

firmed their equality. The most important uses of cod-liver oil, moreover, are observed in a series of cases whose pathology is as obscure as the action of the remedy—such as the “scrofulous” diseases, whether glandular or ulcerative, chronic rheumatism, etc. It must in these cases act in some gentle and peculiar way upon the pathological processes, tending to return them to normal physiological ones, and in this respect is to be classed in the heterogeneous number of medicines called alteratives. Its uses have been mostly noticed in the preceding sentence but may be recapitulated a little more in detail. It is given, more than in any other disease, in phthisis pulmonalis. The long, wasting course of this complaint calls very distinctly for remedies that will prevent waste on the one hand, and promote nutrition on the other. Alcohol and cod-liver oil may be regarded as types of these two therapeutic agents, and experience has long ago shown them to be two of the most generally useful things that can be given. Neither is a specific, neither appears in the slightest degree to change the character of the poison lying at the root of the complaint, but both retard the loss of flesh and strength, each in its peculiar way. The oil is often given alone in the early stages of the disease, and generally with advantage, as alcohol in small doses more readily loses its effect. It is also frequently combined with malt extracts, the hypophosphites, iron, iodine, and other alteratives or aids to nutrition. Besides the general action, the oil has an undoubted favorable effect upon the chronic bronchitis and catarrhal pneumonia present, and it is therefore of value in the cough of consumption. It is also of great service in subacute and chronic idiopathic bronchitis (“colds in the chest”). In the persisting colds of infants and the aged, with a good deal of weakness, it has no equal. In chronic catarrh of various mucous membranes, ear, nose, vagina, urethra, etc., especially if attended with, or depending upon, debility, it is sometimes useful. In hip disease, and similar degenerations of other joints; in glandular abscesses, in chronic ulcers; in short, wherever there are waste, emaciation, and thinness of blood, it is to be tried. A peculiar method of its employment in the fisheries is in half-tumblerful doses, to break up an acute cold.

The great obstacles to the fullest use of cod-liver oil are its taste, which is so repugnant to many that they can scarcely take it, and its liability to disagree with the stomach, and either to produce nausea and vomiting, or, what is equally disastrous, to impair the appetite and so to more than undo all its possible benefit. The different methods of administration mentioned below sometimes overcome this, but most important is the exclusive use of the carefully prepared and nearly tasteless oils referred to above.

ADMINISTRATION.—The dose of the oil is from 12 to 30 c.c. (3 iij. ad 3 i.) two or three times a day. If it can be taken clear it may be so given; the taste, even of the best, is somewhat repulsive, and becomes more so toward the last of the bottle in summer, as it rather easily becomes rancid. It is best, therefore, to purchase only a small quantity at a time, and to keep it as cool as possible. The taste may be disguised by means similar to those used with other oils (e.g., *Custor Oil*, q.v.): rinsing the mouth thoroughly with whiskey, spirit of lemon, peppermint, or some such pungent vehicle; swallowing the oil at once, and again rinsing the mouth, is as good as any of the extemporaneous means used for this purpose. The liquor, if one prefers to do so, may be spit out. Large elastic capsules containing 6 or 8 gm. (3 i. to iij.) are made, but not much used, on account of their expensiveness. The following combination, when liquor is to be given with it, is a well-known favorite:

Cod-liver oil.....	50 parts.
Whiskey.....	35 “
Comp. tincture of lavender.....	15 “

It must be thoroughly shaken for every dose, as the oil immediately begins to separate. The lavender is add-

ed only as a flavor, and may be omitted. All oils appear to be less offensive to children than to adults.

Another method is to mix the oil with about an equal part of one of the syrupy malt extracts; the mixture does not separate so readily as the above. Its taste is well borne by children. Then there are the numerous emulsions made and advertised everywhere. They come under one of the following classes: First, mucilage emulsions, of which the following is an example:

Cod-liver oil.....	50 parts.
Oil of wintergreen.....	2 “
Mucilage of tragacanth.....	15 “
Water of orange flowers, sufficient to make.....	100 “

A little “knack” is required to make it well. The mucilage is the emulsifying agent, and the oil should be added to it very slowly, and most thoroughly stirred until it is divided into invisible particles, before the water is added. The oil of wintergreen is only a flavor, which may be varied to suit. This makes a good, permanent mixture of about the consistence and appearance of thick cream. Instead of tragacanth, mucilage of acacia, about twice the amount, or a decoction of Irish moss, may be used.

Second, egg emulsions: These are made like salad dressings, by using the yolk of egg as the suspending ingredient. The following is a good one:

Cod-liver oil.....	50 parts.
Oil of sassafras.....	3 “
Chloroform.....	2 “
Glycerite of yolk of egg.....	10 “
Rose water, enough to make.....	100 “

Here the oil and the egg must first be “emulsified,” when the other ingredients may be added—the water last. This is a thinner liquid than the preceding.

The pancreatic emulsions are nominally made by emulsifying with pancreatin, and are theoretically the most perfect of all, but are practically attended with some difficulty; the ordinary “pancreatin” of the shops will not make a good result, and of those claimed to be so produced some are made by means of added alkalies, others by the fresh pancreas itself, and some do not even contain any cod-liver oil at all. Considerable care has to be exercised with all proprietary preparations, to see that the percentage of oil is not deficient, as the drawing out of the oil is a favorite method of rendering the preparation palatable. An ounce or two of perfectly sweet pancreas, chopped fine and mixed thoroughly with a gallon of oil, will, it is said, suffice, when the oil is filtered off and mixed with water, to emulsify it perfectly. Like the other emulsions, it can be flavored to taste. Iodine, iron, the hypophosphites, and other suitable additions can be made to all of them, but alcohol and tinctures are incompatible with the mucilaginous ones. If the patient would chew a bit of raw smoked herring before taking the oil, its taste would not be noticed.

The “wines,” and similar preparations, of cod-liver oil, under whatever fanciful names, are utterly unreliable and are to be classed as unscientific.

*Morchuol* is an alcoholic extract of the oil. Very little is yielded by fresh sweet oils, and the yield increases with the degree of putridity of the article. It is therefore to be regarded as essentially a putrefactive product, and whatever useful properties it may claim to possess, it need not be used for the effects of the oil.

Cod liver oil is often given by inunction, with benefit, especially to marasmic babies. W. P. Bolles.

**CÆLOM, COMPARATIVE DEVELOPMENT OF THE.**—In all vertebrates the primitive intestine forms two sets of diverticula which are destined to become permanent tissues, (1) one toward the medullary groove which forms the chorda dorsalis, and (2) two lateral diverticula which form the body cavities. These latter are later on

subdivided into pleural, pericardial, peritoneal, and other cavities. A detailed description of the theory of the formation may be found in Balfour's work, in Hertwig's "Embryologie," and in Minot's "Human Embryology."

the cross piece, thus reversing the relation of the vascular system to the lymphatic, or rather coelomic system. The uprights of the **H** fall to the outside of the body and are swallowed up in the formation of the amnion. Fig. 1392 is a cross-section from a chick at this stage, and shows that the greater portion of the cavity is now on the outside of the body. The cross-piece of the **H** is immediately on the ventral side of the heart, and forms the cavity of the pericardium by the heart growing into it. Its communication with the remaining coelomic cavity is later on cut off in higher vertebrates, while in lower vertebrates it may remain open.

According to Budge two diverticula grow from the cross-piece, one on either side of the chorda, toward the tail of the body, and form the primitive pleuro-peritoneal cavities. Budge's paper was published from fragmentary notes after his death, and I am certain that the above statement is not correct. Professor His has placed before me Budge's specimens, which I think show conclusively that the interpretation of his injections is not

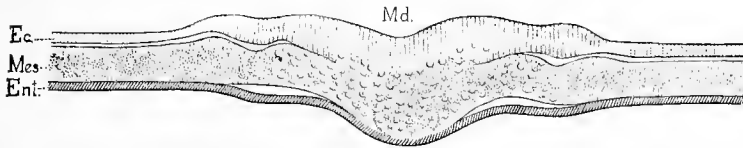


FIG. 1390.—Transverse Section through the Posterior Region of a Chick, with Six Pairs of Myotomes. (After Waldeyer, from Minot.) *Ec.*, ectoderm; *Mes.*, mesoderm; *Ent.*, entoderm; *Md.*, medullary groove.

When sections are made through very young embryos of higher vertebrates, just after the blastodermic membranes are well formed, a solid mesoderm is found, as shown in Fig. 1390. Although in lower vertebrates the mesoderm is produced by lateral diverticula from the entoderm, which are hollow from the beginning, in higher vertebrates the mesoderm is first laid down as a solid mass of cells. Soon the cells of the mesoderm on either side of the chorda divide into two layers, the somatopleure and the splanchnopleure (Fig. 1391, *Som.* and *Spl.*). From the two lateral cavities between these two layers the peritoneal cavity is formed.

The more accurate early formation of the pleuro-peritoneal cavity, in its relation to the other organs, we find carefully studied by Budge, who by means of injection followed it in the chick. With a fine hypodermic syringe he filled the various spaces of the coelom as they appeared, thus showing very clearly the extent of this cavity in various embryos. The splanchnopleure, according to Budge, may be split into two layers, a dorsal or lymphatic and a ventral or vascular. As the first blood-vessels are formed, lymph vessels appear on their dorsal side, which flow together to form networks and accompany the primitive veins to the axial part of the germinal area. Here the lymphatics form two spaces, one on either side of the body, which are soon united by a bridge, or rather duct, on the ventral side of the heart. Therefore, in birds at least, the primitive pleuro-peritoneal cavity appears somewhat as an **H**, the uprights of which are on either side of the body, and the cross-piece on the oral side of the sinus venosus. In its further development the sinus venosus grows to the dorsal side of

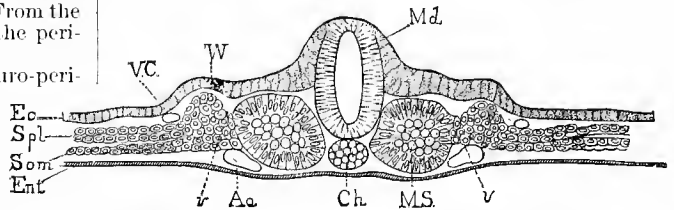


FIG. 1391.—Transverse Section of a Chick of the Second Day. (After Waldeyer, from Minot.) *Som.*, somatic mesoderm; *Spl.*, splanchnic mesoderm; *Ec.*, ectoderm; *Ent.*, entoderm; *V.C.*, vein; *W.*, Wolffian duct; *Md.*, medullary canal; *Ao.*, aorta; *Ch.*, chorda; *MS.*, myotome.

correct. Most of his injections were made into the amniotic fold as the amnion was forming. Cross-sections of embryos show that on either side there is a large cavity (Fig. 1392, *Som.*) which communicates freely with the pleuro-peritoneal (*Coe.*). Before the amnion is complete we have lateral cavities on either side of the body, communicating with each other only by means of the cross-piece on the ventral side of the heart. This is the freest portion of the communication, which also communicates most freely with the pleuro-peritoneal cavities

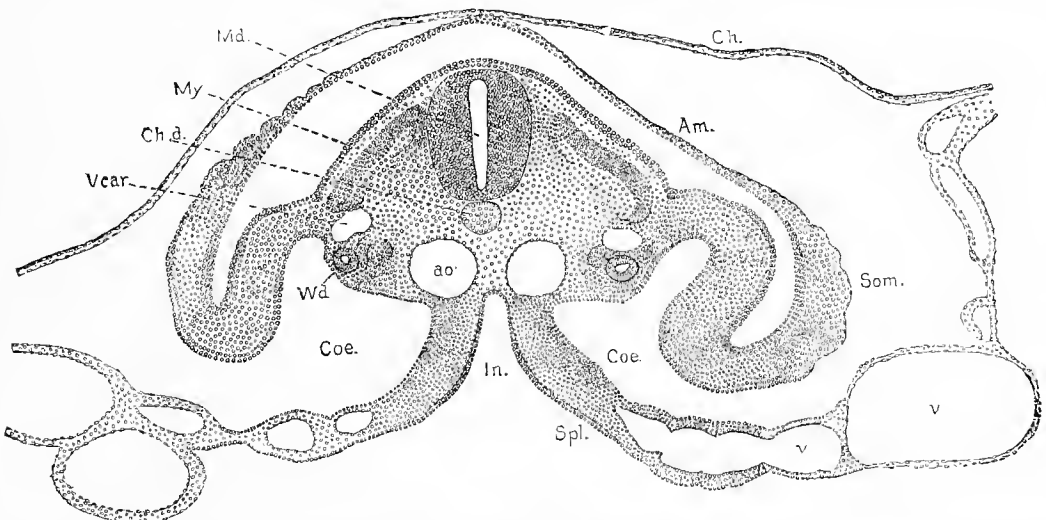


FIG. 1392.—Section through the Body of a Chick of the Third Day. (After Minot.) *Ch.*, Chorion; *Am.*, amnion; *Som.*, somatopleure; *v.*, blood-vessels; *Coe.*, coelom; *Spl.*, splanchnopleure; *In.*, intestine; *do.*, aorta; *Wd.*, Wolffian duct; *Vcar.*, vena cardinalis; *Ch.d.*, chorda dorsalis; *My.*, myotome; *Md.*, medullary canal.

(Fig. 1392, *Coe*). In many embryos the injection passed from the cross-piece into the pleuro-peritoneal cavity and would not extend out into the amniotic portion of the cœlom, thus making it appear

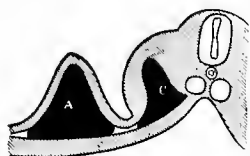


Fig. 1393.—Section of a Chick, to show that the Pleuro-peritoneal Cavity is cut off of the Cœlom, leaving a Portion in the Amnion. The embryo has been injected, but the fluid of the two cavities has not flowed together.

arise as independent diverticula, we must say that they are pinched off from the cœlom cavity after the amnion is formed.

The cœlom cavities which are so intimately united with the lymphatic system unite and again divide into sections, thus forming the various compartments of the visceral cavity of higher vertebrates. In all of the vertebrates the heart, as it is developing, hangs into the ventral transverse portion of the cavity, or the primitive pericardial cavity. This is shown diagrammatically in Figs. 1394, 1395, 1396, and 1397, *P*.

Figs. 1394 to 1397 show the very early condition of things; the cœlom cavities are united by the cross-piece or the primitive pericardial cavity. The dotted lines (Fig. 1394) mark what portion of the cavity is taken up in the amnion (*A.P.*), while the remaining middle portion (*P.P.*) becomes the pleuro-peritoneal. Figs 1395, 1396 and 1397 show in succession the more advanced stages. In higher vertebrates the pericardial cavity is completely closed off from the pleuro-peritoneal, but in elasmobranch fishes a communication between them exists in the adult. The separation of the pericardial cavity from the pleuro-peritoneal is aided materially by the heart growing over to the ventral side of the body, as shown in Fig. 1398. Sections through various parts of the same embryo, from which Fig. 1398 is taken, are shown in Figs. 1399 to 1404. In none of these sections is the communication between the pericardial and pleural cavities shown, but sections nearer the head contain it.

A cast of the cœlom cavity of this same embryo is given in Fig. 1405. There is only a slight communication between the pericardial cavity and the pleuro-peritoneal. The groove in the cast marked *M* indicates the position

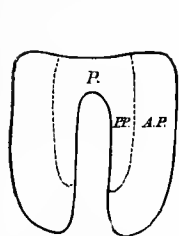


FIG. 1394.

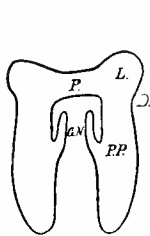


FIG. 1395.

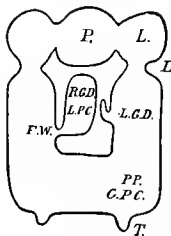


FIG. 1396.

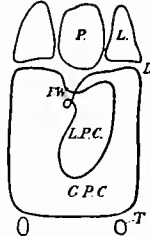


FIG. 1397.

FIGS. 1394, 1395, 1396, and 1397.—Diagrams to Show the Development of the Cœlom Cavity. *P.P.*, Pleuro-peritoneal cavity; *A.P.*, portion of the cœlom cavity swallowed up in the amnion; *P.*, pericardial cavity; *L.*, pleural cavity; *G.N.*, gastric diverticula, right and left; *D.*, position of the diaphragm; *L.G.D.*, left gastric diverticulum; *R.G.D.*, right gastric diverticulum or lesser peritoneal cavity; *F.W.*, foramen of Winslow; *G.P.C.*, greater peritoneal cavity; *T.*, tunica vaginalis.

of the simple mesentery. Its relation to these organs is better shown in the sections (Figs. 1399 to 1404). Fig. 1406 represents a section through a chick at an earlier stage of development, in which the duct communicating between the pericardial and pleural cavities is cut longitudinally.

Thus it is seen that the heart first grows into the primitive pericardial cavity, which is nothing else than the cross-piece of the *H* already spoken of. The pericardial cœlom grows larger and larger, at the same time hanging as it were over the ventral side of the body, and is soon connected with the pleuro-peritoneal cavity only by two ducts, which later on become closed in the higher vertebrates.

In early embryos the veins enter the heart behind, and not in front, as is the case in higher animals. The heart in its whole development undergoes a half-revolution, and in this way the twists, etc., are formed. Before the pericardial cavity is shut off from the pleuro-peritoneal

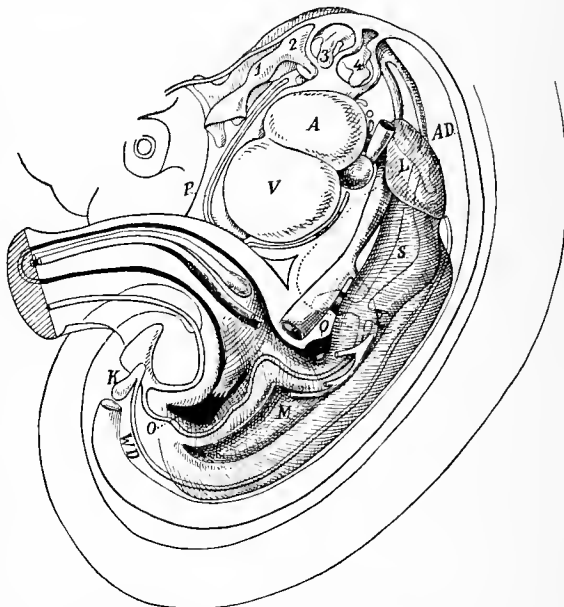


Fig. 1398.—Reconstruction of a Human Embryo. (Enlarged 16 times, viewed from the left side.) *P.*, Pericardial cavity; 1, 2, 3, and 4, branchial pockets; *A.D.*, descending aorta; *A.*, auricle; *V.*, ventricle; *L.*, lung; *S.*, stomach; *P.*, pancreas; *M.*, mesentery; *K.*, kidney; *W.D.*, Wolffian duct; *O.*, openings through which the right and left peritoneal cavities communicate.

the large vessels enter from behind. They are embedded in a mass of mesoblastic tissue which is encroaching upon the pleuro-peritoneal cavity, and has been termed by His the transverse septum. This, by its further growth, forms the diaphragm of higher animals (Figs. 1395, 1396, 1397). In lower animals only a rudimentary diaphragm, or none at all, is present. By the formation of the diaphragm the pleuro-peritoneal cavity is divided into a smaller anterior portion, the pleural, and a larger posterior portion, the peritoneal. The lungs now grow into the pleural, as shown in an early stage in Fig. 1406, and in a somewhat later stage in Fig. 1399.

The peritoneal cavity is at first composed of two distinct portions, one on either side of the intestine, which in lower animals is quite a straight tube, lying in the middle line of the body. Soon, however, two communications are found between the two halves, one in front and one behind the omphalo-mesenteric vessels (Fig. 1399, *O*). These openings enlarge more and more as the intestine becomes more convoluted, and soon flow together, severing completely the omphalo-mesenteric vessels and duct. A por-

tion of the duct may, however, remain in connection with the small intestine to form the diverticulum of Meckel.

As the organs grow the peritoneal cavity surrounds

A section of the chick at this stage is given in Fig. 1406, *G. D.*, making the lesser cavities, or, as they may better be termed, the right and left gastric diverticula. At the beginning of the fourth day the gastric diverticula be-

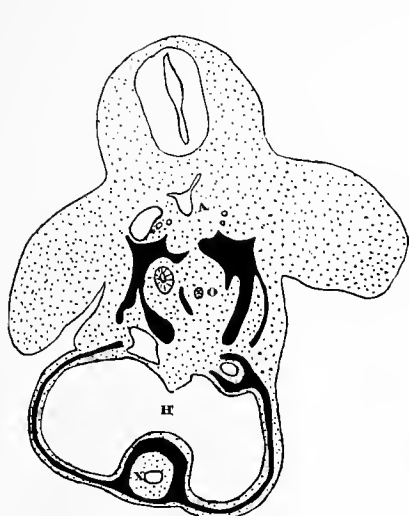


FIG. 1399.

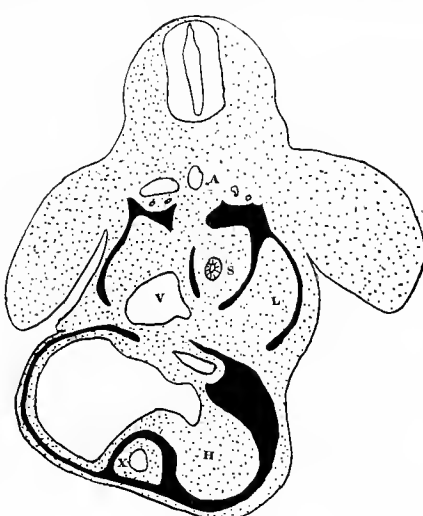


FIG. 1400.

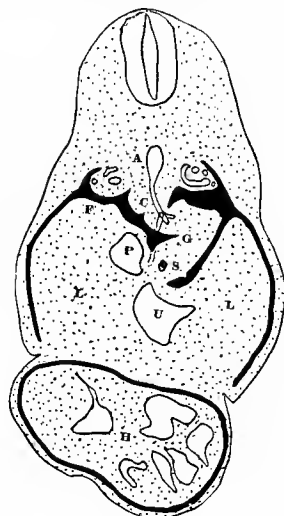


FIG. 1401.

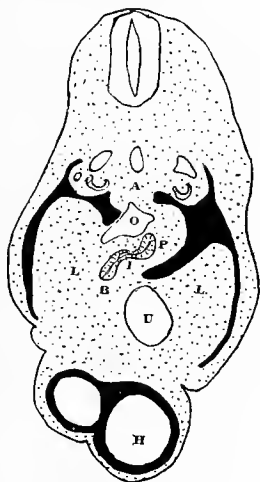


FIG. 1402.

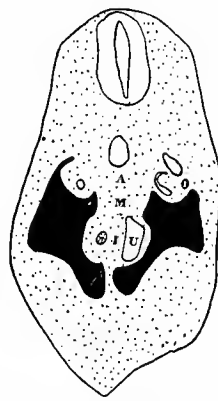


FIG. 1403.

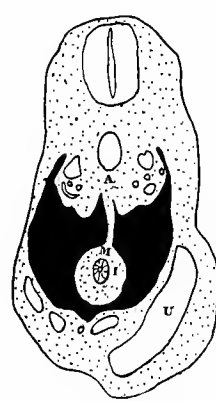


FIG. 1404.

FIGS. 1399-1404.—Sections through a Human Embryo Twenty-six Days Old. ( $\times 25$  times.) O., Esophagus; S., stomach; L., intestine; P., pancreas; B., bile duct; A., aorta; C., coeliac axis; G., right gastric diverticulum; F., foramen of Winslow; M., mesentery; L., liver; P., portal vein; U., umbilical vein; H., heart; X., bulb of the aorta. The pleuro-peritoneal cavity is colored black throughout.

them more or less completely, until the condition of things as seen in the adult is produced.

In lower vertebrates the peritoneal cavity remains quite simple, but in reptiles, birds, and mammals it may become quite complex. Especially is this true regarding the birds, in which these divisions are greatly complicated by the growth of the air sacs from the lungs.

The first trace of the lesser peritoneal cavity is seen in the reptiles. Ravn has shown that in the lizard there are two diverticula from the peritoneum, one on either side of the stomach. From the one on the right side the lesser peritoneal cavity of mammals arises. In general the relation of the lesser peritoneal cavity to the greater is much like what is shown in Fig. 1395. In the true sense of the term there is no lesser cavity, but only the two pouches. These are already present in the embryo, and in the adult they retain their embryonic appearance.

In birds the conditions become more complex. They appear in the chick during the third day of incubation.

come larger, and on transverse section semicircular. Figs. 1407 and 1408 are from casts of the cavities about the stomach of a chick of eighty-eight hours. The right is larger than the left and is markedly cup-shaped, and connects by means of a narrowed opening with the right pleuro-peritoneal cavity (Fig. 1407, *F. W.*). The two together enclose the proventriculus. On account of the relations of the opening of the right diverticulum with the blood-vessels, stomach, and liver, and also for reasons which find their basis in comparative anatomy and embryology, the opening can be nothing else than the foramen of Winslow.

On the left side the gastric diverticulum is much smaller, and in older embryos it disappears altogether.

In a chick of five days and sixteen hours (Fig. 1409) the right gastric diverticulum has about doubled all its dimensions, while the embryonic foramen of Winslow has become much more sharply defined. At this time the liver has greatly increased in size, the right lobe

being larger than the left, both lying anterior to the foramen of Winslow. The original position of the liver being behind the foramen, its rotation necessarily carries the hepatic artery and the portal vein around the fora-

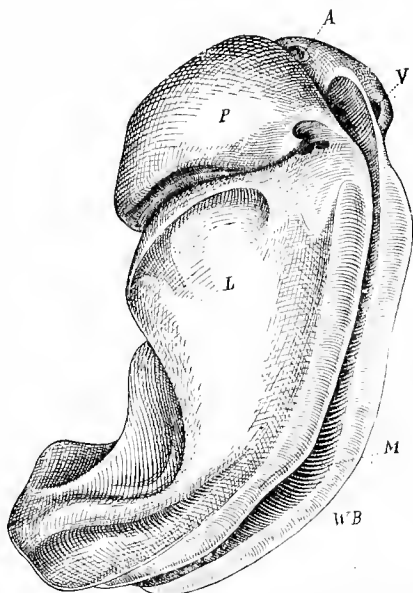


FIG. 1405.—Corrosion Preparation of the Pleuro-peritoneal Cavity of an Embryo Twenty-six Days Old. ( $\times 22$  times.) P., Pericardial cavity; A., opening for the aorta; V., opening for the vein; L., space over the liver; M., slit for mesentery; W.B., space for Wolffian body.

men of Winslow—its adult position. With the growth of the gizzard a space extends from behind the right gastric diverticulum along the dorsal side of this organ, and marks the beginning of the cavity of the great omentum (O.). Nearly the whole of the right diverticulum now lies on the left side of the body; the same position is held by the proventriculus and the gizzard.

The domestic fowl possesses three peritoneal cavities, completely separated from one another, and from one of them the lesser cavity arises. The communication is by means of the foramen of Winslow. After the anterior abdominal walls are removed, two ventral cavities are exposed, separated from each other by a vertical longitudinal septum. Into each of the cavities hangs a lobe of the liver, while into the left the ventral surface of the gizzard projects. On the dorsal side of the liver there are, on each side, three air sacs—an anterior, a middle, and a posterior. The middle one is the smallest, and the posterior the largest, extending as it does throughout the posterior portion of the abdominal cavity. Each sac communicates by means of a special opening directly into the lungs. By allowing the sacs to collapse we find that a very distinct membrane projects backward from the gizzard and cuts off the portion of the abdominal cavity containing the intestines. This is the "pseudo-epiploön" described by Weldon and followed more extensively by Bed-

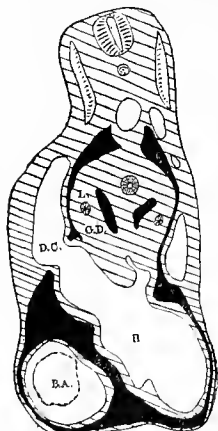


FIG. 1406.—Section through the Region of the Heart of a Chick of Seventy Hours. ( $\times 35$  times.) The section strikes the oral end of the gastric diverticulum (G.D.), and the tips of the pulmonary buds, L. A few sections deeper the gastric diverticula communicate with the pleuro-peritoneal cavity. H., heart; D.C., ductus cœli; B.A., bulbus aortæ.

derd. A similar membrane is present in the crocodile. In all respects, this membrane is situated in the same position as is the epiploön in mammals, with the difference that it is adherent to the abdominal walls along its free border. On the dorsal side of the gizzard the air sacs fill all the space, thus closing off the communication between the cavity in which the intestines lie and the ventral cavities.

When the anterior and middle air sacs on the right side

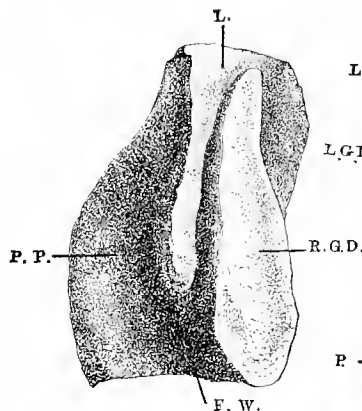


FIG. 1407.

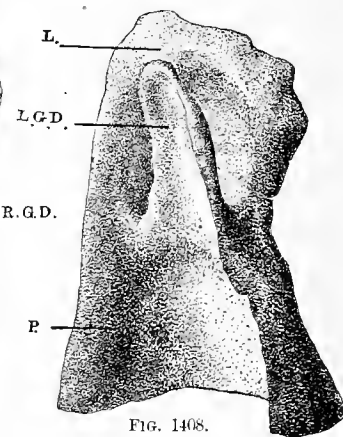


FIG. 1408.

FIGS. 1407 and 1408.—Corrosion Preparations of the Right and Left Gastric Diverticula of a Chick Eighty-eight Hours Old. ( $\times 33$  times.) P.P., Pleuro-peritoneal cavity; R.G.D., right gastric diverticulum; L.G.D., left gastric diverticulum; L., position of lung; F.W., foramen of Winslow.

are separated from the posterior sac on the same side, a slit is shown which extends anterior and dorsal to the hepatic veins. Here it communicates by means of a round opening, about 1 cm. in diameter, with a large cavity lying on the median and dorsal side of the proventriculus and extending to the spleen. The cavity does not extend on the dorsal side of the gizzard. In all respects it corresponds with the right gastric diverticulum of embryos and with the lesser peritoneal cavity of mammals.

The relation of the embryonic omentum with the "pseudo-epiploön" is as yet unknown. However, I

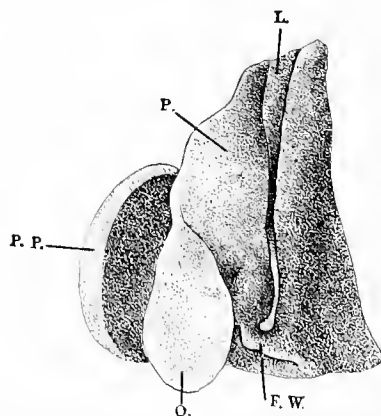


FIG. 1409.—Corrosion Preparation of the Right Gastric Diverticulum from a Chick of One Hundred and Thirty-six Hours. ( $\times 15$  times.) P.P., Pleuro-peritoneal cavity; F.W., foramen of Winslow; L., position of right lung; P., position of proventriculus; O., omental cavity (position of gizzard).

think it probable that the one is changed into the other, and that the "pseudo-epiploön" will prove to be the true epiploön homologous with the same in mammals. We

must imagine only the embryonic omentum attaching itself on the sides of the abdomen followed by a loss of the epiploönic cavity. A subsequent growth of the air sacs backward from the dorsal side of the stomach will produce the condition found in the adult.

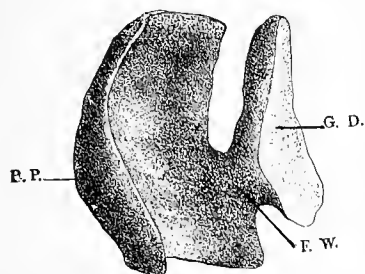


FIG. 1410.—Corrosion Preparation of the Gastric Diverticulum of a Human Embryo, 7 mm. long. ( $\times 35$  times.) P.P., Pleuro-peritoneal cavity; F.W., foramen of Winslow; G.D., gastric diverticulum.

ed black and the position of the section can be made out by the organs which are cut across in the section. A cast of the cavity is shown in Fig. 1405. The portion of the cavity on the right side of the stomach and the liver is shown in Fig. 1410, which is taken from a cast also. Figs. 1399, 1400, and 1401 show sections through the gastric diverticulum of Fig. 1410, Fig. 1401 being through the foramen of Winslow.

The general form of the cavities is shown in Fig. 1410, which is taken from a reconstruction of a human embryo. The peritoneal cavity surrounds the Wolffian body, intestine, omphalo-mesenteric vessels, stomach, liver, and lungs, with the addition of the right gastric diverticulum.

In lower mammals, according to Ravn, there are two diverticula; so the symmetrical arrangement of these cavities in reptiles, is still indicated in the mammals. It is so insignificant, however, that we need not take it into consideration.

The fate of the right gastric diverticulum of mammals has been studied in the dog, and it has been found that it is converted directly into the lesser peritoneal cavity, much as is shown in Figs. 1396 and 1397. In a dog's embryo, 6 mm. long, the diverticulum is much like what it is in the human embryo of about the same size (Fig. 1410). A dog embryo, 10 mm. long, shows a picture more advanced, much like what is seen in the chick of five days (Fig. 1409). In a later stage (Fig. 1411) the stomach has been twisted about, holding in great part the adult

In mammalian embryos, while the stomach is still upright, only one gastric diverticulum is found. It is on the right side in Figs. 1399 to 1401, which are taken from a young human embryo. In each drawing the cœlomic cavity is colored

Fig. 1411 shows the lesser peritoneal cavity as a cast stuck in behind the stomach. The intestine is composed of two loops, one from the stomach, extending into the pelvis, and the other from the cæcum into the umbilical cord. The rapid growth of the large intestine has thrown the cæcum as high as the stomach and to the right of it. The fold of mesogastrium coming from the dorsal side of the stomach passes over the large intestine to form the omentum (Fig. 1411, O.). The general shape of the lesser

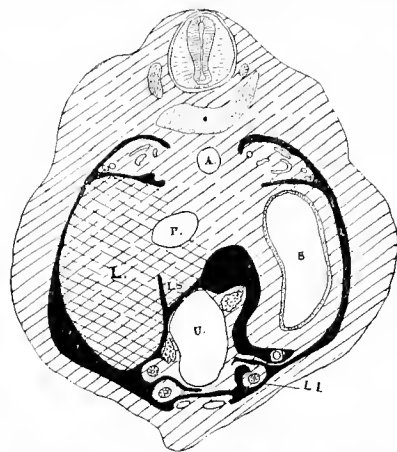


FIG. 1412.—Section through the Foramen of Winslow and Lobus Spigelii of a Dog, 13.5 mm. long. ( $\times 36$  times.) A., Aorta; S., stomach; P., portal vein; U., umbilical vein; L.S., lobus Spigelii; O., omental cavity; L.I., large intestine.

peritoneal cavity is shown in transverse section in Fig. 1412, which can be compared with Fig. 1401. The S-shaped loop of intestine is cut across three times, and the lesser peritoneal cavity with the foramen of Winslow is shown throughout its whole extent.

The omentum from now on rapidly grows over the whole ventral wall of the abdominal cavity, and in man adheres to the colon as first described by Meckel.

A résumé of the comparative development of the cœlom of the embryo is given in Figs. 1394 to 1397.

Franklin P. Mall.

**CÆLOM, HUMAN, DEVELOPMENT OF THE.**—Unfortunately, there are no data regarding the beginning of the cœlom in the human embryo, and in all probability none will ever be found. The smallest human described until recently is that described by Reichert.<sup>1</sup> It was obtained from a woman who had committed suicide, on account of pregnancy, forty-one days after the beginning of the last menstrual period. It was therefore presumably about thirteen days old. This ovum, which is pictured in every text-book, was  $5.5 \times 3.3$  mm. in diameter, was surrounded by a zone of villi leaving two poles bare, and contained in its interior a mass of cells measuring  $1.5 \times 1.75$  mm. All the space between this inner mass and the chorion is the cœlom, and regarding its origin we can no more than speculate.

During the last few years five other human ova, about as large as Reichert's, have been cut into sections, thus permitting a more careful study of their contents.<sup>2</sup> The dimensions and approximate ages of these embryos are given in the table in the first column of the following page.

It is noticeable that in the embryos just mentioned the size of the whole egg does not correspond with the size of the embryo, nor with its age. I do not think that this great variation in the size of the chorionic vesicle is altogether due to the method of hardening the specimen. Just at this time the growth of the chorion is precocious, as is also the case in the dog,<sup>3</sup> rabbit,<sup>4</sup> and monkey.<sup>5</sup>

The papers by Bischoff and by Selenka are worthy of the most careful study by every embryologist, and I take the liberty of rearranging some of Bischoff's data on the

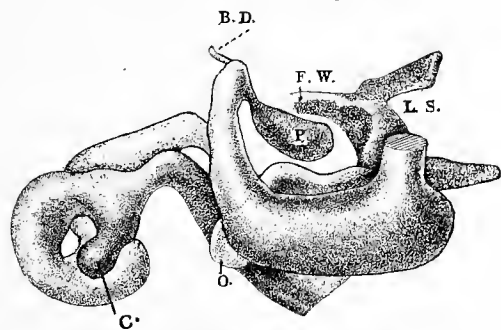


FIG. 1411.—Corrosion Preparation of the Stomach, Intestines, and Lesser Peritoneal Cavity of a Dog, 13.5 mm. Long. Viewed from the Left Side. ( $\times 15$  times.) The lesser peritoneal cavity has been filled with metal. B.D., Bile duct; P., pancreas; C., cæcum; O., omentum; F.W., foramen of Winslow; L.S., position of lobus Spigelii.

position. The liver, which before lay on the ventral side of the stomach, now lies in front, and to a great extent on the dorsal side of it. A model of these parts from a 10-mm. embryo, simply rotated to throw the stomach away from the mouth, gives the condition of things as they exist in the embryo 13 mm. long.

TABLE OF YOUNG HUMAN OVA.

Observer.	Diameter of embryonic vesicle, millimetres.	Diameter of ovum, millimetres.	Time between first lapsed period and abortion.
Peters .....	0.19 × ?	0.3 × 1.5	
Siegenbeck van Henkelom .....	.325 × ?	5.5 × 4.5	
Mall (No. XI.) .....	1.5 × 1.0	10 × 7	13 days.
Reichert .....	1.75 × 1.5	5.5 × 3.3	14 "
Von Spee (v. H.) .....	1.84 × 1.083	6 × 4.5	12* "
Von Spee (Gle.) .....	2 × 2	10 × 8.5	12* "
Mall (No. XII.) .....	2.1 × 2.1	18 × 8	13 "
His (Lgr.) .....	2.15 × 2	15 × 12.5	12 "
Von Spee .....	2.69 × 3	15 × 14	14 "
Janosik .....	3 × 4	8	15 "

\* These are all of the authentic young human ova I can collect from the literature giving all of their measurements as well as the menstrual history of the mother. In both of von Spee's cases the time between the abortion and the end of the last period is given; in embryo v. H. the time is given as "exactly five weeks," while in embryo Gle. "five weeks" is given. If we estimate the duration of menstruation as five days and its frequency twenty-eight days, then the time between the first lapsed period and the abortion is twelve days, as I have given it in the table.

development of the dog. His observations are very extensive, and give us the basis for our present ideas of the passage of the ovum into the uterine tube after fertilization. Unfortunately, they were made before the time of sectioning specimens, yet they are more complete than most researches relating to this subject published since his time.

The portion I tabulate relates to the size of the embryonic mass or vesicle, the size of the ovum, and its approximate age. As far as I have been able to determine, these data taken from the dog are still the most important ones with which we can compare the human ovum. Embryologists are accustomed to state that the age of a human ovum is to be reckoned from the beginning of the first lapsed period, and I think that Bischoff's observation upon the size and growth of the dog's ovum corroborates this view. He found that the ova left the ovary during the rutting period, but the exact date could never be determined. Neither did the time of copulation determine the ovulation. As a rule, it took twenty-four hours or less after copulation for the spermatozoa to reach the ovary, and about the same time is required for the ovum to reach the beginning of the uterine tube after ovulation. So if ovulation and copulation took place at the same time, fertilization of the ovum could not take place until twenty-four hours later.

Bischoff in his tables often rates the age of an ovum from the first or from the last copulation, or from the beginning or from the end of the rutting period. I have attempted to tabulate his specimens from all four of these dates, but in none of the attempts did the size of the ova correspond with their respective dates. Often eggs of a given date were smaller and developed to a less degree than ova presumably younger. After much difficulty I finally constructed a table in which the size of the ovum and its age correspond. A number of the ova published by Bischoff were obtained from the same animal by removing half of the uterus at one time and the remaining half the next day. In each half a number of ova were found, and they were usually of about the same stage of development. By this method of procedure it is possible to determine very accurately the growth of the ovum from one stage to one twenty-four hours later. So, by gradually plodding through the specimens published by Bischoff, it was possible for me to correct his data completely. It is remarkable, as the table shows, how slowly the development takes place in the early stages, and about ten days are required before the ovum is 1 mm. in diameter. On the fifteenth or sixteenth day the ovum is about as large as the human ovum described by Reichert (see table).

Similar results can also be obtained from the various papers published on the rabbit's embryo. Its development, however, is considerably more rapid than the dog's as the period of gestation is but thirty days.

TABLE OF AGE AND SIZE OF THE DOG'S OVUM.  
(Compiled from Bischoff.)

Age.	Diameter of ovum, millimetres.	Diameter of embryonic mass, millimetres.	Stage.
1 day .....	0.15	....	1 cell.
2 days .....	.14	....	2 cells.
3 " .....	.14	....	4 "
4 " .....	.16	....	12 "
5 " .....	.16	....	64 "
6 " .....	.18	....	Mulberry.
7 " .....	.20	....	"
8 " .....	.21	....	"
9 " .....	.28	....	"
10 " .....	.30	.07	"
11 " .....	1.	.16	"
12 " .....	2.	.24	"
13 " .....	3.	.43	"
14 " .....	4.	.5	"
15 " .....	5.	1.	"
16 " .....	5.	2.	"
16½ " .....	6.	3.	"

It has been somewhat difficult to compile this table, as Bischoff's measurements are all given in Paris lines. My measurements are taken in great part from his figures, and I think that these are very accurate.

Recently Selenka has given some of his results relating to the development of the monkey. The most valuable specimen relating to the early development of higher animals was unfortunately lost, but its age and dimensions are preserved for us, and are of value in the determination of the age of human ova. The ovum came from a monkey kept in confinement which was killed eight days after copulation. If we estimate one or two days required before fertilization, this ovum cannot be over seven days old. This suggests that the early stage of this variety of monkey is developed more rapidly than that of the dog.

DEVELOPMENT OF THE MONKEY.

	Diameter of ovum, millimetres.	Diameter of embryonic vesicle, millimetres.
Semnopithecus maurus .....	1.5	0.3 *
Semnopithecus pruinosis .....	6	.5
Cercocebus cynomolgus .....	5	.5
Cercocebus cynomolgus .....	10	2.4 †

The pictures Selenka gives indicate that the development of a monkey's ovum is identical with that of the human ovum. At any rate, the few specimens Selenka publishes give results which are equal to the great number of specimens of human ova which have been published. This only indicates that many of the interesting problems relating to early human development will probably be solved by the study of the monkey's ovum. There is but little doubt now that young monkeys' ova will soon be obtained for study.

\* Not an embryonic vesicle, but only a disc.  
† Neurenteric canal present.

MATERIAL EMPLOYED.

During the last few years I have obtained a number of young human embryos from physicians in different portions of the United States, and to them I am under all obligation for the present study as well as for some others which are to follow. Nearly all of the specimens which I give in a table are well preserved, and a number of them are preserved excellently. All of the specimens were stained in alum carmine, and with the exception of Nos. XVII., XLIII., and LVII. were cut transversely. These three were cut into sagittal sections.

All of the specimens were hardened in alcohol, the value of which method I have repeatedly emphasized to my friends, and do continue to emphasize to those who may preserve specimens for my use in the future.\*

\* Embryologists usually recommended that human embryos should be hardened by placing them in dilute alcohol and then gradually increasing the strength of the alcohol. It has been my experience that by this treatment the specimen is injured by maceration due to the

LIST OF EMBRYOS STUDIED.

No.	LENGTH OF MILLIMETRES.		From whom obtained.
	V. B.*	N. B.	
XI.....	.....	.....	Dr. Kittredge, Nashua, N. H.
XII.....	2.1	.....	Dr. Ellis, Elkton, Md.
III.....	2.2	.....	Prof. His, Leipsic, Germany.
XIX.....	5.	4.5	Dr. Williams, Baltimore, Md.
XVIII.....	7	7	Dr. Douglas, Nashville, Tenn.
II.....	3	7	Dr. C. O. Miller, Baltimore, Md.
IV.....	.....	7	Dr. Williams, Baltimore, Md.
XLIII.....	15	13	Dr. Booker, Baltimore, Md.
VIII.....	17	14	Dr. Ritter, Brooklyn, N. Y.
IX.....	17	14	Dr. Eycleshymer, Chicago, Ill.
V.....	18	17	Dr. Kittredge, Nashua, N. H.
XLII.....	18	15	Dr. Wills, Los Angeles, Cal.
XVII.....	18	16	Dr. Cottrell, Louisville, Ky.
XXVIII.....	19	18	Dr. Sewall, Denver, Col.
VII.....	19.5	18	Dr. Booker, Baltimore, Md.
XXII.....	20	18	Dr. Snively, Waynesboro, Penn.
LVII.....	23	20	Dr. Howard, Cleveland, Ohio.
VI.....	24	.....	Dr. C. O. Miller, Baltimore, Md.
X.....	24	20	Dr. C. S. Miller, Madison, Wis.
XLV.....	28	19	Dr. Douglas, Nashville, Tenn.
XXXIV.....	80	60	Dr. Ellis, Elkton, Md.
XLVIII.....	130	110	Dr. Wilson, Worcester, Mass.

\* V. B. and N. B. indicate the length of the embryo measured from the vertex to the breech and from the nape of the neck to the breech, respectively.

Nearly all of the embryos were drawn or photographed to scale and then carefully cut into sections from 10 to 50  $\mu$  thick. I find that for purposes of reconstruction it is a mistake to cut the sections very thin. Yet in small specimens, as Nos. XI. and XII., the specimens were cut thin to permit of careful cytological studies also. In most of the specimens photographs or an additional series of sections were made of the chorion and amnion in order to study the variation of these structures.

Embryos XI.,<sup>6</sup> XII., and II.<sup>7</sup> were completely reconstructed in wax by the method of Born. Nos. IX., VI., and X. were reconstructed in part by Born's method and finished by His's method of reconstruction. The abdominal viscera of Nos. VI., IX., X., XXXIV., XLV., and XLVIII. were modelled by Born's method.<sup>8</sup>

The mechanical portion of reconstruction has been simplified to a great extent by a special apparatus used in the Anatomical Laboratory,<sup>9</sup> which enables us to employ a modeller. The sections are projected upon a screen, to which the wax plate is attached. By working in a dark room with this apparatus it is easy to direct a modeller to draw the outlines accurately. He can then cut them out, and all that remains to be done is to pile the pieces and then blend them.

### THE CÆLOM IN YOUNG OVA.

All of the young human ova which have been described contain within them a cavity, lined with mesoderm; this is the cœlom, bounded by the somatopleure on the outside and by the splanchnopleure on the inside. This arrangement, as shown by a number of diagrams by recent authors, is very unlike the appearance of the blastodermic membranes of many of the lower mammals, and it is necessary, therefore, that we should revise our

weak alcohol. A few years ago I emphasized the fact that the whole ovum should be placed in a large quantity of strong alcohol as soon as possible. It should be banded as little as possible before hardening it, thus preventing mechanical injury. By leaving the ovum closed the alcohol must first penetrate the chorionic and amniotic fluids before it reaches the embryo, and thus, without placing the embryo first in weak alcohol, it naturally passes through the successive dilutions of alcohol before it is completely hardened.

It is very injurious to these delicate specimens to be wrapped in cotton before they are sent by mail or express. A perfect method is to place the preserved specimen in a bottle filled completely with alcohol, thus imitating the condition of a *fœtus in utero*. If there is no air or cotton in the bottle containing the embryo it is almost impossible to injure the embryo by shaking it.

Since I have emphasized this method of preparation (Johns Hopkins Hospital Bulletin, 1893), I have obtained a number of specimens excellent in every respect. These specimens are not distorted, nor macerated, nor shrunk.

conception of the formation of the amnion in the human embryo.<sup>10</sup>

The ova recently published by Peters and by Graf Spee indicate that the amnion must be formed very early, and, since it is completed before the medullary grooves begin, we must admit now that it is formed much the same as it is in many rodents, *i.e.*, by apparent inversion of the membrane. When Bischoff<sup>11</sup> first described inversion of the membrane in guinea-pigs it seemed like a paradox, but, since the comparative methods of study have been introduced, inversion only means that the amnion is completed before the medullary groove begins to form. This alteration of the development of the amnion and the medullary groove makes the body of the embryo develop on a concave surface instead of on a convex one, thus apparently making the embryo inverted, as is the case in the guinea-pig.

Closely associated with inversion of the blastodermic membrane is the formation of an additional layer of cells, discovered by Rauber,<sup>12</sup> the importance of which has been emphasized by Selenka and others. Rauber's layer is so marked in the rabbit that it was at first believed to be the true ectoderm. The fate of Rauber's layer has not been sufficiently studied to interpret it completely, and our ideas regarding it will not improbably require some revision. In many rodents Rauber's layer becomes markedly thickened on one side of the ovum, forming a support, or *Träger*, for the ovum. The relation of Rauber's layer to the *Träger* is shown beautifully by Selenka<sup>13</sup> on Plate XVI. of his monograph.

The question which interests us here is whether the inversion of the blastodermic membrane as well as the discovery of Rauber's layer aids us in advancing a theory of the development of the germ layers of the human embryo, and thus in turn to explain the large cœlom as found in all of the earliest human ova. I realize fully that any such effort will not be final, yet I believe that it will aid us to understand better the relation of the membranes as found in the human ovum.

In looking over the illustrations of the development of animals closely related to man, one is struck with the similarity of the arrangement of the membranes to those described for the human ovum by Peters and by Graf Spee. One must compare only plates XXXV.-XXXVIII. of Selenka's<sup>14</sup> paper with the two plates accompanying Graf Spee's<sup>15</sup> to be convinced that the early development of monkeys is almost identical with that of man. Yet Selenka's researches on monkeys do not help us a great deal; they only show us that the monkey's development is like that of man. In monkeys we have also the precocious chorion and the early amnion and the large cœlom between the umbilical vesicle and the chorion. The marked difference is that the amnion is attached to the chorion along its dorsal side, while in the human embryo this is only the case along the posterior end of the amnion. The attachment of the amnion along the chorion suggests that the embryonic plate separated from the exterior of the ovum along this point, as Selenka thinks he observed in a very young ovum only 1.5 mm. in diameter. Unfortunately, the most valuable specimen was injured in its preparation,<sup>16</sup> and Selenka did not trust himself to give any illustrations of it.

With the amnion attached at its dorsal end to the chorion, we understand why the entodermal end of the allantois must grow around an angle to reach the chorion (Selenka, Plate XXXVII., Fig. 5). Somewhat the same arrangement has been described by Graf Spee<sup>17</sup> in his embryo Gle., but the curve is by no means as marked, indicating that the attachment of the embryo to the chorion is along its posterior end, as shown by His<sup>18</sup> in his well-known diagram of the formation of the amnion.

Regarding the very early stages of monkeys and man it is better that we make comparisons with animals most nearly related to them, and now we have careful studies of the very early stages of Chiroptera at our disposal. I believe that Selenka's<sup>19</sup> study of the development of *Pteropus edulis* gives us the key for the comparison of the formation of the blastodermic membranes in mam-

mals. Recent investigations by Duval<sup>20</sup> on different families of Chiroptera appear to confirm the work of Selenka on Pteropus.

In order to illustrate these points more clearly I have made diagrams of three of Selenka's figures of Pteropus.

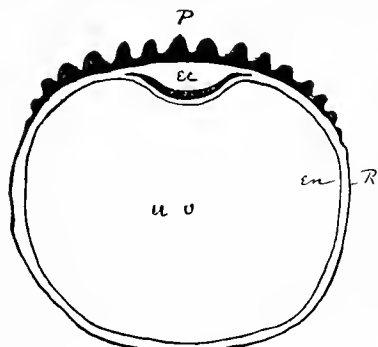


FIG. 1413.

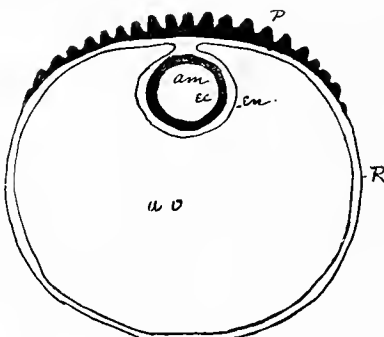


FIG. 1414.

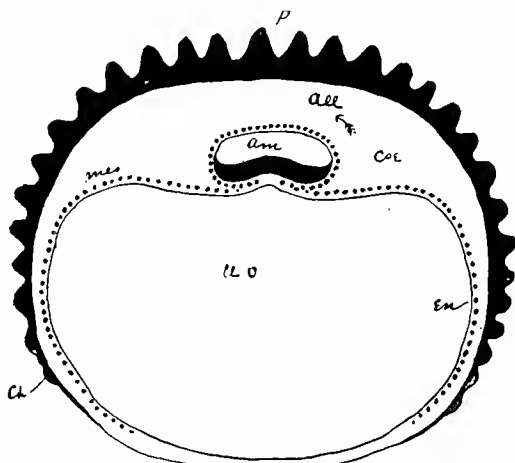


FIG. 1415.

FIGS. 1413-1415.—Diagrams of the Development of Pteropus Edulis, after Selenka. FIG. 1413 is Selenka's Fig. 2; FIG. 1414, Selenka's Fig. 5; FIG. 1415, Selenka's Fig. 9. R, Rauber's layer; P, placenta; ec, ectoderm; en, entoderm; ch, chorion; am, amnion; uv, umbilical vesicle; mes, mesoderm; coe, coelom; all, allantois, with the arrow indicating the direction of its future development.

Fig. 1413 is from an ovum covered completely with two layers of cells, between which at one pole of the egg there is a mass of scattered cells destined to become the permanent ectoderm. The outer layer of cells has a tendency to grow into the form of villi over the embryonic disc, while on the opposite side of the egg it is composed of but a single layer of cells. Since this outer layer remains well separated from the body of the embryo throughout its development, and since it holds the same position to the egg that Rauber's layer does in the rodents, I believe it to be identical with Rauber's layer, and shall speak of it as such. According to Duval this Rauber's layer disappears over the embryonic disc in the Chiroptera much as in the development of the rabbit and the field mouse. This does not necessarily contradict Selenka's observations on Pteropus, for the house mouse begins to develop like the field mouse, but continues during the early stages in the same manner as Pteropus does.

In the next stage the ectoderm has been converted into a hollow mass of cells, Fig.

1414, rather by a process of absorption than by an invagination, as I have expressed it in the diagram. The entoderm lines the whole interior of the egg, and surrounds the ectoderm of the amniotic cavity. The ectoderm of the exterior of the egg, Rauber's layer, is again thickened over the embryonic mass to form the placenta, as Selenka calls it, or the *Träger*, if we were discussing rodent embryology.

In the next stage, as expressed in Fig. 1415, the mesoderm is beginning to form, and has extended completely over the amnion and partly over the umbilical vesicle. The entoderm has retracted itself and touches the ectoderm; only the chorda dorsalis is yet to form. Between the amnion and the placenta, or the *Träger* portion of Rauber's layer, there is a marked space, and the mesoderm does not come in contact with it. The allantois grows as a bag into this space and attaches itself to the thickened part of the ectoderm, as shown by Göhre<sup>21</sup> in his figures. In the Fig. 3 accompanying Göhre's paper he shows the vesicular allantois attached to the support of the chorion (black portion of my Fig. 1415) leaving on either side of the embryo a cœlom. The allantois carries the mesoderm and vessels to the villi of the chorion, and these in turn are embedded in the decidua of the uterus. In so doing the ectoderm of the chorion receives a second layer of epithelium, and I believe that this must account for the two layers of epithelium we have on the chorionic villi of the human ovum. There has been much written on the subject of the double layer of epithelial cells of the human chorion, and I think that a glance at Göhre's Figs. 3 and 4, on Pteropus, as well as at Selenka's Figs. 11 and 12 (Plate XXXV.) and Fig. 6 (Plate XXXVII.) on monkeys, will decide this question more definitely than all the many discussions on the human chorion put together have done.

Having now selected from Selenka diagrams and descriptions of the development of the germ layers of Pteropus, it is easier for me to give a plausible explanation of the development of the human ovum.



FIG. 1416.

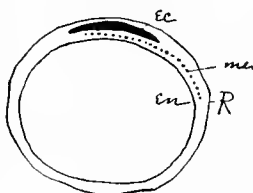


FIG. 1417.

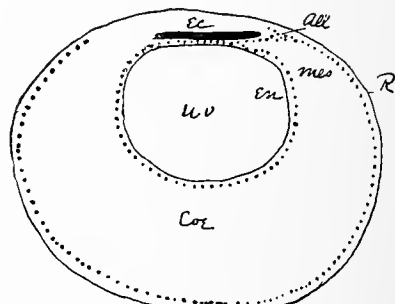


FIG. 1418.

FIGS. 1416 to 1418.—Hypothetical Stages of the Early Development of the Human Ovum. R, Rauber's layer; ec, ectoderm; en, entoderm; mes, mesoderm; uv, umbilical vesicle; coe, coelom; all, position of allantois.

tion of the beginning of the cœlom in the human embryo. If the diagram I have given in Fig. 1415 is compared with Selenka's Figs. 5 and 11 (Plate XXXV.) and Fig. 5 (Plate XXXVII.) of the monkey, as well as with the sections of young human ova published by Graf Spee<sup>22</sup> and by myself,<sup>23</sup> one is struck with the great similarity of the two groups of figures.

Fig. 1426, given further on, is a diagrammatic outline of a longitudinal section of a young human embryo published recently by Graf Spee. It is the one marked v. II. in the table of young human ova given in the beginning of this paper. When, now, this section is compared with the transverse section of Pteropus, in Fig. 1415, the only marked difference is that the umbilical vesicle in Pteropus has retracted, in order to make the arrangement of the membranes as given for the human embryo in Fig. 1426.

In order to make the connection complete, I give hypothetical stages in Figs. 1416, 1417, and 1418. Fig. 1416 represents the human ovum in the two-layer stage. The outer layer, or Rauber's layer, is complete as in the rodents and in Pteropus. The inner layer, or entoderm, is also complete. Between the two is the embryonic shield, or ectoderm of the future embryo. The next figure, 1417,

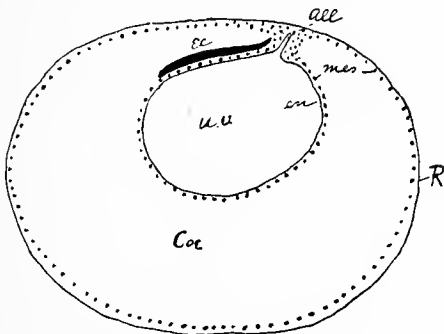


FIG. 1419.—Diagram of a Pathological Ovum which Represents an Early Hypothetical Stage.

shows the beginning of the mesoderm developing toward the tail end of the embryo, as this is the position of the primitive streak, and as the head fold of the amnion in many embryos is often invested only with ectoderm and entoderm. A stage later, Fig. 1418, finds the mesoderm enveloping the umbilical vesicle completely, and also partly lining the outer layer, *R*, of the ovum. The cavity between the two is the cœlom. At the tail end of the embryonic disc the mesoderm of the somatopleure and splanchnopleure are still united, and mark the place of the formation of the rudimentary allantois.

Having carried the development of the human ovum to this stage by means of hypothetical stages, based upon the development of Pteropus, I can now continue the description of the development based upon observation.

**Abnormal Ova.**—Teratologists are accustomed to view a group of abnormal states as arrested development, and in recent years a number of abnormal human ova have been studied by His,<sup>24</sup> by Giacomini,<sup>25</sup> and others. Frequently in the development of an ovum the embryo is destroyed completely, or, according to Giacomini, may wander out of the ovum. In these cases the ova are aborted. Frequently, however, a portion of the embryo is not developed, or it dies and the remaining portion develops for a time, and then the ovum is aborted. I have now in my collection a beautiful example of an ovum of apparently normal structure, the interior of which is lined completely with an amnion, and in place of an embryo there is only an umbilical cord. The ovum was aborted fifty-four days after the first lapsed period, and was 30 mm. in diameter. The cord was 2 mm. in diameter and 9 mm. long. Its embryonic end seemed to be cut off abruptly, and was covered with a small mass

of round cells. I give this example only to show that the embryo may be entirely wanting with a perfect cord and membranes.

TABLE OF VESICULAR FORMS OF PATHOLOGICAL EMBRYOS.

No.	DIMENSIONS OF—		Time between last period and abortion.	
	Ovum.	Vesicle.		
XIII.....	8 × 7	1 × 6 × 6	.....	Amnion formed.
CXXXIV...	17 × 11	9 × 3	33 days.	Amnion partly formed
XI.....	10 × 7	1.5 × 1	41 "	" "
LXXXVII...	24 × 16 × 9	2.5	42 "	Partial amnion.
LVIII.....	20 × 18 × 12	6	71 "	" "
LXXVIII...	36 × 33 × 13	1 × 6	87 "	Multiple amnion.
XXIV.....	21 × 16 × 5	2.6	.....	No amnion.
XIV.....	30	1.5	.....	" "
CXXIII...	17 × 14	2 × 1.5	37 days.	" "
XXI.....	40 × 30	5.5 × 3.5	" "	" "
CXXX.....	15 × 10 × 6	4 × 3 × 1.5	14 days.	" "
CXLVII...	30 × 27 × 20	1	" "	" "
CXLIII.....	.....	25 × 10	" "	" "

A large per cent. of young ova which come into the embryologist's hands are abnormal. According to Professor His' experience over half of the ova less than three weeks old are abnormal, while of those of four and five weeks one-quarter are abnormal. In my collection the per cent. of abnormal embryos is not as high. No. XIII. is His' Embryo XLIV., which is frequently described in the books as a normal specimen, but which unfortunately is an abnormal one. My interpretations of the vesicular forms<sup>26</sup> is that the fibrous degeneration overtook the embryonic vesicle after it had reached the stage of Graf Spee's embryo v. H., my Fig. 1426.

Nos. XXI. and LVIII. came to me as perfect specimens both having been hardened unopened, the first in strong formalin and the second in strong alcohol. No. XXI. was still enclosed in its decidua, and appeared to be a normal specimen until it had been cut into serial sections. The embryonic vesicle proved to be very large, and was composed throughout of two layers, an inner one giving all the appearance of the entoderm and an outer giving all the appearance of the mesoderm of the umbilical vesicle of young embryos. The mesodermal layer contained within it islands of blood cells, as are also present in normal specimens. The whole vesicle was connected to the chorion with a mass of mesodermal cells somewhat as shown in the diagrammatic Fig. 1419. The chorion and decidua appeared to be normal.

No. LVIII. showed considerable change in the mesoderm of the vesicle and chorion, giving somewhat the appearance of fibroid degeneration rich in cells. The chorion was attached to the vesicle by a strong pedicle, as shown in Fig. 1419. The vesicle itself was composed of two layers, an inner and continuous one composed of one layer of cells, and an outer and thickened layer appearing like the mesoderm of the chorion. There were no indications of blood islands. In addition to these two layers there was a third layer fairly well marked near the pedicle and between the vesicle and the chorion. With the exception of the allantois canal, Fig. 1419 is a diagram of this specimen.

Giacomini<sup>27</sup> has described a number of similar vesicles, and he expressly states that the vesicles had the structure of the umbilical vesicle, but that there was no trace of the amnion present in any of them. A number of other vesicular forms have been described, and in general they all appear much like the two specimens I have given.

I do not think that it is rash to assert that these vesicles represent an arrested development of an earlier stage, which, due to impaired nutrition, or whatever it might have been, simply allowed the embryonic vesicle to keep on expanding. That this expansion can keep on is already shown in the simple enlargement of the chorion after the embryo is distorted or wanting altogether. We have in these specimens a thin chorion with atrophic villi, and why can we not have an expanded and atrophic

embryonic vesicle if its development is impaired? In this way I view specimen No. LVIII. It represents a much earlier stage, which has simply expanded and was

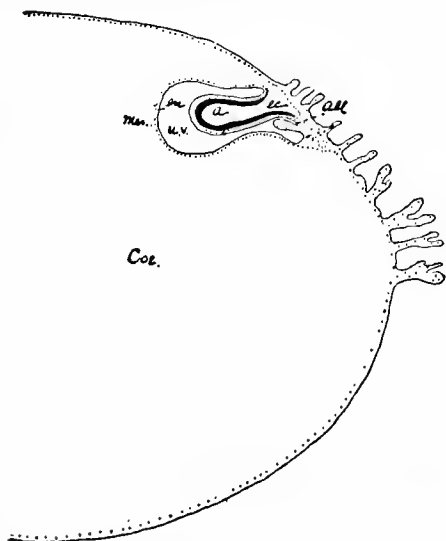


FIG. 1420.—Diagrammatic Section of Half of the Human Ovum No. XI. Enlarged 10 times. The villi are drawn only on the upper side. *cc*, Ectoderm; *en*, entoderm; *mes*, mesoderm; *uv*, umbilical vesicle; *coc*, cœlom; *all*, allantois; *a*, amnion.

ultimately aborted. In No. LVIII, the embryonic vesicle must have ceased its further development a week or so before the abortion, about the time the cœlom was beginning to develop. At that time the fibrous degeneration enclosed the embryonic vesicle as well as extended around the whole chorion into all of its villi. This, then, arrested the further development of the embryo, and the embryonic vesicle simply continued to expand.

This idea is further strengthened by another ovum whose history I published on several occasions several years ago.<sup>28</sup> The specimen is a good one, having been preserved fairly well, and it has every indication of being normal. Since the specimen has been in my hands I have studied it over and over again, have photographed many of the sections, and have reconstructed it. At first it was very difficult for me to interpret it, but finally it appears to me that something definite can be said regarding the arrangement of the membranes and their relation to older as well as to the pathological and presumably younger specimens.\*

*Embryo No. XI.*—"The woman, from whom the specimen was obtained, is twenty-five years old, menstruates regularly every four weeks, the periods lasting from four to five days. She gave birth to a child September 19th, 1892, and had the first recurrence of menstruation December 19th. The second period followed on January 25th, and was very profuse; it lasted until February 1st. The next period should have begun about February 22d, but on account of its lapsing the patient concluded that she was pregnant, and called at my office

a few days later. I did not examine her, but asked her to remain quiet and await developments as I thought possible that she might be pregnant. On the evening of March 1st she fell and sprained herself, and during the same night had a scanty flow. The flow recurred each day, and on the 7th of March she passed the ovum. It was kept in a cool, moist cloth for twenty hours, and when it came into my hands was at once placed in a large quantity of sixty-per-cent. alcohol."†

The ovum is very large for its age, having a long diameter of 10 mm. and a short diameter of 7 mm. It is covered with villi only around its greatest circumference, having two spots without villi, as was the case with Reichert's ovum. The villi of the chorion are from 0.5 to 0.7 mm. long and are branched.

Upon opening the chorion it was found that the germinal vesicle was situated just opposite the edge of the zone of villi. About it was much coagulated albumen, magma reticulare, which I did not remove, and therefore could not obtain good camera drawings. The portion of the chorion to which the vesicle was attached was cut out and stained with alum cochineal and cleared in oil, but even after this treatment it was impossible to obtain any clear picture. The specimen was next embedded in paraffin and cut into sections 10  $\mu$  thick. The series proved to be perfect. From the sections a reconstruction was made in wax, and the accompanying Fig. 1420 is a sagittal section of it.

The dimensions of the different portions of the vesicle are as follows:

Diameter of stem.....	0.4 mm.
Length of stem.....	0.4 "
Length of vesicle.....	1.5 "
Width of vesicle.....	1.0 "
Length of invagination.....	0.8 "
Width of invagination.....	0.5 "
Diameter of opening of invagination.....	0.03 "

The sections and reconstruction show that the embryonic vesicle is attached to the chorion by means of a stem. The greater part of the vesicle itself is composed of two layers, ectoderm and mesoderm. In the neighborhood of the embryonic stem there is a third outer layer which shows all of the characteristics of the ecto-

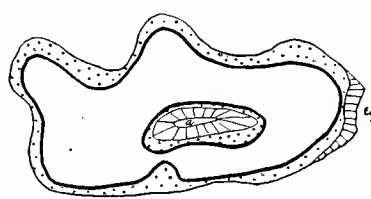


FIG. 1421.

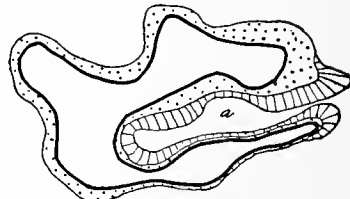


FIG. 1422.

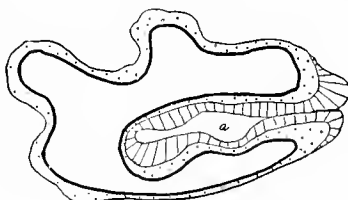


FIG. 1423.

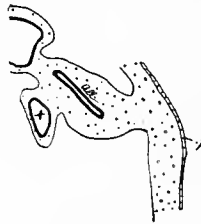


FIG. 1424.

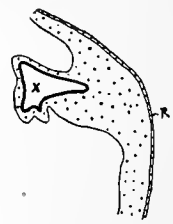


FIG. 1425.

FIGS. 1421-1425.—Sections Nos. 43, 53, 68, 80, and 89 through the Embryonic Vesicle of Embryo No. XI. Enlarged 33 times. The entoderm is a heavy line, the ectoderm is striated, and the mesoderm dotted. *a*, Amnion; *X*, cavity of the umbilical vesicle extending into the stem of the vesicle; *R*, Rauber's layer as the ectoderm of the chorion.

derm. Just beside the attachment of the vesicle to the stem there is a sharp, deep and narrow invagination of all three embryonic membranes, which I have interpreted as the formation of the amnion. The arrangement of

\* An extensive description of the pathology of early human embryos is given by me in the "Contributions to the Medical Sciences," Johns Hopkins Hospital Reports, vol. ix., Baltimore, 1900.

† Letter from Dr. Kittredge, April 27th, 1893.

this invagination is fully pictured in Figs. 1421 to 1425. Within the stem there is a sharply defined allantois which communicates with the cavity of the vesicle just below the cavity of the ectoderm. The ectodermal plate of the invagination is very broad but not of equal thickness throughout its whole extent. It extends to the outside of the vesicle and ends quite abruptly in the neighborhood of the stem. The blood-vessels of the mesodermal layer extend to the stem but do not enter it, nor are there any blood-vessels in the chorion.

Since the first publication of this specimen, embryos both normal and pathological have been studied, all of which indicate more and more that this specimen must belong to the pathological class. The other pathological specimens of my collection as well as the perfect normal specimen described recently by Peters all speak for this conclusion. Yet the presence of all three blastodermic membranes in No. XI., with blood islands in the mesoderm, and an allantois in the embryonic stem, indicate that this specimen cannot be far from the normal, but represents the earliest changes in the blastodermic membranes in a specimen of the Peters stage under pathological conditions.

The next stages in the development of the embryonic vesicle are taken from Graf Spee, and they are of importance to elucidate the changes which take place preparatory to the formation of the body cavity. In Fig. 1426, which represents the younger embryo, the amnion is still surrounded completely with mesoderm, as in embryo No. XI., represented in Fig. 1420. The mesoderm crosses the median line, as the sections given by Graf Spee<sup>29</sup> show. The dorsal side of the amnion is covered with a very thick layer of mesoderm, as the closure of the amnion in embryo No. XI. would suggest.

From the stage represented in Fig. 1426 it is easy to pass to the older embryo represented in Fig. 1427. Now the body of the embryo is well marked, the neural folds are just beginning, and the neurenteric canal has just been formed. The chorda dorsalis is not yet separated from the entoderm, and the blood islands encircle completely the umbilical vesicle and have nearly reached the head end of the body of the embryo preparatory to the formation of the heart.

In my earlier studies I was inclined to believe that embryo XI., Fig. 1420, to be normal, but the recent publication of a normal human ovum younger than Reichert's, by Peters, makes this view improbable. Now we must view the opening in the amnion in XI. as a secondary rupture, for in the Peters embryo, which is so much smaller than any yet seen, and the amnion is closed. Furthermore, Selenka has just described a small ovum of the gibbon in which the amnion is still connected with the epithelial covering of the chorion and almost communicates with the exterior of the ovum. These observations practically set to rest this difficult question. The amnion arises directly from the exterior of the ovum, closes at once, and then the embryo forms within it. There is, therefore, apparent inversion of the germ layers.

In these two ova described by von Spee, the cœlom is much of the same form it was in embryo No. XI., Fig. 1420, and therefore needs no special comment. Yet around the head end of embryo Gle. there is a marked accumulation of mesoderm into which the heart is to grow. In the illustrations of the section of this embryo Graf Spee<sup>30</sup> pictures spaces in the mesoderm which he believes to be portions of the body cavity of the embryo, that is, the cavity of the muscle plates, pericardial cavity or peritoneal cavity. It is impossible to determine definitely which portion of the body cavity these spaces represent, but I do not feel inclined to believe that what he marks pericardial cavity in Fig. 1435 can possibly represent it, for we are to look for the pericardial cavity between the junction of the pharynx and umbilical vesicle

and the head end of the embryo. This portion of the embryo is marked II in my Fig. 1427, and falls anterior to von Spee's Fig. 16. Von Spee's Fig. 16 is the twenty-fourth section of the embryo, beginning at the head, while his Fig. 23 is the eighty-first section.

The various small spaces in different portions of the mesoderm cannot be viewed as the real origin of the body cavities without further discussion. In the von Spee embryo v. H. there are indications already of small spaces in the mesoderm at

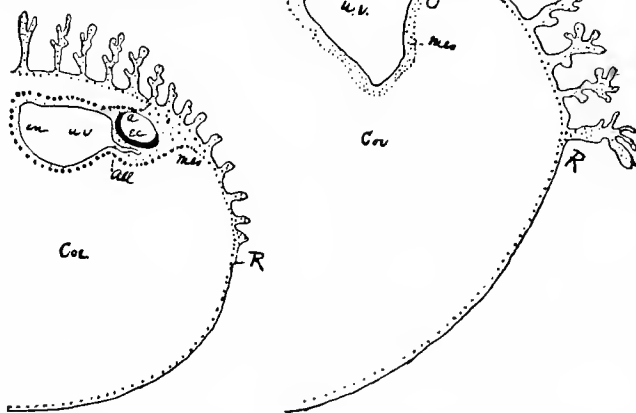


FIG. 1426.

FIG. 1427.

FIGS. 1426 AND 1427.—Longitudinal Sections of Two Young Human Ova. (After Graf Spee.) Enlarged 10 times. Fig. 1426, Embryo v. H.; Fig. 1427, Embryo Gle. Just half of the chorion is drawn, and the villi are outlined only over a portion of the ovum. R, Rauh's layer; a, amniotic cavity; uv, umbilical vesicle; en, entoderm; mes, mesoderm; all, allantois; c, chorda; nc, neurenteric canal; H, position of heart.

the border of the ectoderm of the embryo. Similar spaces are described by Bonnet<sup>31</sup> for the sheep and by Selenka<sup>32</sup> for the monkey. While von Spee and Bonnet believe that these spaces belong to the cœlom, Selenka simply designates them heart, or vascular.

The blood-vessels are intimately associated with the cœlom in their early development, and it is easy to be led into error without an abundance of material. Drasch<sup>33</sup> recently has again emphasized this relation. He has shown in the chick that the blood islands are separated from one another by a number of closed spaces filled only with a fluid. These spaces soon flow together to form the large slit-like cœlom of birds. The same condition of things has been shown to be true, but from a very different method, by Budge.<sup>34</sup> He injected the blastoderm of the chick, and showed that the cœlom was composed of a network of spaces, which gradually flowed together into the large cœlom surrounding the embryo.

Of course in the young human embryos we have at our disposal this stage of the process has long passed, but there is no reason why a remnant of it should not exist at the point of union of the umbilical vesicle with the body. The reason I question von Spee's interpretation of these small spaces in the mesoderm in embryo Gle. is that I believe that all, or certainly nearly all, of the body cavity is formed by an incorporation of the extra-embryonic cœlom within the embryo. What I have observed in human embryos as well as in the injected specimens of Budge shows that this must be true. These small spaces in the mesoderm of the body may belong to the muscle plates and the early blood-vessels, and certainly cannot play any great part in the development of the body cavity. There is no doubt whatever that the whole peritoneal cavity is simply pinched off from the cœlom of the outside of the body, and it is highly probable that

the pericardial cavity and pleural cavities are formed in the same way. The anterior mesentery of the intestine has never existed in the human embryo, and it is therefore needless to explain its mode of disappearance.

My statements are based in great part on embryos Nos. III. and XII., and since No. XII. is such a perfect speci-

dimensions were  $18 \times 18 \times 8$  mm., that is, it was slightly flattened. It was completely covered with long villi. It was carefully opened, care having been taken not to injure the embryo in any way. The cœlom was filled with a clear fluid, and many firm shreds of a fibrin-like body which obscured the embryonic vesicle greatly.

With much difficulty the embryo could be outlined, and these drawings proved to be of great service in making the reconstruction. The portion of the chorion to which the embryo was attached and the embryo were stained in carmine and embedded in paraffin. The whole was cut into sections, at right angles to the body,  $10 \mu$  thick.

Every other section was enlarged 100 times and drawn on wax plates 2 mm. thick, and from them the model of the embryo was made. The model gives the whole central nervous system, the entoderm throughout its extent, the blood-vessels, and the muscle plates.

The shape of the neural tube is given in the diagrammatic outline. It was closed only along the middle of the body, being open in front down to the beginning of the fourth muscle plate. From the beginning of the fourth plate to the beginning of the fourteenth it was closed, and from there on again it was open. In the figure the portions between  $x$  and  $x'$  indicate to what extent the tube is closed. In Figs. 1429 and 1430 the tube is nearly closed, while in Fig. 1432 the tail end of the tube is just beginning to separate from the ectoderm. The cephalic end of the tube already clearly outlines the forebrain, the mid-brain, and the hind-brain; the constriction, Fig. 1428,  $a$ , indicates the junction between the first two. On the ventral side of the fore-brain there are two marked pockets, one on either side, just behind the neuropore, which are no doubt the primary optic vesicles. It shows that in the human embryo these are fully outlined before the brain has separated itself from the ectoderm. Farther behind, very near the dorsal median line and about in the middle of the head, there is a short pocket of thickened ectoderm, the otic vesicle. Toward the hinder end of the embryo the spinal cord communicates by means of a solid band of cells with the entoderm (Fig. 1432). At no point in this communication is there a canal, so it must be viewed as the last remnant of the neurenteric canal. The

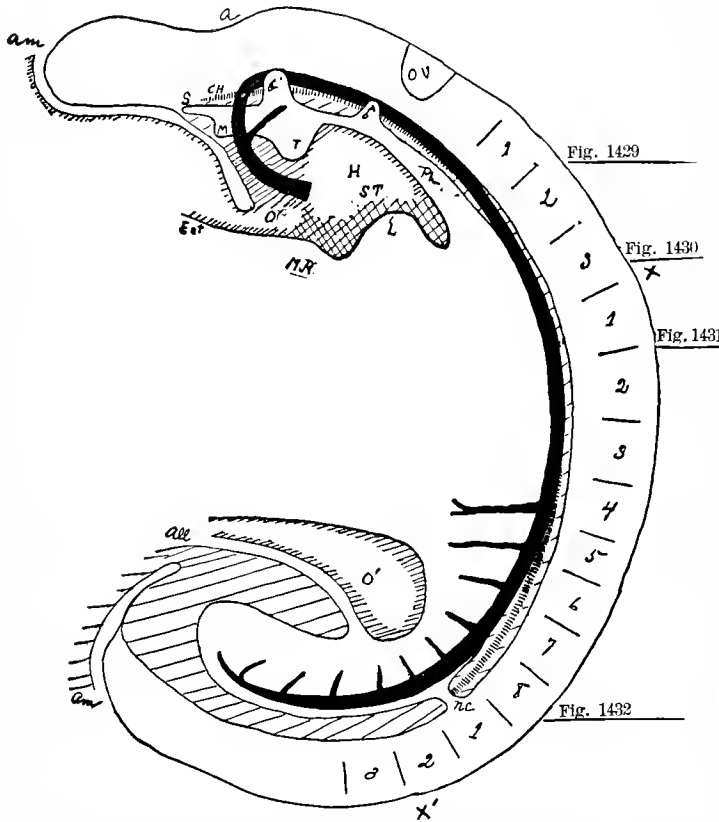


FIG. 1428.—Outline Drawing of a Sagittal Section of the Model of Embryo No. XII. Enlarged 50 times. The heavy line is the aorta. The muscle plates are numbered for occipital, cervical, and dorsal regions, respectively. The mesoderm is striated. *am*, Amnion; *a*, border between forebrain and midbrain; *x* and *x'*, extent of closure of spinal canal; *S*, Seessel's pocket; *ch*, chorda; *O'* and *O''*, first and second branchial pockets; *o v*, otic vesicle; *m*, mouth; *T*, thyroid; *H*, pericardial space; *ph*, pharynx; *ent*, entoderm; *S T*, septum transversum; *l*, liver; *n c*, neurenteric canal; *all*, allantois.

men it is well for me to describe it in greater detail. The embryo is about the same age as Kollmann's<sup>35</sup> embryo Bulle, which unfortunately was never fully published. No. III. is an embryo given me by Professor His. This embryo had been torn from the umbilical vesicle, and was injured in different portions of the body. Yet the head end of it is fairly well preserved, and it is of value in determining the growth of the body walls covering the heart.

*Embryo 2.1 mm. Long.*—The history of embryo No. XII. is as follows: "The woman from whom the ovum was obtained is twenty-three years of age and has been married for three years. She is a very intelligent woman, and her statements are reliable. Her menstrual periods recur every thirty days. She had been married some time before she became pregnant, and after passing two periods aborted July 6th, 1893. She was unwell the 5th of October and again on the 7th of November, this last period lasting five days. She passed her next period and on December 18th aborted the ovum."<sup>36</sup>

The ovum was hardened in strong alcohol without opening it first, and when it came into my hands its

location is opposite the twelfth muscle plate, or in the neighborhood of what will later on be the position of the first rib. The chorda dorsalis extends to the neurenteric canal, but not beyond it. There is no chorda in the tail end of the embryo.

Throughout the central nervous system, immediately about the central canal, there are many karyokinetic figures, showing that the specimen was excellently preserved. In the greater portion of the neural tube the tissue is already marked by two zones, a central one rich in nuclei, and a peripheral containing none. This corresponds with the description already made familiar to us by His.

The general shape of the whole central nervous system is very unlike that of any other young human embryo ever published. It circumscribes the greater portion of a circle, while in the other human embryos of this size it makes more of a straight line. I think that it is probable that this specimen represents the normal, as it was not injured nor handled in any way before it was cut into sections.

The entoderm, as the figures show, is already divided into fore-gut, mid-gut, and hind-gut. The fore-gut makes the pharynx, from which there are four diverticula

\* Letter from Dr. Ellis, January 7th, 1894.

on the dorsal side, one on the ventral side, and two near the mouth. The four on the dorsal side mark the first two branchial pockets on either side of the embryo; the two in front are Scessel's pocket and the entodermal portion of the mouth; while the one on the ventral side of the pharynx is the beginning of the median portion of the thyroid gland (Fig. 1429, *t*).

At the junction of the pharynx with the umbilical vesicle there is a large diverticulum into the septum transversum (Fig. 1430 *b*), the beginning of the liver.

Within the tail end of the embryo, behind the neurenteric canal, the hind-gut is enlarged considerably, and from it the entodermal canal of the allantois arises.

The whole umbilical vesicle is covered with blood-vessels which communicate with the veins and arteries of the embryo. Near the origin of the liver there are two veins which collect the blood from the umbilical vesicle and then enter the heart. These are the omphalomesenteric veins. They with a number of their branches are shown in sections in Fig. 1430, *v*. The heart itself is broken, but there is enough of it left to show that it is bent upon itself and contains a large cavity at the point where the veins entered it. From the heart two arteries arise and pass in front of the first branchial pocket, and each follows the course as shown in black in the reconstruction. The aortæ do not unite, but each sends a number of segmental branches to the umbilical vesicle along the tail end of the embryo. These are, of course, temporary; they may be called collectively the omphalomesenteric arteries. As the permanent omphalomesenteric artery arises more aboral than any of these, it is easy to understand that most of them must degenerate.

The sections show that there are fourteen muscle plates, all of which are hollow and do not in any way communicate with the body cavity in general. Kollmann, who described an embryo of this same age, numbers them from before backward, but I think that they can be designated more definitely. Froriep<sup>36</sup> showed that in all amniotic vertebrates there were a number of muscle plates and dorsal ganglia formed in the occipital region, and studied their fate in the chick and in the cow's embryo. Platt<sup>37</sup> has also followed the order of the origin of the muscle plate in the chick, and found that the first division of the mesoderm was between the third and fourth occipital plates. The first three or four of these segments communicate in the chick, according to Dexter,<sup>38</sup> with the cœlom, and Bonnet<sup>39</sup> has found also that the same is true in the sheep. Bonnet's figures (compare his Plate IV.) show that a sheep's embryo of the same stage as embryo XII. has muscle plates much more sharply outlined than the human. In order to locate the muscle plates more definitely I have made every effort to count the spinal ganglia in embryo XII., but with no definite result. It is impossible for me to define the spinal ganglia, as often they are represented by a few cells only, then again as a band of cells they extend over several segments. The same is true in the occipital region. Had I been able to number them definitely it would still have been impossible to number the muscle plates from them, for His<sup>40</sup> has shown that there is an occipital ganglion in the human embryo as well as in the lower animals.

The fact that the muscle plates reach to the otic vesicle in embryo XII., as well as in Kollmann's embryo Bulle, indicate that the first plates must belong to the occipital region, and I have found that there are three occipital muscle plates in embryo No. II.<sup>41</sup> Moreover, there is every indication of a degeneration of the first two plates in XII., so on this account I am inclined to number them as they are numbered in Fig. 1428. I do not think that any of them ever communicate with the pericardial cavity as Bonnet found them in the sheep. The cavities in all of the other plates are small, and they are separated by a large mass of mesoderm from the cœlom. This all confirms my view.

The chorda extends from Scessel's pocket to the neurenteric canal.

There are also a few segmental ducts, some completely

and some partly separated from the ectoderm, as was the case in Kollmann's embryo. The ducts are small, and extend over one or two sections only, and occasionally one of them is arising at several different points between a given two segments. They are present on both sides between the first and second cervical segments, second and third segments, third and fourth segments, fourth and fifth segments, and only on the left side in the region of the fifth and sixth cervical segments.

The cœlom of this embryo is especially instructive. A sagittal section of the embryo and ovum is given in Fig. 1433. This embryo, when drawn connected with the ovum, is very similar to Graf Spee's embryo Gle, as shown in Fig. 1427. It is very easy for us to conceive the von Spee embryo converted into this embryo, for about all the change that is necessary is that the embryo grow somewhat and bend upon itself. In so doing the attachment of the umbilical vesicle becomes smaller as the amnion encircles the body of the embryo more. The

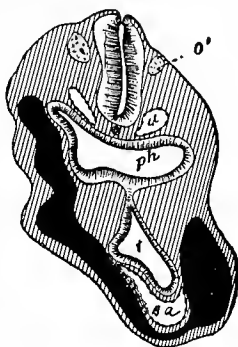


FIG. 1429.

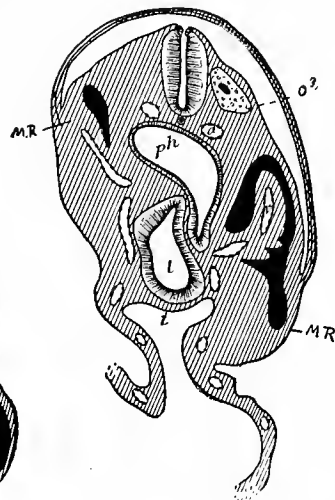


FIG. 1430.

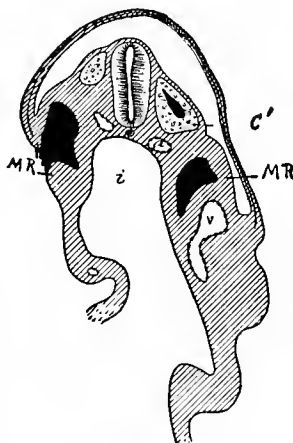


FIG. 1431.

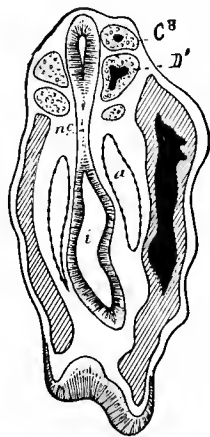


FIG. 1432.

FIGS. 1429-1432.—Sections through Embryo No. XII., as indicated by the Lines in Fig. 1428. Enlarged 50 times. The black is the cœlom within the body. *O'* and *O''*, First and third occipital muscle plates; *C'* and *C''*, first and eighth cervical muscle plates; *D'*, first dorsal muscle plate; *a*, aorta; *v*, omphalomesenteric vein; *t*, thyroid; *l*, liver; *ph*, pharynx; *i*, intestine; *n.c.*, neurenteric canal; *MR*, membrana reuniens.

position of the neurenteric canal, the shape of the allantois, and the formation of the pericardial cavity, all show that the curving must be a normal one.

Nearly all other young embryos of this stage, or a little older, which have been published show a straighter body or even a curve in the opposite direction. I have also in

my collection two embryos of this stage, Nos. I. and XV., which had been taken out of the chorion and torn from the umbilical vesicle, and both of them are straight

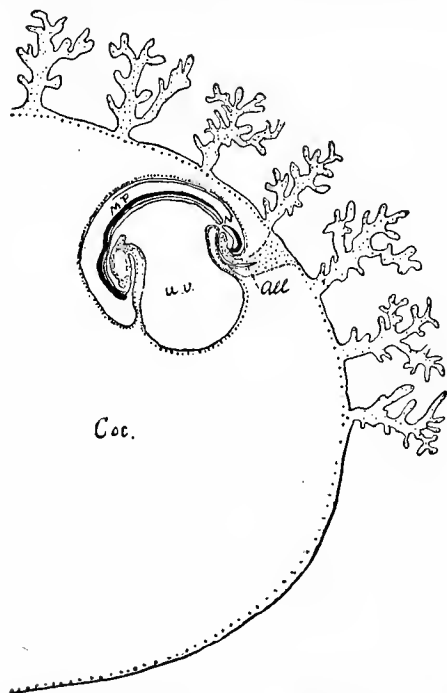


FIG. 1433.—Sagittal Section of the Ovum with Embryo No. XII. Attached. Enlarged 10 times. Coc, Cœlom; u.v., umbilical vesicle; all, allantois; MP, medullary plate.

like Kollmann's embryo Bulle and His's<sup>42</sup> embryo L. It is difficult to conceive how my embryo XII. could possibly be torn out of its membranes without straightening it. We need only recall our experience in hardening embryos of lower animals to be reminded how easily a curved embryo is straightened when it is handled the least bit roughly before it is hardened.

His, in his great monograph on human embryos, emphasizes a curve in the back of the embryo just the reverse of the one given in Fig. 1433. I refer to embryos Sch., BB., and Lg., as well as to Minot's embryo 195.<sup>43</sup> The fact that this inverted bend in the back is not constant (His's Rf., for instance), and that it occurs at the time when any tension upon the umbilical vesicle could produce it, makes me believe that it is an artifact. This view was suggested to me a number of years ago, when I was removing young dogs' embryos from the uterus, and unwittingly distorted a number of them in this very way before they were hardened. The middle of the back is the weakest part of the embryo's body, and the umbilical vesicle is attached to it. Under these conditions the simple weight of the vesicle is sufficient to bend the back of the embryo as pictured by His.

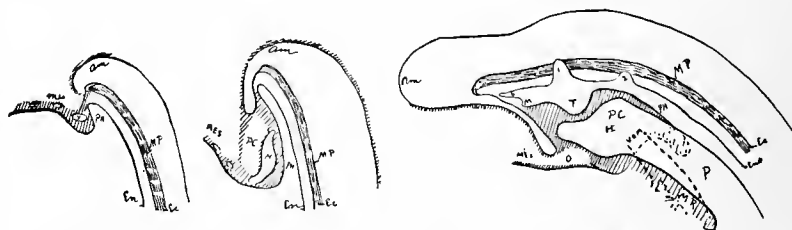
To return to the cœlom. At the hinder end of the embryo the cœlom dips into the body overlapping the hindgut in the neighborhood of the neurenteric canal, as shown in Fig. 1432. This cavity communicates with its fellow on the opposite side through an opening between the umbilical vesicle and the allantois, marked O in Fig. 1428. This communication has already

been described by His<sup>44</sup> for an embryo somewhat older. If, now, the point O in Fig. 1428 is approximated toward NC, with a flexion of the embryo at the same time, this communication is easily explained. In other words, as the hind-gut is being separated from the umbilical vesicle, a groove-like portion of the cœlom is also included in the body of the embryo. At the hinder portion of the embryo, on either side, the cœlomic grooves extend deeper into the body of the embryo, and communicate with each other around the aboral side of the stem of the umbilical vesicle. This communication is shown well by His in Fig. I, B, Plate VI. of his "Atlas," as well as in the same figure, page 299 of Minot's "Embryology." Excellent profile views showing this point are given in all the embryos figured on Plate IX. of His's "Atlas."

I emphasize this point in order to exclude the ventral mesentery for this portion of the embryo. The fact that this mesentery could never have existed in the human embryo is also proved by a careful examination of His's models of human embryos made by Ziegler.

As we pass toward the head in embryo XII. the cœlomic groove communicates freely with the extra-embryonic cœlom until the region of the membrana reuniens is reached. This is shown in Fig. 1431, MR, with the membrana reuniens complete on one side, but not yet united on the other. The membrana reuniens extends up to the heart, and separates the pericardial cavity from the extra-embryonic cœlom, then crosses the ventral median line to return on the opposite side of the embryo. Throughout the extent of the membrana reuniens there is a great increase of mesodermal tissue, which encircles completely the beginning of the liver, as Fig. 1430 shows. A portion of this mesodermal tissue has been described by His as the septum transversum.<sup>45</sup> According to His only that portion of the mesodermal tissue is septum transversum which lies between the posterior part of the pericardial cavity (*Parietelhöhle*), the wall of the intestine, and the point where the veins enter the heart. It extends across the body, and has within it the beginning of the liver. In transverse section this region is shown in Fig. 1430. Now the pericardial cavity communicates by means of a long canal on either side, with the peritoneal cavity, and the omphalomesenteric vein hangs into this, attached to a kind of mesentery, as Fig. 1430 shows. Lower down, near the communication (Fig. 1431), there is an indication of the beginning of the umbilical vein, which unites with the omphalomesenteric vein through the membrana reuniens. The two canals which communicate with the extra-embryonic cœlom are the pleural cavities, and the membrana reuniens aids to separate them from the peritoneal.

All of the tissues from the diaphragm to the opening



FIGS. 1434-1436.—Three Stages to Show the Development of the Blastodermic Layers at the Head End of the Embryo. Fig. 1434, Count Spee's Embryo Gle. Fig. 1435, Embryo No. III. Fig. 1436, Embryo No. XII. V, Vein; ph, pharynx; am, amnion; MP, medullary plate; p.c., pericardial cavity; S, Seessel's pocket; m, mouth; t, thyroid; 1 and 2, first and second branchial pockets; p, pleural cavity; m.r., membrana reuniens; om, omphalomesenteric vein, which is expressed as a dotted line; O, communication between right and left body cavities on the ventral side of the umbilical vesicle.

of the liver duct into the duodenum arise from the septum transversum and the membrana reuniens; the stomach from the fore-gut, the liver from the liver diverticulum, and the diaphragm from the septum transversum and the membrana reuniens. The Cuvierian duct must also

have arisen in the membrana reuniens, in order to pass around the outside of the body cavity to reach the cardinal and jugular veins, as pictured by His<sup>46</sup> for the human embryo.

In the further development of the pleural and pericardial cavities the Cuvierian veins give us our best landmark, as they define the point where the pleural cavity is to be separated from the pericardial. And it really seems as if the greater portion of the diaphragm is formed from the portion of the septum transversum on the ventral side of the vein and from the membrana reuniens, rather than from the portion immediately in front of the intestine. In other words, there is a horse-shoe-shaped ridge of tissue around the neck of the embryo to the ventral side of the pericardial and pleural cavities and parallel to them. The median portion is composed of the septum transversum, and each wing of the shoe is the membrana reuniens, one on either side of the embryo. Its general direction in this stage is parallel with the long axis of the embryo, and within each wing there is an omphalomesenteric vein.

*Origin of Pericardial Cavity.*—With the pericardial cavity opening into the extra-embryonic cœlom on either side as a basis, it is possible to trace back the pericardial cavity to its origin. Figs. 1428 and 1436 show that the ventral wall of the pericardial cavity is composed mostly of mesoderm. This is the portion of the membrana reuniens which is composed of mesoderm, as the sections, Figs. 1430 and 1431, show. An earlier stage is shown in the diagrammatic Fig. 1435. It is taken from embryo No. III. In this specimen, since the ectoderm of the amnion has not reached completely around the body, as both the sagittal and transverse sections show (Figs. 1435 and 1437), it is evident that the pericardial space is first covered on the ventral side with mesoderm and later the ectoderm is added when the amnion begins to close over the head. In embryo III. the canals communicating between the pericardial space and the extra-embryonic cœlom are not as long as in embryo XII., and the ventral walls of the pericardial space are composed wholly of mesoderm. This indicates that the growth of this wall was first by a union of the mesoderm, which was followed by the ectoderm of the amnion to complete the body wall. The process is shown in Figs. 1434 to 1436. Fig. 1434 is a hypothetical stage between Graf Spee's embryo Gle. and my embryo No. III. As the process from Graf Spee's embryo continues, the blood-vessels reach the body to form the heart, as indicated by the outlines marked *e* in Fig. 1434. The mesoderm of the amnion then unites with that of the umbilical vesicle, and the first pericardial

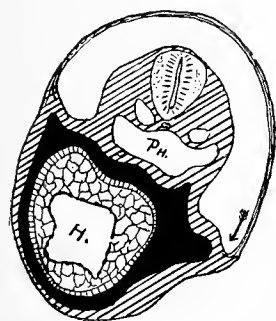


FIG. 1437.—Section through the Head of Embryo No. III. Enlarged 55 times. *Ph*, Pharynx; *H*, heart. The arrow in the amniotic cavity indicates the direction of the future growth of the amnion to complete the ventral body wall.

*Extension of the Amnion.*—After the stage of embryo XII. is passed the amnion rapidly envelops the whole body and soon passes out over the cord. The next stage after No. XII. which I have studied is No. XIX. I have

very perfect photographs of this specimen, and the sections are all good, although the nervous system is macerated. The embryo has rotated in the amnion, throwing the cord to the right side with the left side toward the

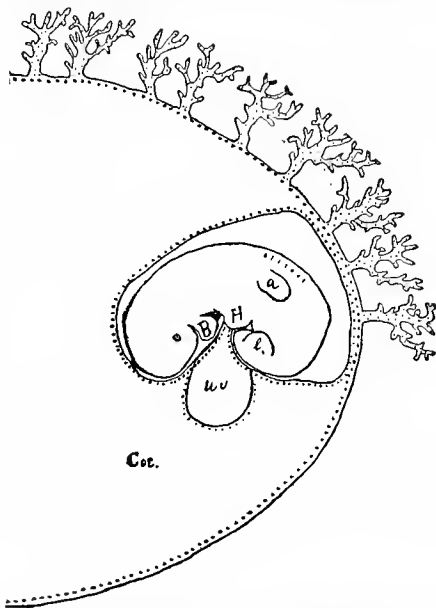


FIG. 1438.—Ovum and Embryo No. XIX. Enlarged 5 times. Just half of the ovum is shown. *a*, Arm; *l*, leg; *H*, heart; *uv*, umbilical vesicle; *B*, branchial arch.

observer. It would have been impossible to obtain a view of the right side of the embryo without cutting the cord. The outlines of this embryo and ovum are given in Fig. 1438. Two sections through the body are given in Figs. 1439 and 1440.

The amnion has become separated from the body with the exception of the part about the cord and also that along the right side of the body, over the heart. The arrow in Fig. 1437 shows how the amnion on that side is extended over the ventral body wall to make the condition shown in Fig. 1440. No doubt the cause of this is the rotation of the body, throwing the cord to its right side and the amnion with it. In nearly all young embryos the cord is on the right side.<sup>49</sup> With the exception of the four instances mentioned below, the rotation has always been so as to throw the left side of the body away from the chorion, and in all of these specimens the amnion must have swept over the body from left to right, as shown in the figures. I find a similar illustration by His in his great monograph.<sup>50</sup>

*Absence of a Ventral Mesentery.*—After the septum transversum has been formed as it is in embryo XII., there is on its ventral side a pretty sharp groove, which indicates that the umbilical vesicle is being constricted at this point.

It is generally believed that the ventral mesentery of the intestine extends to the umbilicus, and that ultimately the round ligament of the liver represents its remnant after most of it has disappeared. This theory is expressed by two diagrams in Minot's "Embryology," page 767. As the liver begins to grow, and while the heart is being pushed down in front of it, the ventral end of the septum transversum is turned down to the umbilicus. While this is taking place the stem of the umbilical vesicle becomes relatively smaller and smaller, but there is no union between the umbilical vesicle and the septum transversum as expressed in Minot's diagram. The first stage of this process is shown in my Fig. 1436, and its successive stages are shown in His's "Atlas," Plate IX. In all six embryos pictured on that plate the successive stages are represented, and in none of them is the um-

bilical vesicle attached to the septum transversum to form a ventral mesentery. From these embryos of His we can pass to embryo XIX., in which the umbilical

macerated. No. II. is a perfect specimen, and has been already described by me several years ago.<sup>52</sup> I shall confine my description of it to the body cavity.

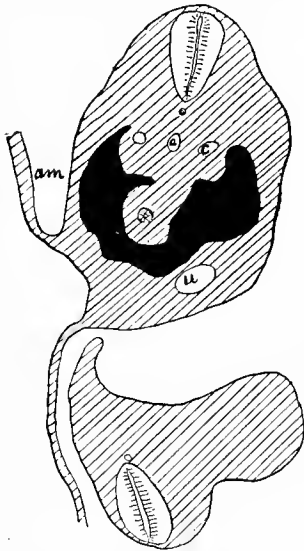


FIG. 1439.

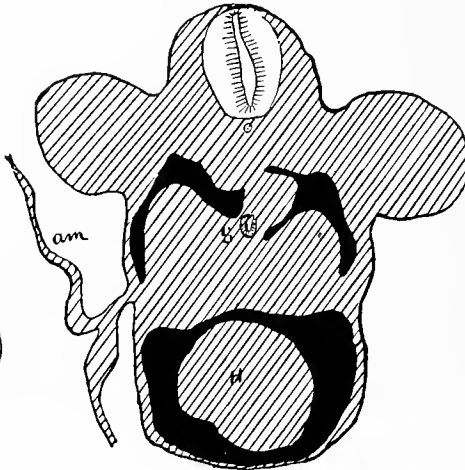


FIG. 1440.

FIGS. 1439 and 1440.—Section through Embryo XIX. to Show the Attachment of the Amnion to the Side of the Body. Enlarged 25 times. *Am*, Amnion; *S*, stomach; *H*, heart; *c*, cardinal vein; *u*, umbilical vein; *a*, aorta.

vesicle communicates by a round canal with the intestine, and the tube is completely encircled with a space which extends to the liver, thus cutting off any possible ventral mesentery at that point. The same thing is shown, but in a later stage, in Fig. 1442, *O*, but a new process has already taken place to complicate matters.

In embryo XII. there is just a beginning of an umbilical vein in the membrana reunions. In Kollmann's embryo the vein is more marked.<sup>51</sup> The vein extends out into the somatopleure, far away from either the intestine or the median line. This same position is again shown in His's embryos BB. and Lr. on Plate IX. in his "Atlas." The left umbilical vein becomes the more prominent, and as the body wall is developed more and more it moves around toward the ventral median line. This movement takes place in common with the movement of the amnion over the body from left to right, as shown in Fig. 1440. In embryo No. II., however, the liver has nearly reached the umbilicus, and the vein has almost moved around to the ventral median line, as shown both in the reconstruction and the sections (Figs. 1442, 1437-1451). After the vein has moved around the body to its ventral surface, and after the liver moves away from the umbilicus up to the permanent diaphragm, it is easy to explain the formation of the round and broad ligaments of the liver as a secondary formation, but not as a remnant of a ventral mesentery. It might be called a portion of the septum transversum, as it is directly continuous with it. A ventral mesentery does exist between the abdominal walls and the liver, and extends only slightly below the liver. It is always slightly to the left of the median line, and is in direct connection with the septum transversum (Fig. 1442, *O* and *ST*).

*Cœlom of Embryo No. II.*—After the body cavity is beginning to separate from the extra-embryonic cœlom, the next important stage is the one after the separation is complete, as from now on the adult body cavities are formed by a simple division and expansion of the cavities already within the body. This stage is represented in embryos XVIII., II., and IV. All of these embryos are nearly of the same size, the successive stages being in the order they are given. No. XVIII. is somewhat distorted in the middle of the body, while No. IV. is slightly

The external form of the embryo within the ovum is given in Fig. 1441. The position of the umbilical vesicle, as well as the extent of the amnion and the relation of the umbilical vesicle and amnion to the chorion, are all given. The umbilical cord is large and lies on the left side of the body, while in most embryos already published it is upon the right side. The cord is short, and midway between the embryo and its attachment to the chorion it shows a decided enlargement. The umbilical vesicle is large, measuring  $5 \times 7$  mm., and is located between the head end of the embryo and the chorion.

The amnion has not grown very much, still leaving a great space between it and the chorion, the extra-embryonic cœlom (compare with Fig. 1438). Within it hangs this large umbilical vesicle, the lumen of which no longer connects with the alimentary canal. The separation is now complete. Around the stem of the vesicle the extra-embryonic cœlom communicates freely with the body cavity, as shown in Fig. 1442. This figure is from a reconstruction, and shows the general

extent of the body cavity within the embryo. It encircles the heart, and then extends to the lungs and over them and to the stomach, over the intestines, and out into the cord. A cast of the whole cavity is also given,

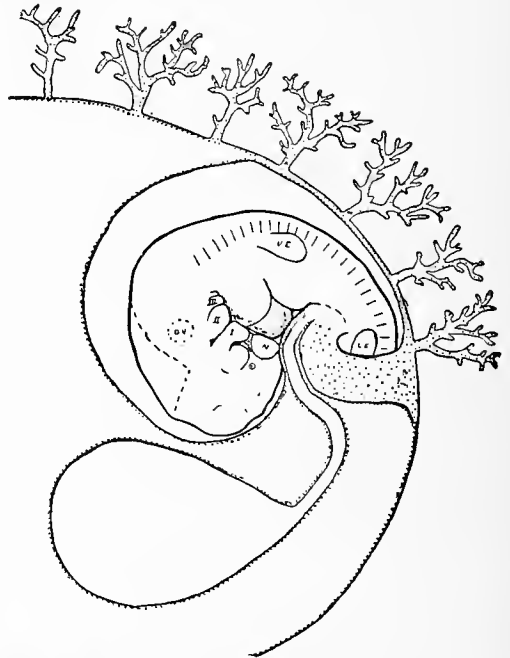


FIG. 1441.—Embryo No. II. Attached to the Chorion. Enlarged 5 times. Just half of the ovum is shown. *o v*, Optic vesicle; *U E*, upper extremity; *L E*, lower extremity; *N*, nose; *I, II, III*, branchial arches.

showing the slit on the dorsal side for the mesentery of the intestine, and the grooves on either side of this for the Wolffian bodies. There are also grooves in the cast

for the veins, and the place where the Cuvierian duct enters the heart is marked *V*. The sagittal section of

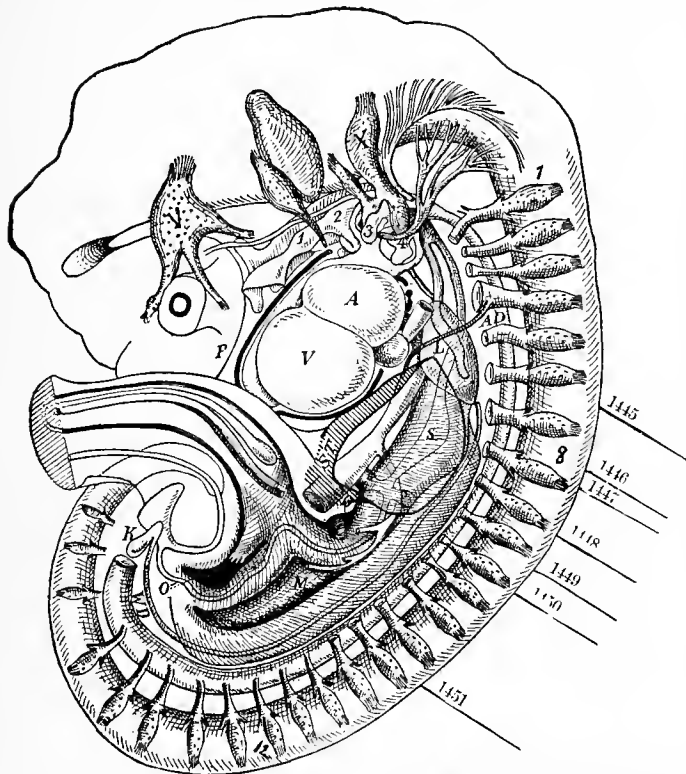


FIG. 1442.—Reconstruction of Embryo No. II. Enlarged 17 times. *V* and *X*, Fifth and tenth cranial nerves; 1, 2, 3, and 4, cast of the branchial pockets; 1 and 8, first and eighth cervical nerves, from the fourth the phrenic arises; 12, twelfth dorsal nerve; *A*, auricle; *V*, ventricle; *L*, lung; *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.

the peritoneal cavity is given in Fig. 1444. The striated line indicates where the cavity crosses the median line of the body, while the other lines outline the cavity beyond. *Lp.* outlines the lesser peritoneal cavity. Figs. 1445–1451 give the extent of the peritoneal cavity in different portions of the embryo, as indicated by the lines in Fig. 1442.

It is not difficult now to imagine the body cavity of embryo XII. converted into the one just described. In that embryo the heart is high in the neck on the oval and dorsal side of the septum transversum. In this embryo it is on the ventral and oral side of the septum transversum, but still above the eighth cervical nerve. The septum transversum has already received its nerve supply from the fourth cervical nerve, as pointed out in the early part of the century by von Baer. This movement of the septum transversum is accompanied by a movement of all the other organs on their way into the thorax and abdomen of the future individual. In the rotation the Cuvierian duct acts much as the fixed point about which the cœlom is bent. The figures all illustrate this beautifully. But as the heart has rolled over the liver, and the septum transversum has undergone a quarter-revolution, the Cuvierian ducts and all have moved away from the head. This is by no means the end of the excursion of the septum transversum, as its dorsal end must move down and beyond the twelfth dorsal segment (compare Fig. 1442).

The pericardial cavity surrounds the whole heart, as the various figures show. The cavity is traversed only where the large veins enter, and where the aorta leaves the heart. The cavity completely surrounds the bulbus

aortæ to its origin (Figs. 1444–1447) in the ventricle. On the dorsal side of the heart the pericardial cavity is separated by a bridge for the transmission of the veins to the heart. Between the bulbus aortæ and the entrance of the veins into the heart the pericardial cavity crosses the median line as three distinct openings, as expressed by the black areas in front of the trachea in Fig. 1442. On the dorsal side of the heart on either side of the lungs the pericardial cavity communicates with the pleural cavities by means of two openings (Fig. 1445), each of which is about  $0.1 \times 0.5$  mm. in diameter. Farther on, the pleural cavities extend as two slits which encircle the lobes of the liver and separate them from the alimentary canal on the one hand and from the body wall on the other (Figs. 1446–1449). The two pleural cavities do not communicate with each other around the lungs, leaving for them both a dorsal and a ventral mesentery.

This appearance of the cœlom about the lungs and the liver can be explained by the two pleural cavities of embryo XII., and this has often made me think that the membrana reuniens of embryo XII. is the main origin of what is called septum transversum in embryo II. If this proves to be the case, then the lower end of the membrana reuniens will form the ventral end of the diaphragm, and not the reverse. A stage between embryos XII. and XVIII. (Fig. 1453) is required to elucidate this point.

In the neighborhood of the stomach the peritoneal cavity on either side of it has become asymmetrical, as Fig. 1448 shows. The mesentery has become bent to the left side, leaving a diverticulum from the right side which extends oralward to the tip of the lung (Figs. 1446 and 1447) to form the beginning of the lesser peritoneal cavity.<sup>53</sup> Further aboralward the cavities become symmetrical again (Figs. 1449, 1450), and then unite along the ventral median line, as

shown in Fig. 1451. The ventral mesentery shown in Fig.

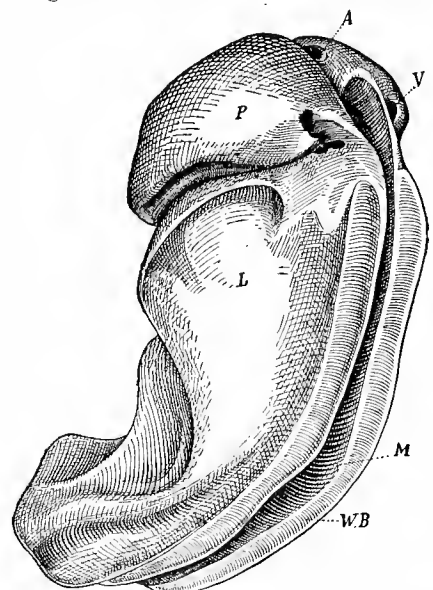


FIG. 1443.—Cast of the Body Cavity of Embryo No. II. Enlarged 22 times. *A*, Position of the aorta; *V*, position of the vein; *M*, position of the mesentery; *W B*, position of the Wolffian body; *P*, pericardial cavity; *L*, cœlom over liver.

1450 does not extend more than a section or two beyond the liver, and is separated by a marked opening from the stem of the umbilical vesicle in this embryo, as is shown in Fig. 1442, *O* (see also No. XII., Fig. 1428, *O*). On the aboral side of the umbilical cord the peritoneal cavities of the two sides unite in both embryos again, marked *O'* in both figures.

*Development of the Diaphragm.*—It has often been stated that the development of the diaphragm, especially in the human embryo, belongs to one of the most difficult problems of embryology, partly because of the difficulty of obtaining the necessary specimens and

partly because there are no fixed points from which to calculate. In its development the whole diaphragm wanders from the head to the abdomen, forming as well as modifying the structures and organs along the way. So while von Baer<sup>58</sup> recognized that the diaphragm wandered in its development, picking up its nerve in so doing, a fairly clear picture of the whole process was not given until Cadiat,<sup>59</sup> His,<sup>60</sup> Uskow,<sup>61</sup> and Ravn<sup>62</sup> studied carefully the development of neck, heart, lungs, and intestine. In so doing His especially recognized the anlage of the diaphragm in a mass of tissue located with the heart amongst structures belonging to the head and containing within it the veins to the heart as well as the anlage of the liver. This mass of tissue His termed the septum transversum. His studies were made upon the human embryo, mainly by the method of reconstruction, and shortly after they were published Uskow made a very careful study of the further growth of the septum transversum. Uskow recognized the great importance of two additional structures in the formation of the pericardium and adult diaphragm from the septum transversum: these

he termed the *pleuro-pericardial membrane*, containing the phrenic nerve and the *pillars* which form the dorsal end of the diaphragm. The pillars of Uskow have been termed the *pleuro-peritoneal membranes* by Bracket, and as this term is more appropriate it should be adopted.

My own studies show that the pleuro-pericardial and pleuro-peritoneal membranes arise from a common structure which grows from the lobe of the liver along the dorsal wall of the ductus Cuvieri to the dorsal attachment of the mesocardium. Later it extends toward the head to complete the pleuro-pericardial membrane, and then toward the tail to complete the pleuro-peritoneal membrane. This structure, which I term the *pulmonary*

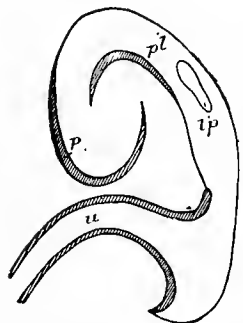


FIG. 1444.—Outline of Cœlom in Embryo No. II. in Sagittal Section. The striated line indicates that the cœlom crosses the median line. P, Pericardial space; pl, pleural cavity; l p, outline of lesser peritoneal cavity.

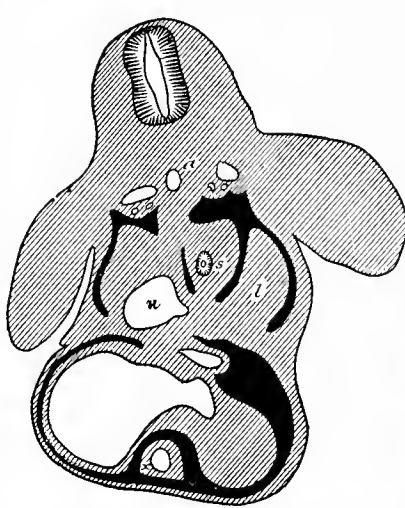


FIG. 1447.

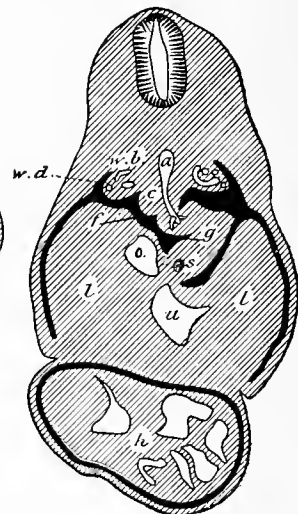


FIG. 1448.

FIGS. 1447 and 1448.—Sections through Embryo No. II. a, Aorta; s, stomach; l, liver; u, umbilical vein; x, bulbus aortæ; h, heart; o, omphalomesenteric vein; g, lesser peritoneal cavity; f, foramen of Winslow; c, coeliac axis; w.b., Wolffian body; w.d., Wolffian duct.

ridge, giving rise to the pleuro-pericardial and pleuro-peritoneal membrane, is located in the sagittal plane of the body cavity with cephalic and caudal horns on its dorsal side. The ductus Cuvieri lies between these horns.

In following the fate of the septum transversum it is necessary to consider the division of the body cavity into the pericardial, pleural, and peritoneal cavities. According to His, the body cavity is divided into the *Parietalhöhle* and *Rumpfhöhlen*. The communication between these spaces he has also termed the *recessus parietalis*. The parietal cavity from its earliest appearance contains the heart and is destined to form the pericardial cavity. This is the pericardial cœlom. A portion of the recessus parietalis forms the pleural cavity; it surrounds the lung buds throughout its development and forms the pleural cœlom. The remainder of the recessus parietalis to the origin of the liver has developed in it the liver and stomach; this is added to the general peritoneal cavity and may be termed the peritoneal cœlom. In the early embryos the whole cœlom lies far out of its final place; in embryo XII. nearly the entire cœlom lies in the region of the head and neck, and in the further development of these parts the cœlom with the surrounding organs wanders away from the head to its permanent location. As long as the serous cavities arising from the cœlom are in the process of wandering and are not fully separated from one another, they may be termed pleural, pericardial, and peritoneal cœlom; when they are fully established they form these cavities.

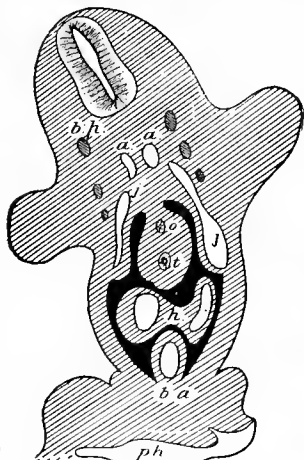


FIG. 1445.

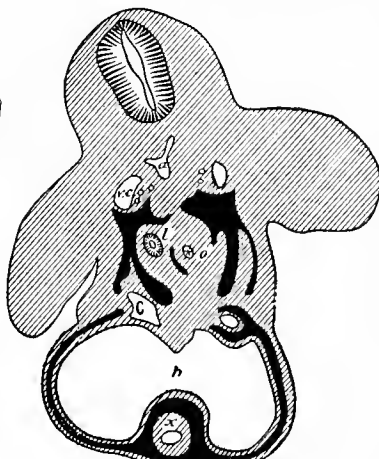


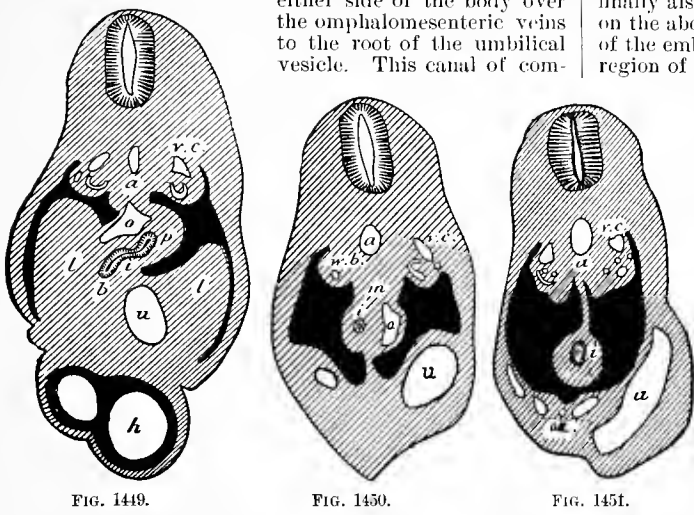
FIG. 1446.

FIGS. 1445 and 1446.—Sections through Embryo No. II. at the Points Indicated in Fig. 1442. Enlarged 22 times. B p, Brachial plexus; a, aorta; b a, bulbus aortæ; ph, pharynx; h, heart; t, trachea; o, oesophagus; j, jugular vein; l, lung; c, cardinal vein; C, Cuvierian duct.

In embryo XII., Fig. 1433, the cœlom of the embryo forms a free space encircling the heart and extending on either side of the body over the omphalomesenteric veins to the root of the umbilical vesicle. This canal of com-

munication has developed within it the lung, stomach, and liver, and throughout its earlier development it always measures in length about one-fourth of that of the body. The appearance of the lung and liver marks the subdivision of the cœlom into the pleural and peritoneal cœlom. With the development of the liver, lung, and stomach the cœlom containing them gradually dilates until the embryo is about 9 mm. long, when the containing canal evaginates, so to speak, and turns the liver and stomach out into the general peritoneal cavity. The Wolffian body, which occupies the dorsal wall of the canal, gradually degenerates, and the lung takes its place. From these statements it is readily inferred that the canal extending from the pericardial cœlom, His's recessus parietalis, gives rise to the pleural cœlom on its dorsal side and to the peritoneal cœlom on its ventral side. The line of division is formed by the pleuro-peritoneal membrane extending from the ductus Cuvieri to the adrenal.

again on its dorsal side. At first the lungs are on the dorsal side of the heart, then on the lateral side, and finally also on the ventral side of it. At first the liver is on the aboral side of the septum transversum in the head of the embryo, then on the dorsal side of it in the cervical region of the embryo, then as the liver is descending in its excursion it is transferred to the ventral side of the septum and extends into the sacral region. At first the Wolffian body extends high into the thoracic region of the embryo, but while it is degenerating and the diaphragm descends, the upper part of the posterior cardinal vein remains, while the lower part is incorporated with its vena cava inferior, as shown by Hochstetter.<sup>63</sup> As the Cuvierian ducts and cardinal vein descend into the thorax, the segmental veins entering the cardinal veins are gradually shifted, so that veins which originally emptied into the posterior cardinal now empty into the anterior cardinal. While the whole process is taking place the arteries arising from the descending aorta also shift, as I have shown in a previous communication.<sup>64</sup> At that time my collection of human embryos was very limited, and it was necessary to include some observations on lower animals to prove my point, but now I can give a complete table of human embryos in which the point of origin of the cœliac axis is recorded.



FIGS. 1449-1451.—Sections through Embryo No. II. *a*, Aorta; *v.c.*, cardinal vein; *o.*, omphalomesenteric vein; *p.*, pancreas; *i.*, intestine; *h.*, bile duct; *l.*, liver; *u.*, umbilical vein; *m.*, mesentery; *w.b.*, Wolffian body; *all.*, allantois.

munication has developed within it the lung, stomach, and liver, and throughout its earlier development it always measures in length about one-fourth of that of the body. The appearance of the lung and liver marks the subdivision of the cœlom into the pleural and peritoneal cœlom. With the development of the liver, lung, and stomach the cœlom containing them gradually dilates until the embryo is about 9 mm. long, when the containing canal evaginates, so to speak, and turns the liver and stomach out into the general peritoneal cavity. The Wolffian body, which occupies the dorsal wall of the canal, gradually degenerates, and the lung takes its place. From these statements it is readily inferred that the canal extending from the pericardial cœlom, His's recessus parietalis, gives rise to the pleural cœlom on its dorsal side and to the peritoneal cœlom on its ventral side. The line of division is formed by the pleuro-peritoneal membrane extending from the ductus Cuvieri to the adrenal.

It is now no great task for me to give the development of the diaphragm in the human embryo, for I have at my disposal excellent sections, as well as definite knowledge of the anatomy of the surrounding organs contributed by the above-mentioned authors.

While the embryo is still straight it is very easy to locate the various organs and their relations to one an-

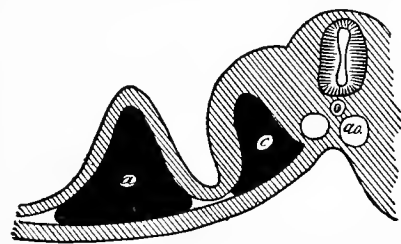


FIG. 1452.—Section of a Chick to Show that the Body Cavity Communicates with the Extra-Embryonic Coelom. Although the embryo has been injected, the injection masses *a* and *c* are not continuous.

other, but through their shifting and the flexion and extension of the embryo the relations are constantly changing, and one must not rely too much upon sections or else erroneous impressions will often be obtained. At first the heart is upon the oral and dorsal side of the septum transversum, then on its ventral side, and finally

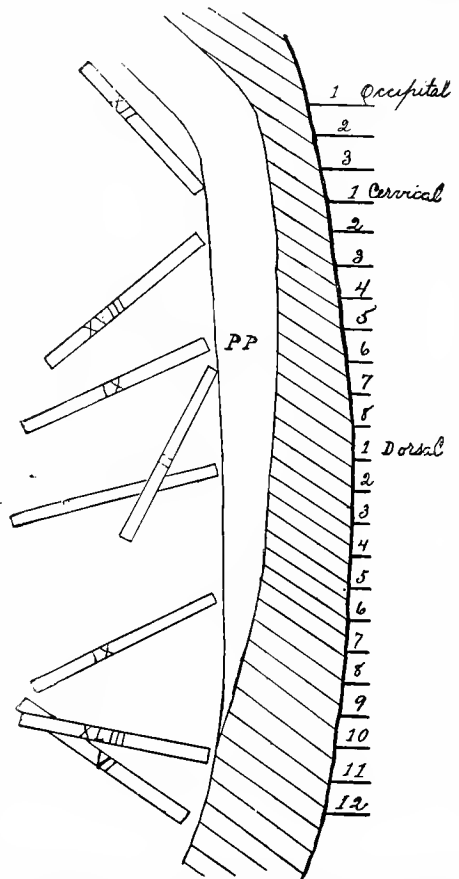


FIG. 1453.—Diagram to Show the Position of the Diaphragm. The numbers on the blocks indicate the embryos from which the diaphragms are taken. *KO* is His's embryo K O; *PP*, the outline of the opening between the pleural and peritoneal cavity, which is finally closed when the diaphragm reaches the tenth dorsal segment.

TABLE SHOWING POINT OF ORIGIN OF CÆLIAC AXIS.

Embryo.	Length in millimetres.	Origin of cœliac axis.
No. XII .....	2.1	Opposite 4th cervical nerve.*
His's Embryo M .....	2.6	" 1st dorsal " " " "
" " B .....	7	" 2d " " " "
No. II .....	7	" 4th " " " "
His's Embryo A .....	7.5	" 6th " " " "
No. XLIII .....	13	" 10th " " " "
" IX .....	14	" 11th " " " "
" XXII .....	18	" 11th " " " "
" XVII .....	16	" 12th " " " "
LVI .....	20	Below 12th " " " "
Adult .....	....	" 12th " " " "

\* In the first two embryos the omphalomesenteric artery is noted, and not the cœliac axis.  
† Compare Fig. 15, Pl. vi., His's "Atlas," with M4, Pl. vii.  
‡ Compare Fig. 35, Pl. ii., His's "Atlas," with Fig. 1, Pl. i.  
§ Compare Figs. 79 and 86, His's "Atlas," with Fig. 4, Pl. i.

The table shows that the arteries arising from the ventral side of the aorta to supply the stomach and intestines are constantly shifting until their definite origin is finally reached. In these specimens the omphalomesenteric artery is shifted ahead of the cœliac axis. In embryo No. II. the omphalomesenteric artery has a double origin from the aorta, which indicates that this movement may be brought about by a new anastomosis forming, which is then followed by an occlusion of the old origin. At any rate it is impossible that the whole aorta shifts with the abdominal viscera, for it is bound to the vertebrae and muscle plates through the segmental arteries.

The various sections and the reconstruction of embryo No. II. show the pleural and pericardial cavities still communicating freely. The same is true in embryos XIX., XVIII., and IV. Immediately after this stage there are no embryos in my collection, so I have no specimen in which the communications between the pleural and pericardial cavities are just closing. In embryos VIII., V., IX., and XLIII. (Figs. 1453-1455), the pleural and pericardial cavities are separated, while the pleural

and peritoneal still communicate. In the embryos with a vertex breech measurement exceeding 17 mm. the pleural and peritoneal have been separated completely.

The separation of the pleural from the pericardial cavity is dependent upon the complete development of the diaphragm. At first the septum transversum and the membrana reuniens are on the ventral side of the pleural cavity, and both are still located within the head. As the septum transversum descends into the body it is next located on the dorsal side of the heart. In other words, the dorsal end of the septum transversum has not moved as rapidly as the ventral end, and thus the whole mass of tissue has turned a quarter revolution. This is accompanied by the extreme flexion of the head, as represented in embryo No. II. At this time the septum transversum has descended to the lower part of the cervical region. Now the septum begins to turn in the other direction again, for with the development of the neck the ventral end of the septum becomes the fixed point and the dorsal end moves more rapidly. The successive stages in the movement of the septum are best shown in the diagrammatic Fig. 1453.

Fig. 1454 shows the septum transversum on the ventral side of the stomach and the pleural cavity communicating with the peritoneal at the point X. The Wolffian body and the suprarenal capsule, which is very large, have receded markedly, and the pleural cavity already forms a pocket on the dorsal side of them. A sagittal section through this region, somewhat distant from the median line, is given in Fig. 1457. A transverse section of the embryo pictured in Fig. 1454 is given in Fig. 1455. This

section is just at the point above the opening, and shows the communication between its pleural and peritoneal cavities closed on one side, but open on the other. There is a ridge on the side of the cavity which projects between the lung and the liver and continues down to the suprarenal capsule. This ridge has been well described by Ravn,<sup>65</sup> who gives an excellent illustration of the opening with the ridge encircling it.

In all the embryos in which the pleural and peritoneal cavities still communicate, the vena cava does not yet communicate with the posterior cardinal vein.

Fig. 1457 is from an embryo slightly larger than the one from which Fig. 1454 was taken. The pleuro-peritoneal communication has just closed by the walls of the ridge having grown together; the extent and shape of the pleural cavity is much as it is in Fig. 1454. The Wolffian body is smaller, and the kidney and suprarenal capsule have come together.

The story, then, is brief: as the diaphragm descends, its dorsal end is in apposition with the suprarenal capsule, and finally, when the capsule approaches the twelfth rib, a ridge of tissue which also includes the capsule unites with a ridge from the septum transversum, and the opening is closed. These two ridges, however, are portions of one and the same ridge, as they form a circle and in section appear as two ridges. The circle is closed much after the fashion of tying up a bag.

All of the abdominal organs, with the exception of the kidney, descend; and the descent is not

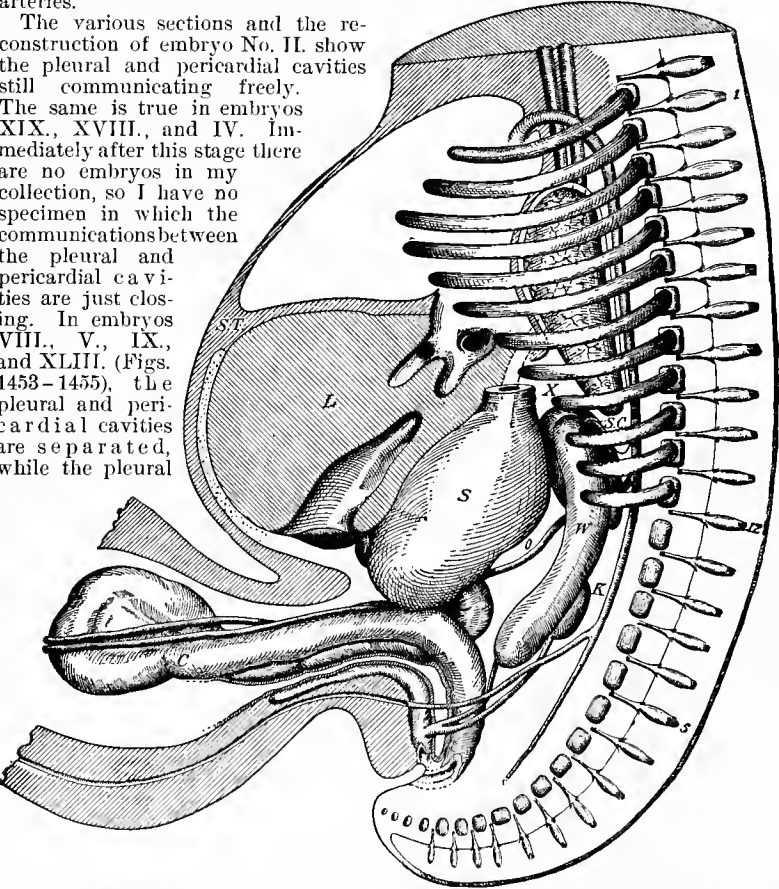


FIG. 1454.—Reconstruction of Embryo No. IX. Enlarged 17 times. S.T., Septum transversum; L, liver; S, stomach; C, cœcum; W, Wolffian body; K, kidney; T-12, dorsal ganglia; o, omphalomesenteric artery. The ventral mesentery of the liver is dotted, as it is only a thin membrane; S.C., suprarenal capsule; X, point of communication between pleural and peritoneal cavities.

completed until the pelvis is formed to admit some of them. In the stages pictured nearly all the small intestine lies in the umbilical cord, as is the case in many

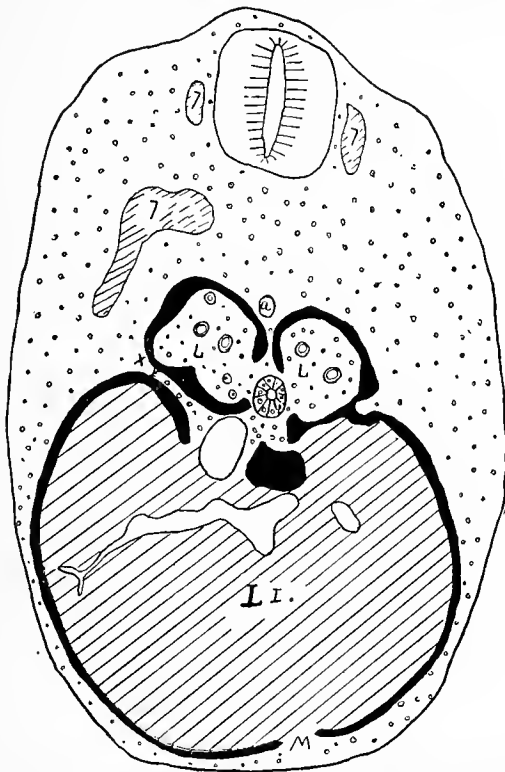


FIG. 1455.—Section through the Point of Communication between the Pleural and Peritoneal Cavities in Embryo No. IX. Enlarged 15 times. 7, Seventh rib; L, lung; Li, liver; M, ventral mesentery of liver; a, aorta. The diaphragm is complete on one side, X, while it is incomplete on the other.

mammalian embryos. In embryo X. (Fig. 1457) a large portion of the liver also projects into the cord. I have also observed a hernia of the liver in another embryo somewhat larger. I do not consider the form of embryo X. altogether normal, but this was not noticed until the reconstruction was complete.

Closely associated with the closing of the pleuro-peritoneal opening is the development of the celiac ganglion. In these young embryos it is extremely large, and can be outlined already, while the septum transversum is still high in the thorax. As the septum descends, the various communicating branches of the nerves are caught up with the celiac ganglion and dragged along. This accounts for the high origin of the splanchnic nerve.

Fig. 1458 (embryo VI.) shows that all the tissues are becoming more definitely outlined, and the whole structure is firmer than in embryo X. The organs of the abdomen are more firmly clustered together, and the intestine has become more convoluted. The lung is much larger, and the pleural cavity extends to the ventral wall of the embryo, obscuring wholly the outline of the heart. In general it confirms everything given in Fig. 1457.

Minot<sup>66</sup> has stated that the pleural cavities are to be considered a portion of the septum transversum, because they lie on the dorsal side of it. From what has already been said above it will be seen that I consider the septum transversum the mass of tissue between the pericardial cavity, the pleural cavities, and the opening between the two sides of the peritoneal cavity immediately below the liver, marked O in Figs. 1428 and 1442. This tissue includes the membrana reuniens, which is really the wings of the septum transversum as described by His. In my account I have employed the term membrana reuniens wherever

possible to avoid confusion, and have usually employed the terms septum and primitive diaphragm as synonyms.

There are developed within the region of the septum transversum the whole liver, including its ventral mesentery, the lesser peritoneal cavity, the stomach, and the suprarenal capsule. This same region which I have marked out by these three boundaries as the septum transversum is still sharply defined in the adult. The point O in Figs. 1428 and 1442 is still as definably marked as ever by the round ligament, foramen of Winslow, and the duct passing from the liver to the duodenum. The round ligament is developed by the umbilical vein shifting around the side of the abdominal walls into the ventral mesentery of the liver, and then when the liver is retracted from the umbilical cord, the vein and mesentery remain as the round and broad ligaments respectively.

*Lesser Peritoneal Cavity.*—I have already discussed the lesser peritoneal cavity in a separate paper,<sup>67</sup> and find that I can confirm all that I have stated at that time. I can only add that the portion of it extending up under the lung degenerates, while the omental sac is growing rapidly. I have also found that it is extremely easy for the omentum to find its way over the large intestine. At the time this takes place the large intestine is in the median line, while the stomach and the omentum are on the left side of the body. After the intestine is retracted

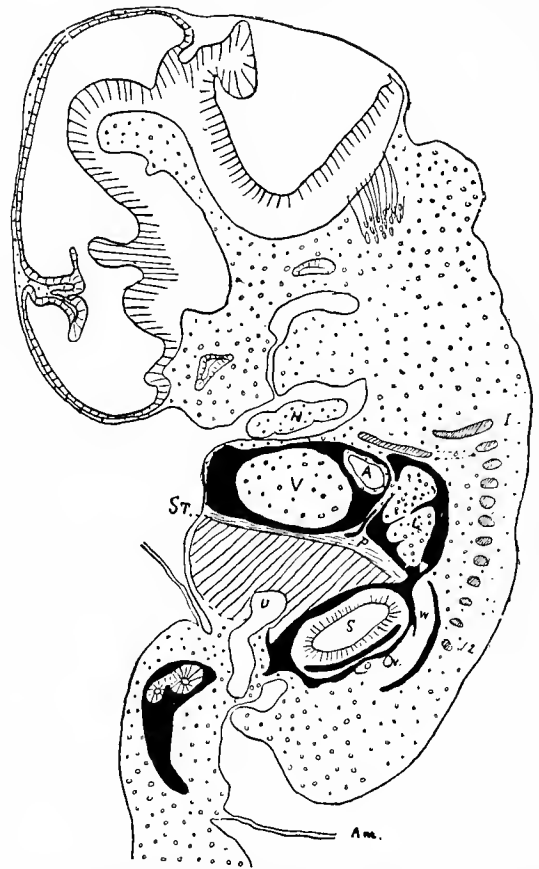


FIG. 1456.—Section through Embryo No. XLIII. Enlarged 8 times. H, Hand; A, auricle; V, ventricle; L, lung; S T, septum transversum; P, phrenic nerve; U, umbilical vein; St, stomach; W, Wolffian body; Ov, ovary; Am, amnion; 1-12, ribs.

from the cord the caecum falls over to the right side of the body, while the descending colon is shifted to the left side, and the omentum then comes to lie on the ventral side of the transverse colon.

*Expansion of the Body Cavity and Obliteration of the Extra-Embryonic Cœlom.*—After the pleural and pericardial

cavities are separated from each other it is very easy to follow their further development. In embryo II., Fig. 1459, the heart is still upright, and a transverse section of

cardial accounts for the location of the phrenic nerve in the adult. In Fig. 1459 the nerve passes to the septum transversum from the lateral body wall, and it is gradually separated from it by the descent of the septum and by the growth of the pleural cavity between the nerve and the body wall, thus locating the nerve in a membrane, as Figs. 1460 and 1461 will readily explain.

The expansion of the peritoneal cavity is by no means as simple. In it there are many bands and mesenteries as well as a marked shifting of the organs. With the descent of the testis a portion of it is cut off to form the tunica vaginalis.

In embryo II. the peritoneal cavity is extremely simple, as the figures show,—a simple cavity on each side communicating the one with the other by means of two openings, one above and one below the omphalomesenteric duct. Later, as the diaphragm descends more and more, the liver rotates, and its lobes soon fill the peritoneal cavity, while the intestine develops out into the core. The Wolffian body, sexual glands, and suprarenal capsule fill the dorsal side of the cavity and the rudimentary pelvis. The whole development of the intestine takes place within the cord, and finally it is drawn into the embryos when it is about 30 mm. in length. By what process this takes place I am unable to determine, but it must take place very rapidly, for I have never seen a human embryo in which it is only partly retracted. In the pig's embryo, however, I have found the stages in which the intestine is in process of retraction.

The liver now fills nearly the whole cavity, and extends down to the pelvis, and in embryo XXII. projects over the

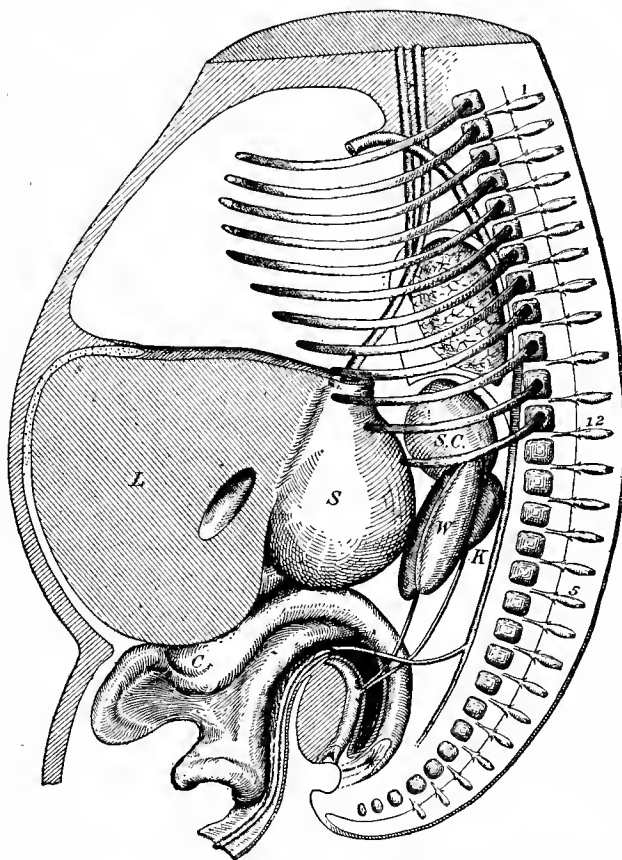


FIG. 1457.—Reconstruction of Embryo No. X. Enlarged 8 times. 1-12, Dorsal ganglia; S.C., suprarenal capsule; W, Wolffian body; K, kidney; L, liver; S, stomach; C, caecum. The dotted area on the ventral side of the liver indicates the extent of the ventral mesentery of the liver.

it is also transverse to the lung. The pleural cavity lies wholly on the dorsal side of the pericardial (Fig. 1444). In the next stage, as the lungs descend more and more, the heart is tilted over so that its base is toward the lung and its apex away from it, as in embryo IX., shown in Figs. 1454 and 1460. The pericardial space has now become separated completely from the pleural, although both have grown at about the same pace. From now on the pleural space grows more rapidly than the pericardial, as shown in Fig. 1461. I have a number of embryos which represent intermediate stages between embryos IX. and XXII., and all of them confirm the idea that the pleural space develops first and then is followed by a growth of the lung. Fig. 1462, which is a section of embryo No. XLV., shows a marked increase in the size of the lung, but the heart and pericardial space are of about the same size as in embryo XXII. A much later stage is shown in Fig. 1463. The scale of enlargement is only half that of Fig. 1462, and when this is considered it is again seen that the heart has not grown very much, but the lung has developed enormously.

It is therefore seen that at first the pericardial cavity is on the oral side of the pleural, then on the ventral side, and is finally enclosed by the pleural cavity growing over it.

The growth of the pleural cavity over the peri-

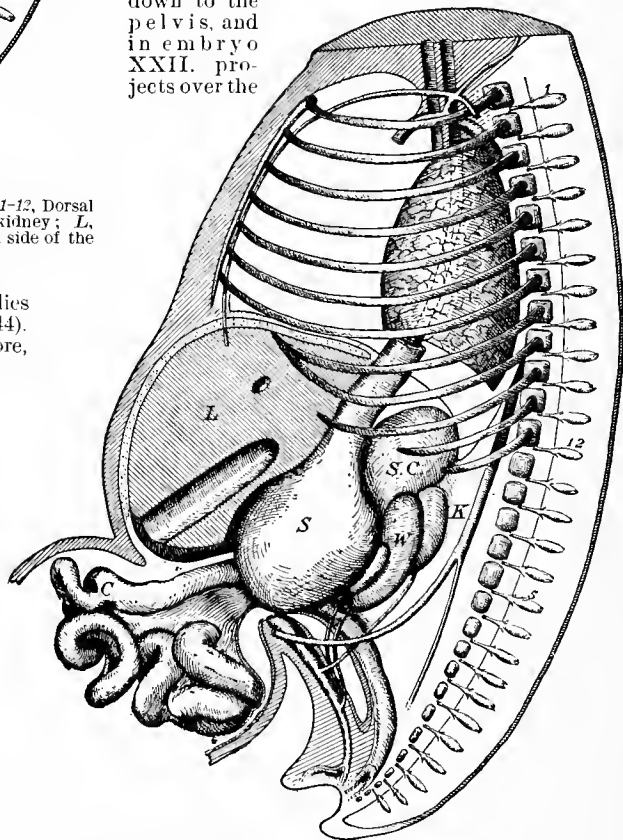


FIG. 1458.—Reconstruction of Embryo No. VI. Enlarged 8 times. 1-12, Dorsal ganglia; S.C., suprarenal capsule; K, kidney; W, Wolffian body; S, stomach; C, caecum; L, liver. The dotted area on the ventral side of the liver indicates the extent of the ventral mesentery.

ovary and is in contact with the rectum. As the intestines are retracted from the cord the liver is relatively higher and higher, for the expansion of the abdominal walls is now greater below the umbilical cord than before, giving more space in this region for the intestine which displaces the liver. In embryos XXXIV. and XLVIII. the intestine has been studied, and it was found that it



FIG. 1459.

FIG. 1460.

FIG. 1461.

FIGS. 1459 to 1461.—Outlines of the Pleural and Pericardial Cavities to Show Their Relative Position and Size. Enlarged 7 times. Fig. 1459, Embryo No. II.; Fig. 1460, Embryo No. IX.; Fig. 1461, Embryo No. XXII. H, position of heart; L, position of lung.

is still located in the ventral portion of the peritoneal cavity, as there is no pelvic cavity large enough to hold any portion of it.

The extra-embryonic cœlom has only a short existence, as it is already completely obliterated in embryo No. XXII. This embryo came to me in an unopened ovum,

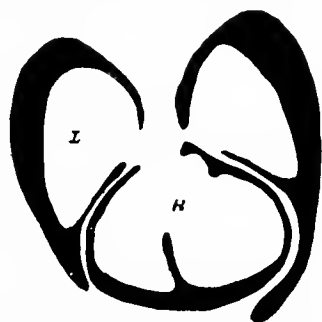


Fig. 1462.—Outline of Pleural and Pericardial Cavities in Embryo No. XLV. Enlarged 7 times.

and on this account is extremely valuable for this purpose. This embryo is about six weeks old, so, reasoning from it, the union of the amnion and chorion takes place earlier than is generally believed. In embryo No. XLIII., which is about five weeks old, the amnion has expanded over the whole embryo and has nearly reached the chorion

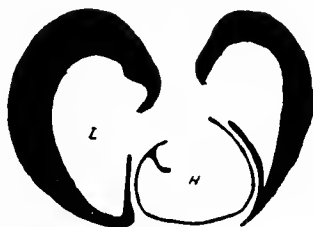


Fig. 1463.—Outline of Pleural and Pericardial Cavities in Embryo No. XXXIV. Enlarged  $3\frac{1}{2}$  times. H, Position of heart; L, position of lung.

The earlier stages are given in the sagittal sections. They show that the amnion is nearest the chorion at the caudal end of the embryo in the earliest stages, and soon the two unite at this point. As the embryo grows, the union of amnion and chorion extends. At the end of the fourth

week the extra-embryonic cœlom is still very large; at the end of the fifth week the space between the embryo and chorion is divided equally between the amnion cavity

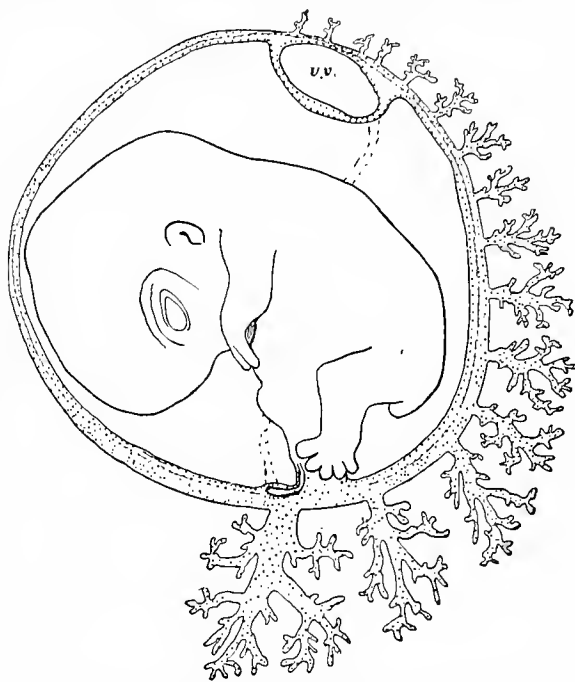


Fig. 1464.—Embryo No. XXII. Within the Ovum. Enlarged 3 diameters. The villi of chorion are outlined on one side of the ovum only. The umbilical vesicle, u.v., has become shifted around to the dorsal and right side of the embryo. The outline is made from a photograph, and is correct in detail with the exception of the attachment of the chord to the chorion. This in reality attaches itself to the chorion immediately to the right of the embryo.

and the cœlom; at the end of six weeks the extra-embryonic cœlom has disappeared. *Franklin P. Mall.*

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