TABLE II.

| No. | Diameter of ovum. | Dimensions of embryonic mass. | Time between last period and abortion. |
|---|---|---|---|
| | mm. | mm. | days. |
| XXXVII | 25 × 18 × 15 | 2 × 2 | |
| CXXX | 15 × 10 × 6 | 7 × 2 | 14 |
| XXXII | 30 | 9 × 2 | 82 |
| XXV | 25 | 6 × 2 | |
| LXXVII | 70 × 40 × 30 | 1 × 0.25 | |

In general, the size of the cord does not correspond to the size of the ovum or to its age when determined from the last menstrual period. In specimens XXXII. and

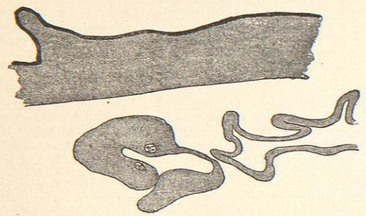

FIG. 1861.—Section through the Head, Umbilical Vesicle, and Chorion of Specimen No. XXXVII. The pharynx and first aortic arches are cut across in the head. × 10 times.

CXXX. the embryonic masses are much alike, and they might well represent the cords of embryos of the second month. The size of the ovum in XXXII. calls for this age, but the time between the first lapsed menstrual period and the abortion is much greater.

In specimen CXXX. the size of the ovum, as well as its history, places it in the early part of the third week, but at this time the cord and umbilical vesicle are much less developed than in this specimen.

It appears to me that we have in the five specimens given in Table II. five stages of a variety of pathological embryos intermediate between ova without any embryos at all and those forming embryos which are greatly deformed. At an early stage, after the formation of the amnion, through unknown causes, the embryos die, or, having been originally deformed, cease to grow, while the amnion, cord, and chorion grow on as if nothing had

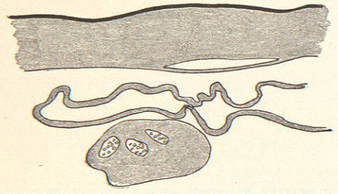

FIG. 1862.—Section through the Umbilical Cord and Vesicle and the Chorion of No. XXXVII. × 10 times.

happened. Therefore the normal villi of the chorion and the comparative absence of magma reticulare. This continues, however, until the circulation through the embryo is greatly needed to keep up the equilibrium between the ovum and uterus and the abortion follows.

The earliest stage of this form of degeneration is represented in specimen XXXVII. (Figs. 1861 to 1863), which is made up of a very atrophic head of an embryo seated upon the tip of the umbilical cord within the amnion.

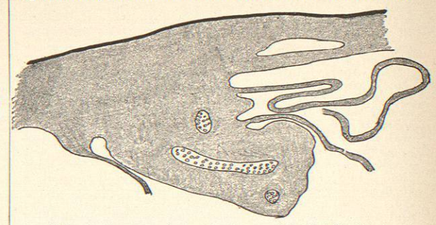

FIG. 1863.—Section through the Attachment of the Umbilical Cord and Vesicle to the Chorion in No. XXXVII. × 10 times.

The umbilical vesicle is attached to the side of the cord but does not extend in any way to the embryo. The very rudimentary nervous system, the absence of the heart, as well as other causes, are sufficient to overthrow the further growth of this embryo had the abortion not occurred.

The next stage is represented in specimen CXXX. (Figs. 1864–1866). Here the embryo is already reduced to a mass of cells which no longer contains nervous system or vascular system. It naturally dies in consequence of the absence of these important members and thus interferes with the equilibrium of the ovum. The cord is filled with blood-vessels and blood, showing again that an embryo must have been present at an earlier date.

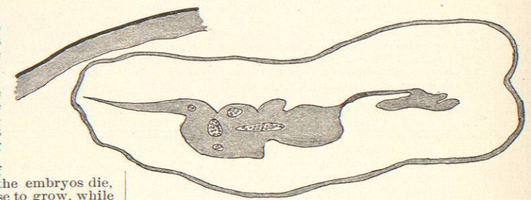

FIG. 1864.—Section through the Amnion, Cord, and Remnant of the Embryo of No. CXXX. × 10 times.

Had the amnion not been complete, the remnants of the embryo would probably have fallen off, converting this specimen into one represented in the next stage.

The relation of the amnion to the cord makes it probable that this specimen is not over three weeks old. The large cœlom also speaks for this. The large and detached umbilical vesicle is difficult to account for. It may be that the early destruction of the embryo and the overthrow of the circulation through the umbilical vesicle may have hastened its growth and favored its separation from the umbilical cord. Of course it is possible that the lasting connection between the vesicle and umbilical cord was separated by traumatic means, but a tear is not visible at any point.

A stage slightly more advanced is represented in specimen XXXII. (Figs. 1867 and 1868). Here the amnion fills the ovum completely, the embryo is entirely destroyed, and the cord shows a number of secondary changes. It may be that this stage is really but little in advance of





the specimen CXXX., as in it the embryo remnants were well protected by the amnion. In both specimens, however, the blood-vessels are well filled with blood, and at points the vascular walls are broken and the cells infil-

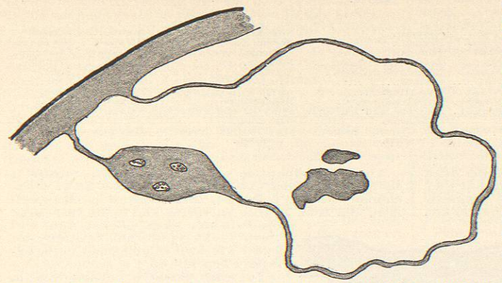

FIG. 1865.—Section through the Amnion, Cord, and Chorion of No. CXXX. × 10 times.

trate the surrounding tissues. These pictures are extremely striking and suggest an attempt at repair by the process of inflammation at this early stage. The tip of the cord is intensely stained by the carmine, suggesting very much a section through an ulcerating wound. The nucleated blood cells are out among the mesoderm cells of the cord and become necrotic as they approach its ragged edge.

The stage as represented in specimen XXXII. is shown in a somewhat advanced form in specimen XXV., Fig. 1869. The stump end of the cord is not so ragged as before; it has become rounded and the larger blood-vessels are not overdistended with blood. It appears as if the stage of great reaction between the blood cells and the necrotic tissue had passed and the wound had nearly healed.

In the five specimens described above, the morphological characteristics of the chorion, villi, and syncytium appear normal. The magma reticulare, however, is greatly diminished in quantity or is entirely wanting. With the exception of the partly deformed embryo, then, there was little to suggest that the specimens are pathological. It appears that the destruction of the embryo with a deficient quantity of magma reticulare is the only sign to account for the abortion. Specimen LXXVII., however, shows that the ovum can be retained in the uterus for a long time after the embryo has been destroyed, and that under these circumstances decided secondary changes may take place. In this specimen the chorion and amnion have both become more fibrous than normal, appearing as if all the delicate mesoderm spaces had disappeared. At the point of juncture between the amnion and chorion there is a nodule which no doubt represents the last remnant of the umbilical cord. The mesodermal tissue of the villi has also become fibrous, and there are no blood-vessels within them. There is no magma. While this stage has been reached on the inside of the ovum, the syncytium and leucocytes on the outside have become most active. With every increased quantity of fresh blood between the villi the syncytium receives new food and continues to grow. Wherever syncytium comes in contact with leucocytes it causes their destruction, as the fragmentation of their nuclei shows. But this cannot continue forever, and finally the syncytium, as well as the leucocytes, attacks the mesoderm of the chorion and its villi, and in specimen LXVII. all stages of this process are shown. Similar pictures are seen in specimen XCIII., which in all probability also belongs to this group of abnormal ova. In CXLII. the syncytial attack is still more intense; it invades the mesoderm of the chorion and its villi, has entered the cavities of the cœlom and amnion, and is attacking the amnion.

The excessive growth of syncytium and its invasion of the maternal tissues, ultimately forming malignant tumors, was first pointed out by Sänger,[9] and has since been confirmed numerous times by competent investigators. Recently, however, Neumann[10] has shown that not only does the syncytium enter the tissues, and ultimately the circulation of the mother, but it also invades the tissues of the chorion and its villi. This observation I can confirm, but am unable to contribute to its diagnostic value. In general, it appears to me that destruction of the chorion and its villi may be accomplished by the syncytium, but this is exceptional. It appears that when the chorion is attacked by the syncytium there are

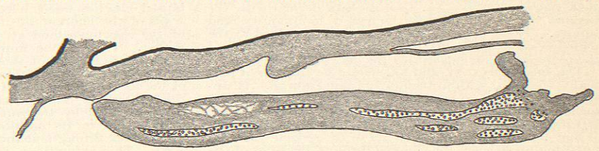

FIG. 1867.—Section through the Cord and the Amnion at its Attachment to the Chorion of No. XXXII. × 10 times.

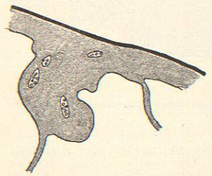

FIG. 1866.—Section through the Attachment of the Amnion and Cord to the Chorion of No. CXXX. × 10 times.

usually great quantities of leucocytes accompanying it, and this condition may also favor the formation of deciduomata. At any rate the fact is established that the syncytium may enter and destroy the chorion and its villi in uterine moles of long standing.

OVA NORMAL IN FORM WITHOUT EMBRYOS AND UTERINE MOLES.—The ten specimens which come under this head differ very much from one another in form and age, but careful consideration of all their structures shows that they belong together. They are all alike in that the embryos are missing, and they must have been destroyed at a very early date; in seven of them this must have taken place before the embryo was six weeks old, as there is no trace of an amnion left; while in three of them (XCIII. and LXXVII.) the amnion is fully formed, but the general appearance of the ova shows that they represent early stages in development.

Table III. gives the general characteristics of the ova which represent all stages of uterine moles. The youngest specimen, LXXI., is an ovum about two weeks old, normal in every respect, with the exception that the embryo is wanting entirely. Within the cœlom, however, there is a small nodule about 1 mm. in diameter, which may represent the remnant of the embryonic mass. It is

TABLE III.—TABLE OF OVA WITHOUT EMBRYOS AND UTERINE MOLES.

| Number. | Diameter of chorionic mass. | Diameter of coelom. | Time between last period and abortion. | Amnion. | Chorion. | Villi. | Syncytium. | Magma. |
|---|---|---|---|---|---|---|---|---|
| LXXI | 10 × 9 × 5 mm. | 8 mm. | 40 days | None. | Normal. | Normal | Normal. | Normal. |
| XX | 20 × 14 × 6 mm. | 16 mm. | | None. | Normal. | Normal | Normal. | Increased. |
| XXIX | 30 mm. | 24 mm. | | None. | Fibrous. | Atrophic | Excessive. | Excessive. |
| LV | 35 × 20 × 14 mm. | 15 mm. | 54 days | None. | Leucocytic invasion | Necrotic | Necrotic. | Granular. |
| CLIII | 50 × 20 × 20 mm. | | 77 days | None. | Leucocytic invasion | Normal | Normal. | None. |
| LXX | 45 × 30 × 28 mm. | 5 mm. | 113 days | None. | Necrotic. | Hypertrophic | Excessive. | None. |
| LXXXII. | 75 × 60 × 40 mm. | | 279 days | None. | Hypertrophic. | Atrophic | Diminutive | None. |
| XCIII | 40 × 20 mm. | 7 mm. | | Present. | Syncytial invasion. | Hypertrophic | Excessive. | None. |
| CLIX | Walnut | | 70 days (?) | Present. | Syncytial and leucocytic invasion. | Syncytial and leucocytic invasion. | Excessive. | None. |
| LXXVII. | 70 × 40 × 30 mm. | 20 mm. | | Present. | Syncytial and leucocytic invasion. | Syncytial and leucocytic invasion. | Excessive. | None. |

composed of twisted discs looking much like the dried blood corpuscles of the frog, being pigmented, but they would not stain. If this mass represents the remnants of the embryo, it must have died long before the abortion took place. Embryo XX. also appears normal with the magma normal or slightly increased in quantity and lumpy. These small nodules of magma appeared to the naked eye like remnants of the embryo, but sections of the ovum easily demonstrated the contrary.

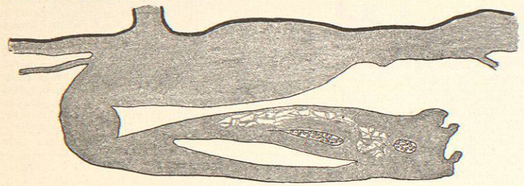

FIG. 1868.—Section through the Attachment of the Umbilical Cord to the Chorion in No. XXXII. × 10 times.

The specimens LXXI. and XX. would be considered normal if they had within them a normal embryo. It appears that to the extent, as represented in these specimens, the chorion develops independently of an embryo, but its further growth is affected if no embryo is present. It may be noted that in the ovum of the second week the nutrition must reach the embryo through the fluid of the cœlom and thence through the umbilical vesicle. Toward the end of the second week the blood-vessels of the embryo reach the chorion,[11] and at this time nutrition must reach the embryo through its blood-vessels, which now reach to the villi of the chorion. So if an early embryo is missing we should find marked changes in the chorion after the beginning of the third week. This proves to be the case in specimen XXIX. The walls of the chorion and its villi are fibrous and thickened. The syncytium is very extensive; its borders are no longer sharply defined, and at points it invades the chorion. Many of the islands of syncytium are enclosed in a mucoid, and sometimes fibrinous, envelope. This process is still further increased in specimen LV., which from its size and history belongs to the beginning of the fifth week. The cavity of the cœlom has become smaller, the villi are matted together, and with their surrounding syncytium appear necrotic. There is much blood and fibrin between the villi and leucocytes have invaded the wall of the chorion. In this specimen we have a typical mole which is two weeks older than the specimen LXXI.

Another modification of the degenerative process is shown in specimen LXX. It is an hydatid mole. The chorion is small, collapsed, deeply buried in the specimen, and from it arise enormous villi with very large spaces within them. Between the villi there is a considerable quantity of blood which gave nutriment to the excessive syncytium.

To what extent a collapsed ovum may grow is shown in specimen LXXXII. A large solid mass the size of a duck's egg was expelled nine months after the last menstrual period. At the end which lay in the os uteri there is an extensive ulceration of the mole; otherwise it is very compact. After it had been hardened, I cut it into sections which, to my astonishment, contained a collapsed chorion sending folds in all directions throughout the specimen. Through the middle of the specimen there are large spaces along the collapsed chorion filled with fresh blood. The opposite walls of the chorion are in apposition throughout most of the specimen, and at points they have grown together. There is no amnion, and on this account I place the beginning of this mole back to the first month of pregnancy. The extensive ramification of the folds of the chorion shows that it must have continued to grow throughout the nine months of its existence, this being made possible by the nutrition brought to it by the fresh blood in its interior. Islands of syncytial cells are located throughout the specimen upon the chorionic wall. This syncytium shows active growth and its cells stain well at numerous points where it comes in contact with fresh blood. All the syncytial masses which are distant from the fresh blood are necrotic, which is undoubtedly due to the lack of nutrition. Nests of leucocytes with fragmented nuclei are scattered throughout the specimen. The walls of the chorion are not invaded by the syncytium.

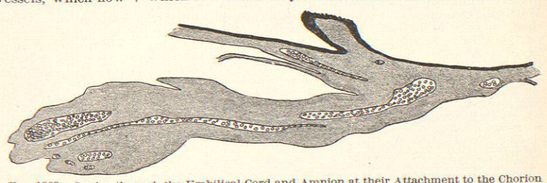

FIG. 1869.—Section through the Umbilical Cord and Amnion at their Attachment to the Chorion in No. XXV. × 10 times.

The above group of specimens shows all stages of mole formation before the amnion is in contact with the chorion. There are, however, three other specimens,





CIII., LXXVII., and CLIX., in which the chorion is lined with an amnion. These must have arisen from specimens like those in which the embryo was destroyed, leaving only the umbilical cord. Specimen LXXVII. I have already discussed with that group in which the embryo is destroyed, leaving only the cord (Table II.), and to it I now add XCIII. in discussing it with this group.

In specimen LXXVII. there is a small stump of the umbilical cord left, while the chorion has a large quantity of blood and syncytium between its villi. At points the chorion and villi are invaded by the syncytium. In XCIII. this process of destruction has increased, the chorion is thickened and irregular, and it is surrounded by hypertrophied villi with great quantities of blood and syncytium between them. Over the entire mass there is a layer of syncytium covered with blood and fibrin, then a space, and then the decidua. Within the mesodermal tissue of the chorion there are occasional islands of syncytium.

The two groups of pathological ova, given in Tables II. and III., are undoubtedly caused by an arrest of development and a destruction of the embryo before the fifth week of pregnancy. In one of the groups this took place very early before the amnion had been fully formed and I am strongly inclined to believe that they represent specimens in which the amnion did not form at all—the so-called vesicular forms. In the second group the embryo and amnion were formed, then the embryo was destroyed, leaving the amnion and chorion. In both sets the equilibrium by which the normal growth of the chorion is favored was overthrown, due to the destruction of the embryo. In case the ovum is not aborted, it continues to grow in an irregular fashion, and the chorion or villi either become atrophic or hypertrophic. The syncytium in all cases continues to grow as long as it receives the proper nutrition, and in certain instances it attempts to destroy the chorion and its villi.

VESICULAR FORMS OF PATHOLOGICAL EMBRYOS.—The different varieties of pathological embryos described above can all be explained as forms of arrested development of the embryo, its partial destruction or its complete destruction. In all instances the chorion proves to be the most resistant tissue and continues to grow after forming a large cyst-like ovum, but occasionally collapsing to form a fleshy mole. When the primary trouble is in the embryo, usually the chorion appears normal; but when the primary trouble is in the chorion the embryo is immediately affected, often resulting in its strangulation. In the younger strangulated embryos the tissue reactions are very marked, while in the older strangulated specimens there is a slow and irregular growth, but not development of the organs.

In addition to the atrophic embryos and moles there is a group of vesicular forms which are extremely difficult to understand. It has frequently been asserted that this group represents early pathological embryos, but as yet no positive proof has been brought forward to substantiate this view. All the specimens at my disposal indicate that the vesicle is the umbilical, for in it there is found the characteristic mesoderm with blood-vessels filled with blood. This is naturally what we would expect to find, as the blood-vessels arise in the umbilical vesicle and grow into the embryo. In the very early normal human embryo, described recently by Peters, we have a very small amnion completely closed with the head end of the amnion not wholly covered with mesoderm. There can be no question about this specimen being normal. I think, on this account, that the young specimen (No. XI.) described by me several years ago must now be considered pathological. Yet this does not indicate that the amnion never communicated with the cœlom. None of the facts are against this hypothesis, and many of the pathological specimens in my collection speak for it. At any rate, the walls of the vesicular forms are not only formed of a layer of mesoderm, in which are embedded blood-vessels and lined with a layer of entoderm cells, but are covered with a layer of epithelium which in a number of specimens form an invagination—the amnion. This outer covering of the vesicle, which I shall term the ectoderm, may represent an early normal form of the ectoderm or it may represent a displaced ectoderm in a stage as early or earlier than the Peters specimen.

The ectodermal covering of the vesicle is usually present in the vesicular forms and nearly always absent from the umbilical vesicle in the normal embryo. In a large collection of serial sections of normal embryos I have found it present but once. These facts can be interpreted in either of the ways given above and need not, therefore, be discussed further. At any rate, the epithelial layer covering the vesicle in the pathological ova is nearly always present, and in my description of them I shall assume that it is the ectoderm.

The fact that there is so great a morphological difference between the vesicular embryos and the older pathological embryos makes it likely that some very marked barrier lies between the two varieties. This undoubtedly is the amnion, for in the one it is absent or not closed, and in the other it is present. In order to bring the vesicular forms into any sort of harmony it is necessary to assume that the ectodermal covering of the vesicle is either a displaced amnion or that it is an arrested development of an extremely early normal stage.

That the cavity of the amnion may have communicated at an early stage of its development with the cœlom is indicated by Giacomini in his thirteenth communication.[12] The pathological embryo in the specimen he describes is not entirely encircled by the amnion, for the head of the embryo protrudes through an opening into the cœlom. A similar, but normal specimen, is described by Siegenbeek Van Heukelom.[13] This specimen dates from the end of the second week. The amnion is not complete. In two successive sections the amnion has in it an opening in the dorsal median line which Van Heukelom believes to be artificial, for free chromatin granules are present in the tissues in the immediate neighborhood of the opening. A similar condition is present in the Peters embryo, as the amnion is not entirely enclosed with a layer of mesoderm but protrudes into the cœlom.

The first vesicular specimen of my collection which I

TABLE IV.—VESICULAR FORMS OF PATHOLOGICAL EMBRYOS.

| Number. | Dimensions of ovum. | Dimensions of vesicle. | Time between last period and abortion. | |
|---|---|---|---|---|
| XIII | 8 × 7 mm. | 1.0 × 6 × 6 mm. | | Amnion formed. |
| CXXXIV | 17 × 11 mm. | 9.0 × 3 mm. | 33 days | Amnion partly formed. |
| XI | 10 × 7 mm. | 1.5 × 1 mm. | 41 days | Amnion partly formed. |
| LXXXVII | 24 × 16 × 9 mm. | 2.5 mm. | 42 days | Partial amnion. |
| LVIII | 30 × 18 × 12 mm. | 6.0 mm. | 71 days | Partial amnion. |
| LXXVIII | 36 × 33 × 13 mm. | 1.0 × 6 mm. | 87 days | Multiple amnion. |
| XXIV | 21 × 16 × 5 mm. | 2.6 mm. | | Multiple amnion. |
| XIV | 30 mm. | 1.5 mm. | | No amnion. |
| CXXXIII | 17 × 14 mm. | 2.0 × 1.5 mm. | 27 days | No amnion. |
| XXII | 40 × 30 mm. | 5.5 × 3.5 mm. | | No amnion. |
| CXXX | 15 × 10 × 6 mm. | 4.0 × 3 × 1.5 mm. | 14 days | No amnion. |
| CXLVII | 30 × 27 × 20 mm. | 1.0 mm. | | No amnion. |
| CXLIII | | 25.0 × 10 mm. | | |