

The Anatomical Considerations of Ectopic Gestation

by Don Carlos Guffey

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OF ECTOPIC PREGNANCY**

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Note: This thesis was placed for some time with others lacking author's name and date. Guffey's thesis was marked "lost". Examination of this thesis whose title is equivalent to that given for Guffey's and whose bibliography indicates it was written in 1908 or soon afterwards, led to the assumption that it is Guffey's 1908 thesis recorded as "The anatomical considerations underlying extra-uterine pregnancy."

THE ANATOMICAL CONSIDERATIONS
OF ECTOPIC GESTATION

Introduction.

Since the first description of extra-uterine pregnancy given by the Arabian physician, Albucasis (1), about the middle of the eleventh century, the subject has been one filled with the greatest professional interest. The literature which has accumulated on this one subject alone would take months for its reading. Scarcely is there an issue of a medico-surgical journal but contains references to this interesting and dangerous condition. Because of the immense amount of work done during the last few years we must not be led into the belief that its recognition is of recent origin.

Scattered throughout the literature we find references to the older writers. As early as 1500 Nufer (2) had performed abdominal section (on his wife, it is said) for extra-uterine pregnancy. The operation was again performed by Dirlawang (2) in 1549. Israel Spach (3) in 1557 published his work on gynecology in which he figured a lithopedion in situ. Mauriceau (3) and de Graaf (3) in 1669 described and discussed the condition fully. It was Mauriceau (3) who recognized the importance of the position of the round ligament in differentiating certain types.

Rupture of an extra-uterine pregnancy was early recognized. Its appalling fatality was universally known. Although Parry (4) in 1876 said "the only remedy which can be proposed to rescue a woman in these unfortunate circumstances (tubal rupture) is to open the abdomen, tie the bleeding vessels, or to remove the sac entire", it was not until 1883 that Tait accepted the challenge and first operated for a rupture of the tube.

It is with great difficulty that the frequency of extra-uterine pregnancy is determined. In the seven years ending in 1886, out of 60,000 women examined in Braun's (5) clinic in Vienna, only 5 cases were reported; Winkel (6) saw 16 in 22,000; Bandl saw 3 in 60,000; and Fasola (5), of Florence, in two years, saw 5 in 1565 multiparae who had remained for some time sterile. These figures by no means represent the true frequency. Formad, coroner's physician of Philadelphia, found 35 cases of tubal pregnancy in 3500 general autopsies, or 1 in 100. It is generally stated that the proportion is about 1 to 500 pregnancies.

Earlier resort to laparotomy and greater skill in the examination of pathological specimens, especially the study of serial sections, have shown this condition to be much more frequent than was formerly supposed. Hirst (6) operated on 13 cases in 9 months; Noble (7) and Kelly (8) have found it in 3 to 4% and 2.3%, respectively, of their laparotomies. Watkins says that in 1904 eight Chicago hospitals reported 56 cases. (9)

By extra-uterine pregnancy is meant the development of the product of conception outside of the normal uterine cavity. In this sense it is synonymous with the term ectopic gestation, first suggested by Barnes in 1873, and includes pregnancy in the undeveloped horn of a bicornate uterus.

Under physiological conditions the ripened Graafian follicle extrudes its contained ovum into the peritoneal cavity. The ovum may then wander about for a time, finally dying and undergoing absorption; it may be picked up by the current of peritoneal fluid produced by the cilia of the tube and wafted into the fimbriated end of the tube; it may pass downward through the tube and uterine cavity and be lost with the menstrual discharges. On the other hand, the ovum may become fertilized at any point in its migration and under proper conditions undergo development without ever gaining the uterine cavity. We can conceive of its passing through the uterine cavity and entering the tube of the other side (internal migration). That the fertilized ovum may originally enter the tube of the opposite side (external migration) is a settled fact. Ordinarily, however, the ovum enters the tube of the same side, is fertilized in the outer portion of the tube and reaches the uterine cavity in from 3 to 5 days.

That most pregnancies begin as extra-uterine pregnancies does not seem so improbable when we remember that the extirpated tube has been known to contain living spermatozoa. Dührssen (8) has seen them in the normal tube three and one half weeks after the last copulation, and Williams (7) goes so far as to speak of the tube as the receptaculum seminis.

Classification.

When the ovum continues its development at the original point of attachment, the pregnancy is spoken of as primary; when it changes its location, as secondary. For example, a primary tubal pregnancy may, by rupture of the tube, become a secondary abdominal pregnancy; a secondary extra-uterine pregnancy results when a fetus develops for a time in the uterine cavity and is then forced out through the site of a cesarean section or rupture, as in the case of Lacluyse (10) where the incision of a cesarean section failed to heal; and a secondary intra-uterine occurs when there is extrusion of a fetus from the tube into the uterus.

Four primary varieties of ectopic gestation are possible; rudimentary cornual, tubal, ovarian, and abdominal. The differentiation into tubal, ovarian and abdominal, was made by Boehmer (2) as early as 1752, and was based on the original site of implantation of the ovum.

The tubal variety is by far the most common. This

is made clear by the fact that the ovum is normally fertilized after entering the tube. Gestation may take place in any portion of the tube, and the type is named accordingly: ampullar, isthmic and interstitial. The ampullar variety is generally considered to be the most frequent. The ovum is attached to the outer portion of the tube. The tubo-ovarian, or infundibular of Webster, is simply a form of the ampullar in which the ovum develops in the fimbria ovarica or in other fimbriae which become glued to the ovary. In the isthmic variety the ovum develops in the ~~in the~~ narrow portion of the tube just outside the uterus. Williams (7) found it oftener than the ampullar. In the interstitial or tubo-uterine form the ovum develops in that portion of the tube which traverses the uterine wall. It was first described by Schmidt (5) in 1801. It is the rarest form of tubal pregnancy. Martin found 1 in 77 cases of extra-uterine pregnancy, while Kelly (8) failed to find a single one in 139 cases. Mauriceau (3) in 1669 described minutely a specimen exhibited by Vassal in which " the child was engaged in a part of the womb which was elongated" - probably a true case of interstitial pregnancy.

The differentiation of these types depends upon the following conditions: In an ampullar or isthmic tubal pregnancy the uterus and round ligaments lie toward the median line, the ovary is intact, and the broad ligament is not spread apart. In the interstitial form the tube

and round ligament are to the outer side of the tumor, the tumor forming a part of the uterus. Pregnancy in a rudimentary horn resembles this closely in that the round ligament is to the outer side. The uterus is, however, rounded off at that side and the pedicle of the tumor is attached low down.

Ovarian pregnancy is extremely rare. It was first described by Mercerus and St. Meurice (7) in the seventeenth century. Since then much uncertainty has existed regarding the possibility of such a condition. Spiegleberg (7) in 1878 formulated four postulates to which all cases must conform, viz.: (a) That the tube on the affected side be intact; (b) that the fetal sac occupy the position of the ovary; (c) that it be connected with the uterus by the ovarian ligament ; and (d) that definite ovarian tissue be found in its wall. Williams (7) found that up to January 1906 only 13 of all the reported cases fulfilled all of these requirements; 17 more were classified as highly probable. Four more positive cases must be added, viz., that of Kelly and McIlroy (1906) (11), that of Popow (1906) (12), that of Webster (1907) (13), and that of Norris and Mitchell (1907) (14). That ovarian pregnancy does occur, therefore, can be doubted no longer. Most of the early cases, however, were really dermoid cysts.

In ovarian pregnancy, Leopold (7) believes that fertilization takes place in the Graafian follicle.

This is certainly true in the case of Kelly and McIlroy (11), since the lutein cell envelope was not broken. It is improbable that the spermatozoon penetrates the wall of the Graafian follicle, rather does it enter through a rent which is too small to permit the exit of the ovum should it become detached from the cumulus oophorus. He also believes that a deeper follicle may rupture into one more superficial without discharging its ovum, which may become fertilized by a spermatozoon entering through the superficial follicle. Nevertheless, not all cases of ovarian pregnancy develop in the Graafian follicle, since Webster's first case (15), and probably his second (13), fails to show lutein cells in the sac wall. This seems to be one of those cases where the ovum becomes attached to the ovarian surface and embeds itself through the germinal epithelium.

The possibility of primary abdominal pregnancy, one in which the ovum is originally attached to the peritoneum, is denied by many on the ground that the ovum would be destroyed by the peritoneum. Knowing that spermatozoa may penetrate to the peritoneal cavity, that the unimpregnated ovum may travel a considerable distance without losing its vitality, that the vitality of the ovum may be increased by fertilization, and that areas of cells, closely resembling decidual cells, may be found underneath the peritoneum, does it seem unreasonable to suppose that the impregnated ovum might not become attached to one of these areas and undergo development giving rise to a true primary abdominal

pregnancy? De Graaf (3) in 1669 expressed the belief in the existence of this form. "It is not difficult to explain how a fetus occasionally develops in the abdominal cavity among the intestines inasmuch as the ova already impregnated fall from the ovaries outside the cavity of the tube and are nourished by the neighboring parts." To deny the possibility of this type of ectopic gestation would be unscientific, but the actual existence of such a condition remains to be proven. According to Turtle (16), the best example of primary abdominal pregnancy is a case reported by Galabin in 1896. The sac ruptured in the 7th. week of gestation and the ovum, 5/8 of an inch in length, was found. The sac was attached to the bottom of Douglas' pouch and to the back of the uterus and broad ligament. Both tubes were free and pervious.

Secondary forms are derived from the primary and may be abdominal, tubo-ovarian, intra-ligamentary, retro-peritoneal, vesical, and the like. Secondary abdominal pregnancy may have its origin in an ovarian, tubal, rudimentary cornual or uterine pregnancy. Tubo-ovarian may result from tubal or from an ovarian pregnancy, in either event the fimbriae become glued to the ovary. The intraligamentary form comes from the rupture of a tubal, rudimentary cornual or uterine pregnancy, between the layers of the broad ligament. Its recognition is difficult. Kelly (8) says "the tumor occupies the same relation to the

broad ligament and the uterus as does an intraligamentary cyst; the meso-salpinx is unfolded, together with the anterior and posterior layers of the broad ligament. The peritoneum may be stripped up. The ovary lies somewhere upon the surface and is not greatly spread out. The tumor lies closely to the uterus and vagina, pushing the uterus to the opposite side. The round ligament lies on the anterior surface of the tumor." If the fetus passes behind the peritoneum a retro-peritoneal type results. An interstitial may be forced into the uterus producing a secondary intra-uterine type. Vesical, intestinal and vaginal forms are the result of ulceration into these cavities.

Cases of multiple (17), double (18) and repeated (19) ectopic gestation have been frequently reported. Simpson (20) collected 113 cases of combined intra- and extra-uterine pregnancy.

Below is given a tabulation of the various types:

Primary	Secondary
1. Rudimentary Cornual	Intra-uterine Intra-ligamentary Abdominal
Interstitial	Intra-uterine, Abdominal, Intra-ligamentary, Tubo-abdominal
2. Tubal Isthmic	Tubo-abdominal Abdominal Intra-ligamentary
Ampullar	Tubo-abdominal Tubo-ovarian Abdominal
3. Ovarian	Ovario-abdominal, Abdominal Tubo-ovarian
4. Abdominal	

Causation.

The question of the causation of extra-uterine pregnancy resolves itself into an explanation of why the ovum never reaches the uterine cavity. The ovum may never leave the Graafian follicle, it may adhere to the ovarian surface or it may fall into the peritoneal cavity, producing, respectively, an ovarian or abdominal pregnancy.

In the production of tubal pregnancy two conditions seem necessary, viz.: (A) Arrest of the ovum; and (B) proper soil for its growth.

(A) Arrest. Having gained the tube, many conditions have been described which might arrest the progress of the ovum. These may be divided into

1. Mechanical factors,
2. Inflammatory conditions in and about the tubes,
3. And conditions causing overgrowth of the ovum.

1. The mechanical factors causing narrowing of the lumen of the tube include

- (a) External pressure, as myomata (especially when in that portion of the uterus through which the tube passes), cysts, and the like;
- (b) Persistence of the fetal type of tube, which has a narrow lumen and is markedly convoluted and lengthened;
- (c) Diverticula, accessory lumina or ostia and cul de sacs;
- (d) Puerperal atrophy of the tubes;
- (e) Congenital or acquired stenosis;
- (f) Polypi projecting into the lumen;
- (g) Oxytoxic drugs causing spasm of the tubes;
- (h) And kinking or torsion of the tube.

2. Inflammatory conditions of the tubes, ovaries or peritoneum include

- (a) Chronic salpingitis, interfering with normal peristalsis;
- (b) Follicular salpingitis in which the rugae become united;
- (c) Inflammatory conditions destroying the cilia;
- (d) Peritoneal adhesions, constricting the lumen or interfering with peristalsis.

Micholitsch, from the study of serial sections in 100 cases, concludes that the most frequent cause of tubal pregnancy is found in anomalies of the tube. Tait believed that destruction of the cilia was the chief cause. His argument was that the absence of the ciliary wave permitted the entrance of the spermatozoa into the tubes. It is generally claimed that the cilia are not destroyed in catarrhal and rarely in suppurative salpingitis, while Williams (7) finds cilia in nearly every case of extra-uterine pregnancy. Puerperal infection of the tubes, especially liable after abortions, is certainly an important factor. Of the 32 cases reported by Heinick (21), a miscarriage had preceded the ectopic pregnancy in 30%. Hirst says that the majority of his cases have been preceded by salpingitis. Schrenck (22) in 1893 found adhesions in 70%, and Duhrssen (22) found tubal disease in 68%.

3. Whatever increases the size of the ovum, as external migration, twins, very long tubes, or absence of the cilia, tends to the production of ectopic gestation.

That external migration of the ovum is a fact cannot longer be denied. Kelly's (8) classic case may be cited: He removed the diseased ovary of one side and the diseased tube of the other. Pregnancy soon occurred and the patient was delivered at term. Later, he removed an ectopic pregnancy in the remaining tube. The corpus luteum was in the remaining ovary. External migration of the fertilized ovum is also a fact - a more important fact, since the ovum grows rapidly appearing in the uterine cavity in the morula or blastula stage. This is of frequent occurrence, Williams (8) having found it in 15% of cases. Vineberg (23) reports a case of ectopic pregnancy in the stump of a removed tube. Usually external migration is the result of prolapse of the tube and the ovary of opposite sides whereby they are brought together. Vineberg's case could not be of this type. The spermatozoon must have come through the intact tube, the fertilized ovum wandering to the opposite stump. Williams describes a case in which the uterine end of the tube was filled with a cyst containing fetal remains (probably of 12 years standing) while the outer end of the tube had ruptured from a four month's fetus. The corpus luteum was in the opposite ovary. Kelly (8) figures a specimen of pregnancy in a rudimentary horn of a bicornate uterus in which migration of the fertilized or unfertilized ovum must have occurred, the corpus

luteum being in the opposite ovary and no communication existing between the rudimentary horn and the uterine cavity of the developed horn.

That an ovum, which is undergoing the rapid development associated with multiple uniovular fetation, is more liable to be arrested in the tube, is easy to believe. This is substantiated by the fact that multiple pregnancy is four times as frequent in ectopic as in uterine pregnancy.

As already stated, cilia are usually found in salpingitis and in ectopic tubal pregnancy, but areas in which the cilia have been destroyed also exist. Since the ovum is incapable of self-propulsion, it may remain indefinitely on one of these areas unless some external factor moves it onward.

Ladinski (19) suggests the possibility of some peculiar condition of the primitive chorion as a causative factor. What the nature of this peculiarity is, he does not intimate.

(B) Proper Soil. Arrest of the ovum is a necessary condition, but is it a sufficient condition? In 1895 Webster (24) advanced the view that the genetic or decidual reaction, ordinarily not occurring outside the uterus, does occur under certain conditions, an extra-uterine pregnancy being possible only at these times. He believes also that only Müllerian tissue is capable of giving this reaction, and that it is a reversion,

either in structure or reaction, to earlier mammalian types. He would explain ovarian and abdominal pregnancy by the production of nests of decidual cells in the ovary or under the peritoneum, the product of growth of scattered Müllerian tissue. He has described nests of decidua-like cells in the ovary and beneath the peritoneum in intra-uterine pregnancy (15). Mechanical factors, he believes, simply determine the site of implantation.

It remains to be determined whether the nests of cells described are true decidual cells. Decidual cells are of connective tissue origin while these decidua-like cells are claimed by some to be of endothelial origin(25). They have also been found in productive peritonitis in the non-pregnant condition (25).

Is the decidual reaction necessary to implantation? It is known to disappear before term, particularly in tubal pregnancy. Peters' specimen shows that implantation in the uterus may occur before the decidua forms. Apparently, therefore, a decidual reaction is not necessary. Williams (7) makes the positive statement that decidual reaction is altogether absent in some cases of tubal pregnancy. There was no decidual reaction in the case of ovarian pregnancy described by Kelly and McIlroy (11). The function of the decidua, therefore, seems to be one of protection to the maternal tissues.

In the experiments of Tainturier (7) and Mandl and Schmidt upon rabbits, the uterine cornua were ligated shortly after copulation with resulting pregnancy in that part of the horn beyond the ligature. When the uterine end of the tube was ligated, pregnancy did not supervene, though dead ova were found in the tubes. These findings would tend to show that arrest of the ovum is not a sufficient condition. The value of these experiments is greatly reduced by the statement of Bland Sutton (7) that extra-uterine pregnancy rarely, if ever, occurs in lower animals. If this be true, it would seem impossible to have any reversion to the lower mammalian types, in either structure or reaction. But, if there is reversion, why does it not occur in the first as often as in succeeding pregnancies?

What explanation is there on the genetic reaction theory for the period of sterility preceding the ectopic pregnancy? Why is it that several years of married life precedes it? If it occurs in an individual once, we would look for its repetition. Repeated ectopic gestation does occur, but rarely.

In the absence of a decidual reaction, Webster's theory presupposes the death of the ovum. How can he explain the existence of those cases in which no decidual change is recognized? It hardly suffices to say that it was there but could not be found.

When the processes involved in the implantation of the ovum are understood, the etiology will be much simplified. It is generally accepted that embedding is the result of the destructive power of the trophoblastic cells. These destroy the endometrial epithelium at the site of implantation. Is there any reason to suppose that these same cells may not have the same power when brought in contact with other epithelium?

Developmental Changes.

The developmental changes incident to ectopic gestation were divided by Cauwenberghe (10) into two groups: Maternal and fetal. Another classification is proposed, viz., (A) Common changes - those associated with all forms; and (B) Specific changes - those resulting from the individual types.

(A) Common Changes. The constitutional and emotional changes of normal pregnancy appear but are less marked. The chief changes are in relation to the vagina, mammae and, in particular, the uterus.

The vaginal changes incident to normal pregnancy appear but are not so pronounced. The vaginal walls are thickened, lax, soft, and dark in color. The scarlet fourchette and violet anterior vaginal wall may be expected. The secretions are increased.

The breasts enlarge and partake of the changes characteristic of normal pregnancy but to a less degree.

Death of the embryo is followed ~~is followed~~ by retrogressive changes. Colostrum appears and if term is reached milk forms as usual.

The uterine changes are more characteristic. The cervix is soft and congested, but less so than in normal pregnancy. The signs of Hegar and Ladinski (a softened spot on the anterior uterine wall at the site of the internal os) do not appear. Uterine enlargement always occurs, but its size does not correspond to the length of gestation. The maximum enlargement is about eight inches, usually four. It is claimed by Bandl that the nearer the sac is to the uterus, the greater the uterine enlargement. Instead of becoming globular it retains its original pear shape. The uterine changes are out of harmony with the stage of gestation.

The endometrium usually undergoes decidual transformation. Vineberg's case shows no decidual cells in the uterus. As a rule, there will be, from time to time, a discharge of more or less of this decidual tissue. Menstruation may cease or continue irregularly. It occasionally happens that the entire decidua is thrown off in the form of a cast of the uterus. Kelly (8) saw 3 in 139 cases and Ladinski (19), 2 in 107. Microscopic examination will show the absence of villi or syncytial cells.

(B) Specific Changes. What are the changes peculiar to tubal pregnancy? The maternal organism makes abortive

attempts at the production of conditions necessary for fetal development and maternal protection. The tube becomes edematous and richly supplied with blood vessels. The muscular fibres in the tubal wall do not apparently undergo hypertrophy as do those in the uterus. It is still an unsettled question whether the tubal mucosa always shows the decidual reaction even in the earliest stages. Indeed, it does not seem so much necessary for the implantation of the ovum as does a simply edematous mucosa. A simple swelling of the connective tissue cells, the result of edema, can hardly be called decidual transformation. Kermanner (26) found none in 35 out of 41 cases and Vassmer(26) found none in 8 out of 20. Kermanner believes that the stiffness and tenseness of the tubal mucosa and chronic inflammatory conditions interfere with decidual transformation. Many observers find decidual cells in the mucosa, in the intermuscular connective tissue and in the intima of the blood vessels. Hensius (26, believes that the nearer the implantation is to the fimbriated extremity, the greater the reaction. Decidual cells have been found in the opposite tube (7), and, possibly, in the ovaries and under the peritoneum (15).

As a result of insufficient decidual reaction placental formation is imperfect. There is no definite and distinct placenta though all the microscopic elements of the placenta are present. The tube at the placental site is especially

thickened and edematous, the muscle fibres are thinned and separated. These fibres are, of course, incapable of much contraction.

The interstitial type presents greater decidual reaction, with a better placental formation, than other tubal types. Moreover, the uterine muscle fibres, which form the wall of the tube, are capable of considerable hypertrophy.

In tubal pregnancy, according to Werth (7), the ovum may become attached to the tip of the folds or plica - columnar implantation - or may sink into a depression between them - intercolumnar implantation. In either case, the trophoblastic cells covering the ovum erode the mucous membrane and bring the ovum into contact with muscular and connective tissues. Blood vessels are opened up and the ovum become covered with fibrin, the beginning of the capsular membrane. This separates the ovum from the lumen of the tube. Expansion of the ovum, without rupture, is limited more in the columnar than in the intercolumnar variety. The villi are formed in the same way as in normal pregnancy. The ovum is surrounded by blood spaces. Growth is in the direction of least resistance, i.e., toward the tubal lumen. When this is occluded, the villi penetrate farther into the tubal wall; they may pierce the capsular membrane and enter the opposite wall of the tube. Thus, implantation in the ampulla will permit of greater development with less involvement of the tubal wall than will an isthmic pregnancy.

The development of the fetal membranes - the amnion and chorion - is the same as in uterine pregnancy. The absence or reduction in decidua renders impossible the formation of a typical placenta. Whatever is formed, is formed chiefly of fetal tissue. In the absence of typical decidua, which presumably protects the maternal tissues, the villi penetrate the tubal wall, open up blood spaces and finally reach the peritoneum. This condition greatly weakens the tubal wall; and the ovum, as Werth says, while making its bed, digs its own grave.

In ovarian pregnancy two types probably occur : internal, the ovum growing within the follicle, being surrounded by lutein cells; and external, becoming implanted on the ovarian surface. Webster's cases seem to belong to the latter type, and that of Kelly and McIlroy to the former. In either event, implantation is the result, again, of the erosive action of the trophoblastic cells. The villi come to lie in direct contact with the ovarian stroma. Imperfect placentation, therefore, results.

Pregnancy in a rudimentary horn of a bicornate uterus gives the same changes as are met with in uterine pregnancy.

What happens in abdominal pregnancy is not known

Terminations.

What may happen to ectopic pregnancy? Several possibilities arise. First, consider tubal pregnancy.

(1) Absorption. In the event of early fetal death, absorption is the rule. This may take place before or after rupture. Many a fetal sac is found which does not contain an embryo; villi and the unabsorbed end of the cord prove the diagnosis. Many cases of tubal disease have really been cases of tubal pregnancy which were recognized as such, only after careful routine pathological examination of sections. How many cases have gone entirely unrecognized!

(2) Intra-tubal Rupture. The delicate capsular membrane is easily ruptured. This may occur spontaneously or as the result of violence. The ovum is set free into the tubal lumen, and the condition is spoken of as intra-tubal rupture. In a collection of 289 cases of tubal pregnancy, Williams found this termination in 78%. If the fimbriated extremity is closed, a blood tumor results - hematosalpinx. If the blood gradually trickles out of the abdominal end of the tube into the pelvic cavity, it may become encapsulated, forming a pelvic hematocele. This may occur also in tubal rupture with a small amount of hemorrhage. Formerly pelvic hematocele was supposed to be a disease entity. Tait (27) was of this opinion. In Linnell's (28) 90 cases of ectopic pregnancy 40% showed hematocele.

(3) Tubal Abortion. Following intra-tubal rupture it frequently happens that the ovum, usually contained in its membranes, is forced out into the abdominal cavity - tubal abortion. The factors responsible for this condition are (a) contractions of the tube, (b) detachment of the ovum by hemorrhage, and (c) the force of the outflowing blood stream. It is much more frequent in the ampullar than in the isthmie type. This is because the ampulla permits of greater distension and the sac expands in the direction of least resistance. The amount of hemorrhage will be determined by the number and size of the blood vessels ruptured, the patulousness of the abdominal end of the tube and the strength of the tubal wall. There may be complete or partial extrusion of the ovum into the peritoneal cavity - complete or partial abortion.

Should the ovum remain in the tube, it may become infiltrated with blood forming a tubal mole. The blood which is found within the chorion is fetal in origin since it contains nucleated red corpuscles, while that without the chorion is maternal. A portion of the placenta may serve as the basis of a placental polypus. In both the mole and polypus the hemorrhage usually persists.

(4) Tubal Rupture (Extra-tubal Rupture). Tait (27) taught that this was the most frequent termination. Since Werth's investigations in 1887 it has been

considered second in frequency. Statistics now show that tubal rupture occurs in not more than 25% of ectopic pregnancies. Noble's⁽³²⁾ analysis of 91 cases shows 15% rupture and 75% abortion and Linnell's of 90 cases shows 10% rupture and 74% abortion.

Rupture occurs usually before the twelfth week. Several factors are responsible for rupture: (a) Stretching of the tubal wall; (b) separation and degeneration of the muscle fibres by the intra-mural growth of the villi; (c) hemorrhage into the sac, around it or into the tube, from ruptured blood vessels, especially when this is sudden and profuse; (d) incomplete development of the decidua reflexa; and (e) blocking of the venous channels by villi (Veit) or decidual transformation of the connective tissue cells of the intima.

Degeneration of the muscle fibres by the pseudo-malignant nature of the trophoblastic cells needs emphasis. Probably no one factor works alone. Rupture will certainly occur earlier when the ovum lies in a diverticulum or in the substance of the tubal wall. It is more likely to occur at the times corresponding to the menstrual periods, on account of increased congestion. It occurs more frequently near the uterine end because this portion is incapable of much stretching. Occlusion of the abdominal end makes ampullar rupture more frequent by making abortion impossible.

In such cases extra-tubal may follow intra-tubal rupture. One or more ruptures may occur without terminating pregnancy, if limited in extent. Great hemorrhage may come, however, from a very small perforation by a villus.

Tubal rupture may take place in one of two directions: into the peritoneal cavity (intra-peritoneal) or between the folds of the broad ligament (intra-ligamentary). The site of rupture is determined largely by the site of implantation of the ovum. This is because the villi persist longer and grow more luxuriantly than at other portions of the chorion. Ampullar rupture is always into the peritoneal cavity because this portion of the tube lies outside the folds of the broad ligament.

Intra-peritoneal Rupture. Hemorrhage is generally severe. As a rule, the ovum dies and is more or less absorbed. If the placental attachment is not too much disturbed, fetal life may continue. The placenta may retain its attachment to the tube or become, through contact attached to other organs. This is the only acceptable explanation for placental transplantation. Usually the fetus is surrounded by its membranes, though full term pregnancies have occurred with the fetus free in the abdominal cavity.

Intra-ligamentary Rupture. By far the smaller number of ruptures, about 2%, occur into the broad ligament.

In 326 collected cases it occurred 5 times. But Ladinski failed to find even one in 107 cases of ectopic pregnancy. It is the most favorable termination for the mother, the amount of hemorrhage being limited. The ovum may continue to grow, either going to term or producing secondary rupture. More frequently it dies forming a broad ligament hematoma. The growing fetus may push its way up beneath the peritoneum, forming a retro-peritoneal pregnancy.

Hemorrhage accompanies all form of rupture. It may occur into the tubal lumen (intra-tubal), into the tubal wall (intra-mural), or outside of the tube (extra-tubal), either into the peritoneal cavity (intra-peritoneal) or between the folds of the broad ligaments (intra-ligamentary). Various combinations of these possibilities may co-exist, as an intra-mural, intra-tubal, and intra-peritoneal hemorrhage.

(5) Pregnancy in the tube may go to term. This is an infrequent termination. Several cases, however, have been reported (21). Should this occur, false labor usually supervenes, the labor pains being due to uterine rather than tubal contractions. The fetus dies unless removed by operation. Rupture is likely to occur. Intra-ligamentary and abdominal pregnancy is more likely to go to term than is the purely tubal.

(6) Should the fetus die, what may become of it? If early death occurs we may have absorption or the production of a tubal mole. If, however, death occurs late, other possibilities arise:

(a) Suppuration. The product of conception may become infected by contiguity or continuity, especially if it is situated near the bowel. A broad ligament pregnancy is particularly liable to infection. Various inflammatory conditions may arise or ulceration occur into the bladder, bowel, rectum, vagina, or uterus, or through the abdominal wall. Many cases are cited in the older literature where portions of the fetus have been expelled through one or more of these routes. Heinick (21) has collected 89 cases which ruptured through the abdominal wall, 164 through the intestinal canal, 42 through the vagina and 34 through the bladder.

(b) Mummification. The liquor amnii may become absorbed and, in the absence of infection, the membranes and even the fetus itself may simply dry up or become converted into a dry, hard, leathery tissue. The placenta, also, is absorbed. Bland (29) has recently reported an interesting case of thirteen years' standing.

(c) Lithopedion Formation. Another curious termination that occurs, according to Beede (24), in about 1% of all cases is the transformation of the fetus into a stony condition by the deposition of lime salts. This gives the lithopedion. It is more likely to develop in

intra-peritoneal pregnancies. This condition was recognized at least as early as the middle of the sixteenth century. Leinzell (10) in 1720 found a lithopedion in a woman of ninety four who had carried it for forty six years. Cheston (16) in 1814 described a case in which the fetus had remained for fifty-two years in the abdominal cavity. This is claimed to be the most innocuous form.

The department of Obstetrics and Gynecology of the University of Kansas has the pleasure of reporting one case of lithopedion formation.

(d) Saponification. In very rare cases the fetus undergoes a peculiar soap-like transformation, called adipocere.

While these changes occur in tubal, they are more frequent in abdominal pregnancy. Reed (31) reports 3 and collects 7 more cases of the latter going beyond term.

What are the possible termination of ovarian pregnancy? Early rupture into the peritoneal cavity is the rule. Eleven out of the 13 analyzed by Williams ruptured before the fourth month. Two of the cases, however, went to term. Popow's case not only went to term, but a living child was delivered. The four additional cases included in this article were removed early before rupture occurred. In 10% of Williams' cases there was lithopedion formation. Here as elsewhere, the pregnancy may be

be terminated early without rupture, an ovarian tumor resulting. More careful microscopic examination may reveal a frequency of ovarian pregnancy little dreamed of.

At least 50% of pregnancies in a rudimentary horn end by rupture, usually prior to the fourth month. This for two reasons: (a) The uterus is not usually sufficiently supplied with muscular fibres to accommodate a full term fetus; and (b) the rudimentary horn does not, as a rule, communicate with the larger horn. About 75% terminate fatally when rupture does occur. In rare cases the fetus may be extruded into the larger horn.

Such are the anatomical conditions which underlie ectopic gestation. The pathological changes are fairly well understood and the dangers which so treacherously await the woman are better realized. With a fuller appreciation of these things, the abdominal surgeon will be able to cope with it as never before.

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