not been mentioned hitherto, belong to the visceral skeleton, some of them being primordial, others covering bones.

The hyoid bone and the auditory ossicles (perhaps also the thyroid cartilage) are primordial parts; they are characterised by very diminutive size and occupy a very subordinate position in comparison with the enormously developed covering bones. The *hyoides* begins toward the end of embryonic life to ossify at several points. The *auditory cartilages* acquire from the periosteum as early as the fourth month a bony investment, within which here and there remnants of cartilage persist even in the adult. According to recent researches, *the malleus is a compound skeletal piece.* The long process is developed as a covering bone on that part of MECKEL's cartilage which penetrates between petrosal and annulus tympanicus. While the cartilage undergoes degeneration, the covering bone fuses with the larger, primordial part of the malleus. It probably corresponds with the os angulare of lower Vertebrates.

The *covering bones of the visceral skeleton*, the maxillare superius, palatinum, pterygoideum, zygomaticum, and maxillare inferius, are developed in the vicinity of the mouth-opening in the connective tissue of the superior and inferior maxillary processes.

The *maxillaria superiores* are a complex of two pairs of bones, which indeed remain separate in most Vertebrates. One pair is developed on the two superior maxillary processes laterad of the cartilaginous nasal capsule. The other pair appears in the eighth or ninth week, according to TH. KÖLLIKER's detailed investigations, upon the part of the frontal process that lies between the nasal orifices. It corresponds to an actual *paired intermaxillary* (premaxillare), and subsequently encloses the fundaments of the four incisors.

The two intermaxillaries in Man early fuse with the fundaments of the two superior maxillaries, the two membranous superior maxillary processes having previously united with the inner nasal processes. The boundary between maxillary and intermaxillary is indicated on the crania of young persons by a suture-like place (sutura incisiva), running transversely outward from the foramen incisivum, which is occasionally retained even in the adult.

There early grow out from the two superior maxillaries into the palatal processes horizontal lamellæ which produce the two palatal bones—the hard or bony palate.

Palatals and pterygoids are developed in the roof and side walls of the oral cavity; they are consequently mucous-membrane bones. The pterygoids apply themselves, as was stated on p. 620, to the cartilaginous downgrowths of the greater wings of the sphenoid. In many Mammals they remain separate from the latter throughout life, but in Man they unite with it and are now distinguished as inner pterygoid plates from the outer plates, which arise by ossification of cartilage.

The development of the visceral skeleton, which has been discussed here and in previous sections (pp. 284, 515), furnishes the basis for the interpretation of the malformations which are quite frequently met with in the maxillary and palatal region in Man. I refer to the *labial*, *maxillary*, and *palatal fissures*, which are simply malformations due to arrested development. They result when the separate fundaments from which are formed the upper lip, the upper jaw, and the palate do not come into normal union (figs. 288-91).

The malformations of arrested development can present very different variations, according as the coalescence is wholly or only partly omitted, and according to whether it affects one or both sides of the face.

In the case of total arrest, in *palatal*, *maxillary*, and *labial fissures of both sides*, both nasal cavities are broadly in communication with the oral cavity by means of a right and a left fissure running from in front backward. From above there projects free into the oral cavity the nasal septum, which is enlarged in front, and here bears the incompletely developed intermaxillary with its rudimentary incisor teeth. In front of it lies a small dermal ridge, the fundament of the middle part of the upper lip. At the sides of the fissures and the nasal openings, which have not been closed in below, there lie the two separated maxillary processes, with the bony upper jaw and the fundaments of the canine and molar teeth. The horizontal palatal plates project as ridges only a little distance into the oral cavity, and have not effected a junction with the nasal septum. A malformation of this kind is very instructive for the comprehension of the normal processes of development previously described.

When the arrest is only partial, coalescence may fail either on the superior maxillary processes only, or on the palatal plates only, and either on one or on both sides. In the first case there is produced a *labio-maxillary fissure*, or even a *labial fissure* (hare-lip) only, while hard and soft palates are formed normally. In the other case the upper jaw is well developed and no external evidence of malformation is visible, while there is a fissure on one or both sides which passes through the soft palate, and sometimes through the hard palate also (*cleft palate*).

The *development of the lower jaw* is coupled with fundamental metamorphoses. As has been previously explained, in the youngest embryos the oral cavity is limited below by the membranous inferior maxillary processes. Within this there is developed (fig. 338) MECKEL's cartilage (*MK*), the cranial end of which becomes (compare p. 611) the fundament of the malleus (*ha*), by means of which MECKEL's cartilage is articulated with the incus (*am*). At its ventral end in Mammals it unites in the middle line with the corresponding part of the other side, whereas in Man a small space remains between them.

Inasmuch as the small cartilages mentioned have arisen in the first visceral arch, they correspond both in position, and also in their mutual connections and many other relations, to the large cartilaginous elements with which we have already become familiar in the Selachians (fig. 330) as palato-quadratum (*O*) and mandibulare (*U*). In the Selachians the palato-quadratum and mandibulare are functional as a genuine jaw-apparatus, for they bear on their margins the teeth, which are attached in the mucous membrane only, and the masticatory muscles are inserted on their surface.

In Mammals and Man the function of the skeletal parts corresponding to them has become essentially different, for they have entered into the service of the auditory apparatus; a profound, and in its final results wonderful and highly important metamorphosis has taken place here. In order to explain this it is necessary to touch briefly upon a few comparative-anatomical facts.

With the beginning of ossifications the primary lower jaw loses in Teleosts, Amphibia, and Reptiles its simple condition, and is converted into an apparatus which is often very complicated. The ossifications are here, just as was the case in the other parts of the head-skeleton, of two different kinds, primary and secondary. One bone, which makes its appearance in the articular part of the cartilage and produces the os articulare, is a primary bone. With this are associated several covering bones arising in the surrounding connective tissue, two of which, the angulare and the dentale, acquire special importance. Both are attached to the outer surface of the cartilaginous [Meckelian] rod, the angulare near the joint, the dentale in front of it and extending to the symphysis.

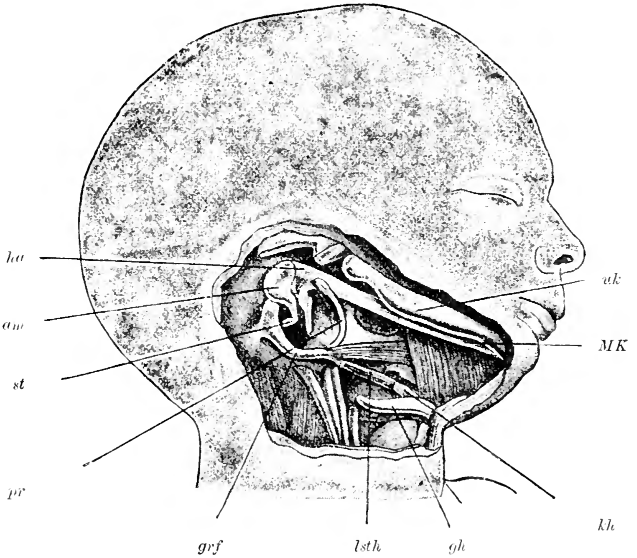

Fig. 338.—Head and neck of a human embryo 18 weeks old with the visceral skeleton exposed, after Kölliker. Magnified.

The lower jaw is somewhat depressed in order to show Meckel's cartilage, which extends to the malleus. The tympanic membrane is removed and the annulus tympanicus is visible.

ha, Malleus, which passes uninterruptedly into Meckel's cartilage, *MK*; *uk*, bony lower jaw (dentale), with its condyloid process articulating with the temporal bone; *am*, incus; *st*, stapes; *pr*, annulus tympanicus; *grf*, processus styloideus; *lsth*, ligamentum stylohyoideum; *kh*, lesser cornu of the hyoid bone; *gh*, its greater cornu.

The latter is an important skeletal element, which attains a considerable size, receives into its upper margin the teeth, and grows around the cartilage of Meckel in such a manner that the cartilage is almost completely enclosed in a bony cylinder. The whole complicated apparatus, composed of several bones and the original cartilage enclosed within them, articulates at the *primary joint of the jaw* between palato-quadratum and os articulare.

The same fundaments are again met with in Mammals and Man.

In the articular part of the cartilage of the lower jaw, which has assumed the form of the malleus (figs. 334, 338 *ha*), there arises a special centre of ossification, which corresponds to the articulare of other Vertebrates. In its vicinity appears, as a covering bone, an exceedingly small angulare, which subsequently fuses with it, producing the long process of the malleus. The second covering bone, the dentale (fig. 338 *uk*), attains, on the contrary, a great size and alone becomes the subsequently functioning lower jaw, whereas the remaining parts, which in the compound mandibular apparatus of Teleosts, Amphibia, Reptiles, and Birds participate in the function of chewing (palato-quadratum,—or quadratum,—articulare, angulare, and Meckel's cartilage), lose their original function and are employed in another manner.

The most important motive to this profound metamorphosis is to be found in the fact that in Mammals and Man *there is developed in place of the primary articulation of the jaw a secondary one.* The primary articulation, upon which the tooth-bearing dentale is moved, lies, as we have seen, between palato-quadratum and articulare. Inasmuch as these elements correspond respectively to the incus and malleus of Mammals, the *primary articulation of the jaw of lower Vertebrates is to be sought in the incus-malleus articulation of the higher Vertebrates.* In Mammals and Man the dentale is no longer moved at this joint, because the dentale itself forms a direct articulation with the cranial capsule by means of a bony projection,—the processus condyloideus (fig. 338),—which it sends upward, and through which it is united to the squamous portion of the temporal bone at some distance in front of the primary articulation. This union constitutes the *secondary articulation of the jaw*, in which only covering bones participate.

The natural result of the formation of a new articulation is, that the primary lower-jaw apparatus has become superfluous for the act of mastication, and that its development is restricted. Incus, malleus, and angulare, which is united with the malleus, are converted into parts of the auditory organ (see p. 613). The remaining part of Meckel's cartilage (*MK*) begins to degenerate, in Man in the sixth month. A portion of it, which is a prolongation of the long process of the malleus, extending from the fissura petrotympanica as far as the entrance into the bony lower jaw at the foramen alveolare, is converted into a connective-tissue cord, the ligamentum laterale internum maxillæ inferioris. A small portion near the front end early acquires a special centre of ossification and fuses with the covering bone. The remainder of that portion of MECKEL's cartilage which is enclosed in the canal of the lower jaw, from the foramen alveolare onward, is gradually broken down and dissolved ; however, remnants of the cartilage are found even in the new-born infant at the symphysis.

At first the bony lower jaw is a paired structure, consisting of tooth-bearing halves. These remain in many Mammals as separate bones, being united in a symphysis by means of connective tissue. In Man they are united in the first year after birth into a single piece by the ossification of the intervening tissue.

A special peculiarity is exhibited by the articular end of the lower jaw, phylogenetically a covering bone. Instead of beginning to be formed, in the manner of the anterior portion, by direct ossification of the connective-tissue foundation, there first arises here a cartilaginous tissue consisting of large vesicular cells and soft intercelluar substance, which is gradually converted into bone. This presents a certain similarity to the development of the primordial bones. But that the resemblance is only superficial is shown by the difference in the structure of the articulation, to which I shall return in a subsequent section.

(c) *Concerning the Relation of the Head-Skeleton to the Trunk-Skeleton.*

In different sections of this text-book—in discussing the primitive segments, the nervous system, and especially now in the discussion of the axial skeleton—reference has been made to many points of agreement that have been recognised between the structural conditions of the head and those of the trunk. In a critical comparison of these two regions of the body there arise many important questions which have for several decades engaged the attention of the best morphologists. It may therefore be well here, after having given the pertinent facts, to take up these questions more particularly, and *determine the relation which head and trunk, and especially that which head-skeleton and trunk-skeleton, sustain to each other.*

Before I elucidate the present state of the question, I will give a brief survey of the history of these researches, which have been grouped together under the name

"*The Vertebral Theory of the Skull.*"

The relation which the anterior and posterior parts of the skeleton of the trunk sustain to each other in the morphology of Vertebrates was for the first time subjected to a thorough scientific discussion at the beginning of the present century, when the school of the "Natural Philosophers" began its career. An attempt to solve the problem was made in very similar ways by two persons, by the natural philosopher OKEN and by the poet GOETHE, without either of them having been influenced by the other.

According to the OKEN-GOETHE *vertebral theory*, the skull is the most anterior part of the vertebral column, and is composed of a small number of modified vertebræ. OKEN distinguished three vertebræ in his "Programme" entitled "Ueber die Bedeutung der Schädelknochen," which appeared in 1807, when he entered upon a professorship conferred upon him in Jena. He named them the ear-, eye-, and jaw-vertebræ.

Each *head-vertebra*, like a trunk-vertebra, consisted in his opinion of several parts—a body, two arch-pieces, and a dorsal spine. OKEN, GOETHE, and their numerous followers believed that this composition was most distinctly recognisable in the last cranial vertebra, the *occipitale*, the base of which was compared to the body of the vertebra, the condyloid parts to the lateral arches, and the squama to the spine of the vertebra.

A second cranial vertebra was discerned in the *body of the posterior sphenoidale*, which together with its greater wings and the two parietal bones formed a second bony ring around the brain.

A third vertebra was constructed out of the *body of the sphenoidale anterius*, the lesser wings and the frontale.

The *ethmoidale* was cited by many investigators as a fourth—the most anterior—cranial vertebra. A number of bones, which would not fit into this scheme, were considered to be structures sui generis, and were in part associated with the sensory organs as sensory bones, in part compared with the ribs of the thorax.

In this form, which underwent numerous modifications in details, the OKEN-GOETHE vertebral theory of the cranium dominated morphology for decades and formed the foundation of many investigations. *It had a stimulating and fruitful effect until, with a deeper insight into the structure of Vertebrates, it was abandoned as defective and erroneous*, giving way before the force of numerous newly discovered facts.

For neither the comparative osteology of the skull nor growing embryological research could point out in a satisfactory way which bones were really to be interpreted as parts of vertebræ. The most dissimilar, and more or less arbitrary, opinions upon this subject made their appearance. An agreement even as to the number of vertebræ contained in the skeleton of the head could not be reached. Some investigators assumed six, others five or four, or even three only.

HUXLEY, in his "Elements of Comparative Anatomy," by a critique based upon facts, was the first to prepare the way for a termination of this unpleasant state of affairs, in which the vertebral theory was held to with tenacity, notwithstanding the contradictions that everywhere arose. In his discussion he argued from *a series of facts which embryological investigation had brought to light.* As such the following, important for the problem of the skull, should be cited before all others.

First, the discovery that the skeleton of the head, like the vertebral column, is developed out of a cartilaginous condition, and that the brain is first enclosed by a primordial cartilaginous cranium (BAER, DUGÈS, JACOBSON).

Secondly, the doctrine established mainly by KÖLLIKER, that the bones of the head-skeleton are separable into two groups according to their development—into the primordial bones, which arise in the primordial cranium itself, and the secondary or covering bones, which have their origin in the enveloping connective tissue.

Thirdly, the insight which was acquired, through the important works of RATHKE and REICHERT, into the metamorphoses of the visceral skeleton, and thereby into the development of the palato-maxillary apparatus and the auditory ossicles.

Through an examination of these various facts, HUXLEY was led to the important and fully justified conclusion, *that not a single cranial bone can be recognised as a modification of a vertebra, that the skull is no more a modified vertebral column than the vertebral column is a modified skull; that, rather, both are essentially distinct and different modifications of one and the same structure.*

While HUXLEY stopped at the negative standpoint, simply denying the vertebral theory, GEGENBAUR has made the question of the relation of skull and vertebral column, raised by GOETHE and OKEN, but from ignorance of the facts incorrectly answered by them, again the object of profound comparative study. Rightly recognising that the problem can be solved only by detailed *investigation of the primordial skeleton,* he selects as the object for his studies the cartilaginous skull of the Selachians, and endeavors in his revolutionising work, "Das Kopfskelet der Selachier als Grundlage zur Beurtheilung der Genese des Kopfskelets der Wirbelthiere," to produce the evidence that *the primordial cranium has arisen by fusion from a number of segments equivalent to vertebræ. Instead of the* OKEN-GOETHE *vertebral theory he propounds the segmental theory of the skull*, as I suggest the doctrine of GEGENBAUR be called.

GEGENBAUR proceeds from the correct conception that the segmentation of a region of the body is recognisable not only in the metamerism of the vertebral column, but also in many other structures—in the method of the arrangement of the chief nerve-trunks, and in the ventral arch-structures attached to the axial skeleton. He investigates, accordingly, the cranial nerves of the Selachians, and arrives at the conclusion that, with the exception of the olfactory and optic nerves, which are metamorphosed parts of the brain itself, they deport themselves like spinal nerves both in their origin and their peripheral distribution. He determines that there are nine pairs of them ; and therefore concludes that the portion of the head-skeleton which is traversed by the nine segmentally arranged cranial nerves must be equivalent to nine vertebral segments, and that it must have arisen by their very early fusion.

The visceral skeleton of Selachians is regarded by GEGENBAUR from the same instructive point of view. He discerns in the maxillary, hyoid, and branchial arches skeletal elements which are represented in the vertebral column by the ribs.

Inasmuch as a vertebral segment belongs to each pair of ribs, a similar relation is also assumed as the original arrangement for the visceral arches. Thus this method of considering the question leads to the same result : that the primordial cranium—since at least nine visceral arches belong to it as ventral arch-structures—has been produced from at least nine segments.

Such an origin GEGENBAUR accepts for the posterior chorda-traversed region of the skull only, in which alone the emerging nerves agree with spinal nerves. He therefore distinguishes this as *vertebral* from the anterior or *non-vertebral portion*, which does not allow the recognition of any segmentation, and which begins in front of the anterior end of the chorda. He interprets the latter as a new formation which has been established by the enlargement in front of the vertebral part of the skull.

GEGENBAUR explains the great differences which exist between skull and vertebral column as adaptations, partly to the enormous development of the brain, partly to the sensory organs of the head, which are received into pits and cavities of the primordial cranium.

Since the time when GEGENBAUR with keen discrimination propounded his segmental theory of the skull, the way has been prepared in many directions, chiefly through embryological investigation, for a better comprehension of the skeleton of the head.

Investigations which I undertook on the dermal skeleton of Selachians, Ganoids, and Teleosts, as well as on the head-skeleton of Amphibia, showed that the difference between primordial and covering bones is much greater than it was originally assumed to be. For as their development shows, *the covering bones are at first structures quite foreign to the axial and head-skeleton, formed at the surface of the body in the skin and mucous membrane.* They are parts of a dermal skeleton, which in lower Vertebrates protect the surface of the body as a scaly armor,—parts which have entered into union with the superficially located portions of the inner, primordial cartilaginous skeleton. Therefore the covering bones of the lower Vertebrates are often tooth-bearing bony plates, which have originated from a fusion of isolated dental fundaments, a condition which may be regarded for many reasons as the primitive one.

A further acquisition of broad significance is the discovery of the *primitive segments of the head*, which we owe to BALFOUR, MILNES MARSHALL, GOETTE, WIJHE, and FRORIEP.

By it an important point of agreement between head and trunk has been made out. The two body-sacs penetrate even into the head; here also the two middle germ-layers are separated into a dorsal portion, lying in contact with the chorda and neural tube, which is divided into nine pairs of primitive segments,* and into a ventral portion (see p. 351).

The head is therefore segmented similarly to the trunk, even at a time when the first traces of the fundament of a vertebral column or a head-skeleton are not yet present.

Thirdly, the insight into the *development of the cranial nerves* (BALFOUR, MARSHALL, WIJHE, and others) is important. An agreement with the development of the spinal nerves has been established in so far as some cranial nerves have a dorsal origin from a neural crest, like the sensory roots of spinal nerves, while others grow out ventrally from the brain-vesicles like anterior roots.

Finally, I would mention as a step in advance, which is not without significance for the interpretation of the head-skeleton, *the altered conception of the meaning of the primitive segments which embryological evidence has compelled us to form.*

The primitive segments are the real fundaments of the musculature

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* [See footnote p. 458.]

of the body. The first segmentation of the vertebrate body affects the body-sacs and the musculature arising from them. The formation of the primitive segments is only remotely and indirectly connected with the development and segmentation of the vertebral column. It is only after muscle-segments have existed for a long time that, at a comparatively late stage of development, the fundaments of a segmented vertebral column are established. But these arise, by histological metamorphosis, from an unsegmented connective-tissue matrix, in consequence of the appearance of a process of chondrification.

All the conditions here only briefly touched upon are of far-reaching significance for the question of the relation of the head- and trunk-skeletons to each other. For, as Gegenbaur rightly points out, since the establishment of his segmental theory "the vertebral theory of the skull has become more and more a problem of the phylogenesis of the whole head."

I desire to give briefly and connectedly my own views upon this subject:—

Theory concerning the Relation of the Head and its Skeleton to the Skeleton of the Trunk.

The segmentation of the vertebrate body begins with the walls of the primary body-sacs, the dorsal portion of which, abutting upon the chorda and neural tube, is divided by the formation of folds into successive compartments, the primitive segments.

Inasmuch as the voluntary musculature is developed from the walls of the primitive segments, it is the first system of organs in Vertebrates to be segmented.

The myomeric condition—"myomerism"—is the direct cause of a segmental arrangement of the peripheral nerve-tracts, for the motor nerves pertaining to a segment unite to form an anterior [ventral] root as they emerge from the spinal cord, and in the same manner the sensory nerves which come from a corresponding part of the skin together constitute a sensory root.

At a time when the segmentation of the musculature and of the peripheral nerve-tracts has already been effected, the skeleton is still unsegmented; for it is represented by the chorda dorsalis alone. The soft mesenchyme, which envelops the chorda and the neural tube, and which becomes the matrix of the subsequently formed segmented axial skeleton, is still a continuous mass of cells, filling in the spaces between these organs.

At this time the differentiation of head and trunk has already taken place. This is accomplished, first by the establishment of the higher sensory organs in the anterior portion of the body, secondly by the enlargement of the neural tube into the voluminous brain-vesicles, thirdly by the formation of a regular series of visceral clefts in the walls of the head-gut, which thus also undergo a kind of segmentation (branchiomerism).

The region of the body which is thus metamorphosed into a head is from the beginning segmented, and is composed, as the Selachians show, of at least nine primitive segments.

The development of visceral clefts produces still further differences between head and trunk. By the appearance of visceral clefts, the front part of the body-cavity is divided up into several successive *head-cavities.* By the disappearance of these cavities, parts corresponding to the thoracic and abdominal cavities have become obliterated. Further, there are developed out of the cells composing the walls of the head-cavities important masses of transversely striped muscles for moving and constricting the separate portions of the branchial region of the alimentary canal, whereas in the trunk the voluntary musculature arises exclusively from the primitive segments. In the trunk these masses of muscle spread out both dorsally over the neural tube and also ventrally into the wall of the thorax and abdomen, whereas in the head they remain limited to a small space and do not undergo any extensive development.

It is only after head and trunk have thus already become in a high degree different that the cartilaginous axial skeleton begins to be formed. The latter is therefore a structure of comparatively recent origin, as it also is peculiar to the phylum, Vertebrata, and even here is wanting in the lowest representative, Amphioxus lanceolatus.

The development of the cartilaginous axial skeleton in the two chief regions of the body is from the beginning partly similar, partly dissimilar.

The development is *similar* in so far as the process of chondrification begins in both head and trunk in the perichordal connective tissue, then extends around the chorda both above and below, ensheathing it, and finally is continued into the connective-tissue layer that envelops the neural tube.

The dissimilarity is expressed in the occurrence or omission of segmentation. In the trunk under the influence of the musculature there arises a segmentation of the cartilaginous axial skeleton into firm vertebral pieces, alternating with intervertebral ligaments which remain in the connective-tissue state. In the head there is developed at once a continuous cartilaginous capsule around the brain-vesicles. *The segmentation, which in this region is expressed in other systems of organs,—in the formation of primitive segments and in the arrangement of the cranial nerves,—does not occur in the corresponding part of the axial skeleton.* Never in the course of the development of any Vertebrate has there been observed, as the first fundament of the primordial cranium, a succession of cartilaginous pieces, alternating with connective-tissue discs, and there seems to be no ground for assuming that a condition of this kind existed in earlier times. In the slight development of the muscles derived from the primitive segments of the head, and in the voluminous condition attained by the brain and sensory organs, are to be discerned, on the contrary, factors which have converted the head, at an early period, into a more rigid portion than the trunk. The cause, which in the trunk has made the segmentation of the axial skeleton necessary, has been wanting in the head.

During the last few years the opinion has been expressed by a number of persons (ROSENBERG, STÖHR, FRORIEP) that in some classes of Vertebrates the occipital region of the primordial cranium is increased by fusion with vertebral fundaments of the neck-region, and thus, as it were, "is constantly advancing caudad." I leave undetermined to what extent this is true. GEGENBAUR combats the interpretation of STOHR, but describes a quite frequently occurring fusion of the cranial capsule with vertebræ in Bony Fishes. One thing only would I point out: the conception of the first unsegmented fundament of the primordial cranium which I have presented is not irreconcilable with the view that subsequently new vertebral segments may be added behind.

Besides the segmented condition of the vertebræ, a segmentation of the axial skeleton is also expressed in the appearance of ventral arches, which are repeated in regular order from before backwards. On the head they are designated as *visceral arches,* on the trunk as *ribs.*

The position of these skeletal parts also is dependent upon the first segmentation which affects the organisation of Vertebrates. For the ribs are developed between the muscle-segments by a process of chondrification in the connective-tissue plates separating them—the intermuscular ligaments; while the visceral arches are dependent upon the visceral clefts, by which the ventral part of the head-region is divided into a number of successive segments.

It cannot be concluded from the existence of ribs and visceral arches that the corresponding skeletal axis must likewise have been segmented. They are only an indication of the segmentation of the region of the body to which they belong.

That the segmentation of the head which is present in the embryo is more or less obliterated in the adult Vertebrate depends upon two causes. First the primitive segments are only slightly developed, furnishing unimportant muscles, and in part wholly degenerate; secondly the visceral skeleton is subjected to profound metamorphoses. Especially in the higher Vertebrates it experiences such a degeneration and metamorphosis, that finally nothing of the original segmental arrangement of its parts (palato-maxillary apparatus, auditory ossicles, hyoid bone) is left.

B. The Development of the Skeleton of the Extremities.

A description of the skeleton of the extremities should be preceded by a few words in regard to the fundaments of the limbs themselves. These at first appear as small elevations [limb-buds] at the sides of the trunk in front and behind (fig. 339). That they belong more to the ventral than to the dorsal surface of the body is evident from the fact that they are innervated by the ventral branches of the spinal nerves.

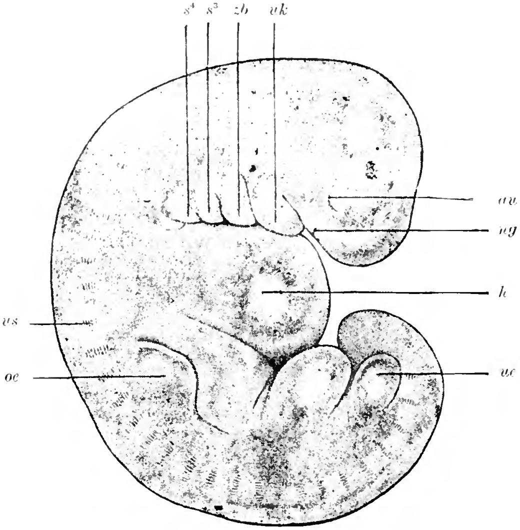

Fig. 339.—Very young human embryo of the fourth week 4 mm long, neck-rump measurement; taken from the uterus of a suicide 8 hours after her death, after Rabl.

au, Eye; *ng*, nasal pit; *uk*, lower jaw; *zb*, hyoid arch; s^3, s^4, third and fourth visceral arches; *h*, protrusion of the wall of the trunk caused by the growth of the heart; *us*, boundary between two primitive segments; *oe*, *ue*, anterior and posterior limbs.

Moreover, *the limbs appear to belong to a large number of trunk-segments. This is to be inferred both from the method of the distribution of nerves and also from the source* *of their musculature.* For the anterior and posterior limbs always receive their nerves from a large number of spinal nerves. The muscles are derived from the same source as the whole musculature of the trunk—from the primitive segments.

It has not yet been possible to establish the derivation of the musculature in Mammals and Man. For the limb-buds consist of a mass of small, closely crowded cells; it is impossible to state which of these belong to the mesenchyme, which to the musculature, or which to the nerves. The conditions in lower Vertebrates, on the contrary, are much more favorable.

In Selachians the fins, which correspond to the limbs of the higher Vertebrates, contain, even at the time of their formation as small plates, distinctly recognisable embryonic gelatinous tissue, which is covered in by the epidermis. An important discovery by DOHRN has established that there grow into the gelatinous tissue of the fin two buds from each of a large number of primitive segments; the buds then become detached from their parent tissue and each is divided into a dorsal and a ventral half—the fundaments of extensor and flexor musculature. *Each fin therefore contains a series of muscular fundaments, which have arisen segmentally and are arranged one behind another,*—a fact which has its weight in many other questions touching the origin of the limbs.

In Man the fundaments of the limbs take on a definite form as early as the fifth week. The outgrowths have become enlarged and divided into two regions, of which the distal becomes the hand, or foot. In the case of the anterior extremity the front margin of the hand already begins to acquire indentations, by which the first fundaments of the fingers are indicated. In the sixth week the three chief divisions of the limbs are recognisable, for the proximal portion is now marked off by a transverse furrow either into arm and fore-arm or into thigh and leg. Now, too, on the foot the toes are indicated by constrictions, but less distinctly than are the fingers on the hand.

In the seventh week there are to be observed at the tips of the fingers claw-like appendages, consisting of epidermal cells—the primitive nails. As HENSEN remarks, "The similarity of the hand at this stage to the anterior extremity of a Carnivore viewed from the sole is striking; in addition to the toe-like brevity and thickness of the fingers, the pads are well developed."

With their enlargement the limbs apply themselves to the ventral surface of the embryo, being directed obliquely from in front backward [and ventrad], the anterior limbs more obliquely than the posterior. In both of them the future extensor side lies dorsal, the flexor side ventral. Both the radial and tibial margins with the thumb and great toe are directed cephalad, the fifth finger and the fifth toe caudad.

By this and by the fact that the limbs belong to several trunk-segments are explained certain conditions in the *distribution of the nerves of the upper extremity.* In the case of the arm "the radial side is supplied with nerves (axillaris, musculo-cutaneus), whose fibres are referable to the fifth, sixth, and seventh cervical nerves. Upon the ulnar side, on the contrary, are found nerves (n. cutaneus medialis, n. medius, and n. ulnaris) whose origin from the lower secondary trunk of the plexus discloses their derivation from the eighth cervical and first dorsal nerves" (SCHWALBE).

In the further course of development both limbs alter their original position,—the anterior to a greater extent than the posterior,—inasmuch as they undergo a torsion around their long axes in opposite directions. In this way the extensor side of the upper arm becomes directed backward [caudad], that of the thigh forward; radius and thumb are now directed laterad, tibia and great toe mediad. These alterations in position due to torsion are naturally to be taken into account in determining the homologies of the anterior and posterior extremities, so that radius corresponds to tibia and ulna to fibula.

In the originally homogeneous cell-mass the fundaments of the skeleton and musculature are gradually differentiated from each other, owing to the fact that the cells acquire a more definite histological character. In this connection the following phenomenon is to be observed:—

The parts of the skeleton of the extremity are not all established at the same time, but follow a definite sequence, in somewhat the same manner as, in the development of the axial skeleton, the process of segmentation begins in front and progresses backward. So in the limbs the proximal skeletal elements (*i.e.*, those which are situated nearer to the trunk) are formed sooner than the distal ones.

This is the most strikingly apparent in the case of the fingers and toes. Whereas the first phalanx has been differentiated from the surrounding tissue in embryos of the fifth and sixth week, the second and third are not at that time distinguishable; the ends of the fundaments of fingers and toes still consist of a mass of small cells in process of growth. In this mass the second phalanx is then differentiated, and at last the third.

Furthermore the formation of the anterior limbs outstrips somewhat that of the posterior.

In the development of the skeleton of the extremities there are to be recognised, as in the vertebral column and the skull, three different stages,—the stage of the membranous, that of the cartilaginous, and that of the osseous fundament.

After these general remarks I turn to the detailed description of (1) the pectoral and pelvic girdles, (2) the skeleton of the appendage, which projects free from the surface of the trunk, and (3) the formation of joints.

(*a*) *Pectoral and Pelvic Girdles.*

The fundaments of the girdles of the limbs consist each of a pair of curved pieces of cartilage, which are imbedded under the skin in the muscles of the trunk, and which bear near the middle an articular surface for the reception of the skeleton of the free extremity. By this each cartilage is divided into a dorsal half, near the vertebral column, and a ventral half. The former is converted in Mammals and Man into a broad shovel-shaped piece; the ventral half, which reaches to, or nearly to, the median plane, is, on the contrary, divided into two diverging processes, an anterior and a posterior. The cartilaginous pieces thus distinguishable ossify from special centres, and thereby acquire a higher degree of independence.

The shoulder-blade (scapula) of Man is at first a cartilage of a form similar to that of the adult, except that the basis scapulæ is less developed. In the third month ossification begins at the collum scapulæ. However, the margins, the spine, and the acromion remain for a long time cartilaginous, and indeed are in part so even at the time of birth. There arise in them here and there accessory centres during childhood.

From the articular part of the shoulder-blade there runs ventrally a cartilaginous process, which is short in Man, but in other Vertebrates is of considerable size and reaches down to the sternum. It corresponds to the posterior of the previously mentioned diverging processes into which the ventral part of the cartilaginous arch is divided, and is known in comparative anatomy as *pars coracoidea.* In Man it is only slightly developed. Its great independence, however, is made evident by its acquiring in the first year after birth a separate centre of ossification. From this there gradually arises a bony element (os coracoideum), which is joined to the shoulder-blade until the seventeenth year by a strip of cartilage, and may therefore be detached. Afterwards it is united with the scapula by bony substance and constitutes the coracoid process. Still later the fusion of the accessory centres previously mentioned takes place, to which, however, no great morphological importance attaches.

There are two different views concerning the place which the *clavicle* takes in the shoulder-girdle.

According to GOETTE, HOFFMANN, and others, it belongs to the primordial skeletal parts, which are preformed in cartilage, and corresponds to the anterior ventral process, which was present in the primitive form of the shoulder-girdle. According to GEGENBAUR it is a covering bone which has entered into union with the cartilaginous skeleton in the same way as the covering bones of the skull have with the primordial cranium.

It is the peculiar method of the development of the clavicle that has caused this divergence of opinion. This is the first bone to be formed in Man; it begins to be ossified as early as the seventh week. The earliest bony piece, as GEGENBAUR was the first to ascertain, is developed out of wholly indifferent tissue. Then there are added at both ends masses of cartilage, which are softer and provided with less intermediate substance than the ordinary embryonic cartilage. They serve, as in other bones that are preformed in cartilage, for the elongation of the clavicle at both ends. There is also developed in the sternal end, between the fifteenth and twentieth years, a kind of epiphysial centre, as KOLLIKER states; this fuses sometimes as late as the twenty-fifth year with the main piece.

The original conditions are the most faithfully preserved in the *pelvic girdle*, even in Man and Mammals. The first fundament of the girdle consists of a right and a left pelvic cartilage, which are united ventrally in the symphysis by means of connective tissue, and each of which has at its middle an articular fossa. Each pelvic cartilage is composed of an expanded part extending dorsally from the articular depression,—the iliac cartilage,—which is joined to the sacral region of the spinal column, and two ventral cartilaginous rods,—pubis and ischium,—which, meeting in the symphysis, enclose the foramen obturatorium.

It is stated by ROSENBERG that the pubic cartilage is at first formed independently, but that it soon fuses with the other cartilages at the acetabulum.

Ossification begins at the end of the third month in three places, and thus are formed a bony *ilium*, *os pubis*, and *ischium* at the expense of the cartilage, of which, however, considerable remnants are still present at the time of birth. For the whole crest of the ilium, the rim and fundus of the acetabulum, and the whole tract from the tuberosity of the ischium to the spine of the pubis is still cartilaginous.

After birth the growth of the three bony pieces advances toward the acetabulum, where they all meet, being however separated, up to the time of puberty, by strips of cartilage, which together form a three-rayed figure. At about the eighth year both the ascending and descending rami of pubis and ischium fuse with each other, so that at this time each hip-bone consists of two pieces joined by cartilage at the acetabulum—the ilium and an ischio-pubic bone. These do not become united into one piece until the time of puberty.

As in the pectoral girdle, so also in the pelvic girdle, there occur accessory centres of ossification; of these one, which sometimes arises in the cartilage of the acetabulum, is the most important, and is described as os acetabuli. Others arise in the cartilaginous crest of the ilium, in the spines and tubercles, and in the tuberosity of the ischium. They are not united with the chief bones until the end of the period of growth.

(*b*) *Skeleton of the Free Extremity.*

All skeletal parts of the hand, fore-arm, and arm, as well as of the foot, leg, and thigh, are originally solid pieces of hyaline cartilage, which early acquire the general forms of the bones that subsequently replace them. They are marked off from their surroundings by a special fibrous layer of connective tissue, the perichondrium.

From the beginning of the third month the process of ossification takes place in the larger skeletal pieces, by means of which the cartilaginous tissue is destroyed and replaced by osseous tissue, in the same manner as in the vertebral column. In this process several general phenomena regularly make their appearance; I shall go somewhat into the details of these, without however taking into account the complicated histological changes, information concerning which is given in text-books of histology.

The process of ossification takes externally a somewhat different turn according as the cartilages are small and uniformly developed in all directions, as in the wrist and ankle, or have become more elongated.

In the first case the course of development is more simple. From the perichondrium vascular, richly cellular connective-tissue processes grow into the cartilage, dissolve its matrix, and unite with one another in its centre. There arises a network of medullary [marrow] cavities, in the vicinity of which there is a deposit of salts of lime (a provisional calcification). The medullary spaces extend farther and farther by destruction of the cartilaginous substance. Then there are secreted by the superficially located medullary cells bone-lamellæ, which gradually increase in thickness. The osseous nucleus thus formed slowly increases in size, until finally the cartilage is almost entirely replaced, only a thin layer of it remaining at the surface as a covering to the bone.

The ossification of the wrist- and ankle-bones is therefore purely *endochondral*, and proceeds ordinarily from one, sometimes from two, centres of ossification. It does not begin until very late—in the first year after birth. The only exception occurs in the foot, where the os calcis and astragalus acquire a bony nucleus in the sixth and seventh months, and the cuboid begins to ossify a short time before birth. In the others ossification takes place after birth, and, as KÖLLIKER states, in the following order:—

I. *In the hand.* (1) Os magnum and unciform (first year); (2) cuneiform (third year); (3) trapezium and lunar (fifth year); (4) scaphoid and trapezoid (sixth to eighth year); (5) pisiform (twelfth year).

II. *In the foot.* (1) Os scaphoideum (first year); (2) internal and middle cuneiform (third year); (3) external cuneiform (fourth year).

Concerning the cartilaginous fundaments of a special centrale carpi, which usually is not retained as a separate carpal element (ROSENBERG), as well as a special intermedium tarsi or trigonum (BARDELEBEN), the text-books of comparative anatomy are to be consulted.

The process of ossification is more complicated in the long cartilages, in which, moreover, it begins much earlier, usually even in the third month of embryonic life. The course of ossification is fairly typical.

At first a perichondral ossification takes place midway between the ends of each cartilage in the humerus and femur, tibia and fibula, radius and ulna. From the perichondrium there is deposited upon the already formed cartilage bony tissue instead of a cartilaginous matrix, so that the middle portion of the cartilage becomes ensheathed in a bony cylinder, which is continually increasing in thickness.

The further growth of the skeletal element thus composed of two tissues proceeds in two ways: first by growth of the cartilage, and secondly by increase of bony substance.

The cartilaginous tissue increases at both ends of the skeletal piece and contributes to the increase of the latter both in length and thickness. In the middle, on the contrary, where it is enveloped in a bony cylinder, it ceases to grow. Here there is a continual addition of new bony lamellæ upon those already formed; they are produced by the original perichondrium, or, as one may now more properly say, by the periosteum.

In this process the successive lamellæ extend farther and farther toward the two ends of the skeletal piece; new portions of the cartilage are being continually ensheathed in bone and restricted in their growth.

The periosteal bony sheath assumes in consequence the form of two funnels united at their apices.

The cartilage which fills up the funnels early undergoes a gradual metamorphosis and degeneration. From the osseous sheath there grow into it connective-tissue strands with blood-vessels, which dissolve the matrix and produce larger and smaller marrow-cavities. Then, by the secretion of osseous tissue at the surface of the persisting remnants of cartilage, there is developed a spongy bone-substance, which fills up the funnel-shaped cavities of the compact bony mantle produced by the periosteum. The spongy bone is, however, only an evanescent structure. It in turn is gradually dissolved, beginning at the middle of the skeletal element, and its place is occupied by a very vascular marrow. In this way there arises in the originally quite compact cartilaginous fundament the large central medullary cavity of the long bones.

During these processes the two ends still remain cartilaginous, and serve for a long time by their growth to increase the length of the skeletal element. They are designated as the two *epiphyses*, in distinction from the middle piece, which is the first to ossify, and which has received the name *diaphysis.* The latter increases in size at the expense of the epiphysial cartilages, for the endochondral process of ossification progresses, with a very distinct line of ossification, toward both ends.

A new complication in the development of the tubular (long) bones arises either a short time before or in the first years after birth. There are then developed in the middle of each epiphysis special centres of ossification, the so-called *epiphysial nuclei*; there are first produced, in the manner previously described, vascular canals, which arise by the dissolution of the cartilaginous substance; the canals unite to constitute large medullary spaces, at the surfaces of which osseous tissue is then secreted.

By a slowly progressing enlargement of the bony nucleus, which continues for years, the epiphysial cartilage is gradually converted into a *spongy osseous disc*, being finally reduced to small remnants. First, there is preserved, as an investment of the free surface, a layer only a few millimetres thick, which constitutes the "articular cartilage." Secondly, there remains for a long time a thin layer of cartilage between the older, bony middle piece and the bony disc-like epiphysis, and this serves to keep up the elongation of the skeletal part. For the cartilage grows vigorously by the proliferation of its cells, and thus is being renewed as fast as its two flat surfaces are dissolved away by the endochondral ossification which takes place at its expense, both by the growth of the bony epiphyses and, to a much greater extent, by that of the more rapidly elongating diaphysis.

Thus it happens that long bones which have not yet ceased growing can be divided into three pieces, if the organic parts are removed by maceration. *A fusion into a single osseous piece does not take place until, at the time of maturity, the increase in the length of the body has ceased.* Then the thin plates of cartilage between the diaphysis and its two epiphyses are broken down and converted into bony tissue. From this time forward a further increase in the length of the bone is impossible.

Besides the three typical and chief centres already described, from which the ossification of the cartilaginous fundament of a tubular bone proceeds, there are established in many cases smaller centres of ossification of secondary importance, which are denominated *accessory bone-nuclei*. They always arise in the later years, when the epiphyses are well developed, and sometimes not until they are in process of fusion with the diaphysis. They then appear at places where the cartilaginous fundament possesses elevations and projections, as in the tubercles of the humerus, in the trochanters of the femur, the epicondyles, etc. They serve for the conversion of these elevations into osseous masses, which are generally the last to fuse with the chief bone.

After this general description, I add some detailed statements about the formation and the number of the more important bony nuclei in the fundaments of the separate tubular bones, concerning which we have the extensive investigations of SCHWEGEL.

1. The diaphysis of the humerus ossifies in the eighth week. Epiphysial nuclei are not formed until after birth, at the end of the first or beginning of the second year. In the second year there appear accessory nuclei in the tuberculum majus and minus; during and after the fifth year in the epicondyles also.

2. The diaphyses of the radius and ulna also begin to ossify in the eighth week. Epiphysial nuclei do not appear until between the second and the fifth years. Accessory nuclei are observed rather late in the styloid processes.

3. The metacarpals begin to ossify in the ninth week, but, with the exception of the metacarpal of the thumb, there arises only one epiphysis, which is at the distal end. This acquires in the third year its own centre of ossification.

4. The ossification begins in the phalanges at the same time as in the metacarpals.

5. The femur begins to ossify in the seventh week. *A short time before birth there is formed in the distal epiphysis a centre of ossification, which is a part of the evidence that a child has been carried to the full time, and therefore possesses a certain importance for forensic purposes.* After birth an epiphysial nucleus soon appears in the head of the femur. Accessory nuclei are formed in the fifth year in the trochanter major, in the thirteenth or fourteenth in the trochanter minor.

6. Tibia and fibula acquire epiphysial nuclei in the first and third years after birth, first at the proximal, then at the distal end, the ossification in the fibula occurring about a year later than that in the tibia. GEGENBAUR regards this as indicating a subordination of the functional importance of the fibula in comparison with the tibia.

7. The patella begins to ossify in the third year.

8. To the metatarsals and the phalanges of the toes applies in general all that has been said about the corresponding parts of the hand.

(c) *Development of the Joints.*

Inasmuch as the separate pieces of cartilage in the body are formed by histological differentiation in the connective-tissue layers, they are at first united to one another by remnants of the parent tissue. This generally acquires a more compact fibrous condition and is converted into a special ligament.

Such a union of the separate skeletal elements is the prevailing method in the lower Vertebrates, as, *e.g.*, in the Sharks. In the higher Vertebrates, including Man, it is retained in many, but not all, places, as, *e.g.*, in the vertebral column, where the bodies of the vertebræ are joined to each other by intervertebral discs of connective tissue. But at the places where the apposed skeletal parts acquire greater freedom of motion upon each other, there appears, in place of the simpler connective-tissue union, the more complicated articular connection.

In the development of the joints the following general phenomena occur :—

Young cartilaginous fundaments, as, *e.g.*, those of the thigh and leg, are in early stages separated at the place where the articular cavity is subsequently formed by a very cellular intermediate tissue (the intermediate disc of HENKE UND REYHER). This subsequently diminishes in extent, because the ends of the cartilages grow at its expense. In many cases it disappears entirely, so that the terminal surfaces of the skeletal parts concerned are for some distance in immediate contact.

The specific curvature of the articular surfaces is by this time more or less well established. This is accomplished at a time when there is as yet no articular cavity, and when, moreover, movements of the skeletal parts cannot be executed, because the muscles are not capable of functioning.

From this it follows that during embryonic life the articular surfaces cannot acquire their specific form under the influence of muscular activity, and that they are not formed, as it were, by attrition and adaptation to each other in consequence of definite recurrent movements in a simply mechanical way, as has been assumed by many. *The early appearing typical form of the joint seems therefore to be inherited* (BERNAYS). Muscular activity can be effective only for alterations at later stages; it is, however, not without influence in the further development and formation of the articular surfaces.

When, after the disappearance of the intermediate tissue, the surfaces at the ends of the developing cartilages come into immediate contact, there arises between them a narrow fissure as the first fundament of the articular cavity. This is bounded directly by the hyaline articular cartilage, which does not here possess any perichondrium. Then a sharper delimitation of the articular cavity from the surrounding connective tissue gradually takes place, inasmuch as a firmer connective-tissue layer, which becomes the capsular ligament, is developed from one cartilage to the other, and additional fibrous tracts are converted into separate tense articular ligaments.

The process of development takes a somewhat different course when the articular surfaces do not fit into each other. In these cases the ends of the cartilages cannot come into immediate contact in the manner previously described; they now remain separated by more or less considerable remnants of the richly cellular intermediate tissue, which then assumes more and more the condition of compact fibrous tissue.

When the intermediate tissue is preserved in its whole extent, there arises a fibro-cartilaginous interarticular disc (intermediate or interpolated cartilage), which is inserted as an elastic cushion between the skeletal pieces. There is formed an articular fissure between the ligamentous disc and the terminal surfaces of each of the articular cartilages, or, in other words, there is developed an articular cavity, which is divided into two by means of an interpolated disc.

Finally, a special modification of the joint occurs when the cartilages are partly in contact and partly remain separated by intermediate tissue. In this case there appears at the place of contact a single articular cavity; laterally, however, this is enlarged by the incongruent parts of the cartilaginous surfaces becoming split off from the intermediate tissue separating them. Thus there arises an articular cavity which, it is true, is single, but into which are thrust from the articular capsule the metamorphosed products of the intermediate tissue, which constitute the so-called semi-lunar fibro-cartilages or the menisci, as in the case of the knee-joint.

As was previously described in treating of the development of the bones of the extremities, there is preserved, even after the termination of the process of ossification, an exceedingly small remnant of the cartilaginous fundament, which forms on the articular surfaces a cartilaginous covering only a few millimetres thick. The articular ends of all bones that are developed out of a cartilaginous fundament possess such a covering.

It is different when bones that have been produced directly in connective tissue (the covering bones) are united to each other by a veritabie joint. Such a case occurs in the articulation of the lower jaw in Mammals. The glenoid process of the lower jaw, as well as the glenoid fossa of the squamous portion of the temporal bone, is in this case covered with a thin layer of unossified tissue. It looks like cartilage, and usually is described as such. But microscopic examination shows that it is composed exclusively of layers of connective-tissue fibres.

As there are bones which are preformed in cartilage and others which are preformed in connective tissue, so a distinction must be made between joints with a covering of hyaline cartilage and joints with a covering of fibrous connective substance.

SUMMARY.

A. *The Vertebral Column.*

1. During development the vertebral column passes through several (from lower to higher) morphological conditions, of which the lower are permanently preserved in the inferior classes of Vertebrates, whereas in the higher classes they appear only at the beginning of development and are then replaced.

2. In the axial skeleton three different stages of development are distinguished:—

(1) As chorda dorsalis (notochord),
(2) As cartilaginous and
(3) As osseous vertebral column.

3. The chorda is developed out of a tract of cells (chorda-entoblast, fundament of the chorda) lying below the neural tube and belonging to the inner germ-layer, from which it is detached by abstriction (chordal folds).

4. The chorda is a rod composed of vesiculated cells and bounded superficially by a firm sheath; it begins with a pointed end beneath the mid-brain vesicle (in the region of the future sella turcica of the cranial floor) and reaches to the blastopore (primitive groove).

5. The chorda persists as a permanent skeletal structure in Amphioxus and the Cyclostomes.

6. A cartilaginous vertebral column is found in the adults of the Selachians and some of the Ganoids, while in the remaining Vertebrates it appears more or less during development as a forerunner of the bony vertebral column.

7. The cartilaginous vertebral column is developed by histological metamorphosis out of embryonic connective tissue, a part of which envelops the chorda as skeletogenous chordal sheath, and a part forms a thin continuous envelope (membranous vertebral arches) around the neural tube.

8. The process of chondrification begins on both sides of the chorda, progresses around it both above and below, and thus forms a cartilaginous ring,—the body of the vertebra,—from which the process of chondrification advances dorsally into the membranous envelope of the neural tubes, producing the arches of the vertebræ and ceasing with the formation of the vertebral spines.

9. It is not until the beginning of the process of chondrification in the unsegmented, connective-tissue, skeletogenous chordal sheath

that the axial skeleton undergoes a segmentation into separate like portions, which are situated one behind another; to accomplish this, remnants of the parental tissue do not chondrify, but become, between the bodies of the vertebræ, the intervertebral discs, and, between the arches, the ligamenta intercruralia, etc.

10. The segmentation of the vertebral column has been dependent in its origin upon the segmentation of the musculature, and has been effected in such a way that skeletal segments and muscular segments alternate with one another, and that the longitudinal muscle-fibres, which lie alongside the axial skeleton, are attached by their anterior and posterior ends to two [adjacent] vertebræ and are capable of moving them upon each other.

11. The chorda is more or less restrained in its growth by the cartilaginous bodies of the vertebræ surrounding it, and degenerates in different ways in the different classes of Vertebrates; in Mammals the part located in the body of the vertebra is completely obliterated, whereas a remnant of it is preserved between vertebræ and becomes the jelly-core of the intervertebral disc.

12. The cartilaginous vertebral column is converted in most Vertebrates into a bony one, by the breaking down of the cartilaginous tissue, which begins at different places, and its replacement by bony tissue. (Formation of bone-nuclei or centres of ossification.)

13. The ossification of each cartilaginous vertebral fundament in Mammals and Man proceeds from three centres, from one in the body and one in each half of the arch, to which subsequently certain accessory centres are added.

14. With each vertebral segment there is associated a pair of ribs, which arise by a process of chondrification in the layers of tissue which separate the muscle-segments (the ligamenta intermuscularis).

15. In Man the various regions of the vertebral column are produced by metamorphosis of the vertebral and costal fundaments.

(1) The thoracic part of the vertebral column (dorsal vertebræ) is characterised by the following peculiarities: the ribs attain to complete development; a part of them become expanded at their ventral ends, and united to form the two sternal bars, by the fusion of which the unpaired sternum is produced. (Fissura sterni, an arrested formation.)

(2) In the cervical and lumbar regions of the column the fundaments of the ribs remain small, and fuse with outgrowths from the vertebræ—the transverse processes—to form

the lateral processes. In the neck-region there is retained, between the transverse process and the rudiment of the rib, the foramen transversarium for the vertebral artery.

(3) Atlas and epistropheus [axis] assume special forms, owing to the fact that the body of the atlas remains separate from the fundaments of its arch, and unites with the body of the axis to form its odontoid process. (Separate centre of ossification in the odontoid process.)

(4) The sacrum results from the fusion of five vertebræ and the sacral ribs belonging to them. The latter by their fusion produce the so-called massæ laterales, which bear the articular surfaces for the ilium.

B. The Head-Skeleton.

16. The skull, like the vertebral column, passes through three morphological conditions, which are designated as membranous and as cartilaginous primordial cranium and as bony cranial capsule.

17. The membranous primordial cranium consists of—

(1) The anterior end of the chorda, which extends to the anterior margin of the mid-brain vesicle, and

(2) A connective-tissue layer, which surrounds the chorda as skeletogenous layer, and also furnishes a membranous investment around the five brain-vesicles.

18. The cartilaginous primordial cranium arises by a histological metamorphosis of the membranous one.

(1) At the sides of the chorda there are first formed two cartilaginous rods, the two parachordals, which soon grow around the chorda both above and below, and become united into a single cartilaginous plate.

(2) In front of the parachordals RATHKE's trabeculæ cranii make their appearance; their posterior ends soon unite with the parachordal cartilages, their anterior ends become enlarged and by fusing with each other produce the ethmoid plate; in the middle they remain for a long time separate and embrace the hypophysis (region of sella turcica).

(3) From the cartilaginous base of the cranium thus produced, the process of chondrification, as in the development of the vertebral column, first extends into the lateral walls, and at last into the roof of the membranous primordial cranium, partly enclosing the higher sensory organs.

19. In the Selachians the cartilaginous primordial cranium is a permanent structure, and possesses rather thick uniform walls; in Mammals and Man, on the contrary, it is of only short duration, serving as foundation for the bony cranial capsule that takes its place; it is therefore less completely developed than in Selachians, for only the base and lateral parts are in all cases cartilaginous, whereas the roof presents large openings closed by dermal membranes.

20. From its relation to the chorda dorsalis, there are distinguishable in the cartilaginous primordial cranium two chief portions,—a vertebral (chordal) and a non-vertebral (prechordal),—or, according to its relations to the sensory organs, it may be divided into four regions—ethmoidal, orbital, labyrinthal, and occipital.

21. As the ribs are associated with the vertebral column in the form of ventral arched structures, so also the visceral skeleton is united to the primordial cranium in the head-region.

22. The visceral skeleton is composed of segmented cartilaginous rods, which have arisen by a process of chondrification in the tissue of the membranous visceral arches between the successive visceral clefts.

23. The cartilaginous throat- or visceral arches are well developed only in the lower Vertebrates (permanently in the Selachians), and are distinguished, according to differences of position and form, as jaw-arch, hyoid arch, and branchial arches, the last being variable in number.

24. The jaw-arch is divided into the cartilaginous upper jaw (palato-quadratum) and the cartilaginous lower jaw (mandibulare); the hyoid arch into the hyomandibulare, the hyoides, and the unpaired copula.

25. In Mammals and Man the cartilaginous visceral skeleton attains only a very rudimentary condition, and is converted into the cartilaginous fundaments of the three auditory ossicles and the hyoid bone.

26. In the membranous jaw-arch arise—

(*a*) The incus, which corresponds to the palato-quadratum of lower Vertebrates;

(*b*) The malleus, which is the representative of the articular part of the cartilaginous mandibulare; and

(*c*) The cartilage of Meckel, which corresponds to the remaining portion of the mandibulare, but which afterwards completely degenerates.

27. The membranous hyoid arch furnishes, [beginning with] its uppermost part,—
   (*a*) The bow of the stapes,—whereas its plate is derived from the cranial capsule and is, as it were, cut out to form the fenestra ovalis,—
   (*b*) The processus styloideus,
   (*c*) The ligamentum stylohyoideum, and
   (*d*) The lesser horn and body of the hyoid bone.

28. The third membranous visceral arch is chondrified only in its lowest [ventral] part, to form the greater horn of the hyoid bone.

29. At no stage of its development does the primordial cranium exhibit evidence that, like the vertebral column, it is composed of separate segments.

30. The original segmentation of the head is expressed in only three ways—in the appearance of several primitive segments (myotomes), in the arrangement of the cranial nerves, and in the fundament of the visceral skeleton.

31. The primordial cranium is therefore an unsegmented skeletal fundament in a region of the body that is segmented in another manner.

32. The ossification of the head-skeleton is a much more complicated process than that of the vertebral column.

33. Whereas in the vertebral column there are developed bones of only *one* kind,—through substitution for cartilage,—there are to be distinguished in the ossification of the head-skeleton, according to their formation and source, two different kinds of bone—primary and secondary.

34. The primary bones of the head arise in the cartilaginous primordial cranium and visceral skeleton, like the separate bone-nuclei in the cartilaginous vertebral column.

35. The secondary bones, covering or membrane-bones, arise outside the primordial skeleton of the head in the connective-tissue foundation of the skin and mucous membrane; they are therefore dermal and mucous-membrane ossifications, and constitute in lower Vertebrates a portion of a dermal skeleton that covers the surface of the whole body.

36. The covering bones are developed in some instances, which can be regarded as reproductions of the original method, by fusion of the bony bases of numerous denticles which arise in the skin and mucous membrane.

37. Primary and secondary bones sometimes remain separate in later stages, sometimes they fuse with each other to form bone-complexes, like the temporale and sphenoidale.

38. After the conclusion of the process of ossification only unimportant remnants of the primordial cranium persist as the cartilaginous partition of the nose and as the nasal cartilages.

C. The Skeleton of the Extremities.

39. The skeleton of the limbs, excepting the clavicle, the development of which exhibits many peculiarities, is established in the cartilaginous stage. (Cartilaginous shoulder-girdle, cartilaginous pelvic girdle, cartilages of arm and leg.)

40. The ossification takes place, in the same manner as in the vertebral column and primordial cranium, from centres of ossification by disintegration of cartilaginous tissue and its replacement by osseous tissue.

41. The most of the small cartilages of the wrist and ankle ossify from a single bone-nucleus, but the larger flat cartilages of the shoulder and pelvic girdles from several centres.

42. The cartilaginous fundaments of the tubular [long] bones ossify at first in the middle, which region is designated as diaphysis, whereas their two ends—the epiphyses—remain for a long time cartilaginous, and are the means of the elongation of the skeletal element.

43. In Man the cartilaginous epiphyses begin to ossify from centres of their own (epiphysial nuclei), some of them in the last month before, others not until after birth.

44. The fusion of the bony diaphysis with the bony epiphyses does not take place until the termination of the growth of the skeleton and body in length, and is accompanied by the removal of the intervening cartilaginous tissue.

45. Before growth is at an end the tubular bones can be divided into a larger middle piece (diaphysis) and two small bony epiphyses.

46. Of the cartilaginous fundament of a tubular bone there is preserved only a small remnant as a cartilaginous covering of the articular ends (articular cartilage).

47. The medullary cavity of the tubular bones is formed by the resorption of the spongy bone-substance that first replaced the cartilage.

48. Whereas the articular ends of bones preformed in cartilage are covered over with hyaline cartilage, the articular surfaces of

bones of connective-tissue origin (covering bones) present an investment of fibrous connective substance (articulation of the jaw).

49. The form of the articular surfaces is determined at a time when an influence on the part of the musculature is not to be considered.

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