

CRITICAL REVIEW.

Recent Work on Tubal Pregnancy.

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At the suggestion of the Editor, I have undertaken to write a critical review of the work on tubal pregnancy published since my own papers "On the Anatomy of the Pregnant Tube" and "The Ætiology of Tubal Pregnancy," which appeared in this JOURNAL in May and September, 1903, respectively. As the former paper was finished in October, 1902, I have now endeavoured to review the subject from the middle of 1902 up to the present time. A large amount of work has been done in this period of three and a half years, as shown by the fact that I have had to consult thirty-eight papers and monographs, some of which are of considerable importance, *e.g.*, those of Berkeley and Bonney, Fellner, Fütth, von Franqué and Garkisch, Heinsius, Hitschmann, Kermauner, Kober, Kroemer, Micholitsch, Raschkes, Runge, Schambacher, Vassmer and Whitridge Williams. At the Congress at Würzburg in 1903, tubal pregnancy was chosen as the subject of a discussion in which Veit, Werth, Wertheim and Heinsius took part.

The literature is chiefly German. There are six English papers and a few reports of cases, two American and two French papers. I have not given references to any paper that appeared before the middle of 1902, as these can be found in my papers above referred to. Much of the work has been done most thoroughly, with the aid of a very large number of serial sections (*e.g.*, over 2,300 sections of one tube, Vassmer). It is well recognized that deductions from a few sections only may lead to the most erroneous views with regard to the minute anatomy of pregnant tubes. The subject can be studied most easily when arranged under the following headings:—

I. THE ANATOMY OF THE PREGNANT TUBE.

(i.) Decidual reaction

(a) In the tubal mucous membrane.

(b) In the submucous and inter-muscular connective tissue and muscle, *i.e.*, the walls of the gestation sac.

(c) In the walls of the maternal blood-vessels.

(d) In the surrounding tissues.

(ii.) The site of the gestation sac. The structure of the "capsularis."

(iii.) The relation of the foetal ectodermal cells to the maternal vessels.

II. THE CAUSES OF TUBAL ABORTION AND RUPTURE.

III. THE ÆTIOLOGY OF TUBAL PREGNANCY.

I. THE ANATOMY OF THE PREGNANT TUBE.

(i.) *Decidual reaction.*

Heinsius²¹ defines a *membrana decidua* as follows: "A tissue consisting of a dense layer of enlarged connective-tissue cells with large nuclei, a tissue, the function of which is to afford protection to both mother and ovum, clothing the whole neighbourhood of the ovum." Such a tissue, he says, is not to be found in the Fallopian tube.

(a) *Decidual reaction in the mucous membrane.* Veit seldom found well-marked decidual changes in the mucous membrane.

Dobbert,⁸ Heinsius,²¹ Vassmer,⁴⁵ and Lange³⁰ found decidual change here and there in the folds.

Schambacher⁴² and Runge⁴¹ found it only in the folds in close proximity to the ovum, not in other parts of the tube.

Berkeley and Bonney⁴ found here and there patches of decidua-like cells.

Kermauner²⁷ found decidual changes in the mucous membrane in only 6 cases out of 41, usually only in the tips of folds on the uterine side of the gestation sac. One case of bilateral tubal pregnancy showed decidual changes in the mucous membrane of both tubes. He considers that the tenseness and stiffness of the tubal mucous membrane have not been sufficiently noticed. They prevent the early occurrence of œdema which precedes and accompanies the characteristic swelling of the connective-tissue cells in decidual reaction. The less marked are the chronic inflammatory changes in the mucous membrane the earlier will decidual reaction be seen, but its appearance will always be later in the tube than in the endometrium in

intra-uterine pregnancy because these chronic inflammatory changes are never altogether absent.

Kroemer²⁹ found decidual changes in the tubal mucous membrane in cases where this tissue took some part in the formation of the gestation sac, but not in those where the site of the ovum was deeply intra-muscular. In one case he found decidual reaction in the other tube.

Fellner¹² finds decidual reaction in the mucous membrane, and thinks that if there is no decidual reaction the ovum cannot go on developing. Kermauner's²⁷ evidence, decidual change in only 6 out of 41 cases, does not support this view.

von Franqué and Garkisch¹³ found much decidual reaction in the mucous membrane of all parts of the tube, even in a labyrinthine congeries of intra-muscular tubules branching off from the main lumen. The changes were so marked as to produce a tissue resembling a young decidua compacta in the uterus. They consider that a *decidua capsularis* and *decidua basalis* are formed in the mucous membrane very early, but are soon destroyed by foetal cells.

Whitridge Williams⁵⁰ found decidual formation not only at the site of implantation of the ovum, but also in folds of the mucosa some distance from it.

Voigt⁴⁷ is the only observer who has failed to find evidence of decidual change in the mucous membrane in any case. Kermauner found none in 35 cases out of 41, and Vassmer found none in 8 cases out of 20.

(b) *Decidual reaction in the submucous and inter-muscular connective tissue and muscle, i.e., in the walls of the gestation sac.* A decidual change in the inter-muscular connective-tissue cells, not sufficient to form a decidual membrane, has been described by many observers.

Thus Heinsius²⁰ says: "There is *some* decidual reaction in the maternal tissues: the musculature of the tube is loosened and oedematous, and the connective-tissue cells are swollen.

Berkeley and Bonney⁴ say: "In our sections the absence of connective-tissue reaction to the invading trophoblast is, perhaps, one of the most striking features. Here and there are patches of small cells with single, rounded, deeply-staining nuclei, whilst scattered irregularly about in the muscle tissue are certain cells with large, oval, vesicular-looking nuclei, which stain faintly with hæmatoxylin. These cells are certainly decidua-like, but with the exception of these the maternal tissues appear to be undergoing a passive destruction."

Dobbert⁸ says: "In the placental site there may be some decidual reaction."

von Franqué and Garkisch¹³ describe decidual change in the cells of the inter-muscular connective tissue. The nuclei were large and well stained, the cell-bodies swollen and decidua-like.

Since Kühne pointed out, in 1897, that what had been described as decidua serotina consisted of Langhans' cells and fibrin, no observer until recently had spoken of any changes producing a tissue worthy of being called "decidua basalis tubaria."

Whitridge Williams, however, in his text-book of "Obstetrics," and Kober, Kroemer and Heinsius, in recent papers have questioned the correctness of Kühne's interpretation of the cell-sheet.

Whitridge Williams⁵⁰ says: "While there is no doubt that a great part of the so-called decidual cells are really foetal in origin, I am, nevertheless, confident that a decidual formation occurs, though to a far less marked extent than was believed by the early observers. . . . The decidua serotina . . . never occurs as a continuous membrane, but at most consists of a few patches of decidual cells, which can be distinguished from the more abundant foetal cells only by the most careful examination."

Kober²⁸ considers that the cell-sheet is partly maternal.

Kroemer²⁹ found, in examination of a 14-day ovum, loosening and hypertrophy in the tissues forming the "serotina," so that in the place of the usual scarcely visible submucous tissue there were here and there broad fields of decidual cells. Wherever villi were found there was decidual reaction. He says, "It is interesting to notice that even the muscular fibres and interstitial connective-tissue cells swell in a decidual manner, and show large clear vesicular characters, when in contact with masses of syncytium."

The drawings illustrating Kroemer's paper show what certainly look like decidual cells in the basalis.

This case, in which there was a well-developed submucous tissue, must be looked on as being quite unusual.

Heinsius²¹ gives a most interesting description of the "basalis" in one case: "At the boundary between the ovum and the tubal muscle, and in some of the vessel walls, in the side towards the ovum, there was a peculiar homogeneous almost glassy tissue containing large cells with large nuclei, spindle-shaped or star-shaped and of varying sizes. The cell-boundaries had disappeared. The cell-bodies contained masses of chromatin which took the same stain as the muscle fibres. The tissue looked like the remains of an old uterine decidua

as seen round the vessels after an abortion." In another, a fresh specimen, he found a similar structure looking "as if the muscle had formed a decidua like that of the uterus and had taken on the same function as a uterine decidua." The nuclei of the muscle fibres were swollen and the boundaries of the fibres had disappeared, so that eventually only a large nucleus was left, surrounded by masses of chromatin, in the middle of a similarly stained tissue. He concludes, "The changes in the tissues of the tube are, to a certain extent, like those produced by an inflammatory process, and appear to be the result of an attempt at affording as good a bed as possible for the development of the ovum."

On the other hand,—

Berkeley and Bonney⁴ agree with Kühne that the cells in the "decidua serotina" are foetal and not maternal.

Voigt⁴⁷ did not find a trace of decidual formation in the basalis.

Werth⁴⁸ says: "there are no decidual cells in the basalis, though some of the ectodermal cells are like decidual cells."

Runge⁴¹ says that the proliferated cells in the wall of the gestation sac are not decidual cells or proliferated epithelium, but certainly Langhans' cells.

Schambacher⁴² agrees with Kühne's interpretation of the cell-sheet, and finds no decidual cells except in the walls of vessels.

Kermauner,²⁷ in forty-one cases, did not once find definite decidual cells in the basalis, and only once did he find cells that somewhat resembled decidual cells. He found in one case some large cells such as those described by Heinsius, and thought that they were probably the result of degeneration, possibly of decidual change.

Heinsius²⁰ attempts to find an explanation of the varying results of observation of decidual reaction in pregnant tubes in—

(1) Individuality of the tissues, the varying energy of the foetal tissues, and the varying reaction of the maternal tissues.

(2) The site of the ovum. The nearer to the fimbriated extremity is the spot at which the ovum becomes implanted, the more marked is the reaction of the tissues.

(3) The stage of the development of the ovum. (However, von Franqué and Garkisch¹³ found very marked decidual reactions in a 3 weeks' pregnancy, and Fellner¹² in a pregnancy of 2-3 weeks. Lange³⁰ cannot find evidence that the amount of decidual change depends on the age of the ovum.)

(4) The time that has elapsed between interruption of the pregnancy and removal of the tube.

(c) *Decidual reaction in the walls of the maternal blood-vessels.*

In 1902 I wrote, "Since Clarence Webster, whose 'proliferated endothelium' is generally considered to have been in reality trophoblast, Mandl is the only writer on tubal pregnancy who has described proliferation of the endothelium of the maternal vessels as being well-marked. There is not the slightest doubt that proliferation of the endothelium of some of the maternal vessels does sometimes occur, as is seen in some of my sections, but what very slight proliferation there is is of no evident importance. In other words, 'trophospongia' as described by Hubrecht in the hedgehog, is not found in the human female. . . . As regards Veit's contention that the foetal cells do not destroy maternal tissue, there are numberless sections showing vessels the walls of which on the side towards the ovum have been completely 'substituted,' the place of muscle, connective tissue, elastic tissue and endothelium having been taken by foetal cells."

Some of the most interesting of the recent work has been done on the changes that occur in the walls of the maternal vessels, and on their relation to the trophoblast.

Kermauner²⁷ found undoubted proliferation of the endothelium in some cases, and Kroemer describes syncytial change in it; but the endothelium no longer occupies the place of interest—this has been taken by the cells of the intima.

Hitschmann²⁴ found that the cells of the tunica intima of some of the arteries had undergone a decidua-like proliferation.

Fellner,¹² who examined three tubes not more than 2-3 weeks pregnant, and very little damaged, finds that the larger arteries in the neighbourhood of the implantation site undergo an autothrombosis; what has been described by several observers as deportation of Langhans' cells into veins is really formation of decidual cells in arteries. That they are arteries is proved by the large amount of elastic tissue in their walls. In most places where an artery communicates with the intervillous space there are heaped-up cells, a few spindle-shaped, but chiefly round or polygonal, under the endothelium. The lumen is more or less obliterated by these cells, which gradually take the place of all the tissues of the vessel-wall. They have generally been called Langhans' cells, but in some places they can be seen to be invaded by Langhans' cells, the difference in character of the two sorts of cells being clearly seen. They can be seen under normal endothelium, large spindle-shaped, round or polygonal, and fairly well-stained cells. Their nuclei are vesicular and contain a few chromatin granules and one or more well-stained

nucleoli. Intermediate forms between unaltered connective tissue cells and these cells can be seen. In the illustrations the differences between Langhans' cells and these decidual cells formed from the intima is very marked. Nearly all the observers to whom Fellner has shown his sections found similar appearances in their own preparations from pregnant tubes.

Kroemer²⁹ also has described decidual cells in the arteries. In some cases he found a many-layered sheet of decidual cells surrounding the lumen.

Schambacher⁴² found that the walls of some of the vessels were infiltrated with large cells of decidual character quite distinct from Langhans' cells. They could be differentiated from the latter by the fact that they, the decidual cells, were two or three times the size of Langhans' cells, were of a different shape, and though they usually contained only one nucleus, often contained two or three or more. They were separated from one another by a good deal of inter-cellular substance, which is not seen in clumps of Langhans' cells. By tracing vessel-walls in serial sections these decidual cells could be proved to arise from cells of the intermuscular tissue of the vessel-walls, and particularly from the intima, under endothelium which often was unaltered. As these cells, round or spindle-shaped, increased in quantity, the muscle and elastic tissue of the vessel-wall disappeared. The cells of Langhans could be seen breaking through the layers of these vessel-wall decidual cells to reach the lumen. Intermediate forms between the decidual cells and Langhans' cells could never be seen. The endothelium usually remained undisturbed until the Langhans' cells broke through the sheet of decidual cells. This decidual change was not seen in all the vessels; in some of the smaller ones the wall was simply destroyed by the Langhans' cells without undergoing any previous change.

Kermauner²⁷ found cells like those described by Schambacher, but only in the side of the vessel towards the ovum. He considers that they originate from Langhans' cells, not from maternal cells.

von Franqué and Garkisch¹³ examined two ova, one of 3 weeks, the other of 6 weeks, cutting 800 serial sections of the former and 730 of the latter. Their evidence supports that of Hitschmann, Fellner, Kroemer and Schambacher. They found decidual changes in the vessel walls, large cells being formed which were not Langhans' cells. In the wall of a large vein there was "a beautiful picture of decidual change, the cells being large, rich in protoplasm, and containing large nuclei."

(d) *Decidual reaction in the peritoneum and surrounding tissues.*

Few writers of recent papers have paid much attention to the changes in the peritoneum.

Berkeley and Bonney⁴ found no decidual cells in the ovary, in the opposite tube, or on the peritoneum.

Kermauner²⁷ found proliferation of the peritoneal cells in almost every case, but no decidual cells on the peritoneum, and very few in the adhesions, although he sometimes found large decidua-like cells in the loose, new, connective tissue of the latter.

Kroemer²⁹ and Whitridge Williams⁵⁰ each found decidual changes in the tube of the other side in one case.

Hirschberg²² described a case of "periappendicitis decidualis," in which the appendix was adherent to the pregnant right tube. There were decidual cells in the peritoneum of the appendix and its mesentery, and on the great omentum. In another case of right-sided tubal pregnancy where the appendix was adherent to the tube he found no such cells.

Penckert³⁷ described a case of considerable interest in which a three-months' ovum was implanted partly on the abdominal end of the tube and partly on the omentum, to which some of the chorionic villi were attached. In the omentum were clumps of gigantic cells, oval, ovoid, or more elongated in shape, typical decidual cells such as are found in the compact layer of a uterine decidua. These clumps of cells were not arranged in any special relation to the large omental vessels, and were certainly not endothelial or perithelial in origin, but were evidently formed from the connective tissue cells of the fatty tissue.

Such a case strengthens the view that primary abdominal pregnancy may occur.

The uterine decidua.

Cazeaux⁶ considers that in every case of extra-uterine pregnancy there is a reaction in the endometrium which undergoes profound changes during the development of the ovum. This reaction is variable and is the more marked the nearer the site of the ovum is to the uterus. The expulsion of a decidual cast does not always occur. Expulsion of a decidual cast does not always imply the death of the ovum, but it has not been proved that it does not coincide with some more or less important disturbance to the ovum.

Kermauner²⁷ thinks that it is not absolutely proved that a uterine decidua is always formed in tubal pregnancy. If formed, it may not be thrown off until four weeks after the death of the ovum

(Lindenthal). He believes that a certain amount of the blood which escapes from the uterus may come from the tube.

I have been unable to find any note as to what changes, if any, can be found in the connective tissue of the broad ligament.

If we accept the above evidence—and there is no reason to doubt the correctness of the greater part of it—we are forced to the conclusion that the amount of decidual reaction undergone by the maternal tissues in the pregnant tube varies considerably in different cases. Some of those in which decidual reaction is described as being present to a marked degree were early cases, so time is not the only important factor. One thing is certain, viz., that tubes in which the gestation sac has been much damaged by bleeding are of little value for purposes of demonstrating decidual change in muscle and inter-muscular tissue. Edema, loosening of tissue and a certain amount of degeneration are always present in the neighbourhood of the ovum, and when to these is added pressure from blood clot the tissues stain so badly that it is difficult or impossible to decide whether doubtful cells are maternal or foetal, and whether changes are to be put down to decidual reaction or to degeneration. It is possible that difference in the methods of fixing and staining are responsible for some discrepancies.

(ii.) *The site of the gestation sac.*

The theory that the ovum is implanted *on* the mucous membrane and has a “free pole” projecting into the lumen of the tube receives no support. The work of Peters on the embedding of the ovum in the uterus, and of FÜTH on embedding in the tube are almost universally adopted. The chief difference of opinion now is as to the means by which the ovum sinks to such a depth in the tissues of the tube.

Veit⁴⁶ describes submucous embedding, and says that the ovum can only occupy pre-existing cavities in the tube wall, and cannot destroy maternal tissue. He still objects to the ovum being looked on as acting in the same way as a malignant growth.

Kroemer²⁹ upholds this view to a certain extent. He thinks that the site of the ovum may be simply submucous if the mucous membrane is loosely attached to the muscle. It may project into the lumen in polypoid fashion, but if it does this it is encapsuled, not free. In other cases it is intra-muscular, but the villi do not devour the muscle, they grow into interstices in the softening maternal tissues.

Standage⁴³ says “the lumen of the tube is patent in its entire length, so the gestation sac did not occur there.”

The large majority of observers are agreed that the site of the ovum is intra-muscular.

Whitridge Williams⁵⁰ says: "The ovum penetrates the surface epithelium and burrows down into the tissue beneath it. Several specimens, which I had previously taken as indicating the development of the ovum in a diverticulum from the lumen of the tube, are to be interpreted in this manner. . . . As there is no distinct decidual membrane to separate the growing ovum from the underlying muscular and connective tissue, the rapidly proliferating trophoblast comes at once in contact with the tube wall, and promptly leads to its necrosis and ultimate conversion into fibrin."

Heinsius²¹ says that in what will be the placental site the muscle is destroyed, looking as if it had been eaten out. The ovum becomes intra-muscular at the uterine end sooner than at the abdominal end of the tube because of the difference in the mucous membrane at the two ends. The trophoblast may grow through the *capsularis* into the opposite wall of the tube.

Füth¹⁵ also has seen this, and says that the ovum undoubtedly enters the tubal tissues by its own activity.

Vassmer⁴⁵ and Raschkas³⁸ agree that the foetal cells destroy or cause atrophy of the tubal muscle.

The presence of a partition-sheet or *capsularis* containing muscle, thus proving the deep intra-muscular site of the ovum, has been noted by many observers.

Andrews² showed sections from a pregnant tube in which the ovum projected into the tube lumen, but was separated from it by a very definite partition-sheet which contained muscle fibres.

Berkeley and Bonney⁴ found the gestation sac separated from the lumen by the circular coat of muscle. They lay a good deal of stress on the way in which the longitudinal coat of muscle is split off from the circular coat. Serial sections from pregnant tubes of 19 and 24 days showed that early tubal gestation is entirely intra-mural. "The depth at which the gestation sac lies from the lumen of the tube, together with the fibrinous track indicating apparently the track of the ovum strongly suggest that burrowing has taken place."

Bosse⁵ found that an ovum embedded in a diverticulum was entirely surrounded by muscle; there was no communication between the gestation sac and the diverticulum or the main lumen.

Duncan¹⁰ describes a case in which "the tubal lumen appears intact and separated from the gestation sac by a well-marked muscular layer (*capsularis*) of considerable thickness."

von Franqué and Garkisch¹³ speak of "the muscle which separates

the bed of the ovum from the lumen of the tube." Some foetal cells lie between the muscle bundles in situations which they could have reached only by their own activity; they could not have been carried there by the blood-stream.

Kermauner²⁷ found in all his 41 cases that there were not too much damaged traces of the capsularis, and in some saw not only muscle-fibres, but even muscle-bundles in the base of this partition-sheet.

Cuthbert Lockyer³¹ demonstrated a case in which the capsularis contained hyaline muscle fibres.

Voight⁴⁷ says "the capsularis contains muscle."

Werth⁴⁸ says that in the ampulla the ovum bulges into the lumen, covered by its capsularis which contains muscle. In the isthmus the ovum surrounds the lumen and the internal layers of the tube soon disappear.

Most observers agree that the capsularis is not often found intact except in early and undamaged specimens. When a "free pole" is found it is to be explained by the fact that the capsularis has been destroyed.

The deep site of the gestation sac is in some cases partly due to embedding of the ovum in a diverticulum. Fellner considers that this explains the deep intra-muscular site more easily than the theory of the pseudo-malignant action of the trophoblast, which he refuses to accept. Most observers who have described diverticular embedding, however, accept the burrowing theory.

Bosse⁵ found that an ovum had been embedded in a diverticulum. The mucous membrane covering the capsularis showed decidual reaction except at one minute spot where there was granulation tissue. He considers that this was undoubtedly the spot where the ovum had broken through into the mucous membrane. "There is not the least doubt that there is here an active invasion of the muscle by Langhans' cells, and that the muscle is infiltrated and destroyed by these cells."

Fellner¹¹ considers that embedding in a diverticulum is not the exception but the rule in tubal pregnancy. He is not certain whether the ovum bores its way into the wall of the diverticulum or not.

Füth,¹⁴ Kroemer²⁹ and Wertheim⁴⁹ report cases in which the ovum was embedded in a secondary lumen.

Micholitsch³⁴ describes 10 cases in which the ovum was embedded in a diverticulum (Kermauner challenges every one of these 10 cases). Micholitsch found in all the cases that he examined, over 30, diverticula of some sort, and it was almost always possible to prove that the

ovum was embedded in one of these. He agrees with Fùth that the ovum becomes intra-muscular by virtue of its own activity.

von Franqué and Garkisch¹³ agree that embedding in a diverticulum may occur, but hold that "cases more than a few weeks old, and apart from serial sections, are practically useless for purposes of demonstrating diverticular embedding."

Kermauner,²⁷ in 1904, did not believe that embedding in a diverticulum had been proved in any case. He thinks that columnar embedding, *i.e.*, embedding in a fold of mucous membrane, does not occur, but that the ordinary method of embedding is intercolumnar, between two folds.

Heinsius²¹ thinks that if an ovum is embedded in a fold the pregnancy soon comes to an end.

With the exception of Veit and Kroemer, and also Fellner to a certain extent, all observers are agreed that the maternal tissue is destroyed by the trophoblast. As proof of this destructive action may be cited the fact that in three cases (Fùth,¹⁵ Heinsius,²¹ von Franqué and Garkisch¹³) the trophoblast had grown through the capsularis and attacked the tube wall on the other side of the lumen.

The appearances in the maternal tissues forming the wall of the gestation sac may be summed up briefly from von Franqué and Garkisch¹³: "Swelling, fibrinous degeneration and finally breaking-down of the muscular fibres which are in direct contact with Langhans' cells."

(iii.) *The relation of the foetal ectodermal cells, trophoblast, to the maternal vessels.*

The way in which communication is established between foetal tissues and maternal blood has received much attention.

Veit⁴⁶ refuses to admit that the trophoblast exercises a destructive action on the walls of vessels. He says that the villi and trophoblast are not found in arteries, but only in veins into which they are carried by the force of the blood-stream, *i.e.*, by "deportation." The veins are so blocked up by villi that bleeding from congestion ensues.

Kroemer²⁹ says that the opening of arteries and veins into the intervillous space is brought about by the force of the circulation acting on tissues which have been altered by a peculiar softening due to pregnancy.

Several observers have noticed "deportation," but look on it as a secondary result of the destruction of vessel-walls by trophoblast.

Heinsius²¹ finds that deportation of villi undoubtedly occurs in both tubal and uterine pregnancy, but at a later stage than the

destruction of maternal tissue by trophoblast. The finding of either process cannot be held to disprove the occurrence of the other. In every tubal pregnancy at least, if not in every intra-uterine pregnancy, many foetal cells are carried into the blood-stream. Carrying away of foetal cells cannot, therefore, be the cause of eclampsia as suggested by Veit. "Invasion of the vessel walls by Langhans' cells has been proved with absolute certainty."²⁰

Berkeley and Bonney⁴ say, "Our sections show very clearly the appearances figured in Russell Andrews' paper, viz., trophoblast cells replacing the tissues forming the walls of the maternal vessels. Nowhere does the foetal tissue grow along the lumen of the vessels in the manner described by some workers on placenta formation. It either directly invades the wall from without, so that the mass of trophoblast replacing the vessel wall is directly continuous with a similar mass lying outside the vessel, or vessels may be seen whose walls have been in part replaced by a cell mass not in continuity with any other part of the trophoblast. It is probable that in these cases the trophic ectoderm has found its way along the perivascular lymphatics."

Bosse⁵ says that villi are carried into veins by the force of the blood-stream, but their entrance into arteries cannot be explained in this way.

Hitschmann,²³ who has made a special study of deportation of villi, finds that the trophoblast actively opens up maternal vessels by destruction of part of their walls. Deportation undoubtedly occurs, villi entering opened veins simply by a process of advance in the direction of least resistance. Most "deported" villi are really still in direct connection with the chorion; there is no solution of continuity.

Fellner¹² is convinced that what many writers have described as deportation of Langhans' cells into veins is really decidual formation in arteries. Villi and trophoblast are found in arteries at some distance from the ovum. Langhans' cells break through the layer of decidual cells in the arterial walls. The lumen is more or less filled up by the decidual formation, autothrombosis, and the force of the blood stream cannot have so much to do with opening of the vessel as has the destructive action of the foetal cells.

Raschkes³⁸ describes the two processes, viz., destruction by trophoblast, and entrance of villi into vessels: "Instead of syncytium at the place where the villus is anchored, we find Langhans' cells arranged in several layers. From these columns of Langhans' cells groups or single cells can be seen invading the wall of the gestation

sac. . . . They are found in great numbers round blood-vessels; they force their way under the endothelium and destroy it. The villi themselves progress only on account of this destruction by the Langhans' cells."

Schambacher's⁴² description of decidual cells in the vessel walls has been quoted above. In many places he saw Langhans' cells breaking through into the decidual layer. The endothelium was usually undisturbed until the Langhans' cells had broken through the decidual cells. In some of the smaller vessels the wall was simply destroyed by the Langhans' cells without undergoing any previous change. After the foetal cells had entered a vessel they underwent proliferation and reached to a considerable distance from their place of entry.

Werth⁴⁸ finds that vessel walls are destroyed by trophoblast. Deportation is not responsible for the communication between foetal elements and maternal blood.

Kermauner²⁷ and von Franqué and Garkisch¹³ find a preparatory change in the wall of the maternal vessels followed by infiltration by foetal cells.

The bulk of this evidence is in favour of the view that the foetal cells act in a malignant or pseudo-malignant manner towards the maternal tissues, in somewhat if not exactly the same way as do the cells of a chorio-epithelioma. The difference seems to be one of degree only, not of kind.

II. THE CAUSES OF TUBAL ABORTION AND RUPTURE.

There is not much that is new to be said about the causes of abortion and rupture.

Most observers are agreed that "abortion" is really an internal rupture, as first insisted on by Krönig.

Werth⁴⁸ speaks of rupture of the "internal capsule" and of the "external capsule."

Berkeley and Bonney⁴ employ the useful expression "rupture of the primary gestation sac," and describe three varieties: (1) extra-tubal, (2) intra-tubal (tubal abortion), and (3) intra-mural rupture. Intra-mural rupture had not been described previously, but Vassmer⁴⁵ has since described a somewhat similar condition. The authors compare it with the condition that results when a saccular aneurysm becomes diffuse. The gestation sac ruptures into the substance of the tube wall. Rupture of the blood sac thus formed may occur into the peritoneal cavity, broad ligament or lumen of the tube. They suggest that the paratubal hæmatocele described by Sampson

Handley¹⁶ may have originated in an intra-mural rupture. Paratubal hæmatocele has been described by Hamilton Bell³ also.

The three factors involved in causing abortion or rupture, apart from such extraneous causes as bimanual examination, etc., are—

- (i.) The destructive action of the trophoblast.
- (ii.) Bleeding.
- (iii.) Contraction of the muscular wall of the tube.

(i.) *The trophoblast* may burrow until it perforates either the peritoneal coat of the tube or the capsularis. If the intervillous space is opened up the pregnancy probably comes to an end.

von Franqué and Garkisch¹³ consider that there is not the least doubt that rupture is due to destructive action of the trophoblast.

Schambacher says that the amount of villus formation varies—if it is well developed, rupture results; if it is less marked, abortion.

(ii.) *Bleeding* into the intervillous space may cause either the formation of a mole or internal or external rupture of the tube.

According to most writers, bleeding into the sac is due to a destruction of the vessel-walls by the growth of the ovum, *i.e.*, by trophoblast. According to Veit,⁴⁶ however, bleeding is due to congestion caused by blocking of veins by deported villi.

In one of Vassmer's⁴⁵ cases rupture was due to villi and blood breaking through into an epithelial-lined tubule in the tube wall.

Whitridge Williams⁵⁰ says: "the underlying causes of rupture are perforation of the tube wall by the growing villi, or acute overdistention as a result of hæmorrhage into a tube whose fimbriated end is occluded. . . . In abortion, the connection between the ovum and the tube wall is loosened, the former being completely or partially separated from its site of implantation as the result of hæmorrhage due to the sudden opening up of maternal vessels by the growing trophoblast and chorionic villi."

(iii.) *Contraction of the tube.* Mainzer³³ and Kermauner²⁷ both recorded cases in which intussusception of the tube occurred, showing that there must have been active contraction.

Dobbert⁸ looks on muscular contraction as being an important factor in the causation of abortion and rupture.

Runge⁴¹ considers that the amount of reaction in the muscle of the tube wall, not simply hypertrophy but also hyperplasia, must help to determine whether the rupture shall be internal or external. If well marked hyperplasia is present there will be internal rupture, if the reaction is less well-developed external rupture will occur.

Heinsius²¹ is doubtful as to the importance of muscular contraction in the causation of abortion and rupture. He considers that the

severity of the bleeding is due to the fact that the damaged muscle cannot contract.

Two clinical cases of interest may be mentioned.

Galabin¹⁶ records a case in which a mass on the right side of the uterus was suddenly felt to collapse during bimanual examination under an anæsthetic. Two days later a mass was felt in Douglas's pouch. Abdominal section was performed several days later and a carneous mole, two and a half inches in diameter, was removed. There was no free blood in the peritoneal cavity.

Amos¹ reports a case in which a full term foetus was found to be still inside the tube. The placenta had perforated the tube wall, making a hole rather less than the size of a 3-mark piece.

INTRA-LIGAMENTARY RUPTURE OF THE TUBE.

My search through the literature brings out one interesting point which, though it is rather outside the scope of this paper, seems worth inserting, viz., that intra-ligamentary rupture is a rarer occurrence than is generally supposed. Among the very large number of cases on which were based the papers that I have consulted there were only two of intra-ligamentary rupture, one reported by Noble³⁵ among his 91 cases, and the other by Whitridge Williams⁵⁰ among his 50 cases. The latter author finds that it was noted in only 4 out of 276 cases collected from the articles of Mandl and Schmidt, Küstner and Fehling. This is the more remarkable since most early ruptures, or "external ruptures of the gestation sac" take place at the placental site, and this commonly involves the attached or mesosalpingeal part of the tube. The tendency of the ovum to travel towards the best blood-supply, viz. the place where the vessels enter, has been noted by several observers, *e.g.*, by Berkeley and Bonney, who say: "It is probable that the ovum travels towards that part of the tube where the nutrition (vascular supply) is most copious, and that in the majority of cases it is primarily implanted in the attached half of the tube wall."

Alban Doran⁹ says that "hæmatoma" (due to intra-ligamentary rupture of a pregnant tube) is probably not so rare a result of interrupted extra-uterine pregnancy as is generally taught.

Cullingworth⁷ considered it "rare" and Taylor⁴⁴ "rather rare." I have not been able to find any suggested explanation of the comparative rarity of the occurrence of intra-ligamentary rupture, and I do not think that the fact that an explanation on anatomical grounds is difficult to find has received attention before.

One might theorize on the subject, suggesting that the loose

connective-tissue of the mesosalpinx could undergo decidual reaction and so resist a threatened rupture, but if the intervillous space were opened into the mesosalpinx a great amount of decidual formation would be necessary to prevent escape of blood into the tissues, and we have no evidence that such decidual reaction occurs in the connective tissue of the broad ligament.

III. THE ÆTIOLOGY OF TUBAL PREGNANCY.

(a) *Diverticula.*

The presence of diverticula, secondary lumina, and small epithelium-lined prolongations and branchings from the lumen is looked on by many observers as the cause of tubal pregnancy.

A case recorded by von Franqué and Garkisch¹³ is of considerable interest. The tube lumen consisted of two overlapping parts, one leading from the ostium abdominale and blind at its uterine end, the other leading from the uterus and blind at its external end. A minute communication existed between the two overlapping portions. Each lumen, except at this spot, was surrounded by its own muscle. The ovum had become implanted in the portion of the lumen the uterine end of which was blind, on the uterine side of the communication between the two portions. The tube showed marked inflammatory changes. External to the ovum, in a part of the tube through which it had passed, was a labyrinth of folds of such number that a section of the tube resembled a sieve. The authors consider that their case proves that a high degree of adhesions between folds does not necessarily prevent the further progress of the ovum as Opitz suggested.

If pregnancy had progressed further in this case the two parts of the lumen would have been thrown into one by the growth of the ovum, and the proof of the peculiar structure of the tube would have been lost. The authors look on diverticula as one of the least certainly proved causes of tubal pregnancy. Cases in which the pregnancy is of more than a few weeks' duration, or not investigated by the aid of serial sections are practically useless for purposes of demonstrating embedding in a diverticulum.

Micholitsch³⁴ recorded 10 cases of embedding of the ovum in secondary processes of the lumen, and found invaginations of mucous membrane, either congenital or acquired, in every one of 30 cases that he examined. In almost all it was possible to prove that the embedding had taken place in one of these secondary processes.

Kermauner²⁷ refuses to accept any of these cases as proved, and

does not consider that embedding in a diverticulum has ever been conclusively demonstrated.

Fellner¹¹ considers that diverticular embedding is very common. If other observers disagree with him, he thinks that they cannot have cut serial sections. He holds that the ciliary stream acts towards the blind end, and that muscular contraction would tend to prevent the escape of an ovum from a diverticulum rather than to further it. The absence of these diverticula in the tubes of animals explains the non-success of experimental attempts at producing tubal pregnancy in rabbits, bitches, etc.

Füth¹⁴ considers that diverticula are an important cause of tubal pregnancy.

As regards the origin of these diverticula—they may be congenital, due to Wolffian relics, or acquired as the result of inflammation (vide Hoehne below), such as salpingitis isthmica nodosa, or adenomatous proliferation, or may be due to the presence of adenomyoma of the uterine end of the tube (*Tubenwinkel*).

Whitridge Williams,⁵⁰ speaking of diverticular embedding says: "I believed for a number of years that a considerable number of my cases had originated in this way," but "after further examination of my specimens, while not wishing to deny such a possibility, I am of the opinion that these conditions can be more satisfactorily explained by supposing that the fertilised ovum had burrowed beneath the mucosa of the tube."

Berkeley and Bonney⁴ failed to find any evidence of diverticula.

Werth⁴⁸ thinks that some of the small diverticula, inter-muscular branchings and invaginations described by many observers are the result of proliferation during pregnancy.

Heinsius¹⁹ says that it has been proved that in tubal pregnancy the ovum *may* be embedded in a diverticulum, but it is by no means proved that it *must* be so embedded.

(b) *Salpingitis*.

Kermauner²⁷ thinks that there is undoubtedly some connection between salpingitis and tubal pregnancy, but cannot say what it is. Some of the appearances ascribed to inflammatory changes are the result rather than the cause of tubal pregnancy, *e.g.*, oedema and small-celled infiltration as found by Mandl in cases of intra-uterine pregnancy. The adhesions between folds of mucous membranes, to which attention was drawn by Opitz, Kermauner looks on as being possibly the result of a proliferation during pregnancy, and not the cause of the arrest of the ovum.

Noble,³⁵ Runge⁴⁰ and Werth⁴⁸ look on salpingitis as an important cause of tubal pregnancy.

Hoehne²⁶ examined a tube in which an abscess in the wall communicated with the lumen. The mucous membrane was prolapsing into the abscess cavity the wall of which was partially clothed by epithelium derived from the lumen. He considers that this method of formation of intramuscular offshoots from the lumen is the commonest. Among 136 tubes which he examined, there was not one with epithelial diverticula which did not show evidence of old inflammation.

Gottschalk¹⁷ is convinced that salpingitis is a cause of tubal pregnancy, although he has not found the adhesions between folds described by Opitz. He considers that the difference between inflammatory changes and changes due to pregnancy can be made out with certainty.

von Franqué and Garkisch¹³ consider that endosalpingitis may occur in virgins without any symptoms and leave behind it changes which, although they cannot be recognised by palpation or by naked-eye examination, may lead to the occurrence of tubal pregnancy in later years.

It would be very difficult to prove that this statement is correct. It appears to be of the same class as the statement that endometrium is never normal.

Berkeley and Bonney⁴ found no evidence of salpingitis in their cases.

Orthmann³⁶ and Reifferscheid³⁹ both record cases in which there was absolutely no sign of inflammation.

Schambacher⁴² does not consider that inflammation plays an important rôle in the ætiology of tubal pregnancy.

Vassmer⁴⁵ finds that ova often manage to pass along the lumen of tubes in spite of very marked abnormalities in the mucous membrane.

von Franqué and Garkisch¹³ found an ovum on the uterine side of a labyrinth of folds.

Hitschmann and Lindenthal²⁵ suggest that the ovum can only implant itself at a certain stage in its development, and that the cause of tubal implantation is that the passage of the ovum has been delayed in some way so that it is still in the tube when this stage is reached. This is very much like Sippel's modification, in 1901, of his original theory. His original theory was that the ovum was too large to pass through the tube, having been delayed in some way, *e.g.*, by "external wandering." His later theory was that the delay had given it time to acquire the power of boring its way through epithelium.

Vassmer,⁴⁵ also, is of opinion that purely mechanical hindrance to the passage of the ovum is one of the most common causes of tubal pregnancy. During its slow progress it reaches the stage when it can embed itself.

The theories of Hitschmann and Lindenthal and Vassmer fit in with every cause of delay in the passage of the ovum from the ovary to the uterus, but do not help us to a better understanding of the actual causes of tubal pregnancy.

Heinsius²¹ does not expect that any single cause will ever be proved to be applicable to all cases, but looks on tubal pregnancy as being due to a concatenation of causes. He finds¹⁹ that diverticula are present in many normal tubes, yet uterine pregnancy occurs.

Vassmer⁴⁵ adds another to the list of cases in which a mucous polypus in the tube has formed a mechanical hindrance to the onward passage of the ovum.

It has been proved that in a few cases the ovum has been caught in a diverticulum or prevented from passing along the tube by the presence of a mucous polypus. Beyond this our knowledge as regards the ætiology of tubal pregnancy must be admitted to be most unsatisfactory. It is, unfortunately, likely to remain so, as undamaged and early specimens of tubal pregnancy are seldom obtained for examination, and there are not many trained observers who can spare the time to cut serial sections of large numbers of healthy tubes, inflamed tubes, pregnant tubes, and tubes from cases of intra-uterine pregnancy, and compare the microscopical appearances. Until this has been done we shall be in doubt as to whether certain appearances should be looked on as being (i.) congenital, (ii.) due to inflammatory changes, or (iii.) due to changes produced by pregnancy. It is evident that there is nearly if not quite as much difference of opinion as to what should be considered a departure from the normal in the structure of the tubal mucous membrane as there is about the endometrium. Some German microscopists seek to explain as much by "endosalpingitis" as by "endometritis," and stronger evidence than a mere statement is required to prove that intra-muscular branchings of the tubal mucous membrane in an apparently healthy young woman are due to a symptomless endosalpingitis which occurred in childhood. Other skilled observers consider that similar changes are the effect and not the cause of tubal pregnancy. Sections of an ovum caught in the act of implanting itself on the tubal mucous membrane would be necessary to prove the theories of Sippel, Hitschmann and Lindenthal, and Vassmer.

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