

STUDIES OF THE DEVELOPMENT OF THE HUMAN SKELETON.

- (A). THE DEVELOPMENT OF THE LUMBAR, SACRAL AND COCCYGEAL VERTEBRÆ.
- (B). THE CURVES AND THE PROPORTIONATE REGIONAL LENGTHS OF THE SPINAL COLUMN DURING THE FIRST THREE MONTHS OF EMBRYONIC DEVELOPMENT.
- (C). THE DEVELOPMENT OF THE SKELETON OF THE POSTERIOR LIMB.

BY

CHARLES R. BARDEEN.

Professor of Anatomy, The University of Wisconsin.

WITH 13 PLATES.

The following studies on skeletal development are based upon embryos belonging to the collection of Prof. Mall, at the Johns Hopkins University, Baltimore. I am greatly indebted to Prof. Mall for their use.

A.

THE DEVELOPMENT OF THE LUMBAR, SACRAL AND COCCYGEAL VERTEBRÆ.

Recently I have given an account of the development of the thoracic vertebræ in man (This Journal, Vol. IV, No. 2, pp. 163-175). In the present paper it is my purpose to describe the special features which characterize the differentiation of the more distal vertebræ.

During the early stages of vertebral development the skeletal apparatus of the various spinal segments is strikingly similar. This is shown in Fig. 1, Plate I, which illustrates the spinal column of Embryo II, *length 7 mm.* Yet even during the blastemal stage some regional differentiation becomes visible. The costal processes of the thoracic vertebræ, for instance, develop much more freely than those of other regions. It is, however, during the chondrogenous period that the chief regional features appear.

To what extent morphological similarity in the sclerotomes and scleromeres indicates equal formative potentiality experiment alone can determine.

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mine. While it is unlikely that experimental studies of the required nature can ever be made on mammalian embryos it is quite possible that they may on embryos of some of the lower vertebrates. From the evidence at hand it seems probable, however, that the primitive vertebræ are to a considerable extent potentially equivalent and that their subsequent development depends upon the demands of their regional environment. The strongest arguments in favor of this view come from a study of variation in the adult. It is well known that at the regional boundaries vertebral variation is frequent. Thus the 7th vertebra often carries a short "cervical" rib (Gruber, 69), and rarely it has two cervical ribs which run to the sternum (Bolk, 01). On the other hand the 8th vertebra, usually the first thoracic, may assume all the characteristics of a cervical vertebra (Leboucq, 98, Low, 01).

At the thoraco-lumbar margin variation is more frequent than at the cervico-thoracic. Thus out of 1059 instances described statistically in the literature I found, 1904, that the 19th vertebra, commonly the last thoracic, had no free ribs and was hence of the lumbar type in 30 instances, 2.8%, and that on the other hand the 20th vertebra, commonly the first lumbar, had free costal processes in 23 instances, 2.2%. Cases have also been reported where the 21st vertebra, usually the 2d lumbar, has carried free ribs (Rosenberg, 99). Variation takes place in the articular processes as well as in the costal elements of the vertebræ at the thoraco-lumbar border (Topinard, 77).

Variation of the lumbo-sacral boundary is likewise frequent. Thus out of the 1059 instances above mentioned in 28 instances, 2.7%, the 24th vertebra, commonly the 5th lumbar, was the first sacral and in 47 instances, 4.4%, the 25th vertebra was of the lumbar type. The 25th vertebra may exhibit one of many transitions from the sacral to the lumbar type. This subject has been well treated by Paterson, 93. Papillault, 00, has contributed an interesting paper on lumbar variations and Cunningham, 89, on the proportion of bone and cartilage in the lumbar region.

At the sacro-coccygeal border variation is even more frequent than in the regions more anterior. Paterson, 93, found diminution in the number of sacral vertebræ in 2.62%, and increase in their number in 35.46% of the 265 sacra he examined; and Bianchi, 95, in 17.5% of the female, 23.3% of the male, and 21.23% of the total number (146) of sacra examined. In this count he excluded sacra in which compensation for lumbo-sacral alterations was to be seen. Bianchi thinks that the 1st coccygeal vertebra belongs properly to the sacrum. In the 1059 instances mentioned above I find that the 30th vertebra, usually the 1st coccygeal,

was reported sacral in nature in 91 instances, 8.6%, and the 29th, commonly the last sacral, coccygeal in 27 instances, 2.5%. It is possible that variations of this nature were sometimes overlooked by those making up the tables from which the above data were obtained.

Variation other than border variation has been reported most frequently in the cervical region. Ribs have been found not only on the 7th and 6th vertebræ but also on those more anterior (Szawlowski, 01).

It seems fair, however, to assume that the primitive vertebræ become differentiated according to the demands of their environment. Thus the factors commonly exerted on the 8th to 19th costo-vertebral fundaments causing them to develop into thoracic vertebræ with free ribs, may be so exerted as to call into similar development the 7th to 18th, the 7th to 19th (20th), the 8th to the 18th, the 8th to the 20th (21st), or the 9th to the 19th (20th). While the thorax may be segmentally extended or reduced at either end, extended at both ends, or extended at one end and reduced at the other, a simultaneous reduction at both ends has not been reported (Rosenberg, 99).

Differentiation in the post-thoracic region depends apparently in the main upon the position of the posterior limb (Bardeen, 00, Ancel and Sencert, 02). When the developing ilium becomes attached to the costal processes of the 25th, 26th (and 27th) vertebræ the conditions of the lumbar, sacral and coccygeal regions are commonly normal. But the developing ilium may become attached further anterior than usual, either directly to the costal process of the 24th vertebra or so far forward that a close ligamentous union is established with it. In such instances the 12th rib is usually either very rudimentary or absent and often the 29th vertebra is of the coccygeal type. In rare instances the thorax may at the same time advance a segment into the cervical region. On the other hand the developing ilium may take a position more posterior than usual, leaving the 25th vertebra either free to develop into the lumbar type or but incompletely united to the sacrum (Paterson, 93). When this occurs the 20th vertebra is very apt to have ribs developed in connection with it and the 30th vertebra usually becomes an integral part of the sacrum.

The coccygeal vertebræ, with the exception of the first, which is more directly than the others subjected to the differentiating influences of the developing limb, are relatively more rudimentary in the adult than in the embryo.

Rosenberg, 76, advanced the opinion that the ilium is attached more distally in the embryo than in the adult. I have recently, 1904, shown that this is not the case. On the contrary, as might have been inferred

from the distribution of the nerves to the posterior limb, the ilium is differentiated in a region anterior to the site of its permanent attachment and the differential activities which it stimulates in the sacral vertebræ are exerted first on the more anterior of these vertebræ.

The two limbs do not always call forth a similar response on each side of the body. Thus Paterson, 93, found asymmetry of the sacrum in 8.3% of the instances he studied.

Assuming the specific differentiation in the lumbar, sacral and coccygeal regions of the spinal column represents a response to stimuli arising in part from the developing limb, we may turn to a consideration of the differentiation thus brought about in each of these regions. Attention will here be directed chiefly to the more salient differences between development in the distal half of the vertebral column and that recently described for the thoracic region.

LUMBAR VERTEBRÆ.

Rosenberg, 76, seems to have been the first to take up a detailed study of the early development of the lumbar vertebræ in man. He described the costal rudiment of these vertebræ and found in several embryos that this rudiment of the 20th vertebra had given rise to a cartilaginous 13th rib. A careful study of a large number of human embryos has led me, however, to the conclusion (1904) that a 13th rib is no more frequent in the embryo than in the adult and that in the series studied by Rosenberg it must have been unusually frequent. Holl, 82, found no 13th rib in the embryos which he examined. He also came to the conclusion that the transverse processes of the lumbar vertebræ do not represent ribs. Most investigators rightly disagree with him on this point.

The development of the external form of the lumbar vertebræ in a series of embryos belonging to the Mall collection is shown in Figs. 1-13, Plates I-V.

The bodies of the lumbar vertebræ during the earlier periods of differentiation are essentially like those of the thoracic vertebræ. In embryos over 12 mm. long, however, the former become progressively thinner, broader and longer than the latter. The intervertebral disks and the enveloping ligamentous tissue are similar in both regions. In the thoracic region the canal of the chorda dorsalis lies nearer the ventral surface of the vertebral column than it does in the lumbo-sacral region. The marked alterations in the curvature of the spinal column which occur during embryonic development seem especially associated with changes in the intervertebral disks.

The *neuro-costal processes* of the lumbar vertebræ are also at first similar in form to those of the thoracic vertebræ. This is the case in Embryo II, *length 7 mm.*, Fig. 1, Plate I; CLXIII, *length 9 mm.*, Fig. 2, Plate II; and CIX, *length 11 mm.*, Figs. 3 and 4, Plate II.

Marked differences in the costal processes are to be seen when chondrofication begins. Thus while the costal process of the 12th thoracic vertebra has early a separate center of chondrofication (Embryo CLXXV, *length 13 mm.*, Fig. 14, Plate VI and Embryo CXLIV, *length 14 mm.*, Fig. 5, Plate III), the processes of the lumbar vertebræ remain for a considerable period dense masses of mesenchyme (Embryo CLXXV, *length 13 mm.*, Figs. 15 and 16, Plate VI, and Embryo CCXVI, *length 17 mm.*, Figs. 18 and 19, Plate VI). Finally, however, they undergo chondrofication at the base (Embryo XXII, *length 20 mm.*, Figs. 21 and 22). I have been unable to determine whether this chondrofication always takes place from a separate center, as it certainly often does, or sometimes represents merely an extension into the costal mesenchyme of cartilage from the transverse process. I incline to the former view.

Sometimes the costal element of the 1st lumbar vertebra may remain for a considerable period separate from the cartilage of the transverse process. This is true of the right side (left in the figure) of Embryo XLV, *length 28 mm.*, Fig. 24. But usually at an early period the costal and transverse processes become intimately fused (Embryo XXII, *length 20 mm.*, Fig. 21; XLV, *length 28 mm.*, Fig. 24, right side of figure; and Fig. 25; Embryo LXXXIV, *length 50 mm.*, Figs. 27 and 28). The "transverse" process of the adult lumbar vertebra represents in the main an ossification of a membranous, not cartilagenous, extension of the fused costal element (C. Pr., Fig. 28).

At first the *neural processes* of the lumbar vertebræ are essentially like those of the thoracic (Embryo CXLIV, *length 14 mm.*, Fig. 5, Plate III). Union of the pedicles with the cartilage of the body takes place and the laminæ extend out dorsally in a similar manner in each. It is in the transverse and articular processes that the chief characteristic differentiation takes place.

The lumbar transverse processes are broader and much shorter than the thoracic. At an early period, as mentioned above, they become intimately united to the costal processes. In the dense mesenchyme between the region of the transverse process and the costal element there is commonly developed no loose vascular area such as serves to separate the neck of the developing rib from the transverse process in the thoracic region. The occasional appearance of a foramen in a transverse process of a lumbar vertebra has led to the supposition that they may occur

regularly in the embryo (Szawlowski, 02, Dwight, 02). The differences between the transverse processes of the 12th thoracic and the first two lumbar vertebræ in several embryos are shown in Plates VI and VII, Figs. 14 to 28.

The articular processes in the lumbar, as in the thoracic, region are at first flat plates connected by membranous tissue, Fig. 5, Plate III. But in the lumbar region the superior articular process develops faster than the inferior so that each superior process comes partly to enfold the inferior process of the vertebra next anterior. These conditions may be readily followed in Figs. 9, 12 and 13, Plates IV and V, and in Figs. 20-28, Plates VI and VII. The mammillary and accessory processes of the adult lumbar vertebræ probably represent an ossification of muscle tendons attached to the transverse and articular processes.

During the development of the vertebræ in embryos from 30 to 50 mm. in length alterations preliminary to ossification, similar to those in the thoracic, occur in the lumbar vertebræ. No actual ossification occurs in any of the centers in the latter in embryos less than 5 cm. long in Prof. Mall's collection. It begins in the bodies of the more anterior of the lumbar vertebræ in embryos between 5 and 7 cm. long, and in those 8 cm. long it has usually extended to the more distal. Meanwhile, ossification of the neural processes has extended from the thoracic into the lumbar region and soon may be seen throughout the latter. See Bade, 00.

SACRAL VERTEBRÆ.

Although much has been written about the ossification of the sacral vertebræ comparatively little attention has been devoted to their early differentiation. Rosenberg, 76, contributed several important facts, although the general conclusions which he drew concerning the transformation of lumbar into sacral, and sacral into coccygeal vertebræ are unwarranted. Holl, 82, studied more especially the relation of the ilium to the sacrum in adults and embryos and added materially to the knowledge of the sacro-iliac articulation. Petersen, 93, has given an incomplete description of the sacrum in several early human embryos, and Hagen, 00, of one 17 mm. long.

Figs. 1 to 13, Plates I to V, show the general external form of the sacral vertebræ in embryos of the Mall collection. In Embryo II, *length 7 mm.*, Fig. 1; CLXIII, *length 9 mm.*, Fig. 2; and CIX, *length 11 mm.*, Figs. 3 and 4, the sacral appear to resemble the lumbar in all essential particulars, although there is a progressive decrease in size from the mid-lumbar region distally. No line of demarcation can be drawn in these embryos between the sacral and lumbar vertebræ on the one side and the sacral and coccygeal on the other.

Soon after the stage shown in Figs. 3 and 4 the iliac blastema approaches more closely the vertebral column, usually in the region opposite the costal processes of the 25th and 26th vertebræ. These, then, are stimulated to more active growth and extend in their turn out toward the ilium. The costal processes of the 27th, 28th and 29th vertebræ are likewise stimulated into more active growth. Lateral to the ventral branches of the spinal nerves the tissue derived from the costal elements of these five vertebræ becomes fused into a continuous mass of condensed tissue (Fig. 37, Plate IX; and Figs. 5 and 6, Plate III). Against the anterior and better developed portion of this the iliac blastema comes to rest (Figs. 5 and 37). From the time of the fusion of the costal elements of the sacral vertebræ into a continuous lateral mass of tissue these vertebræ may be distinguished from the lumbar and coccygeal. Variation in the vertebræ entering into the sacrum occurs in the embryo as in the adult (Bardeen, 04).

At the period when the iliac blastema comes into contact with the costal mass of the sacrum centers of chondrofication have appeared in the bodies of the sacral vertebræ. The bodies, compared with the intervertebral disks, are progressively smaller from the first to the fifth (Embryo CXLIV, *length 14 mm.*, Fig. 6). Otherwise they present no characteristics of special note. In older embryos this difference becomes less and less marked.

The neuro-costal processes present features of more specific interest. In Embryo CXLIV, *length 14 mm.*, centers of chondrofication may be observed in the neural processes of the first two sacral vertebræ. They are not yet united to the bodies of the vertebræ and are simple in form. No cartilage has as yet appeared in the neural processes of the other vertebræ. In somewhat older embryos, CCXVI, *length 17 mm.*, Fig. 38, and CLXXXVIII, *length 17 mm.*, Fig. 39, the neural processes of all the sacral vertebræ have become chondrofied and distinct. Separate centers of chondrofication may be seen in each of the costal elements. At a slightly later stage, Embryo XXII, *length 20 mm.*, Fig. 10, Plate IV, the extremities of the costal elements of the first three sacral vertebræ have fused with one another and have thus given rise to a cartilaginous auricular surface, and each has fused with the neural arch of the vertebra to which it belongs. The costal elements of the 4th and 5th sacral vertebræ are likewise fused to their corresponding neural arches and all of the sacral neural arches are fused to their respective vertebræ.

Cross-sections illustrate well the relations of the neural and costal processes to the vertebræ. Embryo CIX, *length 11 mm.*, Fig. 29, Plate VIII, shows an early blastemal stage in which the sacral vertebræ resem-

ble the thoracic. Figs. 30, 31 and 32 represent cross-sections through the 1st, 2d and 3d sacral vertebræ of Embryo X, *length 20 mm.* The neural and costal processes in this embryo show cartilagenous centers, but these are fused neither with one another nor with the vertebral body. Embryo CCXXVI, *length 25 mm.*, Figs. 33 and 34, shows fusion of neural and costal processes with the body. The costal processes have by this period given rise to a continuous lateral cartilagenous mass, a portion of which is represented in Fig. 40. This shows an oblique section through the 3d and 4th sacral vertebræ of Embryo LXXXVI, *length 30 mm.* This cartilagenous lateral mass may likewise be seen in the sacra of Embryo CXLV, *length 33 mm.*, Figs. 11 and 12, and LXXXIV, *length 50 mm.*, Fig. 13.

From the primitive neural cartilages there develop pediclar, transverse, articular and laminar processes. The pediclar and transverse processes become intimately fused with the costal element as described above. In none of the embryos examined was there seen a separation of costal from transverse process marked by blood-vessels, such as one might perhaps expect to find because of the occasional appearance in the adult of transverse foramina in the lateral processes of the sacral vertebræ (Szawlowski, 02).

The articular processes in the older embryos retain a more primitive condition than do those of the lumbar and thoracic regions. Figs. 33, 34, 35 and 36 show cross-sections through the articulations of the neural processes.

The laminar processes of each side are still separated by a considerable interval in embryos of 50 mm., although at this period the lumbar region is nearly enclosed. Compare Figs. 28 and 36.

Changes in the cartilages preliminary to ossification occur both in the bodies and in the neural processes of the sacral vertebræ at a period quickly following their appearance in the lumbar region. Thus in Embryo LXXIX, *length 33 mm.*, changes of this nature may be followed as far as the 5th sacral vertebra. It is well known, however, that actual ossification in the more distal sacral vertebræ takes place considerably later than in the thoracico-lumbar region. The primary centers of ossification correspond with the centers of chondrofication except that there is a single center in place of two centers for each body, and one center instead of two for each neuro-costal processes of the two more distal sacral vertebræ. Posth, 97, has recently contributed a valuable paper on the subject of sacral ossification.

COCCYGEAL VERTEBRÆ.

Since the valuable contributions of Fol, 85, who described 38 vertebræ in the early human embryo, considerable attention has been devoted to the development of the coccygeal vertebræ, especially from the point of view of the number of vertebræ in embryos. The literature on the subject has been summed up by Harrison, 01, and more recently by Unger and Brugsch, 03. The later stages in the development of the coccyx have been described by Steinbach, 89, who studied a large number of spinal columns of fœtuses, infants and adults. In a recent paper, 1904, I have given a summary of the number of coccygeal vertebræ found in various embryos and of the number of hæmal processes found in the embryos belonging to the collection of Prof. Mall.

Without attempting here to enter into a detailed account of the conditions found in these various embryos we shall pass at once to a consideration of the more characteristic features of coccygeal development. The differentiation of the coccygeal sclerotomes begins at about the end of the fourth week, Embryo II, *length 7 mm.*, Fig. 1, Plate I. As a rule at least six or seven membranous vertebræ are developed. The highest relative differentiation of the coccygeal vertebræ occurs in the fifth and sixth weeks. At this time dorsal processes connected by interdorsal membranes extend as far as the 4th and 5th vertebra, Figs. 3 and 4, Plate III, Fig. 41, Plate X. No distinct costal processes are, as a rule, developed on any except the first coccygeal vertebra, but at the height of development most of these vertebræ have distinct hæmal processes, first described by Harrison, 01. These processes may also be seen on the more distal sacral vertebræ, Fig. 41, Plate X. They usually disappear before the embryo has reached a length of 20 mm., but the coccyx described by Szawlowski, 02, suggests that occasionally they are retained until adult life.

Usually the bodies of the first five coccygeal vertebræ become chondro-fied. The chondrofication of the more distal of these vertebræ is, as pointed out by Rosenberg, 76, often very irregular. There may be separate bilateral areas of cartilage or the two areas may be connected merely anterior to the chorda dorsalis. The bodies of successive vertebræ may be irregularly fused.

As a rule the neural processes of the first coccygeal vertebra alone become chondro-fied and fused to the vertebral body. The others, as well as the connecting interdorsal membranes, disappear.

The cartilagenous coccygeal vertebræ are thus relatively less developed than the membranous. It is probable that the osseous are less developed than the cartilagenous. Thus although Steinbach, 89, has made a strong

plea for the presence of 5 vertebræ in the adult coccyx, the more commonly accepted number of four seems to be a truer estimate of the definite number of bones usually found present.

The bend of the coccyx which takes place during the third month is an interesting phenomenon. It seems to be associated with the development of pelvic structures.

SUMMARY.

In the earlier stages of development the lumbar, sacral and coccygeal vertebræ resemble the thoracic. The blastemal vertebræ arise each from the contiguous halves of two original segments of the axial mesenchyme. Each vertebra exhibits a body from which neural and costal processes arise. The neural processes are connected by "interdorsal" membranes.

As the blastemal vertebræ become converted into cartilage specific differentiation becomes more and more manifest. The cartilagenous vertebral bodies and the intervertebral disks are all formed in a similar manner and except for size manifest comparatively slight differences in form. The more distal coccygeal vertebræ are, however, irregular. But the chief specific differentiation is seen in the costal and neural processes.

In the blastemal neural processes of the thoracic vertebræ cartilagenous plates arise from which spring pedicular, transverse, articular and laminar processes.

In the lumbar vertebræ similar processes arise from the neural cartilages. The pedicular processes resemble the thoracic but are thicker; the transverse processes are shorter, much thicker at the base and remain bound up with the costal processes; the superior articular processes develop in such a way as to enfold the inferior; the laminar processes are broad, grow more directly backward than do the thoracic, and on meeting their fellows in the mid-dorsal line fuse and give rise to the typical lumbar spines. The mammillary and accessory processes are developed in connection with the dorsal musculature.

In the sacral vertebræ the neural cartilages give rise to very thick pedicular processes; to articular processes the most anterior of which develop like the lumbar, while the others long maintain embryonic characteristics; to transverse processes which in development are bound up with the costal processes; and to laminar processes which are very slow to develop and of which the last fail to extend far beyond the articular processes.

In the coccygeal vertebræ the neural processes of the first, and rarely

the second, alone give rise to cartilagenous plates. From these only pedicular and incomplete articular and transverse processes arise. The cornua of the adult coccyx represent fairly well the form of the early neural semi-arches. The transverse processes develop in close connection with the costal processes.

In the thoracic vertebræ cartilagenous ribs develop from separate centers in the blastemal costal processes.

In the lumbar vertebræ separate cartilagenous centers probably always arise in these processes, but they are developed later than those of the thoracic vertebræ and quickly become fused with the cartilage of the transverse processes. The transverse processes of the adult lumbar vertebræ represent at the base a fusion of embryonic cartilagenous costal and transverse processes, but in the blade an ossification of membranous costal processes.

In the sacral vertebræ separate cartilagenous costal centers are developed but they soon become fused at the base with the transverse processes of the neural plates. Laterally by fusion of their extremities the costal processes give rise to an auricular plate for articulation with the ilium.

In the coccygeal vertebræ the costal processes of the first become fused with the transverse processes and develop into the transverse processes of the adult coccyx. I have been unable definitely to determine whether a separate costal cartilage is developed in these processes or cartilage extends into them from the neural processes. The costal processes of the other coccygeal vertebræ have merely a very transitory blastemal existence.

For a brief period the more distal sacral and the coccygeal vertebræ have membranous hæmal processes.

Centers of ossification correspond in general with centers of chondro-fication, but, as in the case of the vertebral bodies and the more distal sacral neuro-costal processes, a single center of ossification may represent two centers of chondro-fication.

B.

THE CURVES AND THE PROPORTIONATE REGIONAL LENGTHS OF THE SPINAL COLUMN DURING THE FIRST THREE MONTHS OF EMBRYONIC DEVELOPMENT.

In 1879 Aeby contributed an important paper dealing with the length of the various regions of the spinal column at different ages, the height of the constituent vertebræ and the thickness of the intervertebral disks

in man. He showed that in young embryos the cervical region is relatively longer than the lumbar region but that as growth proceeds there is a constant proportional increase in length of the latter over the former. Taking the cervical region as 100, for instance, he found that in embryos below 10 mm. in length the lumbar region equals 69, while in the adult it is equivalent to 150. Thus, too, while from infancy to maturity the spinal column increases three and one-half times in length and the thoracic region at about the same relative ratio, the lumbar region increases four times in length and the cervical but three. Other investigators, including Ballantyne, 92, and Moser, 89, have in general confirmed these results. Of those who have studied the proportional length of the various regions in the adult Ravenel, 77, and Tenchini, 94, have made noteworthy contributions.

The post-natal lengthening of the lumbar region is associated with those changes in the lumbo-sacral curve which accompany the assumption of an erect posture during early childhood. Do similar alterations in relative regional length accompany the straightening of the spinal column which takes place during the first three months of embryonic development?

In Fig. 44, Plate X, I have represented by curved lines the vertebral columns of several embryos of this period and an adult column. The cervical, lumbar and coccygeal regions are represented by heavy, the thoracic and sacral regions by light lines. The 5th, 6th and 7th thoracic vertebrae are made to coincide in each instance.

The *anterior half* of the spinal column is considerably curved in Embryo II, *length 7 mm.* It gradually becomes straightened in successively older embryos until in Embryo CLXXXIV, *length 50 mm.*, it is nearly straight. The subsequent anterior convexity in the adult is associated with the assumption of an upright position of the head.

It is, however, in the *posterior half* of the spinal column that the chief alterations in spinal curvature are to be noted. In Embryo II, *length 7 mm.*, the ventral surface of the sacral region faces the mid-thoracic region; in Embryo CIX, *length 11 mm.*, the anterior end of the vertebral column; in Embryo CLXXXIV, *length 50 mm.*, almost directly ventrally; and in the adult, in a posterior direction.

The relative lengths of the various regions of the spinal column during the first three months of development may be gathered from the following table, which is based in part upon data obtained from embryos belonging to the Mall collection and in part upon those of the Born and His collections studied by Aeby.

TABLE A.

THE LENGTHS OF THE VARIOUS REGIONS OF THE SPINAL COLUMNS OF EMBRYOS OF THE SECOND AND THIRD MONTHS, AND THE PROPORTIONAL LENGTH OF THE THORACIC COMPARED WITH THE OTHER REGIONS.

Embryos.			Regions of the spinal column.								
Designation.	Collection.	Length in mm.	Cervical.		Tho- racic.	Lumbar.		Sacral.		Coccygeal	
			Length in mm.	% of Thoracic region.	Length in mm.	Length in mm.	% of Thoracic region.	Length in mm.	% of Thoracic region.	Length in mm.	% of Thoracic region.
II.	Mall.	7	2	60.6	3.3	1.2	36.4	.9	27.3
CCXXI.	"	13 (1)	2	62.5	3.2	1.3	46.1	1.25	39.1	1.0	31.2
1 (Aeby).	His.	10	2.95	76.6	3.85	1.75	45.5	1.95	50.6 (2)
CIX.	Mall.	11	2.7	67.5	4	2	50.0	1.7	42.5	1.3	32.5
CXLIV.	"	14	2.3	62.2	3.7	1.7	46.0	1.34	36.2	1.1	29.8
XLIII.	"	16	2.9	61.9	4.34	1.9	43.7	1.55	35.7	1.41	32.5
2 (Aeby).	His.	10	3	65.2	4.6	2.25	48.9	1.88	40.9 (2)
3 (Aeby).	"	16	3	64.5	4.65	2.25	48.2	2.65	57.0 (2)
XXII.	Mall.	20	5.5	3	54.5	2.0	36.4	1	25
4 (Aeby).	His.	21.5	3.9	61.9	6.3	3.1	49.2	3.4	53.9 (2)
CVIII.	Mall.	22	4.34	61.9	7.0	3.5	50.0	2.8	40	1.2	16.1
CXLV.	"	33	5.1	59.5	8.55	4	46.8	3.5	35.6	1.75	20
CCXXVII.	"	30	5.4	60.0	9.0	4	44.4	3	33.3	1.38	15.3
5 (Aeby).	Born.	..	6.0	54.5	11	5.2	47.3
XCV.	Mall.	46	8.25	59.0	14	7.25	51.8	5.5	39.3	3.75	26.8
CLXXXIV.	"	50	8	61.1	13	6.35	48.8	4.65	35.8	2.65	20.4
6 (Aeby).	Born.	..	10	58.8	17	8.5	50.0	9.5	55.8 (2)

1. This is the measurement recorded before the embryo was sectioned. The embryo was cut sagittally. The length of the sections in the median line is 7.5 mm. The general development corresponds with that of an embryo of this length.

2. These figures represent the length of the pelvic portion of the spinal column.

This table discloses considerable individual variation. The length of the cervical region is about 60% of that of the thoracic. In Embryos CIX, 1 and 2, this ratio is much exceeded. The measurements for CIX are calculated from obliquely transverse sections and hence are subject to some error. The data concerning the measurements for 1 and 2 are not given by Aeby.

The lumbar region, at first less than 40% in length of the thoracic, in most embryos approximates 50%. The length of the sacral region varies from 33 to 42.5% of the thoracic. The coccygeal region, with a nearly constantly diminishing comparative length, shows marked variations.

There is no good evidence that the straightening of the spinal column is accompanied by a marked increase in relative length of the lumbar region after the early stages in Embryos II and CIX.

A comparison of the spinal columns of embryos of the second and third months with those of older embryos and of children shows that it is during the latter half of foetal life and early childhood that the chief relative lengthening of the lumbar region takes place.

According to Aeby the average length of the cervical, thoracic and lumbar regions in the new-born is respectively 45.1, 83.9 and 47.5 mm. This makes the length of the cervical region 53.5% and that of the lumbar region 56% of that of the thoracic. Corresponding figures from Ballantyne, 92, for full-term foetuses are: cervical, 33.6 mm. (42.8%); thoracic, 78.4 mm. (100%); lumbar, 42.8 mm. (54.3%); and sacro-coccygeal, 39.8 mm. (50.8%). Thus Ballantyne finds a greater proportional reduction of the cervical region.

The conditions in the adult, as given by various investigators, are as follows:

TABLE B.

PROPORTIONAL LENGTHS OF THE VARIOUS REGIONS OF ADULT SPINAL COLUMNS.

Investigator and date.	Sex and Size.	Average length of regions in mm.				Ratio of other regions to the thoracic as 100.		
		Cervical.	Thoracic.	Lumbar.	Sacro-coccygeal.	Cervical.	Lumbar.	Sacro-coccygeal.
Ravenel, 1877.	Male.	133	280	182	..	47.5	65.0	..
	Female.	120	260	178	..	46.1	68.5	..
Aeby, 1879.	Male.	129.9	273.4	184.1	..	47.5	67.3	..
	Female.	122.9	265.8	190.3	..	46.2	71.6	..
Tenchini.	Male.	98	222	125	151	44.1	56.3	68
	Medium.	100	240	137	158	41.7	57.1	65.8
	Tall.	104	240	134	168	43.3	55.8	61
Dwight, 1894.	Male.	133	287	19.9	..	46.3	69.3	..
	Female.	121	265	18.7	..	45.7	70.6	..

The chief point of interest in this table is the difference between the results found by the German and American investigators and those of the Italian. Apparently the Italians have proportionately shorter cervical and lumbar regions than the Americans and Germans, but it is possible that different ways of measuring were used. It is a subject worthy of further investigation.

Both Tenchini and Ancel and Sencert, 02, have treated of variations in measured length of individual vertebræ associated with numerical vertebral variation.

C.

THE DEVELOPMENT OF THE SKELETON OF THE POSTERIOR LIMB.

One of the most studied subjects in morphology has been the development of the vertebrate limbs. Fortunately critical summaries of its immense literature have recently been given by several keen investigators, among whom may be mentioned Wiedersheim, 92, Mollier, 93, 95, 97, Gegenbaur, 98, 01, Klaatsch, 00, Rabl, 01, Fürbringer, 02, Ruge, 02, and Braus, 04. Therefore no attempt will here be made to review previous work except in so far as it deals directly with the development of the human limb.

During the third week of embryonic life the limb-buds become filled with a vascular mesenchyme (Bardeen and Lewis, 01, p. 17, Figs. 18 and 19). The source of this tissue is uncertain. In part it may come from the primitive body-segments, but it seems probable that in the main it comes from the parietal layer of the unsegmented mesoderm.

During the fourth week the mesenchyme increases in amount and the limb-bud begins to protrude further from the body-wall. Observed structural differentiation does not, however, begin until the early part of the fifth week, at the time when the lumbo-sacral spinal nerves are beginning to form a plexus. At this period the tissue at the center of the base of the limb becomes greatly condensed, Embryo CLXIII, *length 9 mm.*, Fig. 45, Plate XI. The boundaries of the mass are not perfectly definite, but a wax-plate reconstruction based upon drawings made as definite as possible gives rise to the structure shown in Fig. 2, Plate II. The relations of this tissue mass to other structures are shown in Plate II, Fig. B, and Plate III, Fig. C, of the article by Bardeen and Lewis, 01. The condensation represents the acetabulum and the proximal end of the femur. This is indicated by its relations to the nerve plexus.

Once begun skeletal differentiation proceeds rapidly. In Embryo CIX, *length 11 mm.*, Figs. 3 and 4, it may be seen that from the original center of skeletal formation the condensation of tissue has extended both distally and proximally, but much more rapidly in the former than in the latter direction. Distally the sclero-blastema shows femur, tibia, fibula, and a foot-plate; proximally, an iliac, a pubic and an ischial process. A series of sections through the skeletal mass (Figs. 46 to 52) shows that in the femur, tibia and fibula chondrofication has begun. At the centers of the blastema of the ilium, ischium and pubis a still earlier stage of chondrofication has made its appearance. The leg of this embryo, therefore, represents a stage of transition from the blastemal to the chondrogenous stage of development. Fig. 55, Plate XII, shows a longitudinal

section through the leg of Embryo CLXXV, *length 13 mm.* The development is slightly more advanced than in Embryo CIX.

The further general development of the skeleton of the limb may be followed in Figs. 8 to 13. For the sake of convenience the development of the several parts of the skeleton will be taken up in turn as follows: (a) pelvis; (b) femur, hip-joint, tibia and fibula, and knee-joint; (c) ankle and foot.

A. PELVIS.

Petersen, 93, has given a good account of the early development of the human pelvis. His work was based upon embryos belonging to the His collection. In embryos Ru, *length 9.1 mm.*, Ko, *length 10.2 mm.*, and N, *length 9.1 mm.*, the formation of the lumbo-sacral plexus has begun and there is a condensation at the center of the limb-bud. The conditions here resemble those in Embryo CLXIII, *length 9 mm.*, Fig. 2, described above. Petersen believed that the condensation of tissue in embryos Ru and Ko represents the germinal area for the muscles and skeleton of the lower extremity while that of N shows a further differentiation of the diaphysis of the femur. The last ends anteriorly in a small undifferentiated cell-mass but there is nothing further to indicate the future pelvis. Yet, as I have mentioned above, the relations of this cell-mass to the nerves arising from the plexus indicates that it is the fundament of the future pelvis. The nerves pass about it as they do later about the acetabulum. In Embryo S₁, *length 12.6 mm.*, Petersen found what he considers the first traces of a definite pelvic fundament. This embryo is evidently of about the same stage of development as CIX, *length 11 mm.*, Figs. 3 and 4 and 46 to 53. But CIX is slightly more advanced and shows early stages of chondrofication not seen in S₁. The pelvis of S₁ has a slightly more anterior position and the iliac blastema extends rather toward the 24th than the 25th vertebra (Fig. 1, Plate I, of Petersen's article).

The pelvic scleroblastema of embryos of the stage found in CIX undergoes a rapid development. Its iliac portion extends in a dorsal direction toward the vertebræ which are to give it support. The costal processes of the latter at the same time become fused into an auricular plate. With this the iliac scleroblastema comes into close approximation, Figs. 5 and 6, Plate III, although for some time separated by a narrow band of tissue staining less densely than the blastema, Fig. 37.

Anteriorly the iliac blastema extends toward the abdominal musculature, to which it finally serves to give attachment.

While the blastemal ilium is thus becoming differentiated the pubic

and ischial processes of the pelvic blastema extend rapidly forward and ventral to the obturator nerve they become joined by a condensation of the tissue lying between them. Thus the obturator foramen of the blastemal pelvis is completed, Figs. 5 and 6. Between the crest of the ilium and the ventral extremity of the pubis dense tissue is formed to give attachment to the oblique abdominal musculature. This represents the embryonic Poupart's ligament and completes a femoral canal, Figs. 5 and 6.

While the blastemal pelvis is being differentiated the formation of cartilage in the ilium, ischium and pubis extends rapidly from the centers indicated in Embryo CIX. In CXLIV, *length 14 mm.*, Figs. 5, 6 and 54, the three cartilages are distinct.

The iliac cartilage is a somewhat flattened rod with anterior and posterior surfaces, Fig. 38. The anterior surface of the iliac cartilage at first faces slightly laterally as well as anteriorly. Lubsen, 03, in an interesting paper has shown the importance of this from the standpoint of mammalian phylogeny. He considers a flat plate with median and lateral surfaces to be the probable primitive form of ilium from which the triangular form, on which Flower, 70, laid stress, is derived by a lateral projection serving to divide the lateral surface into an anterior iliac and a posterior gluteal portion. In man and some other mammals the anterior iliac surface, according to Lubsen, comes to be turned medially by a great extension of the lateral projection and a secondary union of the abdominal musculature to this. In man, however, the primitive iliac cartilage is a rounded plate of which the long axis of the cross-section lies nearly at right angles to the median plane of the embryo. On the whole it suggests the prism described by Flower.

The pubic and ischial cartilages when first formed are mere rounded masses of tissue lying in the center of their respective blastemal processes. The acetabulum at this time is composed mainly of blastemal tissue but the iliac and ischial cartilages form a part of its floor, Embryo CXLIV, *length 14 mm.*, Figs. 5 and 6, Plate III. The pelvis of CR, *length 13.6 mm.*, described by Petersen and pictured in Fig. 2, Plate I, of his article, is of a stage of development similar to that of CXLIV. The cartilages are slightly more advanced in development. The iliac cartilage is broader in an antero-posterior direction and extends to the sacrum. He observed no dense tissue completing the obturator foramen but this tissue is quite plain in the corresponding embryos of the Mall collection, and it is described by Petersen for embryos Wi, *length 15.5 mm.*, and Ob, *length 15 mm.*, which are slightly more advanced than CR.

While the human embryo is growing from 15 to 20 mm. in length, there occurs a rapid development of the pelvic cartilages. About the head of the femur each gives rise to a plate-like process. The fusion of these processes produces a shallow acetabulum, Figs. 9 and 10, Plate IV. Those from the ilium and ischium are larger than that of the pubis and fuse with one another before the pubic cartilage fuses with them. The proportional areas of the acetabulum to which each pelvic cartilage contributes seem to be essentially the same as those later furnished by the corresponding pelvic bones, $\frac{2}{5}$ + ischium, $\frac{2}{5}$ — ilium, $\frac{1}{5}$ pubis. While growing about the hip-joint so as to complete the acetabulum each of the pelvic cartilages has a centrifugal growth within the blastemal pelvis. It is convenient to consider each cartilage in turn.

The iliac cartilage of the stage represented in Embryo CXLIV, Figs. 5 and 6, represents essentially that portion of the ilium which borders the entrance to the true pelvis and which has hence been called the pelvic portion of the ilium. From this cartilage extends dorsally into the sacral area of the blastemal pelvis, Figs. 9 and 10, and there gives rise to the sacral portion of the cartilagenous ilium. At the same time cartilage extends into the blastema which passes anteriorly to give attachment to the abdominal musculature and from this arises the abdominal portion of the cartilagenous ilium. A slight extension of cartilage into the anlage of Ponpart's ligament forms the anterior superior spine, but the blastemal covering of the femoral canal is not converted into cartilage as is the similar covering of the obturator.

While the cartilagenous ilium is being developed the ischial and pubic cartilages extend ventrally into their corresponding blastema. The ischial cartilage rapidly increases in thickness and at the same time gives rise to two processes. One of these, the ischial spine, extends toward the sacrum. This seems to indicate a commencing enclosure by cartilage of the ilio-sciatic notch. The other projects toward the developing hamstring muscles and gives rise to the ischial tuberosity.

The pubis broadens as it extends forwards and beyond the obturator foramen sends down a process which fuses with a longer one extending up from the ischium.

The various stages in the formation of a cartilagenous innominate bone have been followed in detail by Petersen in a series of six embryos from 17.5 to 22 mm. in length. In general what he describes coincides well with the appearances presented in a somewhat more extensive corresponding set of embryos belonging to the Mall collection. The distal position of the ilium, represented in Fig. 12, Plate VII, of Petersen's article, is to be looked upon as an individual variation and not as a

regular step in the process of attachment of ilium to spinal column. This I have previously pointed out (1904). Hagen, oo, has given an account of the pelvis of an embryo of 17.5 mm., which corresponds with the description given above.

During the further development of the cartilagenous pelvis the ventral extremities of its two halves, at first widely separated, in embryos of 20 mm. in close proximity, are finally united by a symphysis when the embryo reaches a length of 25 mm. In an embryo of this length, CCXXVI, the blastemal tissue of each half is fused in the median line but the cartilages are separated by $\frac{1}{2}$ mm., although the width of the pelvis at the rim is only 3 mm. In this embryo the obturator foramen is completely enclosed by cartilage. In embryos of 30 mm. the pubic cartilages are closely approximated in front.

Petersen reconstructed the pelvis of an embryo of 29 mm., Lo₁, and has given an extensive description of it. In essential features it corresponds with the pelvis of Embryo CXLV, *length 33 mm.*, Figs. 11 and 12. The sacrum of this latter embryo is, however, composed of the 25th to 29th vertebræ, while Petersen found the 30th vertebra of Lo₁ belonging to the sacrum. This variation is common in the adult.

Of the characteristic features common to Lo₁ and CXLV may be mentioned the relatively great development of the sacral portion of the ilium, with a large posterior-superior spine, the relatively slight development of the abdominal portion, and the comparatively large part of the pelvic entrance which is bounded by the sacrum. In the adult, according to Engel, the sacrum bounds 26.2% of this. For the new-born female the following figures are given by Fehling: sacrum, 28.9%; ilea, 29.2%; pubes, 42.8%; for the new-born male, 30.4%, 26.9% and 42.2%. For Lo₁, the percentages are: 37.0%, 31.7% and 31.3%; for CXLV, 34%, 33% and 33%.

In Lo₁ the rim of the acetabulum is deepened by dense blastemal tissue. In CXLV this has been in part converted into cartilage by extension of processes from the ilium, ischium and pubis. The processes of the ischium and pubis are fused with that of the ilium but not with one another, so that the cotyloid foramen is well marked.

In both embryos the iliac blades bend more sharply than in the new-born and resemble in this respect the adult. The ischial spines are relatively more developed and project more into the pelvis than do those of the adult.

The pelvis of Lo₁ is that of a female; the pelvis of CXLV that of a male. It is of some interest to determine whether or not sexual differentiation is apparent. Fehling, 76, showed that during foetal life differ-

ences of this nature, though by no means marked, are none the less to be made out. His conclusions have been confirmed by Veit, 89, Romiti, 92, Konikow, 94, Thomson, 99, and Merkel, 02. Petersen has made most careful comparisons between the measurements of the pelvis he reconstructed and the structural data furnished by Fehling. The variations due to sex are, however, so slight that they are likely to be obscured in wax reconstructions of early embryos. Allowance must be made for errors of technique and for the difficulty of determining corresponding points between which measurements are to be taken. Thus, for instance, the proportional widths of the entrance to the true pelvis, the pelvic cavity and the pelvic exit I find to be in CXLV as 100:75:54, while Petersen makes them for Lo_1 as 100:74.7:46.1. According to theory the width of the exit should be proportionately less in the male than in the female pelvis. For foetuses of 30 to 34 cm. Fehling gives for females 100:88:70; for males 100:87:60; for new-born females 100:84:76; for new-born males 100:82:65; for adults 100:92:81. Without the possibility of a direct comparison of the two reconstructed pelvis it is therefore scarcely possible to determine accurately to what extent they may show sexual differences. A characteristic on which Merkel, 03, lays especial stress, the more posterior position of the greatest width at the pelvic entrance in the male, does, I think, exist in CXLV in comparison with Lo_1 .

These two embryos show that at the beginning of the third month of development the cartilagenous pelvis is well formed. At this time, also ossification begins in the ilium. Preliminary changes in the cartilage may be seen in embryos of 25 mm. in an area corresponding to that in which chondrofication commenced. These changes are further advanced in CXLV, but in this embryo neither deposit of calcium salts nor true ossification has commenced in the ilium although ossification is under way in the clavicle, inferior and superior maxillæ, occipital, humerus, radius, ulna, femur, tibia and fibula. Another embryo of the same length, 33 mm., LXXIX, does, however, show a well-marked area of ossification, Fig. 58. In the endochondral region calcium salts are deposited while on each side of this perichondral ossification takes place. In an older embryo, LXXXIV, length 50 mm., this latter process shows well, Fig. 36. It is known that ossification of the ischium and pubis takes place considerably later, that of the ischium beginning in the 4th month and that of the pubis in the 6th to 7th (Bade, 00).

Aside from the ossification of the ilium nothing especially noteworthy seems to take place in the development of the pelvis during the period

when the embryo is growing from 30 to 50 mm. in length. Fig. 13 shows the form of the pelvis in an embryo of the latter size.

The relations of the pelvis to the sacrum during the second and third months of life deserve some attention. I have endeavored to illustrate them in Fig. 44. The curves of the spinal columns of several embryos and an adult are there shown. A point "a" represents the place where a line joining the centers of the two acetabula would cut the median plane of the embryo. From this point dotted lines are drawn to each extremity of the sacral region and one is projected perpendicularly to a line joining these two extremities. A fourth line from point "a" indicates the direction of the long axis of the femur.

In Embryo II, *length 7 mm.*, the leg skeleton is not differentiated. "a" represents there the approximate position where the pelvic blastema will first become marked, as in Embryo CLXIII, *length 9 mm.* The perpendicular falls on the body of the 1st sacral vertebra and points toward the mid-thoracic region.

In Embryo CIX, *length 11 mm.*, the perpendicular falls on the 1st sacral vertebra; in CXLIV, *length 14 mm.*, about at the junction of the 2d and 3d; in CVIII, *length 22 mm.*, on the 3d; in CXLV, *length 33 mm.*, at the junction of the 2d and 3d; in CLXXXIV, *length 50 mm.*, on the anterior portion of the 3d.

At birth, judging from the figure of Fehling, the perpendicular would strike at about the junction of the 2d and 3d. In the adult the area where it strikes shows much individual variation, but in most of the specimens which I have examined it strikes on the 2d sacral vertebra not far from the junction of this with the 3d. In some specimens it strikes the 3d. The material at my disposal has been chiefly dried specimens from the dissecting room and has been subjected to some warping.

Fig. 44 shows that when first differentiated the pelvis occupies a position anterior to that which it takes when it becomes attached to the vertebral column, but that after this attachment the position of the central area of the acetabulum is altered but slightly with respect to the sacral region of the vertebral column. At the beginning and at the end of the period under consideration it probably occupies a position slightly more anterior than that which it takes during the latter part of the second and first part of the third month of development. The chief alteration of the position of the pelvis with respect to the long axis of the body is due to change in the position of the sacrum in relation to the rest of the spinal column.

Merkel, 02, has contributed an important paper on the growth of the

pelvis and refers to the previous literature on that subject. He shows that the sacrum and the innominate bones exhibit a certain independence in rate of growth.

B. FEMUR AND HIP-JOINT, TIBIA, FIBULA, AND KNEE-JOINT.

The rapid development of the blastemal skeleton of the lower limb has been briefly described above. Soon after the fundament of the femur makes its appearance condensation of tissue marks out the anlage of the tibia and fibula and the skeleton of the foot. This last seems to be at first a somewhat irregular continuous sheet of tissue. It is not clear whether or not the anlage of the tibia and fibula also begins as a continuous tissue sheet which becomes divided, by ingrowth of blood-vessels, into tibial and fibular portions. The incomplete development of the interosseous fissure in Embryo CIX, *length 11 mm.*, Figs. 3 and 4, suggests this. The blastemal anlages of the tibia and fibula are here very incompletely separated.

In Embryo CIX the femoral blastema is continuous at one end with that of the pelvis, at the other with that of the tibia and fibula and that of the last two with the foot-plate.

Within the blastema of the femur, tibia and fibula chondrofication begins as soon as the outlines of the blastemal skeleton are fairly complete (Figs. 3 and 4). The embryonic cartilage appears slightly knee-wards from the center of the shaft of each bone and then extends toward the ends. In CIX, Figs. 3 and 4, and 46 to 53, the cartilage of the femur consists of a bar largest at the knee whence it tapers off toward the hip. The cartilages of the lower leg lie nearly in a common plane. That of the tibia is larger than that of the fibula and toward the knee it broadens out considerably. At this stage the joints consist of a solid mass of mesenchyme, Fig. 55. The tissue uniting the femur and tibia has something the appearance of precartilage.

The further development of the thigh and leg may be conveniently studied by taking up at first the development of the femur and hip-joint, and then that of the tibia, fibula and knee-joint.

The cartilagenous femur expands rapidly at the expense of the surrounding blastemal perichondrium and at the same time acquires adult characteristics.

In an embryo of *14 mm.*, CXLIV, Figs. 5 and 6, the shaft of the femur extends almost directly into the hip-joint. Here there is a simple rounded head, distal and dorsal to which a slight projection marks the beginning of the great trochanter. There is nothing corresponding to a true

"neck." Similar conditions have been pictured by Hagen, oo, for the His embryo So, *length 17 mm.*

In Embryo XXII, *length 20 mm.*, Figs. 9 and 10, the head of the femur is proportionately larger and between it and the great trochanter the cartilage has developed in such a way as to give rise to a short neck. Blastemal extensions serve to give attachment to the musculature of the hip and indicate the lesser trochanter and the intertrochanteric ridge. In Embryo CXLV, *length 33 mm.*, Figs. 11 and 12, the cartilage has extended into these projections and the main characteristics which distinguish the proximal end of the femur have become established. Even at this stage, however, the neck is proportionately very short and thick. In an embryo of *50 mm.*, LXXXIV, Fig. 13, the neck is relatively more slender and the head of the femur has become more rounded.

The hip-joint is represented at first by a dense mass of scleroblastema, Fig. 55. The development of the acetabulum by ingrowth and fusion of processes from the iliac, ischial and pubic cartilages has already been described. The cartilagenous joint-cavity is at first quite shallow, Fig. 56. But extension of cartilage into the blastemal tissue which passes from the pelvis over the head of the femur serves greatly to deepen it on all sides except in the region of the cotyloid notch.

The joint-cavity is at first completely filled with a dense blastemal tissue, Fig. 56. While the embryo is growing from 20 to 30 mm. in length cavity formation begins in the tissue lying between the cartilagenous floor of the acetabulum and the head of the femur. The first stage in the process is marked by a condensation of the capsular tissue immediately bordering upon the joint and of the perichondral tissue which at this stage covers the cartilages on their articular surfaces as well as elsewhere. In the region of the ligamentum teres a fibrous band is likewise differentiated from the blastema of the joint. The rest of the tissue becomes looser in texture and ultimately is absorbed, Fig. 57. Henke and Reyher, 74, gave a good account of the development of the hip-joint. Moser has discussed the ligamentum teres.

The shaft of the femur at the stages of Embryos CIX and CXLIV, Figs. 3, 4, 5 and 6 is proportionately very short and thick. For a time it then grows so rapidly that it may become distorted and bent from the resistance offered at each end. But soon adjustment takes place between the skeletal and the neighboring parts and the femur becomes straight and slender. Yet in Embryo CXLV, *length 33 mm.*, Figs. 11 and 12, it is relatively thicker than in the adult.

The linea aspera is marked during the early development of the femur by a thickening of the perichondrium in the region where the various

muscle tendons and fascia are inserted. But in embryos up to 50 mm. in length there is no extension of cartilage into this area. Since by this period the shaft is ossified it is evident that no cartilagenous linea aspera is formed.

Ossification begins at an early period kneewards from the center of the shaft. Endochondral calcification begins here in embryos about, or slightly less than 20 mm. in length. Perichondral ossification usually begins in embryos about 25 mm. long, although in Embryos LXXXVI and LXXV, *length 30 mm.*, the clavicle alone shows actual bone formation. Ossification of the femur takes place at about the same time as that of the humerus, radius and ulna, and very slightly, if at all, precedes that of the tibia. Ossification of the clavicle and the superior and inferior maxillary bones seems always to begin a little earlier, that of the scapula, ilium, occipital, and ribs, slightly later.

The distal extremity of the femur is large at an early period of differentiation, Embryo CIX, Figs. 3 and 4. In Embryo CXLIV, *length 14 mm.*, Figs. 5 and 6, it has expanded laterally and each lateral process has extended dorsally so that fairly well-marked condyles are apparent. These are better formed in Embryo XXII, *length 20 mm.*, Figs. 9 and 10. In CXLV, *length 33 mm.*, Figs. 11 and 12, the form of the distal extremity of the femur resembles the adult.

The tibia and fibula at first lie nearly in the same plane, Embryo CIX, *length 11 mm.*, Figs. 3 and 4. As the head of the tibia enlarges toward the knee-joint it comes to lie dorsal to the proximal extremity of the fibula. This may be seen in Embryo CXLIV, Figs. 5 and 6, and more marked in Embryo XVII, *length 18 mm.*, Fig. 59; XXII, *length 20 mm.*, Figs. 9 and 10; and CXLV, *length 33 mm.*, Figs. 11 and 12. In the last embryo the relations of the head of the fibula to that of the tibia are nearly like the adult.

In Embryo CIX, Figs. 3 and 4, the fibula points toward the lateral condyle of the femur and the tibia toward the median, but the long axis of the femur much more nearly meets that of the tibia than that of the fibula. As the head of the tibia enlarges the anterior extremity of the long axis of the bone is carried toward the center of the distal end of the femur while the head of the fibula is pushed toward the side, Figs. 5, 6, 59, 9, 10, so that the long axis of the fibula comes to point lateral to the extremity of the femur. The head of the fibula is held in place by ligaments developed from the skeletal blastema.

The development of the *knee-joint* in man has been studied by a number of competent observers. Bernays, in 1878, gave a good review of the previous work of von Baer, Bruch, Henke and Reyher, and an

accurate description of the processes which take place. Of the more recent articles that of Kazzander, 94, deserves special mention.

Until the embryo reaches a length of about 17 mm. the knee-joint is marked by a dense mass of tissue, Fig. 59. The medullary tissue at the knee, like that at the hip and other joints, is less dense than the surrounding cortical substance, so that when the cartilages of the femur, tibia and fibula are first differentiated they seem to be connected by a tissue which, in some respects, resembles the prochondrium of which they are composed, Fig. 55. But as the cartilages become more definite the apparent continuity disappears. As the musculature becomes differentiated a dense tendon for the quadriceps is formed in front of the knee-joint. This is shown well in Fig. 56. In it the patella becomes differentiated.

In embryos of about 20 mm. the tissue immediately surrounding the cartilages becomes greatly condensed into a definite perichondrium. The peripheral blastemal tissue at the joints becomes transformed into a capsular ligament strengthened in front by the tendon of the quadriceps. Within the joint most of the tissue begins to show signs of becoming less dense, Fig. 56, but the semi-lunar disks and the crucial ligaments, like the ligaments of the capsule are differentiated directly from the blastema, Figs. 61 to 65. A knee-joint cavity first appears in embryos about 30 mm. long.

The shafts of the tibia and fibula are incompletely separated in the blastemal stage. The cartilages which arise in the scleroblastema are, on the other hand, separated by a distinct interval, Fig. 50, and as the blastemal elements give way to cartilage the interosseous space becomes larger. This is shown in Figs. 3, 4, 5, 6, 9, 10, 11, 12 and 59. At first short and thick the shafts gradually become more slender in proportion to their length. The fibula at all times smaller, becomes increasingly more slender in comparison with the tibia. In embryos of 30 mm., Figs. 11 and 12, both bones, and especially the fibula, are relatively thick compared with the adult bones.

During a period of rapid development, in embryos of 15 to 20 mm., the tibia and fibula, like the femur, may extend so rapidly in length as to become temporarily distorted by resistance at the ends. This is often especially marked in hardened specimens. Holl, 91, Schomburg, 00, and others have called attention to this distortion.

Ossification begins in the tibia at about the same time that it does in the femur and a little earlier than it does in the fibula. It is usually under way in embryos 25 mm. long. In older embryos it is generally well marked, Figs 11 and 12, Plate V. It begins in both bones knee-wards from the center of the shaft and from here spreads toward the

ends of the bones (Fig. 13, Plate V). The development of the distal extremities of the tibia and fibula may best be taken up in connection with the development of the foot.

C. ANKLE AND FOOT.

Of the papers dealing with the early development of the skeleton of the human foot the more important are those of Henke and Reyher, **74**, Leboucq, **82**, v. Bardeleben, **83**, **85**, Lazarus, **96**, and Schomburg, **oo**.

Since the work of Schomburg is the most recent of these and is based on a considerable number of well-prepared embryos, I shall discuss his results somewhat at length in connection with the results which I have obtained. He recognizes four periods in the development of skeletal structures, a mesenchymal, a prochondral, a cartilagenous and an osseous. For the sake of ready comparison I shall take up each of these periods in turn. The fourth period falls within the scope of this paper only in so far as it overlaps the third.

Mesenchymal (blastemal) period.—This commences during the fifth week of embryonic development. The free extremity of the limb-bud becomes flattened and differentiated into the anlage of the foot and its axial blastema becomes differentiated into a foot-plate, from which later the bones of the foot are derived. Schomburg states that the axial blastema becomes distinct at the end of the fourth week. In Embryos CCXLI, length 6 mm.; II, length 7 mm.; CLXIII, length 9 mm.; and CCXXI, length 13 mm.,¹ I find no distinct signs of a foot-plate. In each of the following embryos I find a foot-plate which has not distinctly undergone further differentiation: CIX, length 11 mm.; CLXXV, length 13 mm.; and CVI, length 17 mm. The last is a somewhat pathological specimen. In Fig. 3 a reconstruction of the foot-plate of CIX is shown, in Figs. 51 and 52 transverse sections through this are represented, in Fig. 66 is pictured a longitudinal section through the foot-plate of CLXXV.

Toward the end of the fifth week, in embryos usually 14 to 16 mm. long, the first differentiation of definite bones is manifested by a condensation of tissue in specific areas. Within these areas of condensed tissue precartilage soon makes its appearance. Schomburg says that the first metatarsal is differentiated distinctly later than the other metatarsals. This I find to be the case in none of Prof. Mall's embryos. I do, however, agree with Schomburg that the metatarsal bones become well differentiated before the tarsals. When the metatarsals and phalanges

¹ See note 1, Table A, p. 277.

become differentiated the portions of the foot-plate between them serve for a short time to form a thick web, Fig. 67.

Prochondrium period.—Schomburg gives a detailed account of the early differentiation of the anlagen of the bones of the foot and illustrates his belief as to their nature by several diagrams. Unfortunately he does not picture the wax-plate reconstructions which he reports having made of a number of early embryos. In Prof. Mall's embryos I find no evidence of the archipterygium-like conditions which Schomburg describes. While it may be true that the somewhat slow development of cartilage in the tarsus is owing to the great alterations from primitive conditions which the human foot has undergone during its phylogeny, and to a certain extent has to repeat during its ontogeny, still the development of the bones of the foot is far more direct than Schomburg's diagrams indicate. In the embryos studied I also fail to find the rudimentary tarsal bones described by v. Bardeleben, 83, 85. I have examined six embryos between 15 and 20 mm. long without finding a trace of either the os intermedium tarsi or the triangularis tarsi. In only one instance have I found the I cuneiform distinctly portioned out into dorsal and plantar divisions by a lateral fissure. Study of adult variation statistically, as so admirably carried out by Pfitzner, 96, for the foot, coupled with comparative anatomy, in this, as in so many other fields, throws more light on a possible phylogeny than is gained from ontological investigation.

Embryo CXLIV, *length 14 mm.*, is, of those I have studied, the youngest showing definitely tarsal and metatarsal elements. The general form of the skeleton is shown in Figs. 5 and 6. The differentiation of the tarsal elements is difficult to make out, that of the metatarsals is clear. Webs between the latter still persist, Fig. 67. Webbed digits are sometimes found in the adult (Robertson).

It is to be noted that the elementary condition of the foot of CXLIV corresponds with none of the diagrams given by Schomburg. On the whole the cartilagenous anlagen have a position much more nearly resembling the adult. Embryo XLIII, *length 16 mm.*, exhibits pedal characteristics almost identical with those of CXLIV.

It may here be mentioned that in none of the embryos I have studied is the fibula so long as the tibia. Schomburg states that at first it is longer.

The metatarsals when first formed are spread wide apart and gradually become approximated. The diagrams of Schomburg indicate a different condition.

Cartilagenous period.—This Schomburg distinguishes from the preceding by the fact that cartilage cells at the centers of the areas of chondrofication show definite cell boundaries and become larger than the surrounding prochondral cells. These changes take place in the various skeletal anlagen in the order in which the anlagen were originally formed. With the active production of cartilage cells the broad surrounding zone of mesenchyme gives way to a narrower, denser perichondrium. At the same time the form of the skeleton becomes more definite, so that, as Schomburg says, the cartilages of the foot of an embryo at the middle of the third month give a good picture of the adult bones of the foot. The articular surfaces acquire more or less their definite form. I quite agree with Schomburg, in opposition to Henke and Reyher, that the joints of the foot, like the other joints of the body, are laid down at the start in their definite form and are not moulded into shape by use.

The skeleton of the foot at the time when the cartilage cells at the centers in most of the bones are beginning to be distinctly outlined, has the form shown in Figs. 7, 8 and 59. The tibia is much larger than the fibula and extends further distally. The astragalus has somewhat the form of a rhomboid plate which runs dorsally from the fibular side toward the tibial side on the plantar surface. The calcaneus is rather small and is in direct line with the long axis of the fibula but in a plane lying further plantarwards. The navicular is in a direct line with the astragalus. Its tibial edge lies near the lower end of the tibia. The three cuneiform bones are proportionately broader and thicker than in the adult skeleton. The cuboid is in direct line with the calcaneus. The metatarsals lie less spread apart than at an earlier stage, Figs. 5 and 6. The first phalanx has developed in all of the toes, and in the second toe, the second phalanx as well. At the region of the phalangeal joints there is a swelling of the blastemal tissue.

If now these figures be compared with Figs. 9 and 10, which show the foot of an embryo of 20 mm., the most noticeable change will be seen in the astragalus. This has become considerably thicker. It extends further than the calcaneus. Between the tibia and the navicular it has so increased in size that the foot is bent toward the fibular side. A much greater interval than in Embryo XVII, Figs. 7, 8 and 59, exists between the two bones.

The calcaneus has extended considerably in length both in a proximal and in a distal direction. The cuneiform bones are becoming crowded together. The cuboid is larger than in XVII. The phalanges are at a similar stage of development. The joints between the metatarsals and phalanges are surrounded by a mass of dense tissue, while the tissue of the joints themselves is of a light texture and resembles prochondrium.

In Embryo CXLV, length 33 mm., Figs. 11 and 12, the process of cartilage formation has given rise to structures which resemble adult bones. The tibia has greatly expanded at its distal extremity and now articulates directly with the fibula. These two bones in turn articulate with the well-developed superior articular process of the astragalus. The malleolar process of the tibia is larger and extends further distal than that of the fibula. In an embryo of a corresponding age, however, Schomburg shows that the fibula extends further distal than the tibia. Individual variation may exist.

The astragalus exhibits perhaps more marked alterations in form than any other bone of the foot during the period when the embryo is growing from 20 to 30 mm. in length. Toward the tibia and fibula it develops a well-marked articular process. While this resembles closely the similar process in the adult it is less developed on its fibular side than it is in the adult. As Schomburg has shown the definite adult form is not reached before the fourth month. Toward the calcaneus the bone is well developed and against it exhibits the two characteristic articular surfaces. The posterior of these, compared with the adult, is relatively undeveloped. Distally the bone sends forth a rounded process to articulate with the navicular. In the material at my disposal the whole complex astragalus seems to arise from a single primary center.

The calcaneus, like the astragalus, undergoes marked changes in form during the latter part of the second and the first part of the third month of development. Toward the heel a well-marked tuberosity has made its appearance in Embryo CXLV, Figs. 11 and 12. Distally the bone extends to form a joint with the cuboid. Tibially it has developed a sustentaculum tali for articulation with the astragalus. It is still, however, short in proportion to its width as compared to the adult.

The navicular exhibits no marked changes. On its plantar side and tibial edge it shows a distinct tuberosity.

The cuneiform bones are crowded together and have their characteristic wedge shape. The internal cuneiform is the largest and extends farthest distal. The middle is the smallest.

The cuboid shows a tuberosity. The phalanges, all of which are developed, present no points of special interest.

The joint-cavities begin to develop while the embryo is growing from 25 to 30 mm. in length. As in other cases, so here the blastemal tissue in which the cartilages are developed becomes condensed at their articulating ends and about the joint, while in the region of the joint the tissue becomes less dense and finally disappears leaving a joint-cavity. In

embryos of about 30 mm. the joint-cavities of the foot are filled with a loose fibrous tissue, in embryos of 50 mm. definite cavities are to be made out. The sesamoid bones develop later than the period to which this investigation extends.

During the progress of form differentiation above described the shape of the foot is markedly altered. At the beginning of the development of the foot the tarsal and metatarsal bones lie nearly, though not quite, in the same plane as the bones of the leg, Figs. 7, 8 and 59. They are so arranged, however, that the foot is convex on its dorsal surface and concave on the plantar, and the projections of the calcaneus and astragalus serve to deepen the plantar fossa. The metacarpals spread widely apart. As differentiation proceeds the metacarpals come to lie more nearly parallel to one another and the tarsal elements become compacted in such a way as to give rise to the tarsal arch. The foot at the same time is flexed at the ankle and turned slightly outwards. The toes are flexed. Fig. 68 shows the extent of the tarsal arch in an embryo of 23 mm.

In the further development of the skeleton of the foot the various constituent structures are elaborated and the foot gradually becomes more flexed and turned toward the fibular side. Yet even in the infant the head of the astragalus is directed more inwards than in the adult. Leboucq, 82, pointed out that the first metatarsal is relatively short in the foetus and points more toward the tibial side than later.

Ossification.—This begins in the metatarsals and phalanges during the third month and is perichondral in nature. The tarsals begin to be ossified considerably later. The center for the calcaneus appears in the sixth month, that for the astragalus in the seventh month of foetal life. The ossification of the other bones begins during the first five years of life. Authorities differ as to the exact time at which the process begins in the various bones. In Quain's Anatomy the following dates are given: cuboid, at birth, external cuneiform, 1st year; internal cuneiform, 3d year; middle cuneiform, 4th year; navicular, 5th year.

I have studied the ossification in the third and fourth months of embryonic life. In an embryo about 4 cm. long, cleared according to the Schultze method, I have found centers of ossification in the 2d, 3d and 4th metatarsals, and in the terminal phalanx of the big toe of each foot. In Embryo XCVI, *length 44 mm.*, there is a very thin layer of bone being laid down about the center of the shaft of the 2d, 3d and 4th metatarsals. I have been unable definitely to determine whether or not bone has been deposited in the terminal phalanx of the big toe. In Embryo XCV, *length 46 mm.*, ossification has begun in the 2d, 3d and 4th metatarsals and in the terminal phalanges of the 1st and 2d toes; in Embryos

LXXXIV and CLXXXIV, *length 50 mm.*, it is apparent in the 2d, 3d and 4th metatarsals and in the terminal phalanges of the first three toes. In a cleared embryo, 6 cm. long, there are centers of ossification in all of the metatarsals and terminal phalanges; in one, 8 cm. long, in the first two basal phalanges as well; while in one, 10 cm. long, ossification has begun in all of the metatarsals and the basal and terminal phalanges. We may therefore conclude that ossification in the foot begins in the three central metatarsals and in the terminal phalanx of the first toe toward the end of the third month, and that it is thence extended to the other metatarsals and terminal phalanges before beginning in the basal phalanges.

For a consideration of the development of the individual bones of the foot reference may be made to the excellent paper of Schomburg, 00. The chief points in which my observations conflict with what he describes have been pointed out above. Hasselwander, 03, has recently published a good account of the ossification of the bones of the foot; and Spitzzy, 03, of the structure and development of the infant foot.

SUMMARY.

In general the development of the skeleton of the limb in man corresponds closely with that which is known to take place in other digitates and which has been recently admirably summarized by Braus, 04. Three stages may be recognized, a blastemal, a chondrogenous and an osseogenous. During the chondrogenous stage the chief features of form are reached which characterize the adult structure. The centers for chondro-fication correspond closely with those for ossification. The development throughout is fairly direct. No distinct evidences of phylogenetic structures discarded during ontogeny were found in the embryos studied.

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LIST OF ABBREVIATIONS USED IN LETTERING THE FIGURES.

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| <i>A. A. Pr.</i> —Anterior articular process. | <i>M. D. R.</i> —Membrana reuniens dorsalis. |
| <i>Cæl.</i> —Cælom. | <i>N. Pr.</i> —Neural process. |
| <i>Chd.</i> —Chorda dorsalis. | <i>O. F.</i> —Obturator foramen. |
| <i>Co.</i> —Coccygeal. | <i>O. N.</i> —Obturator nerve. |
| <i>C. Pr.</i> —Costal process. | <i>Pd.</i> —Pedicle. |
| <i>Cu.</i> —Cuboid. | <i>Pch. S.</i> —Perichordal sheath. |
| <i>C. V.</i> —Cardinal vein. | <i>P. L.</i> —Poupart's ligament. |
| <i>Der.</i> —Dermis. | <i>P. A. Pr.</i> —Posterior articular process. |
| <i>Disk.</i> —Intervertebral disk. | <i>P.</i> —Pubis. |
| <i>D. L.</i> —Dorsal ligament. | <i>Rib.</i> —Rib. |
| <i>D. M.</i> —Dorsal musculature. | <i>S.</i> —Sacral vertebra. |
| <i>F. D. M.</i> —Fascia of dorsal musculature. | <i>S. Bl.</i> —Scleroblastema. |
| <i>Fi.</i> —Fibula. | <i>S. N.</i> —Sciatic nerve |
| <i>F. N.</i> —Femoral nerve. | <i>Sptm.</i> —Perichordal septum. |
| <i>F. Pl.</i> —Foot-plate. | <i>Sp. C.</i> —Spinal chord. |
| <i>F. v. E.</i> —Fissure of v. Ebner. | <i>Sp. G.</i> —Spinal ganglion. |
| <i>H. Pr.</i> —Hæmal process. | <i>Sp. N.</i> —Spinal nerve. |
| <i>Ids. M.</i> —Interdiscal membrane. | <i>Sp. Pr.</i> —Spinous process. |
| <i>Idr. M.</i> —Interdorsal membrane. | <i>T. R.</i> —Tendon of r. abd. muscle. |
| <i>Il. Bl.</i> —Iliac blastema. | <i>T.</i> —Thoracic. |
| <i>Is.</i> —Ischium. | <i>Ti.</i> —Tibia. |
| <i>Is. A.</i> —Intersegmental artery. | <i>Trap.</i> —Trapezius muscle. |
| <i>L.</i> —Lumbar. | <i>Tr. Pr.</i> —Transverse process. |
| <i>Ls. Pl.</i> —Lumbo-sacral plexis. | <i>V. L.</i> —Ventral ligament. |
| <i>L. T.</i> —Ligamentum teres. | <i>V. B.</i> —Vertebral body. |
| <i>Myo.</i> —Myotome. | |

DESCRIPTION OF PLATES.

PLATES I-V.

FIGS. 1-12. A series of figures drawn from models made by the Born wax-plate method. Fig. 13 from an embryo cleared by the Schultze alkaline, glycerine method.

PLATE I.

FIG. 1. Skeleton of Embryo II, length 7 mm. About 20 diam. In part the reconstruction was made free-hand from drawings.

PLATE II.

FIG. 2. Right half of the distal portion of the skeleton of Embryo CLXIII, length 9 mm. 25 diam.

FIGS. 3 and 4. Right half of the distal portion of Embryo CIX, length 11 mm. 25 diam. (4) lateral, (5) median, view. The prochondrium of the pubis, ilium, ischium, femur, tibia and fibula are represented by stippling.

PLATE III.

FIGS 5 and 6. Distal portion of the right half-skeleton of Embryo CXLIV, length 14 mm. 25 diam. The prochondrium of the neural arches, the

vertebral bodies, the ilium, ischium, femur, tibia, fibula and of the bones of the foot is represented by stippling. The last are but slightly differentiated at this period.

PLATE IV.

FIGS. 7 and 8. Dorsal and plantar views of the cartilages of the left leg and foot of Embryo XVII, *length 18 mm. 20 diam.*

FIGS. 9 and 10. Lateral and median views of the distal portion of the right half of the cartilagenous skeleton of Embryo XXII, *length 20 mm. 20 diam.*

PLATE V.

FIGS. 11 and 12. Median and lateral views of the distal portion of the right half of the cartilagenous skeleton of Embryo CXLV, *length 33 mm. 10 diam.* The centres of ossification of the femur, tibia and fibula are shown.

FIG. 13. Lateral view of the left leg of an embryo 5 cm. long. *5 diam.* For the sake of facilitating comparison, a mirror picture has been drawn and a technique has been used similar to that employed for illustrating the models. The centers of ossification of the ilium, femur, tibia, fibula, the three middle metatarsals and the terminal digits are shown. The position of the various structures has probably been somewhat distorted during the preparation of the specimen.

PLATES VI and VII.

FIGS. 14-28. Transverse sections through the twelfth thoracic and first two lumbar vertebræ of a series of embryos. *14 diameters.* FIGS. 14-16, Embryo CLXXV, *length 13 mm.*; FIGS. 17-19, Embryo CCXVI, *length 17 mm.*; FIGS. 20-22 Embryo XXII, *length 20 mm.*; FIGS. 23-25, Embryo XLV, *length 28 mm.*; FIGS. 26-28, Embryo LXXXIV, *length 50 mm.*

PLATE VIII.

FIGS. 29-36. Transverse sections somewhat oblique through several vertebræ of various embryos. *14 diam.* FIG. 29, 4th sacral vertebra of Embryo CIX, *length 11 mm.*; FIGS. 30-32, 1st, 2d, and 3d sacral vertebræ of Embryo X, *length 20 mm.*; FIGS. 33 and 34, 1st and 2d sacral vertebræ of Embryo CCXXVI, *length 25 mm.*; FIG. 35, 2d sacral vertebra of Embryo XLV, *length 28 mm.*; FIG. 36, 2d sacral vertebra of Embryo LXXXIV, *length 50 mm.*

PLATE IX.

FIGS. 37-40. Obliquely cut frontal sections through the sacral region of several embryos. *14 diam.* FIG. 37, Embryo CLXXV, *length 13 mm.*; FIG. 38, Embryo CCXVI, *length 17 mm.*; FIG. 39, Embryo CLXXXVIII, *length 17 mm.*; FIG. 40, Embryo LXXXVI, *length 30 mm.*

PLATE X.

FIGS. 41-43. Sections through the coccygeal region of several embryos. *14 diam.* FIG. 41, frontal section of Embryo CLXXV, *length 13 mm.*; FIG. 42, sagittal section of Embryo CXLV, *length 33 mm.*; FIG. 43, frontal section of Embryo LXXXIV, *length 50 mm.*

FIG. 44. Diagram to show the curvature of the spinal column, the proportional lengths of the various regions, the relation of the acetabula to the sacral region and the direction of the long axis of the femur in a series of embryos 7 to 50 mm. in length, and in an adult. Each curved line represents the chorda dorsalis of an individual. The cervical, lumbar and coccygeal regions of this are represented by the heavy, the thoracic and sacral by the light portions of the line. The approximate position where a line joining the centers of the two acetabula would cut the median plane is represented at "a." For Embryo II, in which the skeleton of the leg is not yet differentiated the position of the future acetabula is deduced from Embryo CLXIII, length 9 mm. (See Fig. 2.)

The line passing in each instance from "a" and terminating in an arrow point represents the long axis of the femur. For Embryo II, this line is pointed toward the centre of the tip of the limb-bud. From "a" in each instance a perpendicular is dropped to a line connecting the two extremities of the sacral region. The numbers refer to the following embryos:

2, II.....	Length	7	mm.
109, CIX.....	"	11	"
144, CXLIV.....	"	14	"
108, CVIII.....	"	20	"
145, CXLV.....	"	33	"
184, CLXXXIV.....	"	50	"
Ad. Adult.			

PLATE XI.

FIG. 45. Longitudinal section through the center of the limb-bud of Embryo CLXIII. *14 diam.* Compare with Fig. 2.

FIGS. 46-52. A series of cross-sections through the right leg of Embryo CIX, length 11 mm.

FIG. 53. Outline of the blastemal skeleton with the regions marked through which the sections 46-52 pass. *14 diam.* Compare with Figs. 3 and 4.

PLATE XII.

FIG. 54. Section from Embryo CXLIV, length 14 mm., showing the pubic, iliac and ischial cartilages. *14 diam.*

FIG. 55. Section passing longitudinally through the femur and tibia of Embryo CLXXV, length 13 mm. A portion of the foot-plate is shown cut obliquely. *14 diam.*

FIG. 56. Longitudinal section through the ilium, femur, and tibia of Embryo XXII, length 20 mm. *14 diam.*

FIG. 57. Section through the pubis, ilium, ischium and head of the femur of Embryo CCXXVII, length 30 mm. The hip-joint cavity shows well. It does not extend into the region of the ligamentum teres. *14 diam.*

FIG. 58. Section through the ilium, ischium and head of the femur of Embryo LXXIX, length 33 mm. Calcification is beginning in the ilium.

PLATE XIII.

FIG. 59. Section through the leg and foot of Embryo XVII, length 18 mm. The section does not pass through the cartilage of the 1st metatarsal.

FIG. 60. Section through the pubis, ischium, femur, fibula, calcaneus, cuboid and the 4th metatarsal cartilages of Embryo LXXIV, length 16 mm. $1\frac{1}{4}$ diameters.

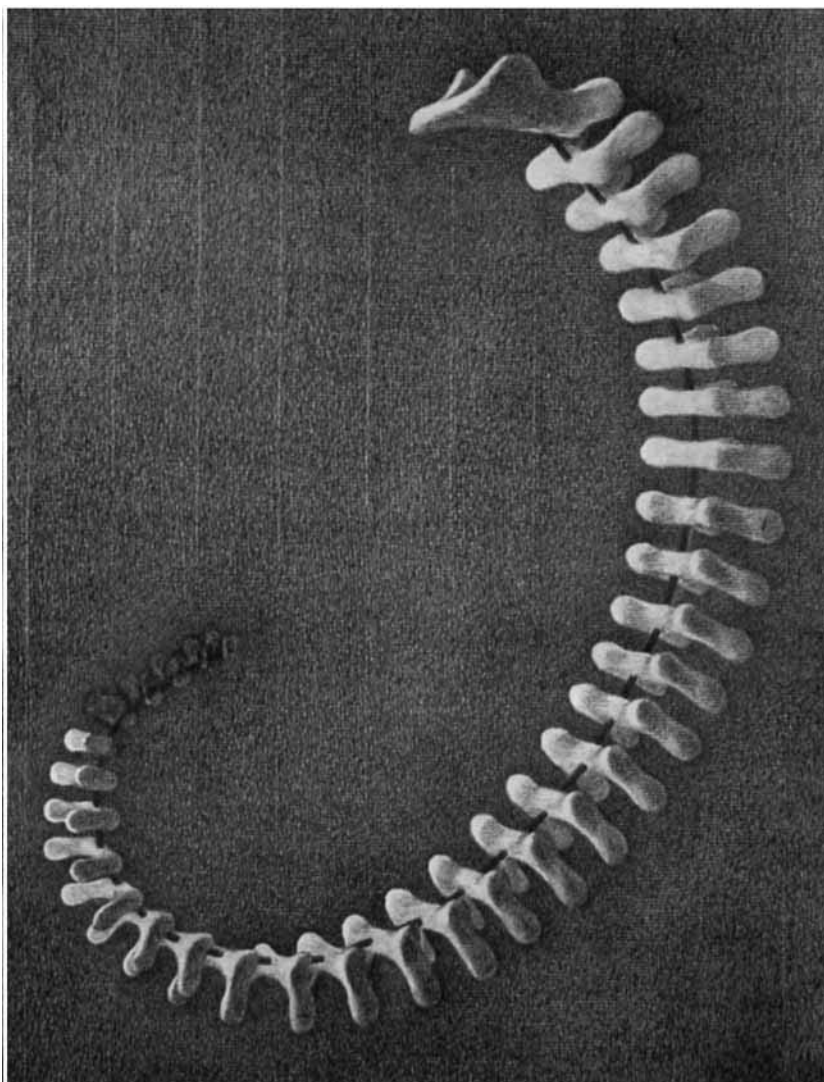
Figs. 61-65. Sections through the knee-joints of several embryos. 14 diam.; 61, CCXXIX, length about 20 mm.; 62, LXXXVI, length 30 mm.; 63, LXXV, length 30 mm.; 64 and 65, CXLV, length 33 mm.

FIG. 66. Longitudinal section through the knee-joint, tibia and foot-plate of Embryo CLXXV, length 13 mm.

FIG. 67. Section through the foot of Embryo CXLIV, length 14 mm.

FIG. 68. Section through the foot of Embryo LVII, length 23 mm.

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II, LENGTH 7 MM.

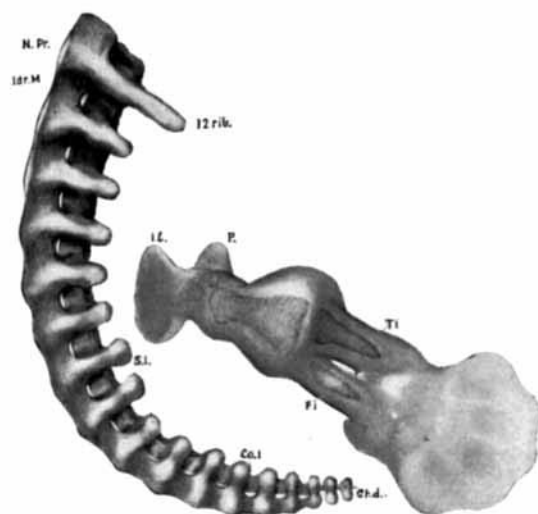


Fig. 3

CIX, LENGTH 11 MM.

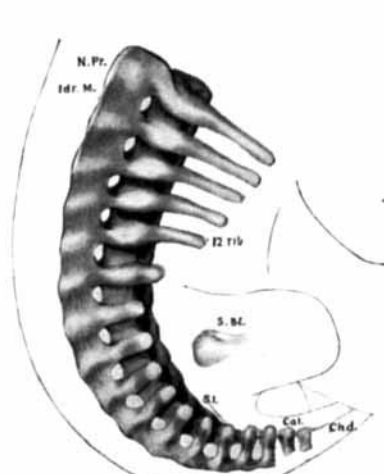


Fig. 2

CLXIII, LENGTH 9 MM.

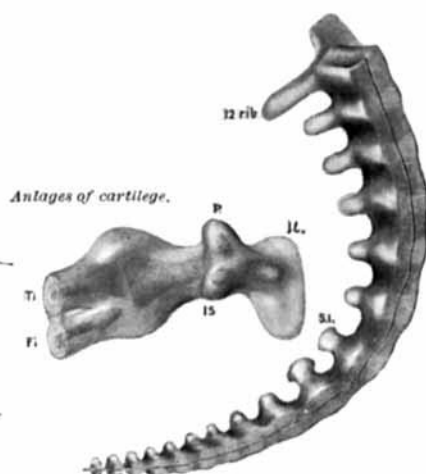
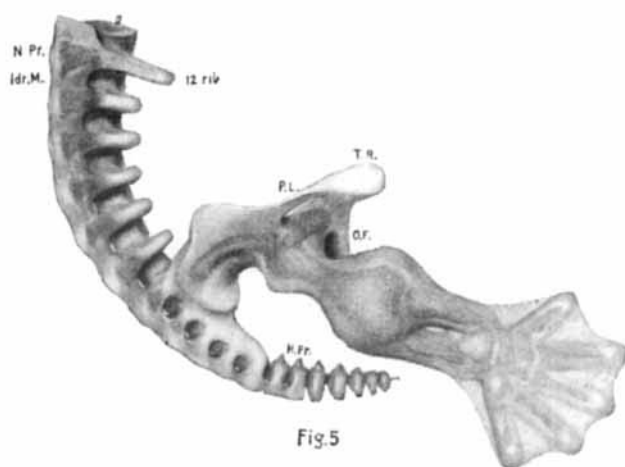
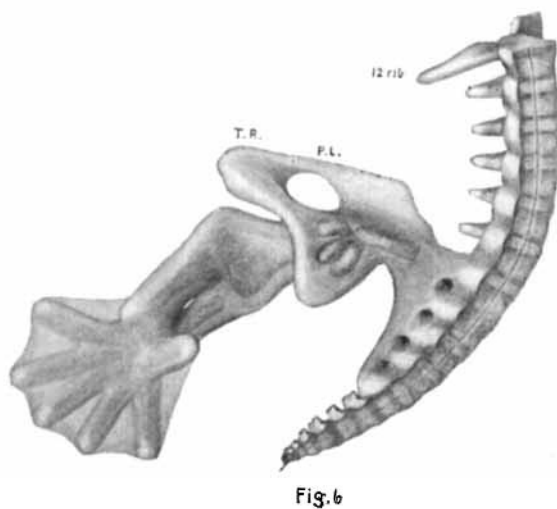


Fig. 4.

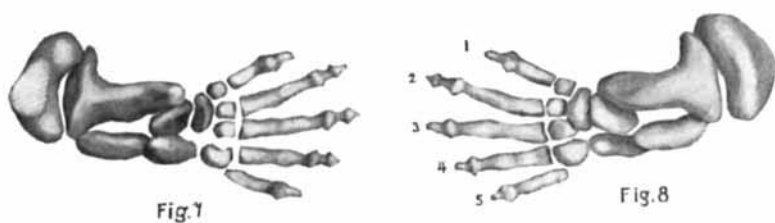
CIX, LENGTH 11 MM.



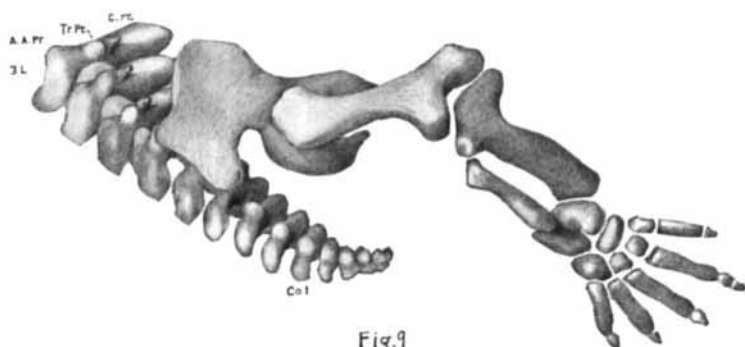
CXLIV, LENGTH 14 MM.



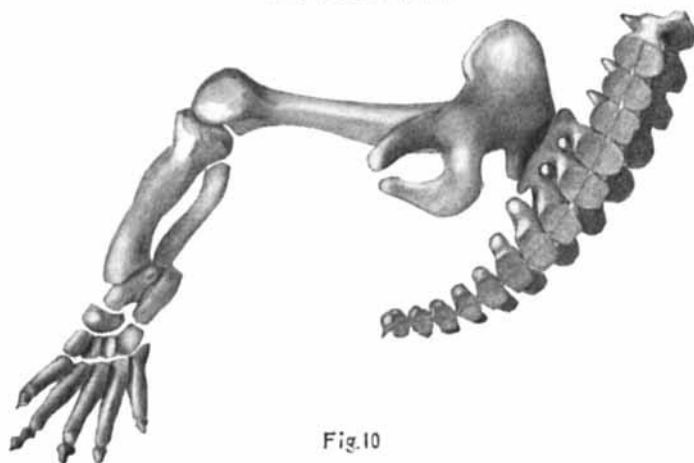
CXLIV, LENGTH 14 MM.



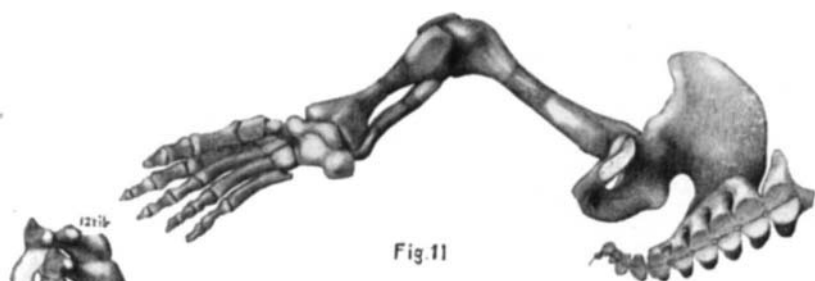
XVII, LENGTH 18 MM.



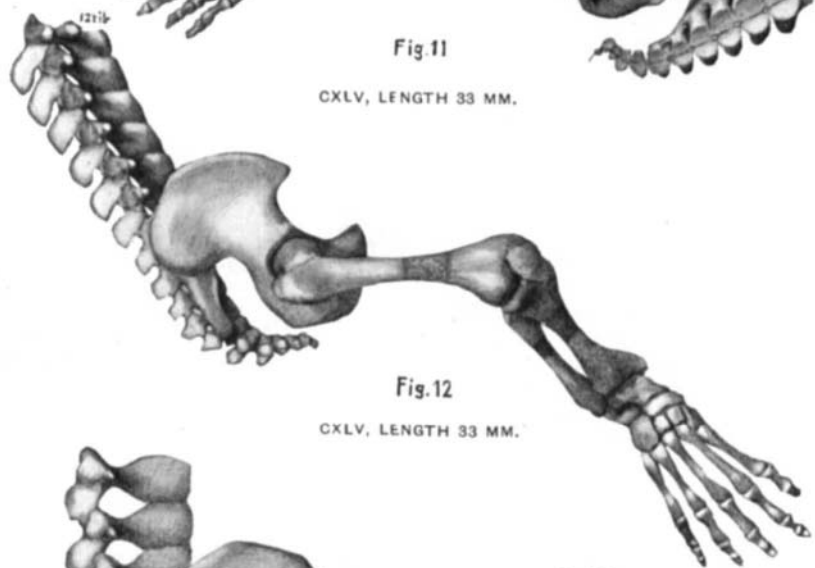
XXII, LENGTH 20 MM.



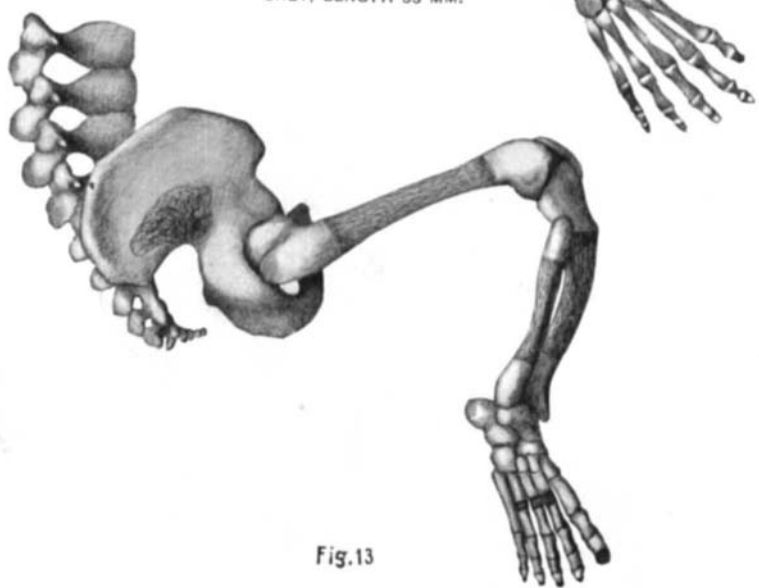
XXII, LENGTH 20 MM



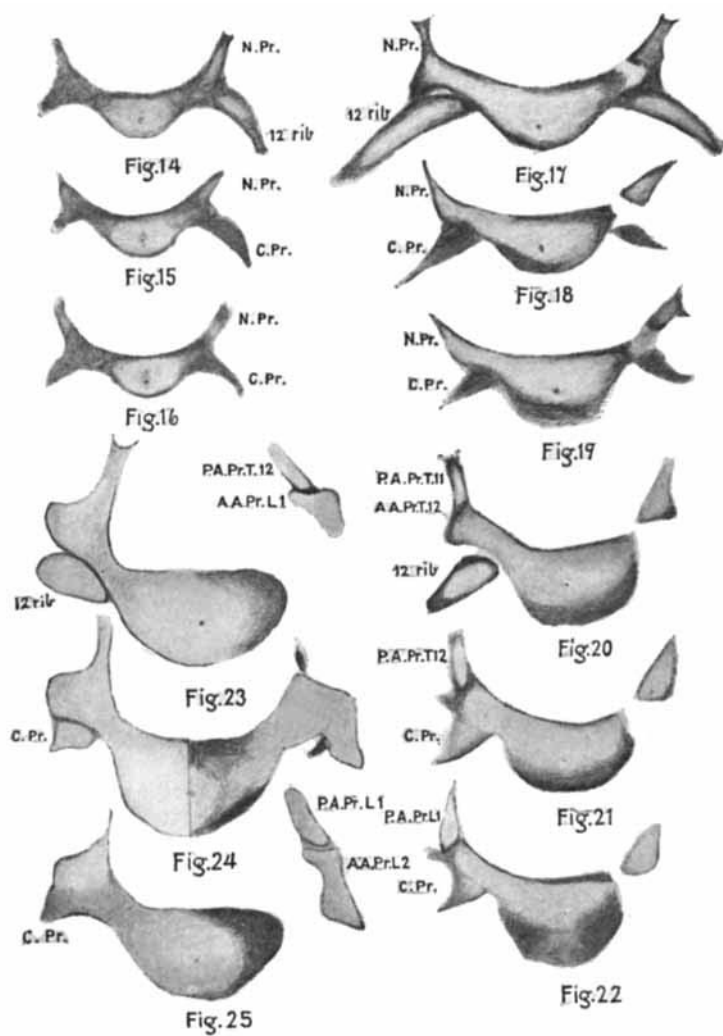
CXLV, LENGTH 33 MM.



CXLV, LENGTH 33 MM.



LXXXIV, LENGTH 50 MM.



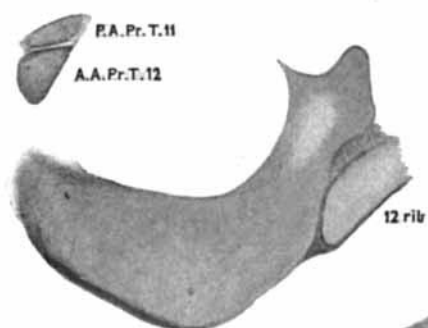


Fig.26

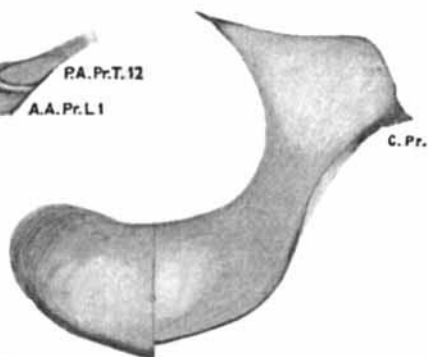


Fig.27

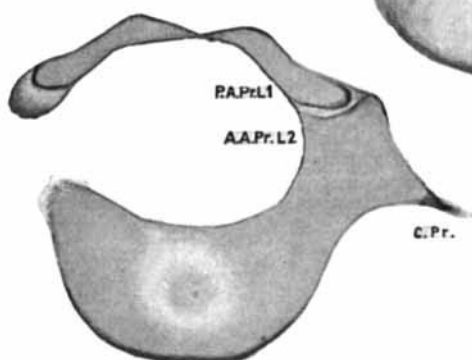
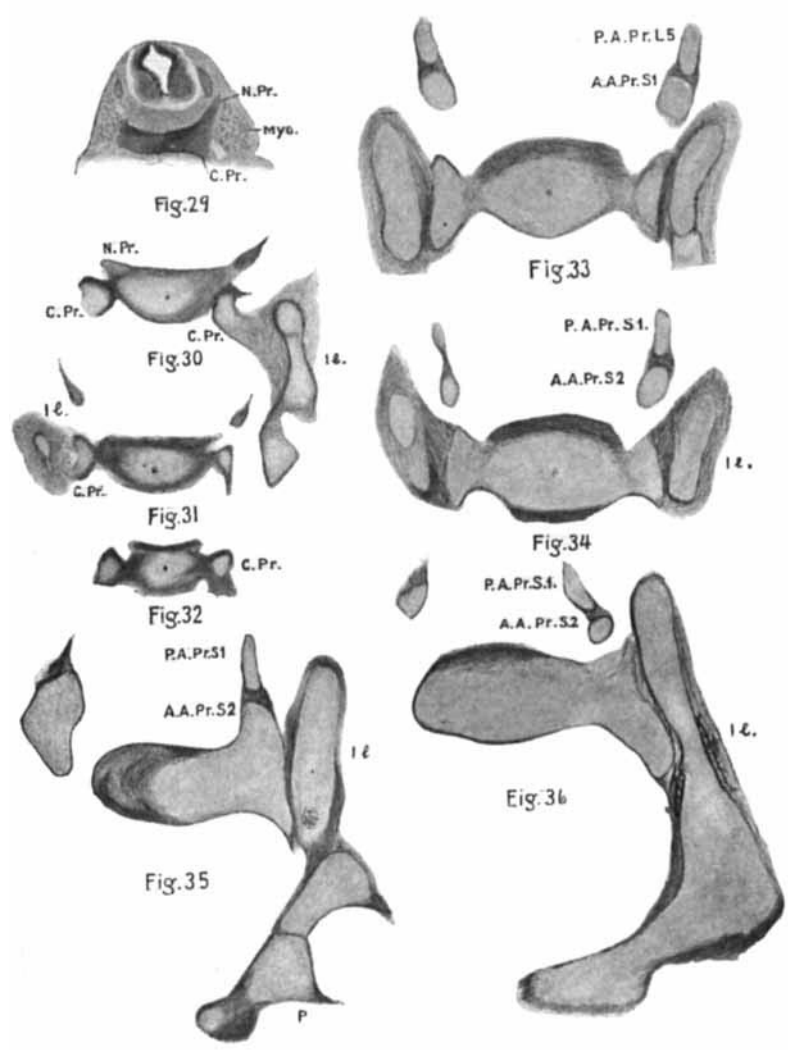
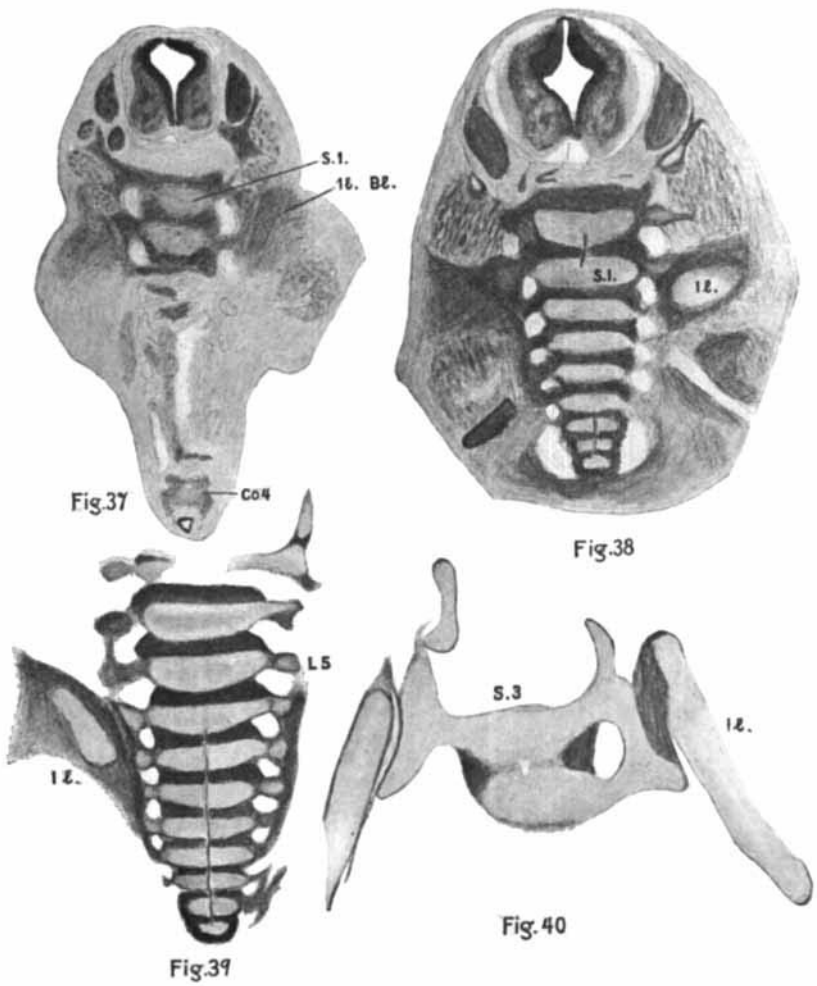


Fig.28





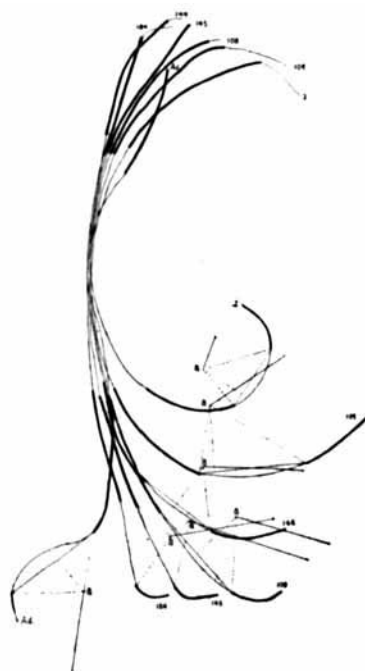


Fig. 44

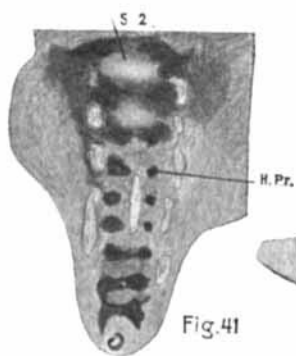


Fig. 41



Fig. 42

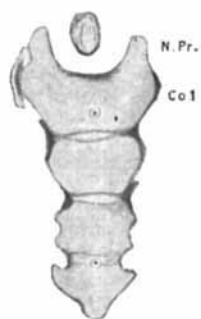
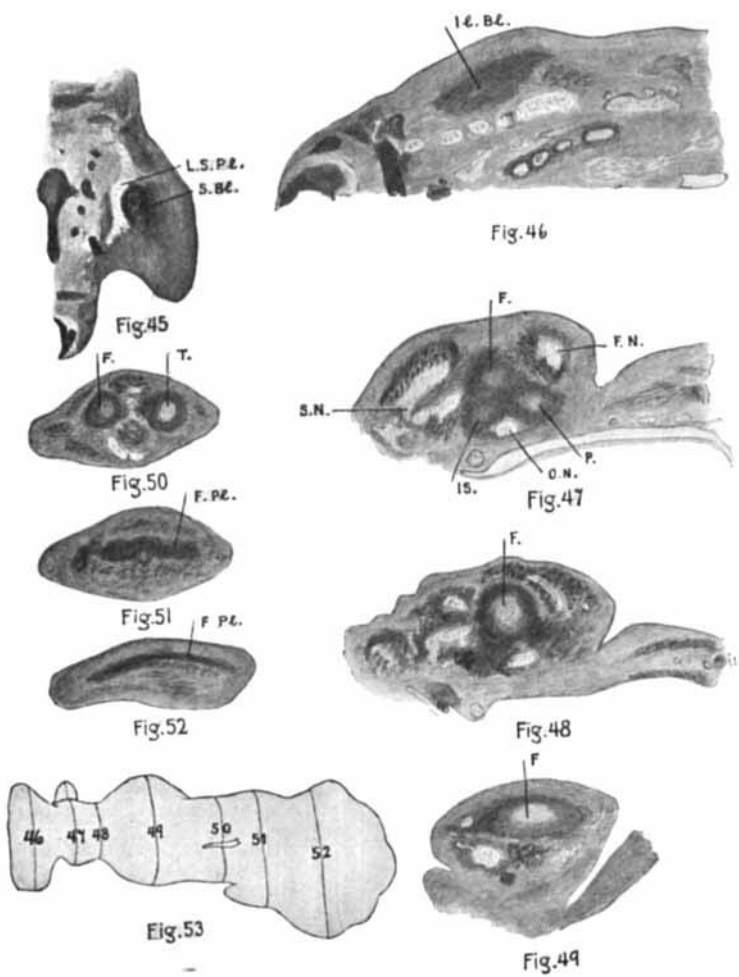


Fig. 43



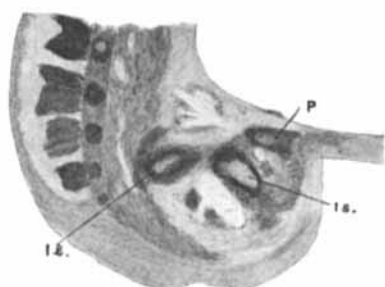


Fig. 54



Fig. 55

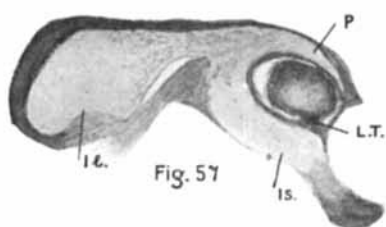


Fig. 57



Fig. 56

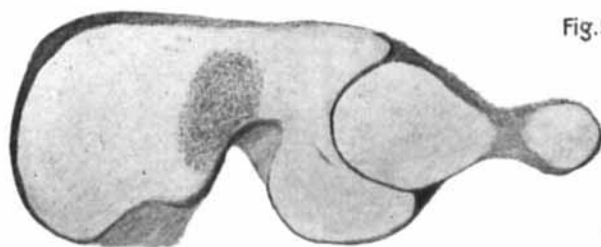


Fig. 58

