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	
Siegenbeek van Henkelom	.325 × ?	5.5 × 4.5	13 days.
Mall (No. XI.)	1.5 × 1.0	10 × 7	14 "
Reichert	1.75 × 1.5	5.5 × 3.3	12* "
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 (Lg.)	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 pruinosus	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 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 handled 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 shrunken.

LIST OF EMBRYOS STUDIED.

No.	LENGTH OF MILLIMETRES. V. B.*	N. B.	From whom obtained.
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.
XIX	19	18	Dr. Sewall, Denver, Col.
XVIII	19.5	18	Dr. Booker, Baltimore, Md.
VII	20	18	Dr. Snively, Waynesboro, Penn.
XXII	23	20	Dr. Howard, Cleveland, Ohio.
LVII	24	....	Dr. C. O. Miller, Baltimore, Md.
VI	24	20	Dr. W. S. Miller, Madison, Wis.
X	28	19	Dr. Douglas, Nashville, Tenn.
XLV	80	60	Dr. Ellis, Elkton, Md.
XXXIV	130	110	Dr. Wilson, Worcester, Mass.
XLVIII			

* 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 μ 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.[6] XII., and II.[7] 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. VII., IX., X., XXXIV., XLV., and XLVIII. were modelled by Born's method.[8]

The mechanical portion of reconstruction has been simplified to a great extent by a special apparatus used in the Anatomical Laboratory,[9] 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 CŒLOM 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 conception of the formation of the amnion in the human embryo.[10]

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[11] 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,[12] 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[13] 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[14] paper with the two plates accompanying Graf Spee's[15] 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,[16] 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[17] 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[18] 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[19] 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[20] 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.

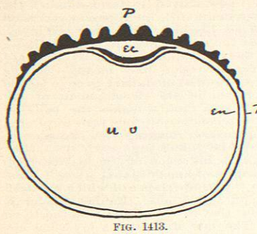

FIG. 1413.

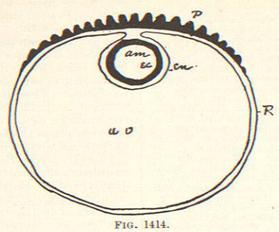

FIG. 1414.

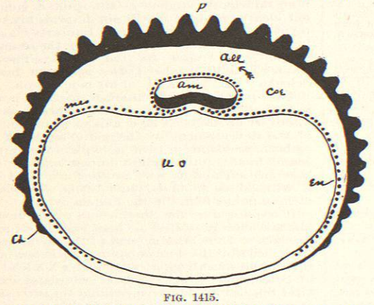

FIG. 1415.

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; *u v*, umbilical vesicle; *mes*, mesoderm; *coe*, cœlom; *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[21] 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 explana-

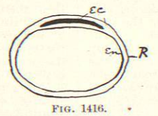

FIG. 1416.

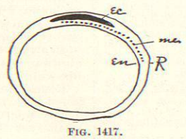

FIG. 1417.

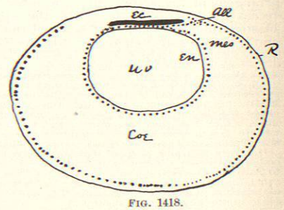

FIG. 1418.

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*, cœlom; *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[22] and by myself,[23] 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. H. 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,

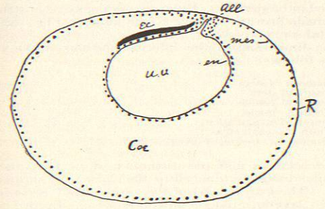

FIG. 1419.—Diagram of a Pathological Ovum which Represents an Early Hypothetical Stage.

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,[24] by Giacomini,[25] 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— Ovum.	Dimensions of— Vesicle.	Time between last period and abortion.	
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	30 × 18 × 12	6	71 "	" "
LXXVIII	36 × 33 × 13	1 × 6	87 "	Multiple amnion.
XXIV	21 × 16 × 5	2.6	.....	" "
XIV	30	1.5	.....	No amnion.
CXXIII	17 × 14	2 × 1.5	27 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[26] 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[27] 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

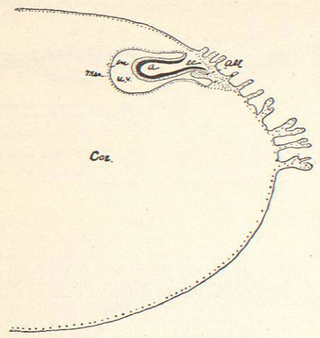

FIG. 1420.—Diagrammatic Section of Half of the Human Ovum No. XI. Enlarged 10 times. The villi are drawn only on the upper side. *ec*, Ectoderm; *en*, entoderm; *mes*, mesoderm; *uv*, umbilical vesicle; *coe*, cœlom; *all*, allantois; *a*, amnion.

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.[28] 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 resconstructed 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 μ 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-

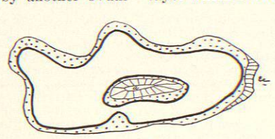

FIG. 1421.

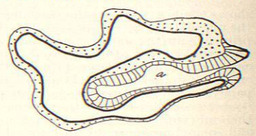

FIG. 1422.

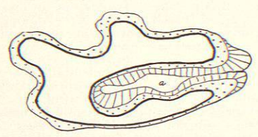

FIG. 1423.

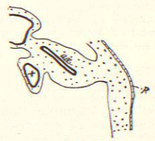

FIG. 1424.

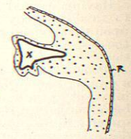

FIG. 1425.

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-vesssels 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[29] 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[30] 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 H 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

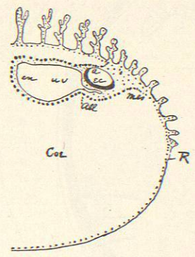

FIG. 1426.

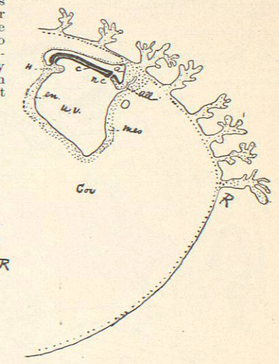

FIG. 1427.

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*, Rauber's layer; *a*, amniotic cavity; *u v*, umbilical vesicle; *en*, entoderm; *mes*, mesoderm; *all*, allantois; *c*, chorda; *n c*, neurentic canal; *H*, position of heart.

the border of the ectoderm of the embryo. Similar spaces are described by Bonnet[31] for the sheep and by Selenka[32] 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[33] 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.[34] 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