hypoblastic spheres now passes to the centre of the ovum; and the four epiblastic spheres, which are at the periphery, divide, each one into two, making eight epiblastic and four hypoblastic spheres. When this has occurred, the epiblastic spheres are smaller and more transparent than the hypoblastic spheres. The four hypoblastic spheres now divide into eight. The epiblastic spheres then divide into sixteen, the hypoblastic spheres in turn divide, and this goes on until the process of segmentation is completed. In the rabbit, this occurs usually about seventy hours after impregnation (Van Beneden). As segmentation progresses, the epiblastic cells ex-

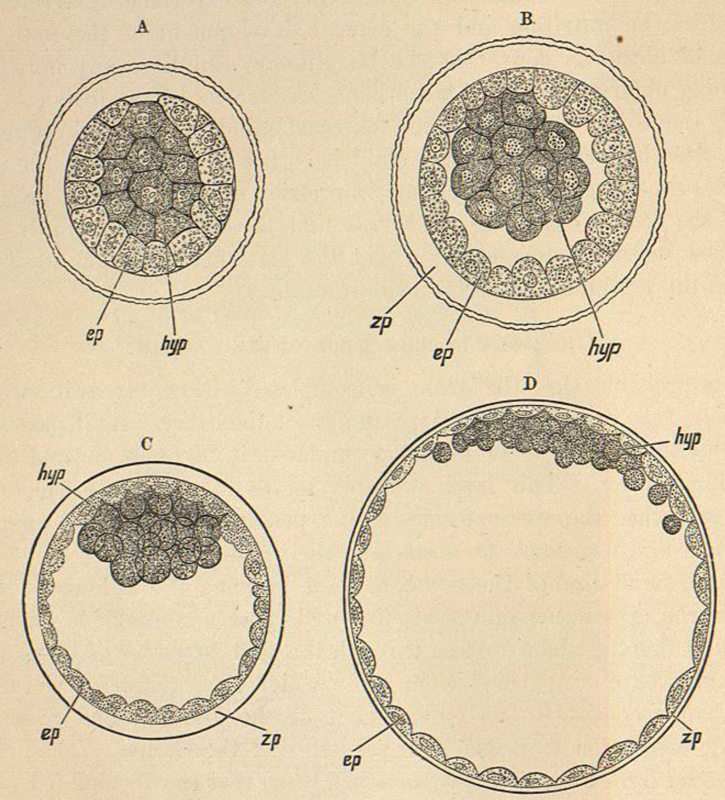


FIG. 293.—*Formation of the blastodermic vesicle* (Van Beneden).
A, B, C, D, sections of ova in successive stages of development in the rabbit; *zp*, zona pellucida; *ep*, epiblastic cells; *hyp*, hypoblastic cells.

tend over the hypoblastic cells, and become irregularly polygonal in form. The hypoblastic cells occupy the central portion of the ovum. At first there is a circular space upon the ovum where the epiblastic cells do not cover the cells of the hypoblast (see Fig. 293, A); but this soon becomes closed by an extension of the cells of the epiblast (see Fig. 293, B). The hypoblastic cells, at the close of segmentation, are slightly larger than the cells of the epiblast and are darker and more rounded. The ovum is now called the morula, on account of its fancied resemblance to a mulberry; and the cells of which it is composed are called collectively blastodermic



cells. The ovum is probably in this condition when it passes from the Fallopian tube into the uterus.

Most of the phenomena of segmentation have been observed in the lower forms of animals; but there can be no doubt that analogous processes take place in the human ovum. In the rabbit, forty-five and a half hours after copulation, Weil observed an ovum with sixteen segmentations, situated in the lower third of the Fallopian tube. He observed an ovum, ninety-four hours after copulation, with a delicate mosaic appearance, presenting a small, rounded eminence on its surface. It is impossible to say how long the process of segmentation continues in the human ovum. It is stated that it is completed in rabbits in a few days, and in dogs, that it occupies more than eight days (Hermann).

After segmentation has been completed, a cavity filled with liquid appears between the hypoblastic and epiblastic cells, except at that portion which has last been covered by the epiblast. Here the cells of the hypoblast are in contact with the epiblast. The liquid in the interior of the ovum gradually increases in quantity, the ovum becomes enlarged to the diameter of $\frac{1}{50}$ to $\frac{1}{25}$ of an inch (0·5 to 1 mm.), and is now called the blastodermic vesicle. The epiblastic cells surround the blastodermic vesicle completely, forming a single layer over the greater portion; and the hypoblastic cells form a lenticular mass attached to the smaller portion of the inner surface of the layer of epiblastic cells (see Fig. 293, C and D). It is at this portion of the ovum that the embryonic spot or area afterward appears.

The albuminous covering which the ovum has received in the upper part of the Fallopian tube gradually liquefies and penetrates the vitelline membrane, furnishing, it is thought, matter for the nourishment and development of the vitellus. In the Fallopian tube, indeed, the adventitious albuminous covering of the ovum presents an analogy to the albuminous coverings which the eggs of oviparous animals receive in the oviducts; with the difference that this albuminous matter is almost the sole source of nourishment in the latter and exists in large quantity, while in viviparous animals the quantity is small, is generally consumed as the ovum passes into the uterus, and in the uterus the ovum forms attachments to and draws its nourishment from the vascular system of the mother.

*Primitive Trace.*—Soon after the formation of the blastodermic vesicle, at a certain point on its surface there appears a rounded elevation or heap of smaller cells, forming a distinct spot, called the embryonic spot. As development advances, this spot becomes elongated and oval. It is then surrounded by a clear, oval area, called the area pellucida, and the area pellucida is itself surrounded by a zone of cells, more granular and darker than the rest of the blastoderm, called the area opaca. The line thus formed and surrounded by the area pellucida is called the primitive trace. This primitive trace, or primitive groove, however, is a temporary structure. After the groove is formed, there appears, in front of but not continuous with it, a new fold and a groove leading from it. This is the "head-fold," and the groove is the true medullary groove, which is subsequently developed into the neural canal.

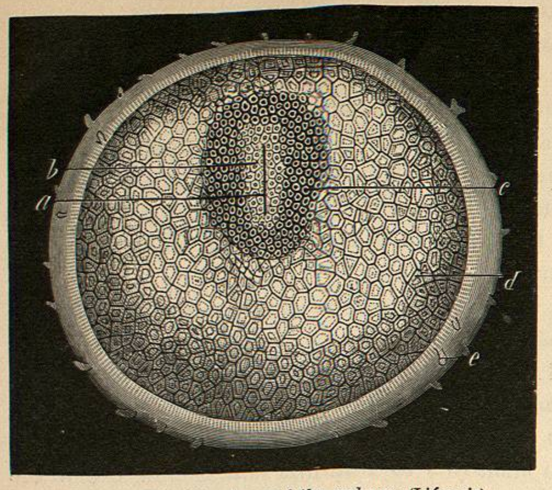


Fig. 294.—*Primitive trace of the embryon* (Liégeois).
*a*, primitive trace; *b*, area pellucida; *c*, area opaca; *d*, blastodermic cells; *e*, *e*, villi beginning to appear on the vitelline membrane.

*Blastodermic Layers.*—The blastodermic cells, resulting originally from the segmentation of the vitellus, are first split apparently into two layers, the external, or epiblast, and the internal, or hypoblast. The epiblast is developed into the epidermis and its appendages, the glands of the skin, the brain and spinal cord, the organs of special sense and possibly some parts of the genito-urinary apparatus. The hypoblast is developed into the epithelium lining the mucous membrane and glands of the stomach and intestinal canal. There is a thickening of both of these layers at the line of development of the cerebro-spinal system, with a furrow that is finally enclosed by an elevation of the ridges and their union posteriorly, forming the canal for the spinal cord.

As the spinal canal is developed, a new layer of cells is formed between the epiblast and the hypoblast, which is called the mesoblast. The mesoblast itself afterward splits into two layers. All the parts not enumerated as developed from the epiblast or hypoblast are developed from the two layers of the mesoblast. The outer layer of the mesoblast, or the epiblastic mesoblast, unites with the epiblast, and the two membranes together form what is sometimes called the somatopleure. The inner layer of the mesoblast, the hypoblastic mesoblast, unites with the hypoblast to form what is called the splanchnopleure. The cells lining the vessels, including the lymphatics, which exist in a single layer, are called endothelial cells. This name is also applied to the cells lining the serous membranes.

### Formation of the Membranes.

In the mammalia a portion of the blastoderm is developed into membranes by which a communication and union are established between the ovum and the mucous membrane of the uterus. From the ovum two membranes are developed; one non-vascular, the amnion, and another, the allantois, which is vascular. The two layers of decidua are formed from the mucous membrane of the uterus. At a certain part of the uterus, a vascular connection is established between the mucous membrane and the allantois,



and the union of these two structures forms the placenta. The fœtal portion of the placenta is connected with the fœtus, by the vessels of the umbilical cord, and the maternal portion is connected with the great uterine sinuses.

The external covering of the ovum, during the first stage of its development, is the vitelline membrane. As the ovum is received into the uterus, the vitelline membrane develops upon its surface little villosities, which are non-vascular and are formed of amorphous matter with granules. These are the first villosities of the ovum, and they assist in fixing the egg in the uterine cavity. They are not permanent, they do not become developed into the vascular villosities of the chorion and they disappear as the true membranes of the embryon are developed from the blastodermic layers. The vitelline membrane disappears soon after the passage of the ovum into the uterus, when it is replaced by the amnion.

*Formation of the Amnion.*—As the ovum advances in its development, it is observed that a portion of the blastoderm becomes thickened, forming the epiblast, the two layers of the mesoblast and the hypoblast. At about the time when this thickening begins, a fold of the epiblast and of the external layer of the mesoblast makes its appearance, which surrounds the thickened portion and is most prominent at the cephalic and the caudal extremity of the furrow for the neural canal. This fold increases in extent as development advances, passes over the dorsal surface of the embryon and finally meets so as to enclose the embryon completely. At a certain period of the development of the amnion, this membrane consists of an external layer, formed of the external layer of the fold, and an internal layer; and the point of union of the two layers, or the point of meeting of the fold, is marked by a membranous septum.

The two amniotic layers are formed in the way just described, and a complete separation finally takes place, by a disappearance of the septum formed by the meeting of the folds over the back of the embryon. This process occupies four or five days, in the human ovum. The point where the folds meet is called the amniotic umbilicus. When the amnion is thus completely formed, the vitelline membrane has been encroached upon by the external amniotic layer and disappears, leaving this layer of the amnion as the external covering of the ovum. At this time there is a growth of villosities upon the surface of the external amniotic layer, which, like the villosities of the vitelline membrane, are not vascular.

Soon after the development of the amnion the allantois is formed. This membrane is vascular. It encroaches upon and takes the place of the external amniotic membrane, and is covered with hollow villi, which take the place of the villi of the amnion. Over a certain portion of the membrane the villi are permanent. The mode of development of the amnion is illustrated by the diagrammatic Fig. 295. This figure illustrates the formation of the amnion, the umbilical vesicle and the allantois. The last two structures are derived from the hypoblast and the internal layer of the mesoblast.

When the allantois has become the chorion, or the external membrane of the ovum, having taken the place of the external layer of the amnion, the structures of the ovum are the following: 1. The chorion, formed of the two layers of the allantois and penetrated by blood-vessels. 2. The umbili-

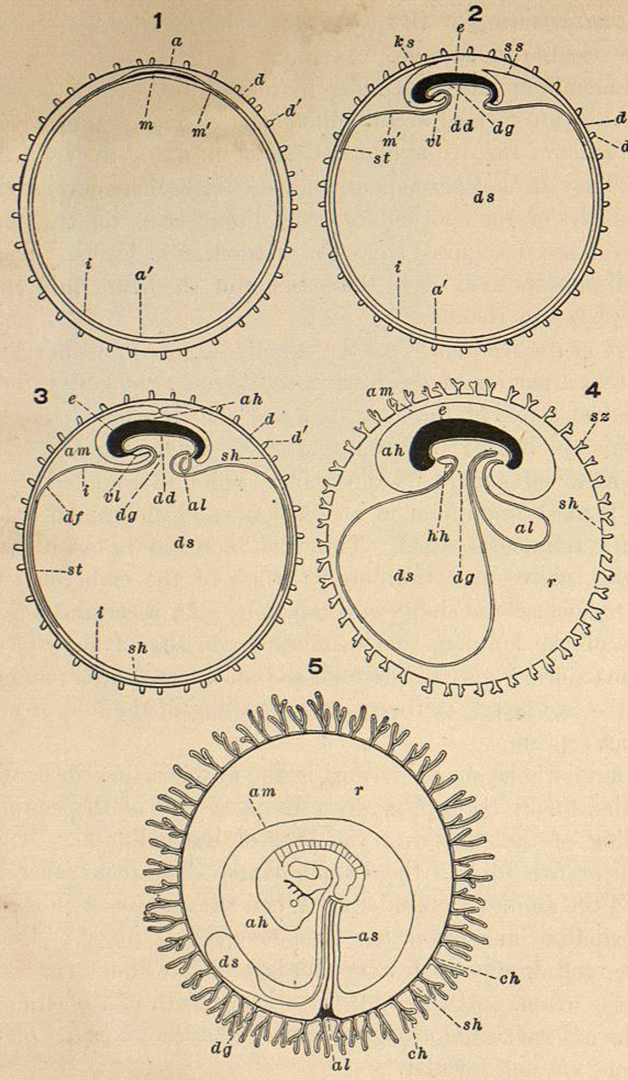

FIG. 295.—*Five diagrammatic representations of the formation of the membranes in the mammalia* (Kölliker).

1: *a*, *a'*, epiblast; *d*, vitelline membrane; *d'*, villi on the vitelline membrane; *i*, hypoblast; *m*, *m'*, mesoblast.
2: *a'*, external layer of the amnion; *d*, *d'*, vitelline membrane; *e*, embryon; *d s*, umbilical vesicle; *v l*, *k s*, *s s*, folds of the amnion; *d d*, *m'*, *s t*, hypoblast; *d d*, connection of the embryon with the umbilical vesicle.
3: *d*, *d'*, vitelline membrane; *v l*, internal amniotic layer; *e*, embryon; *a h*, amniotic cavity; *s h*, *s h*, external amniotic layer; *a m*, space between the two layers of the amnion; *d d*, hypoblast; *d f*, *s t*, *i*, walls of the umbilical vesicle; *d g*, omphalo-mesenteric canal; *d s*, cavity of the umbilical vesicle; *a l*, first appearance of the allantois.
4: *s h*, external layer of the amnion; *s z*, villi of the external layer of the amnion, which has now become the chorion, the vitelline membrane having disappeared; *h h*, *a m*, internal layer of the amnion; *e*, embryon; *a h*, amniotic cavity; *d g*, omphalo-mesenteric canal; *d s*, cavity of the umbilical vesicle; *a l*, allantois; *r*, space between the two layers of the amnion.
5: *c h*, *s h*, *c h*, *a l*, allantois (which has now become the chorion, the external amniotic layer having disappeared), with its villi; *a m*, amnion; *a s*, amniotic covering of the umbilical cord; *r*, space between the amnion and the allantois; *a h*, amniotic cavity; *d s*, umbilical vesicle; *d g*, omphalo-mesenteric canal.

Pl. III.

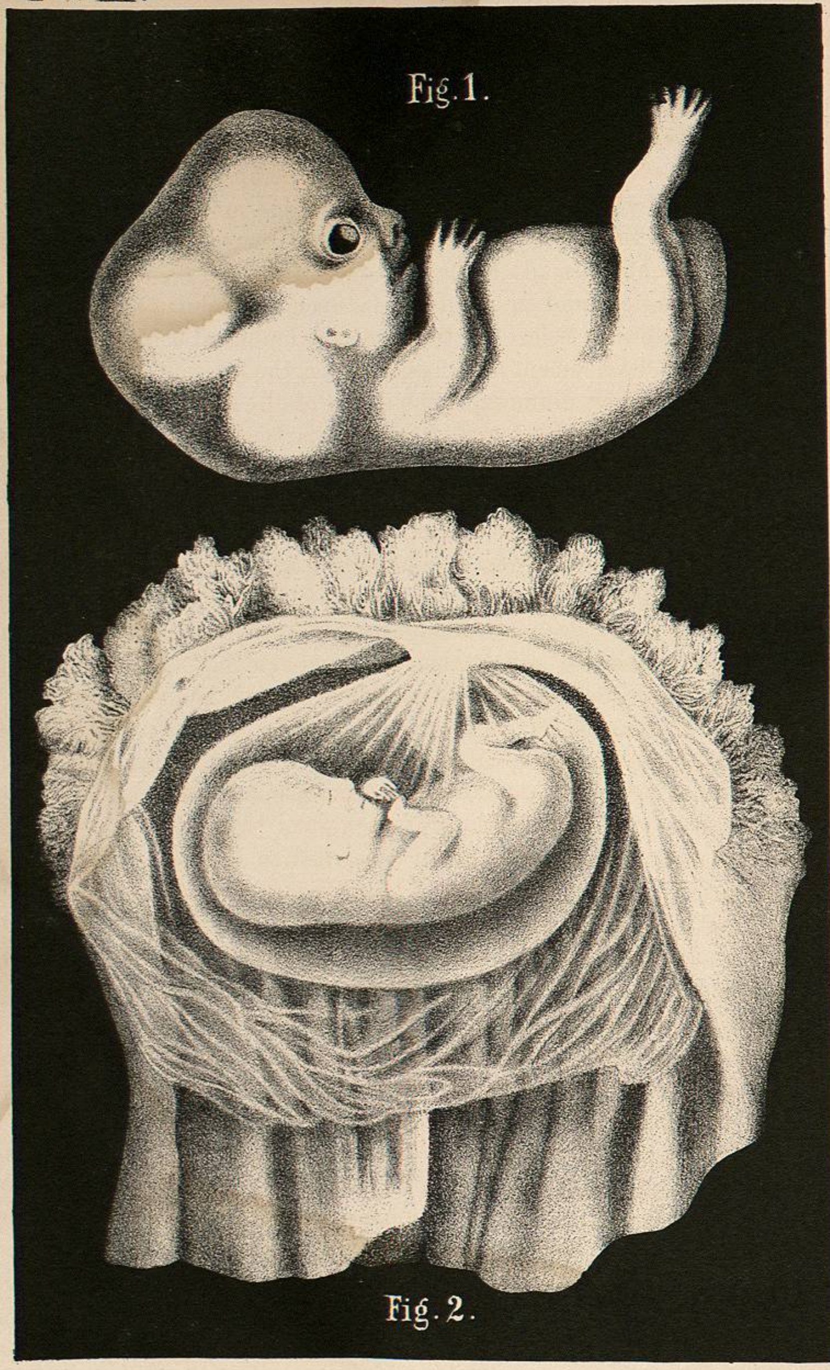


FIG. 1.—Human embryon, at the ninth week, removed from the membranes; three times the natural size (Erdl).

FIG. 2.—Human embryon, at the twelfth week, inclosed in the amnion; natural size (Erdl).



cal cord, which connects the embryon with the placental portion of the chorion, and the umbilical vesicle, formed from the same layers as the allantois. 3. The amnion, which is the internal layer of the amniotic fold, persisting throughout fœtal life. 4. The embryon itself.

During the early stages of development of the umbilical vesicle and the allantois, the internal amniotic layer, or the true amniotic membrane, is closely applied to the surface of the embryon, and is continuous with the epidermis, at the umbilicus. It is then separated from the allantois by a layer of gelatinous matter; and in this layer, between the amnion and the allantois, is the umbilical vesicle. At this time the umbilical cord is short and not twisted. As development advances, however, the intermembranous gelatinous matter gradually disappears; the cavity of the amnion is enlarged by the production of a liquid between its internal surface and the embryon; and at about the end of the fourth month, the amnion comes in contact with the internal surface of the chorion. At this time the embryon floats in the amniotic cavity, surrounded by the amniotic fluid.

The amnion forms a lining membrane for the chorion. By its gradual enlargement it has formed a covering for the umbilical cord; and between it and the cord, is the atrophied umbilical vesicle. The amnion then resembles a serous membrane, except that it is non-vascular. It is lined by a single layer of pale, delicate cells of pavement-epithelium, which contain a few fine, fatty granulations. At term the amnion adheres to the chorion, although it may be separated, with a little care, as a distinct membrane and may be stripped from the cord. From its arrangement and from the absence of blood-vessels, it is evident that this membrane is simply for the protection of the fœtus and is not directly concerned in its nutrition and development (see Plate III, Fig. 2). The gelatinous mass referred to above, situated, during the early periods of intraüterine life, between the amnion and the chorion, presents a semi-fluid consistence, with very delicate, interlacing fibres of connective tissue and fine, grayish granulations scattered through its substance. These fibres are gradually developed as the quantity of gelatinous matter diminishes and the amnion approaches the chorion, until finally they form a rather soft, reticulated layer, which is sometimes called the membrana media.

*Amniotic Fluid.*—The process of enlargement of the amnion shows that the amniotic fluid gradually increases in quantity as the development of the fœtus progresses. At term the entire quantity is variable, being rarely more than two pints (about one litre) or less than one pint (about half a litre). In the early periods of utero-gestation it is clear, slightly yellowish or greenish, and perfectly liquid. Toward the sixth month its color is more pronounced and it becomes slightly mucilaginous. Its reaction usually is neutral or faintly alkaline, though sometimes it is feebly acid in the latest periods. It sometimes contains a small quantity of albumin, as determined by heat and nitric acid; and there generally is a gelatinous precipitate on the addition of acetic acid. The following table gives its chemical composition (Robin):

COMPOSITION OF THE AMNIOTIC FLUID.

| | |
|---|---|
| Water | 991·00 to 975·00 |
| Albumin and mucine | 0·82 " 10·77 |
| Urea | 2·00 " 3·50 |
| Creatine and creatinine (Scherer, Robin and Verdeil) | not estimated |
| Sodium lactate (Vogt, Regnauld) | a trace |
| Fatty matters (Rees, Mack) | 0·13 to 1·25 |
| Glucose (Bernard) | not estimated |
| Sodium chloride and potassium chloride | 2·40 to 5·95 |
| Calcium chloride | a trace |
| Sodium carbonate | a trace |
| Sodium sulphate | a trace |
| Potassium sulphate (Rees) | a trace |
| Calcareous and magnesian phosphates and sulphates | 1·14 to 1·72 |

The presence of certain of the urinary constituents in the amniotic fluid has led to the view that the urine of the fœtus is discharged in greater or less quantity into the amniotic cavity. Bernard, who is cited in the table of composition of the amniotic fluid as having determined the presence of sugar, has shown that in animals with a multiple placenta, the amnion has a glycogenic action during the early part of intraüterine existence.

With regard to the origin of the amniotic fluid, it is impossible to say how much of it is derived from the general surface of the fœtus, how much from the urine, and how much from the amnion itself, by transudation from the vascular structures beneath this membrane. The quantity apparently is too great, especially in the early months, to be derived entirely from the urine of the fœtus, and there probably is an exudation from the general surface of the fœtus and from the membranes. After the third month the sebaceous secretion from the skin of the fœtus prevents the absorption of any of the liquid. An important property of the amniotic fluid is that of resisting putrefaction and of preserving dead tissues.

*Formation of the Umbilical Vesicle.*—As the visceral plates, which will be described hereafter, close over the front of the embryon, that portion of the blastoderm from which the intestinal canal is developed presents a vesicle, which is cut off from the abdominal cavity but which still communicates freely with the intestine. This is the umbilical vesicle. On its surface, is a rich plexus of blood-vessels; and this is a very important organ in birds and in many of the lower forms of animals. In the human subject and in mammals, however, the umbilical vesicle is not so important, as nutrition is secured by means of vascular connections between the chorion and the uterus. The vesicle becomes gradually removed farther and farther from the embryon, as development advances, by the elongation of its pedicle, and it is compressed between the amnion and the chorion, as the former membrane becomes distended.

When the umbilical vesicle is formed, it receives two arteries from the two aortæ, and the blood is returned to the embryon, by two veins, which open into the vestibule of the heart. These are called the omphalo-mesenteric vessels. At about the fortieth day one artery and one vein disappear, and soon after, all vascular connection with the embryon is lost. At first there is a canal of communication with the intestine, called the omphalo-mesenteric canal. This is gradually obliterated, and it closes, between the thirtieth and the thirty-fifth day. The point of communication of the vesicle with the intestine is called the intestinal umbilicus; and early in the process of development, there is here a hernia of a loop of intestine. The umbilical vesicle remains as a tolerably prominent structure as late as the fourth or fifth month, but it may often be discovered at the end of pregnancy.



The umbilical vesicle presents three coats; an external, smooth membrane, formed of connective tissue, a middle layer of transparent, polyhedric cells, and an internal layer of spheroidal cells. The membrane, composed of these layers, encloses a pulpy mass, composed of a liquid containing cells and yellowish granulations.

*Formation of the Allantois and the Permanent Chorion.*—During the early stages of development of the umbilical vesicle, and as it is shut off from the intestine, there appears an elevation at the posterior portion of the intestine, which rapidly increases in extent, until it forms a membrane of two layers, which is situated between the internal and the external layers of the amnion. This membrane becomes vascular early in the progress of its development, increases in size quite rapidly, and finally it completely encloses the internal layer of the amnion and the embryon, the gelatinous mass already described being situated between it and the internal amniotic layer before this membrane becomes enlarged. While the formation of the two layers of the allantois is quite distinct in certain of the lower forms of animals, in the human subject and in mammals it is not so easily observed; still there can be no doubt as to the mechanism of its formation, even in the human ovum. Here, however, the allantois soon becomes a single membrane, the two original layers of which can not be separated from each other. The process of the development of the allantois is shown in the diagrammatic Fig. 295 (3, 4, 5).

It is the vascularity of the allantois which causes the rapid development by which it invades and finally supersedes the external layer of the amnion, becoming the permanent chorion, or external membrane of the ovum. At first there are two arteries extending into this membrane from the lower portion of the aorta, and two veins. The two arteries persist and form the two arteries of the umbilical cord, coming from the internal iliac arteries of the fœtus; and one vein, the umbilical vein, which returns the blood from the placenta to the fœtus, is permanent. These vessels are connected with the permanent, vascular tufts of the chorion.

The development of the allantois can not be well observed in human ova before the fifteenth or the twenty-fifth day. When the allantois becomes the permanent chorion, it is marked by a large number of hollow, branching villi over its entire surface, which give the ovum a shaggy appearance. As the ovum enlarges, over a certain area surrounding the point of attachment of the pedicle which connects the chorion with the embryon, the villi are