

DECIDUOMA MALIGNUM.

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AT a meeting of the Leipzig Obstetrical Society, July 16 1888, Sänger⁵⁰ reported what he designated as "two unusual cases of abortion," one of which occurred in a twenty-three-year-old woman, who aborted in the eighth week and died seven months later, with four large, soft, spongy, reddish tumors in the uterine wall and metastases of the same character in the lungs, diaphragm, tenth rib, and right iliac fossa.

He stated that the microscopic examination showed that he had to deal with a very hemorrhagic tumor made up of cells similar to those found in the decidua, and that he had before him a "malignant metastasising deciduoma," a tumor never before observed, which belonged in the sarcoma group.

He reported the case more in detail before the German Gynecological Society⁵¹ in 1892, when several of the members, particularly Müller⁴¹ and Hegar,¹⁶ stated that they had observed similar cases. And in 1893 he made it the basis for an extensive monograph, which appeared in the *Archiv für Gynækologie*,⁵² and in which he collected all that was known of this class of tumors and compared his case with those which had been reported since his first publication.

The year following his first report, Pfeiffer,⁴⁰ a pupil of Chiari, described a similar case, and, without knowledge of Sänger's previous work, likewise proposed to call it a de-

ciduoma malignum. He stated at the same time that Chiari⁶ considered that three cases, which he had previously reported as carcinoma of the uterus following the puerperium, were of the same character.

Numerous more or less similar cases have been reported since Sanger⁵⁰ first called attention to this class of tumors, which have increased very rapidly in number since the appearance of his monograph. The majority of the cases have been reported by German observers and a few by French, but as yet no one in this country or England has reported a well-authenticated case.

The case which we are about to report occurred in Baltimore last summer. My friend, Dr. Wm. T. Howard, Jr., Professor of Pathology in the Western Reserve University of Cleveland, performed the autopsy and very kindly placed the specimens at my disposal. The specimens were exhibited before the Johns Hopkins Hospital Medical Society last November, and a brief report of the case appeared in the Johns Hopkins Hospital *Bulletin* of December, 1894.

For the clinical history of the case we are indebted to Dr. Wm. E. Harris, of Baltimore, who attended the patient in her last confinement and for some time subsequently.

CLINICAL HISTORY. R. W., aged thirty-five years, was a full-blooded negress, both her parents having been born in Africa. Her family history was good, both parents being still alive. She had been treated by Dr. Harris for malaria some two years previously, and for bronchitis about six months before her last pregnancy. She has had five pregnancies, the third ending in a miscarriage at the sixth month, and the others at full term; in all of which, with the exception of the last, she was attended by a midwife.

During her last pregnancy she felt somewhat apprehensive as to the result and engaged Dr. Harris to attend her. The pregnancy was perfectly normal, excepting a transient attack of slight albuminuria a few days before confinement.

April 15, 1894, she was delivered spontaneously of a dead

child. The labor was slow and lasted about thirty hours, a good deal of blood being lost during the third stage. The placenta was "soft and boggy," but there was no loss of blood after its expulsion. The puerperium was not entirely normal, the temperature remaining at about 100° F., and she felt very much prostrated. Dr. Harris saw her for eight days, when he discontinued his visits, leaving her with a chalybeate tonic.

About one week later, the patient's mother informed him that there was a small and painful nodule, about the size of a pea, on the right labium majus, for which he prescribed some soothing wash without seeing the patient. Three weeks after the labor, he was called once more to the case and found the right labium swollen to about the size of a hen's egg and very painful. In it was a bright-red tumor the size of a walnut, which rapidly increased in size and soon became gangrenous and ulcerated on its surface, so that a month after labor it had attained the size of a hen's egg, was markedly necrotic on its surface, and was accompanied by a very odorous discharge. There were no symptoms indicating any involvement of the uterus, and as the patient was rapidly growing worse he advised her to enter the Maryland German Hospital, which she did on May 16th, and died there July 12, 1894.

When admitted to the hospital, she was suffering with septi-cæmia; and examination showed a large sloughing mass, which occupied nearly the whole of the right labium and the adjacent tissue, in the centre of which there was a large fistulous opening into the rectum, through which fæces were discharged. The temperature varied from 99° F. in the morning to 103° F. in the afternoon, but during the last three weeks of life it did not rise above 100° F. Death was from exhaustion, with marked emaciation. The clinical diagnosis was "sloughing hæmatoma of the vulva with septicæmia."

Abstract of autopsy protocol. There are a few scattered flakes of grayish-white lymph on the intestinal peritoneum, the peritoneum is pale and the peritoneal cavity contains about 50 c.cm. of clear fluid. The genital tract and rectum were removed *en masse*.

At the entrance of the vagina, involving its posterior and

lateral aspects and both labia majora, there is an irregularly-shaped raised mass of a dark grayish-red mottled appearance, which is marked by deep furrows of ulceration. This is about 10 c.cm. in circumference and extends for about 6 c.cm. up the posterior vaginal wall. At the upper border of this mass, on the posterior wall of the vagina, there is an irregularly-shaped opening 2 c.cm. in diameter, which communicates with the rectum. Its edges are not raised. On section the mass is of a mottled-gray and red color, is soft and friable, and is separated from the underlying tissue by a paler grayish zone.

On the left lateral wall of the vagina, 4 cm. below the cervix, there is an oval area raised 5 mm. above the surrounding tissues, which measures 1.5 by 1 cm., is of a grayish-red color, and presents a granular appearance. It is soft and readily breaks down under the fingers. On section, it is also of a grayish-red color and extends through the vagina into the underlying tissues.

The cervix is soft, considerably dilated, and has very thin walls. On the right side of its vaginal surface there is a small ulcer; its canal is free from ulceration and new growth.

The body of the uterus is about twice the normal size and its cavity is considerably dilated. On section, its wall is very pale and softer than usual. The mucosa is pale and free from ulcerations. From the posterior wall of the body of the uterus an irregular oval mass, 3.5 cm. long and 2 cm. wide, projects 1.5 cm. into the cavity of the uterus. Its surface is uneven and grayish-white in color, marked here and there by greenish-gray areas. At its lower portion, just above the os internum, there is an irregularly-shaped superficial loss of substance, which is covered by a loosely adherent, foul-smelling slough. On section, the tumor presents a grayish-red granular appearance. In the fundus, beneath the mucosa, there is a smaller tumor the size of an almond, which on section presents the same appearance as the larger tumor.

The left tube is of the usual size, its fimbriated extremity is free, and a thin milky fluid can be expressed from it. The left ovary is smaller than normal, and from its hilum a dark-red tumor, the size of a hazlenut, arises, which is soft, and breaks down readily under the finger, and on section closely resembles

placental tissue. Adjacent to this, and corresponding to the parovarium, is a small multilocular cyst, the size of a lemon, which contains clear fluid.

The right tube presents the same appearance as the left. The left ovary is irregularly nodular in shape, and on section contains several small cysts with hemorrhagic margins and clear contents.

Lungs: Left lung. There are numerous thin adhesions, particularly on the upper and anterior surface of the superior lobe. On its surface, as well as on section, the lung is seen to be occupied by a large number of irregularly-shaped round or oval nodules, which vary from a pea to a walnut in size; the majority being situated in the peripheral portions of the lung. They are grayish-red in color, some presenting soft grayish areas in their centre. They easily break down under the finger, and are readily enucleated from the surrounding lung substance, and closely resemble placental tissue in appearance. At one point, upon enucleating a nodule, a vessel of considerable size is seen, whose walls are infiltrated by the growth, which appears to project into its lumen.

The right lung is likewise studded by large numbers of similar nodules. In both lungs the tissue between the nodules presents its usual appearance and crepitates. The bronchial mucous membrane is normal, as are also the bronchial glands.

Heart: The heart is normal, but several atheromatous patches are seen in the upper part of the aorta.

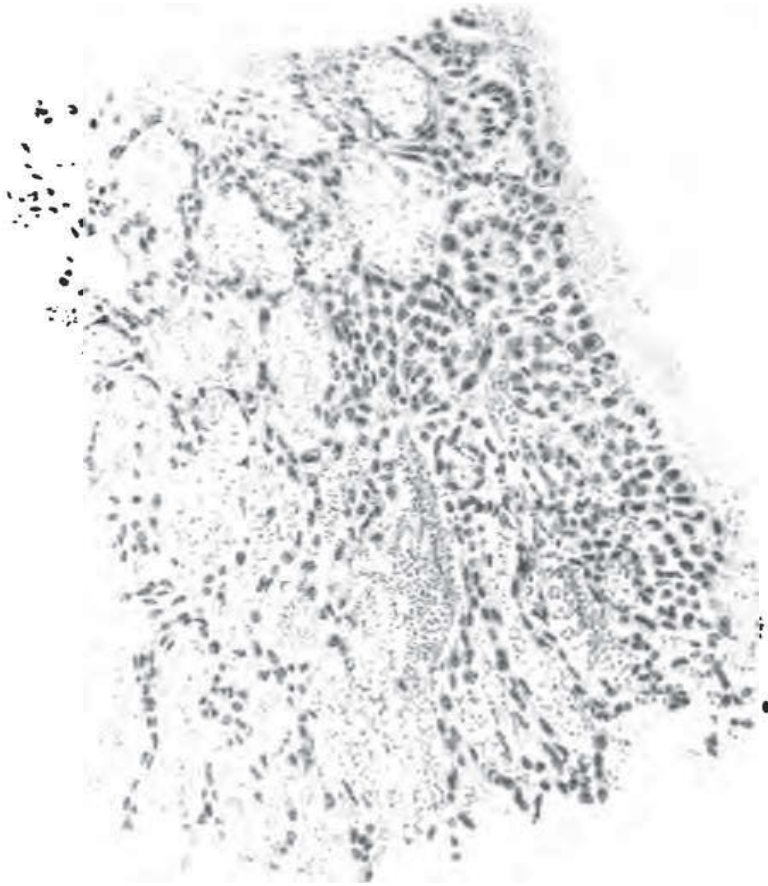
Liver: The liver is not enlarged. It presents markedly fatty degeneration, and scattered through it are numerous hemorrhagic nodules, the largest not exceeding a hazlenut in size.

Spleen: The spleen is twice its normal size, is soft and almost diffuent, the entire organ being the seat of an infarction. It also contains several small metastases.

Kidneys: The kidneys are not enlarged, but present marked fatty degeneration. In the cortex of both, just at the base of the pyramids, are several dark-red hemorrhagic areas, with whitish or grayish centres, which vary from 2 to 10 mm. in diameter.

The renal pelves, ureters, bladder, suprarenals, and pancreas are normal. The mucous membrane of the stomach and intestines is very pale, but otherwise normal. Agar cultures from the lungs, spleen, liver, and kidneys were sterile.

FIG. 1.



Section from primary uterine tumor, showing its alveolar structure, with the cavities filled with blood. \times 60 diam. Leitz, ocular 3. Objective 3.

Microscopic examination. Small pieces from the various organs were immediately placed in 95 per cent. alcohol, from which very satisfactory sections were obtained.

Sections were first made through the larger nodule on the posterior wall of the uterus and the adjacent portions of the uterine wall. The mucosa covering the uterine wall adjacent to the tumor was very slightly changed. Its surface epithelium was intact, and in places ciliated, and its glandular structures presented their usual appearance. The interglandular connective tissue was increased in amount, and scattered through it were considerable numbers of round cells and leucocytes. The mucous membrane could be traced for a considerable distance up along the sides of the tumor, where it gradually disappeared, the surface epithelium disappearing first, while the stroma and glands persisted longer. Nowhere in the mucosa could any trace of decidual tissue be found, nor did it present any suggestion of sarcomatous change.

It was found that the new growth had invaded portions of the muscularis, which were still covered by but slightly changed mucosa, and had consequently undermined it to some extent, but by far the greater part of the growth was uncovered by mucosa.

The entire superficial portion of the nodule is composed of necrotic material, which indeed makes up its greater part. The most superficial portions are entirely necrotic, and we are able to distinguish only threads of fibrin and very dense leucocytic infiltration. Lower down, as we approach the real substance of the tumor, the necrosis becomes less absolute, and in the necrotic masses we are able to distinguish the outlines of cells, whose nuclei have disappeared. As we approach still nearer, we find very large individual cells scattered through the threads of fibrin, in whose meshes are large quantities of blood-cells, which are accompanied by many more leucocytes than normal. These cells are very large, and present a decidedly epithelial appearance, though they are somewhat suggestive of the large epitheloid decidual cells. The boundary line between the necrotic tissue and the new growth is very irregular, as is also the line of demarcation between the latter and the subjacent muscular tissue.

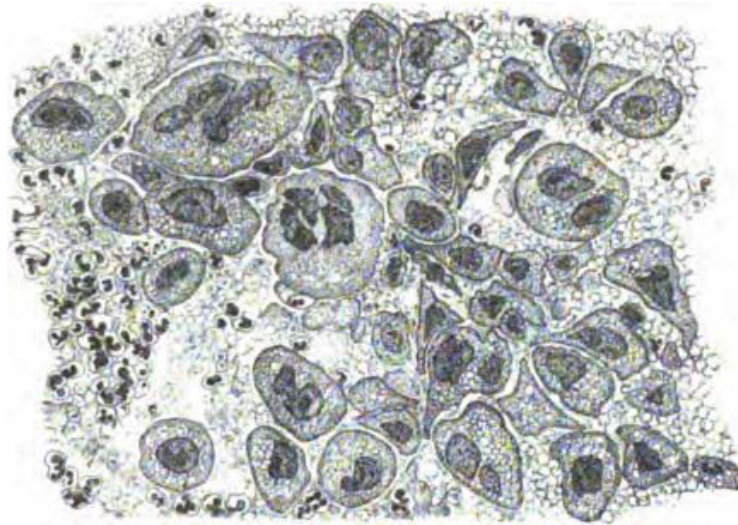
Under the low power, the most striking feature of the growth

is its marked alveolar structure, its greater part being made up of irregularly-shaped cavities of varied size and shape, which are filled with blood and fibrin, and contain numerous leucocytes. (Fig. 1.) Nowhere in these cavities are we able to discover any trace of an endothelial lining. They are separated from one another by irregularly-shaped bars of tissue, which are made up of large epithelioid cells of varying shape and size, which likewise form the boundaries of the blood spaces. Where the cells are closely packed together they are usually more or less spindle-shaped, with a nucleus filling the greater part of the cell, and staining moderately deeply, while the cell body stains readily with eosine, and presents a distinctly granular appearance, and contains vacuoles of varying size. Where they are less closely packed together, and especially where the individual cells are separated from one another by hemorrhage, they assume a polygonal or rounded shape, and closely resemble epithelial cells. (Fig. 2). In other places, especially where the bars of tissue separating the alveolar spaces are very thin, the cells may present irregular branching outlines, and send out long branching processes, which apparently anastomose with similar projections from other cells.

In some instances, only a single layer of cells separates one blood-space from another, and at times they appear to be separated only by the anastomosing branching processes, and not even by the whole thickness of a cell body. Some of these cells resemble stellate connective-tissue cells in shape, but differ from them by their much larger size.

The nuclei are usually round or oval, and vary considerably in size, but are sometimes very irregular in shape, corresponding to the general outlines of the cells which they occupy. They stain quite deeply with the usual stains, and present a well-marked chromatin network. In most of them we observe a single nucleolus, and not infrequently two, which are large and very prominent. A considerable difference in staining, however, appears in nuclei belonging to cells of apparently the same character, some staining much more deeply than others. Considerable numbers of the cells contain two or more nuclei, giving rise to pictures similar to those obtained in normal decidual tissue. It is rare,

FIG. 2.



Portion from lower margin of Fig. 1, more highly magnified, showing the structure of the cells and the absolute lack of intercellular tissue, the cells being separated by blood cells and leucocytes. $\times 275$ diam. Zeiss, ocular 4. Objective DD.

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however, in this part of the tumor, to find cells containing more than six or eight nuclei. In some of them we observe typical and in others atypical mytotic figures.

Throughout this portion of the growth we are unable to find any trace of intercellular tissue or reticulum, most of the cells lying in apposition, and when they are separated from one another it is only by blood or threads of fibrin; thus giving the tissue a decidedly epithelial appearance. Nowhere in the cell bars are we able to find any trace of blood or lymph vessels, consequently necrotic areas are of frequent occurrence.

The boundary line between the new growth and the muscularis is very irregular, as it is being invaded in all directions by offshoots from the tumor. In places we may see bands of cells making their way between the muscle cells, and frequently causing their degeneration and atrophy; and in other places we see masses of the characteristic tumor cells making their way along the lumen of what appear to be venous channels. And here and there we find small areas of tumor formation in the muscularis, at some distance from and without any apparent connection with the main growth. A marked zone of leucocytic infiltration always precedes and surrounds the new growth as it invades the muscularis.

At one side of the tumor there is an area, which at first sight presents an absolutely different appearance. (Fig. 3.) Here we find a mass composed of long, wavy, more or less parallel bands of cells, connected at one end with the main body of the tumor, but with its free end projecting into a cavity, which is partially lined by endothelium, and is apparently of venous origin. On closer examination, we find that we do not have to deal with individual cells at all, but with long, narrow, worm-like bands of protoplasm with nuclei imbedded in them, but presenting absolutely no trace of division into cells. For the most part, these bands contain only a single row of nuclei, but in other places they are arranged in groups, giving rise to structures similar to giant cells. Their protoplasm is quite granular and stains readily with eosine, and contains many vacuoles. The nuclei vary greatly in shape, but are mostly round or oval. They contain a thick chromatin network and stain deeply, and usually present one or two sharply marked nucleoli. (Fig. 3.)

The muscular tissue adjoining this area presents a large amount of leucocytic infiltration. And many of the muscle nuclei are enlarged and swollen, and contrast markedly with the normal muscle cells, which are at some little distance from them, and between which all stages of gradation may be observed. At first, it appeared as if the above-mentioned protoplasmic bands were derived from them, but closer examination shows that this is not the case; for the larger the muscle nuclei become, the more faintly do they stain, and the less resemblance do they bear to the nuclei in the protoplasmic masses or syncytium. And it is evident that we only have to do with degenerating muscle cells and not with those which are being transformed into tumor elements.

Not far distant from this area containing well-marked syncytium, we find other areas presenting a similar but not so well-marked structure. And at one point we find an areolated area, which at first glance resembles a mass of large fat cells. (Fig. 4.) But, on closer examination, we find that we have before us a considerable number of quite large, round, or irregularly-shaped cavities, which lie in a mass of protoplasm, which shows no trace of division into individual cells, and which corresponds to the syncytium above described. The partitions separating the cavities, which appear to be empty or filled by transparent contents, are generally quite thin, usually being but a small fraction of the diameter of the cavities in thickness. Many of the nuclei lie in the partition walls, and are then usually spindle-shaped, while those in the other portion of the mass are more oval in shape. Both the protoplasm and its enclosed nuclei correspond exactly in structure and staining qualities to those found in the protoplasmic bands (Fig. 3); and there can be no doubt as to their identity, their only difference consisting in the presence of the alveolar spaces.

After carefully examining these areas, and then going back to the main portion of the tumor, we find that many portions, which at first appeared to be made up of individual cells, are really small masses of syncytium, and some of the blood-spaces likewise appear to be bounded by it. In fact, the likeness becomes so striking in many places that we cannot help asking if it is not possible that even the cells which still appear as individuals

FIG. 3.



Uterine wall at margin of growth, showing syncytial masses invading a venous channel. $\times 256$ diam. Leitz, ocular 1. Objective 7.

may not have a similar origin, and perhaps be due to transverse or oblique sections through syncytial bands. Sections through narrow worm-like bands, giving rise to the smaller mononuclear cells, and those through thicker masses appearing as multinuclear or even giant cells; analogous to the appearances obtained on section through the placenta in its early stages, where we find mononuclear as well as giant cells scattered through the intervillous spaces, which are undoubtedly produced by sections through chorionic syncytium.

Sections through the entire thickness of the fundus, including the smaller nodule, show that it presents essentially the same structure as the larger nodule, except that it is much more necrotic. This nodule is almost entirely covered by uterine mucous membrane, which is of the same character as that which partially covers the larger nodule. In several places, deep down in the tissue, we found several cut-off portions of uterine glands, whose epithelium is desquamated and lies loose in their lumina. At first sight they appeared to be isolated areas of tumor formation, but a casual examination reveals their true nature and their marked difference from the cells of the new growth.

The chief point of interest in these sections is that we find in the uterine wall, at least 1 cm. distant from the tumor mass, several apparently normal veins, which contain thrombi composed of typical tumor cells, which are imbedded in a mass of fibrin and lie loose in the lumina of the vessels, and are apparently in transit to some remote portion of the body, probably the lungs, where they might have given rise to other metastases.

We next cut sections through the necrotic tumor mass at the entrance of the vagina. At its margin, it is covered by the typical stratified epithelium of the epidermis, with the characteristic pigmentation in its deeper layers (the woman being a negress). Beneath this is the subcutaneous connective tissue, with bundles of striated muscles crossing it in all directions.

The greater part of the tumor formation is composed of well-preserved blood, which is not contained in vessels, and in which there are many more leucocytes than usual. The cellular part of the metastasis is only clearly marked at the margins of the growth when it is seen to present the same general structure as the nodules in the uterus.

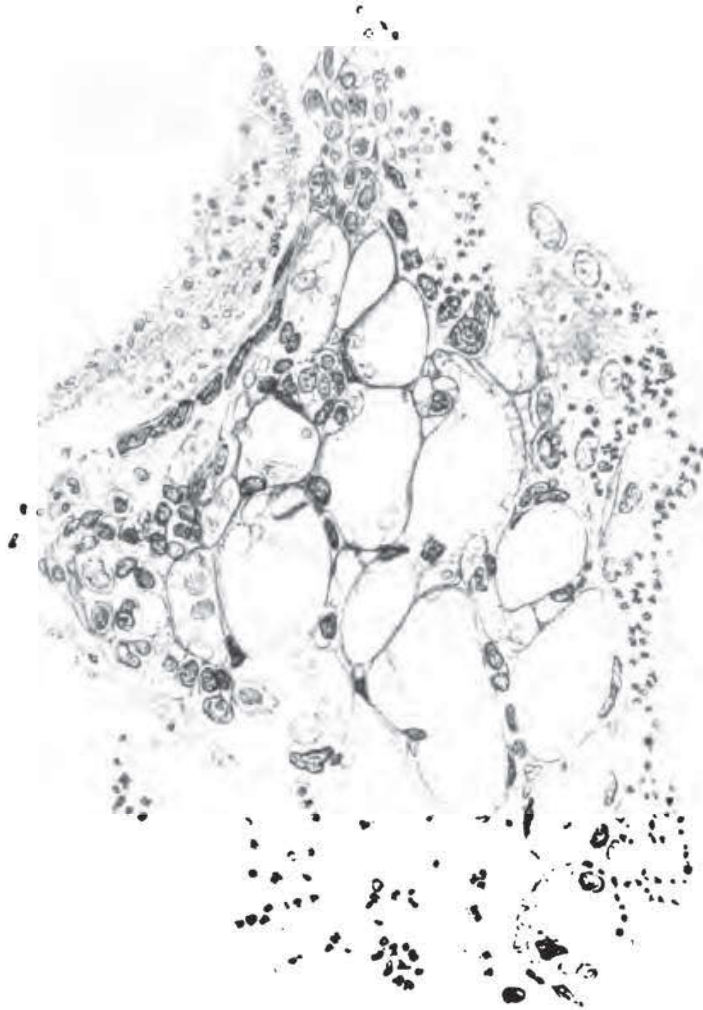
Here we observe the same alveolar structure, only more highly developed, the greater part of the metastasis being composed of free blood and blood in spaces, and the same two varieties of cells(?). Here the protoplasmic bands or masses of syncytium appear in much greater abundance, and are more clearly marked than in the primary tumor, and assume all sorts of bizarre forms. In some places we find structures almost resembling cross-sections of chorionic villi; that is, more or less circular bodies surrounded by a protoplasmic band, which contains nuclei arranged in a single row, but presenting absolutely no trace of division into cells, in whose centre there are a number of polygonal epithelioid cells, whose nuclei, as a rule, stain less deeply. In none of these structures, however, do we find any trace of bloodvessels or real stroma, nor any trace of a second layer of definite epithelial cells (Langhan's Zellschicht), beneath the syncytium. In other words, we are unable to find more than a superficial resemblance to chorionic villi.

In other places, the definitely characteristic syncytium appears to form a distinct border, beneath which there are several layers of what appear to be definitely marked epithelial cells(?). And in other places it forms large finger-like masses with nuclei scattered all through them, which lie free in the blood and do not appear to be in connection with any other form of cells. (Fig. 5.)

We also observed most beautiful giant cells, with large numbers of irregularly placed nuclei, which are clearly produced by sections through syncytial masses. Some of the alveolar spaces are apparently completely bounded by syncytium of varying thickness, which in places sends out long branching process, just as in the primary uterine tumor.

The protoplasm composing this syncytium is finely granular and takes on a yellowish-red stain with eosin. Scattered through it are numerous vacuoles, which vary in size from cavities scarcely visible, under a high power, to very large cavities, some being empty and others containing blood, but none of them presenting any trace of an endothelial lining. Some of them appear to be produced by the degeneration and final disappearance or dropping out of nuclei; while others have certainly no connection

FIG. 4.



Area near Fig. 3, showing areolated arrangement of syncytium.
× 150 diam.

with nuclear changes, as the majority of them are far smaller than the smallest nuclei observed in the growth.

The nuclei are of various shapes and sizes, and occasionally assume very bizarre forms. They all contain a definite chromatin network, but vary greatly in their staining properties, some staining intensely and others quite lightly. This is strikingly observed in some of the finger-like bands of syncytium, which lie perfectly free in the blood, and in which there is absolutely no trace of cell division, when one nucleus may stain very intensely and possibly the one adjoining it very lightly. So that if they occurred in separate cells, there would be no hesitation in saying that they were totally different, and, perhaps, of different origin. On the whole, however, they stain very intensely. In most of them one or more nucleoli can be observed.

The individual cells, to which we have already referred as being bounded by or enclosed within masses of syncytium, present a distinctly epithelial appearance. There is absolutely no trace of reticulum between them, and they are frequently packed very closely together. The greater part of these cells are occupied by large nuclei, which, as a rule, stain less intensely than those in the syncytium, but correspond entirely with the syncytial nuclei, which stain lightly. The small amount of protoplasm, which surrounds the nuclei, is slightly granular and stains exactly as does that of the syncytium, and likewise contains numbers of small vacuoles.

The boundary line between the metastasis and the surrounding tissue is marked by a layer of leucocytic infiltration, and tumor cells may be seen invading it in all directions. At several points it is clearly seen that the tumor cells have broken through vessel walls, and in some instances have partially or entirely replaced their endothelial lining.

Small thrombi, composed apparently of individual cells or giant cells, may occasionally be detected in the small veins of the subcutaneous tissue, at a very considerable distance from the metastasis itself.

Sections through the metastases in the various organs present identically the same structure as that at the entrance of the vulva, varying from it only in the fact that they are surrounded

by different tissue; and it is therefore unnecessary for us to consider them in detail. They all present the same markedly hemorrhagic character, and the cellular elements are only well preserved at their margins. The pulmonary metastases are much more necrotic than those in the other organs, but otherwise do not differ from them. In all the organs the metastases are surrounded by marked areas of leucocytic infiltration. In the kidney there is marked increase in the cells about the glomeruli, combined with marked degeneration of the epithelium of the convoluted tubules, which is presumably fatty. In the spleen there are various infarcted areas, and in the lungs many of the alveoli are filled with leucocytes, desquamated epithelium, and fibrin.

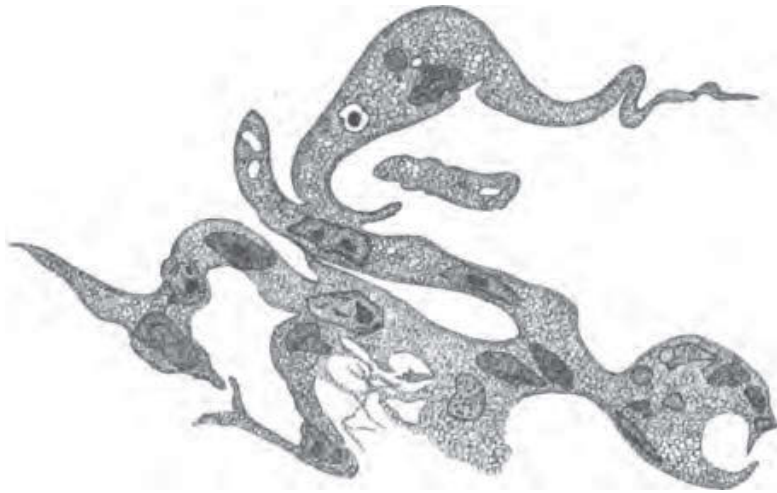
It is thus seen that we have to deal with a very remarkable new growth, which cannot readily be classed among any of the well-known tumors occurring in the uterus.

The greater part of the original tumor, as well as the metastases, is made up of blood, which lies either free in the tissues or enclosed within cavities formed by the tumor cells; while its cellular part is composed of large elements, some of which appear as epithelial cells(?) and others as larger or smaller masses of syncytium.

Nowhere in the tumor can any trace of bloodvessels or reticulum be discovered, and it appears to be composed solely of epithelial cells(?) and masses of syncytium, which are grouped together with apparently no attempt at tissue formation; but which lie free in areas of hemorrhage without apparent integral connection with the surrounding tissues.

The metastases present the same characteristics, and appear to be thrombotic or embolic masses of cells, which multiply in the vessels and cause their rupture, with consequent hemorrhage into the surrounding tissue. In these hemorrhagic areas, the cells live on and multiply until they form masses too large to be nourished simply by osmosis, when they undergo necrotic changes. Accordingly, the onkological interpretation of the tumor is no easy matter, not to speak of the difficulties involved in positively settling its histogenesis.

FIG. 5.



Single syncytial mass from vulval metastasis, which lay apparently free, and was entirely surrounded by blood. $\times 275$ diam. Zeiss, ocular 4. Objective DD.

ONKOLOGICAL RELATIONS AND HISTOGENESIS. It is evident from the microscopical examination that our tumor, while closely resembling Sanger's in its gross appearance and clinical history, differs very essentially from it in its finer structure. Both present the same alveolar structure and are characterized by their markedly hemorrhagic nature; but Sanger's new growth is apparently composed of decidual cells, while ours is made up of cellular elements whose significance is not beyond all question.

It is our object, in this article, to consider carefully the nature and histogenesis of our tumor, and then to compare it with the various new growths, which have been described as malignant deciduomata or by more or less cognate terms.

It is apparent, from an anatomical standpoint, that the most striking feature of our tumor is the presence of the protoplasmic masses or syncytium. And anyone, who is at all conversant with the structure of the normal placenta in its early stages, must be impressed with the marked similarity existing between the syncytial masses in our tumor, and the so-called chorionic epithelium. In both we have the same protoplasmic masses, without division into definite cells, and the same deeply staining nuclei, and in both the occurrence of vacuoles of varying size, which are either absolutely empty or filled by transparent contents; and we do not consider that we shall go far wrong in concluding without further argument that this portion of our tumor is either derived from or very closely connected with what is generally termed chorionic epithelium.

We do not stand alone in making this assertion, for other observers, especially H. Meyer,³⁹ Klebs,²⁴ Gottschalk,¹² L. Fraenkel,⁸ and Marchand,³⁶ have observed the same, and have not hesitated to conclude that they had to deal with growths which were derived either wholly or in part from chorionic epithelium.

The nature of the individual cells, which also constitute a considerable portion of our tumor, is, however, not so clear,

and before attempting to establish their identity we think it would be well to consider briefly the more intimate structure of the chorionic villi, and some of the more recent works concerning their development.

Langhans,³¹ in 1882, was the first, we believe, to call attention to the fact that the chorionic villi are covered by a double layer of epithelium, and all subsequent observers have confirmed his statements; the only exception, so far as we are aware, being Hofmeier,¹⁷ who still believes in the existence of only a single layer.

The outer layer, that is, the layer nearest the uterine wall, is composed of a band of protoplasm, in which very deeply staining nuclei of varying shape are deposited without any trace of division into individual cells. The nuclei are arranged for the most part in a single row, and to this tissue the term syncytium has been very aptly applied. Beneath it comes a single layer of definitely marked epithelial cells, which are generally cuboidal or cylindrical in shape and possess nuclei, which stain considerably less intensely than those of the syncytium. This layer is readily seen to be composed of individual cells, and is generally designated as Langhans's cell layer (*Zellschicht*), and beneath it comes the connective-tissue stroma of the villi, with its blood and lymph vessels.

Thus far all observers are agreed, with the exception, as stated above, of Hofmeier;¹⁷ and anyone who is able to examine young embryos can readily convince himself of the correctness of their observations.

But here the unanimity ceases, for as soon as we begin to consider the origin and development of two layers of chorionic epithelium, we are met by several absolutely conflicting opinions. Thus, Langhans³¹ formerly believed that the syncytium represented the foetal ectoderm, and that the cell layer beneath it was of mesoplastic origin; but later, and especially in the works of his various students, he changed his opinion, and now considers that the cell layer represents the foetal ectoderm while the syncytium is most probably of maternal origin.

Kastschenko²³ believes that the syncytium represents the foetal ectoderm, and that the cell layer is developed from it secondarily. Minot⁴⁰ and Gottschalk¹⁰ likewise believe in the foetal origin of both layers; while Turner⁵⁹ and Ercolani⁷ consider that the syncytium is of maternal origin, the former supposing it to be derived by the transformation of decidua cells, and the latter from maternal endothelium.

Most recent observers, however, believe that Langhans' cell layer represents the foetal ectoderm, while the syncytium is derived from metamorphosed uterine epithelium.

This mode of development is particularly advocated by Kossman²⁸ and Merttens³⁸ for the human placenta, and their arguments are rendered far more convincing by the study of placental development in other animals; for Selenka⁵⁶ has apparently conclusively demonstrated it in the monkey, and Strahl⁵⁷ in the dog and cat; while Frommel⁹ has rendered it fairly probable in the bat.

Merttens³⁸ in his "Contributions to the Normal and Pathological Anatomy of the Human Placenta" almost conclusively demonstrates this mode of origin. The article is based in great part upon a human embryo, seven to eight days old, which was accidentally obtained by curetting the uterus. It was still in connection with portions of the decidua vera and serotina, and he clearly and definitely demonstrated that the surface epithelium of the decidua, as well as portions of its glandular epithelium, was transformed into syncytium. As a portion of the syncytium is derived from the glandular epithelium, a certain amount of it must necessarily be found deep down in the decidua between the true decidual cells; and he likewise demonstrated that offshoots from the surface epithelium also make their way down between the decidual cells. The entire article is of great interest, and we heartily recommend its perusal to those interested in the subject.

Kossman²⁸ demonstrated similar changes in the epithelium of a tube, which was the seat of a four to five weeks pregnancy; and Gunsser,¹³ in a similar case, could demonstrate

the transformation of tubal epithelium into a syncytium, which grew over the chorionic villi, and so provided them with a second layer of epithelium ; and in one of the cases of tubal pregnancy, which we have examined, we also found changes in the epithelium which are capable of similar interpretation.

After this imperfect survey of the subject, it is 'apparent that the weight of evidence is decidedly in favor of regarding the syncytial covering of the villi as derived from uterine or tubal epithelium, as the case may be, and consequently of maternal origin ; while Langhans's cell layer represents the foetal ectoderm.

At the same time, it must not be forgotten that several competent recent observers, especially Minot,⁴⁰ do not incline to this view and still regard both layers of chorionic epithelium as foetal in origin. For our own part, while we cannot express an opinion based upon positive experience, we incline strongly to the maternal origin of the syncytium.

This being the case, we have but little hesitation in regarding the distinctly syncytial portions of our tumor as maternal in origin, as we have already identified it with the so-called chorionic epithelium or syncytium.

The identification and histogenesis of the apparently individual cells, which make up a considerable portion of our tumor, unfortunately is a much more difficult matter, and we must confess in advance our inability to arrive at more than a probable conclusion concerning them. For it is well known how very difficult it is to settle questions of histogenesis in a perfectly satisfactory manner, especially when we are obliged to base our conclusions upon the general appearance of individual cells, which apparently do not stand in direct connection with the tissues from which they are derived.

As stated above, these cells in general present a decidedly epithelial appearance. Marchand,³⁶ in his very suggestive article upon this subject, states that we must consider the possibility of their being derived from anyone of four sources,

namely : 1. The decidual cells *per se* ; 2. The syncytial covering of the villi ; 3. The foetal ectoderm (Langhans' cell layer); and 4. The mesoblastic stroma of the villi. In other words, they may possibly be either maternal or foetal in origin.

In the preliminary communication upon our case, we stated that the growth was composed in great part, at least, of decidual cells, and that it corresponded very closely to Sanger's original case.

There is no doubt that the cells do resemble decidual cells very closely ; for we meet with the various modifications in shape and size and arrangement of the nuclei, with which we are familiar as occurring in the normal decidua. But careful examination teaches us that the resemblance ceases here, and that they lack several of the characteristics of cells derived from connective tissue. In the first place, we were absolutely unable to find any trace of ground substance or reticulum separating the cells from one another, and instead find them lying in direct apposition, or, when that is not the case, separated only by blood or threads of fibrin, and thereby conforming to epithelial cells in arrangement ; and, again, the growth is completely lacking in blood or lymph vessels of any description, its hemorrhagic character being due in great part to free hemorrhage into the surrounding tissues, and when the tumor proper contains blood it is within cavities, whose walls are formed entirely by tumor cells, upon which absolutely no trace of endothelium can be discovered. In view of these considerations, we believe that we are amply justified in concluding that our tumor is not made up of decidual cells.

There likewise appears to be absolutely no ground for believing that they are derived from the stroma cells of the chorionic villi, partly for the reasons already adduced against their decidual origin, but principally because no one, except Gottschalk,¹² as supposed that they can ever take on such decidedly epithelial forms, as are presented by the cells in our tumor.

Marchand,³⁶ in the histological description of Ahlfeld's case of "Deciduoma" following a tubal pregnancy, has appar-

ently met with the same two varieties of cells as in our case, namely, the syncytium and individual epithelial cells. He concludes, just as we have done, that the former is derived from chorionic syncytium and is of maternal origin, and believes that the latter, in all probability, are derived from Langhans's cell layer of the villi, and are therefore of foetal origin. He states that he has convinced himself as to the morphological identity of the two forms of cells by comparison with various specimens of Langhans's cell layer, especially those derived from hydatidiform moles.

He states that the cells of Langhans's cell layer are usually small polyhedral cells with a tolerably homogeneous nucleus, but that they may undergo a very considerable increase in size at the ends of villi of attachment (*Haftzotten*) and in the cell masses between the villi.

"The behavior of the nuclei is particularly characteristic, which are provided with a tolerably wide-meshed chromatin network and one or several large round or lancet-shaped nucleoli. Several nuclei may be also found in the same cell; the elements of the cell layer divide by indirect cell division."

Then, speaking of his tumor, he says:

"This relation of the two varieties of tissue is especially characteristic, and recalls to a marked degree that of the cell masses between the villi and in the neighborhood of the attachment of the villi to the surface of the decidua. Accordingly there appears to me to be no doubt that the tumor mass is composed of the same two elements, which form the normal chorionic epithelium, namely, the syncytium and the ectodermal cells.

"The peculiar symbiosis, which normally characterizes these elements, likewise explains their combination in the tumor formation. This peculiarity extends to the entire arrangement of the two forms of tissue, and to the formation of blood spaces within the syncytium and the lack of other vessels."

From the statements which we have just adduced, it does

not appear to us that Marchand³⁶ has proven, as conclusively as he believes, that the cells in question are derived from the foetal ectoderm ; his entire argument being based upon the resemblance of the two forms of cells to one another.

But, at the same time, it must be confessed that he has suggested a possibility, which, at least for his case, deserves careful consideration.

We do not, however, believe that this mode of origin applies to the cells in our case ; for, as we have already stated, the differences between their nuclei and protoplasm and those of the syncytium is not so marked as in his case.

As we stated in the microscopic description of our case, it was difficult not to suppose that a part at least of the individual cells were due to cross or oblique sections through syncytial masses or bands.

We pointed out that the nuclei of the individual cells, as a rule, stained less deeply and presented a less marked chromatin network than the nuclei of the syncytial masses ; but, at the same time, they varied greatly among themselves, some of them staining quite as intensely as the syncytial nuclei.

And we also called attention to the fact that all the syncytial nuclei did not stain equally intensely, nor contain an equally well-marked chromatin network, and that they frequently presented variations between themselves quite as great as those observed between the individual epithelial(?) cells.

Such being the case, it does not appear necessary to consider the two classes of cells as essentially different in origin, especially when we recall the fact that the protoplasm of both varieties of cells, as a rule, presents the same general appearance and staining qualities.

When we recall the fact that many of the cells differ very greatly in size, some being two or three times as large as others, and that the nuclei likewise vary considerably in the amount of cell space which they occupy, it appears to us that these differences may be most readily explained by supposing that what appear as individual cells are really only sections

through syncytial masses or bands. Sections through narrow bands giving rise to small cells, whose nuclei are surrounded by only a small amount of protoplasm, for the nuclei occupy nearly the entire width of many of the narrower bands; while sections through wider bands would give rise to larger cells with more protoplasm, and sections through still larger syncytial masses would give rise to large multinuclear cells and giant cells. The individual cells would then be analogous to the giant cells and cell masses observed in the normal placenta.

This mode of origin certainly applies to considerable numbers of these cells, and we are inclined to believe to all of them; but at the same time it is impossible to exclude the possibility of some of them being derived from the foetal ectoderm or even from the decidua cells.

The syncytial origin of the tumor readily explains its markedly hemorrhagic character, and its superficial resemblance to placental tissue; for all the intervillous spaces of the normal placenta are lined by syncytium, which is in direct contact with the blood, except for a very short period at the beginning of pregnancy, when they are supposed by most observers to be lined by a thin layer of maternal endothelium, which, however, soon disappears.

Kossmann,²⁸ on the other hand, believes that the intervillous spaces are at no time lined by maternal endothelium, but are produced simply by the dilatation and coalescence of the vacuoles, which are so characteristic of the syncytium.

According to this conception of its structure and histogenesis, we have to deal with an epithelial tumor of maternal origin. And, although it differs very considerably from the usual forms of carcinoma, in that it does not tend to the reproduction of any definite form of tissue and is totally lacking in stroma, we believe that it is most fittingly designated as a carcinoma, which has arisen from transformed uterine or chorionic epithelium or syncytium.

On comparing our specimen with those described in the

literature, we find that it presents a very marked resemblance to the cases described by H. Meyer,³⁹ Gottschalk,¹² L. Fraenkel⁸ and Ahlfeld,¹ and Marchand.³⁶

In 1888 Meyer³⁹ described under the title "A Case of Destructive Proliferation of Retained Myxomatous Chorionic Villi" a tumor which resembles ours in many respects.

It occurred in a woman, aged fifty-five years, who had three children and died from anæmia, resulting from frequent and profuse uterine hemorrhages nine months after the manual removal of an hydatidiform mole. Only an incomplete autopsy was permitted, so that it is impossible to say whether metastases had been formed. The uterus was considerably enlarged, and its interior presented an irregular, nodular, eaten-out appearance, and scattered through its walls were numerous round nodules of a felty appearance, which varied from a grain of sand to a lentil in size.

On section, they were found to be composed of cylindrical structures, some of which contained a slight core of connective tissue but without any trace of bloodvessels, but their most prominent feature was that they were covered by a thick layer of syncytium, which in many instances made up the entire structure. All of them lay within blood or lymph vessels, and he considered that they were derived from myxomatous villi, which had remained in the uterus after the removal of the mole and undergone proliferation. He classed it among the carcinomata and proposed to designate it as "epithelioma papillare corporis uteri."

Klebs,²⁴ in his work on *General Pathology*, refers to the same case, and states that it is undoubtedly derived from chorionic epithelium, but should not be classed among the carcinomata, but proposes to call it a placental papilloma. He regards it undoubtedly of foetal origin, and considers it a most beautiful example of parasitism. When in Baltimore a short time ago, Prof. Klebs kindly examined our case and said that it corresponded with his case, and had no hesitation in regarding it as a parasitic growth of foetal origin.

It is only necessary to compare Meyer's³⁹ illustration with our own to see a marked resemblance, though his case differs from ours in its distinctly villous form, and in the fact that some of the villi contain a definite connective-tissue stroma, and possibly, also, in the absence of metastases; but owing to the partial autopsy it is impossible to be positive in this regard.

Gottschalk,^{11,12} in two communications, has likewise described a tumor, which presents many points of resemblance to ours, and which we are inclined to regard as practically identical with it.

It occurred in a woman, aged forty-two years, in whom very profuse and continual hemorrhage followed an abortion in the third month. The hemorrhages persisted, and her uterus was dilated several times, and a large amount of what appeared to be placental tissue was removed.

Gottschalk then saw the case and removed with his finger from the uterus about 150 gm. of red tumor masses. He could have removed much more, but the growth had so far penetrated the uterine wall that he feared lest he should perforate it. The portions removed consisted of villi, which expanded at their ends into roundish masses, some of which were as large as a hazelnut.

The microscopic examination showed that he had to deal with "sarcoma of the chorionic villi(?)."

He removed the uterus per vaginam, the woman continuing well for six months after it, but died two months later with placental-like metastases in the lungs, spleen, and right kidney.

The uterus was very considerably enlarged, and at its upper right-hand margin and involving the fundus and the adjoining anterior and posterior walls was a large, jagged, villous growth, of reddish color, which had almost perforated the uterine wall. It corresponded in structure to the masses previously removed, and on section was found to be composed of syncytial masses, between and within which he found large

polygonal cells with oval nuclei, which closely resembled decidual cells, but which he regarded as sarcoma cells derived from the stroma of the villi. Nowhere in these masses did he find any trace of bloodvessels. The metastases were composed entirely of syncytial masses, and showed absolutely no trace of sarcomatous stroma cells.

In his first article he designated the growth as "sarcoma-chorion-deciduo-cellulare," and considered that the primary change had occurred in the chorionic villi, which in some way had infected the cells of the decidua and caused them to take on a sarcomatous growth. He also stated that he believed that Sanger's case, as well as the other cases which had been reported as deciduomata, had a similar origin. In his later and more elaborate article he discards the term sarcoma-chorion-deciduo-cellulare and proposes instead to designate his case as sarcoma chorii. He recognized the fact that its greater part was composed of syncytium, which he considered was derived from the chorionic epithelium, but believed that the changes in the stroma of the villi were of more importance; and, while admitting that he had to deal with a tumor of both epithelial and connective-tissue origin, preferred to call it a sarcoma of the chorionic villi.

We have carefully read Gottschalk's^{11,12} articles, and can only agree with Marchand³⁶ in believing that he has failed to adduce positive proof in support of the sarcomatous nature of the cells in question, and especially of their origin from the stroma cells of the villi.

It is true that Waldeyer⁶⁸ examined his specimens, and at a subsequent meeting of the Berlin Medical Society fully indorsed Gottschalk's position; but to us his proof appears no more convincing than Gottschalk's. And when we recall the fact that he likewise expressed himself in favor of the sarcomatous nature of the changes which Landau and Abel described in the endometrium associated with carcinoma of the cervix, and which later work has demonstrated were simply cases of hyperplastic endometritis, we do not feel that we are

bound to accept his verdict in this instance without question. Especially when we recall the fact that the pulmonary metastases in Gottschalk's case were composed entirely of syncytium, and showed absolutely no trace of the sarcomatous stroma cells. Now, had the case been a sarcoma or even a mixed sarcoma and carcinoma, we should expect to find in the metastases at least some traces of its sarcomatous nature; but finding none, and learning from his own description that the metastases were pure epithelial, *i. e.*, syncytial in character, we must confess that we are very skeptical as to its sarcomatous nature, and therefore consider his designation—sarcoma chorii—at least ill-chosen, if not absolutely erroneous.

We believe that the cells in question were most likely produced, as in our case, by cross or oblique sections through syncytial bands, or perhaps were derived from Langhans' cell layer of the villi, as believed by Marchand.³⁶

As stated, when considering the development of the epithelial layers of the chorionic villi, Gottschalk¹⁰ believes that they are both of foetal origin, and consequently considers his tumor of foetal origin, and therefore of a parasitic nature.

It is evident, however, from his description and the considerations just adduced, that his tumor is very similar to if not identical with our own.

L. Fraenkel⁸ has recently reported a case as "carcinoma of the uterus, arising from the epithelium of chorionic villi, following an hydatidiform mole," which closely resembles our own. It occurred in Pernice's clinic in Greifswald, and its clinical history was reported by Perske,⁴⁴ in a Greifswald dissertation for 1894.

In July, 1892, a woman, aged twenty-five years, expelled an hydatidiform mole in the third month of pregnancy. In March, 1894, twenty-one months later, she returned to the clinic in very poor condition, having a markedly enlarged uterus with tumor masses on either side of it. She complained of a great deal of pain and passed blood by the bladder. The tumors on either side of the uterus were removed

by laparotomy and were found to be small ovarian cystomata. The uterus was stitched to the abdominal incision and opened, when it was found filled by soft, reddish, placental-like masses. She suffered a great deal from cough and headache, and died three months later with metastases in the vagina, and a soft, red, spongy tumor arising from the abdominal incision.

Only a partial autopsy was permitted, but metastases were found in the spleen, bladder, parametria, and vagina. The uterine wall had been ulcerated through and its cavity communicated with the parametrial metastases, which in turn communicated with those found in the vagina. The clinical symptoms, likewise, indicated the formation of metastases in the lungs and brain.

Sections through the tumor masses, which were removed from the uterus at the time of operation, were very necrotic and presented a marked hemorrhagic character. When its structure could be made out, it was seen to be composed of very large, irregularly shaped individual cells, which were separated from one another by a definite reticulum, and he accordingly concluded that they represented decidual cells and that he had to deal with a deciduoma malignum. Upon examination of the tumor masses obtained at the autopsy, however, he was surprised to find that all trace of the individual cells had disappeared, and that he had to deal with an alveolar and hemorrhagic tumor, which was made up of large masses of syncytium, by which the majority of the blood cavities were bounded; while others were bounded by endothelium which had been partially replaced by syncytial masses.

He stated that there was nothing about the growth indicative of sarcoma, and, even though there was no tendency to the formation of villous-like structures, he had no hesitation in concluding that the syncytium corresponded to that of the chorion, and that he had to deal with a carcinoma produced by its proliferation.

As the tumor showed no trace of myxomatous changes, he is doubtful whether it is derived from myxomatous villi.

He does not express himself as to the origin of the chorionic syncytium, but it is to be inferred that he regards it as foetal.

The case of Ahlfeld¹ and Marchand,⁸⁶ to which we have already referred, occurred in a seventeen-year-old girl, whose menses had been regular up to Christmas, 1893, after which they became more profuse than usual, so that in April, 1894, she was obliged to consult a physician on account of profuse hemorrhages, which had lasted for three weeks. Upon rest in bed they ceased, and she was well until June, 1894, when she had another profuse hemorrhage, which came from a soft, reddish tumor, the size of a walnut, which was situated on the lower part of the anterior vaginal wall.

This was removed and the uterus curetted. The uterine scrapings showed nothing abnormal; while the examination of the vaginal tumor by Marchand showed that it contained long villous structures, which he considered identical with those observed by Gottschalk¹² in his case of sarcoma chorii.

The vaginal growth recurred with great rapidity, and soon another appeared alongside of it. At the same time a tense tumor appeared above the symphysis. July 4th she developed the symptoms of peritonitis, and, during a laparotomy for it, her respiration ceased and she died.

The autopsy showed that the uterus was perfectly normal and that the growth arose from the left tube, which had been the seat of a tubal pregnancy. Beside the metastases in the vagina, there were numerous small placental-like thrombi in the lungs, but none in other organs.

We have already referred to the microscopic structure of the tumor, and stated that Marchand considered it composed of maternal syncytium and foetal ectoderm.

The only respect in which the syncytial masses in this case differed from those in ours was in the fact that portions of its free margins presented a row of thin protoplasmic offshoots which upon superficial examination appeared as cilia, but

which closer examination showed were due to the formation of large numbers of very small vacuoles along its edges.

It is thus seen that four cases have already been recorded in the literature which bear a very close resemblance to our own case. Those of Gottschalk¹² and Marchand³⁶ being practically identical with it, as far as their histological structure is concerned, but differing markedly from it according to the interpretation of the observers. As pointed out above, we differ absolutely from Gottschalk¹² in the interpretation which he places upon his case, and are inclined to consider it identical with our own.

We might say the same of Marchand's³⁶ case, were it not vouched for by so able an observer; but, under the circumstances, we hesitate to question the correctness of his interpretation, and shall only suggest the possibility that the cells, which he considers derived from the foetal ectoderm, may after all only represent cross-sections through syncytial masses.

It is evident that our case, as well as those just referred to, differ very materially in their minute structure from those described by Sanger,⁵² Pfeifer,⁴⁹ Chiari,⁶ and others. For in their cases the cells, which make up the solid portions of the tumor and form the walls of the blood spaces, correspond in all respects to typical decidual cells. In none of them were syncytial masses found and all presented a well-marked connective-tissue stroma. All these observers lay considerable stress upon this point, and Sanger,⁵² in his monograph, gives a drawing, which positively demonstrates its presence in his case.

All these tumors presented a distinctly sarcomatous structure and appear to have been well characterized by the term *sarcoma uteri deciduo-cellulare*, which Sanger first proposed for them.

In all the cases, however, the matter was not so clear, for in several, especially those described by Pestalozza,⁴⁵ Lohlein,⁵³ Nove-Josserand and Lacroix,⁴² and Klien,²⁶ beside the well-marked decidual cells, other smaller cells of a distinctly sarco-

matous appearance were observed, and in some cases composed the greater part of the growth. Thus, Pestalozza⁴⁵ did not designate his case as a decidual cell sarcoma at all, but simply as a hemorrhagic infectious sarcoma, and Löhlein³³ described his case as "sarcoma uteri partim deciduo-cellulare post-myxoma chorii."

The tumors which were very briefly described by Schmorl¹⁴ and Koettnitz²⁷ were stated to be composed of both foetal and maternal tissue, and their significance was so obscure that Schmorl¹⁴ hesitated to express himself as to their exact nature, and proposed to designate them by the neutral term "blastoma chorion-deciduo-cellulare."

It is thus apparent that the growths, which have been described as malignant deciduomata or by other more or less cognate terms, differ very materially among themselves, and an idea as to the difficulty of their correct interpretation is, perhaps, best given by simply enumerating the various designations which have been applied to them.

Thus, for example, Sängner⁵⁰ first designated his case as deciduoma malignum, and later as sarcoma uteri deciduo-cellulare; Gottschalk¹¹ at first called his case sarcoma chorion-deciduo-cellulare, and later sarcoma chorii; Schmorl¹⁴ designated his cases and the one observed by Koettnitz²⁷ by the neutral term, blastoma chorion-deciduo-cellulare. Pestalozza⁴⁵ called his case infectious hemorrhagic sarcoma; Fraenkel,⁶ carcinoma arising from the chorionic epithelium; Guttenplan,¹⁴ hemorrhagic sarcoma; Meyer,³⁰ epithelioma papillare uteri; Klebs,²⁴ placental papilloma; and Klien,²⁵ deciduo-sarcoma uteri giganto-cellulare.

But, in spite of differences in anatomical structure, these variously designated tumors form a distinct clinical group. They all follow closely upon some form of pregnancy, either abortion, full-term pregnancy or hydatidiform mole, and quickly lead to the death of the patient with the very rapid formation of metastases, especially in the lungs and vagina.

They all present the same hemorrhagic structure, and in their gross appearance resemble placental tissue.

Now, is it not possible to group all these tumors together under some distinctive designation, which will enable us to speak of them from a clinical standpoint, without at the same time committing ourselves as to their intimate structure and origin? We believe that it is, and we consider that the term *deciduoma malignum*, which Sanger⁵⁰ first proposed for his case, is best suited for the purpose.

We must remember that the decidua represents the metamorphosed uterine mucous membrane, and accordingly consists of both epithelial and connective-tissue elements; while the hypertrophied connective-tissue cells, of course, represent its most striking and characteristic feature.

The tumors, to which Klotz²⁶ and Kustner³⁰ were the first to apply the term *deciduoma*, consisted of small tumor formations, which were made up of hyperplastic decidua and contained both decidual cells and glandular structures. Now, we likewise believe that malignant tumors may be derived from either the connective-tissue or epithelial elements of the decidua, or perhaps from both at the same time, and all of them, clinically speaking, may, not improperly, be designated as malignant *deciduomata*.

If the new growth be derived entirely from the connective-tissue cells, we shall have the typical *sarcoma deciduo-cellulare* of Sanger;⁴² but if it be derived from the epithelial elements, which normally form the syncytium which covers the chorionic villi, we shall have a tumor made up of syncytial masses, similar to ours and those of Meyer,³⁹ Gottschalk,¹² Fraenkel,⁸ and others, which are essentially *carcinomata*.

As Merttens³⁸ has demonstrated that not only the surface epithelium of the decidua, but also portions of the glandular epithelium as well, are transformed into syncytium, and also that syncytial processes make their way from the surface epithelium a certain distance down into the stroma, it is possible to conceive that both tissues may simultaneously take on a

malignant growth, and give rise to a mixed tumor composed of both decidual cells and syncytial elements, which are very intimately blended together.

No one has as yet definitely described such a tumor, but it is possible that the cases which Schmorl⁶⁴ and Koettnitz⁶⁷ considered were made up of both foetal and maternal elements may belong in this category, as they probably regarded the syncytium as foetal in origin. This is, however, a mere supposition, for they failed to publish a minute anatomical description of their specimens.

We believe, however, that the case, which Menge⁶⁷ has lately described as deciduo-sarcoma uteri, belongs in this category. In it he clearly distinguishes two well-marked varieties of cells. "One, which resembles the epithelial cell, in which the protoplasm has remained almost unstained; and another, which recalls an hypertrophic muscle cell, and in which the protoplasm stains in about the same way as in the unchanged muscle." And later on he says: "The relation of the two kinds of cells to one another does not appear to be quite without rule (regellos), but one often gets the impression as if a small group of the pale epithelioid cells were surrounded or framed in by two or more of the large intensely stained elements, so that depressions or hollows appear to be formed on their margins, into which the smaller cells fit."

He considers that the epithelioid cells are derived from decidual cells, which is apparently borne out by finding a small amount of connective-tissue stroma between them; while he believes that he has definitely proven that the other cells, with the deeply staining nuclei and protoplasm, are derived from muscle cells. This latter point, however, does not appear so clear to us.

Dr. Menge, on hearing of our case, very kindly sent us several slides from his tumor for comparison. There is absolutely no doubt that his tumor is made up of two distinct varieties of tissues: the epithelioid cells and those which he considers are derived from the muscle cells. We are inclined

to agree with him as to the decidual origin of the epithelioid cells; but close examination showed us that the elements which he considers represent hypertrophic (*gewucherte*) muscle cells are not individual cells at all, but consist of a granular protoplasm, in which intensely staining nuclei are deposited without any trace of division into individual cells; in other words, are syncytial bands, just as in our case.

It will be remembered that we were at first inclined to consider the syncytial bands in our case as transformed muscle cells, but closer examination revealed our error.

The syncytial tissue in his case is quite similar to that in ours, and we are disposed to consider it identical with chorionic epithelium.

Accordingly, in his case, we have to deal with a tumor made up of decidual cells (admitting their connective-tissue origin), and syncytium, or a tumor derived from both the connective-tissue and epithelial elements of the decidua, if we accept the maternal origin of the latter.

From an onkological standpoint, therefore, admitting our interpretation, Menge's³⁷ case is a mixed sarcoma and carcinoma or a carcino-sarcoma of the uterus, which has followed an hydatidiform mole, which, anatomically speaking, should be distinguished from the other varieties of *deciduoma malignum*. But it closely resembles the other cases in its clinical history and gross appearance, and from a clinical standpoint should be classed among them.

We would, therefore, designate this entire group of tumors by the term *deciduoma malignum*, as they are all, with the possible exception of Marchand's³⁸ case, derived from one or both of the component parts of the normal decidua. We, however, wish it distinctly understood that we recommend this general term purely for convenience in clinical work, and do not wish anyone to imagine that we consider the various tumors identical in anatomical structure. For they differ absolutely among themselves, some being sarcomata, some carcinomata, and others mixed tumors, and we do not wish to

be placed in the same category with Beach,³ who says: "When the entire literature presents some sixteen cases of deciduoma, it would be worse than useless to attempt to divide them into different forms and varieties."

In the articles of Pestalozza,⁴⁵ Nove-Josserand and Lacroix,⁴² Klien,²⁵ and Menge³⁷ it is stated that a certain proportion of the cells, which compose the tumor, are derived from the muscle cells. We were at first inclined toward a similar origin for some of the cells in our case, but, as stated above, more careful examination showed that the changes in the muscle cells were of a degenerative character, more or less similar to those observed by Bacon² in a case recently described from Chiari's laboratory. We believe that we have likewise shown that Menge³⁷ was in error in believing that a part of his tumor was derived from them. Nor do we find anything in the cases of Nove-Josserand and Lacroix⁴² and Klien²⁵ which lend marked support to this view. We would not, however, absolutely deny the possibility of such changes, for we ourselves⁶⁴ were the first to demonstrate conclusively the direct transformation of muscle into sarcoma cells.

The malignant deciduomata, and especially those which are made up wholly or in great part of syncytial cells, are no doubt closely related to the so-called destructive hydatidiform moles (interstitielle, destruirende Molenbildung), which have been described by Wilton,⁶⁶ Volkmann,⁶² Jarotsky and Waldeyer,¹⁹ and Krieger,²⁹ in which myxomatous villi have made their way into the vessels of the uterine wall and almost completely destroyed it. In Wilton's⁶⁶ case, the uterine wall was perforated by the growth, and the woman died from hemorrhage into the peritoneal cavity. Unfortunately, none of these cases were examined microscopically, so that we are ignorant of their finer structure.

Beach³ has lately described a case as deciduoma malignum, which was demonstrated before the Anatomical Society of Paris by Hartmann and Toupet,¹⁵ in which the patient died from uterine hemorrhage after the uterus had been cleaned out

several times. Only an incomplete autopsy was permitted, but no metastases were found in any of the abdominal organs. The left angle of the uterus and its posterior wall were occupied by a blackish mass, which resembled placental tissue, and two nodules, the size of a hazelnut, were situated on its fundus and posterior wall. On section through the uterine wall they were seen to be grayish white in color, pulpy, and less consistent than the surrounding tissue. They extended through the entire thickness of the uterine wall and were continuous with the placental-like mass of its interior. The uterine wall was studded by many similar but smaller nodules, all of which were developed within veins. They consisted of villous structures, which contained a connective-tissue stroma, containing bloodvessels, outside of which was a layer of syncytium. They apparently represented but slightly changed chorionic villi, which had gained access to the vessels and there undergone proliferation.

We cannot agree with Beach³ in regarding the case as a deciduoma malignum, and consider it related to the destructive hydatidiform moles, to which we have just referred, or perhaps more nearly to the destructive placental polyps, which have been described by von Kahliden²¹ and Zahn.⁶⁷ It is evident, from his own words, that he does not comprehend the nature and significance of the malignant deciduomata; for, in summing up the anatomical study of his case, he says: "The nature of this tumor is very plain; it is a tumor composed of placental tissue, and if, moreover, we notice how much vitality belongs to this neoplastic tissue, how profoundly it infiltrates the uterine muscle, it is impossible not to see that we have the characteristics of a malignant tumor, thus the name deciduoma malignum seems most appropriate to this variety of neoplasm."

FREQUENCY. There is no doubt that malignant deciduomata are of much more frequent occurrence than is generally supposed, and many cases have been observed and described as carcinoma, sarcoma, or carcino-sarcoma of the uterus.

We have already stated that Chiari⁶ described his first three cases as carcinomata, and many others have doubtless done likewise.

Up to the present twenty-five cases, including our own, have already been described as deciduoma malignum, sarcoma uteri deciduo-cellulare, or by more or less cognate terms. This includes three cases of Chiari,³ two of Schmorl,⁵⁴ and one each of Sanger,⁵⁰ Pfeifer,⁴⁹ Blanc,⁴ P. Muller,⁴¹ Lohlein,⁵³ Koettnitz,²⁷ Gottschalk,¹¹ Menge,³⁷ Pestalozza,⁴⁷ Paviot,⁴³ Nove-Joss-erand and Lacroix,⁴² Klien,²⁵ Jeannel,²⁰ Boldt,⁵ Beach,³ Ahlfeld,¹ Schauta,⁵³ Bacon,² Tannen,⁵⁸ and ourselves.⁶⁵ As we shall show later, it is doubtful whether four of these cases should be included under this broad heading, namely, those of Blanc,⁴ Paviot,⁴³ Boldt,⁵ and Beach,³ thus leaving twenty-one cases which have been definitely described and which undoubtedly belong in this category.

There is likewise no doubt that the two cases which Pestalozza⁴⁵ described as infectious hemorrhagic sarcoma, and one described by Guttenplan¹⁴ as hemorrhagic sarcoma, as well as the epithelioma papillare of Meyer,³⁹ and the carcinoma chorii of L. Fraenkel,⁸ all belong in the same group. Thereby giving us twenty-six cases, which, at least from a clinical standpoint, should surely be classed among the malignant deciduomata.

The case which Blanc⁴ describes as a deciduo-sarcoma certainly does not belong in this category. It possibly represents a fibroid degeneration of the decidua serotina, as suggested by Sanger,⁵² or may simply be a partially organized placental infarct, which remained in the uterus after the manual removal of the placenta. All anatomical details are lacking in the very short report of Boldt's⁵ case, so that it is impossible to be sure with what he had to deal; and we have already shown that Beach's³ case should be classed among the destructive placental polyps.

Paviot's⁴³ case occurred in a woman, aged forty-eight years, who had suffered with uterine hemorrhage for thirteen years. At the autopsy the uterus was as large as a foetal head, its left

and inferior portion being made up of an adenomatous growth, while its right and superior portion was made up of a dense, somewhat fragile, and granular tissue. There were metastases in the peritoneal cavity, the mesenteric and prevertebral glands, lungs, liver, and kidneys, which were reddish in color, slightly granular, sharply marked off from and readily peeled out from the surrounding tissue. The uterine growth and the metastases were composed of large epithelioid cells, with granular protoplasm and one or two deeply staining nuclei, between which there was a marked connective tissue-stroma. Neither the uterine growth nor the metastases presented the markedly hemorrhagic structure which was so characteristic of the other cases of deciduoma. Nor were we able from his description or his highly diagrammatic drawings to identify the epithelioid cells with those of the decidua. When we add to this the fact that the woman was a widow, who had never become pregnant in twenty years of married life, and who gave no history of a pregnancy preceding her last illness, we are obliged to hesitate to class the case among the malignant deciduomata; though, of course, we do not desire to deny its possibility.

We also agree with Sānger⁵³ that it would be unwise to attempt to class the cases which R. Maier⁵⁵ designated as a deciduoma among the tumors in question; for it is impossible to determine from his description exactly what it is, but it evidently does not belong among the malignant deciduomata.

On the other hand, it is more than probable that the case mentioned by Zweifel,⁶⁸ in the discussion on Menge's paper before the Leipzig Obstetrical Society, in which the woman died with persistent uterine and pulmonary hemorrhages some months after the expulsion of an hydatidiform mole, belongs in this category. And the same may be said of one of Jacobusch's¹⁸ cases, in which death resulted from intraperitoneal hemorrhage four months after a four months' abortion. The hemorrhage being due to the rupture of a bluish-red nodule, the size of a hazelnut, which was situated on

the posterior wall of the uterus. In addition to which there was a tumor of similar character (5 by 6 cm.) in the fundus of the uterus, and six other smaller nodules, varying from a pea to a walnut in size. Jürgens, who performed the autopsy, designated the case as "sarcoma teleangiectodes hemorrhagicum multiplex uteri et metastaticum colli uteri," but no microscopical examination was made.

Sänger,⁵² likewise, includes among the probable cases a case of sarcoma of the uterus following an hydatidiform mole, which was reported by Kaltenbach;²² and a case of Lebensbaum,³² which was reported as "carcinoma of the vagina, resulting from implantation from carcinoma of the corpus." But in both cases the microscopic description was too meagre to enable one to express a positive opinion concerning them.

It is also possible that two cases, which Veit^{60,61} described as carcinoma of the body of the uterus, may also have been deciduomata. Especially one, to which he refers in the article by Ruge and himself,⁶¹ on carcinoma of the body of the uterus, which he stated was analogous to the tumors described by Chiari (but which the latter subsequently stated were malignant deciduomata). It was examined by Jürgens, who left the diagnosis between carcinoma and sarcoma in suspenso, and Veit said "er hielt es für ein Mischform beider, ein Vorkommen, das jedenfalls durch die den Sarkomzellen ähnlichen Deciduazellen gerade kurz nach einem Abort möglich erscheint. Wir führen den Fall weil nicht von uns näher betrachtet, hier nicht in extenso, an, wollen ihn aber gerade bei der Aehnlichkeit mit Chiari's Fällen erwähnen."

There can be no doubt that at least some of these cases were really malignant deciduomata; but leaving them out of account, as well as the doubtful cases of Boldt⁵ and Paviot,⁴³ it is seen that at least twenty-six cases have already been described, which, from a clinical standpoint, should undoubtedly be classed among the malignant deciduomata; and no doubt they will increase very rapidly in number now that general attention has been directed to them.

ETIOLOGY. Just as is the case with all other malignant tumors, the etiology of the growth before us is unknown. The most striking etiological factor in connection with them is the marked relationship in which they stand to some form of pregnancy; all the cases having followed labors at full term, abortions, or hydatidiform moles. The only exception in this regard being the problematical case of Paviot,⁴⁸ in which there was no history of a pregnancy preceding the formation of the tumor; and to overcome it, Paviot himself supposes that an early abortion had occurred, which was masked by the continuous uterine hemorrhage, which had existed for years.

It is interesting to note that a very considerable proportion of the cases followed hydatidiform moles, and upon analyzing the 26 cases, which we consider undoubtedly belong in this group, we find that 11 cases followed hydatidiform moles; 6 cases followed full-term pregnancies; 5 cases followed abortions; 1 case followed a tubal pregnancy; and in 3 cases it was not definitely stated what form of pregnancy had preceded the appearance of symptoms.

When we consider the marked infrequency of hydatidiform moles in general, and the very large proportion of the cases of deciduomata which have been preceded by them, it is difficult not to believe that they stand in some sort of causal relation to them. And Sanger,⁵² in his monograph, carefully divided the cases into two groups, according as they followed hydatidiform moles or not.

It does not appear to us, however, that any particular histological difference can be noted in the cases which were preceded by moles and those which followed ordinary pregnancies. And it appears to us, if the moles played any very important part in the production of the growths, that we should find something in their structure to indicate this mode of origin. But we find both typical decidual cell sarcomata as well as tumors composed wholly or in part of syncytium following moles and normal pregnancies without distinction. It is quite possible

that this may be the case in those instances in which symptoms appear soon after the expulsion of the mole; but it can scarcely apply to the cases in which a year or eighteen months elapse between the expulsion of the mole and the first appearance of symptoms. An observation of Pestalozza,⁴⁸ however, would tend to indicate that there is some definite relationship between the two. For he has reported two cases of hemorrhage following moles, which persisted after curettement and compelled him to remove the uterus. In both uteri he found giant cells as well as masses of cells with nuclei rich in chromatin, which he considered very similar to chorionic epithelium, and which he considered were probably derived from the epithelium of the myxomatous villi.

In the present state of our knowledge, however, we believe it would be unwise to attempt to prove that the mole may give rise to the deciduoma, or the reverse, and must content ourselves by simply stating the fact that, in eleven of the twenty-six cases to which we have referred, the occurrence of symptoms was preceded by the expulsion or manual removal of an hydatidiform mole.

In our case the occurrence of vulval metastases, less than two weeks after the full-term labor, would lead one to suppose *à priori* that the primary tumor had developed during pregnancy rather than in the very short interval which elapsed between the completion of labor and the appearance of the metastasis at the vulva. But the small size of the primary tumor at death, three months after the labor, militates somewhat against this view; for it must be supposed that it increased in size during this period, and consequently must have been much smaller at the time the first metastasis was developed. On the other hand, it is quite possible that they developed during pregnancy, but owing to their small size did not interfere with it and allowed it to go on to full term.

The occurrence of metastases in less than two weeks after the labor is not, however, inconsistent with the development of the tumor after the completion of labor. For Schmorl,⁵⁶

in his very valuable contribution to our knowledge of puerperal eclampsia, has shown that we may find thrombi in the pulmonary arteries, which are composed of placental giant cells, without any trace of tumor formation about the uterus or placenta. And it would be only necessary to suppose these cells endowed with malignant properties to account for the very rapid formation of metastases. In several cases of tubal pregnancy we have likewise found thrombi of chorionic epithelium in venous channels of the tube wall, far removed from the site of pregnancy. And Pestalozza,⁴⁶ in one instance, following the expulsion of an hydatidiform mole, found pulmonary thrombi composed of apparently unchanged myxomatous chorionic villi.

These observations all teach that it is possible for chorionic and perhaps decidual elements to make their way into venous channels and reach remote portions of the body either during or just after pregnancy in conditions which have nothing to do with tumor formations. This being the case, we can readily imagine that the same may occur in the earliest stages of malignant growths connected with the placenta or decidua, and thus give rise to metastases at a very early period, which, under favorable local circumstances, may exceed the primary growth in size.

CLINICAL HISTORY. In contradistinction to the usual forms of malignant uterine growths, the vast majority of the cases of deciduoma malignum occur in young women. An analysis of the 26 cases shows that they all occurred before the menopause and were divided as follows:

1 case occurred at the seventeenth year; 12 cases occurred between twenty and thirty years; 5 cases occurred between thirty and forty years; 4 cases occurred between forty and fifty years; 1 case occurred at fifty-five years; and in 3 cases the age was not given.

The most constant symptom is uterine hemorrhage following some form of pregnancy. In some cases it begins almost immediately after the completion of the labor or abortion,

but in others it does not make its appearance until some months later. The hemorrhage, as a rule, is not continuous, but occurs at intervals and is generally of a gushing character, indicating the invasions of a vessel. The uterus is enlarged, and upon dilating it and introducing a finger its cavity is found to be more or less completely filled by a soft reddish placental-like mass, which is readily scraped away, when the finger sinks into an irregular depression, which in some cases extends almost through the entire thickness of the uterus.

The tumor masses recur rapidly after removal, and within a few days the uterus may be once more filled with them. In other cases, however, the uterine hemorrhage is not a prominent symptom. In Sanger's⁵⁰ case it ceased entirely after a single curettement and thus completely masked the real nature of the disease; while in our own case it did not occur at all, and attention was first called to the case by the appearance of vulval metastases. In Sanger's case the absence of uterine hemorrhage and the occurrence of cough, hemoptysis, and the development of a fungoid tumor in the iliac fossa caused the case to be regarded as one of tuberculosis, although no bacilli could be found in the sputum.

The rapid formation of metastases and early death are the characteristic features of this form of tumor. Metastases are most frequently observed in the lungs and vagina; pulmonary metastases being observed in nearly every fatal case; while vaginal metastases were observed in 58 per cent. of the cases. The occurrence of vaginal metastases is very characteristic; for they are rarely noted in carcinoma of the uterus, and only occasionally follow the usual forms of uterine sarcoma.

Several observers are inclined to regard the vaginal metastases as due to implantation of bits of tissue from the uterus, but their very frequent occurrence and especially the fact that they occurred in Ahlfeld's¹ case, in which the tubal situation of the primary tumor apparently excluded such a mode of origin, renders it apparent that they do not all originate in that way. And in certain cases, at least, must be due to in-

fection through lymphatic or venous channels, though the arrangement of the pelvic vessels renders such a mode of origin difficult of explanation.

The cases run a very rapidly fatal course and death usually occurs within six months from the first appearance of the symptoms, our case dying in less than three months after the completion of labor.

DIAGNOSIS. Now that attention has been directed to this class of cases, a probable clinical diagnosis may readily be made in advanced cases. The occurrence of uterine hemorrhage following soon after a normal pregnancy, abortion, or hydatidiform mole, which soon recurs after curettement and associated with vaginal metastases or symptoms indicating pulmonary involvement, presents a clinical picture which leaves but little room for doubt.

The diagnosis of the early stages of the growth is not, however, so easy a matter, and can be made only by means of the microscope. In view of the rapidly fatal character of these tumors, and their intimate connection with some form of pregnancy, their early diagnosis is a matter of the greatest possible moment; for it is only by very early operation that we can hope to prevent the formation of metastases.

Consequently, we must regard with anxiety hemorrhage occurring in the later part of the puerperium or in the period immediately following it, especially when the pregnancy terminated in the expulsion of an hydatidiform mole. In such cases, we shall not do our duty by our patients if we procrastinate and suppose that we have to deal only with hemorrhage resulting from retained membranes, a placental polyp, or an endometritis post partum; for a few days' delay may afford the short period necessary for the formation of metastases and render futile all operative interference. But in all such cases we should promptly dilate and curette the uterus, preceding the latter by a digital exploration of its cavity if possible, and then submit the scrapings to a competent microscopist for examination.

If we have to deal with a malignant deciduoma, the presence of decidual cells or masses of syncytium, making their way between the muscles, will enable us to make a positive diagnosis. Diagnoses have been made in this way by Gottschalk,¹¹ Löhlein,³³ Menge,³⁷ Nove-Josserand and Lacroix,⁴² Schauta,⁵³ and Tannen,⁵⁸ and have been verified by the examination of the uterus after operation or death.

In Ahlfeld's¹ case a diagnosis of sarcoma chorii (Gottschalk) was made by Marchand upon the examination of the vaginal metastasis.

TREATMENT. Owing to the very rapid formation of metastases, many cases will occur in which all operative procedures will be futile. But when the diagnosis is made early, and there is no evidence of the formation of metastases, total extirpation of the uterus, with its appendages attached, is urgently indicated.

Thus far seven cases have been operated upon in this manner by Gottschalk,¹² Löhlein,³³ Menge,³⁷ Nove-Josserand and Lacroix,⁴² Jeannel,²⁰ Schauta,⁵³ and Tannen.⁵⁸ The cases of Menge, Gottschalk, and Löhlein all died from recurrence of the growth, six, seven, and twelve months, respectively, after the removal of the uterus. The other four cases recovered from the operation, but sufficient time has not elapsed since to enable us to judge of its ultimate success.

Thus no subsequent report was made upon Jeannel's case. The case of Nove-Josserand and Lacroix was well three months after the operation. Schauta's case had a vaginal metastasis when operated upon, and naturally offers a very gloomy prognosis. Tannen's case was perfectly well nine months after the operation, having gained twenty pounds in weight.

It is thus seen that the operative treatment has not been crowned with very great success, and it is probable that several of the four cases just mentioned will succumb to a recidive. It is, however, the only chance of saving the

patient's life and should be resorted to as soon as a diagnosis is made, if metastases are not already present.

P. S.—Marchand's article was not concluded when this article was written, consequently its latter portion is not referred to by us. It may be found in the July number of the *Monatsschrift für Geb. u. Gyn.*

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