not been demonstrated. Section of the trigeminus, on the theory that the nerve stimulus is perverted, should be considered. Various contrivances have been devised for correcting the resulting deformity. Sachs has used a pad or rubber plate in the mouth. Eckstein has improved the appearance with subcutaneous injections of paraffin. *T. Stuart Hart.*


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**FACIAL HEMIHYPERTROPHY** is a rare affection consisting of circumscribed enlargement of one side of the face. The process usually involves the skin, connective tissue, blood-vessels, muscles, and bone. In some cases

Fig. 5139.—Facial Hemihypertrophy in a Child. (After Sabrazès and Cabannes.)

the skin is harsh and rough, while the sebaceous glands are much hypertrophied and clogged with an abnormally thickened secretion of gummy consistence. The hair is often thick and coarse. In the case reported by Dana the bones were alone involved in the process; the soft tissues were not hypertrophied. The external ear may take part in the enlargement. Here either the cartilage alone or all the tissues may be involved. The hypertrophy may extend into the mouth implicating the gums, soft palate, and jaw. The hypertrophy may be limited to a part of the face on one side, or may extend somewhat across the median line.

But little is known of causes underlying the condition. Of the twenty-three cases collected by Sabrazès and Cabannes eighteen were congenital. In Schick's case the hypertrophy commenced in the second year with no known cause. In Berger's case there was an obstinate antecedent neuralgia of the fifth nerve. Montgomery's patient had brain fever when two years old. There was no neuralgia. When nine years of age the patient had an osteomyelitis of the left maxilla. About one year later hypertrophy first appeared in the gums of the left side. In Dana's case the patient was also affected with gigantism. It is probable that several distinct conditions have been described under the term of hemifacial hypertrophy. Among the theories advanced as to the etiology of the acquired cases may be mentioned irritation of the fifth nerve through its roots or the Gasserian ganglion, and chronic hyperæmia of vascular origin.

The enlargement may be first noticed in the bones, particularly about the orbit, giving the eyeball the appearance of being depressed in its socket. The bony hypertrophy gradually extends until the entire side of the head is included. In other cases (*e.g.*, Montgomery's) the process may begin in the soft parts, and the gums, skin, sebaceous glands, hair, connective tissue, muscle, and the bones become later involved. The enlargement of the blood-vessels may cause a reddening of the skin. The flow of saliva may be considerably increased.

There are few conditions which could be confounded with hemifacial hypertrophy. It has been suggested that it might be mistaken for hemifacial atrophy of the other side of the face; but anything more than a cursory examination could not fail to disclose the differences.

We know of no cases in which the hypertrophied tissues have been replaced by normal ones; but after a progression covering a period of several years it is probable that the condition may become stationary.

Treatment thus far has proved unavailing, either in limiting the course of the disease or in reducing the hypertrophy. *T. Stuart Hart.*


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Montgomery: Medical News, July 15th, 1893.
Dana: Journal Nervous and Mental Disease, November, 1893.
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**FŒTUS, DEVELOPMENT OF.**—Our knowledge of the development of the fœtus was in an exceedingly fragmentary condition until Wilhelm His, the distinguished German anatomist, published twenty years ago his noteworthy "Anatomie menschlicher Embryonen." This was the first, and is to-day the most important work on human embryology. Previously there were isolated descriptions here and there of embryos of the first two months of pregnancy. Uncertainty as to the normal appearance often leads to the description of abnormal for normal ones, and the great difficulty in obtaining embryos of the first two months of pregnancy renders progress comparatively slow. The main sources of such material are from post-mortem examinations, operations, and abortions; so the human embryologist is thus dependent upon the courtesy of physicians and surgeons for his material.

*Age.*—In regard to the ages of embryos of the first two weeks much uncertainty exists. Length is not entirely reliable, owing to distortions and variability in size. In attempting to determine age from the last day of the last menstrual period as the date of conception, there is often the difficulty of inexact history. The following table indicates in a fairly accurate way the length and ages of embryos:

| Age. | Length. | Age. | Length. |
|---|---|---|---|
| Two weeks | 2 mm. | Three months | 50 mm. |
| Three weeks | 5 " | Four months | 100 " |
| Four weeks | 8 " | Five months | 200 " |
| Five weeks | 11–12 " | Six months | 300 " |
| Six weeks | 16 " | Seven months | 370 " |
| Seven weeks | 20 " | Eighth months | 425 " |
| Eight weeks | 25 " | Nine months | 500 " |

According to Mall their ages in days corresponds to the formula $\sqrt{100 \times (\text{length in millimetres})}$ for all embryos from 1 to 100 mm. long. Multiply the length of the embryo from vertex to the breech in millimetres by one hundred, and extract the square root, and the result will be its age in days. In embryos from 100 to 220 mm. long from vertex to breech their length in millmetres equals their age in days. Fig. 5140 indicates the relative sizes during the first eight weeks.

There are but few good collections of embryos in the world; the one at Leipsic and the one at Baltimore are the most important.

In development it is convenient to distinguish the three stages suggested by His. The stage of the ovum embraces the first two weeks; the embryonal stage from the third to the fifth week, during which time the characteristic embryonal features and the principal organs are established; lastly the fœtal stage, during which time the embryonal features change to those of the fœtus and full-term child.

*The Ovum Stage.*—There are no observations on normal ova of the first nine or ten days. It is evident





from the material of the latter part of the stage of the ovum that there is an early and precocious development of the chorion and villi.

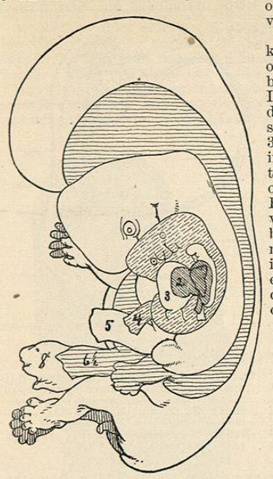

Fig. 5140.—Six Human Embryos taken from His' Standard Chart. Enlarged three times. The figures in the cut indicate the ages of the embryo in weeks. 2 is His' embryo S R.; 3, embryo Lr.; 4, embryo A.; 5, embryo O"; 6½, embryo XCI.; 8, embryo Wt. (After Mall.)

The youngest known normal ovum was described by Peters in 1899. It is ten to eleven days old and consists of a vesicle 3 × 1.5 × 1.5 mm. in size. A section through the entire ovum is seen in Fig. 5141. The vesicle is formed by the chorionic membrane, consisting of an outer layer of epithelial cells covered by numerous villi which are in contact with the uterine wall of the mother, and an inner layer of mesenchyme. Attached to this inner layer at one side is the small embryo, but .19 mm. in length. It is apparently simple in structure, consisting of an epithelial plate facing the small amniotic cavity lined by flat epithelial cells, which are continuous with the epithelial cells of the plate. On the other side of the plate is a layer of mesenchyme, and projecting from this is the yolk sac lined by entodermal cells. The epithelial plate of the embryo, as well as the epithelium of the amnion, was probably at an earlier stage continuous with the epithelium of the chorion and the embryo, subsequently cut off after its sinking down or projecting into the vesicular cavity. One stage of such a process has been found in the monkey by Selenka. The projecting embryo is surrounded by mesenchyme continuous with that lining the chorion, as well as with that between the yolk sac and epithelial plate.

Already, then, in the youngest known ovum the so-called three primary germ layers are present. From these at a later period various structures arise. From the epithelial layer develop the epidermis of the skin and its appendages, such as hairs, nails, sweat glands, etc., the central nervous system, and portions of the eye and ear, mouth and nose. From the middle or mesenchymal layer develop the skeletal, muscular, circulatory, and urogenital systems; and lastly from the inner or entodermal layer, which is here represented by the lining of the yolk sac, develop the alimentary tract (pharynx, œsophagus, stomach, and intestines), the trachea and lungs, liver and pancreas, and bladder.

The next important human ovum was described by Spee in 1896. It measures 7 × 5.5 mm. and the embryo within is 0.37 mm. in length. Its age is about eleven days. The chorion is covered with villi and lined with mesenchyme (see Fig. 5142). The embryo is attached at one side by a broad pedicle, the so-called belly stalk. The amniotic sac is small and is continuous with the epithelial plate of the embryo, as in the preceding ovum. The primitive streak is represented in this embryo by a slight groove along the centre of the epithelial plate. Mesenchyme separates the epithelial plate from the large

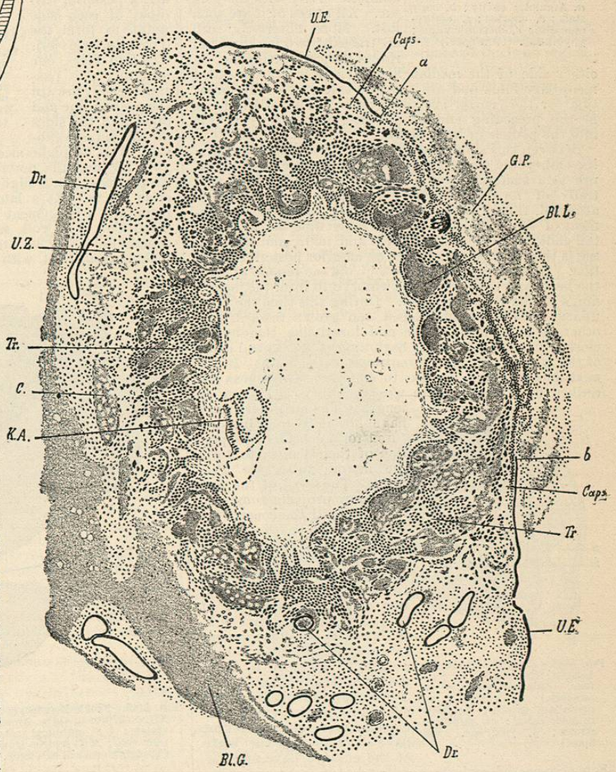


Fig. 5141.—Peters' Early Ovum. (Enlarged about 35 diameters.) *U.E.*, Uterine epithelium; *Bl.L.*, lakes of blood; *Caps.*, decidua reflexa; *G.P.* "Gewebspilz"; *Dr.*, uterine glands; *U.Z.*, decidua vera; *Tr.*, trophoblasts; *C.*, capillaries; *K.A.*, beginning embryo; *Bl.G.*, large blood-vessels; *a–b*, point of entrance of ovum.

yolk sac, and a small diverticulum of the sac projects into the mesenchymal pedicle, constituting the first trace of the allantois. We thus see that the embryo in this ovum, although about twice as long as the Peters embryo, shows very little advance in structural differentiation. Both are in the primitive streak stage.

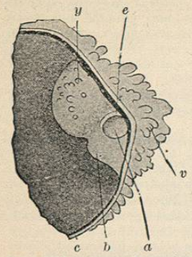


FIG. 5142.—Ovum Measuring 6 × 4.5 mm. (Enlarged about 10 diameters.) The left half of the chorion has been removed to show the embryo. *a*, Amniotic cavity; *b*, belly stalk; *c*, chorion; *e*, embryonic disc; *v*, chorionic villus; *y*, yolk-sac. (von Spee.)

Spee also described an ovum 10 × 8.5 × 6.5 mm. containing an embryo 1.54 mm. in length and about eleven and one-half days old. The chorion is covered by large branching villi, lined by mesenchyme, and attached at one side by a short pedicle is the embryo (see Fig. 5143). The primitive streak still persists, and near its anterior end the neurenteric canal has formed, thus connecting the amniotic cavity with the yolk sac. All traces of it are soon lost. More anteriorly still are traces of two longitudinal ridges, short distances on either side of the median line. These are the so-called medullary folds and are the first traces of a differentiation for the central nervous system. The allantois as in the preceding embryo projects from the yolk sac into the pedicle or belly stalk.

Between this stage and the next one we shall consider, the embryonic plate changes from a flat discoidal structure to a somewhat cylindrical body by a bending ventrally of its lateral edges, to which the amnion is attached, thus gradually constricting the broad attachment of the yolk sac. At the same time the head and tail ends begin to project more and more, and the yolk sac is thus also constricted in an anterior posterior direction. Connecting pockets of the yolk sac remain at both the head and tail ends of the embryo to form the beginnings of the digestive tract. During this time the medullary folds have lengthened and grown toward each other, so as to meet in the mid-dorsal line, thereby enclosing a central canal, the beginning of the central canal of the spinal cord and the ventricles of the brain. In the next oldest ovum we are to consider, which was described by Eternod, there was an embryo 2.11 mm. in length. The medullary folds have not only met, but are fused for a considerable portion of their length to form the neural tube (see Fig. 5144). The head of the embryo now projects some distance beyond the constricted yolk sac, and on the ventral side of this head fold is a slight invagination of the ectoderm for the mouth. Between the mouth invagination and the attachment of the yolk sac the heart is in the process of development from two lateral tubes, which soon fuse together to form the simple tubular heart. The blood-vessels which have developed in the extra embryonic area and those that have developed in the body of the embryo have now become connected with the heart, and at its head end arises the ventral aorta dividing immediately into three pairs of branchial arches, which pass around the primitive foregut to unite beneath the medullary plate into the dorsal aorta.

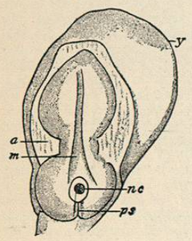


FIG. 5143.—Embryo 1.54 mm. in Length, from the Dorsal Surface. (Enlarged about 20 diameters.) *a*, Amnion; *m*, medullary groove; *nc*, neurenteric canal; *ps*, primitive streak; *y*, yolk sac. (von Spee.)

From the dorsal aorta are given off the omphalo-mesenteric and the umbilical arteries. The first veins to develop are those which accompany the first formed arteries, namely, the omphalo-mesentericS, connected with the yolk sac, and the umbilicals, connected with the allantois. Soon after these are formed the veins within the body of the embryo develop, the first ones being the anterior cardinals, or internal jugulars and the inferior cardinals, the latter draining the blood from the caudal portion of the body. An anterior and a posterior cardinal of each side unite to form the ductus Cuvieri. The two ducts, one on either side, pass transversely toward the median line and open into the sides of the sinus venosus. The omphalo-mesenteric veins coming from the yolk sac and the umbilicals from the allantois join the sinus venosus at a slightly earlier date than do the Cuvierian ducts. At a later stage we shall see how this primitive arrangement is modified to form the adult condition. The yolk sac in this embryo is somewhat constricted along its attachment, leaving pockets of entoderm connected with it that lie in the head and tail

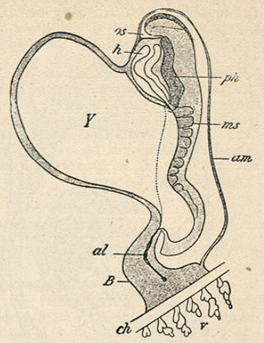


FIG. 5144.—Reconstruction of Embryo 2.11 mm. Long. (Enlarged about 25 diameters.) *al*, Allantois; *am*, amnion; *B*, belly stalk; *ch*, chorion; *h*, heart; *ms*, mesodermic somite; *os*, oral fossa; *ph*, pharynx; *v*, chorionic villi; *Y*, yolk-sac. (After Eternod.)

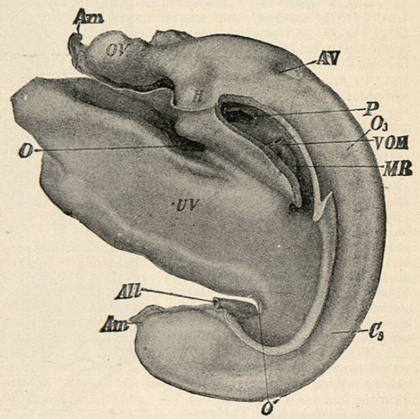


FIG. 5145.—Profile Reconstruction of the Embryo, 2.11 mm. Long. No. XII. × 37 times. *Am*, Amnion; *OV*, optic vesicle; *AV*, auditory vesicle; *UV*, umbilical vesicle; *H*, heart; *VOM*, omphalo-mesenteric vein; *MR*, septum transversum; $O_3$, third occipital myotome; $C_8$, eighth cervical myotome. (After Mall.)

ends of the embryo. They form the primitive foregut and hindgut. At either side of the neural tube the mesenchyme has become differentiated into eight prim-





itive segments or myotomes, from which later much of the muscular system becomes differentiated.

A slightly older embryo, of about the same length, described by Mall, consists of an ovum measuring 18 × 8 × 8 mm., and containing an embryo 2.1 mm. in length. The age is about two weeks (see Fig. 5145).

Many important changes have taken place. The embryo is connected to the chorion by a thinner stalk of mesenchyme containing the blood-vessels that carry on the circulation between the embryo and chorion, the latter being in close contact with the uterine wall, and thus affording opportunity for nourishment and oxygen to pass from the mother through the thin walls of the villi, to supply the rapidly growing embryo with the essentials for growth and life. The embryo itself has greatly increased in length, and is curved into a semicircular form. The medullary plate is converted into a tube and the groove into its canal. At the anterior end of this tube are enlargements marking the beginnings of the brain. The remainder of the tube forms the spinal cord. The yolk sac, which is covered by blood-vessels that communicate with those of the embryo, is more constricted and the fore- and hindguts are longer than in the preceding stage. From the foregut arises the pharynx with two gill pockets and a thyroid pocket. The neurenteric canal connects the hindgut with the central canal of the central nervous system. So while from the yolk sac are differentiating the two ends of the alimentary tract, the main portion is still embodied in the large sac. Near the origin of the foregut is a slight projection of the yolk sac for the beginning of the liver. In the anterior wall of the yolk sac, posteriorly to the mouth and beneath the pharynx, is the tubular heart. There are now fourteen pairs of mesenchymal segments or myotomes—three in the head, eight in the neck, and three in the thoracic region. The amnion at this period forms a small sac about the dorsal surface of the embryo.

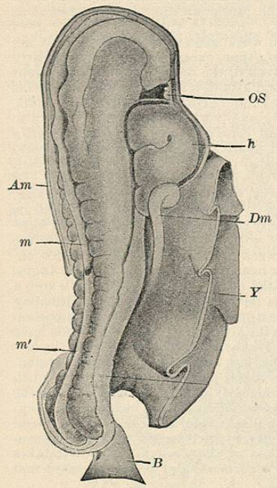


FIG. 5146.—Embryo 2.5 mm. Long. (Enlarged about 33 diameters.) *Am*, Amnion; *B*, belly stalk; *h*, heart; *m*, closed and *m'*, still open portions of the medullary groove; *Om*, omphalo-mesenteric vein; *OS*, oral fossa; *Y*, yolk sac. (Kollmann.)

In an embryo described by Kollmann (Fig. 5146), and measuring 2.5 mm. in length, the edges of the medullary folds have come in contact throughout their entire length except for a short distance anteriorly, and thirteen pairs of mesodermic somites or myotomes are visible. The constriction of the yolk sac is even more pronounced than in the preceding embryo, and the hind end of the body has become defined, the belly stalk no longer seeming to be a posterior continuation of the body, but arises from the ventral surface. The oral fossa is more marked.

The general shape of this embryo is quite different from that of the preceding one, the embryo being nearly straight; and it has probably been distorted, as has also the His embryo (Fig. 5147), as the normal curve of the medullary tube at this period is probably somewhat semicircular, as seen in Figs. 5145 and 5149. This so-called dorsal flexure, which is often pictured in text-books as a normal condition at this stage, I have been able to produce in pig embryos of a corresponding stage by rough handling while removing them from the uterus. Others from the same uterus, which were more carefully handled, do not show such a dorsal flexure, and we naturally conclude that similar treatment has produced a similar effect in the human embryo.

The His embryo Lg, 2.15 mm. long, contained in an ovum 15 × 12.5 mm., is the next important one to consider. Its age is about fourteen days. (Fig. 5147.) The forebrain has a marked ventral bend. Between the forebrain and the heart is now a well-marked invagination of the skin to form the mouth cavity. It is not as yet connected with the pharynx. Projecting from the forebrain are the optic vesicles, and farther back are invaginations of the ectoderm for the internal ear. Two gill clefts and three branchial arches are present, and branches of the aorta pass through the latter. The heart consists of a much bent tube.

The branchial arches and clefts are of great morphological importance, since they determine to a large extent the arrangement of the various organs of the head region. In the human embryo four clefts and five branchial arches appear on each side. The last arch is very indistinct.

We thus see that during the first two weeks, which constitute the ovum stage, there has developed from the simple one-celled ovum or egg an embryo with its membranes, the amnion and chorion, the latter having over its entire surface numerous long branching villi, and in the embryo are already present the beginnings of the central nervous system, the alimentary tract, the circulatory system, the muscular and skeletal systems, the latter being represented by the chorda dorsalis, which has differentiated from the dorsal wall of the entodermal sac and canal. The primitive urogenital system has also begun to appear. The yolk sac remains throughout this stage the dominant feature of the embryo.

*The Embryonal Stage.*—During the third week the embryo grows rapidly in size and attains a length of about

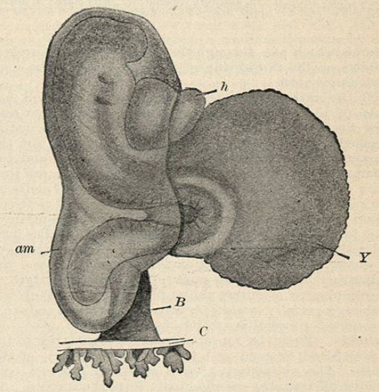


FIG. 5147.—Embryo Lg., 2.15 mm. Long. (Enlarged about 30 diameters.) *am*, Amnion; *B*, belly stalk; *C*, chorion; *h*, heart; *Y*, yolk sac. (His.)

4 mm. The brain increases in size and shows the three primary divisions. The optic and otic vesicles become more prominent. Two more gill clefts and three more gill arches appear caudal to the ones already formed. The attached area of the yolk sac has diminished. The

mouth cavity communicates with the pharynx. By the twenty-first day the limb buds appear (see Fig. 5148). Internally the heart is enlarged and takes the form of an S-shaped tube. From the aorta now arise five pairs of

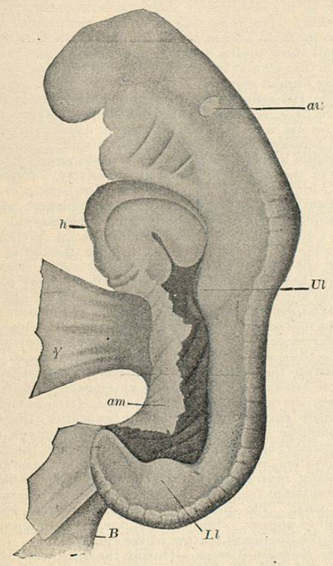


FIG. 5148.—Embryo Lr., 4.2 mm. Long. (Enlarged about 23 diameters.) *am*, Amnion; *au*, auditory capsule; *B*, belly stalk; *h*, heart; *Ll*, lower and *Ul*, upper limb; *Y*, yolk-sac. (His.)

arteries which pass through the five pairs of gill arches, joining on the dorsal side of the pharynx into the common dorsal aorta.

By the narrowing of the attachment of the yolk sac more of the primitive gut has been folded off, so that now the foregut, midgut, and hindgut are to be distinguished. In the foregut can already be made out the pharynx with its diverticula, the œsophagus, and the stomach. Of the pharyngeal diverticula there are four pairs of gill pockets corresponding to the gill clefts on the external surface and separated from the gill clefts by a thin membrane. The diverticulum for the respiratory tract has begun to bud from the œsophagus. The first indication of the lungs and trachea is found in embryos of about 3.2 mm. in length in the form of a groove, the pulmonary groove, along most of the ventral surface of the œsophagus. During the embryonal stage this groove deepens especially toward the stomach, where it ends in a a rounded projection, which lengthens and gives off branches. These, by repeated branching, give rise to the various-sized bronchi and the epithelial portion of the lungs. The pulmonary groove gradually becomes constricted off from the œsophagus to form the trachea. At the upper end, however, it remains open into the pharynx, in the region of the fourth branchial diverticulum, to form the glottis. The midgut gives rise to the small intestine and to a portion of the large intestine. From it have arisen diverticula which give rise to the liver and pancreas. The hindgut gives rise to the rest of the large intestine and to the rectum.

The primitive urogenital system has appeared as two longitudinal ridges projecting into the cœlom along its dorsal wall, one at either side of the median line in the posterior half of the embryo. This ridge contains the Wolffian duct, the pronephros with its two tubules and rudimentary glomeruli. The Wolffian duct, which is the first to appear, develops from the mesenchyme, and extends from the heart region to the cloaca. Soon after the non-functional pronephros is formed, the mesonephros begins to develop and its tubules join the Wolffian duct. The mesonephros is a much more important structure than the pronephros, and we shall consider it again later. The beginning of the Müllerian duct is also present at this stage.

During the fourth week growth is relatively more active than at any other time, except during the very early stages of the first week or ten days. The embryo about doubles in length, and attains a length by the end of this week of about 6 or 7 mm. During the first part of the week the embryo becomes very much flexed, so much so that the head and tail nearly touch. The brain vesicles are better developed, as are also the gill clefts and arches, the eyes, ears, and nasal pits. The heart, which is much enlarged, lies in the cervical region, near the mouth, and produces with the liver, which is now of considerable size, a large ventral bulge. The simple tubular heart with its single cavity is rapidly changing into a complicated four-chambered structure with imperfect partitions. By the end of the fourth week (see Fig. 5149) the anterior enlarged portion of the head has become bent at right angles to the main axis of the body. From the first gill arch a maxillary process is developing which will ultimately form a portion of the upper jaw. From the main portion of the arch will form the lower jaw. The limb buds have increased in size. The arm bud projects from the cervical region and the leg bud from the lumbar region. The yolk sac is very small and the amniotic sac is much enlarged. During the early part of the fourth week the intestinal tube, composed of its several characteristic segments, lies in the sagittal plane attached to the dorsal wall of the body cavity by the straight primitive mesentery. Toward the last of the week rapid growth takes place, the intestine lengthens, and becomes coiled and twisted.

The nerves have begun to grow from the medullary tube or central nervous system into the mesenchyme. Plexuses are forming, but the nerves are not attached to their end-organs. There are now thirty-eight primitive segments or myotomes which have been formed from the mesenchyme lateral to the spinal axis. Muscle fibres are beginning to differentiate from the cells of these segments. Their ventral ends have begun to grow into the primitive abdominal wall formed by the growing around of the amnion. Condensed mesenchyme marks portions of the vertebral column. In the arm bud the mesenchyme is beginning to differentiate to form the skeletal core of condensed mesenchyme. The Wolffian ridge has increased in size and the Müllerian duct is now formed and runs parallel with the Wolffian duct. A diverticulum from the lower end of the Wolffian duct near the cloaca indicates the beginning of the permanent kidney and its duct, the ureter. On the Wolffian ridges are also seen the first traces of the sexual glands, but they are indifferent in type, and not until the fifth week can sex be determined by microscopical examination.

By the middle of the fifth week the embryo is 9 mm. in length. The amniotic sac is now so much enlarged that it is everywhere in contact with the chorion. A true umbilical cord of some length has developed by the enclosure of the entire belly stalk and yolk stalk within a tubular prolongation of the embryonic ectoderm and somatic mesoderm of the embryo. The embryonic ectoderm at the end of the cord is continuous with the extra embryonic ectoderm of the amnion, and the somatic mesoderm with that of the amnion, which is in contact with that of the chorion. So, strictly speaking, the umbilical cord is a portion of the embryo, the amnion having been carried farther and farther from the umbilicus by extension of the embryonic ectoderm. The head is as large as the rest of the body, and bent at right angles to it. Its





large size is due to the rapid growth of the brain. The three primary divisions of the brain are more marked and bent upon each other. From the forebrain the cerebral hemispheres have begun to grow. The spinal cord forms a thick-walled tube of nervous tissue. The various cranial and spinal nerves now extend some distance into the body and the motor nerves of the head and shoulder reach the premuscle masses. The rami communicantes are already present at this stage and connect with the sympathetic cord. The latter forms a continuous column of cells in front of the vertebræ, and has not as yet separated into ganglia. The sympathetic nerve cells have reached this position by migration from the ganglia of the dorsal roots.

At about this time the suprarenals commence their development and are found, at the beginning of the third month, occupying their characteristic position as a cap fitted over the head of the kidney. They rapidly acquire a very large size and at birth have their permanent volume. There is no developmental relation between the suprarenals and the kidney. The suprarenals are probably derived partially from the mesonephros and partially from the sympathetic nervous system, the latter giving rise to the medullary portion and the former to the cortical portion.

The gill clefts and arches are undergoing marked changes. From the first arch the upper and lower jaws

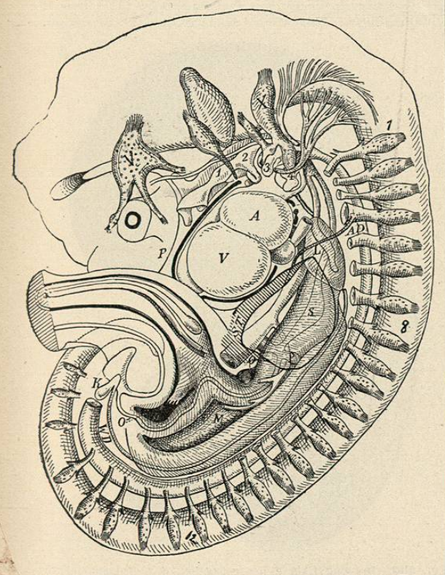


FIG. 5149.—Reconstruction of Embryo No. II., Johns Hopkins University Collection. (Enlarged 17 times.) *V* and *X*, Fifth and tenth cranial nerves; *1*, *2*, *3*, and *4*, cast of the branchial pockets; *I* and *8*, first and eighth cervical nerves, from the fourth the phrenic arises; *12*, twelfth dorsal nerve; *A*, auricle; *V*, ventricle; *L*, lung; *S*, stomach; *P*, pancreas; *W D*, Wolffian body; *K*, kidney; *M*, mesentery; *S T*, septum transversum; *O*, openings which communicate with the peritoneal cavity of the opposite side. The black line around the heart marks the pericardial cavity. (After Mall.)

are developing. From the first cleft the external auditory canal and ear drum are forming, and from the pharyngeal portion of the cleft the Eustachian tube and middle ear. The malleus and incus of the ear arise from the dorsal portion of the cartilage of the first gill arch, and from its ventral portion Meckel's cartilage. From the second arch are forming the stapes, styloid process, and the hyoid apparatus, to which later the tongue muscles become attached. The remaining arches and clefts are beginning to disappear by sinking into the depth of the neck, remaining connected with the surface, however, by a deep sinus, the so-called cervical sinus. Occasionally one may persist to adult life as a sinus or cyst. The arm and leg are enlarged and show two segments (see Fig. 5150). The skeletal system consists of a condensed mesenchymal tissue and precartilage. The premuscle masses of the head and arm are differentiating from the mesenchyme. Those of the trunk arising from the myotomes contain muscle fibres and are more advanced, while those of the limbs appear to develop *in situ* about the preskeletal mesenchyme, and show no fibrillation The heart still lies close to the mouth in the neck region. It is much changed in shape and is imperfectly four-chambered. The truncus arteriosus is undergoing division into two tubes by the formation of the aortic septum.

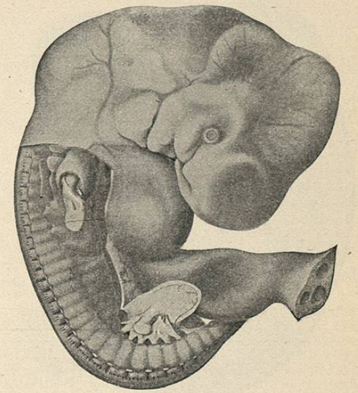

FIG. 5150.—Lateral View of a Human Embryo 9 mm. in Length and About Four and One-half Weeks Old. No. CLXIII., Johns Hopkins University Collection. (Enlarged about 8 diameters.) The areas from which the skin has been removed are drawn from reconstructions, the remaining portions from excellent photographs. The myotomes are growing into the body wall. Portions of the premuscle masses of the arm are seen and also the preskeletal tissue of the arm and leg with the beginnings of the lumbar sacral plexuses. (After Bardeen and Lewis.)

The modification of the primary arterial system is progressing rapidly. The main portions of the first two arches have disappeared, giving rise with the third arch to the common carotids and their branches. From the last arch the pulmonary arteries are developing, and from the fourth, which seems to be a combination of the fourth and fifth, develop the large aortic arch on the left side and innominate and subclavian on the right side. The latter, however, still retains its connection with the dorsal aorta, giving a condition found in reptiles. The important connection of the last arch on the left side with the aorta remains of large size, and that portion of it between the pulmonary artery and the aorta forms the ductus arteriosus, a very important fœtal structure, as it enables the venous blood from the right side of the heart to pass into the aorta without going through the lungs. The growth of the liver has also been an important factor in bringing about modifications in the venous system. With the diminution of the umbilical vesicle the extra embryonic portion of the omphalo-mesenterics disappears, but the embryonic portions of the two veins form the portal

system. Of the two umbilical veins, the left persists entire, to form the single umbilical vein of the embryo and cord. The right umbilical vein degenerates into an unimportant vein. The presence of the liver has also modified the proximal ends of the umbilical veins. The left one becomes divided into a capillary net, which

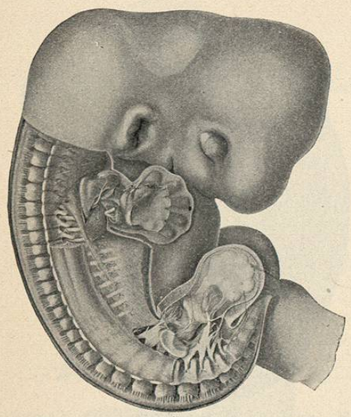

FIG. 5151.—Lateral View of a Human Embryo 11 mm. in Length and About Five Weeks Old. No. CIX., Johns Hopkins University Collection. (Enlarged about 7 diameters.) The dissected area was drawn from a reconstruction. (After Bardeen and Lewis.)

again collects into a short vein that opens into the sinus venosus. The development of the ductus venosus soon forms a channel for most of the blood carried by the umbilical vein. The proximal portion of the inferior vena cava is developed as a new structure. The distal end of this unites with the right inferior cardinal in the region where the renal arteries arise; and the caudal continuation of the cardinal from this point of union becomes the inferior portion of the vena cava. The remaining portions of the two cardinals form the azygos veins. A cross anastomosis develops from the left jugular to the right jugular, and from the common stem thus formed develops the superior vena cava. The proximal portion of the ductus Cuvieri on the left side then loses its connection with the jugular and becomes the coronary sinus of the heart.

By the time the embryo is five weeks old it has attained a length of 11 mm. (see Fig. 5151). The head is still very large and bent at right angles to the main axis of the body. The maxillary and nasal processes, which fuse at a later stage to form the upper jaw, are now more marked and approaching each other. The external nares are nearing the middle line. The external ear is represented by several small protuberances about the first cleft. The general body musculature is well advanced and has its nerve supply. The ribs and the muscles of the thorax and abdomen have grown some distance into the thin membrane, membrana reuniens, which in early stages constitutes the ventral body wall. The limbs are much enlarged and contain a skeletal core of cartilage surrounded by the developing muscles. The arm keeps about two weeks in advance of the leg in its internal differentiation. The vertebral column and ribs are formed partially in cartilage. The fourth pair of the aortic arches still persists entire and the others are modified in various ways to form the larger arteries in this region. The liver has been increasing rapidly in size, and in this embryo as in the preceding stage forms with the heart most of the large projecting abdomen and thorax. The allantois forms a long narrow tube extending from the hindgut into the umbilical cord as far as the chorion. At a later stage the umbilical portion becomes obliterated, while the portion near the hindgut enlarges into the bladder.

During the fifth week the œsophagus elongates and the stomach acquires its characteristic form, as well as an obliquely transverse position, its former left side becoming directed anteriorly and upward, and its former right side looking backward and downward. This explains the distribution of the left vagus nerve to the front of the stomach and the right to the back; for, before this twisting of the stomach began, these nerves had already reached the stomach. The connection of the yolk stalk or vitelline duct with the intestinal canal rapidly becomes less marked, and by the end of this week only a small duct attaches the yolk sac to the intestine.

During the last part of the embryonal stage and the first part of the fœtal stage there are very important shiftings or migrations of various organs in the body. That of the heart and diaphragm from the cervical region into the thoracic region is of especial interest, as other structures are dragged along with them. The large blood-vessels are pulled downward, and such nerves as the recurrent laryngeals indicate this process. Originally they passed directly from the vagus to the larynx just posterior to the fifth aortic arch, and by the migration of the heart and large blood-vessels they are brought into the position seen in the adult. The diaphragm in its descent obtains muscle tissue and its nerve in the cervical region,

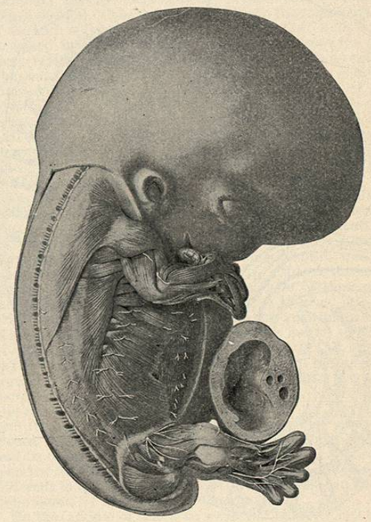

FIG. 5152.—Drawing from a Reconstruction of a Human Embryo 20 mm. in Length and About Seven Weeks Old. No. XXII., Johns Hopkins University Collection. (Enlarged about 5 diameters.) The muscular systems of the limbs and body wall are seen to be well developed. (After Bardeen and Lewis.)

and both are then carried down to the lower part of the thorax. The limbs also exhibit a migration, the arm from the cervical to the thoracic region giving the caudal inclination to the brachial plexus, which originally went straight out into the arm without this caudal inclination. The leg likewise migrates. Many individual muscles also take part in this shifting and migrating, such as the trapezius from the upper cervical region and the





latissimus dorsi from the lower cervical. The path of the nerve from its exit at the intervertebral foramen to its point of entrance into the muscle indicates the path the migrating muscle has taken, while the branching within the muscle probably indicates the direction in which the muscle has increased in size.

During the embryonal stage the yolk sac has diminished to an organ of relatively small size and importance, while the central nervous system, with its greatly enlarged anterior end, the brain, giving to the head its great prominence, becomes the predominating feature of the embyo. The head throughout most of this stage is about equal in bulk to the rest of the body of the embryo.

*Fœtal Stage.*—In an embyro seven weeks old and 20 mm. long the early fœtal features are fairly well marked. The head is nearly erect. The fusion of the maxillary and nasal processes is proceeding rapidly to form the upper jaw, and the nasal pits have approached nearer to the median line. Failure of fusion between these processes gives rise to the various forms of cleft palate and harelip. The arms and legs are much elongated, and show the three segments seen in adults. Fingers and toes are also to be distinguished. Practically every muscle of the body can now be recognized, and has also its nerve supply (see Fig. 5152). Most of the skeletal elements are present in cartilage. Portions of the skull, however, are never so represented, but ossification takes place directly from the condensed mesenchyme. The ribs have extended nearly to the mid-ventral line. The thoracic and abdominal muscles have likewise pushed farther out into the ventral wall of the body.

By the end of the second month the permanent kidney is fairly well formed and the Wolffian body, which so far in the life of the embryo has performed the function of an excretory organ, begins to lose its importance. All but the middle portion, which later forms the sexual gland, atrophies. Its duct in the male forms the vas deferens, in the female degenerates, while in the female the Müllerian ducts form the Fallopian tubes and uterus, and in the male degenerate. Thus by the end of the second month most of the organs which are found in the adult are formed. The main processes which now take place until birth are the growth and shifting about of these organs.

The *third month* establishes the human form, although the head still unduly predominates. The limbs have acquired their definite shape, and the imperfect nails are present on both fingers and toes. The external organs of generation become definitely differentiated, although they make their appearance several weeks earlier.

In the female the genital tubercle remains much less developed to form the clitoris. The genital furrow remains open to form the vestibule and the genital swellings the labia majora. The prepuce and labia minora developing from the genital folds, lie at either side of the genital sinus. The genital swellings in the male when they develop into the scrotum have layers identical with those of the abdominal wall, as seen in the following scheme:

| *Abdominal Walls.* | *Scrotum.* |
|---|---|
| Integument. | Integument. |
| Superficial fascia. | Dartos. |
| External oblique muscle. | Intercolumnar fascia. |
| Internal oblique muscle. | Cremasteric. |
| Transversalis muscle. | Infundibuliform fascia. |
| Peritoneum. | Tunica vaginalis. |

The tunica vaginalis lines the sac, communicating above with the peritoneal cavity; and into this sac later the testicle descends. The anterior end of the ureter now reaches the neighborhood of the suprarenal where it ends in the kidney, which consists of about eighteen lobes, one for each group of tubules connected with the ureter. This lobulation persists until after birth. The suprarenals now fit caplike over the anterior end of the kidney. At the end of the month the fœtus weighs about 120 gm. (3¼ ounces), and measures about 5 cm. (2 inches) in length.

During the *fourth month* hairs devoid of pigment appear on the scalp and other parts of the body, which is now covered with firmer skin of a rosy hue. The eyelids, nostrils, and lips are closed. The anus opens, and the coils of intestine, which before extended into the umbilical cord, now lie entirely within the abdominal cavity. The point of emergence of the umbilical cord lies low down close to the pubes. The head forms about one-fourth of the entire body. The bones of the skull while ossifying are still widely separated. The sexual distinctions of the external genital organs are well defined. By the end of this month the fœtus weighs about 230 gm. (7½ ounces), and measures about 10 cm. (4½ inches) in length.

During the *fifth month* the lower extremities become longer than the arms, nails are well formed, and hairs are more plentiful, but devoid of color. The fœtal movements are distinctly felt by the mother. The sudoriparous glands arise during this month as solid cylindrical outgrowths from the primary ridges of the epidermis into the dermis. Later they become coiled and a lumen appears. The heart and liver share with the head in the undue preponderance which these parts present. At the end of this month the fœtus measures 20 cm. (8 inches) in length, and weighs about 500 gm. (1 pound).

During the *sixth month* the surface presents many wrinkles and is of a dirty reddish hue; the sebaceous coating, the vernix caseosa, begins to appear. This whitish substance is composed of shed surface epithelium, mingled with the secretions of the sebaceous glands; its primary function seems to be the protection of the integument from maceration by the amniotic fluid. The eyebrows and eyelashes begin to grow. The length of the fœtus by the end of this month is about 30 cm. (12 inches), and its weight about 1,000 gm. (2 pounds).

*The Seventh Month.*—The formation of fat causes an appearance of greater plumpness, although the surface is still somewhat wrinkled. The hairs are longer, about 5 mm. in length. The eyelids are now permanently open. The liver is still relatively large; the testicles have descended as far as, or even into, the inguinal canals. Children born at the end of this month may live. The fœtus measures at the end of this period about 37 cm. long (15 inches), and weighs about 1,500 gm. (3 pounds).

*The Eighth Month.*—This and the ninth month complete the fœtal period. The chief changes are great increase in weight, as by the end of the eighth month the fœtus weighs from 2 to 2.5 kgm. (4 to 5 pounds) and measures about 42 cm. in length. The scalp is well supplied with hair, and the finger nails almost reach the finger tips. The lanugo or embryonal down begins to disappear. The subcutaneous fat has increased considerably, giving a more rounded form to the body.

*The Ninth Month.*—During this month there is a relatively large increase in weight, from 2 to 2.5 kgm. to about 3 or 3.5 kgm. (6 to 7 pounds), while the increase in length is only from about 42 to 50 cm. (20 inches). The skin is less highly colored and the lanugo has almost entirely disappeared. The testicles have descended into the scrotum; in the female the labia majora are in contact. Centres of ossification usually appear in the epiphysis at the lower end of the femur, and often in the upper epiphyses of the tibia and humerus.

*Warren Harmon Lewis.*

**GIGANTISM, GENERAL.**—The word giant is derived from the Middle English "geant," the equivalent of the French "géant," which may be traced back to the Greek γίγας.

Very early in the world's history we meet with references to huge beings of supernatural strength. Even before the flood, in the story of Noah, we are informed that "there were giants in the land in those days," and there are stray allusions to giants, Emmim and Anakim, in the accounts of the early Jewish conquests, in the sight of whom the people were "as grasshoppers," to use