On Chorionepithelioma and the Occurrence of Chorionepitheliomatous and Hydatidiform Mole-like structures in Teratomata.

A pathological and clinical study

by

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Contents.

PART ONE.

Introduction.

Chorionepithelioma or Deciduoma Malignum is not a new subject to the author of the present memoir. It was taken up again after an interval of 4 years with a view to reporting a new case which had been put into his hands for examination in October 1901. Shortly afterwards, another case (Case III) in which the difficulties of diagnosis of this disease are illustrated was also obtained, and, about a year later, a third case (Case II) very similar to the first.

Although it is only 14 years since the recognition of Deciduoma Malignum as a special disease, the literature of this subject is already very large. Hardly any tumour has given rise to so much discussion or to so many divergent views as to its origin & nature. Within the last four or five years, however, we seem to have attained a considerable degree of certainty on these points. Matters of detail there are yet to be settled, and particularly the practical questions of diagnosis & treatment are still in an unsatisfactory condition. Examination of the literature of the subject showed that, whatever might be the state of opinion regarding its pathology on the Continent, in this country it was far from unanimous, and the most constant stumbling

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X "A case of Deciduoma Malignum" by J. K. Kelly, M. D. and John H. Teacher, M. A. M.B.C.M. Journ: Path: & Bact: October 1898, p. 358.

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block appeared to be the decision of the Obstetrical Society of London as the outcome of the discussion which they held in the year 1896 that these tumours were only Sarcomata of the uterus. Not only in Obstetrical and Gynaecological text books, moreover, but also in special works on tumours, and in the reports which one saw in the Journals of cases of Deciduoma Malignum, it was apparent that in England at any rate this same opinion was still the cause of much confusion. Some even questioned the existence of such tumours. On the other hand, all who have reported cases in Scotland have followed the view of the disease which is associated with the name of Marchand, and recently that opinion has won many adherents in England also.

Having regard to the amount of importance still attached to the discussion in the Obstetrical Society of London, and the fact that in spite of the great advances in our knowledge, no more recent thorough discussion has been held by the Society, I approached them last September with a request that they would allow me to communicate my cases to them. The idea of using the subject for a thesis had also occurred to me. At this time, I was just starting on a visit to the German Schools of Medicine, and, what I saw & heard there confirmed me in my opinion that it would be well worth while doing a new English review of the whole subject. In Austria & Germany, I had the privilege of studying many of the classic cases and also most of the best material relating to the development & structure of the placenta, with which Deciduoma Malignum is so closely bound up.

On the Continent I found, then, that any case of Deciduoma

Deciduoma/

Malignum was an object of considerable interest, but it was not on account of the question of its nature or origin; that is regarded as settled by the demonstration in numerous cases of the actual development of the growth out of the Epithelium of the Chorionic Villi. The nature of the Epithelium also seems now to be fairly well determined and with it the question of classification of the tumour. · The name "Deciduoma Malignum" is still often used, but the view implied by it is completely abandoned in favour of that of Marchand expressed in the term "Chorionepithelioma". A great deal of interest was also manifested in what is called the "English opinion", meaning that of the Obstetrical Society of London. This usually ended with the remark that it needed revisal.

Attending the Versammlung ~~of the~~ Deutscher Naturforscher und Aerzte in Carlsbad in September 1902, the Author became acquainted with certain recent discoveries which had greatly increased the interest felt in the subject. These were contained in a paper published in May 1902 by Friedrich Schlagenhaufer of Vienna on 2 cases of malignant tumour of the testis in which were found structures identical, histologically & in their behaviour to the adjacent tissues, with Chorionepithelioma; and in one of them, structures closely resembling hydatidiform mole, which had spread from the testicular tumour into the veins and even into the cavities of the heart. Schlagenhaufer's cases formed the subject of a lively discussion in the pathological section of the Congress, and I have since then had the pleasure of meeting him in Vienna & examining them in detail. His conclusion was that these

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tumours were teratomata, a conclusion which was very generally accepted as valid. These tumours are of great interest in themselves. They have also a special interest, for in them apparently we meet again the "Sarcoma of the Testis" which was shown to the Committee of the Obstetrical Society of London by the late Professor Kanthack & Dr Eden, which was one of the reasons for the decision of the Society.

The practical importance of Chorionepithelioma is shown by the number of cases that have been reported since it was recognized A considerable number of these certainly were cases which had previously been recorded under other names, but, after excluding them, there are more than sufficient to shew that it is by no means the great rarity that it was supposed to be. After rejecting a number of cases which appeared doubtful, I have been able to tabulate from the literature 188 well authenticated ones/ the principal details of which were accessible to me, have seen sections of about 40. In addition to these, there are a good number of the ordinary cases of the disease lying unpublished, only the unusual ones being now recorded. By the kindness of Professor Weichselbaum, I obtained portions of the specimens which have been added to the museum of the General Hospital in Vienna between February 1901 and August 1902. Of these, seven in number, only two have been published. The rest were examined and then placed in the museum. All of them were fatal cases. In addition, I was informed that several others in the same period had been simply examined and thrown out as if they were ordinary cases of carcinoma of the cervix. The published cases are those

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of Hubl; they are a primary vaginal one and an exceptionally large uterine one which had ruptured into the peritoneal cavity. Schlagenhaufer informed me that he had reported on 6 cases since 1897, but of these, he had only published two. A like state of affairs, though perhaps not concerning so many cases, I encountered in Prague & Dresden; and in Kiel & Leipsic, I saw sections of several new cases which are being worked up for publication. In some parts of the world, it would appear from the above, Chorion-epithelioma is not an uncommon tumour. In the period of 18 months above mentioned, there would be, I was informed, about 2700 post-mortem examinations in connection with the General Hospital of Vienna; practically all patients who die there are examined by the pathologist. Even 7 deaths in that number is no inconsiderable share for a disease which was supposedto be a rarity; and when one considers that most of the victims are women in the prime of life and who have enjoyed good health up to the fatal pregnancy, the importance of the disease appears still greater. Although not so many cases have been reported from other countries, still British, Italian, French, Russian, Scandinavian, & American literature shows a considerable & rapidly increasing tale of them. One of the American cases, that of Williams, occurred in a negress. On the other hand, although the pathologists of Budapest have been on the look-out for cases for several years, Dr Krompecher informed me that there has not yet been found one in that city. It may be that it is almost equally rare in London. With a population more than twice that of Vienna, only some(7)seven cases

seven cases/

have been recorded. From other parts of England, 5 cases, From Ireland one case, and from Scotland, including those here reported, 9 cases have been put on record, and I am aware of one more which has been observed. Probably others have been dismissed as Sarcomata and others have escaped notice through the rarity of post-mortem examinations in this country. A very suggestive story is that of a case recorded by Baldwin in the American Journal of Obstetrics of November 1902. "He was called to remove a cancer of the uterus, this being the diagnosis of the attending physician. He found the woman had been delivered at full term without difficulty 6 or 8 weeks previous to his visit. The after-birth was delivered by itself and so far as the attending physician knew, it was normal. Two weeks later, trouble continuing, another physician was sent for who examined her & found a piece of after-birth which he removed, curretted, and supposed there would be no further trouble. Criticism was indulged in and a suit for mal-practice was in the air. The second physician, 2 or 3 weeks later, on examining the woman, found more afterbirth. Dr Baldwin again examined the woman carefully and found malignant disease, and told the physician it was deciduoma malignum. Vaginal hysterect-omy was made. There was no involvement of the vagina. He was careful however to pull down the omentum and found a secondary nodule as large as the end of his finger. Recovery was satis-factory, but a few weeks later, the woman developed cachexia and died. He believed he had seen half a dozen such cases in his practice".

At the same time already evidence is not wanting that too hasty operations have been performed. The extreme malignancy of the earliest reported cases gave grounds for the opinion that operation could not be done too early, but the records of numerous cases more recently reported show that the extremely malignant disease is but one type and that there are all degrees of malignancy, just as in the other classes of tumour. The histological test has been proved to be by no means infallible, and neither clinically nor pathologically is it possible to draw a sharp line of distinction between the cases which are merely retained placenta and curable by removal of the foreign material, and those cases which run on into chorionepithelioma or destructive hydatidiform mole. It is especially with regard to the last mentioned variety of the tumours that difficulties are met. The recognition of chorionic epithelium or chorionic villi is easy & certain; but to decide whether the villi are those of a simple hydatidiform mole or whether they are potential malignant growths is a very different matter.

Chorionepithelioma or Deciduoma Malignum ~~k~~ may be defined generally as follows:-

It is a malignant tumour of the uterus arising in connection with a confinement or abortion which in typical cases destroys life with a rapidity almost unequalled by any other kind of growth. Clinically it is characterized by the occurrence within a shorter or longer period of the pregnancy ~~by the occurrence~~ of irregularly recurring haemorrhages, progressive anaemia, & cachexia.* The morbid anatomy of the ~~v~~ase shews a haemorrhagic

* Sometimes also rigors and fever.

haemorrhagic/

tumour situated most commonly in the cavity of the uterus, occupying the fundus and adjacent portions of the anterior & posterior wall of the body of the uterus, i.e. the commonest site of the placenta. Malignancy is shewn, in addition to the violent haemorrhages, by more or less ulceration, infiltration, & destruction of the uterine tissues and the rapid occurrence of metastatic growths, which are most common in the vaginal veins and the lungs, corresponding to dissemination by the blood stream. Histologically it presents a very characteristic picture, but at the same time a complex and rather confusing one owing to the numerous modifications which the component cells undergo, so that they present an extraordinary variety of forms.

The most typical elements are

(1) Small well defined polyhedral cells, with large vesicular nuclei closely packed together in masses without any connective tissue stroma between them.

(2) Large multi-nucleated irregular masses of protoplasm (plasmodia or syncytia) in which no definite cell boundaries are recognizable.

(3) Large cells, sometimes mono-nucleated, sometimes multi-nucleated, some of which present some resemblance to decidua cells, while others are identical in character with the multi-nucleated giant cells which occur in the decidua serotina. These are, in some parts, arranged in cell masses without intervening connective tissue stroma, in other parts they are

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infiltrating and destroying adjacent tissues after the manner of Sarcoma.

Among the cell masses are seen the remains of the normal tissues, and a large amount of blood, sometimes clotted, sometimes fluid, as if in sinuses, giving the tissue its haemorrhagic character. The tumour has no proper connective tissue stroma, or blood vessels of its own, nor does it convert the adjacent normal tissues into a stroma. Instead, a particularly active destruction of them is characteristic, and specially it attacks and burrows into the uterine blood vessels. To this feature it owes its haemorrhagic character and its mode of dissemination.

According to what may be called the accepted view, the connection with the pregnancy is essential and it is a quite peculiar growth originating from a structure peculiar to the gravid uterus, viz:- the epithelium of the chorionic villi; the cells of the first class corresponding to the Langhans' layer; the second to the syncytium and the third containing derivatives of both layers. Its place in a system of classification depends on the view that is held of the nature & source of that epithelium. The original view was that it was a tumour composed of decidua cells is quite abandoned. The other views are the English one already mentioned, and what may be called the view of Veit, according to which the tumour is a Sarcoma originating from uterine tissues, and the foetal elements, which he admits to be present, are non-essential and due to the superposition of a pregnancy on a primary maternal disease.

Part 2. - The History of Chorionepithelioma.

A very elaborate discussion of the history & literature of Deciduoma Malignum has been rendered unnecessary by the publication of a very long & able Zusammenfassendesrefe/rat by Max Munzer in which practically all the cases that had been described up to the beginning of 1902, and all the opinions that have ever been held are most carefully, and, as I can vouch from my own reading, accurately epitomized & discussed. This, and the papers of Marchand for the details, contain certainly nearly all that anyone need read for a thorough knowledge of the general aspects of the subject. For the excentricities there are other monographs which will be referred to later. For those to whom German presents a difficulty, the older literature is very well presented in Whittridge William's paper of 1895, and the position in 1899 is summarized with exemplary brevity by Haultain. There are a number of other papers which give valuable information among which may be mentioned those of McKenna, Gaylord, Fothergill Berry-Hart, Ladinski, & Pierce.

The history of the Deciduoma Malignum considered as a special disease begins with the description by Sanger in 1889 of a case of very malignant Sarcoma-like growth of the body of the uterus, arising after an abortion in the eighth week. This he regarded not merely as a Sarcoma coinciding with the pregnancy but as a special tumour allied to the Sarcomata in which pregnancy was an essential feature,& the growth developed from a tissue peculiar to the gravid uterus, viz:- The Decidua, and he called it Decidduoma Malignum. In 1890, Pfeiffer, a pupil of Chiari, published an

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account of a very similar case,& classed along with it three cases which had been described in 1877 by Chiari as Carcinoma of the uterus coinciding with pregnancy. Pfeiffer quite independently came to the same conclusion as Sänger,and also called the growth Deciduoma Malignum. From Italy too, Pestalozza in 1891 reported three cases of a highly malignant tumour of the uterus connected with pregnancy. One of these was a case of malignant hydatidiform mole. The whole three,he described as haemorrhagic or infectious Sarcoma. Pestalozza recognized the importance of the pregnancy as giving to the tumour special characters, but he doubted the origin from decidua cells and regarded it as modified sarcoma of the uterus. Cases more or less similar to that of Sänger were also reported by Schmorl, Müller, Gottschalk, Lebensbaum, who did not, however, altogether accept Sänger's interpretation of the disease.

In 1893, Sänger published his monograph on the subject in which he collected all the earlier described tumours that seemed to present affinity to his case, and included also a number of old cases of destructive hydatidiform moles of which there had been no proper microscopic examination, and considered a number of other diseases of the placenta which had no direct connection with deciduoma and need not be further considered here. Sänger now divided the malignant tumours directly connected with pregnancy into three classes -

(1) Sarcoma Decidua-Cellulare, i.e. the Sarcoma composed of decidua cells corresponding to the original deciduoma malignum The name was altered to be more precise by excluding the glands

the glands/

of the decidua, which played no part in the tumour.

(2) Sarcoma Decidua-Cellulare with participation of Chorionic villi. (a) after hydatidiform mole, (b) with a Sarcomatous condition of the mesoblast of the villi (Schmorl's & Gottschalk's tumours.)

(3) The malignant interstitial hydatidiform moles and placental polypes.

The third class he held to be quite distinct from the decidual tumours; being a sort of parasitic growth of chorionic villi into the maternal tissues which remained passive except for some inflammatory re-action. The second group formed the bridge between the real decidual tumours and the pure malignant moles. In the tumours he held the decidua cells to be the essential malignant tissue, and the chorionic elements which had been described in Gottschalk's and one of Schmorl's cases were adventitious. The views of Sänger as to the pathology of the condition have proved to be erroneous in many respects, but the great merit remains to him that he focussed the attention of gynaecologists and pathologists on the disease and paved the way for a proper understanding of a condition, the practical importance of which has been indicated. Very soon it was proved that the tumour which he may be said to have discovered, although not exactly common, was by no means a great rarity. Cases began to be reported in considerable numbers, many of them being old ones which had formerly been reported under different names.

Most of them were reported as deciduomata in the sense of Sänger, but divergent views also appeared, the number of which is indicated in the great number of names which were conferred upon the disease.* Gottschalk in his full publication in 1894, dissented from the view of Sänger and emphasized his view that the disease was originally of the foetal tissues, being essentially a Sarcoma of the chorion arising from the Langhans' layer (regarded by him as of foetal mesoblastic nature) and the stroma of the villi. Schmorl also regarded the participation of foetal tissues as essential to the tumour, but did not publish his views in detail, and Menge reported two cases taking the view that they were Sarcomata originating from the uterine muscle. Cases were also reported as deciduomata in the sense of Sanger by Bacon, Tan[illegible], Löhlein, Schauta and others.

In 1895, L. Fränkel reported a case in which the growth consisted almost entirely of syncytium and called it Syncytioma Malignum or Carcinoma Syncytiale, because he regarded it as originating not from the decidua but from the syncytium of the chorionic epithelium. As to the exact nature of the syncytium he did not commit himself to an opinion.** He also described the

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* Gottschalk -sarcoma chorion-deciduo-cellulare; later sarcoma chorii; Schmorl - blastoma chorion-deciduo-cellulare; Pestalozza - infectious haemorrhagic sarcomata; Guttenplan - haemorrhagic sarcoma; Meyer - epithelioma papillare uteri; Klebs - placental papilloma; Klien - deciduo-sarcoma uteri giganto-cellulare.

decidua-like infiltrating cells but did not commit himself to an opinion as to their nature either.

About the same time, Marchand published the papers which brought order out of this chaos. According to his view, the tumours were composed of cells derived from both layers of the chorionic epithelium; they were, therefore, accepting the ruling opinion as to the nature of that structure of mixed maternal & foetal origin. The difficulty of admitting that a tumour could be composed of foetal & maternal tissues was fully met by the conception of the chorionic epithelium as so specialized a structure, and the symbiosis of these two elements as so characteristic & essential a physiological feature that they were entitled to be considered together as if one tissue. It was on this ground as well as on the ground of their clinical history & histological structure - resemblances to both carcinoma & sarcoma - that Marchand regarded these growths as neither carcinoma nor sarcoma, but as sui generis. He suggested that they might be called serotinal tumours since they arose from tissues which occurred only in the region of the decidua Serotina, and which were characteristic of the Decidua Serotina and the placenta.

William s of John Hopkin's Hospital in the same year independently recognized the connection of Deciduoma Malignum with the chorionic epithelium, but, while recognizing elements resembling Langhans' layer cells, he considered the syncytium the important element. He was inclined to regard the latter as a derivative of the uterine epithelium and considered the foetal

epiblastic nature of the former & difficulty in the way of believing that the individual cells of the tumour could be of this nature. He preferred to leave the question of their nature open. The three last mentioned authors, then, at least agreed in referring the tumour to the Chorionic Epithelium; and as the particular view which has prevailed was that of Marchand, the origin from the Chorionic Epithelium came to be generally associated with his name.

Indeed, it is to Marchand that the credit is chiefly due for unravelling the confusion in which the subject had become involved and setting the pathology of it on a sure foundation of accurate observation and careful generalisation.

Marchand's theory of the nature & origin of the tumour was founded on a thorough investigation of the histology of the human placenta in which he was able to trace a close resemblance - physiologically & anatomically - between the Chorion epithelium and the tissues composing the tumour. The frequency with which hydatidiform disease of the Chorion precedes Deciduoma had been noted and had been held by some observers to be no accident. In the study of hydatidiform mole in situ within the cavity of the uterus, Marchand demonstrated that the generally accepted view, that of Virchow, ~~with~~ that hydatidiform mole was a myxoma of the Chorion was erroneous. The stroma of the villi is connective tissue and in the young placenta it has the characters of embryonic connective or mucous tissue. Marchand found that the actual condition of this in the mole was dropsical degeneration.

In the small vesicles (the early stage) there was plenty of mucin as was natural considering the nature of the tissue, but in the large vesicles there was scarcely any, the contents being a watery fluid. Active proliferation of the mucous tissue, there was none. The connective tissue was poor in nuclei and reduced to a thin rind beneath the epithelium. But there was excessive and irregular proliferation of both layers of the Chorionic Epithelium. This Marchand regarded as the important change. Later observers have in the main agreed with him. The condition may vary somewhat in different cases. There may be excessive proliferation as well as degeneration of the mesoblastic cores of the villi in some cases; but the important tissue, especially with regard to tumour formation, is the epithelium. The subject has recently been reviewed by Kermauner. He finds this work of Marchand the classic memoir and his views the generally accepted views.

Besides setting the histology of the hydatidiform mole on a satisfactory basis, Marchand was able to trace an extremely close likeness between hypertrophied epithelium in mole and the cells composing deciduoma malignum. Not only were the cell forms which arose out of it the same, but they infiltrated the maternal tissues, and invaded the blood vessels in a similar way. This he showed further, was but an exaggeration of the conditions found about the attachments of the villi to the decidua in the young placenta. His conclusion was that no sharp line could be drawn histologically between the long ago observed but rare malignant hydatidiform moles, and the new deciduomata. In both

diseases, the active element was the chorionic epithelium which had taken on an excessive and aberrant growth after the manner of the epithelial structures in carcinoma. Unfortunately also, he was likewise forced to consider it impossible to distinguish sharply between the proliferation in a simple mole and that in a malignant one; a conclusion which still holds good. It is interesting to note that although he accepted the different origin of the two layers, he traced all the intermediate cell forms, and noted that this agreed with the older observations of Kastchenka who had believed in their common origin from foetal epiblast.

According to the view of Marchand then, the so-called deciduoma malignum or, as he called it in his monograph of 1898, Chorionepithelioma, may be regarded as a member of a series of diseased conditions of the chorionic epithelium which shows many varieties, and a progression in degree of malignancy comparable with the progression from simple adenoma to malignant adenoma or papilloma and carcinoma. Like other malignant tumours, it has its physiological prototype, the characters of which it reproduces in an aberrant and excessive manner. The young chorionic epithelium, or to use the name which is now commonly applied to it, the trophoblast is an extremely peculiar and active tissue. Its histological structure is as characteristic as that of any other tissue of the human body; there is none with which it can be confused by anyone of reasonable histological skill. Physiologically also, it is quite characteristic, discharging, as it does, the functions in the first place of establishing a connection between the mother and the embryo, and, secondly, of

maintaining it up to the time of birth. In respect of the former, it shows indeed a striking resemblance to a malignant tumour. As Hubert Peters observed in comparing the trophoblast of the earliest known human ovum with the tumour, "the young trophoblast has a striking power of growth and in respect to its physiological relations in the early stages of the embedding of the ovum, (destructive effects on the enclosing zone) does indeed manifest a destroying (malignant) action on maternal tissue." The epithelium also of villi and ova of slightly later date also show a very luxuriant growth which is quite normal (Fig: 4.) and even in placentæ of 2 or 3 months, villi may be found which show considerable masses of epithelium (fig 3) - vide Part III.

In actual diseased conditions there are

(1) The simple hydatidiform mole, which may be a dangerous disease even apart from any actual malignancy.

(2) Malignant hydatidiform moles, which differ from the preceding but little in their structure - a little more overgrowth of the epithelium, a little more infiltration of the decidua, the invasion of vessels and the establishment of metastatic growths, which may also contain villi, in the vaginal vessels and the lungs. In the combination of epithelium which is the essential malignant structure with a stroma which may show growth but no malignancy, this may be compared with malignant papillomata.

(3) The pure Chorionepithelioma in which no trace of foetal mesoblastic tissue is to be found.

(4) Connecting these two, tumours composed almost entirely of

epithelial tissue in which a few villi, either normal or more or less hydatidiform, are seen.

The tumours of the last class are the crucial ones in which the whole of the tumour tissue in all its very varied cell forms can be traced directly to its source.

The relationship between the normal placenta, the moles and the tumours was worked out in a masterly manner by Marchand, but a case of the last class to actually demonstrate his conclusions was yet wanting. A very interesting link was supplied by the consideration of the case of Meyer published in 1888, in which, sometime after the removal of a large hydatidiform mole in a woman aged 55 years, violent haemorrhage & rigors set in, leading in a few months to a fatal issue. The uterus was considerably enlarged and shewed an irregular ulcerated internal surface. This was regarded as a tumour, and Meyer himself accurately indicated the Chorionic Epithelium as the essential element of the growth. Klebs in his text book of Pathology, referred to the case as a beautiful example of "parasitism" - foetal tissues invading and destroying the maternal - he called it a papillary epithelioma of the body of the uterus. Certain structures in it he regarded as Chorionic villi to which the epithelial tumour belonged. Marchand referred to it as a link between the malignant moles and the Chorionepitheliomata, although he doubted if the structures described by Klebs as Chorionic villi were really of that nature; he thought they were only masses of fibrin amid the epithelial cell masses. In 1896, the gap was filled by the publications of Apfelstedt & Aschoff and of Julius Neumann. In their papers,

several cases of characteristic deciduoma malignum in which villi were present, and in which the origin of the tumour tissues from them was readily traceable, were described. Other monographs followed in which the same connection was demonstrated. There is no clearer example of the tracing of a tumour to its physiological prototype than Chorionepithelioma. Such evidence there is no getting past.

Aschoff's paper also contained an admirable study of the normal placenta in which he came to the conclusion that the view then most generally held in Germany, and which Marchand had accepted, that the syncytium of the chorionic villi was a derivative of uterine epithelium, while the Langhans' layer represented the foetal epiblast was erroneous. His conclusion was that both layers were foetal epiblastic in nature and were capable of being transformed one into the other. Marchand also from further studies of the normal placenta was in his second paper (1898) more inclined towards this conclusion. He has now fully accepted it. About this date too, the preliminary communications of Peters and Siegenbeek van Heukelom on extremely young human ova appeared. Both of them regarded the chorionic epithelium as purely a foetal epiblast, a conclusion which is adhered to in their full publications; vide Part III. At any rate, Marchand then was clear that whatever might be their nature, the origin of the tumour from both layers was no longer open to question.

The effect of Marchand's work may be characterized as revolutionary. Nearly all authors who have published cases since then have accepted his views, and many of the

old ones have been re-described in the same sense. Gottschalk re-examined the cases of Tannen and Hartman and Toupet, and reported them as tumours of the chorionic epithelium in the sense of Marchand, abandoning his former view of Sarcoma of the chorion. Schmorl, who had prepared the microscopic specimens of Sänger's original tumour, re-examined them & also declared in favour of the Marchand view. Sänger adhered to his old opinion. Subsequently, he admitted that many of those cases might be epithelial tumours, and Austerlitz, in reporting a case from Sänger's clinic in 1902 gives what may rest as his final opinion. "Sänger accepts in its essentialities the explanation given by Marchand, but with the reservation that the possibility of the formation of Sarcoma cells out of decidua cells in respect to his first case, which does not correspond in all points with those of Marchand, cannot be excluded". I have examined Schmorl's preparations and I am of the opinion that the original deciduoma malignum was a typical chorionepithelioma, many of the cells of which presented the resemblance to decidua cells, which is seen in all those tumours. The opinion that a real sarcoma composed of decidua cells may occur is also held by Chiari. In conversation, Professor Chiari referred me to the case of Bacon, reported from his laboratory originally as deciduoma malignum. In the year after the publication of Marchand's papers, this was examined and reported again by E. Fränkel as a typical tumour of the Chorionic epithelium. This, Chiari said, might be taken to represent the acceptance by his school of the Marchand view. Although he has not published any other paper on the subject, he had frequently expressed that

opinion in meetings of Societies, for example, in the discussion on Schlagenhaufer's communication at Carlsbad last summer, but he would make the reservation that a true deciduoma malignum may occur. Dr Whittridge Williams*, in a letter to me, states "In view of the changes in embryology which have occurred since I wrote my article, I have found it necessary to change my views upon the subject and at present I believe that the syncytium as well as the isolated cells represent Chorionic epithelium and are derived primarily from the foetal ectoderm. Accordingly, I share the views of the German investigators who designate the growth as Chorionepithelioma, and only use the term Deciduoma malignum from the clinical point of view." This is practically the universal attitude of German pathologists. A few, like Kossmann and Pfannenstiel, while agreeing that the tumour arises from the chorionic epithelium, having not yet accepted the above view as to the nature of that structure. vide Table. The views of Marchand were also accepted by the Italian, French, Russian, Swedish and American observers whose names will be found in the table of cases.

On the other hand, in 1896, the members of the Obstetrical Society of London, in a discussion on cases reported by Herbert Spencer, Malcolm, and Rutherford Morrison were mostly against the idea that there was anything special about these growths; and the pathological Committee to which the specimens were handed over for full examination decided unanimously that the tumours shown to them were sarcomata and that there was nothing in their histological characteristics to justify the supposition that they were of

* Dr Williams' "Obstetrics" has now appeared: it contains an excellent account of the subject

decidual origin, and that the term deciduoma malignum was therefore an inappropriate one. In the discussion, the opinion of Marchand was quoted and the case of Apfelstedt and Aschoff was cited. In the report of the Committee, they are not directly referred to, but they seem to have had considerable influence in moulding that report to the extremely guarded form which it took. In 1897, Dr. J. K. Kelly and the author reported the first case which was observed in Scotland. In sections of the secondary tumour in the lung we had the fortune to find masses of the young tumour tissue growing amid uncoagulated blood, and therefore presenting appearances unmodified by contact with the maternal tissues or by degeneration. Comparing this with our preparations of the placenta, we had no difficulty in recognizing the identity of the tumour tissues with the expansions of the Chorionic epithelium which is seen particularly about the tips of the villi where they are attached to the decidua - the so-called "haftzotten", and we therefore accepted the view of Marchand. The actual origin of the tumour from the villi has since been demonstrated in this country by Haultain and recently by Prowse. The discussion in the Obstetrical Society of London was held at an unfortunate time, when there was still great confusion regarding deciduoma. I think it was a pity, considering the amount of influence which their decision has had and the great clearing up of difficulties which occurred within the two years succeeding their discussion, that they did not accept the advice tendered them by Marchand in 1898, and have a thorough reconsideration of the subject long ago. Certainly there was a discussion in London on Haultain's case. No

preparations could demonstrate more conclusively than his the origin of the tumour; and the cases since then have usually been reported as Chorionepitheliomata.

On the Continent, practically the only opposition now to the opinion of Marchand comes from the school of Veit. The essence of the tumour, Veit holds to be sarcoma of the maternal tissues associated with pregnancy. He admits the presence of foetal structures, but he regards them as adventitious. The course of events under his theory presupposes a sarcoma in the body of a uterus which afterwards becomes the seat of a pregnancy. The case which he published was clinically a typical example of deciduoma malignum. The tumour presented quite characteristic appearances and contained a number of villi; large cells, many of them multi-nucleated, lined the adjacent blood vessels, and also appeared among the uterine tissues, including the muscle. These cells he regarded as sarcoma cells of maternal origin constituting the real tumour ~~x~~ tissue. Evidence that they were invaders, he could not find. The occurrence of pregnancy in a uterus already the subject of a sarcoma of the body, he admits has not been demonstrated. This account of the sequence of events, although it has now been in evidence many years, remains purely hypothetical. Winkler, who has revived the old error of treating the syncytium as a derivative of uterine muscle, need not be considered. His more gross inaccuracies have been exposed.

In 1901, Veit published a paper on deportation of Chorionic villi. That the metastasis of tumours has a prototype in the escape (~~xxxxxxxxx~~ deportation) or Verschleppung of portions of

villi, or fragments of chorionic epithelium into the maternal vessels, was made known by the work of Schmorl on puerperal eclampsia some years ago, and it has been confirmed by various observers, Lubarsch, Aschoff, Veit, and, still more recently, Poten, and I have also been able to observe it for myself in two specimens of the uterus with the placenta in situ. Williams has also observed it. Formerly it was supposed to occur only in diseased conditions, but it has now been observed under such circumstances as to favour the belief that it occurs in the majority of normal pregnancies. Usually the escaped materials undergo dissolution in the maternal blood, and give rise to no symptoms; but under conditions about which ~~[illegible]~~ a little is known, they give rise to those abnormal cases of Chorionepithelioma in which the primary tumour is situated outside the ordinary seat of implantation of the ovum. The fact of deportation, Veit demonstrated in a case of extrauterine pregnancy. That the deported villi may attach themselves to the interior of the maternal blood vessels just as they attach themselves to the decidua in their normal seat, Veit allows, but only under abnormal

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An interesting speculation on the influence of such deported villi I have encountered in the papers of Veit and Kollmann. This material, which becomes dissolved in the maternal blood, represents the male "germ plasm" as well as the female; it is suggested, therefore, that it may be the material basis of telegony! Also of Syphilis by "Choc en retour."

conditions of the maternal organism. He holds, as a general rule that disease of the mother cannot arise from the foetus. Where the foetus or placenta is diseased, the cause is always primarily in the mother.

From study of the Siegenbeek van Heukelom ovum he has satisfied himself that the theory of imbedding of the human ovum by removal of the uterine epithelium and attachment by means of foetal epiblast to maternal connective tissue (Peters and v. Heukelom) is probably correct in the main, but he will not admit that destruction of the maternal tissues or infiltration of maternal tissues by foetal, after the manner of a malignant growth, has been demonstrated. The large supposed infiltrating cells in the decidua enclosing a normal ovum and in the walls of the blood vessels wherever deported villi are attached (which are generally accepted as derivatives of the chorionic epithelium) he regards as formed in situ from maternal elements - practically as decidua cells. Thus the difference between the views of Veit and Marchand turns on the interpretation of the large infiltrating cells which Sänger originally regarded as the decidua cells composing the tumour. I shall return to this later.* From discussion with Professor Veit, I gathered that he is not quite so strongly of the opinion that those cells are not of foetal origin, but even if he were to allow that point and abandon his view that the Sarcoma is the primary element in the disease, he would still hold that some disease of the mother preceded the disease of the ovum. (n.s.) The actual cause of these tumours is unknown. What the conditions of origin of the tumours might be, Marchand discussed in his publication, while admitting

* V. Histological details p 80.

that there is much to be said in favour of the state of the maternal tissues being the cause, he considers the primarily foetal origin to be the more probable. Either observer might be right without in any way disproving that the actual tissues which behave as tumour are foetal. Whatever may be thought as to the source of chorionepithelioma. the essentiality of the connection with pregnancy is beyond question. This is so clear from the clinical facts alone that it is hardly worth while discussing it. Even excluding the malignant moles, there are many cases in which the disease was continuous with the pregnancy. Cases there are in which the clinical history shows an interval greater than one year between the pregnancy and the first symptoms of disease, and in two or three the preceding pregnancy was not clearly demonstrable; but one is quite justified in treating these as exceptional. Tumours which do not show that feature should be accepted as chorionepitheliomata only on the clearest histological evidence being produced.

I regard the controversy, then, as having been summed up by Marchand in his paper of 1898, and I think that his theory that deciduoma malignum and destructive (malignant) hydatidiform mole are diseases of the chorionic epithelium might then have taken a place among the proved facts of pathology. The problems which remained for solution were the expiscation of all aberrant forms of the tumours, the practical ones of diagnosis and treatment, and the the nature of the chorionic epithelium. The latter we will now proceed to consider.-

Part III.

The physiological prototype of Chorionepithelioma.

Our knowledge of the structure of the placenta is much more favourable to a consistent explanation of the peculiarities of the tumour at the present time than it was in 1896. The foetal epiblastic nature of the whole chorionic epithelium seems to be proved. The magnificent monograph of Hubert Peters on the earliest stage of human placentation yet discovered seems to leave little room for doubt; notwithstanding that the veteran Langhans still holds the uterine epithelial origin of the syncytium to be discussable for the human subject, and Selenka in the last part of his work on the apes maintains that "the uterine epithelium plays an important role" in them in the formation of the placenta. In my opinion, the conclusion of Peters must be held valid unless material yet more favourable than his unique specimen should be found and should demonstrate the contrary.

All the literature of human, and, in less detail, comparative placentation up to 1899 is reviewed by Peters; an excellent summary of the subject, containing evidence of much original research, and giving a very full account of Peters' work has recently been given by Clarence Webster in his "Human Placentation." The position of the comparative anatomy of the placenta is indicated in some of the more recent papers of Hubrecht in German, and is summarized in English by Jenkinson.

The description of the placenta is best approached by considering its structure in the second month. Abortions of six to eight weeks are fairly easily obtainable. After the fourth

month regressive changes have advanced so far that for the most part only the one layer of the epithelium - the syncytium - remains. (fig 4d.)

The decidua ever since William Hunter recognized that it was the uterine mucous membrane modified to subserve the needs of pregnancy, and first described its gross relations to the ovum, has been regarded as a maternal tissue. The decidua vera presents no difficulty, and contains no elements about which doubt can arise; the similar tissues in the serotina and reflexa are judged by comparison with it. The problems are connected with the so-called epithelial wandering cells of the decidua serotina and the epithelium of the chorionic villi. Taking the villus in the early stage, say about the sixth week of gestation, the mesoblastic stroma containing the blood vessels is found to be enclosed in a double layer of epithelium. This fact was recognized by Goodsir and S. von der Kolk (according to Virchow), but the classical description we owe to Langhans.

The epithelium consists of

(1) An inner single layer of cubical cells having clear protoplasm and round or oval vesicular nuclei of relatively large size, moderately rich in chromatin and shewing a well marked intra-nuclear network; multiplication is by indirect division and karyokinetic figures can usually be found without much trouble. The protoplasm contains glycogen. This is known as Langhans' layer, and the cells as the individual cells. They rest on the connective tissue core, the line of junction often being a well marked basement membrane. (fig 4a. 4c. etc.)

(2) Enclosing that and separating it from the maternal blood in

the intervillous space is the syncytium, a layer of protoplasm in which no definite cell boundaries are recognizable. (Plate II.) The protoplasm has an opaque appearance and takes the usual contrast stains somewhat deeply. In specimens fixed with osmic acid, it is usually found to be richly loaded with finely divided fat. The nuclei are generally smaller than those of the Langhans' layer, oval or more elongated in shape, solid, and staining more deeply. The appearances and especially the distinctness of the two layers vary considerably according to the state of preservation & character of the fixative agent used. (fig. 4a) In material which is not very fresh the distinction is difficult to make out. The syncytium frequently spreads out into buds which may even be detached from the main layer and lie apart as multi-nucleated giant cells free in the maternal blood, or it may be merely a thin layer resembling endothelium. Nuclear multiplication is by a process of direct division. The free edge of the syncytium shews more or less distinctly a fringe of protoplasmic processes which have been described as cilia, but they are not of this nature, being non-motile. (Pl. XII fig. 17.) Doubtless they have to do with the absorptive and secretory functions of the epithelium. A better comparison of them would be to the striated border of the intestinal epithelium or the fine processes in the prickle cells of the epidermis.

Here and there the Langhans' layer spreads out into masses of considerable size. These occur in the intervillous space (forming cell knots) (fig. 4c) but are best developed at the attachment of villi to the decidua - the haftzotten - villi of attachment. At these points they form a layer several cells deep between the tip of the

connective tissue core and the tissue to which it is attached. The cells composing these masses commonly retain their clear protoplasm but both nucleus & cell body tend to be considerably increased in size. The syncytium instead of enclosing these cell masses divides on either side and is applied to the surface of the decidua lying between the attachments of villi. At this stage there is commonly no mingling of the Langhans' layer cells with the decidua, the two being separated from one another by what is usually called the canalised fibrin layer (fibrin layer of Nitabuch) a dense stratum of necrosed tissue mixed with fibrin. (fig 3a, & 4.) The cell knots (fig. 4c.) often contain more or less fibrin or degenerated material and the cells then tend to be enlarged and altered in character. Thus they may form masses of somewhat large cells with very large nuclei more or less embedded in fibrin, which present a superficial resemblance to the Decidua cells. They were formerly regarded as processes of decidua; now, however, their origin has been traced from the chorionic epithelium. Apparently for the most part, they are derivatives of the Langhans' layer, the modification being of the nature of hypertrophy with more or less of degeneration, the exact limits of the two processes being very difficult to determine. Masses of what are plainly syncytium may also be seen in those cell knots and there are cells also mono-nucleated or with two or three nuclei, but with the opaque protoplasm characteristic of the syncytium. In the decidua and in the fibrin layer lining it, similar cells may be observed. (fig. 3.) There are also large isolated cells with protoplasm similar to the syncytium and multiple nuclei to be found in varying number inthe decidua, and even in among the

(Fig. 3.)
uterine muscle cells. These are generally taken to be infiltrating detached buds of the syncytium and are referred to as "syncytial wandering cells". In the cell knots and masses at the tips of villi all forms intermediate between the typical individual cells and the syncytium are described. In my preparations, however, the two layers are in general sharply defined from one another. This question of the transformation of the one layer into the other will be taken up under the histology of the tumours. The infiltrating giant cells and large individual cells are found in the decidua serotina and reflexa, but not in the decidua vera.

The idea that the placenta was an organ of mixed foetal & maternal origin may be traced to William Hunter. According to him the villous chorion was everywhere interpenetrated right up to the membrana chorii by processes of decidua. In the joint organ there were two circulations which were quite distinct, the interchanges between mother and foetus being by "transudation;" the foetal blood flowed through the vessels of the villi, while the maternal circulated in the "intermediate spaces" (intervillous spaces) which he compared to the cells of the corpus cavernosum penis. He regarded the placental cells as an extension of the maternal circulation.

The influence of these views is seen in many of the theories which have held as to the constitution of the organ. By Reid, for example, it was supposed that the lining membrane of the maternal vessels was everywhere applied to the surface of the foetal tissues, and the intervillous space was therefore actually

dilated maternal vessels. The later representative of this was the view which interpreted the syncytium as a derivative of maternal endothelium, (Winkler, Waldeyer, and Pfannenstiel). Langhans, in his classical description, regarded the inner layer as foetal mesoblast while the syncytium he regarded as foetal epiblast; but this view he abandoned, and, along with many others, came to regard the syncytium as a proliferation of the uterine epithelium (the old view of Goodsir and Turner) while the Langhans' layer cells represented the foetal epiblast. The return to this particular opinion was largely due to the comparative anatomical studies of Selenka, Strahl, Gunser, and Kossmann, and Merbtens and Keibel appeared to have rendered it fairly probable for the human subject also. By 1895, the view that both layers were of foetal epiblastic and therefore of common origin, which had been held by Minot & Kastchenko, was generally discredited in Germany.

On the other hand, others had observed (Hensen and Van Beneden) that in the embedding of the ovum in rodents & bats, the uterine epithelium was destroyed and the ovum appeared to attach itself to the deeper maternal tissues. In 1889, appeared Hubrecht's monograph on the placentation of the hedgehog and about the same time Duval's on the placenta of the rodents (rabbit and guinea-pig) in which the disappearance of the uterine epithelium and the attachment of the ovum to maternal connective tissue by a proliferation of foetal epiblast was described from most complete material worked up by histological technique of a very high order.

Huxley, in his paper "on the application of the Law of

Evolution to the arrangement of the Mammalia" had indicated the insectivora as a very central and primitive type. In the hedgehog in particular, "we possess the key to every peculiarity which we meet with in the primates, carnivora and ungulata". Fairfield Osborne and other American paleontologists have since confirmed this position. On these grounds it was, that Hubrecht chose the hedgehog for placental research. To the naked eye its placenta also strongly resembled the human.

Hubrecht was able to demonstrate the manner of the embedding of the ovum of the hedgehog in the uterus, tracing it from the stage while it was yet free in the cavity through all stages of development up to the mature placenta. At an early stage of segmentation it comes to rest in a hollow or furrow in the uterine mucous membrane. Around it the mucous membrane swells up, forming a deep cleft in which the ovum lies. Then the epithelium in the immediate vicinity of the ovum degenerates and disappears. A similar fate overtakes the adjacent subepithelial structures. Maternal blood-vessels in this way are opened and a certain amount of haemorrhage occurs around the ovum. The extravasated blood coagulates and the ovum is cut off from the uterine cavity by a plug of blood-clot which glues together the lips of what is now termed the decidual swelling. As segmentation advances, the ovum is differentiated into two classes of cells, an outer set and an inner set. The inner, the hypoblast, remains comparatively small in amount; the outer, the epiblast, proliferates rapidly into a thick layer of cells, which at one part becomes still thicker, and projects inwards against the

hypoblast. The greater part of the epiblast - in fact all except that knob of cells lying towards the centre of the ovum - takes no part whatever in the formation of the embryonic shield, but becomes specialized as an organ for the nutrition of the ovum. This thick layer of primitive epiblastic cells, Hubrecht named on account of its nutritive function, the trophoblast, otherwise trophic-epiblast. (Fig 49. Plate IV.) In the early stages of development, the trophoblastic portion grows much more rapidly than the embryonic portion of the ovum, and thus the condition is attained of a relatively large nutritive organ enclosing a very small embryonal rudiment. Stated without details, the development of the placenta may be described as follows:-

Around the ovum destruction of the maternal tissues occurs to a considerable extent, the degenerated remains probably being used up by the trophoblast for its nourishment. Then a reaction in the maternal tissues outside the zone of destruction sets in and they begin to proliferate, forming what is called in the human subject, the decidua. An equilibrium becomes established between the trophoblast and the proliferating uterine tissues, union of foetal and maternal tissues then takes place and where maternal blood-vessels have been opened, the trophoblast becomes hollowed out into a sponge work of cavities containing maternal blood. This does not coagulate; On the contrary, the cavities take the place of vessels, become as it were a part of the maternal circulation, and a primitive placenta is complete. There has been no extension of the maternal endothelium into these cavities to form a lining to them. Like the maternal epithelium, the endothelium in

contact with the trophoblast simply disappears and its place is taken by foetal cells. Later, with the growth of the embryonic rudiment and its differentiation into the three primitive layers, the foetal mesoblast, bearing blood-vessels, enters into combination with the trophoblast, and villi are formed consisting of cores of foetal mesoblast covered with trophoblast which thus becomes the epithelium of the villi, and the cavities in it, the intervillous spaces. Here then is a proper placenta containing a circulation of maternal blood and a circulation of foetal blood, the tissues of which are entirely foetal. In the early stages, Hubrecht recognized a considerable proliferation of the maternal endothelium; and along the edge of attachment of foetal to maternal tissues. it was far from easy in the later stages to draw a sharp line between them. Recently one of his pupils, Van Resink, has re-examined all the hedgehog preparations and material, and his results in the main confirm the earlier ones. Where they differ it is in the direction of still further limiting the share of the maternal tissues in the formation of the placenta. The proliferating maternal tissues, especially the endothelium of the vessels, form a layer which he called the trophospongia. The greater part of this and the layer of large multinucleated cells called deciduofracts, he now regards as part of the trophoblast. The trophospongia as at present defined is in the fully developed organ, a very thin layer. All the organ which performs the metabolic interchanges between mother & foetus Hubrecht now regards as of foetal origin.

The work of Duval led to results practically identical. The

organ of attachment he found to be a proliferation of foetal epiblast which he named ectoplacenta; a term which may now be treated as synonymous with trophoblast. Later, Duval came to similar conclusions for the cheiroptera, and Van Beneden who had favoured other views in his earlier work on the same order, stated in a letter to Duval his conversion to those of the latter. Nolf also brought confirmatory evidence.

Hubrecht forecast that the attachment of the human ovum to the uterus and the formation of the decidua reflexa would be found to resemble what occurred in the hedgehog; his hypothesis may be taken as the modern representative of the old idea that the decidua reflexa is formed by the rising all round the ovum of a fold of uterine mucous membrane, the edges of which eventually meet and unite over it. A different mode of formation of the decidua reflexa was suggested by Von Spee. (Plate IV.) Following up the work of Hensen on the guinea-pig, Von Spee was able to confirm his observations that the ovum in that rodent breaks through the uterine epithelium between the mouths of the glands and burrows into and embeds itself in the connective tissue. Von Spee pointed out that this form of embedding would account for the fact that in his very early human ovum (of 11 m/m longest diameter) no glands opened into the cavity of the decidua reflexa as they would on Hubrecht's hypothesis, and there was no lining of uterine epithelium to that cavity. His observations at this time were still incomplete and his full account of them has only recently appeared; even this covers only the embedding and not the formation of the placenta. But it covers the most important

stages. The hole in the epithelium is blocked by the last part of the ovum remaining in contact with the edges; (fig 4k) here at first there is no widespread destruction of the epithelium. Round the rest of the periphery of the ovum, the maternal cells swell up and gradually lose their distinct outlines and flow together into a symplasma or syncytium of degenerative nature. This was erroneously described by Selenka as developing into a part of the placental epithelium. Instead, it gets broken down into a fluid (histolysis) and by its destruction a space (fig 4k) (implantations-hof) is formed for the ovum to grow in. Outside the zone of degeneration, there is proliferation of the maternal tissues into a "sort of granulation tissue that about 10 to 16 hours after the commencement of implantation perhaps hinders or at least limits the destruction of the uterine tissues".

Professor Graf Von Spee showed me some of his later stages along with those already published. I think there can be no doubt that in the guinea-pig as in the hedgehog, the ovum "like a sort of parasite" attacks and destroys the maternal epithelium and underlying tissues until it forms a cavity in which to rest. Reaction of the maternal tissues follows as round a foreign body and the result is embedding of the ovum in maternal connective tissue by means of a proliferation of the epiblast.

Study of the convenient rabbit here as elsewhere in embryology has had results by no means happy. The uterine epithelium in the gravid uterus exhibits extensive formation of syncytium. This has been, and still is, regarded by many observers as the syncytium of the placenta, and they have applied

their results without reservation to the syncytium of the human placenta. The other interpretation appears to me more probable, according to which this is a mere temporary structure which disappears when the trophoblast comes into contact with it. I have preparations which shew this disappearance but they are two few to allow me to form an independent judgment on the whole question. As to mice and rats, opinions likewise differ. Jenkinson holds that the entire trophoblast is foetal epiblast. The lower orders of mammals in which proliferated uterine epithelium is persistent differ so radically from the human subject in placentation that they need not be considered.

The hypothesis of Hubrecht while in details different from that of Von Spee is in full agreement with it so far as the main principles are concerned. There is no essential opposition between the two. In 1893, Berry Hart, & Gulland in an admirable study of human placentation in material from the fourth week onwards, recognized that there was no proliferation of maternal tissues forming the chorionic epithelium, but, on the contrary, there was evident destruction of uterine epithelium and endothelium. The chorionic epithelium was described very much as I have done it; both layers they regarded as of common origin and foetal epiblastic nature. They adopted Hubrecht's terminology in so far as to apply the name trophoblast to the cellular expansions at the tips of the villi and recognized its destroying action on the decidua. As a working theory, they put forward " the hypothesis that the human ovum could only graft itself on connective tissue, a view which might be added to Hubrecht's speculation". It was possible

that it embedded itself by destroying a portion of the superficial epithelium and boring into the decidua (as Spee had already suggested). On the other hand, they thought that the removal of the epithelium was due to menstruation, which prepared a suitable place on which the ovum might ingraft itself. The human ovum then was an "embedded one";—not attached to the serotinal epithelial surface and with the epithelial vault of the serotina arching over it to form the so-called reflexa, but one actually growing in the serotina. The foetal epiblastic nature of the chorionic epithelium was also maintained by Clarence Webster in his work on extrauterine pregnancy.

Placentation differs greatly in different orders and even in different species in the same order. Each ovum seems to be a law unto itself; Therefore great caution must be exercised in applying the results of comparative research to the attachment of the human ovum. Nevertheless, it appears highly probable that the problems of the formation of the decidua reflexa and the nature of the placenta have at last been solved. The demonstration that the human ovum is an embedded one has come only with the discoveries of Hubert Peters. The same observer and Siegenbeek Van Heukelom have apparently proved the foetal epiblastic nature of the human trophoblast and its later form the epithelium of the chorion.

The Peters' ovum is the only one yet discovered in which the decidua reflexa is not complete. According to the evidence it affords, the embedding resembles that of the guinea-pig ovum more than that of the hedgehog. Instead of being enclosed by swelling up of the

mucous membrane around it, which would be equivalent to the old circumvallation theory of the formation of the decidua reflexa, the ovum bores its way into the mucous membrane, destroying the epithelium and underlying the maternal tissues until it has reached a sufficient depth. The hole by which it entered is closed over it by a blood-clot. The Peters ovum shews this stage quite clearly. The pregnancy was probably of not more than five or six days duration. It was obtained from the body of a woman, who, on the non-appearance of menstruation along with the occurrence of subjective symptoms suggesting pregnancy (vomiting), swallowed caustic potash solution and died in about 3 hours. Three hours later (the exact time is not stated in Professor Peters' monograph; he told me it was as stated above and requested me to let the fact be known) the uterus had been opened and the ovum discovered by prosector Kretz, who presented it to Professor Peters. The area of decidua containing the ovum was at once removed and placed in Muller's fluid which at first was changed every hour.

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After fixation it was embedded in paraffin and converted into an unbroken series of sections about 10μ in thickness.

The Peters' ovum has been greatly criticised. It has been said that as it was taken from a dead body, it could not be fresh enough to be reliable; that it is badly fixed; that it is pathological, and that even it is not early enough to prove the nature of the chorionic epithelium. By the kindness of Professor Peters, I was able to study the preparations and my impression is that it is a thoroughly reliable specimen. More favourable circumstances one could hardly have. The fixation is exceedingly good. It has the faults of Muller's fluid fixation to a slight degree - the cellular details are less clear than is the case by certain other methods of fixation. Otherwise there is no fault that can be found with it. It was not possible to study the distribution of glycogen or fat. It has recently been restained with haemalum & eozin and the structure of the trophoblast is now plainer than when the original description was written, but no changes require to be made. Probably the spaces of the trophoblast are somewhat overfilled with blood, but certainly to a much less degree than is the case in the other early ova which the author has seen, and not to an extent which in any way disturbs the relation of parts. Apparently there has been a considerable degree of congestion of the uterine mucous membrane. Further, no one can say that it is pathological, for there is no other so young with which to compare it. Considering it as the youngest member of the series consisting of Von Spee's 3 ova (one as yet unpublished) the Van Heukelom ovum, and the two youngest Leopold

ova (all of which I have examined) one can have no hesitation in accepting the opinion of Von Spee that it is normal, as fully warranted. From the point of view of histology as distinguished from that of embryology Marchand and Von Spee agree in regarding it as irreproachable. For those to whom the original is inaccessible, the account of this ovum by Webster can be highly recommended, but there is no work which can fill the place of the original monograph. The relationship of the ovum to the uterine mucous membrane may be seen in fig: 4 e. which is re-produced from Peters' original figure. The ovum which measured 1.6 by 0.8 by 0.9 m/m is completely embedded in somewhat oedematous tissue. There was no projection of the decidua over it and it was discovered by Dr. Kretz only by the detection of a paler area in the somewhat thickened and congested mucous membrane covering the posterior wall of the uterus. The greater part of the uterine mucous membrane shews only a condition of swelling, true decidua formation having commenced only in the immediate neighbourhood of the ovum. The ovum itself consists of a thick sphere of trophoblast which is irregularly hollowed out by spaces containing maternal blood. Within that, the embryonal rudiment, consisting of a very small epiblastic shield with the amnion already closed over it, and the rudiment of a yolksac, and a very small amount of mesoblast between them is slung in a net-work of delicate connective tissue - the extra-embryonic mesoblast or mesoblast of the chorion - which connects it with the trophoblast. There are no foetal blood vessels and no sign of an allantois. The outermost layers of the chorionic mesoblast are somewhat denser than that

filling the general cavity of the trophoblast. The surface shews a few slight projections in it, corresponding to depressions of the trophoblast, but actual formation of villi had not yet taken place. Between the mesoblast and trophoblast in places is a slight cleft which is artificial. The innermost layer of the trophoblast consists of small cubical cells, exactly corresponding to those of the later Langhans' layer. External to this and obviously continuous with it are considerable masses of cells which are somewhat larger and shew much larger nuclei; and between these and the blood in the spaces of the trophoblast is a complete layer of syncytium which in some parts is in considerable masses, in others is so thin as to look like an endothelium lining the blood spaces. Both by the relatively large size of its nuclei and the character of its protoplasm it differs entirely from real endothelium. The appearance is one I am familiar with in the tumour and in the normal placenta. Its interpretation presents no real difficulty.

In the large cell masses of the trophoblast, Peters can trace all the intermediate forms between the individual cells and the syncytium. The primitive type of cell is the clear cubical mono-nucleated cell of the inner layer. Where the trophoblast is united with the maternal tissues, the individual cells appear to be in contact with the connective tissue and there is a certain degree of mingling of foetal elements with maternal elements. Outside the zone, which is clearly trophoblastic, are seen large cells, sometimes multi-nucleate, which Peters takes to be wandering elements of the syncytium. In the maternal tissues, although there is a slight modification of some of the cells in the direction of decidua cells, and apparently new formation of

blood vessels, there is no such proliferation as even to suggest that the trophoblast had developed out of the maternal tissues. On the contrary, there is clear evidence of destruction of the maternal tissues where they are actually in contact with the trophoblast. In special the uterine epithelium both of the surface and of the glands in the immediate neighbourhood of the ovum gives evidence of degeneration (Fig: 4c.) and the destruction of the maternal endothelium is also clearly demonstrated (Fig: 4f.) The work of Van Heukelom on a somewhat older ovum which was obtained under conditions almost equally favourable for the study of the relationships between the foetal and maternal tissues also led to the conclusion that the whole trophoblast is of foetal blastic origin. The broad lines of distinction between foetal and maternal are quite clear. With regard to cells here & there, there is admittedly a difficulty which is experienced in all placental research, viz:- that the union between the maternal & foetal is so intimate and the variety of cell forms appearing in the border zone is so great that there are some cells about whose origin one would not commit one's self. This is the case even where, as for example in the work of Hubrecht on Erinaceus, Tarsius spectrum, and Tupaya javanica (insectivora), the material contains all stages from the free ovum in the uterine cavity up to the mature placenta; but this does not affect the main principles.

The only member of the Primates which has been worked out with full material is the curious aberrant one, formerly classed with the Lemurs,- Tarsius spectrum. In this, Hubrecht finds the

connection to be established by a process homologous with that in the hedgehog. The ovum in this case is not wholly embedded; the trophoblast develops over a limited area only. The completely foetal nature of that structure is very clear in this animal.

The true monkeys and the apes would perhaps be as well left on one side just now. Turner and Waldeyer found a very close resemblance between the placenta of the monkeys and the human placenta. Selenka described the villi as covered by a double layer of epithelium exactly similar to that in the human placenta. The syncytium, he regarded as formed by proliferation of the uterine epithelium while the individual cells represented the foetal ~~ectoblast~~ chorioblast. This opinion was controverted by Hart & Gulland, who considered that the chorionic epithelium in the monkeys to be of the same nature as they had described for the human subject, and they considered that Selenka's illustrations did not prove his view. Kollman recently has expressed the same opinions. In the last part of Selenka's great work recently issued "as a fragment" under the editorship of Keibel, he still adheres to the opinion that in the formation of the ape's placenta, the uterine epithelium plays an important role. It is probably better, however, seeing that the work is but a fragment, to leave the placenta of the apes entirely out of account until we have the promised full publication of them by his pupils Hubrecht, Strahl, & Keibel.

In concluding this part of my paper, I have to acknowledge the great kindness of Professor Peters, Hubrecht, Marchand, Von Spee, Veit, and Dr Leopold in not only allowing me to see their preparations

but in giving valuable time to demonstrating them to me.

Addendum.

Since the above was written three important papers have passed through my hands, viz. those of Sobotta on the "Development of the ovum of the mouse," of Hitschmann and Lindenthal on a very young human ovum, and of Andrews on "tubal pregnancy." All of these confirm and strengthen the position which has been maintained in the preceding pages.

PART IV.

Reports of the cases.

Of the 3 new cases, two are quite typical examples of chorionepithelioma arising after abortion. The third must be classed as a doubtful case, being possibly only hydatidiform mole. The case formerly published along with Dr Kelly forms a good supplement to the group. All the new cases were submitted to operation. That of Dr Kelly shews the course of the disease in the very malignant type, undisturbed by operation. It is therefore recapitulated at some length.

Case of Kelly and Teacher. Clinical history. 2nd Febry 1897. Mrs L. aged 27, 2-para, now in her third pregnancy, consulted her medical attendant on account of slight haemoptysis. This was supposed to be due to incipient phthisis, as the expiratory murmur at the apex of the right lung was prolonged. This slight haemoptysis recurred from time to time. Probably it was not connected with the growth. On 20th April, there was some vaginal discharge.

On 18th June, labour came on and a mole about the size of a Jaffa orange, which was not hydatidiform, was expelled. No tumour was then observed in the vagina. Haemorrhages from the vagina continued to occur, and on 7th August a small tumour like a foreign body, about the size of a shilling lying on the anterior wall, was detected. An attempt to remove it caused such severe haemorrhage that the vagina had to be plugged.

On August 10th "an ulcerating hematoma" was removed from the anterior vaginal wall. It was not examined microscopically. Bleeding having persisted, the patient was removed into the Royal

Infirmary on the 20th of September. At this time there was an elongated finger-like mass in the anterior vaginal wall and a rounded nodule in the posterior wall, and the uterus itself was enlarged. On the 24th of September, there was a severe uterine haemorrhage, followed by collapse of the patient. On the 28th of September, a slight cough commenced with streaks of blood in the sputum. On the 3rd of October, recurrence of the uterine haemorrhage; and thereafter rapid increase in the size of the uterus, and decline of strength; and death on the 19th of October - 4 months after the abortion. The body of the patient appeared well nourished, but was extremely blanched. The post-mortem examination showed that the lungs were the seat of numerous secondary nodules, but the other organs of the thorax and the abdominal organs presented no important abnormality. The uterus was about the size of the pregnant organ at the end of the fourth month. (Fig. 2a & 2b.) The enlargement affected particularly the posterior wall and fundus, which were rounded out by the tumour. This surface of the uterus was of a peculiar mottled red & pink colour owing to the large amount of blood in the tumour, which had almost reached the peritoneum. In the right fallopian tube, there was a small globular nodule of dull red colour, enclosed in a thin capsule of tube wall. Several rounded tumour masses projected into the vagina. The lymphatic glands in the neighbourhood of the rectum are said to have been enlarged but they were not kept for microscopic examination. The uterus was opened by an incision right through the tumour. This filled the whole cavity. It rose from the fundus and posterior wall. In section, it presented the appearance of blood-clot mixed with lighter coloured strands of

tissue. In its outer part it, to some extent, resembled placental tissue. The uterine muscle had been almost completely destroyed in the seat of the tumour, but there was not any actual perforation. The rectum and bladder were not involved. Dense swellings could be felt on either side of the vagina and cervix which, on dissection, were found to be secondary tumours, partly in the vesical, uterine and vaginal veins, partly in the lymphatic glands in the base of the broad ligament. Separate from these, there were a number of nodules which looked like thrombosed varicose veins. They were in fact veins dilated by tumour invasion. Along either side of the vagina, extending about half way to the ostium were large masses of the same nature, in appearance exactly like thrombosed varicose veins. This is the usual description of these vaginal metastases. The tumours in the base of the broad ligament were about the size of a walnut. They were quite detached from the side of the cervix uteri, separated from it by a thin layer of normal tissues through which the ureters were traced. The blood-vessels between these nodules and the uterus were not thrombosed. The microscopic examination demonstrated that the lymphatic glands were involved in the tumour, and at the time the authors were inclined to regard this as a primary lymphatic infection. The proof of this, however, is not absolute. Lymphatic gland tissue there is in the nodules, but the relations of the tumour tissue to it do not preclude the possibility that, just as emboli had fallen down into the vaginal veins and given rise to secondary tumours there, so they may have rested in the iliac veins about the junctions of the vesical uterine & vaginal branches, where they attached themselves ~~there & grown outwards~~ and grew outwards, and thus

ing
invad~~e~~ the lymphatic glands. Lymphatic infection is quite exceptional, having been recorded only in 8 cases, all of these being very advanced. In case 2 of Marchand (Everke), the relationship of the tumour cells to the ~~lymphatic~~ lymphoid tissue appears to prove that they were infected through the lymphatics. On the other hand, metastasis by way of the blood stream has been recorded in the majority of the fatal cases. For the tumour, as for Sarcoma, it is the usual route.

Microscopic examination of the primary growth shewed that, as usual, by far the greatest part of it was composed of blood-clot mixed with a certain amount of necrosed tumour tissue. The actual living tumour formed the floor of an extensive ulcer, as it were, between the blood-clot and the uterine muscle. Plugs of it burrowed in among the muscle fibres and along the cavities and walls of the veins. Thrombosis of the larger veins near it was common, but the thrombi were of quite recent formation, probably not long before the death of the patient. The mucous membrane was in a condition of ulceration and inflammation. Decidua cells were not observed. The lungs were studded with round firm nodules of a dull red colour; those on the surface projecting somewhat. In section they were rounded, and well defined, and did not, as a rule, present much resemblance to either haemorrhagic infarcts or pneumonic patches except in colour. They had a drier, older & better defined appearance. They were composed principally of blood-clot with living tumour tissue recognisable only around the edges. The neighbouring alveoli contained red blood corpuscles, catarrhal cells and some plugs of fibrin. The diagnosis of the

tumour as a derivative of the chorionic epithelium was made, as already mentioned, from one of these secondary nodules in which masses of very well preserved tumour were found growing in fluid blood. (fig 9c.) The resemblance of these to the masses of Langhans' layer and syncytium around the attachment of villi to the uterine tissues in the normal placenta was so exact that it was impossible to doubt their identity and little difficulty was experienced in determining that the other elements in the tumour were derived from these two structures. Actual villi were not present in either the primary or the secondary tumours. The destructive action of the tumour tissues on the walls of the blood vessels was very clearly recognized in dissecting the masses at the side of the vagina & cervix. The walls of the large veins were quite rotten and microscopic examination demonstrated that this was due to their erosion by infiltrating processes of tumour cells. Another point which may have an important practical bearing was the condition of many of the secondary nodules. The tumour in the fallopian tube and several of the small intravenous ones were very dense, and on being incised, shelled out of their capsules. Serial sections were prepared to investigate the reason of this and demonstrated that the entire tumour tissue in the nodule was in a state of necrosis. Various observers, from Gottschalk onwards, have commented on this apparent destruction of the tumour by the haemorrhage which it has itself evoked, and some, e.g. Halltain, have regarded it as a possible explanation of the fact that patients have covered after removal of the primary tumour although symptoms pointed strongly to the occurrence of metastasis in the lungs.

This will be referred to further in discussing the question of prognosis & treatment.

New case, No 1. Dr John Edgar's. To Dr John Edgar I have to express my indebtedness for the specimen, for the clinical notes of the case, and for many valuable suggestions.

History. Mrs P. aged 32, married 6 years, no children. Her health previous to 1897 was good, monstruation was regular every four weeks. On the 29th March 1897, she aborted after two months amenorrhoea. There had been no morning sickness and no breast symptoms. Dr Burges removed the ovum with his fingers. The subsequent haemorrhage was slight and only lasted for a day or two. On 6th September 1898 there was a second abortion like the first, but breast symptoms were present and the ovum came away spontaneously. In November 1898 the patient had an attack of appendicitis. In February 1899, Dr Burges inserted an intrauterine stem pessary on account of ante-flexion of the uterus. In March 1900, Dr Burges dilated the cervix uteri. This was done not because of dysmennorrhoea, but because of the patient's desire for pregnancy. On 20th September 1900, after two months amenorrhoea with breast symptoms but no morning sickness, the patient sent for Dr Burges on account of uterine haemorrhage. It was slight and lasted only a few hours. There was no pain. Thereafter there was a slight but almost constant bloody uterine discharge, dark in colour & odourless. In December, this increased in quantity & became red & mixed with clots. On the 16th of December, a fleshy mass about the size of a hen's egg was extruded into the vagina and was removed by Dr Burges. He states that it

did not look like an ovum. He regarded it as a fleshy mole, but did not keep it nor get it examined microscopically. He is certain that it was not a vesicular mole. The bleeding continued until 1st of January. A few days later a slight brown discharge reappeared. On the 7th of January, intrauterine application of Ac: Carbolic: On the 23rd January severe rigor with pyrexia lasting three hours. On the 7th Febry, Dr Edgar removed with the curette several small pieces of tissue like placental remains. Microscopic examination gave no definite results. The discharge ceased. In July it reappeared after a menstrual period which had been delayed a week and continued off and on. On the 31st August, Dr. Burges was called in on account of the increase of the discharge. On the 3rd of September there was a second pyrexial attack beginning with a rigor and lasting a few hours. On the 5th of September, Dr Edgar curetted a second time and brought away pieces of tissue similar to the last. No definite result was obtained from microscopic examination of these pieces, but the clinical features of the case were so suggestive of deciduoma that on the 25th of September another portion was removed and sent to me. Characteristic masses of tissue were found ~~xx~~ in this (Fig: 9a) On the 5th of October 1900, Dr Edgar performed vaginal hysterectomy. The operation was a difficult one owing to the narrowness of the vagina and the size of the uterus. Clamps were used instead of ligatures. They were removed in 48 hours. Dr Burges states that the uterus was reduced in size by the curettage of 5th September and then rapidly enlarged. The haemorrhages recommenced on the 10th. Just after the operation, the patient

spat up a mass of tough bloody mucus. Microscopically it showed recently shed blood and a considerable number of leucocytes & catarrhal cells. There were no elements suggestive of Deciduoma malignum. Tubercle bacilli could not be detected. The tubes & ovaries were left. Dr Edgar examined them. There was no sign of secondary growths in them or in the veins of the vagina and broad ligaments. Patient was dismissed on the 20th of September, well.

Description of the Tumour.

The uterus was pear shaped and considerably enlarged, measuring in total length 14 c/m, of which 8 c/m was body. The breadth between the tubes was 8 c/m, thickness back to front 6½ c/m. The cervix was lengthened measuring 5 c/m by 3 c/m x 2.2 c/m. The enlargement of the body was directed towards the right cornu and the uterus bulged more in front than behind. There was no sign of tumour externally. A few inflammatory adhesions over the posterior surface had to be torn before removal could be effected. On slitting open the uterus from the anterior surface, the cavity was found to be considerably dilated; the tumour covered the fundus and extended down both the anterior and posterior walls for some distance to within about 2.5 c/m of the os internum. On either side there was a wedge shaped area of mucous membrane, free of tumour, running up into the fallopian tubes, which were quite clear. The tumour was a somewhat dense fleshy mass of dull red colour with a few haemorrhagic patches in it. Its surface for the most part did not appear to be ulcerated. In section, the tumour seemed not to infiltrate the uterine muscles but to lie on it, projecting into the cavity of the organ. Towards the growing edge especially bands of the uterine muscle appeared drawn up into the tumour

(Figs: 1 & 2)

It looked as if composed largely of blood clot with strands of pale pink tissue through it and along the surface of the uterine muscle there was a well defined zone of this tissue mixed with patches of blood, producing an appearance which suggested the site of attachment of a placenta. Microscopic examination showed this to be the growing zone of the tumour; further details are given in the histological report.

The contraction of the uterine muscle was very striking on laying open the organ; it accounts for much of the pouting over-hanging appearance of the tumour in Fig: 1.

The history is somewhat indefinite, but probably the symptoms of September 20th 1900 which were those of threatened abortion, might be taken as the beginning of the case. As early as February 1901, Dr Edgar suspected that he had to deal with a case of deciduoma malignum; the subsequent good health lulled his spspicions, but he and Dr Burges continued to watch the case. The operation was performed 12½ months after the first symptoms of abortion and after about two months of renewed symptoms of uterine disease. After the operation, the patient made a good recovery and enjoyed good health until 29th of May 1902, when, while out for a walk, she had a sudden attack of giddiness. After rest in bed, the symptoms passed off, but on the 5th of June a similar attack occurred, in consequence of which Dr Burges was consulted. As there were no definite symptoms, the patient was placed on tonic treatment. She got quite well, but on the 25th June had a sudden attack of frontal headache with severe retching and vomiting which lasted all day. During the two following days, the patient became

worse, and on the evening of the 27th began to be drowsy, gradually passing into a condition of stupor. She gradually improved and on the 3rd July was quite bright and intelligent, and took food well, but on the following day the symptoms returned. On the 4th the pulse ran as high as 165; temperature rose to 102.5 F. and breathing was of the Cheyne-Stokes type. On the 5th, the temperature reached 104.6, rapid action of the heart continued and the patient looked moribund. On the 6th, there was some improvement. On the 7th, she was very much better, but on the 8th, she again became drowsy. On the 11th, she was quite unconscious. Vomiting occurred repeatedly, and she died on the 14th of July without recovering consciousness. Dr Edgar saw the patient on the 30th of June. The vaginal examination shewed that there was no local recurrence of the tumour. The patient then looked fairly well and was able to speak to Dr Edgar. Although the importance of obtaining a post-mortem examination was pointed out, the patient's friends would not consent to its being made. The termination of the case then is decidedly unsatisfactory.

The occurrence of metastatic tumours in the brain has been determined in 12 cases, those of Jurassowsky, Inglis & Bruce, Busse, two by Marchand, E. Fränkel, Gebhard, Scherer, Tibaldi, Krewer (2 cases) and one of the cases which Professor Weichselbaum allowed me to examine. The symptoms have usually been rather indefinite. It seems therefore fairly probable that in this case the fatal result was due to secondary growths in the brain. In the case of Inglis & Bruce, the cerebral tumours had the appearance of simple cerebral haemorrhages and their connection with the

uterine tumour was demonstrated only by the microscopical examination. In this case, and those reported by Marchand, the presence of deciduoma malignum was not suspected, but the patient died with symptoms pointing to the presence of a cerebral tumour, and the post-mortem examination demonstrated the actual nature of the disease. nil. From the point of view of treatment, the result is in so far satisfactory that she made a perfect recovery and enjoyed 9 months of good health after the operation. The haemoptysis which occurred after the operation was certainly of pulmonary origin and was regarded as probably indicating secondary infection of the lungs. Possibly the amount of manipulation of the tumour may have given rise to embolism, but beyond the sputum there was nothing to suggest this. The character of the sputum reported in several cases was similar.

Case 3. Dr Munro Kerr's. To Dr Kerr I have to offer thanks, not only for the specimen, but for much encouragement and for assistance in obtaining the literature of the subject. Mrs D. aetat 23, was admitted to the Western Infirmary on the 17th May 1902, suffering from pain in the abdomen and haemorrhage from the uterus. There was a history of a miscarriage in the preceding September. In March she was curetted, but a definite history in regard to this was not obtained. After this she states that she suffered from pain in the abdomen and constant bleeding, and felt ill & feverish. On admission, she appeared very x ill. She was very anaemic. On the 23rd of May the uterus was cleared out with the curette and the fingers. Several masses of what were regarded as placental tissue were removed and thrown away without being examined microscopically

Next day the temperature rose to 106 degrees F. but fell within 24 hours and remained normal for about a month. Then it began to shew an evening rise, on one occasion going as high as 105 F. Some septic condition was suspected and intrauterine douching was resorted to. It was followed by a very severe haemorrhage. Deciduoma malignum was indeed suspected. On the 31st July, Dr Munro Kerr, acting for Professor Murdoch Cameron, extirpated the uterus per vaginam. The preliminary examination provoked an extremely violent haemorrhage. The patient appeared almost moribund, but the operation was gone on with and the uterus removed as rapidly as possible, She died later in the day. Post-mortem examination was not allowed and it is therefore impossible to state whether metastasis had occurred. Some hard cords were felt in the vagina which suggested secondary tumour, but it was impossible to examine them properly at the time of the operation. The total duration of the case was 10 months.

The tumour is almost identical with that from the preceding case. It is not quite so large and it is situated towards the right side of the uterus, covering the orifice of that tube. The histological appearances in these two tumours are also very similar. Both of them shew all the characteristic cell forms and owing to the favourable circumstances in which they were obtained, the fixation of the material for histological examination is perfect. The relative amount of syncytium & Langhans' layer cells and of infiltration, and the large sarcoma-like cells varied in different parts of the tumour. The histological description which follows is largely founded on these two tumours although the

sections of the old case and a number of preparations given to me by Professors Marchand and Veit, Drs Schmorl, & Haultain were also used freely. In neither of them were villi present. The uterine mucous membrane in Dr Edgar's case in part had the appearance of an ulcerating surface with few remains of glands in its deeper parts. Probably this was the area which had been traversed by the curette on the 25th of September. In the area which was overhung by the tumour, the surface epithelium was well preserved and many of the deeper cells had the character of young decidua cells. The mucous membrane covering the surface of the tumour was deeply eroded and in parts reduced to a mere layer of granulation tissue or necrosed tissue and fibrin. Changes in the uterine gland or surface epithelium into syncytium, which Gebhard and Marchand have observed in one or two of their cases, I did not find. These two cases belong to the somewhat slow going ones, contrasting with the first one, which is a typical example of the rapidly fatal tumour which originally attracted the attention of Sänger and the other early observers of this disease.

Case III, Dr Elizabeth Pace's. This case, as already mentioned, must be regarded as a doubtful one, but it is of special interest as being one of the connecting links between deciduoma malignum and the hydatidiform mole. No regular case of destructive hydatidiform mole has, as yet, been recorded with proper histological details in Britain; that of Champney[20] appears to have been of this nature, and one of the oldest cases is the classic one of Wilton. The connection of the tumour with the chorionic villi has been directly demonstrated in this country in the case of

Haultain, one of Prowse's (Thesis as yet unpublished) and the case of Inglis & Bruce.

The case of Haultain as will be seen from Fig: 8 & 9, was a typical example of the deciduoma malignum in which a few villi were present. Haemorrhage commenced 3½ hours after the expulsion of a hydatidiform mole. A few days later a large fibrinous mass "not unlike a carneous mole" was expelled. Along with this there was very severe haemorrhage, sub-involution was suspected, and the uterus was cleared out by Dr Haultain. The haemorrhage which accompanied this was so violent that deciduoma malignum was suspected and the material was kept for microscopical examination, with the result that deciduoma malignum was definitely diagnosed one month after the abortion. As the patient had improved greatly within the few days between the curetting and the diagnosis from microscopical examination, she refused further operation, but 7 weeks later a haemorrhage occurred which was almost fatal. After allowing 3 days for the patient to recover somewhat, Dr Haultain extirpated the uterus per vaginam. The tumour was a small one and consisted of blood clot and a few villi shewing the enormous proliferation of the epithelium which is shewn in the figures, and the characteristic infiltration of the uterine muscle and the invasion of the blood vessels. Clinically & histologically, there cannot be the slightest doubt of the malignancy of this case, but, thanks to the early operation, the patient made a good recovery, & is still alive & well. If my third case be accepted, this, and Lewers' case are the only British ones with a favourable termination. I have to thank Dr Haultain for permission to use

Fig: 8 & 9a which are taken from his specimens.

History of case No 3. Mrs McA, aged 23, 2 children, was admitted to the Victoria Infirmary under the care of Mr. Maylard on October 31st, 1900, as an urgent case of haemorrhage following the expulsion of a large hydatidiform mole. At the end of July 1900, while still nursing the youngest child, the patient noticed a little red discharge from the vagina, which she regarded as a return of menstruation. During August, she had occasional slight bleeding with a certain amount of pain. In September, the bleeding became more severe. On October 30th, labour came on with severe bleeding, and a vesicular mole was expelled. The vagina was plugged by Dr Weir and the patient sent into hospital. On the 31st, the plug was removed and the uterus douched out. A considerable red discharge mixed with shreds of tissue continued until the 6th of November when patient was examined under an anaesthetic. At this time she appeared fairly well nourished, but was very anaemic. The uterus was enlarged and could just be felt above the pubis. The fundus felt somewhat thin. On the anterior wall were masses of soft tissue which broke off readily. The cavity was cleared out as thoroughly as possible with the finger by Dr Pace, douched and plugged with iodoform gauze. There was very little bleeding. The right ovary could be felt to be cystic and about the size of a walnut. The left ovary was not felt. The same evening, the patient had a rigor; the temperature rose to 104 F. The gauze was removed and the uterus douched out. The temperature came down at once and remained normal until the patient was sent to the Convalescent Home on the 17th of November.

There had been no red dischaege since the 6th, and the uterus had diminished very much in size. Dr Anderson, Pathologist to the Hospital, reported on 10th of November that the tissues removed were typical hydatidiform mole.

On the 1st of December, i.e. 32 days from the abortion, a bad flooding occurred, which was checked by rest, hot douching and ergot. On the 10th, there was a little bloody discharge which continued, and on the 11th & 14th there were haemorrhages of an alarming character. On the 15th, the patient was brought back to the Victoria Infirmary. The temperature, on admission, was 102.4F On the 16th, under an anaesthetic, the cervix was dilated with Hegar's dilators. The examining finger came upon small soft projections, especially in the left cornu; some fleshy pieces were scraped out with the finger. Some of these were as large as peas. There was not much bleeding. The uterus was thoroughly scraped, washed out with boracic acid and plugged with iodoform gauze. The uterine wall in the region of the left cornu, during the operation was felt to be thin. For 3 days, the temperature remained above 101. On December 19th, it fell to normal and remained so. Dr Anderson reported that the scrapings shewed sarcoma-like elements and epithelial cells which suggested deciduoma malignum. Comparisons with sections from Dr Kelly's tumour strengthened this impression. The patient was extremely weak & anaemic, but as she appeared to be improving, it was decided not to perform any radical operation immediately. But before allowing her to leave the Infirmary, a thorough examination was to be made and she was to be kept under observation.

On the 8th January 1901, 71 days from the abortion and 23 days from the last curetting, this was undertaken. She was prepared for operation if that should be found necessary. There was no discharge from the uterus which was found to be smaller than on last examination, but still somewhat enlarged. The sound on being introduced passed without encountering any but the very slightest resistance for an unusual distance into the abdomen, and was felt presenting against the abdominal parietes. Perforation of the uterus in the left cornual region was diagnosed. Vaginal hysterectomy was at once performed; the ovaries and tubes were removed along with the uterus. The patient made a slow but complete recovery. She reported herself in December 1901, being then in good health. Some time later, pulmonary symptoms developed which were regarded with suspicion and recurrence was feared, but they disappeared and she reported herself recently in good health.

The uterus was expected to reveal on examination deep erosion by a malignant ulcer. Actually it was a very soft, flabby, slightly enlarged organ which, on being slit open, shewed no tumour but only an appearance of having been somewhat recently thoroughly curetted. The sound had passed through in the left cornu quite close to the orifice of the fallopian tube. Sections were prepared from several places, including the seat of puncture. At the last point, nothing resembling tumour could be seen, but there was an area over which the wall was abnormally thin. Owing to the method of preparation, the presence of fatty degeneration could not be properly investigated, but the muscle was very soft, brittle & pale. In one series of sections from a part

on the anterior wall which to the naked eye suggested the placental site, were found a few syncytial masses embedded in the remains of mucous membrane and one or two which had even penetrated in amongst the muscle, and one or two lay free in blood-vessels. The muscle was almost completely denuded of mucous membrane. There was some superficial round-celled infiltration. Nothing else abnormal could be found.

The case was handed over to me for investigation along with that of Dr Edgar, Dr Pace supplying the clinical particulars, and Dr Anderson giving me his sections, and what remained of the curettings of the uterus; From Dr Weir I received the mole. All the tissues had been preserved in formalin solution. The last was a typical hydatidiform mole of large size and very much torn. Part of it had a covering of decidua which was very ragged. Sections prepared from several different parts shewed that the greater part of the villi were necrosed and embedded in blood-clot. Others, however, shewed the typical structures of vesicular mole, the epithelium of some of the villi being considerably hypertrophied in places, both layers participating; but the overgrowth was no greater than, nor in any way different from, that seen in several specimens of innocent hydatidiform mole with which it was compared. In the sections of the curettings removed on the 16th of December, on which Dr Anderson had founded his diagnosis, (Fig. 56.) there were a number of villi, some of which were slightly hydatidiform whilst others were, as regards their mesoblastic cores, quite normal. Most of them shewed very marked hypertrophy of the epithelium; and in some of the syncytium and masses of Langhans'

layer cells there were nuclei of very large size. Here & there in the connective tissue of the villi were large cells similar to the syncytial wandering cells - the so-called "Neumann's cells". The shreds of mucous membrane did not shew the characters of decidua; one or two of the portions included uterine muscle. In the mucous membrane there were no epithelial wander cells, but the shreds of muscle shewed infiltration by these cells in considerable number. With the experience which I then had, I would have agreed with Dr Anderson in regarding the case as probably deciduoma malignum of the variety containing a few villi, and I would have advised extirpation of the uterus. The clinical indications also pointed in this direction.

Cases in which repeated haemorrhage, leading to anaemia and loss of health after abortion ~~from~~ or hydatidiform mole are not uncommon, and these symptoms usually disappear after the retained placental tissues have been removed. In this case, a thorough clearing out of the uterus had been done 7 days after the birth of the mole. The patient had been much reduced by the repeated oozing of blood prior to the birth of the mole, and the severe haemorrhage which accompanied it, and she improved considerably after this operation. 25 days later, there was a flooding, which was repeated 3 times within the next fortnight, and was so severe as to be alarming. The patient became extremely weak and was of a yellowish pallor suggestive of pernicious anaemia or cancerous cachexia. The examination of the uterus revealed considerable enlargement and in its cavity was a soft friable protuberance resembling tumour tissue. All this strongly pointed to malignant disease.

Now, in the light of what was shewn to me on the Continent, and further study of hydatidiform moles recorded in the literature of deciduoma malignum, I would not care to give such a confident opinion. It is clear that one must be most careful in dealing with all cases in which villi are present. Repeatedly it was demonstrated to me that curetting after a simple hydatidiform mole may bring to light villi which are very little different from those found in the fatal malignant moles. It seems at present impossible to draw a distinction between the simple moles and the malignant moles, and chorionepitheliomata, either in respect of their early clinical history or the histological appearances. With a history so suggestive and considering also the undoubted danger of peritonitis after perforation with the sound, there can be no doubt that the immediate removal of the uterus was the right course to adopt. Had this accident not occurred, the comparatively small size of the organ and the absence of discharge, and the slight improvement which the patient had shewn would probably have determined Dr Pace in the policy of delay.

The history of the malignant cases shews that the uterus fills up again very rapidly after curetting. For example, in Dr Edgar's case it was as large as ever within 20 days; in that of Von Franqué in 12 days. In the Hartman & Toupet case, the symptoms recurred within 8 days and in Graefe's the tumour reached the size of a hen's egg in a month. On the other hand, there are cases in which curetting has been followed by a long period of quiescence suddenly broken by the re-appearance of malignant symptoms, rapid development of a tumour in the uterus, metastasis,

and a fatal result; e.g. in Butz's case the interval of quiescence was nearly a year with regular menstruation, yet she died just a year after the curetting. (Compare also the cases of Klien and Krebs).

The condition of the uterus here by no means proves that operation was unnecessary. The presence of masses of syncytium shews that chorionic remains were present which might have developed into a tumour. Whether, apart from malignant disease, such cells would be found 71 days after the removal of the mole and 65 days after thorough clearing out with curette and fingers, is a question to which no definite answer can, I think, be given. Villi, however, it must be remembered, were present 23 days before the radical operation. In a case of vesicular mole which proved to be innocent, Poten & Vassmer found similar cells in the uterine muscle removed with the curette 52 days after manual clearing out.

Probably, therefore, less importance should be attached to those few portions of syncytium than to the clinical history of the case and the report on the second curettings. It is a serious matter to castrate a young married woman, yet when the whole history of the case is taken and compared with those of fatal deciduomata, & when the good subsequent state of the patient is considered, I cannot but feel that the accident was not an unfortunate one.

A similar accident occurred in the case of Marchand (Everke); and in the cases of Menzel and v. Fleischmann, the Recamier blunt spoon was pushed through the diseased uterine wall. In the deciduomata of Gottschalk, Axel, Reinicke, and the malignant moles of Wilton and Gottschall, spontaneous rupture of the uterus in consequence of deep ulceration by the tumour occurred.

The case of Menzel is particularly à propos. A woman of 23 years had 4 full time children in 4 years. All the confinements were perfectly normal. 3 weeks after the last irregular haemorrhages set in, and she wasted rapidly and became intensely anaemic. 6 weeks after the confinement she applied for treatment. The uterus was 1½ times its normal size and of very soft consistence. There was a bloody slimy discharge. The first impression was retention of placental tissue, and sub-involution. Next day the os was dilated and the cavity of the uterus explored with the finger. In the fundus, towards the insertion of the right fallopian tube was felt a ragged depression in the wall which admitted the finger tip. Bimanually the wall could be felt to be thin and palpation was painful. As the finger nail failed to detach pieces for microscopic examination, the Recamier curette was very cautiously applied. Suddenly it perforated the thin spot. It was immediately withdrawn. The uterus was not washed out; - simply packed with iodoform gauze. No particular bleeding nor fever followed. Microscopic examination shewed the tissues characteristic of deciduoma malignum. In consequence of this report, the uterus and appendages were removed next day. Patient made an uninterrupted recovery. 8 months later she was seen again. Her condition had improved vastly, and there were no unfavourable indications. The microscopic examination of the uterus shewed that the depression was a deep chorionepitheliomatous ulcer. The rest of the uterine cavity was already clothed with regenerated mucous membrane. The muscle was soft and shewed among the cells spaces filled partly with loose connective tissue, partly with

young connective tissue and numerous blood-vessels, a condition resembling that described by Gérard (Cent: fur Gyn: 1901 p. 1138) in two cases of perforation as myometritis with hyaline degeneration. Menzel remarks that an examination of the literature of the last 15 years shews that perforation of the uterus is no rarity, and that nearly every busy gynaecologist will have had the experience. With proper treatment it seldom gives any trouble or necessitates extirpation. The warning as to the dangers of the curette is given in every text book, yet the accident occurs in the hands of the most ~~xxxxxxxx~~ skilful and cautious. Menzel concludes that in most of such cases the blame should rest, not on the operator who has taken all reasonable care, nor on the instrument which must often be used, but on the tendency of the uterus under certain conditions to be extraordinarily soft & brittle. Of these conditions the process of involution after pregnancy is a common one, and deciduoma malignum a comparatively rare one. But it is far from being a negligeable one.

Part V.

Histological details.

The specimens in cases Nos. 1 and 2 were obtained immediately after the operations. Portions were at once cut out and fixed in corrosive sublimate-acetic acid fluid. From case II in absolute alcohol and Herman's Platinum-osmium-acetic fluid also. The whole uterus was then placed in Formalin and Salt fluid for conversion into a museum preparation. Sections were also prepared from portions treated in this way, and the fixation of these was found to be tolerably good. Various processes of staining were tried, the most satisfactory being Haemalum & eosin or Haemalum & Van Gieson for the sublimate, alcohol & Formalin tissues. For those fixed in Herman's fluid, Iron haematoxylin gave particularly beaufitul results. Saffranin & Lichtgrün were less satisfactory. Staining for Glycogen was not successful as the alcohol fixed material was lost. The sections were cut by the paraffin process and complete series of considerable length were used.

The four cases which I have examined, while they all present certain special features which either have been referred to in the clinical reports or will be taken up later, correspond so closely in the general histological characters that one description will apply to all of them.

The tumour springs from a broad base and usually projects considerably into the cavity of the uterus. In the Kelly and Teacher, [redacted] and the Edgar cases, there is an overhanging portion projecting into the lower part of the cavity. Into this the muscle seems to be drawn up to some extent Fig: 2. The greater part of

the tumour mass in section is of a dull red colour, fairly uniform in texture and looks like old blood-clot; microscopic examination shews that it is in fact of this nature, but mixed with remains of uterine tissues, and tumour tissue in a state of necrosis. Practically all the central parts of the growth are in this state. Nearer the uterine muscle, the tumour presents a patchy red & white appearance, suggesting placental site in section. This zone consists of tumour masses, some actively growing, others more or less necrotic, mixed with areas of blood which simulate the uterine sinuses. The actual growing tumour for the most part lies between this layer and the uterine tissues and may be seen in places as a somewhat irregular layer of tissue 1 to 2 m/m broad, which is just distinguishable from the muscle by being of a whiter and less glancing appearance. This distinction is too delicate to be properly appreciable in the figure. The nature of these layers was determined by the microscopic examination.

With a low power it is found that outrunners of the tumour burrow deeply into the muscle, especially along the tracks of the blood vessels, loosening it out and pushing layers of it up into the body of the tumour. This may give rise to a somwhat alveolar arrangement of the tumour (Fig: 6) but it is quite irregular & coarse, and totally different from the typical alveolar structure characteristic of carcinoma. Connective tissue stroma or blood-vessels of its own the tumour does not contain. Like its physiological prototype it is a parasite on the maternal tissues and depends for its life on the maternal blood. Masses of the sort shewn in fig: 6. may be found deep in the muscle quite separate from

the main tumour and are, in fact, metastatic tumours. This was recognized in case I but not in case II . Figure 15 represents a section of one of the burrowing processes in the course of a blood vessel; the wall of which was almost completely replaced by tumour. A less advanced stage of this is seen in fig: 12; a small metastasis in fig. 16.

Many of the difficulties that have arisen in the interpretation of these tumours are due to the variety of cell forms which occur. Some of the appearances are due to degenerative changes leading up to necrosis. Others correspond to what is seen in the placenta, which is there presumably physiological, and others may be an expression of the intense activity of the malignant growth. Between these classes of changes in the typical cells, it is not easy to make a sharp distinction. Fig: 6 shews most of the types of cell formation under a low magnification. In this, which was taken from a preparation stained with iron haematoxylin, there is seen to the left the uterine muscle of a lighter colour and shewing only small nuclei and a decidedly fibrous appearance. The darker masses are the tumour which in this place is infiltrating the uterine tissues principally in large masses, giving rise to the irregular alveolar arrangement already referred to. Fig: 7 shews a part of the regular layer of tumour forming the floor as it were, of the malignant ulcer, from about the middle of the growth. It shews in striking contrast the two main types of tumour cells. In both figures it will be seen that there are two principal cell forms,

(1) The syncytium, (syncytia or plasmodia); large multi-nucleated

masses of protoplasm of various shapes & sizes, rounded or oval giant cells, long drawn out bands and whorls and quite irregular sprawling masses. These are frequently riddled with vacuoles which may contain fluid blood and which frequently spin it out into meshworks of very fine threads. Fig: 11. The nuclei are generally small, oval, dense, and stain uniformly and deeply with the ordinary chromatin stain, therein corresponding with the syncytium which is seen in the normal placenta; but not infrequently in the syncytium nuclei of other types are seen; especially there occur large clear & vesicular ones with well marked intranuclear network and one or more nucleoli, and shewing a comparatively light staining appearance. Fig: 15 & 16) Karyokinetic figures do not occur, but appearances suggestive of direct division are to be found. The protoplasm typically shews an opaque appearance and stains deeply with eosin and other plasma stains. The depth of staining varies considerably. The differentiation of the syncytium from the other leading cell form is particularly well brought out by haemalum and Van Gieson's stain. With this combination the colour of the cytoplasm varies from a deep green through lighter shades of green to yellow, drab, and brown. The lighter shades of green are characteristic of tissue which, to judge by the regular oval fleshy vesicular nuclei, are young & active. It distinguishes further the outrunners of syncytium which are found in considerable number infiltrating the adjacent muscle, and differentiates them sharply from the muscle fibres which are stained of a pure yellow colour. (Fig: 6, [illegible]). The syncytial masses in a state of necrosis may be

of a very dark green colour or they may shew more or less of yellow (in some cases brownish); in the advanced stages a pure yellow colour very similar to that which the muscle fibres shew. The nuclei in this condition are small, shrunken, indented, & deeply staining (pyknotic nuclei). Such cells are frequently loaded with fat globules; this appears to be fatty degeneration, though sometimes it is seen in healthy looking masses and may there represent the physiological fat of the normal syncytium.

Examined with an oil immersion objective, the cytoplasm presents the characteristic of a sponge work or foam (alveolar structure.) (Fig. 22) This varies greatly in its fineness, being extremely close in the younger masses, while in those which are older and especially some of the much vacuolated masses, it is quite a coarse sponge work. This is totally different from and independent of the vacuolation. An appearance which is not infrequently observed is that along the borders of haemorrhages, where the tissue had been pushed aside and stretched the meshwork is drawn out so as to simulate the longitudinal fibrillations of the muscle cells, but it is far less fine and delicate and wants the regularity which these present. Some of the syncytial masses among the muscle are very fine and long drawn out and through being of somewhat paler colour than the parent tissue in general give rise to the impression that they might be modified muscle cells. (fig 6. 4h.cm) The origin of sarcoma cells from uterine muscle is well-known and doubtless it was appearances such as those described above that led Menge, and recently K. Winkler to regard the deciduoma as a sarcoma originating from uterine muscle. Whittridge Williams, who was

one of the first to trace this origin of sarcoma cells, also was at first inclined to regard his tumour as a sarcoma originating from the uterine muscle and did describe it as such in his preliminary note, but subsequently recognized and pointed out this error. Isolated mono-nucleated cells with protoplasm identical with that of the syncytium are also seen. These will be discussed later.

The modifications of syncytium which were observed in the tumour, I have been able for the most part to trace in the normal placenta or in hydatidiform mole which did not give rise to a malignant growth. The large size and character of the nuclei in the syncytium must be regarded as an evidence of extreme activity and in a question of diagnosis, I would regard it as abnormal. They cannot be regarded as a sure sign of malignancy, for they are seen in innocent hydatidiform mole and in young trophoblast of ova, such as the Peters, and the Siegenbeek van Heukelom ones. The so-called "ciliated" border is frequently very beautifully shewn in the tumours. Fig: 17.

(2) Individual well-defined mono-nucleated cells which in a case containing villi are seen to be derived from the Langhans' layer, (Fig: 8 & 9). These usually form masses of some size intimately united with the syncytium. The regular relationship which is seen on the villi where the syncytium fomms a thin layer enclosing the individual cells, is also observed in the tumour, but in general the relationship between the two is irregular; it is an exaggeration of what is seen in the cell knots and epithelial expansions at the attachment of villi to the decidua. Where the

tumour is in contact with the maternal tissues, the syncytium, just as in the placenta, appears at the sides of the cell masses, and the individual cells are seen in actual contact with muscle or whatever the tissue may be, and even to some extent, infiltrating it. (Fig: 13: 23:). The syncytium may form a mere endothelium -like edge to the cell masses or it may be a broad border and also send in irregular processes among the individual cells. (Fig: 6, 7, 10, 11 etc.) Remains of connective tissue, amidst the tumour cells, as fine shreds of a bright red colour (fig 12) are frequently to be seen. (fig. 23.) The individual cells in the youngest stage are small, polyhedral in shape, & closely packed together. Fig: 8 shews at once their source of origin and their character. The nuclei are round or oval, clear, vesicular, with well-marked intranuclear network, large nucleoli and stain moderately deeply. Relatively to the cell-body, they are very large. The cytoplasm with a low power is clearer than that of the syncytium and does not stain readily with eosin. In a haemalum and Van Gieson preparation, it has a somewhat greenish gray colour, (Fig: 10) and is not very clear. With a high power, the opacity is found to be due to the presence of a darkly staining fine close reticulum - this is quite unlike the alveolar structure of the syncytium. (fig. 19. 20) The older cells are clearer and larger and their edges are sharply defined; in the way they are packed together they are characteristically epithelial cells. The reticulum is opener and less deeply stained; the nuclei are larger but the cell bodies are relatively still more enlarged. Multiplication is by karyokinesis. (fig. 8. 19. 20) The karyokinetic figures are perfectly regular, and multiple mitoses were not observed. Their

number varies greatly in different fields; in fig: 8 they are numerous. The cells in division are large and clear, the reticulum is very open and looks at first sight as if retracted from the figure; (fig 19.) actually in this part of the cell it is so fine as to be almost invisible.

(3) Large cells of very varied shapes and sizes which do not conform to either of the types already mentioned. They are large cells and contain from 1 or 2 to 10 or more nuclei. They occur under two conditions

(a) In masses which in the section are either attached to the uterine wall or may appear as if lying detached amid blood (fluid or clotted) or they may be imbedded in fibrin (Fig: 10)

(b) Infiltrating the maternal tissues. (Fig. 13. 14. 23.)

These are the cells which have given rise to most of the differences of opinion in the interpretation of the tumour, and their origin and relations have been described ad nauseam. The continuity of them with the first two classes of cells of the ordinary tumours and with the epithelium of the villi in the cases in which these are present is plain. They correspond to the cell knots and the expansions at the tips of villi; and the infiltrating epithelial wander cells which over & above the regular syncytial wandering cells have been referred to in part III. (Fig: 3. 4b. 4c.). But the variety of cell forms and the degree of infiltration of uterine tissue is far greater than can be seen in ordinary preparations of the placenta. In the masses of hypertrophied epithelium of innocent hydatidiform mole (fig 5a.) the variety

of cell forms is more closely paralelled so that a sharp line of distinction on these grounds is impossible. The relationship to adjacent tissues is also an exaggeration of what can be found in the normal placenta. There they are usually shut off from the decidua by the canalized fibrin layer (Fig: 3 & 4.) or if they are infiltrating it, the degree of infiltration is small (Fig: 4b). They may be found at the mouths of blood-vessels, attached to their walls or even under the endothelium. Cells of this class deep in the uterine wall, I have not seen: only the wandering masses of syncytium passing beyond the layer of decidua cells.

In the hydatidiform moles which have been examined in situ, however, an increased amount of infiltration is characteristic; so that here again no sharp line can be drawn. Cells of all sorts which can be traced to the chorionic epithelium are found deep in the decidua and even well in among the muscle.

In case I quite typical young decidua cells were found near the border of the tumour where the overhanging edge had protected it from the curette. (fig. 24.) There were no tumour elements in the decidual portion. Along the edge of the tumour, the tissues for the most part shew a certain amount of inflammatory reaction. The blood, both in the vessels and extravasated among the tumour whether fluid or clotted, contains a high proportion of leucocytes principally polymorphonuclear. Many cells of this class are seen in among the tumour cells (of all sorts) and many of them are seen actually within tumour cells; these frequently lie in vacuoles and present degenerative appearances; i. e. the syncytium and the large cells at present under consideration show

phagocytes properties.

The invaded maternal tissues may be uterine muscle or connective tissues or blood-vessel walls. Masses of tumour cells among the muscle fibres are not infrequently seen; occasionally tumour cells appear to be actually embedded in the muscle substance; but for the most part the muscle in the immediate neighbourhood of the tumour has atrophied and disappeared before the invaders reached it in any number. The tumour cells therefore lie principally in connective tissue, which may have a ragged eroded appearance and shew hyaline degeneration, or may have been converted into granulation tissue. The former is represented in fig: 23. H. P. photo) where shreds of connective tissue without many nuclei and rather hyaline in character are seen permeated by the tumour elements. The granulation tissue character is seen in fig: 13 and fig 7.

In such places the tumour has quite the look of an infiltrating sarcoma, but the character changes at once when you follow it back to the cell mass; there is no trace of connective tissue stroma among the cells there and no blood-vessels.

The mixture of cells in the infiltration zone is a very complex one. By the exercise of diligence one could construct an unbroken series of intermediate forms between the huge tumour cells and almost any of the neighbouring tissues, mesoblastic or epiblastic, and found thereon a theory of origin, but such a process is not comparable with the obvious continuity between the typical tumour masses and the infiltrating elements. (Fig: 6, 7, 13, 14) The resemblance to the decidua cells is slight.

On the other hand, the same tissue which develops into decidua when it develops into a sarcoma shews elements not unlike the chorionepithelioma, but the resemblance is only to the one part of it; when the whole is considered, the tumours are utterly different. The photographs on pl. XIV. shew the differences between decidua, sarcoma, and the infiltrating tumour better than any description. See also part VI. The nuclei of the decidua cells (Pl. XII. fig 24) are much paler than those of the tumour cells, the intranuclear network is less developed, and they are smaller both actually and, still more, relatively to the cell bodies. The cytoplasm of the decidua cells of tumour No 1 is very similar to that of the clear individual cells; the reticulum is very delicate; it had not attained the closeness and opacity seen in older decidua cells. Both classes of cells are described as containing glycogen. This I was not able to investigate. There is no fat in the decidua cells, whereas many of the others contain a few minute globules of it. Apart from these differences in details, the general look of the two tissues is quite different. The decidua cells also plainly arise out of the connective tissue corpuscles. The typical small Langhans' layer cell is usually confined to the cell masses. All the infiltrating cells are more or less enlarged. Many of them are exactly like the larger clear well-defined derivatives of this layer already referred to, but karyokinetic figures in the zone of infiltration are rare. For the most part the cells are much larger still. It is as if the cells invading the maternal tissues had laid aside their reproductive faculties and taken on an exaggerated vegetative

growth. Thus many of the mono-nuclear cells are of very large size, 6 or 7 times that of the parent cell, and have correspondingly large nuclei which may contain a very large amount of chromatin. The contrast between these cells and the leucocytes in fig: 11 & 12 indicates their enormous size better than any measurements. In many of them again the nucleus has divided, and the cytoplasm also shews changes in the direction of that characteristic of the syncytium. Lastly, many of the infiltrating cells are typical syncytium. These changes are better appreciated in the cell masses where there is no interstitial tissue to complicate the picture.

Fig: 10. shews a typical mass of these large cells. None of the smallest Langhans' layer cells appeared in the field drawn; but they are seen just outside of it; at the lower part are several of the somewhat enlarged ones. In the centre is a giant cell containing eleven nuclei in a clump in the centre; other cells in the mass contain 2 or 3 nuclei. With increase in size of the cells there is also a change in the character of the cytoplasm: the reticulum becomes closer and more opaque and stains more deeply and also changes from the grey tint of the typical Langhans' layer cell to light green or greenish yellow. Karyokinetic figures are rare in these large cells, but I have seen typical examples of them alongside cells of similar character (fig. 21.) which contained two or more nuclei; I regard this as evidence of direct & indirect nuclear division occurring side by side in cells of common stock which are diverging into different lines of growth. Sharply contrasting with these cells are the dark

processes and masses of syncytium seen in the figure, but in other similar cell nodules further stages intermediate between the giant cell in the centre and the dark green alveolar vacuolated syncytium shewn in fig: 11 can be readily found. This progression is less easily followed than that from the Langhans' layer cell into the giant cell. The intermediate forms are not to be found all in the one clump of cells. The continuity of the series is however very plain.

Besides the forms of intermediate character, there have already been mentioned individual cells with one or two or more nuclei and dark cytoplasm typically of the syncytial order; these are seen here & there in free masses as well as infiltrating. Their relations to the syncytium are not always that of cross sections of bands, as Williams originally supposed. They appear to be produced by giving off of numbers of very small syncytial buds - a direct proliferation and breaking up of the syncytium.

Among all these forms then one arrives at the position of other observers viz:- that it is impossible to tell where Langhans' layer ends and syncytium begins. Whether it is legitimate to regard this as homologous with the process of development of the syncytium out of the primitive individual cells as it occurs in the normal placenta or of the trophoblast, or whether it is a peculiarity of the tumour, is another matter. In my opinion the problem of the formation of the syncytium is the problem of the origin of giant cells in general, and the evidence of the tumours has some value.

Long before Fränkel stated his conclusions that many tissues

of the human body were ~~exclusive~~ inclined to form syncytium (or take on a syncytial form) besides the chorionic epithelium, this was a vexed question of histology. The statement therefore is quite a valid one; but the conditions under which, and the steps by which, syncytium formation occurs are obscure. Peters sees in the trophoblast of his ovum all the intermediate cell forms (p. 48 of this monograph); they are plainer there than in any other normal trophoblast I have seen; his conclusion that the individual cells adjacent to the chorionic mesoblast are the primitive type out of which all the other forms arise has been mentioned. I hold it justified. I am aware that Professor Peters is engaged on a fresh cell stucy of the re-stained preparation; criticism of his original description might perhaps therefore be left to himself. But with regard to the suggestion that the syncytium originates by a flowing together of the outer layers of the individual cells of the trophoblast in contact with the maternal blood which exerts some corroding influence on the cells & causes them to lose their distinct outlines (p. 50) I must express my doubts. Evidence of such flowing together to form syncytium, I do not find in the tumours. This would correspond to the formation of the symplasma in the maternal tissues round the guinea-pig ovum which von Spee describes and which appears to be a degenerative process; I see nothing like that in my tumours.

On the contrary, the large cells of the tumour closely resemble the giant cells of the trophoblast of various animals, e.g. Tarsius spectrum (Pl IV. fig 4m.), the development of which by growth and nuclear multiplication of the primitive polyhedral cells of the trophoblast

without division of the cell body can be followed in all its stages. I believe the development of the syncytium of the human placenta is of the latter nature and not a process of fusion of originally distinct cells. The giant cells then either spread themselves out round the individual cells, or the latter become invaginated into the former; either way the arrangement characteristic of the later stages of the placenta (human or Tarsius) is attained. I look forward with interest to the results of Professor Peters re-investigation.

Besides the breaking up of the syncytium into the individual cells already referred to, the differentiation of cells having the characteristics of Langhans' layer cells within the syncytium has been described by various observers. A nucleus becomes surrounded by a clear space containing a delicate reticular cytoplasm and sharply defined from the syncytium. A very common appearance in my specimens is of a few such clear individual mono-nucleated cells completely surrounded by syncytium. Where this forms part of a tumour mass, it is reasonable to infer that the explanation of the appearance is the invagination of Langhans' cell derivatives into the mass of syncytium. I was unable to satisfy myself that it occurred in pieces of syncytium which were quite detached. Fig: 17 is unfortunately from the end of a series. The free tumour cells in blood-vessels were almost always syncytium only. Potential emboli containing both, I did not find; but processes of tumour containing both which looked as if they might easily get detached are plentiful enough. That the masses of plain syncytium can attach themselves to the wall of a vessel and grow

to some size is proved by the subject of fig: 16. That it was actually detached, was proved by tracing it through a considerable length of a series and that it had grown in situ was indicated by the fact that the branch of blood vessel on either side of it was very much smaller than ~~that~~ it. ~~[illegible]~~ It contains no individual cells, but, apart from that, it has quite the look of a commencing tumour. If it were so, the endogenous formation of Langhans' layer cells from syncytium would be proved. I have to leave the matter open. Probably only a few of these syncytial masses in the vessels ever become tumour nodules, the bulk of them disappearing like the deported syncytium & villi of the normal placenta. Many of them are in an advanced stage of fatty degeneration. Exactly ~~xyx~~ similar syncytial masses occur much more frequently in the immediate neighbourhood of the growing tumour lying not within blood vessels but in the interstices of the tissue, yet, as mentioned above, the invasion of the lymphatics, and the secondary infection by lymphatic glands is quite the exception in this form of tumour.

The relationships between the different cell forms in the tumour and in its physiological prototype then are as follows:-

(1) The primitive type from which they all originate is, of course, a mono-nucleated cell;—the undifferentiated blastomere. In the differentiated trophoblast or chorionic epithelium, it is represented by the individual or Langhans' layer cell. The syncytium develops out of these by growth of the cell and division (amitotic) of the nucleus without division of the cell body; i.e. it arises by a proliferative process and not by the

fusion of pre-existing distinct cells.

(2) Both the Langhans' layer elements and the syncytium have each an extensive power of growth into cells of their own type. They are thus in a sense capable of independent development although they usually grow in intimate association. This is shewn in the continuance of the syncytium after the disappearance of the Langhans' layer in the later months of pregnancy. Also the syncytium gives off buds which may be mono-nucleated or multi-nucleated, and preserve more or less exactly the cytoplasmic characters of the parent tissue (the wandering cells).

(3) A regression of syncytium into Langhans' cells possibly occurs by the differentiation within the former of clear cells which have the characters and mode of multiplication (mitotic) of the latter.

. The degenerative changes are less interesting than the proliferative; yet they are important, for in a portion of tumour scooped out for diagnostic purposes, degenerated tissue is fully more likely to be obtained than fresh. The principal in the individual cells are retraction of the cytoplasm from the nucleus, crushing together of the cells producing an irregular spindle shape, shrinking of the nucleus and loss of the distinct intra-nuclear structure. The cells may also become loosened out in other cases. The syncytium preserves its recognisability longer; indeed, in degeneration the distinction of the two layers becomes lost. Thus, if there is any living tissue, it will probably be a mass of large cells of very various sizes and shapes up to the large syncytia. The appearance suggests malignant growth of some sort.

. The tumour appears to have a special affinity, on which

some of its most characteristic features depend, for the blood-vessels. Several more or less distinct types of invasion of blood-vessels, which were all described by Marchand, are recognisable in my specimens.

(1) The tumour grows into the mouths of the uterine sinuses, attaches itself and invades them from within (Fig: 12) just as the detached masses already referred to attach themselves.

(2) The advancing tumour attacks the vessel from without destroying and replacing the wall, (Fig: 7). When it reaches the endothelium the tumour cells tend to spread along just under it for some distance, so that the vessel may come to have the appearance of a tube of endothelium in a sheath of large tumour cells. (Fig: 13, 14 & 15). Sometimes a plug of tumour regularly invaginates the endothelium into the lumen. The invaded blood-vessels (at least those attacked from within) dilate (fig. 16.); this peculiarity is particularly striking in the vaginal metastases which are usually taken to be varicose veins; this is referred to in the summary of case Kelly & Teacher, at the beginning of Part V. Finally the endothelium disappears or gives way. When this occurs, on the one hand the tumour cells enter the vessels and on the other extravasation occurs into the tumour.

Marchand and other observers have attributed to the invading tumour elements a blood clotting influence. Peters on the other hand believes rather that they have the power of preventing coagulation, a power which I attributed to them in 1898. Their action perhaps is not very different from that of the endothelium which they replace, or of the syncytium of the intervillous space.

Probably the clotting or remaining fluid depends on the amount of blood which has been extravasated and the amount of damage that has been done to the tissues into which it has escaped. In Fig: 13 there is a thrombus where the endothelium is just disappearing; but in other sections of this series there is clear evidence of extravasation having occurred, and further out in the tumour there has been clotting. There is also a shred of thrombus in Fig: 12. On the other hand there is no sign of it in Fig: 16, or in the vessels in the middle and at the top of fig: 7. An active power of hindering clotting, on the other hand, seems doubtful. The outlying masses of tumour are usually imbedded in clot or surrounded by a layer of fibrin. The same is seen in abortions where a large haemorrhage into the placenta leads to clotting. Here, there has been a gross laceration of tissue, a lesion which is usually followed by clotting, no matter what tissues are concerned.

Whereas in the normal embedding, the vessels which are opened by the trophoblast or burst into it are only capillaries or very small veins, in the tumour veins of very considerable size may be seen with their walls completely destroyed. The thick walled arteries as a general rule appear not to be much affected by the tumour. These relationships explain at once the violent haemorrhages which are such a characteristic feature of the growth and the metastasis by the blood stream, and the tendency to degeneration and necrosis of the cells.

Part VI.

The Chorionepithelioma of Teratomata.

The fact that tumours identical with chorionepithelioma in structure was first noted by Kanthack and Eden under the ~~xxxxx~~ circumstances already referred to; but Schlagenhaufer cites two cases of "Sarcoma of the testis" in the description of one of which Langhans' compared the structure to the Chorionic Villi, and in the other the description by Malassez and Monad is almost exactly that of chorionepithelioma, but both of these occurred when that was yet unknown.

By the kindness of Dr Eden, I saw some of the specimens which he and Kanthack shewed to the Committee of the Obstetrical Society of London; in my opinion "the secondary tumours in the liver and lymphatic glands" are indeed histologically identical with secondary tumours from an ordinary chorionepithelioma. The primary tumour presents a very different appearance. The case, so far as I am aware, has never been reported in detail notwithstanding that it was one of the principal factors in bringing about the decision of the Society and its Committee. Indeed the occurrence of such tumours apart from pregnancy was the most telling point in the case of the opponents of the new views, and the only one which was not capable of explanation there & then. Chorionepithelioma in the uterus apparently quite independent of pregnancy has also been observed by Lubarsch. The history is as follows:

An exploratory laparotomy in a girl of 13 years who had never menstruated revealed a large tumour which appeared to grow

from the uterus. Owing to widespread adhesions, extirpation was not performed, but portions were removed. The growth to the naked eye, and still more on the microscopic investigation, resembled chorionepithelioma so closely that Lubarsch described it as a "double" of that tumour. Before he knew the history of the specimen, he had indeed no doubt that he was investigating a chorionepithelioma. The patient was unfortunately taken away by her friends and the case could not be fully investigated.

Schlagenhaufer remarks that "these are two concrete cases which with full knowledge of the chorionepitheliomatous tumours could be advanced as evidence on the one hand against the specific nature of these tumours, and on the other hand against the prevalent opinion that they originate from the epithelial covering of the chorion".

To them may be added a third observed by Bock in which a typical hydatidiform mole was passed by a virgin of 12½ years.

The patient, who had always enjoyed good health, menstruated for the first time at the age of 12 years & 2 months. The flow was moderate in quantity, contained some small clots and was painless. With rest in bed it ceased after 8 days. The second was accompanied by pains in the region of the kidneys and very little discharge. On the second day a clot enclosed in a whitish membrane was passed, and the pain then ceased, and the discharge flowed in a normal manner for 4 days. The third menstruation was also painful and clots representing casts of the cavity of the uterus were passed. The fourth, still more painful. resulted in the passage after three days, of a typical hydatidiform mole about

the size of a walnut. It consisted of a circular membrane 3-4 mm. thick, about the size of a two francs piece, from which hung a series of strings of vesicles varying in size from that of a pin head to that of a pea. Dr Bock informed me that there were 20 to 30 such strings. The specimen was apparently examined with the microscope in the fresh state only; and it is no longer in existence; but there appears to have been absolutely no doubt as to its nature. The patient has menstruated regularly and without trouble ever since. She is of good family and her parents gave absolute guarantee that so far as careful surveillance was concerned she was a virgo intacta. The physical examination and circumstances of the case - the regular menstruation for the four months - also go against any idea of pregnancy having occurred. Bock suggested that the mole was a "foetal inclusion".

Before taking up the cases of Schlagenhaufer the sense in which the term Teratoma is used must be explained, as it bears a somewhat different significance in English and in German scientific writings. Bland Sutton reserves it for such tumours as clearly arise from the remains of an included foetus.

German authors, of whom Marchand, Bonnet & Wilms may be taken as representatives, use it in a much less restricted sense. The position is most briefly and systematically stated by Marchand. The symmetrically formed but unequally developed double monsters are excluded from the teratomata. There remain the true parasitic monsters - implantationes or inclusiones foetales, in which the united Anlagen are in form, size and reciprocal relations quite unsymmetrical; the parasite is as a rule quite rudimentary, very

irregularly developed and quite dependent for its nourishment on the other (autosite). These are divided into two groups:-

(a) Intra-amniotic, including the parasites of the anterior end (epignathus) which are attached to the surface of the head, more rarely included within it, and the sacral teratomata;

(b) Extra-amniotic and enclosed by the closure of the body cavity i.e. within the thorax or abdomen (coelom-parasit) or from there developed in the tissues of mesoblastic origin.

"To the foetal inclusions are connected without sharp boundary line the so-called Dermoid cysts which are commonly reckoned as tumours. Firstly, a distinction must be made between

(1) Those forms which arise through sequestration from the skin, and therefore consist of a simple sac clothed with skin, the walls of which occasionally contain cartilaginous, bony or glandular tissues; these are without difficulty explained as dislocations of rudiments of organs in the neighbourhood. Such are the dermoids one finds on the head and neck in the region of the primitive branchial clefts, in the skull and in the mediastinum;

(2) Dermoids or teratomata consisting of a complicated agglomeration of tissues which occur almost exclusively in the sexual organs, especially in the ovary, much less often in the testes."

Most of the tumours in the last class, Bland-Sutton would term dermoids, and would derive all their structures from pre-existing tissues of the person that bears them. Especially he lays stress on the fact that the predominating elements are epidermal structures and he regards the tall columnar epithelium of the graafian follicle and the adjacent ovarian stroma as capable of giving rise

to them all. On the other hand, Marchand, Bonnet & Wilms have demonstrated in these tumours representatives of all three embryonic layers. They regard them as representing a three-layered blastoderm (Keimanlage) which is formed after the fashion of a human foetus; whereby the first differentiated tissues and organs,- viz:- the epiblastic ones and the head region come to predominate. They would be, then, "rudimentary ovarian parasites". The same hypothesis they apply to the solid mixed tumours of the ovary, and other organs. On it most at any rate of these complicated tumours originate not from the tissues of the organism which encloses them, but from some included cell which has the morphological value of a matured and fertilized ovum. Either at once (congenital tumours) or after an interval (mixed tumours of later life) this develops into an imperfect organism - a teratoma or embryoma.

Into their transcendental speculations as to the nature of this cell, it is not possible to enter more deeply here. The facts on which the theory is based can be found in the works already cited. Nor can the interesting speculations of Dr Beard of Edinburgh on the origin of tumours in general be considered. In view of the ascertained facts, then, I regard the German classification of the whole series of tumours as the more logical, and the theory of origin as not less probable than that of Bland Sutton, with whom may be coupled Bandler. Both views contain a very large element of speculation.

In ovarian dermoids occasionally quite complicated structures have been seen in addition to nearly all the tissues of the human body;—

fat, etc. cartilage, bone, teeth, glands of various sorts, mammary gland, breast warts, fingers with nails, striated muscle, portions of central nervous system, pigmented epithelium identical with that of the retina have all been observed in them. Occasionally dermoids of the ovary behave as malignant tumours. The mixed tumours of the kidney and testis have a bad reputation in this respect also. Malignancy of sacral teratomata is not unknown.

The tissue which behaves in this way may be sarcomatous or carcinomatous. In the malignant congenital sacral tumour observed in Glasgow by Coats, which I have re-examined in the hope of finding chorionepithelioma, a large part of the primary tumour and the secondary growths in the lumbar lymphatic glands present the characters of carcinoma. A remarkable tumour is the teratoma of the ovary described by Saxer (which he very kindly shewed to me) in which the malignant growth was embryonic nervous ("neuroepithel") tissue. When so many structures can be found in these tumours, it is not surprising that chorionic tissues should occasionally occur. Nor is it surprising, in view of what we know of them in their normal seat, that being there they should manifest malignant activity.

Schlagenhaufer's first case.

A man of 43 years, from whom no account of his illness was obtained, died on 24th July 1900. The diagnosis was leftsided pleurisy and pneumonia, possibly infarction of the lungs. The post-mortem [redacted] diagnosis was Sarcoma of the left testicle, with metastases in the left lung, thyroid gland, and right kidney. Perirenal haematoma from haemorrhage in the renal metastasis and perforation of the capsule of the kidney.

The tumour which was received after hardening in 5% Formalin was of roughly oval shape, measuring 11 by 8 cm. It was enclosed in a firm white connective tissue capsule from which tense bands passed in, dividing it into several lobules. Testis and epididymis were not recognizable to the naked eye. In section the tumour consisted of a brown red crumbly tissue. Only in one more fibrous part were some little cysts to be seen, which were empty or contained a glancing white material. It resembled, in fact, an ordinary uterine chorionepithelioma after hardening. The pulmonary metastases were indistinguishable from secondary nodules of chorionepithelioma in the lungs. Schlagenhaufer's very clear description of the histological characters may be summed up so far as most of the primary tumour and the whole of the secondaries are concerned, as, identical with those of chorionepithelioma to the last detail. (Fig: 26b, 26c.) The relations of the two elements to the blood vessels were particularly clearly made out. The chorion-epitheliomatous tissue and blood clot made up most of the primary tumour, but the cells were well preserved in only a small part of it. (This may be contrasted with Schmorl's case where the chorionepithelioma was found in only a very small area of the primary tumour although the secondary growths were very extensive, and with Wlassov's first where out of ten large pieces he found it in only one) In addition, the primary tumour contained at one part round the edge long-drawn-out flattened tubules lined with columnar epithelium one or two cells deep, evidently remains of the rete testis. Near these, but more into the middle of the tumour were found cavities filled with horny stratified epithelium

and epithelial pearls. Dermal appendages were wanting. Larger cysts with cylindrical epithelium were also seen, and in one place tissues resembling embryonic lung, lymphatic follicle, young connective tissue and involuntary muscular fibre. Clearly, he says, we have to do with a teratoma of the testis; all three layers of the blastoderm and the trophoblast are represented. The enclosing albuginea and the testicular remains prove that it was a tumour of the testis itself. The secondary tumours on the other hand were pure chorionepitheliomata, the malignancy being confined to the representatives of the trophoblast (or chorionic epithelium). This corresponds to what is commonly seen in ordinary chorionepithelioma, where the metastatic growths are usually purely epithelial even when villi have been present in the primary.

In Schlagenhaufer's second group, not merely were there cells corresponding to the epithelium of chorionic villi, but there were also mesoblastic tissues - in fact, if the theory of origin be admitted, whole villi, mostly in a state of hydatidiform degeneration, and the case would be not inappropriately described as one of malignant hydatidiform mole in the male. He has collected five cases in which structures resembling hydatidiform mole in their naked eye characters have been found in the blood vessels in connection with tumour of the testis. These were described as peculiar myxomata by Waldeyer and by Breus: as carcinoma by Kanthack and Pigg, as adeno-carcinoma myxomatodes by Silberstein, and as lymphendothelioma by MacCallum. Breus' case is that which Schlagenhaufer has re-examined. It had lain 20 years in 60% spirit and the microscopic preparations are therefore not good, but they are fairly distinct.

History from Breus' original report. W. H. aet 40, had noticed for 6 weeks a distinct & painful swelling of the scrotum and complained of great difficulty of breathing and pains in the whole right side of the body. Examination shewed a hard tumour of the right testicle; locally diminution of the pulmonary resonance and râles; cardiac area normal; weak apex beat; a loud double murmur at the apex; tenderness of the lower part of the abdomen. The tumour increased in size very rapidly and he died 4 weeks later.

The lungs were studded with secondary growths, some exactly like the secondaries in a case of chorionepithelioma, others more like infarctions; the latter class shewed emboli consisting of plugs of the villous processes in the vessels supplying the areas. In the left auricle, hanging from the region of the fossa ovalis a "gelatinous bunch of grapes like new growth which might best be compared to the vegetations of a hydatidiform mole" Fig: 26. Waldeyer also compared the growth in his case to hydatidiform mole. The testis and epididymis were easily shelled out of the scrotum; they formed a tumour about the size of a fist and consisted of a firm fibrous meshwork enclosing cysts. From the upper end of this stretched the thickened spermatic cord, the dilated veins of which were filled with long string like growths that extended right up into the right auricle and through the foramen ovale into the above described mass. Nowhere was the growth adherent to the walls of the veins. This condition is paralelled in the malignant mole of Solowij and Krysztkowski in which similar masses mixed with clot extended up the spermatic veins to the vena cava. MacCallum's case is extremely like

Breus's; he described the intravascular growths as follows:- "These curious growths resemble nothing so much as the villi of the hydatidiform mole". Fig: 26g. MacCallum regarded his tumour as of endothelial origin. On the other hand, Schlagenhaufer not only could not trace the origin of his to endothelium, but he saw destruction of the blood-vessels just as in chorionepithelioma. The villous masses shew the structure of hydatidiform chorionic villi including the characteristic two layered epithelium; but this was not made out without considerable difficulty owing to the bad preservation of most parts. Further, the manner in which the villi were pressed together in places resulted in an appearance like tubules lined with a peculiar epithelium embedded in a fibrous stroma; appearances which suggest a resemblance to that described by Wlassov. There were also real glandular tubules in these masses, which indicated their teratomatous nature. The occurrence of the whole of the chorionic villus is explained by the embryonal anlage having early gained access to the interior of veins, where the placental portions of it found space and suitable conditions for luxuriant growth.

Soon after the publication of Schlagenhaufer's paper appeared another by Wlassov in which four more tumours of similar nature were described. Wlassov came quite independantly to the same conclusion, viz, that the tumours were teratomata. He takes, however, a different view of the origin of the chorionepitheliomatous tissue, which he believes he has traced to the epithelium of the glandular tubules in the tumour in two of his cases. Following the strict theory of the teratoma, he would have regarded it as

derived from an actual monstrous trophoblast, and did so at first. In his tumours there were no epiblastic structures, but only hypoblastic and mesoblastic were present. On this account, he considers the trophoblastic origin an unproved hypothesis. (This was writing without knowledge of Schlagenhaufer's work). He sums up the tumour as an epithelioma sui generis of the testis developed out of the incompletely differentiated epithelium of embryonic gland tubules; - not tubuli testis; — these he sees undergoing destruction. The mesoblastic tissues are not the stroma of a carcinoma, but the product of the mesoblastic part of an embryonic anlage. They do not re-appear in the secondaries, which are composed only of the epithelial elements just as in the case of chorionepithelioma.

At Carlsbad, sections of another tumour of the testis were shewn by Schmorl and yet another was referred to by Bostroen; the latter, however, occurred not in the testis but in the pelvic connective tissue of a man. It was also suggested that the case of Kleinhaus, of chorionepithelioma in the ovary, might be of this nature, instead of an ovarian pregnancy. None of these cases has yet been published in detail.

Another testicular tumour of this class was shewn to me by Marchand, but I am not aware that it has reached publication yet. It has also been suggested that some of the tumours already described as chorionepitheliomata are of this nature; this might well be the case in such as that of Busse, vide table.

In the end of last year, L. Pick described a "cystic teratoma; so-called dermoid cyst" of the ovary in which "instead of

chorionepitheliomatous tumour or metastatising hydatidiform mole was a hydatidiform-mole like growth of innocent type". Pick suggests that such tissue may occur in most of these tumours, but in such small amount that it has been overlooked. Lastly, by permission of Dr Ritchie of Oxford, I am able to refer to a case which will be published shortly, of malignant dermoid of the anterior mediastinum in a man. In this case, a tumour of considerable size occupied the anterior mediastinum and the lungs were studded with large growths of typical chorionepitheliomatous aspect. There were also many metastases in other organs. The primary tumour consists principally of tissue identical with chorionepithelioma in which the Langhans' layer elements predominate. Fig: 26a. Cysts lined with horny stratified epithelium and containing hairs also occur and tissues of mesoblastic origin. Probably we are only at the beginning of a controversy as to the nature of these curious structures, but in the meantime the view of Schlagenhaufer holds the field. The theory of Wlassov is no less open to objection than that of Schlagenhaufer; and against it is the fact that no exact imitation of chorionepithelioma by tumour derived from glandular epithelium has yet been discovered. The histological details of Schmorl's tumour are not yet published but the sections shew gland tubules and in the small area which is all that presents the placental anlage, there is something very like a gland tubule from which the tumour evidently is springing. Fig: 26d. But the epithelium of this and the connective tissue below it resemble strongly a portion of a

chorionic villus, and it is moreover something quite different from the glandular cysts around it which make up a large part of the section. Wlassov's photographs do not demonstrate to my satisfaction what they are supposed to do.

In conclusion then, I believe the view of Schlagenhaufer that these tumours are teratomata originating from some structure which has the morphological value of an included ovum, and the chorion-epitheliomatous tissues represent the actual trophoblast (Chorionic epithelium) of the included ovum, to be the most probable. In any case, the specificity of chorionepithelioma is not affected. The chorionic epithelium, as already remarked, is as characteristic a structure as any known to the histologist; and its specificity for the placenta is no more affected by its presence in dermoid tumours of the testis or other organs, than the specificity of hairs for the skin or teeth for the mouth because they occasionally crop up in the rectum.

Part VII.

Aetiology: Diagnosis: Prognosis: Treatment.

The chief problem of Deciduoma malignum as of other tumours is how to make our observations of its nature and origin applicable in the treatment of the patient. The aim of this chapter then will be to glean from the preceding all that bears on this question and corellate it with the results of an exhaustive investigation of the literature directed chiefly towards the same end. The record of the four cases shews that the diagnosis of deciduoma malignum in time to offer reasonable chances of successful treatment, yet avoiding the danger of unnecessary radical operation, is not altogether easy. Many of the cases are sufficiently straightforward. Speaking generally, the early symptoms and signs in no way differ from those of retained placenta or sub-involution; but they do not yield to treatment, the patient becomes gradually (often rapidly) more and more gravely ill. The violence of the haemorrhages especially awakes suspicion and finally microscopic examination of removed tissues or the appearance of metastatic growths settles the question. Now that the condition is well known, such cases should not escape detection, and radical treatment at an early period. There are aberrant cases which present special difficulties; some of these must be referred to; but they are the rarities. The really important cases for the elucidation of which the physician must bring into action all his diagnostic armamentarium, both clinical and pathological, are those in which the diagnosis lies between simply hydatidiform mole on the one hand, and malignant or destructive hydatidiform mole and chorionepithelioma with

presence of villi on the other.

Aetiology. This is as mysterious as that of other tumours: the papers of Marchand (94) Schlagenhaufer ( ) and Veit's handbuch should be consulted by those who wish to study the problem. A few points may be referred to here.

The age incidence of the disease is peculiar, differing from that of either carcinoma or sarcoma. The average age of the patients is about 33. This corresponds to the period of greatest sexual activity; the frequency of cases in the different decades is approximately proportional to the frequency of births in the same period. There seems to be a slight rise at either end which may be related to the tendency of the immature uterus and that which is nearing the end of its functional life to produce abnormal conceptions, especially hydatidiform moles. Out of 169 tumours, 6 occurred between 17 & 20 years (3 following moles and two being tubal); 73 between 21 and 30; 54 from 31 to 40; 28 from 41 to 50; and 9 from 51 to 55. 22 cases occurred in women over 45. Of these, 16 followed hydatidiform moles, 4 abortions; and 2 confinements at term. Of the 9 included in this number which occurred beyond 50, all followed mole with the doubtful exception of the case of McCann in which there had been no pregnancy for 9 years.

As regards the nature of the preceding pregnancy analysis of the 188 cases summarized shews, 74 after mole; 58 after abortion; 49 after full time confinements (3 somewhat premature ones being included); and 7 tubal or ovarian. The greatest majority of the cases therefore followed an abnormal pregnancy; but yet a

considerable number followed delivery at term; which was generally described as having been perfectly normal. So many of the patients moreover enjoyed perfect health up to the fatal pregnancy, that it seems unjustifiable to regard preceding ill-health as an important factor. Some of the "abortions", I would suspect to have been really the throwing off of the mass of blood-clot and necrosed tissue which composes most of the tumour. If this were so, the numbers which followed normal pregnancy would be somewhat increased. Possibly too, the premature expulsion of the ovum is frequently not the condition, but the result of the commencement of malignant deviation.

Hydatidiform mole, however, occurs in such a large proportion of cases that it must be regarded as of special significance as a predisposing condition. The cause of [redacted] hydatidiform mole itself is obscure.

The proportion of hydatidiform moles to normal labours is given by Gebhard (quoting König) as 1 to 728; by Williamson (St Bartholomew's Hospital) as 1 - 2400. The proportion of tumours to molar as compared with normal pregnancies is therefore a high one; yet the proportion of tumours to moles is probably not above 1 to 1000 (Berry Hart). Hysterectomy for fear of development of tumour in these cases is therefore absolutely unwarrantable apart from special indications. Repeated hydatidiform mole I did not notice recorded in any of the cases; but in two, there was an innocent mole, and the tumour followed, in the one abortion, in the other a normal confinement. The parasitic causation of chorionepithelioma has not received much attention. The usual

cell inclusions are common; the tumour cells being marked by phagocytes. Fig: 18 shews two little bodies enclosed in clear round spaces in a mass of syncytium which resemble some of the so-called cancer parasites. I interpret them as the earliest stages of vacuoles. Lessened resistance on the part of the maternal tissues due to excessively frequent pregnancies, endometritis, defective formation of the decidua, especially the fibrin layer have all been suggested as causes. On the other hand, a primary foetal cause has been supposed for the heightened activity on the part of the trophoblast, which appears to be capable of preserving its embryonic powers of growth in many cases even to the end of pregnancy, or even of resuming them after that time, vide Peters (No, 150). I fear that, in spite of the intermediate stages between the mole and the tumour, we are not yet able to strip the mystery off the latter; we must infer that some unknown quantity has been added in those cases which develop into malignant growths. ~~Clinical=signs=and=symptoms.~~

Clinical signs and symptoms. The most constant is haemorrhage, characteristically irregular in its recurrences, sudden, and severe. About equally constant is discharge;- serous, sanguineous or brown and putrid. Haemorrhage has been almost absent in six case, but the other symptoms were sufficiently striking in all of these. They were wasting, weakness and anaemia amounting to cachexia, and rigors in some cases. Between the termination of pregnancy and the onset of disease, there is frequently an interval of quiescence, but in 54 (exclusive of malignant moles) out of the 188 summarized, the disease ran continuously with the pregnancy,

or severe bleeding occurred within less than 14 days. In other 35, it appeared within a month. Only 8 began after more than a year's interval: it is difficult to exclude the occurrence of a fresh pregnancy. In several cases, menstruation has been re-established and in four (Helleman, Lohlein, McCann, Treub Doermann) the menopause was supposed to have been passed in the interval. Rigors are not uncommon, and have been taken to mean the occurrence of sepsis. In this way they may prevent the recognition of the true nature of the disease, e.g. case 2. Probably in some cases, just as in other forms of malignant disease, they do indicate some septic absorption, which the presence of a putrid mass in the uterus may well account for. But in others they seem to be related to the occurrence of metastasis. In several cases, the primary and the secondary tumours have been carefully examined for microbes with the result that they were found only in the superficial parts of the former. Their presence is certainly not an essential feature of the disease. Pelvic pain has been noted in a few cases. Cough and haemoptysis may occur very early and naturally suggest phthisis pulmonalis, but when they are associated with uterine symptoms in a recently delivered woman, they should always awaken other suspicions. Curetting and microscopic examination of the removed tissues would probably decide the matter at once; cf. Pestalozza (129). Post-mortem examinations prove that they signify metastasis to the lungs. The impossibility of drawing a sharp distinction on histological grounds between the villi of simply hydatidiform mole and those of chorionepithelioma or malignant mole has been insisted on. This fallacy, notwithstanding,

* Ledinski also regards as characteristic of an enlarged hyperplastic uterus with patulous cervix.

one can hardly ~~xxxx~~ overestimate the value of the histological test in these cases. Now that the fallacy is known, it should not give rise to much trouble. Still the rule that the diagnosis should not be allowed to rest on the microscopical evidence only applies at least as strongly to this as to other tumours; not that there seems to be much danger of that occurring. Indeed only too frequently, in the history of recent cases even, occurs the statement that portions of retained placenta were removed and thrown away without being submitted to microscopic examination. Then after a loss of weeks or months, when the clinical signs are so urgent that hardly a doubt remains, the diagnosis is clinched by this means, but too late. Krebs for example points out that 4 months was probably lost in the case which he described through microscopic examination of the curettings being limited to the identification of it in the fresh state as placental tissue. In the cases of Austerlitz and Graefe, the warning actually was given; but was disregarded; in the latter case because villi were present.

As a matter of routine, in all cases with suspicious clinical history, the whole of the curettings should be submitted to the pathologist in proper condition. Where a mass of curettings is available, it should usually be possible by a careful search in saline solution to find material which will give a valuable result. Where, on the other hand, a few fragments are removed "for microscopical examination," if the case be deciduoma, one is ~~xxx~~ rather apt to obtain only the superficial clots. Even in them

however, masses of large degenerated cells such as those shewn in fig: 25 may be found, which, if not distinctive of chorion-epithelioma, would at least suggest the presence of some malignant growth; which in conjunction with the clinical signs would be enough for practical purposes.

When masses of tissue such as those figured (Fig: 6 to 12 or 96, which is from that on which a diagnosis was given to Dr Edgar) are found apart from villi after a reasonable interval, the diagnosis of chorionepithelioma may be given with confidence.

Where villi are present the case is very different. The danger of malignant mole must not be forgotten, but the clinical signs are here more to be considered than the microscopical evidence. The histological characters which have been supposed to indicate malignancy have been considered on pp. 76, 78 & 79. "Neumann's cells" have been referred to. These are large cells like syncytial wandering cells which are found in the stroma of the villi, usually just under the epithelium. Julius Neumann described them in his early cases as indicating malignancy, but later investigations have quite discounted their significance. Ruge & Pick found them in cases of non-malignant mole. Poten & Vassmer found them in the non-malignant case referred to on p. 68. I have found them in a mole which proved perfectly innocent as well as in the doubtful case No 3. Schlagenhaufer & Peters hold them of no value prognostically. They were absent from the malignant mole described by Marchand in his second paper, & Voigt in his malignant mole found them sparingly and considers them of no account. The precise amount and character of epithelial

overgrowth that would warrant a diagnosis of malignancy cannot be laid down. Fig: 5 is from a case of Marchand in which suggestive symptoms led to curetting and undisturbed recovery followed. Berry Hart has recently published very similar photographs from a case which had a like happy issue. On the other hand, the case from which fig: 9 (also a preparation given to me by Prof: Marchand) was taken terminated fatally. An ordinary degree of hypertrophy in an innocent mole is shown in fig: 5b.

Tumours simulating chorionepithelioma in microscopic structure need hardly any consideration. Syncytial conditions of the uterine gland epithelium are known, but do not present any close resemblance. A carcinoma was shewn to me by Veit in which the cell forms were most faithfully reproduced, and fig: 26 is from a double of it which occurred in the Western Infirmary, Glasgow. The mode of growth is however totally different, being typically carcinomatous. There are a few peculiar cases in which diagnosis was difficult. There were the tubal ones, two in which the primary tumour is not definitely located (Busse & Schmorl-Fiedler) and the cases of Chrobak & Holzapfel in which a uterine tumour lay imbedded in the wall. In these, curettings gave negative result. Operation in the former case was done on the strength of the clinical signs; in the latter, microscopic examination of a vaginal metastasis revealed the nature of the case. The cerebral cases discovered at the autopsy have already been considered.

Prognosis. As already mentioned, although the prognosis in cases of deciduoma malignum on the whole must be regarded as bad,

it is recognized that it is by no means so hopeless as was supposed from the records of the earlier cases. In very large numbers of the fatal cases, there was no radical operation performed at all. Generally, the treatment was repeated curetting, followed by temporary cessation of the uterine symptoms, but after a time the appearance of symptoms indicating involvement of the lungs, and then rapid fatal termination. The cases in which a primary tumour was found in the vaginal veins while the uterus was sound form a group which is particularly interesting in reference to the practical questions. Doubt as to the fallibility of the histological diagnosis had hardly been expressed up to the description of the first case of primary vaginal tumour with sound uterus, that of L. Pick. In this case a small nodule somewhat resembling a thrombosed varix was found in the vagina in a patient 4 months pregnant. This was excised, or more strictly speaking, torn out. 3 days later, a large hydatidiform mole was expelled from the uterus. The wound in the vagina healed rapidly. Histological examination, however, shewed that the varix was actually a mass of hydatidiform villi imbedded in a capsule of blood-clot. Hysterectomy was suggested but patient refused operation and disappeared. 3¼ years later, she was found in blooming health, four months pregnant, and 5 months later she gave birth to a fine girl. Pick concluded that here was an example of a villus which had been given off by a simple mole and instead of disappearing harmlessly from the circulation like ordinary deported villi had formed a metastatic tumour, but not a malignant one. He compared it with Neumann's cases (115 & 117)

in which there was chorionepithelioma with villi in the uterus and mole in a vaginal metastasis which appeared during the pregnancy. In both of these cases, excision of the uterus and secondary tumours was followed by perfect recovery. He spoke of the condition as chorionepithelioma benignum. At the same time, however, Schmorl demonstrated a primary vaginal tumour which appeared 18 weeks after a normal birth. The uterus, tubes & ovaries were quite free from tumour. This patient died 6 months after the confinement with secondary growths in the lungs, liver, kidneys, & intestines. There were no villi in the growth. Here was a malignant metastasis from an apparently innocent placenta. It appears to me the more probable view of the origin of such tumours that the escaped trophoblast developed malignancy in its new seat than that a malignant ovum after giving off metastatic growths was expelled from the uterus. Other primary vaginal cases which ran a benign course have been recorded by Schlagenhaufer and Schmit (No. 1) connected with hydatidiform mole; and Schmit (No. 2) with abortion. On the other hand, in the cases of Hubl and Wehle (2 cases) after normal confinements, Lindfors and Vestbury after a somewhat premature but otherwise normal confinement, and Peters after abortion, excision of the primary vaginal growth was followed by rapid recurrence and fatal result. The cases of Zagorjanski-Kissel (186) and Langhans (80) are referred to later. The opinion of Schauta expressed in the discussion on Hubl's case is probably not far wrong, viz:- that the favourable results in the earlier Vienna cases of this sort were due less to any inherent benignity than to their position early attracting

attention, and consequently early removal. This set of cases then also illustrates the remarkable fact that the tumours related to hydatidiform mole are much less malignant than those related to a pregnancy carried to the full term. Explanation of this fact there is not as yet. Perhaps it will be obtained when the placentae with which they were connected shall have been kept and examined microscopically. This has not yet been done, but it is recorded in several cases that to the naked eye, the placenta appeared to have come away entire and to have been perfectly normal. In very few cases were their signs of anything wrong during the pregnancy.

In those of Williams and Schlagenhaufer (second) however, the disease does appear to have commenced during the pregnancy. In the former the patient, who had passed through several previous normal confinements, felt apprehensive during the pregnancy. The child was born dead and the patient was very prostrated, after the puerperium. The placenta was noted as being soft & boggy. There was no special haemorrhage after its expulsion; but within a week, a secondary tumour appeared in the vagina which grew rapidly and sloughed. Death resulted from haemorrhage and apparently septic absorption within 3 months; the post-mortem examination shewed wide dissemination of secondary growths; cultures from liver, lungs, spleen, and kidneys were tried but were ~~xxxxxxx~~ sterile. In Schlagenhaufer's case, the patient complained in the later months of pregnancy of pains in the pelvis and left side, and attacks of breathlessness, and she was low-spirited, languid, anaemic and of a yellowish pallor. The

confinement was rapid. The placenta was expelled spontaneously & appeared quite normal. The patient improved somewhat after the confinement and was able to suckle the child. The lochia were practically normal. The child was weakly from the first, and ~~x~~ died in about 3 weeks. The mother within 17 days from the birth suffered from extreme dyspnea, had a rise of temperature, cough, & rusty spit which were supposed to signify an attack of pneumonia. 34 days after the confinement she died and examination revealed a tumour of the uterus and innumerable ~~xxxxxxx~~ secondary tumours in the lungs, spleen, kidneys, & vagina. The clinical history in its latter stages suggested an acute pyaemic process. Microbes were found in the necrotic tumour in the uterus, but only on the surface. The metastases were quite free from bacteria and undoubtedly the wide extension of the tumour and not sepsis was the cause of death.

Almost equally malignant were the cases of Cock, death in 20 weeks from a normal birth; the case of Baldwin already referred to (p.6); Eugene Frankel's second, in which the symptoms appeared within 7 days and ~~xxx~~ death resulted in 2½ months. In all of these, no operation was done, the disease running such a rapid course that interference was regarded as hopeless. A number of cases equally malignant have followed abortions. e.g. Kelly and Teacher, and Simmonds, but more of them have run a comparatively slow course like that described in cases 1 & 2.

Among the molar cases there are a number of very malignant ones which were pure chorionepitheliomata without villi, but the most malignant are those to which the term destructive

hydatidiform mole applies. As typical examples of these may be taken the old Wilton case, and those of Voigt which recovered, and of Gottschall, Krieger, & Waldeyer.

In the case of Wilton, the patient suffered from repeated flooding, and the uterus enlarged very rapidly, as is usual in hydatid mole cases; but the termination came suddenly from rupture of the uterus and haemorrhage into the peritoneum in the fourth month of pregnancy. In the case of Gottschall, an apparently simple abortion cleared out manually was followed by rupture of the uterus on the patient making an effort 3 months after the operation, death resulting from shock & haemorrhage in a few hours. In this case rupture during pregnancy was diagnoses and a laparotomy was performed. The abdomen was found full of blood-clot; the uterus was the size of the foetal head at term. It was ruptured across the fundus and out of the rent in it protruded clots and the vesicles of a hydatidiform mole. As post-mortem examination was not allowed, it is not known whether metastasis had occurred; but in the uterus the villi burrowed deeply into the muscle, & plugs of typical chorionepithelioma were seen in the blood vessels. Such cases spoil the otherwise relatively fair prognosis in the cases following hydatidiform mole.

On the other hand, there is now quite a large series of cases in which operation has been done with favourable result in spite of the fact that metastasis had already occurred. In several cases there were actual extensions of the tumour which it was found impossible to remove. Such are the cases of Marchand

Kolomenkin (69), Albert (3) the only tubal one which recovered, and Noble's second case. In the last, a mass was left adhering to the fundus of the bladder. This was felt on examination 3 months later, but 5 months later, it had disappeared and the patient was perfectly well.

In the cases of Chrobak (24) Von Franqué (33), Zagorjanski-Kissel (186) Ladinski (78), Kworostansky (77) Lonnberg & Mannheimer (91), Neumann-Schauta (115), Pestalozza No 4, the presence of metastasis in the lungs was inferred from haemoptysis and cough and the general condition of the patient. In the last mentioned, the case was supposed to be phthisis, but other symptoms directed attention to the uterus which was found to be enlarged. Curettings were removed which microscopic examination shewed to be deciduoma malignum. The uterus was removed and the phthisical symptoms disappeared.

In the third case of Neumann, and those of Holzapfel, Lonnberg & Mannheimer, and Poten & Vassmer metastasis was also present in the vagina. In that of Cazin-Segond, the ovary contained a secondary tumour. The secondary nodules were removed along with the uterus. Chrobak's case was reported immediately after the operation. The others were reported well at periods varying from 6 months up to one year & 5 months in the case of Von Franque, and 2 years and 9 months in that of Marchand. In reply to an enquiry by letter, Dr Ladinski has informed me that his patient is still living, more than 19 months after the operation. In this case, the patient was extremely weak and ill, but the operation was nevertheless undertaken in view of the good

result in the case of Von Franque.

In the case described by Zagorjanski-Kissel, the tumours were present in the vagina 2 weeks after an abortion in the third month. Diagnosis of primary vaginal tumour with sound uterus was made by Landau & Pick. Both nodules were excised and the uterus curetted. Nothing suspicious being found in the latter, it was not removed. The patient's health improved immediately. She had had rigors & haemoptysis which, after a few days, ceased. Throughout, the physical signs in the lungs were negative. 8 months after the operation, she had an abortion in the sixth week, and at 15 months she was 3 months pregnant, and while not in the best of health, shewed no sign of recurrence of tumour.

Spontaneous healing of a vaginal tumour occurred in Langhans' second case. A supposed primary vaginal tumour was removed. It recurred in a fortnight. The recurrent tumour burst a week later, through off a slough, & healed. Haemorrhage from the uterus occurred a few weeks later. It was curetted, a number of villi removed; and she got well and was reported well 10 months after.

But the strangest case of all is that of Von Fleischmann, published in April 1903. On May 5th, 1899, a hydatidiform mole was removed. 30 days later, there was a haemorrhage which gave rise to the suspicion of deciduoma malignum. The uterus was curetted. Microscopic examination gave a negative result and the condition was then regarded as sub-involution. Thereafter for 8 or 9 months she menstruated regularly. Then the periods became less and occurred less often, and, after two years, they ceased entirely. 6 months later, on Febry 12th, 1902, the patient applied for treat-

-ment,

complaining of amenorrhoea and general loss of health. She did not regard herself as pregnant. Examination revealed a characteristic tumour in the vagina. The uterus was ante-flected and of the size of a 6 to 8 weeks pregnant organ. The uterine appendages were normal. The patient refused radical operation, but allowed removal of the vaginal tumour. A week later, there was severe arterial haemorrhage from the wound and 2 days later renewed haemorrhage from the wound and from the uterus. As there was a doubt whether the uterus contained a normal ovum, a mole or a tumour, the os was dilated and the contents cleared out with a blunt curette. Suddenly the curette passed very deeply in towards the right. Perforation was diagnosed. The uterus and vagina were plugged with iodoform gauze. The microscopic investigation of the vaginal tumour shewed a growth consisting of large polymorphous cells which were regarded as chorionepitheliomatous. Extirpation was not performed. Septic infection happily did not occur. About 10 days later, on March 2nd, there was renewed bleeding from the vagina. The artery from which it came was detected and ligatured. The patient had become very anaemic. On March 18th, the vaginal wound was healing and the uterus was becoming smaller. To the right of the uterus there was a resistant mass of considerable size. On the 20th, the patient, by her own wish, was allowed to return home. On June 23rd, she reported herself. Subsequent to her dismissal there had been no haemorrhage. She felt & looked well. There was a small pale scar in the vagina. The uterus was small & movable. Menstruation returned in September and she reported herself well on

December 8th, 1902 - 10 months after the operation. The impression of the tumour elements which I take from the description and the illustrations is that they resembled those of the cell masses in case No 2, i. e. they were of the forms intermediate between Langhans' layer and syncytium, and for the most part they presented characters which suggest some degeneration. Fleischmann regarded the case as a very atypical infiltrating chorionepithelioma and in this opinion Marchand, to whom the sections were submitted, concurred. The remarkable features in the clinical history are

1st. The long latency. The relationship to a preceding pregnancy Fleischmann holds quite certain. If the tumour were referred to the mole, the latency would be $2\frac{3}{4}$ years, but it is possible that the amenorrhoea for 6 months before it was discovered, indicated a renewed pregnancy.

2nd. The comparative absence of haemorrhage.

3rd. The perforation of the uterine wall by the curette.

4th. The recurrence of bleeding after the extirpation of the vaginal tumour. Evidently the growth had not been completely removed.

5th. The healing of the vaginal wound and the restoration of the uterus to its physiological condition as shewn by the return of menstruation, and the uninterrupted recovery of the patient.

The case is a remarkable illustration of the vis medicatrix maturae, but the author regards it as highly exceptional in view of the general malignancy of chorionepithelioma. This, and the case of Langhans, are the only examples so far as I am aware of

spontaneous recovery in this disease and there is no obvious explanation of it. Certainly there was no killing off of the tumour elements by haemorrhage in this case. As a mere speculation, one might put forward the hypothesis that in certain cases, the tumour retained the tendency of its physiological prototype to grow actively for a limited period and then gradually to undergo a retrogression.

Statistics of Cases.

In the 188 cases, radical operation was performed 99 times.

Table I. All cases.

Preceding Pregnancy.	No. of cases.	Deaths.	Recoveries.	Percentage of recoveries.
Hydatidiform mole.	73.	39	34.	46.6
Abortion.	59 (1).	40	19.	31.5
Confinement at term.	49.	39.	10.	20.4
Tubal or ovarian,	7.	5 (2).	1.	
All cases.	188.	123.	64.	34.2

(1) Two cases in which preceding condition is not known to me placed here.

(2) The result in the case of Nikiforoff is not known to me.

Table 2. Cases submitted to radical treatment.

Preceding Pregnancy.	No. of cases.	Deaths.	Recoveries.	Percentage of recoveries.
Hydatidiform mole.	42.	9	33.	78.5
Abortion.	36.	16	20.	55.5
Confinement at term.	19.	10.	9.	47.3
Tubal.	2.	1.	1.	
	99.	36.	63.	63.6

Out of the 36 deaths, 11 occurred within a few days; these may be set down as incidental to the weakened condition of the patient by the time operation was undertaken and such complications as tremendous haemorrhage on the attempt being made. There are several cases in which radical operation had to be abandoned on account of this. 25 died after a longer or shorter interval; in the cases which came to post-mortem examination, this was due to recurrence in internal organs. In 16 of them, there was no marked improvement or interval of good health after the operation. In 9 there was good recovery, and in 5 an interval of several months good health before rapid recurrence of the disease and death. In 5 only of these did the disease recur at a longer interval than 6 months. The longest was in the case of Lohlein;-1 year. When the 63 recoveries are examined it is found that 32 were reported well 6 months or more after the operation, and out of these, 24 were over the year, and out of them 13 over 2 years. Knowing the tendency to report successful operations while the failures are sadly laid aside, it is more than probable that the above statistics convey far too favourable an impression of the results of operation. Nevertheless, it is clear that Deciduoma Malignum is not the hopeless disease it was once taken to be. Further, the list of cases beginning with those of Neumann and Schauta, and Von Franqué, and ending with Zagorjanski-Kissel, in which operation was done in the face of metastasis having occurred, proves that no patient need be abandoned to her fate who seems the least likely to stand operation. ~~A dissertation on treatment by pathologist would be out of place. In most of the cases in the operations~~

Treatment. A dissertation on treatment by a pathologist would be out of place; but a few points may be touched upon.

In the "Operations Table"where the contrary is not specified, vaginal hysterectomy has as a rule been performed. The possibility of the manipulations favouring metastasis has been suggested; it was felt by Dr. Edgar in his case , where the tumour was large relatively to the outlet.

It is hardly necessary to insist on the importance of early diagnosis and treatment, in spite of the fact that favourable results have been obtained in many cases of the more chronic type even after the disease had been in existence many months, e.g. Lewers' and Sticher's cases. Two thirds of the successful operations were performed within three months of the first symptoms.

Classification.

It is generally agreed that the best classification of tumours is that which takes as its basis the nature and origin of the tissue from which they spring. The tendency of recent research has been to show that this was the least inconstant point of distinction between the atypical forms of the epithelial as against the endothelial and the connective tissue tumours.

Chorionepithelioma, then, belongs to the epithelial group. But, as we have shown, it differs in its structure and mode of growth and dissemination from the typical epithelioma or carcinoma. When its source is considered the difference is sharper still. The trophoblast or chorionic epithelium cannot be classed along with

the epithelial tissues of the body. It is, indeed , of common origin with them in as much as it springs from the primitive epiblast of the ovum; but it is differentiated from them and specialized before the stage of the three-layered blastoderm is reached, and even in some animals (including man apparently) before there is any hint of an embryonal anlage at all; and it takes no part in the formation of the body. It is not a tissue of the maternal body, but a parasite upon the maternal organism; nor is it a tissue of the foetal body. Physiologically also it is quite peculiar.

The tumours to which it gives rise are, therefore, something different developmentally and physiologically from either carcinoma or epithelioma;- they form a class apart. Chorionepithelioma Malignum may be an unhandy name, but it is the most appropriate.

Of the other terms in use Chorioma, which has been employed by some American writers, and chorion carcinoma are the least objectionable. Syncytioma disregards one of the essential elements - the"pure syncytial" tumour, if it exists at all, is an unimportant variety. Carcinoma Syncytiale is absolutely wrong; it is a suitable name for the tumour illustrated in fig. 86. The old name Deciduoma Malignum has such a hold that it might be retained for clinical use,along with the pathologically correct designation Chorionepithelioma Malignum sui generis.

Summary of Conclusions.

I think it is proved that,

(1) the so-called Deciduoma Malignum is a tumour arising in connection with a pregnancy, and originating from the chorionic epithelium (or its fore-runner the trophoblast), which is of foetal epiblastic origin.

(2) That these tumours form a quite characteristic group clinically, pathologically and developmentally; and that they should be classified neither as sarcomata nor as carcinomata, but as a distinct group sui generis. The most appropriate name is Chorionepithelioma Malignum*. Malignant hydatidiform mole may be treated as a variety of this disease.

(3) That, in addition to the common tumours developing from a pregnancy, there are tumours containing precisely similar structures which are not connected with a pregnancy, and may occur in other parts of the body than the uterus, and in either sex. The most probable explanation of them is that they are teratomata, originating from some structure which has the morphological value of an included matured and fertilized ovum, and the chorionepitheliomatous tissues represent the actual trophoblast (chorionic epithelium) of the included ovum.

(4) That special care must be exercised in the diagnosis between certain cases of hydatidiform mole and chorionepithelioma arising in connection with that condition.

(5) That while the prognosis in all cases of chorionepithelioma is a grave one, early recognition and early radical operation offer a fair chance of recovery. The fact that meta-

* Or as it is frequently written "Chorio-Epithelioma Malignum."

stasis has occurred does not necessarily preclude successful operation, although it materially diminishes the chances of success.

Glasgow. June 1st 1903.

Description of the Illustrations.

Abbreviations.

Bl.V. blood-vessel: Ca. maternal capillary: C.T.M. maternal connective tissue: C.T.V. connective tissue core of villus: En. endothelium: Ep.U. Uterine epithelium: EP.W. epithelial wandering cells: L.Langhans' layer: Sy. syncytium: Tr. trophoblast: V. chorionic villus.

Plate I. Tumours.

Fig.1, Dr Edgar's tumour. The uterus laid open from before showing the tumour within it. Owing to the contraction of the muscle when the organ was opened the prominence of the growth is considerably exaggerated. On the right where the fresh section has been made the pale tumour tissue is just distinguishable from the dark clots and the uterine muscle; the last is seen to be drawn up into the tumour in the overhanging edge opposite X. In this neighbourhood the uterine mucous membrane had the character of young decidua;- see Pl.13. The cervix was somewhat patulous. About half natural size.

Fig.2. The same specimen in section. The darkest patches are recent haemorrhages. The thickness of the uterine wall is much exaggerated as already explained.

Fig.2a. The tumour in the Kelly and Teacher case, from before. a, top of fundus uteri; b, tumour in the fallopian tube;

c, uterine artery; d, tumour in the vaginal veins; about ½.

Fig. 2b. The same as the preceding from behind; the posterior wall of the vagina cut away; the tumour split in the middle line and its two halves drawn apart to show its appearance in section. a. tumour nodule in fallopian tube; b,lower end of tumour projecting into the cervix uteri;c, cervix uteri; d, the ureters; e, uterine vessels on the left side with a bristle passed under them; f, on the left a large vesical vein distended with tumour; g, on the right a large vein distended with tumour , and a wedge removed for microscopic examination; h, similar tumour incised at autopsy; i, vaginal tumours in section; j, uninvolved vaginal veins.

Plate II.

Fig.3. A section of a placenta about the end of the third month in situ. It shows a villus with trophoblast still persistent at the tip, free syncytial giant cells in the intervillous space among the maternal blood, canalized fibrin layer,, decidua serotina, syncytial wandering cells in its deeper layers,and the edge of the uterine muscle.

Winkel 14 mm. apochromatic; Oc.I. x 60.

Fig.4. The developing placenta about the twelfth day. From left to right in order are seen a portion of the chorionic vesicle, villi which show very large masses of trophoblast at their peripheral ends, and a layer of granulation tissue-like

material composed of a mixture of trophoblast cells, swollen maternal connective tissue cells(decidua cells) and leucocytes of various kinds. Many of the cells are degenerated or necrosed, and among them is granular matter (fibrin) and extravasated red blood corpuscles. At some points there was a well-formed"fibrin layer". The decidual change was limited to a very narrow zone around the ovum; outside that the uterine mucosa preserved its normal characters almost unaltered. The trophoblast is somewhat loosened and broken up , it is supposed , owing to post mortem changes. There was almost no blood in the intervillous spaces. From a preparation given to the author by Professor Marchand.

Winkel 14 mm. Oc.1. x 60.

Fig.4a. section of the same ovum showing the characters of the trophoblast. The distinctness of the two layers is somewhat impaired by the post mortem changes. Large masses of the Langhans' layer derivatives occupy most of the field; the syncytial border and syncytial masses here and there are quite distinct.

Winkel 14mm. apo. and Oc.4. x 150.

Fig.4b. A villus attached to the decidua; third month. The fibrin layer is defective at this point and the trophoblast and decidua cells mix to some extent;- villus and trophoblast to left, decidua to right and above. The distinctness of the tro-

phoblast cells is lost through degenerative changes (or bad fixation) but the large size and deep staining of their nuclei contrasts with the small size relative to the cell bodies and those of poorness in chromatin of the decidua cells.

Winkel 14mm. and Oc.4. x 200.

Fig.4c. Chorionic villi in the fourth week showing the two layered epithelium and a cell-knot. The Langhans' layer is best marked close to the point of outgrowth of the cell-knot. Detached syncytial cells are seen in the intervillous space and vacuolated syncytium in the cell-knot.

Winkel 14mm. Oc.4. x 150.

Fig.4d. Villi of a normal placenta at term showing the epithelium reduced to a thin rind of syncytium with small darkly staining nuclei. The foetal blood-vessels are injected with blood pressed back from the umbilical cord.

Reichert 8mm. semi-apochromatic; Zeiss projection Oc.4. x 150.

Plate III.

Fig.4e. General view of a section through the centre of the Peters ovum.

G.P. the mushroom-like cap of blood-clot closing the hole (a - b) through which the ovum effected its entry into the uterine mucous membrane; Bl.L. blood-lacunae of the trophoblast; Cap. decidua capsularis(reflexa); Comp. decidua compacta; Dr. uterine glands; K.A. Keimanlage; M. Foetal mesoblast commencing to

form villi; Tr. trophoblast; U.E. uterine epithelium, which is partly thinned and degenerated. U.Z. umlagerungszone - surrounding zone of maternal tissue.

From Peters, "Die Einbettung des menschlichen Eies." fig.1.

x about 50.d.

Fig.4f. The trophoblast of the Peters ovum, showing the character of the cells composing it and its relations to the maternal tissues.Ca. cavity of opened maternal capillary; Ekt. the primitive ectoblastic(epiblastic) basal layer of the trophoblast corresponding to Langhans'layer. P.en. maternal endothelium; rest of latters as above. The Bl.L. blood lacuna is lined by a thin sheet of syncytium so delicate as to resemble endothelium.

Ibid. fig 22. Magnified about 150 d.

Plate IV. Imbedding of the Ovum.

Fig 4g. Ovum of the Hedgehog in situ. The blastocyst is imbedded at the bottom of a furrow in the uterine mucous membrane. Its outer wall all over has developed into a thick layer of cells -the trophoblast -which is intimately united with the maternal connective tissue. To the left is the open end of the furrow now blocked by coa.a plug of blood-clot, on either side of which is seen the broken edge of the epithelium e. At Sp. spaces or lacunae of the trophoblast filled with the remains of maternal blood. G. uterine glands partly destroyed by the

trophoblast; T. thickening of the primitive epiblast (Trager of Selenka) where the embryo will be formed; Hy. hypoblast. From Hubrecht "Placentation of Erinaceus Europaeus" fig.39. Magnified about

Figs. 4g,h,i,j,k, four figures illustrating the imbedding of the ovum of the guinea-pig, from Graf v. Spee "die Implantation des Meerschweincheneies."

Fig 4h. ova free in the uterine cavity, and (fig.7) in a very early stage of the imbedding. All the ova are still enclosed in the zona pellucida. x about 125.

Fig.4i. The partly imbedded ovum 6 days and 12½ hours after the coitus (fig.9b.) U.E.uterine epithelium; Bg. edge of connective tissue the cells of which were swollen and had lost their distinct outlines -symplasma. x about 320.

Fig 4j. another ovum of the same period showing the destruction of the maternal connective tissues much further advanced, and the hole in the epithelium somewhat narrowed and blocked by the outermost cells of the ovum. (fig.II.) x about 320.

Fig. 4k. Imbedded ovum of the guinea-pig 6days and 16 hours after the coitus. Around it there is a space which contained a nutritive fluid, and the destruction of the connective tissues has extended considerably.(fig. 13A.) x about 320.

Fig. 4l. Schema of the imbedding of the human ovum from Peters; ibid. Pl. 14. Figs. 4,4a, and I represent the stage of the Peters ovum.

Plate V.

Fig. 4m. Section of the trophoblast and trophospongia of Tarsius spectrum to show the great variety of cell forms in the former. The trophospongia is the base of maternal tissue on which rests the thick rounded mass of proliferating foetal trophoblast. Mes. foetal mesoblast showing projections, mzo, the commencement of villi; kbw, wall of blastocyst; nbl, new formed bloodvessels of the trophospongia; Dl, uterine glands; D4, the same completely degenerated. x about 40.

From Hubrecht ("Placenta von Tarsius und Tupaya." fig. 64.

Fig. 5. Chorionic villus showing very marked hypertrophy of the epithelium, both layers participating. From a case in which curettement was followed by complete cessation of symptoms which had suggested chorionepithelioma. From a preparation given to the author by Prof. Marchand.

Winkel 14mm. apo. Oc. 4. x 85.

Fig 5a. rather degenerated chorionic villi and masses of epithelium (both layers) from case 3.

Reichert 8mm. semi-apo. and Zeiss Comp. Oc. 8. x 150.

Fig 5b. Villus from a case of simple hydatidiform mole, showing hypertrophy of both layers of the epithelium, and the vacuolation of the syncytium.

Winkel 14mm. apo. and Oc. 1. x 60.

Plate VI. Chorionepithelioma.

Fig. 6. Typical masses of chorionepithelioma invading the uterine muscle. Case 1. The tumour tissue is distinguished by its darker shade. The remains of uterine muscle(pale yellow) among the tumour processes produce a sort of alveolar structure. The dark greenish masses with many nuclei are the syncytium. Here and there detached masses of it are seen, some of which (Ep.W.) simulate hypertrophied muscle fibres.

Drawing by Jacob Wenzl, Vienna. x 85.

Fig.7. Chorionepithelioma tissue from an area in which it formed a regular ~~x~~ layer like the floor of an ulcer. Here it happened to consist principally of Langhans' layer cells, with irregular dark masses of syncytium scattered through it. The blood-vessels (bl.v.) at the border of the tumour have the walls on the side next it replaced by tumour tissue. The connective tissue is converted into a sort of granulation tissue. There is an outlying mass of tumour ~~in~~ amidst it.

Drawing by Wenzl. x 85.

Plate VII. Chorionepithelioma with presence of villi.

Fig.8. A small portion of a villus showing the origin of the tumour from the epithelium; the continuity of the various cell formations with one or other layer is obvious. Karyokinetic figures are numerous in the Langhans' layer cell masses. Compare next figure. From Dr. Haultain's case.

Drawing by Wenzl. x 820.

Fig.8a. Photograph of the same section, showing the villus, which is in a state of hydatidiform degeneration, the extensive epithelial outgrowth, and a slight degree of infiltration of the uterine muscle. x indicates the position of the preceding figure.

Zeiss aa, 24 mm. no Oc. x 24.

Plate VIII. Chorionepithelioma.

Fig 9. Portion of a hydatidiform villus with epithelial hypertrophy, and the uterine wall which is slightly infiltrated.

From a preparation given to the author by Prof. Marchand. (Case no.XII, fatal, patient aet 53.)

Winkel 14 mm. Oc.1. x 60.

Fig 9a. Chorionepithelioma with villi or malignant mole. several villi are seen to the left, one of which is almost normal. From one of the cases of Julius Neumann. Preparation given to the author by Dr. Hitschmann, Vienna.

Zeiss aa. 24 mm. No Oc. x 24.

Fig. 9b. Typical masses of chorionepithelioma somewhat degenerated(or badly fixed- warm alcohol) consisting of individual cells principally, enclosed in a thin rind of syncytium. This is the field on the strength of which a diagnosis was given to Dr. Edgar. Magnification etc as in fig 9.

Fig 9c. Typical masses of chorionepithelioma - Langhans' layer cells and syncytium growing in fluid blood in a secondary tumour in the lung. Kelly and Teacher case. fig.8.

Reichert 8mm. semi-apo.Zeiss C.Oc.8. x 260.

Fig 9d. Part of a typical mass of chorionepithelioma showing the two leading cell forms. From case I.

Same as above. x 300.

Plate IX. Chorionepithelioma.

Fig.10. Cell mass from case 2 showing the large decidua-cell-like elements, and forms intermediate between the Langhans' layer and the syncytium. The mass is surrounded by blood and thrombus. Compare Plate XIII.

Drawing by Wenzl. x 130.

Fig. 11. Vacuolated syncytium with masses of Langhans' layer elements imbedded in it. To the left is uterine tissue infiltrated with epithelial wandering cells; compare fig 12. This and the preceding figure show the large number of leucocytes which are usually found in the neighbourhood of the tumour tissue, and their small size compared with the tumour cells.

Drawing by Wenzl. x 130.

Plate X. Chorionepithelioma.

Fig. 12. The tumour growing into the mouth of a uterine sinus. The vessel is for the most part lined with syncytium; to the left are traces of the endothelium. The uterine tissues are infiltrated with tumour cells of very varied shapes and sizes and number of nuclei; they have themselves to some extent assumed the character of granulation tissue. The resulting confusion of cell forms is difficult to unravel, but less so with the microscope than in the drawing; most of the large vesicular nuclei indicate tumour elements. To the right and below is a mass of typical tumour. Ca. a capillary with well preserved endothelium and tumour cells just outside it. From case 2. Compare fig. 13.

Drawing by Wenzl. x 220.

Fig. 15. Transverse section of a process of tumour extending along the wall of a blood-vessel. The lumen is filled by the tumour and not much of the wall remains. From Case 1.

Drawing by Wenzl. x 170.

Fig. 16. An isolated mass of syncytium in a blood vessel of the uterus, attached to the wall and in process of forming a metastatic growth; see p. 86.

Drawing by Wenzl. x 240.

Plate XI. Chorionepithelioma.

Fig 13. A uterine blood-vessel invaded by tumour. The attacking cells have appeared under the endothelium at two points and large wander cells of intermediate character have also crept round to the other side of the vessel. The uterine tissues show reactive round-celled infiltration. In the vessel, at a point where the endothelium has already broken down, there is a small thrombus. In the vessel there is a clump of tumour cells .

Drawing by Wenzl. x 85.

Fig 14. Photograph of part of the same vessel, from the next section of the series.

Winkel 14 mm. Oc.4. x 150.

Plate XII. Chorionepithelioma.

Fig.16a. A mass of Langhans' cells in a uterine blood-vessel.

Drawing by Wenzl. x 240. x 150

Flg. 17. A mass of syncytium showing the bristle edge (so-called ciliated border) and clear individual cells differentiated (?) within it. See p.85. A number of deeply stained threads of fibrin are seen among the ends of the protoplasmic processes and also a number of red corpuscles and leucocytes. The syncytium is attached to lung tissue. Kelly and Teacher case.

Drawing by Wenzl. x 640.

Fig. 18. A young syncytial cell (intermediate form) showing two small round bodies in round clear spaces in the cytoplasm near the nuclei, which represent the beginning of vacuolation.

Drawing by Wenzl. x 640.

Plate XIII. Chorionepithelioma. High power photomicrographs to illustrate especially pp.83 to 87.

Zeiss 3mm apo. N.A.1.40. and 4 proj. Oc. Watson Parachromatic condenser. x 600.

Fig. 19. Slightly hypertrophied individual cells (Langhans' layer) showing karyokinetic figures and the delicate protoplasmic reticulum. x 600.

Fig. 20. A similar mass showing karyokinetic figures and also cells with double nuclei and undivided cell-body. x 600.

Fig. 21. A similar mass of tumour cells showing intermediate cell forms; cells with two or three nuclei; two small giant ♂ cells with several nuclei, and a large vacuolated mass of syncytium with similar cytoplasmic characters.

Reichert 8mm semi-apo. Zeiss Comp.Oc. 8. x 300.

Fig 22. Old syncytium showing the alveolar structure of the cytoplasm. This and the adjacent individual cells are drawn our by a haemorrhage in the neighbourhood. The same mass of syncytium but in a different section is seen in fig 13, Sy.

x 600.

Fig. 23 Large wandering cells of Langhans' layer infiltrating uterine tissues. The deeply stained ~~xxxxxx~~ fibrous matter is remains of connective tissue. x 600.

Flg 24. Young decidua cells from case 1, for comparison with the tumour cells. x 600.

Plate XIV. Chorionepithelioma and other tumours.

Fig. 25. cells from a degenerated and partly necrosed mass of chorionepithelioma. Kelly and Teacher case.

Reichert 8 mm. etc x 300.

Fig.25a. Mixed celled sarcoma of the body of the uterus, showing giant cells.

ditto. x 300.

Fig 25b. Degenerated and compressed chorionepithelioma tissue. Kelly and Teacher case.

Reichert 8mm etc. x 260.

Fig. 25c. Degenerated chorionepithelioma tissue. Kelly and Teacher case.

same as preceding. x 260.

Fig.26. Carcinoma syncytiale;- a carcinoma of the body of the uterus showing cell forms similar to chorionepithelioma, but a totally different mode of growth. see p.110.

Winkel 14 mm. apo. Oc 4. x 150.

Fig. 26a. Chorionepithelioma of Teratoma; Dr. Ritchie's case.

p.101. syncytial masses and smaller individual cells, surrounded by blood-clot and degenerated tissue.
Winkel 14mm etc. x 150.

Plate XV. The chorionepithelioma of Teratomata.

Fig. 26b. Typical tissue from Schlagenhaufer's first case;- primary tumour in the testis.

Copied from the drawing (by Wenzl) about half size. x about 80.

Fig. 26c. Chorionepitheliomatous tissue from the metastatic tumour in the lung in the same case.

Copied from the drawing (also by Wenzl) about half size. x80.

Flg 26d. Part of the small mass of chorionepitheliomatous tissue in the primary tumour in Schmorl's case.

Winkel 14 mm. Oc. 4. x 200.

Flg.26e. From a secondary tumour in the intestine in the case of Schmorl.
Winkel 14 mm. Oc.1 x 60.

Fig 26f. The heart and vena cava from Schlagenhaufer's second case, showing the villous intravascular growth. The actual preparation is far more like hydatidiform mole.

Copied from the drawing by Keilitz.

Fig. 26g. The abdominal tumours in the case of MacCallum (lymphendothelioma testis) after removal of the viscera. The

long string of tumour is seen distending the spermatic and renal veins and vena cava upwards towards the heart and downwards as far as the bifurcation into the iliac veins. The large tumour masses not laid open are in veins. The separate sketch below shows some of the isolated "papillary masses." see pp. 97 and 99. Copied from the drawing in MacCallum's paper, by Max Brodie.

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Heukelom; Siegenbeck v.; Archiv. f. Anatomie. p 1.

Statistical tables.

A few words of explanation of the following tables are necessary. Table I. contains the principal facts about 188 cases of chorionepithelioma and malignant hydatidiform mole, of which a sufficiently detailed account has been accessible to the author, and about which the nature of which there seemed to be no doubt. In a large majority of the cases the original report has been consulted.

Table II. is a list compiled from table I of the cases in which radical operations were performed, and the most essential data.

The headings of the columns for the most part need no explanation. Corresponding to the numbers in the first column are the reference numbers in the first part of the literature list. In column 4 all the pregnancies including that which immediately preceded the tumour are enumerated. "Birth" has been employed as the shortest and most convenient equivalent for confinement at term. Abortion is used in the customary sense; a number of cases in which the nature of the preceding pregnancy was not clear have been placed for simplicity under this heading. "Mole"is used with the meaning hydatidiform mole, as is commonly done in Germany. The meaning of the periods mentioned and the dates from which they are reckoned is explained in the footnotes on sheet 1 so far as is necessary.

The cases of Blumreich, Boldt (2), Bulius (1 &2), Freund, Monod Chabry and Macaigne, and Paviot included by Ladinski have been rejected as not chorionepithelioma, as well as a num-

ber of other cases which have been formerly rejected by other tabulators, viz. Beach, Blanc, Klotz, Kustner, R.Maier, Superno, and Zahn. Menge's second case has been allowed to stand, but the opinion of the author himself on it is quoted. Six genuine cases wanting details are mentioned at the end of table I.

Tables:

No 1. Cases [illegible]

No.	Date	Reporter.	Age.	Pregnancies	Last Pregnancy.	Signs: Symptoms: Date of onset. (2)	Treatment. (3)
1	1896	Aezel	22	1 normal birth 2 abortions	Normal birth.	Haemorrhage; 7 mos; (2) cough + haemoptysis; supposed Phthisis.	
2	1895	Ahlfeld (Marchand)	17	1st pregnancy	Tubal.	Metrorrhagia for 4 months. Haemorrhage from secondary tumour in vagina.	Vaginal nodule scraped out. Recurrence. Exploratory laparotomy.
3	1900	Albert, I	21	1st pregnancy.	Tubal.	Extreme wasting + weakness.	Tumour removed in pieces: very profuse bleeding.
4	1900	Albert, 2.		4 normal births.	Normal birth.	Slight haemorrhage, 4 days. Repeated severely.	Curetted 6 weeks. Hysterectomy 8½ weeks.
5	1900	Anders.	41	6 normal births. 1 abortion.	Abortion.	Haemorrhages. Irregular: 3 months. Severe: 10 months.	Attempted removal of vaginal tumour + curetting of uterus, 11 months.
6	1900	Anders	25	1 normal birth. 1 mole.	Mole.	Recurrent bleeding. stinking discharge, during 1 year after confinement.	Scooped out secondary tumour beside cervix. Had to stop on account of haemorrhage. 12 mo

(1) The reference will be found under the corresponding number in
(2) This is stated in terms of the time which elapsed between the onset of symptoms of disease.
(3) As in 2, — dates from the termination of the
(4) In fatal cases dates as in 3; in cases of

Result (4)	Primary Tumour	Metastases	Remarks.
Death at 9 months (4)	Deep ulcer in fundus uteri.	Cervix, uteri vagina: lungs. intestines.	Recognized post mortem. Reported at first as Sarcoma. Spontaneous rupture of uterus. Villi present (?)
Death.	Round firm mass, size of fist, to left of & above uterus, many adhesions.	Vagina. Haemorrhagic infarcts in lungs.	Marchand's first case of Chorio-epithelioma. p. 14 et seq. Curettage of uterus revealed normal condition. Diagnosis from vaginal growth. Peritonitis. Pyaemia.
Reported well some mos. later.	Tumour size of mans head, along side uterus. many adhesions.		The only recovery in a tubal case. (ovarian?)
Recovery from operation.	Small tumour deep in uterine wall near right tube.		
Death 12 months.	Tumour like Edgar's in uterus.	Both ovaries. vagina. Infarcts (?) in lungs.	Radical operation abandoned as some thrombosed veins could not be removed. Regretted it later.
Death 5 days after Op:	Very small tumour deep in uterine wall; Right cornu contained villi.	Large mass of hydatidiform mole behind cervix uteri.	Diagnosis from microscopic Exam: of tumour behind cervix. Uterine growth found at autopsy.

Features of Class Division A. cases.
Termination of the last pregnancy, and the occurrence,
of pregnancy.
Recovery "A." "reported well" from the operation.

No.	Date.	Reporter	Age	Pregnancies	Last pregnancy.	Signs: Symptoms: Date of onset.	Treatment.
7	1896	Appelstedt & Aschoff.	33	2 births 1 abortion	Abortion 4th month.	Haemorrhages, (Menorrhagia); 2 months.	Curetted 4 mos. Hysterectomy in 8th month.
8	1896	Appelstedt & Aschoff.	42	2 births. 1 mole.	Mole: 5th or 6th month.	Discovered a tumour in labium minus 8 days after delivery. Haemorrhage from uterus & secondary tumour.	The tremendous haemorrhages on attempt to interfere, prevented operation.
9	1902	Austerlitz	23	5 normal births. 1 abortion.	Abortion,	"continuous" bleeding from an abortion 6 months before she was seen.	Curetted 6 mos. Repetition 9 mos. Vaginal hysterectomy 10 mos.
10	1895	Bacon	48	6 normal births; 2 ab: 1 mole.	Mole, 9th month.	Severe haemorrhage 5 weeks later.	Removal of retained placental tissue.
11	1902	Baldwin			Normal birth.	"Trouble continued."	Removal of retained placenta 2 weeks. ditto 4 weeks. Hysterectomy, 8 weeks.
12	1895	Boldt I	33		Abortion, 4th month.	Sanguinary discharge shortly after. Profound anaemia, Pleurisy	Curetted shortly after
13	1901	Brothers	24	1 abortion	Abortion? at 1 month 1 year after the first.	Repeated haemorrhages 2½ weeks.	Curetted twice. Hysterectomy 4½ months.

Result.	Primary Tumour.	Metastases.	Remarks.
Death 8½ months	Moderately large in uterus.	Lungs, stomach Mesentery. Pancreas Intestines. Bone marrow.	Vaginal hysterectomy. Death 28 days later.
Death 4 months. Haemorrhage & Sepsis.	In uterus. a small tumour penetrating deeply.	Vagina. Lungs. Spleen.	The tumour in the vagina was a mass of hydatidiform mole. Malignant mole. See p. 19.
Death, with symptoms of secondary tumours 14 mos	In uterus. like Dr Edgar's	Lungs symptoms. Fro. P. In.	Diagnosis of Chorionepithelioma from the curettings; symptoms ceased therefore did not operate. Recurrence a month later: same diagnosis from 2nd curetting. Radical op: too late. See p. 21. From Sangers Clinic.
Death, 6 months.	Large tumour, In uterus.	Detached nodules in uterus. Broad ligament.	From Chiari's Institute. Reported at first as Deciduoma Malignum. Re-examined & redescribed as Chorionepithelioma 1897, p. 21.
Death 3-4 months.	In uterus.	In omentum	Recovery after operation, Good: rapid development of cachexia, see p. 6. Fro. P. In.
Death 6 or 7 mos.	Uterus greatly enlarged.	Fro. P. In.	Micro: Exam: showed the "characteristic decidual cells".
Recovery. Reported soon after.	In uterus.		Curetted the day before, radical operation. Had to stop on account of severe bleeding.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms: Date of onset	Treatment
14	1901	Bucist.	42	7 Births 2 abortions	? Had not missed a period	"Flooding with clots" Repeated several times in 4 months.	Curetted. 2½ mos. Hysterectomy 4 months.
15	1901	Bucist.	24	1 normal birth. 1 abortion	Abortion 3 months.	Irregular haemorrhages 7 months.	Curetted 7 mos. Hysterectomy 16½ months.
16	1901	Buschbeck	51	8 births, 1 mole 1 abortion	Mole	Haemorrhages: loss of strength: foul discharge. A few weeks.	Hysterectomy 8 months.
17	1902	Busse	40		Abortion	6 months later, hemiplegia: embolism.	
18	1901	Butz.	44	8 births 1 abortion 1 mole.	Mole	Haemorrhage. 13 days.	Curetted twice.
19	1896	Cazin-Segond	30	3 births 1 mole	Mole	Haemorrhage, 3 months.	Curetted 3 mos Hysterectomy 9 mos
20.	1896	Champneys	18	1 birth 1 mole.	Mole 7 months	Severe haemorrhage 3 months. Brown discharge. Rigors Anaemia.	Mole cleared out, Repeated curettings.

Result:	Primary tumour	Metastases	Remarks
Death 28 hours after op:	Irregular ulcerating mass on upper part of anterior wall of uterus.	No autopsy.	Some "cysts" found after second bleeding, may have been mole tissues. Chorioepithelioma, Prof. Sutherland. Not published in detail yet.
Death 12½ mos.	Large mass in uterus.	Lungs, liver, kidneys, Pancreas, heart, ovary.	Improved after operation. Died from generalised recurrence 2 months later. Characteristic tissue in secondaries (Letter from Prof. Sutherland.)
Recovered, Well 2 mos later.	In uterus, Size of fist.	No symptoms of them.	Nearly died of haemorrhage.
Death 6 months.	Uterus & adnexa free. Primary not clear, see remarks.	Heart, spleen, Intestines, kidneys, Pulmonary & hepatic veins.	There were thrombi of somewhat firm, dry character in right & left ventricles which proved to be tumours. That in right ventricle (size of a hen's egg) was regarded as most probably the primary.
Death 1 year after last op:	Tumour mostly of syncytium in uterus.	Many in lungs.	The uterus was cleared out after the mole. After the haemorrhage it was curetted. All symptoms were absent for nearly a year, & she menstruated regularly. Then haemoptysis, cough, rapid development of cachexia and death.
Reported well 3 yrs later	Posterior wall of uterus.	Right ovary.	<u>Recovery in spite of metastasis.</u>
Death 8 months.	Uterus enlarged, sloughy condition inside.	Lungs.	Abscesses alongside uterus.

No.	date	Reporter	Age	Pregnancies	Last pregnancy.	Signs: Symptoms: Date of onsets	Treatment.
21	1877	Chiari	24	1 pregnancy.	Normal birth	Repeated haemorrhages, Later haemoptysis.	
22	1877	Chiari	23	Three	Normal birth.	Bleeding 4 weeks Haemoptysis.	Evacuation of uterus.
23	1877	Chiari	42	one	Abortion in 6th month.	Bleeding, 6 days.	
24	1896	Chrobak	33	2 births 1 abortion?	Abortion?	Haemorrhage severe then: curetted: renewed haemorrhage 5 mos Rigors, haemoptysis, foul discharge, Fever.	Repeated curettings, hysterectomy abt 8 or 9 months.
25	1896	Cock.	30	4 normal births.	Normal birth.	Slight haemorrhage on 14th day. Severe a few days later: fever: lethargy.	Uterus curetted 1 months
26	190	Broom	44	5 births 2 abortions	See remarks.	Amenorrhoea, Leucorrhoea: swelling of abdomen: emaciation, secondary nodule in labium.	

Result.	Primary tumour	Metastases.	Remarks.
Death 6 months.	Irregular mass in whole fundus & corpus uteri	Isolated nodules in uterus. Broad ligaments, Lung.	Described at first as carcinomata, now regarded by Chiari as Chorion-epithelionata, see p. 21.
Death 6 months.	Irregular tumour of fundus uteri	Lungs.	
Death 6 months	In uterus	Isolated nodules in uterus. Vagina, ovary, pelvis, lymphatic glands Lungs.	
Recovered from op:	Tumour in uterine wall covered by mucous membrane.	Lungs?	Micros: Exam: of curettings negative. Extirpation on clinical grounds in spite of signs of metastasis. See p.
Death 8 weeks.	Small tumour in uterus.	Lungs. Ovary.	The placenta was examined & was supposed to be healthy.
Death abt 6 months from amenorrhoea	A very large tumour of uterus, 6" + 4" + 4 3/4"	Lungs, vagina, parametrium,	Diagnosis from examination of secondary nodule. Death before they could operate. Absence of haemorrhage remarkable. Last pregnancy 6 years before, but amenorrhoea for 4 months before discovery of tumour.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms Date of onset	Treatment
27	1903	Grossen + Fisch	48	11 births 3 abortions 1 mole	Mole	Severe haemorrhages 6 weeks. Sanguino-purulent discharge.	Curetted 11 weeks. Hysterectomy a few days later.
28	1903	Fleischmann	30	3 births 1 mole.	Mole	Amenorrhoea: 27 months, Loss of health. Tumour in vagina found 33 months.	Curetted 20 days. Excision of secondary, and clearing out of uterus 33 mos. perforation of uterus.
29	1897	Fränkel. E.	29	1 Birth 1 abortion	abortion no details	Uterine discharge. Wasting: pain in abdomen + head. Supposed metritis	Seen too late.
30	1897	Fränkel E	31	2 births	Normal birth.	Haemorrhage. 7th day. Foul discharge. Metastasis in vagina 2½ months.	
31	1897	Fränkel E	48	5 normal births. 1 mole.	Mole 3rd month.	Haemorrhage: 4 weeks. repeated	Hysterectomy 2 months
32	1895	Fränkel L. (Hecker)	26	First pregnancy.	Mole 3rd month.	Pain; haematinis Wasting. Seen at 21 months.	Exploratory ofuration only.
33	1896	v. Franqué	32	6 births	Perfectly normal birth	Intermittent haemorrhage 4 weeks. weakness, haemoptysis	Curetted 4 mos hysterectomy 4½ mos.

Result.	Primary tumour	Metastases	Remarks.
Reported well 6 months later	In uterus; size of walnut.	Scattered nodules in uterine wall.	
Well, 10 months later	Uterus size of 6–8 weeks pregnancy.	Vagina	Spontaneous recovery after perforation & abandonment of operation; see p. 117.
Death 4½ mos.	Size of fist in uterus.	Vagina, cervix uteri, Lungs. Liver, kidneys Spleen; brain	Described as Sarcoma in 1896. Histo micro: Exam: 1896. Chorion-epithelioma. Absence of haemorrhage.
Death 2½ mos.	In uterus very small.	Several very large, in vagina Lung, uterine veins.	Described in 1892, as Sarcoma clinically. Micro: Exam: flat celled epithelioma. 1896 Chorionepithelioma.
Well, 7 mos later	In uterus like Edgar's. Posterior wall.		Last normal birth 10 years before.
Death 24 mos.	In uterus.	Vagina, Spleen Parametria Bladder,	Regarded as hopeless & operation abandoned: survived 3 months. Symptoms of metastasis in lungs & brain. Partial T. In. only. See p. 13
Recovered rapidly. well 17 mos. later. (Hermann)	In uterus	Lungs probably.	Diagnosis of retained placenta 4 mos. Uterine wall felt "Papier dunn". 12 days after clearing out the uterus was as big as ever. Recovery in spite of metastasis.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms Date of onset	Treatment:
34	1897	Gebhard	30	8 normal births	Normal birth.	Haemorrhage 7 weeks. Pain in abdomen.	Hysterectomy 6 months.
35	1897	Gebhard	23	1 birth at 8 months. 2 abortions. 1 mole.	Mole, 2½ mos.	Mole cleared out. Severe haemorrhage 3 weeks later!	Hysterectomy 4 weeks. Diagnosis from micro: exam.
36	1897	Gebhard	26	1 normal birth. 1 tubal pregnancy.	Tubal pregnancy.	Supposed abortion in 2nd month. Haemorrhage continued. Pain in head, loss of memory.	Extirpation of vaginal tumour
37	1892	Gottschalk	42	2 births 2 abortions	Abortion 3rd month.	Severe haemorrhage after the abortion, repeated many times.	Uterus cleared out 4 times. Hysterectomy 6½ mos.
38	1900	Gottschall	?	1 birth 1 abortion	Abortion removed manually 4 mos.	Rupture of uterus 3 mos. later on making an effort.	Laparotomy. Death 3 hrs later.
39	1895	Götze	21	1 normal birth.	Normal birth.	Bleeding 6 mos. later	Tumour removed from uterus 6 mos. Laparotomy 12½ mos. inoperable

Result.	Primary Tumour	Metastases	Remarks
Well, 11 mos. later.	uterus size of child's head. Tumour size of fist. Posterior wall.		
Recovered from op:	Small tumour in uterus.		Villi (mostly hydatidiform) with marked epithelial overgrowth in blood vessels deep in uterine wall: — <u>early destructive mole.</u>
Death 4 mos.	Tumour in left fallopian tube.	Cerebrum; Lungs, Spleen Mesentery Prevertibral, lymphatic glands.	Found metastasis in vagina at 3 months.
Death 13½ mos.	Big ragged ulcer in fundus & corpus uteri.	Pelvis, lungs, spleen, kidney Brain?	At first described as Sarcoma Chorion-decidua-cellulare. Villi (? Marchand, Well for 6 months after op: Death with symptoms of tumour in the brain
Death 3 months.	Tumour, size of foetal head, in uterus ruptured over fundus.	No. P. Ex.	Described as "Malignant hydatidiform mole, passing into Syncytioma malignum"
Death 13 mos.	Tumour in fundus uteri.	Detached nodules in uterine wall. Vagina: lungs liver, kidney	Tumour in vagina 10 days after the curetting: diagnosis of sarcoma-decidua-cellulare: Laparotomy abandoned without touching the uterus. Death 10 days later.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms: date of onset.	Treatment.
40	1902	Gräefs	37	1 normal birth. 1 abortion?	Menstruation delayed 8 days. Ab: in first mo:?	Brown discharge after abortion. Haemorrhage; 2 months: Severe anaemia.	Curetted after the abortion & at 4 mos.
41	1899	Guérard	40		Mole 2 months	haemorrhage; 4 weeks	Mole was cleared out: curetted 3 mos. Hysterectomy 3½ mos.
42	1883	Guttenplan	28	7 births 1 mole.	Mole: cleared out.	Suppressed retained placenta. Anaemia	Curetted 3 mos.
43	1895	Hartman & Toupet.	25	1 birth 1 abortion?	Normal birth or abortion?	Oozing of blood after the abortion: severe haemorrhage. 6 months.	Curetted. Recurrence of symptoms in 8 days. See remarks.
44	1899	Haeltain			Mole, 10 weeks.	Haemorrhage 3½ weeks. A few days later expulsion of mass "not unlike a fleshy mole". Severe bleeding.	Curetted. 1 mo: Hysterectomy 11 weeks.
45	1903	Hawkins-Ambler.	39	12 births. 3 abortions	Abortion. Severe haemorrhage	6 weeks, severe bleeding. Two years later discovery of tumour. Brown discharge. Anaemia Breathlessness.	Curetted after the abortion. Inoperable when next seen.

Result.	Primary tumour	Metastases	Remarks.
Death 5 months	Size of hen's egg in uterus. Grew in one month.	None	Birth 1 year before abortion: regular menstruation in interval. Villi found in the second curettings, therefore they delayed radical op: Sepsis: recovered: Died a few days later.
Well in 1902 ($3\frac{1}{2}$ years later)	In anterior lip of os uteri like a carcinoma.		Curetted on account of "erosions". Diagnosis from micro: exam: of curettings.
Death 4 mos.	Uterus	Lungs Vagina	Called "haemorrhagic sarcoma" with large spindle & multinucleated cells.
Death $7\frac{1}{2}$ mos.	Small nodule in cavity of uterus. Two others in wall.	Ov: & Ur. Removed uterus.	Hysterectomy was to be done, but haemorrhage set in which soon ended fatally in spite of all treatment. "Decidioma". Re-examined by Segall & Gottschalk. p. 21.
Recovery, well in 1903. 5 years.	Ulcerated nodule, size of a walnut in uterus.		Suspected sub-involution. Haemorrhage so severe that curettings were examined. Diagnosis from them. Operation refused. Nearly died of next haemorrhage 7 weeks later. See p. 61
Death 2 years.	In uterus		English case: considers Marchand's view proved.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset.	Treatment.
46	1898	Helliers	39	7 normal births	normal birth.	Continued reddish discharge. Became offensive. 16 weeks. Haemoptysis	Too ill for operation.
47	1901	Hitschmann	38	4 normal births	Obscure: missed 1 period.	Severe bleeding 1 month after missed period. Continued bleeding.	Hysterectomy 5 months.
48	1897	Holleway (Eierwann)	52	9 births 1 mole	Mole, July '92	Haemorrhage see remarks.	Curetted 4¼ years, hysterectomy 4¾ years.
49	1901	Holzapfel	37	Pluripara	Abortion 3 months.	Haemorrhage: indefinite, found secondary tumour 2 years.	Excision of secondary tumour & hysterectomy.
50	01	Horrocks	48	8 births 4 abortions	Abortion 3 months	Haemorrhage; greenish discharge, 22 months. Passage of fleshy masses.	Hysterectomy 27 months.
51	1902	Hubbard	34	5 Births 3 abortions	Delayed menstruation procured abortion.	Menorrhagia? Sub-involution. Severe bleeding 6 months.	Curetted 6 mos. Repeated 7½" Hysterectomy 9 mos.

sults	Primary tumour	Metastases	Remarks.
Death 20 weeks	Large tumour in uterus: adhesions: perforation into signoid flexure	Omentum Broad ligament, lungs, Ovary	Regarded at first as retained placenta & sepsis. "Sarcoma" (Eden) "Decidnoma malignum" (Targett)
Death 3 weeks after operation	Large tumour in uterus.	General dissemination; brain: thyroid kidneys, liver intestines: lungs: vagina spleen	Langhanscoma: i.e. minimal amount of syncytium
Well 4 months later.	Small soft tumour in uterus.		After the mole bleeding which ceased without operation: Spring '93, monopause 3½ years later sudden severe haemorrhage ~~4½ years latency~~. Chorionepithelioma according to Marchand.
Well in Nov. 1902. 2 years.	Tumour in uterine wall.	Vagina	Curetting showed "decidua". Diagnosis myoma + incomplete abortion: correct diagnosis from micro: exam: of secondary.
Good recovery. Death 33 months.	Deep ulcer in uterus.	Pro. P. In.	Chorionepithelioma (Bellingham Smith)
Recovery. Well 6½ months.	Large tumour in uterus	Detached nodule in uterine wall.	

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset	Treatment
52	1902	Hubl.	36	5 Births 2 abortions	Full time birth: child dead.	Haemorrhage 7 weeks. Severe 8 weeks. Haemoptysis 3 months.	Excision about 3 months.
53	1902	Hubl.	23	First pregnancy.	Mole	Haemorrhage: 14 days. Anaemia: cachexia.	Curetted 3 mos Exploratory laparotomy.
54	1901	Inglis & Bruce.	22	1 Birth 1 mole	Mole 5 months	Epileptic fit. 6 mos. later.	
55	1882	Jacubasch	26	2 normal births, 1 abortion	Abortion in 4th month.	Haemorrhage. Weakness.	
56	1868	Jarotzky & Waldeyer	36	3 Births, forceps, rhachitis, subject healthy otherwise; 1 ab.	abortion 5th month.	Haemorrhage persistent, foul discharge: anaemia; wasting.	Louis treatment.
57	1894	Jeannel	26		Abortion	Haemorrhage 13 months.	Hysterectomy 15 months
58	1900	Jorgenson	49		Abortion?		Hysterectomy very early

Result.	Primary tumour	Metastases	Remarks
Death 4 mos.	Size of walnut in vagina. ulcerated.	Vagina, lungs, liver, Ovary.	Primary vaginal case. Uterus sound. Recurrence in 20 days after Op: Perforation from vagina into bladder.
Death 4 mos.	Large tumour in uterus: posterior wall. Extensive adhesions.	Anterior wall of uterus: cervix: lungs.	In museum preparation, the fundus is ruptured.
Death 6 months	In uterus	Lungs Brain	Death 3 days after an epileptic fit. Tumour found at P. M. Villi.
Death 4 months.	ulcerated mass in uterus, size of apple, rising from fundus.	Uterine wall, vagina	No micro: Exam: Death from intraperitoneal haemorrhage from small nodule on back of uterus.
Death about 4 months	Uterus much enlarged; full of hydatidiform vesicles	None	Uterine wall riddled with the vesicles, in the venous sinuses. Death, practically from haemorrhage, in 24 hours, two months after first complaint.
Recovery.	Haemorrhagic, polypoid tumour in uterus.		From Marchand.
Well 1 year later	In uterus. uterine vessels full of tumour tissue		History not clear. Pregnancy diagnosed from finding villi in the curettings.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset.	Treatment.
59	1897	Jurassowsky			Mole		Hysterectomy 2 years.
60	1891	V. Kahlden	30		normal birth	Haemorrhage 3 weeks. Rigors	Uterus cleared out.
61	1907	Kaiser	35	3 Births	Hydatidiform mole, 3rd month.	Haemorrhage, continued until curettement. Recurred at 9 mos. Cachexia.	Curetted 4 mos. + at 10 months.
62	1890	Kattenbach (Rummel)	46		"Colossal" mole.	Uterine tumour found 5 months.	uterus cleared out 5 months.
63	1892	Karstrom & Vestberg.	32	1 abortion 1 mole.	Mole, 3 months	Haemorrhage. Pain in pelvis. Rigors 6 months.	Hysterectomy & excision of secondary tumour in vagina.
64	1896	Karstrom & Vestberg.	36	3 Births 3 abortions	Abortion 3 months	Haemorrhage 6 months	Hysterectomy 6 months
65	1898	Kelly & Teacher	27	2 births 1 abortion	Abortion 5 months.	Haemorrhages, secondary tumour in vagina; haemoptysis	Excision of vaginal nodule.
66	1902	Kleinhans					Hysterectomy Excision of secondaries.
67	1902	Kleinhans			see remarks		

Result.	Primary tumour	Metastases	Remarks
Death just after	In uterus	Brain	
Death 3½ months.	Posterior wall of uterus.	None.	"Destructive placental Polyp." Villi with epithelial overgrowth in blood-vessels of uterus. (Marchand)
Dying 12 months.	Very large tumour in uterus.	Lungs? Ilias crest.	Radical Op: abandoned on patient developing haemoptysis. Patient regarded as dying when case was reported.
Death 9 months.	Several nodules in uterus.	- None.	Perforation of uterus in 3 places. Intraperitoneal haemorrhage.
Recovery reported less than 1 year.	In uterus	Vagina	Recovery in spite of metastasis having occurred.
Recovery	In uterus		
Death 4 months	In uterus	Vagina; Parametria; lungs Lymphatic glands	p. 48.
Recovery.	In uterus	vagina	No details published yet. Recovery in spite of metastasis having occurred. Preparations seen. J. H. T.
Death	In left ovary.	Vagina; lungs Fallopian tube	Ovarian pregnancy or teratoma? Saw preparations. J. H. T.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms: date of onset.	Treatment.
68	1895	Kleins	27		Mole 3½ months.	Bleeding "some time after." Ceased after curetting.	Curetted 2 months.
69	1900	Kolmenkin	41	11 normal births.	normal birth.	Persistent bloody discharge. 2 mos. Pain in abdomen 3 months.	Hysterectomy
70	1894	Kottnitz (Schmorl)	25	3 Births	normal birth	Haemorrhage continuous from the confinement. Tumour found 33 days. Rigors	Vaginal tumour rutinus cleared out with fingers & spoon: three operations.
71	1900	Krebs	23	First pregnancy	perfectly normal birth.	Haemorrhage, continuous from the confinement to first curetting. Acute sepsis with Haemorrhage 6¼ mos	Curetted. 2 mos Septic abortion removed 6½ months.
72	1902	Krewery	33		Menorrhagia Abortion?	Haemorrhage. Cough Haemoptysis. Consolidation of lung. Hemiplegia.	
73	1902	Krewery	29		Mole	Hemiplegia 4 mos. after the confinement.	
74	1872	Kriegery	25		Malignant mole.	Haemorrhage of 8 months duration. Peritonitis.	

ult.	Primary tumour	2° Tumour Metastases	Remarks.
Death 8 months	Of considerable size. In uterus.	Lungs, vagina Base of cervix	Quiescence after curetting; tumour found 6 months. "Sarcoma giganto-cellulare" Chorionepithelioma (1897) of atypical infiltrating variety.
Well, 6 months later.	Small deep ulcer in uterus. Perforation. Adhesions	Beside cervix	Adherent intestine peeled off: not resected. Recovery in spite of metastasis having occurred.
Death 3½ months	In uterus like Edgar's	Vagina: Broad ligament, lungs Brain? under peritoneum near uterus.	Haemorrhage from "vaginal varices." Apparent sepsis; no pyaemia. P. M. Went insane. Exam: of head not allowed.
Death 6½ months. Day after op.:	Uterus full of shreddy putrid mass.	Incomplete P. M. Peritonitis.	Supposed herself pregnant 2 months after the curetting. Haemorrhage absent for 4 months. supposed retention of mole 2 months; Acute sepsis: death in 5 days. "Pure syncytial." see p. 108 and p. 123.
Death 9 weeks	Size of apple. Fundus uteri	In many organs	Brought to hospital as case of apoplexy. Death soon after.
Death abt 4 months.	In uterus.		Uterus about normal size. Thickened endometrium; cicatrix causing adhesion between the two sides in which tumour was found.
Death.	Large tumour in anterior wall of uterus nearly perforating.		Observed in 1854 "Destruirende interstitielle Blasenmole". From Marchand. On Blasenmole: p. 461.

No.	date	Reporter	Age,	Pregnancies	Last pregnancy.	Signs: Symptoms: date of onset.	Treatment.
75	1895	Kuppenheim	33	5 Births	Birth in 7th Month.	Haemorrhage, 3 weeks, Repeated soon after operation. Cachexia	Uterus cleared out 3 weeks. Hysterectomy 2½ mos.
76	1901	Kworostansky. (1)	27	2 Births 1 abortion,	Abortion 3 mos.	Bleeding: 2 months Tumour found, 2 weeks later.	Manual removal of abortion. Curettage 2½ mos.
77	1901	Kworostansky (2)	24,	2 Births 1 abortion	Abortion 6 mos.	"Menorrhagia". Severe bleeding 6 months. Cough: spit: tubercle bacilli in sputum.	Curetted 6 mos + 7 mos. Hysterectomy 7½ mos.
78	1902	Ladinski	19	1 Birth 1 mole	Mole, 2 months.	Haemorrhage: continuous with the pregnancy, Cough haemoptysis. Patient very ill.	Abdominal hysterectomy, 9 weeks.
79	1902	Langhans	22.	First pregnancy.	perfectly normal birth.	Severe haemorrhage, 4 mos. Irregular bleedings.	Curetted 11 mos. Hysterectomy 12½ months.
80	1901	Langhans	29	1 Birth	Normal birth.	Profuse haemorrhage, 3 mos. 2ndary found in vagina 6 mos. extreme weakness + anaemia.	Scraping of vaginal tumour 6 mos. Uterus curetted 8½ months.

Result.	Primary Tumour	2ndary Tumour	Remarks
Well: 2 years & 4 months.	Size of fist in uterus.		Quoted from Giermann.
Death abt 3 mos.	Tumour like Kelly's: in uterus.	Lungs	Diagnosis from micro: Exam: of curettings: postponed hysterectomy to allow recuperation: sepsis: pyaemia
Well 4½ mos.	Like Edgar's in uterus		Spit disappeared as she got well. Metastasis in Lungs?
Recovery. Well, 18 months later.	Small deeply burrowing tumour in uterus, containing villi.	Lungs?	Symptoms indicating involvement of the lungs appeared during the pregnancy; disappeared after confinement, reappeared, & finally disappeared after the hysterectomy. Recovery in spite of metastasis
Well, 1 year later	Small tumour in uterus.		Diagnosis by micro: exam: of curettings. Menstruation between confinement & onset of illness: menorrhagia after 6 weeks interval: abortion (?) 2½ months after confinement.
Well 10 months later	Villi in uterus regarded as a tumour.	Tumour size of walnut in vaginal wall.	After scraping recurrence in vagina in 2 weeks (1/6/5/00): tumour burst 22/5/00: extruded slough; healed 1/6/00. Haemorrhage from uterus 4/6/00, curetted 9/6/00, no further trouble. Spontaneous healing of vaginal tumour.

No	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset	Treatment
81	1901	Langhans	30	3 normal births. 1 mole	mole	Haemorrhage continued for 2 months.	Curetted 2 months. Hysterectomy 2½ mos.
82	1894	Laver & Wilkinson	21	1 Birth 1 abortion	Abortion 3 mos.	Constant slight bleeding for 5 mos: then menorrhagia: anaemia.	Curetted 10 mos. Recurrence in 3 weeks. Hysterectomy 12 mos.
83	1892	Lebensbaum, (Steinhaus)	27 (37)	6 Births	Normal birth.	Haemorrhage, 4 weeks. Recurred 11 days after curetting "Vaginal varix," 4 months.	Curetted 4 weeks. Hysterectomy 5 mos.
84	1895	Leopold			normal birth	Irregular menstruation from 3rd week after. Pain in abdomen. Collapse, Intraperitoneal haemorrhage.	Abdominal. Hysterectomy one year.
85	1897	Lewers	24	First pregnancy.	Abortion	Red discharge, continuously after abortion.	Curetted 10 mos Hysterectomy 11 mos.
86	1897	Lindfors & Vestberg	44	2 Births	No definite abortion: a menorrhoea 2 mos.	Haemorrhage, 2 mos. Foul discharge. See remarks.	Curetted 4 mos. Hysterectomy 5 months.

Result.	Primary Tumour	Metastases	Remarks
Well, 7½ months	In uterus		The curettings consisted of hydatidiform villi with epithelial overgrowth characteristically chorionepithelioma-atous. Similar tissue in excised uterus.
Death 14 mos.	In uterus	Ilio. P. In.	After operation: rigors: Sepsis?; signs of metastasis in lungs. From Ladinski.
Death 5 months (6 days after op:)	Body of uterus distended to size of 4 mos pregnancy.	Vagina	Originally described as "Carcinoma" Re-examined by Steinhaus 1900; chorionepithelioma.
Recovered from op:	In fundus uteri: growing into muscularis.	Uterine wall.	Haemorrhage from a sub-peritoneal uterine nodule was cause of collapse.
Well in 1902 (5 years)	Rough surface in uterus on posterior wall.		English group of cases "Sarcoma".
Death 5 days after op: see remarks	Large ragged ulcer in uterus.	None	Curettings described from micros: exam: as placental remains. (Marchand gives this case as after mole: death from tuberculosis of lungs without metastasis 5 months later.)

No.	date	Reporter	age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset	Treatment
87	1900	Lindfors & Vestberg	22		Confinement natural but premature	Tumour found in vagina 1 month.	Extirpation of vaginal nodule. Curetting of uterus.
88	1902	Lockyer	42	7 Births 3 abortions	Normal birth 3 yrs or abortion	Persistent haemorrhage since 4 mos before; incomplete abortion?	Inoperable when seen
89	1895	Löhlein	47	6 births 1 mole.	Mole, 7 mos.	Haemorrhage: foul discharge, 20 mos. Tumour found 2 yrs.	Hysterectomy 27 mos.
90	1896	Lomberg & Mannheimer (1)	~~38~~	Multipara 1 mole	Forceps delivery at full time	Haemorrhage, 4 weeks. Tumour found 3 mos.	
91	1896	Lomberg & Mannheimer 2	42	2 births 1 mole.	Hydatidiform mole, 4 mos.	Bleeding 7 weeks. Bloody discharge: Pain in thorax & abdomen 1 year Anaemia.	Hysterectomy & removal of vaginal tumours 2 years.
92	1896	Malcolm (Hebb).	27	3 Births 3 abortions	Abortion? 3 mos or normal birth 17 mos before.	Septic infection after abortion, curetted 2 weeks, Tumour found 3 mos. Brown discharge.	Uterus found perforated: hysterectomy abandoned.
93	1895	Marchand[2] (Zwerke)	34	9 Births	Normal births	Haemorrhages 3 weeks.	Curetted, 4½ mos Hysterectomy 5 mos

Result	Primary Tumour	Metastases	Remarks
Death 8 months	Uterus sound, characteristic tumour size of chestnut in vaginal wall.	Large tumour in lungs: many other organs riddled with metastatic nodules.	Patient made good recovery: well 4 mos later: 2 mos after that cough, loss of strength (influenza?) pleurisy, death in 5 weeks. Primary vaginal
Death 4 mos.	In uterus	Lungs.	The uterus was found to be perforated by the tumour.
Death 3 yrs & 3 mos after mole	In uterus	Lungs	A very slow case. Apparent menopause. Complete recovery after operation; 10 mos later pleurisy: death in 2 mos from metastasis in lungs.
Death 6 mos.	In uterus small flat tumour on anterior wall.	Vagina: Lungs, liver: spleen: kidneys: lymphatic glands.	Reported in 1872 as "epithelial cancer". On later microscopic exam: reported along with next case as Chorionepithelioma.
Recovery well 18 mos (Biermann)	Tumour in uterus	About 20 nodules "like varices" in vagina.	Very slow course. Apparently metastases in lungs 1 year. Very much reduced, but made rapid recovery. "Carcinoma Syncytiale" after Marchand. p. 22.
Death 3 mos.	Ragged ulcer in uterus. Perforation	Lungs Parametria	English group ~~containing a thrombosed vein (tumour?) had to be left.~~ "Sarcoma".
Well 33 mos later (Biermann)	Large growth in fundus. Ruptured during removal.	See remarks.	An adhesion containing a thrombosed vein (tumour?). Had to be left.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset.	Treatment.
94	1898	Marchand 3	42	5 Births 1 mole.	Mole 3 mos.	Profuse haemorrhage 3 weeks, Discharge	Hysterectomy 2½ mos.
95	1898	Marchand 4.	22	First pregnancy.	Mole, 4 mos.	Haemorrhage 4½ mos: decline in health.	Removed vaginal nodules 5½ mos.
96	1901	Marchand	43	9 Births healthy.	No history of abortion or recent confinement.	Cough. Haemoptysis Gradual hemiplegia 3 mos later.	
97	1901	Marchand	-	-	Mole	Hemiplegia, 4 mos later	
98	1902	Marchand (Gunther)	52	Multipara Last 13 yrs before	Mole	Haemorrhage during pregnancy + after the confinement.	Hysterectomy 2 mos.
99	1897	Martin + Kieffer	28	4+ pregnancies	Abortion 4+ mos.	Continued bleeding after the confinement for 14 mos.	Hysterectomy 14 mos.
100	1903	McLaren	53	10 Births: the last an abortion in 3rd mo: 9 yrs before.	?	Sudden haemorrhage, which recurred every 3 or 4 days. Brown discharge. wasting.	Hysterectomy 5 mos after the first haemorrhage
101	1901	McDonald	30	2 Births 1 abortion	Normal birth probably.	Haemorrhage. Abortion(?) 3 weeks before seen.	Curetted twice

Result:	Primary Tumour	2ndary Tumour	Remarks
Recovery reported 2 mos.	In uterus		Villi in tumour.
Death 7½ mos.	In uterus	Vagina, lungs, ovary, Lymphatic glands.	Hysterectomy was not done on account of involvement of the vaginal veins.
Death.	Large tumour in fundus uteri	Abdominal wall: vagina: lungs: heart: liver: kidney: intestines, brain.	Diagnosis of metastatic tumour in brain; found many small brown nodules in it.
Death	Lungs?	Brain: lungs: kidney.	Similar to preceding. No tumour in uterus: decidual condition of mucous membrane: primary supposed to be in lungs.
Recovery.	In uterus		Villi deep in uterine wall in blood vessels, marked epithelial overgrowth.
Recovery.	In uterus		Patient was markedly cachectic yet made a good recovery.
Death 6 days after op:	Very vascular uterine wall: clots: tumour between clots + muscle.	None	Pronounced "deciduoma malignum" by the Pathological Committee of Obstetrical Society of London. Both cell forms present. Uterus size of 3 mos pregnancy organ. Menopause 13 mos before onset.
Death 5½ mos. exhaustion	In uterus.	No: P. Inj	Curettings termed "Placental tissue". Quoted from Ladinski.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset.	Treatment.
102	1900	McFarland (Noble)	30	2 Births (last 2½ yrs before)	?	"Profuse menstruation Sept. 92 to June '93. Cough: haemoptysis Anaemia. Nov. 93.	Sloughing mass cleared out of uterus June '93.
103	1903	McMurtry.	35	6 Births	Apparently abortion 2nd month.	Haemorrhages continued after abortion; Sepsis.	Abdominal. Hysterectomy 6 weeks.
104	1795	Meckel-Gregorini			Mole at end of 10 mos.	Chlorosis: ascites; anasarca; phthisis pulmonalis.	
105	1894	Menge	36	10 pregnancies	Mole, 6 mos removed.	Haemorrhage 5 mos.	Hysterectomy 7 mos.
106	1894	Menge	18	First pregnancy.	Mole	Haemorrhage & tumour in uterus 6 weeks.	Growths removed. Recurred, in 8 days Hysterectomy about 8 weeks.
107	1902	Menzel	23	4 normal births in 4 years.	Normal birth.	Irregular haemorrhages from 3 weeks onwards. Washing: intense anaemia. Bloody slimy discharge.	Curettage abt 6 weeks. Perforation. Hysterectomy next day.
108	1900	Metor (Bonnaire)	31	1 normal birth, 1 mole	Mole, removed in 2nd month.	Haemorrhage; 27th day. Alarming; Syncope.	Hysterectomy 33rd day.

Result	Primary Tumour	Metastases	Remarks
Death Dec. '93 6 mos.	Posterior wall of uterus.	Lungs?	Improvement after curetting: 5 mos. later widenes of recurrence in lungs. Death a month later. Originally reported as "round celled sarcoma". From Ladinski.
Good recovery.	In uterus		Reported a few months later.
Death about 1 year.	Tumour in fundus & body of uterus		Tumour grew into cavity of uterus & also out into abdomen: perforation? bloody assites. From Marchand.
Death 13 mos.	Small tumour in uterus	Pelvis; vagina: lungs: Stomach Intestines, bone marrow, lymphatic glands.	Originally reported as "Deciduo-sarcoma". Seen J.N.T. Bronchial lymphatic glands infected.
Well, 1 year later.	Uterus.		In letter to Biermann, Krenge wrote that in view of the course of the disease after operation he withdrew the diagnosis of Deciduoma.
Well, 8 months later.	a small deep ulcer in fundus uteri		See p. 69.
Death 35th day	Uterus size of foetal head at term: elevated area on posterior wall.		Villi with stinking hypertrophy of epithelium & infiltration of uterine muscle. Malignant mole.

No	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset	Treatment
109	1900	Nestor (Legry)	26	1 mole, 2 abortions	abortions at 6 weeks, Oct. 98	Metrorrhagia: 4 months later: severe Oct. 99 & Dec. 99.	Curetted Dec. 98 & May 1900.
110	1888	Meyer	55	3 births 1 mole	Mole, removed 4 mos:	Bleeding continuous after mole. rigors.	Uterus cleared out 6 mos
111	1898	Morales Arjona					Hysterectomy
112	1896	Morrison	35	9 normal births	Normal birth.	Profuse haemorrhage 6 weeks: syncope, haemoptysis 4 mos after op:	Curetted, 9 weeks Hysterectomy 15 weeks.
113	1899	Muller. E.	25	2 normal births, 1 mole	Mole, 4 mos.	Thereafter bleeding & wasting.	Curetted 4 mos. Hysterectomy 2 weeks later
114	1891	Muller P.	39	6 normal births 1 mole.	Large mole 5 mos, cleared out:	Repeated haemorrhage	Curetted several times
115	1896	Neumann. (Schaerta)	29	3 normal births, 1 ab: 1 mole.	Mole.	Haemorrhage, 1 mo Anaemia; Tumour in vagina 6 weeks	Curetted 6 weeks. Hysterectomy & excision of vaginal nodule.
116	1896	Neumann (Illiel)	52	12 normal births, 1 mole,	Malignant mole	Severe haemorrhage during pregnancy.	Extirpated uterus along with the mole.

Result	Primary Tumour	Metastases	Remarks
	Large mass scooped out of left cornu of uterus.		The mass removed in Dec. 99 showed the structure of chorionepithelioma. She was in feeble health in May '00. Later history not known.
Death 8 mos.	Ragged ulceration of interior of uterus.	?	See p. 19. From Marchand 1895.
Well 1 yr later	On posterior wall of uterus		Tumour felt upon intra uterine digital exam: suspected decidioma: confirmed by micro: (Ladinski)
Good recovery. Death 8 mos.	Characteristic tumour in uterus	No. R. Inguinal Lungs ?	English group "Sarcoma". Diagnosis from curettings "squamous epithelioma".
Recovery, well 6 mos later	In uterus		Curetting showed decidua & mole vesicles: diagnosis of chorionepithelioma.
Death 7 mos	In uterus	Vagina Gluteal region	"Sarcoma Haemorrhagicum, seu infectiosum". Re-examined by Langhans 1901. Chorionepithelioma decidua in uterus.
Recovery. Well 2 yrs 2 mos (Biermann)	Uterus Villi deep in uterine wall.	Vagina	Hydatidiform villi in primary tumour, absent from secondary in vagina. Recovery in spite of metastasis.
Death 12 days. Pneumonia	Villi burrowing deep in the uterine wall	None	Malignant hydatidiform mole.

No.	date	Reporter	Age	Pregnancies	Last pregnancy	Signs: Symptoms date of onset	Treatments
117	1897	Neumann	40	3 normal births, 1 mole	Mole, 4 mos.	Haemorrhage: found secondaries in vagina	Hysterectomy & excision of secondary growths 2 weeks
118	1896	Neumann	37		normal birth.		Hysterectomy 4 mos.
119	1898	Neumann			Normal birth:	Haemorrhage from uterus	Hysterectomy
120	1894	Zikiroff			Tubal pregnancy	Communicated to Tarcha	
121	1902	Noble	30	2 births 1 abortion	normal birth.	Persistent Haemorrhage. 22 mos. Consolidation of right lung & pleural effusion	Hysterectomy 30 mos.
122	1902	Noble	24	2 abortions	Abortion 6 weeks.	Discharge like menstrua. Diagnosis Myoma. Very ill.	Abdominal Hysterectomy 3 mos.
123	1894	Nove-Josserand & Lacroix	24	2 births 1 mole.	Large mole, 6–8 weeks cleared out.	Haemorrhage 1 mo. Brown discharge. Cough.	Curetted 5 weeks Hysterectomy 6 months
124	1900	Pehamy	25		Abortion	Continued haemorrhage	Hysterectomy abt 7 mos.

Results	Primary Tumour	Metastases	Remarks
Recovery Well 2 mos later	Elevated area like placental site. Villi	Vagina (containing villi)	Secondary tumour appeared in vagina during the pregnancy.
Death 7 mos.	In uterus	Lungs.	Curettage at 3 mos. revealed only decidua. Death from metastasis in the lungs.
Death 6 mos after op:	In uterus	Lungs: very numerous.	Good recovery from op: some time later "bronchitis" with purulent sputum, areas of condensation, & friction:
in a letter: Photograph enclosed showed Langhans layer cells & syncytium, (From Marchand)			
Good recovery, Death 3.6 mos.	In uterus	Skin of breast, loin & thigh, lungs? liver. Ov. P. In.	Reported as Sarcoma (endothelioma) in 1893. Now as chorion-epithelioma.
Recovery. Well 5 mos. later	Bluish mottled tumour of fundus.		Suspected malignant tumour at the abortion. Perforation: adhesion to omentum & bladder. Mass on bladder left: felt 3 mos later; gone at 5 mos. Recovery although parts of tumour were left.
Well. 3 mos later	In uterus		Diagnosis of carcinoma from curettings.
Death ?	Small tumour in uterus extending along veins.	Vagina, Lungs involved	Recurrence in vagina 4 weeks after Op: Regarded as dying 2 weeks later.

No:	date	Reporter	Age	Pregnancy	Last pregnancy	Signs: Symptoms Date of onset:	Treatment
125	1891	Pestalozza	25	2 Pregn:	Abortion 4th Month.	Haemorrhage from a vaginal tumour Dyspnoea.	
126	1891	Pestalozza	33	5 normal births	Normal birth.	Haemorrhage. Vaginal tumour found: cough: Haemoptysis.	
127	1891	Pestalozza	45	9 normal births.	Mole 4th month	Irregular bleedings continuous with the abortion. Haemoptysis.	
128	1895	Pestalozza	32	7 births	Full time birth.	Haemorrhage 7-8 days. Anaemia Haemoptysis: tumour in vagina	Curetted
129	1895	Pestalozza	22.	1 birth. 1 mole.	Mole 2 months.	Anaemia: Haemorrhage: Cough. Haemoptysis.	Hysterectomy 3 months.
130.	1902	Pitres.	30.	1 birth. 1 abortion.	Abortion.	Haemorrhage: 8 days: tumour in vagina: 2 months.	Extirpation of tumour: curettement of uterus: 2 months.
131.	1890.	Pfeiffer.	36.	5 normal births 1 mole.	Mole in 2nd month.	Haemorrhage 9 months. Cough. Purulent Sputum.	

Results	1ary Tumour.	Metastases	Remarks
Death 6 mos.	Ulcerated nodule in body of uterus.	Vagina; Broad ligaments, lungs.	Originally described as Sarcoma. Now regarded by Pestalozza as chorionepithelioma.
Death.	Ulcerated nodule in body of uterus	Vagina. Lungs.	
Death 5 mos.	Extensive tumour of fundus & anterior wall	Lungs. Isolated nodules in uterine muscle.	
Went home dying, 5 months.	Like Kelly's	Lungs?	Radical operation regarded as hopeless.
Well. 1 year later.	In Uterus.	Lungs?	Diagnosis of subinvolution and Phthisis Pulmonalis. No T. B. in Sputum: curetted: micro: ex. decidnoma. Recovery in spite of Met[illegible]
Death 8 months.	Primary Vag- inal: uterus sound.	Brain? No P. M.	Rapid recurrence in vagina near scar of operation: refused further operation. Hemiplegia 4 months.
Death 13 months.	Size of fist in fundus uteri.	Lungs. Vagina.	See p 10.

No.	Date	Reporter.	Age.	Pregnancies.	Last pregnancy.	Signs: Symptoms Date of Insult.	Operations.
132	1897	Pick. A.	52.	5 births. 3 abortions. 1 mole.	Mole. 4 months?	Haemorrhage: 4 weeks: severe: cough: sputa: anaemia.	
133.	1897	Pick. A.	37.		Normal Birth.	Post partum haemorrhage: renewed 1 month:	Curetted 3 months
134.	1897	Pick. A. (Löffel)	26.	4 births. 1 mole.	Mole. 4 months	Severe haemorrhage: 3 weeks. Tumour in uterus.	Hysterectomy 1 month.
135	1897	Pick. L.	22.	1st preg-nancy.	Mole 4 months.	Vaginal nodule found during the pregnancy.	Excision of tumour.
136.	1900	Porter and Vasmer.	36.	2 births 1 mole.	Mole 4 months.	Haemorrhage led to exam. and discovery of vaginal tumour.	Excision of tumour: hysterectomy with mole in situ.
137.	1899	Prochownik & Rosenfeld.	37.	5 birth 3 abortion.	Abortion 2nd. month. (uterus cleared out)	Haemorrhage. 14 days: anaemia cough: severe bleeding.	Several times curetted. Hysterectomy 4½ months.
138.	1902	Crowse	43.	10 births. last 12 years before 1 mole.	Mole.	haemorrhage: regress: septicaemia	hysterectomy 6 weeks.
139.	1902	Crowse.	39.		Abortion 7th. month.	Thwarter bleeding and offensive discharge: regress: anaemia.	Curetted 4 months.

Result.	Seat of tumour.	Metastases.	Remarks
Death 4 months.	Small: in uterus.	Lungs. Spleen.	
Death 4 months.	In uterus.		Curettings revealed nature of the disease.
Well 4 months later.	In uterus. Posterior wall.		Diagnosis from micro. exam. of Mole. Cited from Eisenmann.
Well 4 years later.	"Thrombosed varix" in vagina.		Hydatidiform villi in vaginal veins: patient refused hysterectomy. Mole discharged 3 days later: see p. 111.
Well 5 months later.	Malignant Mole. Deep infiltration of uterus.	Vaginal (a mass of villi.)	Metastasis during the pregnancy. Recurrence in vagina after the hysterectomy: removal 20 days later. No mention of death of patient in paper (Potter) of 1902.
Death 8 months.	Small tumour in Uterus.	Brain? Lungs? No P. M.	Diagnosis from curetting (Marchand.) Good recovery from operation: death with cerebral symptoms: like Edgar case.
Death 8 days after Op.	Large deep ulcer in posterior wall of uterus.	No P. M.	Uterine wall almost perforated. Villi with characteristic epithelial overgrowth deep in uterine tissues. Malignant Mole.
Death 8 months.	Like in Kelly & Teacher's case.	Lungs.	"Extremely ill condition of the patient prevented any operative interference".

No.	Date	Reporter.	Age.	Pregnancies.	Last Pregnancy	Signs: Symptoms. Date of onset	Treatment.
140.	1897.	Reinicke	24.	1 birth 1 abortion.	Abortion 2 months	Bloody discharge: started after blow on abdomen. 3 mos.	Porro's amput. uterus & uterus.
141.	1893	Resinelli.	28.	3 normal births 1 abortion.	Abortion	"in a short time" malaise: debility: foetid discharge: severe bleeding 2 months. tumour in vagina 3 months.	
142.	1897	Rosner.	20.	1 birth. Tubal Pregnancy?	Tubal pregnancy?	Haemorrhage 5 months after the normal birth. Tumour beside uterus: vaginal nodule. 1 year.	Excision of vaginal tumour.
143.	1898.	Rousse.	41.	12 normal births. 1 mole.	Mole 5 months.	Severe haemorrhage at confinement: recurred at 2 months.	Hysterectomy 2 months.
144.	1896	Runge	44.	Several normal births. 1 mole.	Mole.	Repeated haemorrhage.	Hysterectomy 5 months.
145.	1899	Saenger.	23.	1 birth. 1 abortion.	Abortion in 2nd month	Haemorrhage. Vaginal discharge Sepsis.	
146.	1898	Scherer.	33.	5 births 1 mole.	Mole.	Brown foetid discharge: 14 days: Haemorrhage 2 months: Cough: rigor.	Hysterectomy 5 months.

Result.	Uterine tumour.	Metastases	Remarks.
Well 3 months later.	Size of apple. Ruptured over fundus.		Chorionepithelioma of atypical infiltrating type (Maitland.)
Death 4½ months.	Ulcer of Anterior wall of uterus.	Vagina: Lungs Liver: fallopian tube.	Operation regarded as out of the question owing to presence of vaginal metastasis: also cough & haemoptysis.
Death about 18 months after the birth.	Large tumour beside uterus. Latter contained decidua only.	Vagina.	Vaginal tumour typical chorion-epithelioma: No autopsy: supposed large growth to be tubal.
Good recovery.	Myoma with chorionepithelio-matous tissue round it in uterus.		Possibly remains of mole only: patient not young and was very anaemic. Hom Metog.
Well 12 weeks later.	In Uterus.		Remains of mole with typical chorionepithelioma-tous infiltration in uterus. (Aschoff.)
Death 7 months.	Several dark red masses in wall of uterus.	Pituitary fossa: Lungs: diaphragm. 10th rib.	Haemorrhage into pleural cavity. Hy original deciduoma malignum Sept. 10.
Death 5 days after Op.	Small: in body of uterus.	Lung & liver: Brain.	Diagnosis from micro: exam of small portion removed for the purpose.

No.	Date.	Reporter.	Age.	Pregnancies.	Last Pregnancy.	Signs: Symptoms Date of Onset.	Treatment.
147.	1898.	Scherer.	26.	1 normal birth.	Normal birth or an abortion a year later	Endometritis. Metrorrhagia 5 months after the abortion: Cough: Phth:	
148.	1899.	Schlagenhauser.	38.	4 births 1 abortion.	Abortion in 4th mo.	Haemorrhage 2 months: curetted 4 months: bleeding from "vaginal varix" 6 months later.	Removal of "vaginal varix"
149.	1899.	Schlagenhauser.	27.	2 births. 1 abortion.	Normal full time birth.	Pain in pelvis. Breathlessness. Weakness and anaemia during the pregnancy.	
150.	1902.	Schmidt. O.	23.	First Pregnancy.	Mole 3½ months.	Weakness: illness: pain in head. Haemorrhage 8 days: extreme anaemia.	Curetted twice. Hysterectomy about 3 months.
151.	1900.	Schmit-1.	36	Five births. 5 abortions. 1 mole.	Mole.	Haemorrhage for 6 weeks: vaginal tumours found 3 months:	Excision of tumours.
152.	1901.	Schmit-2.	41.	2 abortions.	Abortion 7th week.	Severe haemorrhage from vaginal tumour: 7 weeks.	Excision of tumour.
153.	1902	Schmit-3.	29.	5 births [redacted]	Normal birth.	Pain in body: fever: emaciation. Uterine bleeding some months later.	Laparotomy.

Result.	Any tumour.	Metastases.	Remarks.
Death 13 months after the abortion.	In uterus.	No P. M.	Supposed to be endometritis after abortion and Phthisis pulmonalis: diagnosis from micro. exam. of curettings too late.
Well 22 months.	"Vaini in vagina:"		Choriomepithelomatous nature of the "vaini" discovered accidentally: uterus clear: no further operation. No rills: see p. 112.
Death 34 days.	Large tumour in uterus.	Uterine veins: lungs: spleen: kidneys:	Placenta appeared normal: expelled spontaneously: no uterine haemorrhage: resembled acute pyaemia: no suppuration see p. 114.
Good recovery: well 4 months later.	Large cells infiltrating uterine muscle.		Apparently simple mole: diagnosis from micro. exam. (1 piece out of 6) Hb reduced to 15%. 2 months after Hb. 25%.
Uninterrupted healing Well 1½ years later.	In vagina. (1) size of hen's egg. (2) size of walnut Like varices.		Curettings of uterus showed interstitial endometritis. 1st vaginal case: contained rills.
Well 22 months later.	Size of hazel nut in vagina.		Consisted of a few rills imbedded in blood-clot — a haematoma: ulcerated. 1st vaginal case.
Death same night.	Large tumour between layers of broad ligament.	None.	

No.	Date.	Reporter.	Age.	Pregnancies.	Last Pregnancy.	Signs: Symptoms. Date of Onset.	Treatment.
152	1893.	Schmorl. 1.			Normal birth.	Haemorrhage 12 weeks.	
153	1897.	Schmorl 2.	38.		Normal birth.	Discovery of vaginal tumour 18 weeks.	
156	1900.	Schmorl 3. (Fiedler.)	23.	2 births.	Normal birth.	Progressive failure of health: anaemia: pulmonary disease: tumour in abdomen. Collapse.	
157	1896.	Schultze.	40.	2 births One Abortion?	Abortion?	Haemorrhage. Foetid discharge. Curetted 20 days later. Recurrence of Bleeding.	Hysterectomy 36 days.
158	1902.	Senarclens.	38.	13 normal births. 1 abortion. 1 mole.	Mole.	"Menorrhagia" 11 months: bloody discharge: Cachexia.	Curetted 16 months. Hysterectomy 21 days later.
159	1902.	Senarclens.	38.	1 normal birth ten years before.	Tubal pregnancy?	Malaise: pain in pelvis: discharge from vagina: blood.	Abdominal section: extirpation by morcellement.
160	1902.	Simmonds.	20.	First pregnancy.	Abortion.	"Pernicious anaemia."	

Result.	Primary tumour.	Secondary tumours.	Remarks
Death 6 months.	Characteristic tumour in uterus.	Lungs.	
Death 6 months	Primary Vaginal tumour. Uterus and tubes free.	Lungs. Liver. Kidneys: intestines.	p. 114.
Death about 9 months.	Lungs?	Omentum: kidney. uterus: suprarenal: retroperitoneal lymphatic glands.	Death from rupture of a large tumour in omentum attached to under side of liver. Decidua in uterus. Primary supposed to have been in lungs. Autopsy abdomen only.
Dismissed 6 weeks later Well.	Small tumour in uterus.		Last child ten years before. From Ladinski.
Death 22 months.	Large ragged ulcer in uterus.	Broad ligament: vagina. Lungs.	Menstuated regularly for some months after the confinement. Nothing striking about mole.
Death 3½ months. (2 days after op.)	Tumour size of head in pouch of Douglas.	Lungs: anterior mediastinum. Heart. Thyroid. Kidney: suprarenal. Both fallopian tubes.	No tumour in uterus: supposed to have come from a tubal pregnancy.
Death 2 months.	Size of goose's egg. in uterus.	Broad ligaments. Vagina: lungs liver: spleen: bone-marrow.	

No.	Date	Reporter	Age	Pregnancies	Last Pregnancy	Signs: Symptoms. Date of onset	Treatment
161.	1900.	Smyly	33.	4 births	Confinement at 8 months.	Haemorrhages: 4 months: severe: Anaemia.	Curetted 6 months.
162.	1900.	Solowij & Krzyzkowski.	47.	10 normal births. 1 mole.	Malignant Mole.	Cachexia:	Removal of mole 2½ months.
163.	1896.	Spencer.	27.	2 births.	Normal birth.	Passage of masses of growth: 20 days.	
164.	1898.	Stankiewicz	31.	4 births 1 mole.	Mole. 4th month.	Irregular bleeding and appearance of Vaginal tumours during Pregnancy.	Cleared out mole.
165.	1900.	Steinhaus.	28	4 births 1 abortion.	Abortion 3 months	Bleeding after the abortion: 2nd day tumours in the Vagina.	Excision of vaginal nodule: hysterectomy: a few weeks.
166.	1900.	Stickler.	34	5 births 1 mole.	Mole. 4 months.	Haemorrhages after mole:	Curetted 1 year. Hysterectomy 18 months.
167.	1895.	Tannson.	23.	1 birth. 1 abortion 1 mole.	Mole 3 months	Irregular bleedings: 8 months.	Curetted 9 months and 10½ months. Hysterectomy 11 months.

Result.	Any tumour.	Metastases.	Remarks.
Death 6 months	In uterus.		Development of pulmonary symptoms "precluded" radical operation. "Sarcoma modified by pregnancy."
Death 5 days.	Uterus much enlarged and full of mole tissue.	Lungs: tubes: spermatic veins up to vena Cava.	The metastases were masses of hydatidiform villi: See p. 98.
Death 10½ weeks	Ulcerated gangrenous growth in placental site. Uterus.	Lungs: cervix uteri: brain?	"English group:- "Sarcoma."
Death 4 months later.	Masses of soft growth in uterus.	Vagina; —d Lungs (?)	Refused radical operation. Malignant Mole (Sobolewski and Kryszkowski)
Death a few days after op.	Necrotic masses in uterus. Deep excavation.	In vagina.	Last child 3¼ years before: disease apparently continuous with the abortion.
Well 6 months later	In uterus. Very superficial.		Remarkably slow course: disease diagnosed microscopically at 12 months: refused operation then: Contained villi which showed regressive changes.
Well 8 years later (Tanner.)	In uterus.		Menstruation between delivery and first symptoms.

No.	Date	Historian.	Age.	Pregnancies	Last Pregnancy	Signs: Symptoms. Date of Onset.	Treatment.
168.	1903.	Teacher. (Edgar)	32.	3 abortions	Abortion 2nd month.	Bloody discharge thereafter: Rigors 4 months.	Curetted 5 months. Hysterectomy 12½ months.
169.	1903.	Teacher. (Kerr)	23.	First pregnancy.	Abortion.	Haemorrhage and pain in abdomen continuous with abortion: Rigors.	Curetted 6 months and 8 months. Hysterectomy 10 months.
170.	1903.	Teacher. (Pace)	23.	2 births mole.	Mole. 3rd month.	Post Partum Haemorrhage: repeated violent bleedings.	Curetted 7 days and 48 days. Hysterectomy 71 days.
171.	1896.	Tidenat.	47.	3 births.	Full time birth: Dead Child.	Violent bleeding 8 months: pantous discharge.	Curetted 8 months and again soon after.
172.	1896.	Tedenat.	33.		Mole.	Severe Haemorrhage at delivery Repeated 2 months.	Curetted 2 months. Hysterectomy a few days later.
173.	1882.	Tibaldi.	31.	Five births	Normal birth.	Continuous metrorrhagia.	
174.	1898.	Trantenroth	38.	6 births.	Normal birth.	Haemorrhage 3 days later: repeated: extreme anaemia.	Curetted. 12 weeks. Again 4½ months. For diagnosis. Hysterectomy 4½ months.
175	1898.	Trantenroth	48.		Abortion?	Pain in abdomen. Haemorrhage from uterus.	

Result.	Part of tumour.	Metastases.	Remarks.
Death 22 months.	In uterus.	Lungs? Brain?	No P.M. Good health for 9 months after operation.
Death 10 months.	Characteristic tumour in uterus	Vagina?	Death from haemorrhage.
Well 2½ years later.	In uterus.		Perforation by sound while examining: villi:
Death. About 9 months.	In uterus.		From Metoz.
Death. 13 months.	Posterior wall of uterus.		Enjoyed 7 months of good health between operation and return of symptoms. From Metoz.
Death 4 months.	In uterus.	Lungs: kidneys Brain: Ovary intestines.	"Carcinoma Haemorrhagica" Ref. 1895 by Pestalozza as Chorionepithelioma.
Death 5 months.	Medium sized in uterus.	None.	Death from cardiac failure. 12 days after operation.
Death.	Large putrid tumour in uterus.	Broad ligament. Vagina: lungs: liver: intestines: kidneys.	Complete history not obtained.

No.	Date	Reporter.	Age.	Pregnancies.	Last Pregnancy.	Signs. Symptoms. Date of Onset.	Treatment.
176.	1897.	Ulesco-Stroganowa.	26.	First pregnancy.	Mole.	Haemorrhage: a few months: menstruated: haemorrhage recurred, 6 months:	Curetted about 18 months. Hysterectomy 3 months later.
177.	1898.	Veit.	32.	6 normal births. 1 abortion.	Abortion in first month. Incomplete.	Removal of Placental remains: Haemorrhage and discharge persisted.	Curetted 3 months. Hysterectomy 4 months.
178.	1867.	Volkmann.	46.	8 healthy normal births. 1 mole.	Malignant Mole.	Haemorrhage four weeks after amenorrhoea: weakness: wasting.	
179.	1899.	Voigt.	53.	8 normal births. 2 abortions. 1 mole.	Mole removed in 3rd month.	Recurrent haemorrhages: After curetting fever and rigors.	Curetted 9 weeks. Hysterectomy 10 weeks.
180.	1901.	Wehle.	46.	7 births.	Normal birth.	Tumour in labium: 6 months:	Excision of vaginal growth. Recurrence in 8 days.
181.	1901.	Wehle.	39.	6 births.	Normal birth.	Bloody slimy discharge: five months.	Scooped out tumour and Cauterized. Recurred in 10 days.
182.	1895.	Williams.	35.	~~1~~ birth 1 abortion.	Full time birth.	Tumour in vagina 1 week: sloughed at one month: no uterine symptoms.	

Result.	Appearances of tumour.	Metastases.	Remarks.
Recovery from Operation.	Deeply infiltrating, in uterus.		Perfectly well for about a year after clearing out of uterus: then nearly died of haemorrhage.
Well 4 years later.	In uterus. Small: covered by mucous membrane.	In iliac fossa after scraping: (disappeared after a time)	Villi penetrating deeply along the cavities of the blood-vessels.
Death in 6th month of pregnancy	Masses of mole partly in cavity partly burrowing in wall of uterus.		"Exquisite" destroying character. Invasion specially of the sinuses.
Well some months later.	Uterus enlarged. No distinct tumour: villi burrowing deep into wall.		Suspicion of deciduoma: uterus supposed retained: extirpation — not septic but tumour found! malignant mole.
Death 7 months.	Right labium magna; like a haematoma.		Tumour grew very rapidly: ~~fatal~~ Primary Vaginal: uterus free.
Death expected daily. 6 months.	Posterior wall of vagina.		Primary Vaginal: uterus free.
Death 3 months.	Small and not ulcerated: in uterus.	Uterus wall: vagina: ovary: lungs: liver: spleen: kidneys.	Felt apprehensive during pregnancy. Child born dead: no post partum haemorrhage: no septicaemia. Sept 22.

No.	Date.	Reporter.	Age.	Pregnancies.	Last Pregnancy.	Signs: Symptoms. Date of Onset.	Treatment.
183.	1840.	Wilton	37.	4 births / abortion / mole.	Malignant Mole.	Repeated flooding.	
184.	1901.	Winkler	33.	3 normal births.	Normal birth 4 years before an abortion.	Irregular haemorrhage for 4 months abortion probably.	Regarded as inoperable.
185.	1901.	Winkler.	26.	First Pregnancy.	Mole.	Pain in abdomen / year after the mole.	
186.	1902.	Jagorjanski-Kessel.	20.	First Pregnancy.	Abortion in 3rd month complete:	Rigors and haemorrhage Hypnosis 2 weeks: tumours in vagina.	Excision of tumours: curetting of uterus. 2 weeks.
187.	1897.	Zondeck.	43.	12 births 4 abortions / mole.	Mole removed in 7th month.	Haemorrhages: 2 weeks: repeated 6 weeks: rigor 4 weeks.	Curetted after mole, first bleeding and rigor. Hysterectomy 11 weeks.
188.	1894.	Zweifel.			Mole.	Haemorrhage continued: haemoptysis. Consolidation of Lungs.	Uterus cleared out 4 weeks and 8 weeks with fingers.

Cases not included in the Statistical Analyses.

Bulius. 2. Like Sänger's case. Marchand.

Davis and Harris.

Result.	Ist. of tumour.	Metastases.	Remarks.
Death 3 months after 1st bleeding	Villi burrowing deeply in uterine wall.	Ovary.	Rupture of uterus: death from shock and haemorrhage.
Death 5½ months (from onset of bleeding)	In uterus: Perforation into sigmoid flexure.	Lungs. Vagina. Cervix uteri.	A "blast" was attended at the beginning of the haemorrhages
Death 1 year.	Large tumour in uterus (like Kelly's)	Lungs: vagina: broad ligament. Bronchial lymphatic glands.	See p. 24.
Well 15 months later.	Two small nodules about ostium vaginae. Larger was ulcerated: villi.		Uterus free of tumour: symptoms ceased at once after operation: 8 months later abortion; 15 months again pregnant: no recurrence of tumour. See p. 117.
Good recovery from Op.	Tumour like Edgar's.		Reported only 3-4 weeks after operation.
Death. Some months.	No P.M. In uterus.	Lungs?	Examination for tubercle bacilli negative. "Placental Polyp" removed at 2nd operation.

Cases not included in the statistical analysis. contd.

Sänger 2.	no particulars.
Sänger	after normal birth: diagnosed 2½ months Rays.
Freud-Doormann.	after normal birth: diagnosed 2½ months: Rays. Two years after male in a woman of 51 years.

Table III.

No.	Reporter.	Last preg. namg.	After first symptoms.	Bid. or Recurr.	How long after the operation.	Remarks.
3.	Albert, 1.	Tubal.	?	R.	Some mos.	Removed in pieces.
4.	Albert, 2.	B.	8 W.	R.	Some mos.	
7.	Apf. & Asch.	Ab.	6 M.	D.	4 weeks.	General metastasis.
9.	Austerlitz,	Ab.	10 M.	D.	4 mos.	Recurrence in lungs.
11.	Baldwin,	B.	8 W.	D.	6-8 W.	
13.	Brothers.	Ab.	4 M.	R.	Some W.	
14.	Buist.	Ab.	4 M.	D.	28 hrs.	
15.	Buist.	Ab.	3½ M.	D.	2 M.	Generalized metastasis.
16.	Buschbeck	M.	7 M.	R.	2 M.	
19.	Cazin-segond	M.	6 M.	(R) R.	3 yrs.	Secondary in ovary.
24.	Chrobak,	Ab.	4 M.	R.	Soon.	Signs of metastasis.
27.	Crossen & Fisch.	M.	5 W.	R.	6 M.	
31.	Frankel E. S.	M.	4 W.	R.	7 M.	
33.	Franqué, V.	B.	3½ M.	R.	17 M.	Signs of metastasis.
34.	Gebhard, 1.	B.	4 M.	R.	11 M.	
35.	Gebhard, 2.	M.	4 W.	R.	Soon.	
37.	Gottschalk.	Ab.	6 M.	D.	7 M.	Recurrence in brain?
41.	Guerard.	M.	2½ M.	R.	3½ yrs.	
44.	Haultain,	M.	7½ W.	R.	5 yrs.	
47.	Hitschmann	Ab.	4 M.	D.	3 W.	Generalized metastasis.
48.	Hollemann	M.	6 M.	R.	4 M.	
49.	Holzapfel	Ab.	?	R.	2 yrs.	Metastasis in vagina.
50.	Horrocks	Ab.	5 M.	D.	6 M.	
51.	Hubbard.	Ab.	3 M.	R.	6½ M.	
52.	Hubl, 1.	B.	1 M.	D.	1 M.	
57.	Jeannel	Ab.	2 M.	R.	?	
58.	Jörgenson	Ab.	Soon	R.	1 yr.	

No.	Reporter.	Last Agency.	After first Symptoms.	Did or Recurred?	How long after operation.	Remarks.
59.	Jurassowsky,	M.	? long time	D.	Soon.	Metastasis in brain.
63.	Karstrom & Vestberg.	M.		R.	Soon.	
64.	- do -	Ab.		R.	Soon.	
66.	Kleinhans.	?.	?.	R.	?.	Metastasis in vagina.
69	Kolomenkin,	B.	?.	R.	6 M.	Metastasis had occurred?
75	Kuppenheim,	B.	2 M.	R.	2-3 yrs.	
77.	Kworostansky	Ab.	6 W.	R.	4½ mos.	Metastasis in lungs?
78	Ladinski,	M.	9 W.	R.	18 mos.	Metastasis in lungs?
79.	Langhans, I	B.	8½ M.	R.	1 Yr.	
81.	Langhans, III	M.	2½ M.	R.	7½ M.	
82.	Lauer & Wilkinson,	Ab.	7 M.	D.	2 M.	Metastasis: Sepsis:
84.	Leopold.	B.	?	R.	Soon.	
85.	Lewers.	Ab.	11 M.	R.	5 yrs.	
86.	Lindfors.	Ab.	3 M.	D.	5 days?	See large table.
87.	Lindfors.	B.	1 M.	D.	7 M.	Recurrence general.
89.	Lohlein,	M.	7 M.	D.	1 yr.	Recurrence, Lungs.
91.	Lonnberg,	M.	1 yr at least)	R.	1½ yrs	Metastasis in lungs?
93.	Marchand,	B.	5 M.	R.	2¾ yrs	Thrombosed vein left
94	Marchand, 2,	M.	2 M.	R.	2 M.	
98	Marchand, 6,	M.	2 M.	R.	Soon.	
99.	Marten & Kieffer.	Ab.	14 M.	R.	Soon.	Patient was very cachetic,
100.	McCann,	Ab.	5 M.	D.	6 days.	
102.	McMurtry,	Ab.	6 W.	R.	Soon.	
105	Menge, 1.	M.	2 M.	D.	6 M.	Recurrence, general.

No.	Reporter.	Last Pregnancy.	After first symptoms.	Died or Recovered.	How long after operation.	Remarks.
106.	Menge, 2,	M.	2 W.	R.	1 yr.	Doubtful if D. Malig:
107	Mengel,	B.	3 W.	R.	8 M.	Perforation.
108.	Metoz, 1.	M.	1 W.	D.	2 days.	
111.	Morales-Arjona.	?	?	R.	1 yr.	
112.	Morrison,	B.	9 W.	D.	5 M.	Recurrence in lungs?
113.	Muller, E.	M.	4½ M.	R.	6 M.	
115.	Neumann, 1	M.	2 W.	R.	2-6 M.	Metastasis in vagina.
116.	- do - 2.	M.	Malig: Mole	D.	12 days	Pneumonia.
117.	- do - 3,	M.	2 W.	R.	2 M.	Metastasis in vagina.
118.	- do - 4,	B.	4 M.	D.	3 M.	Recurrence in lungs,
119.	- do - 5,	B.	?	D.	6 M.	- do - - - do -
121.	Noble, 1.	B.	8 M.	D.	6 M.	Recurrence.
122.	Noble, 2.	Ab.	3 M.	R.	5 M.	Part of tumour left.
123.	Nove-Josserand.	M.	1 M.	R.	3 M.	
124.	Peham.	Ab.	7 M.	D.	2 M.	Recurrence in 4 weeks.
129.	Pestalozza,	M.	3 M.	R.	1 yr.	Metastasis in lungs?
130.	Peters,	Ab.	2 M.	D.	6 M.	Rapid recurrence: refused further operation.
134.	Pick, A. 3.	M.	1 W.	R.	4 M.	
135.	Pick, L.	M.	at once	R.	4 yrs.	Metastasis during pregnancy
136.	Poten & Vassmer,	M.	Malig: mole	R.	2½ yrs.	- do - - - do - - - do -
137.	Prochownik	Ab.	4 M.	D.	4 M.	Recurrence, ?lungs, brain,
138.	Prowse,	M.	6 W.	D.	8 days.	
140.	Reinicke	Ab.	3 M.	R.	3 M.	Uterus ruptured.
143.	Rousse,	M.	2 M.	R.	Soon.	
144.	Runge,	M.	5 M.	R.	12 W.	

No.	Reporter	Last Pregnancy	After first symptoms	Dead or Recovered	How long after operation	Remarks
146.	Scheuer, 1.	M.	5 M.	D.	5 days.	Exhaustion.
148.	Schlagenhaufer.	Ab.	4 M.	R.	22 M.	
150.	Schmidt.	M.	3 M.	R.	4 M.	
151.	Schmit, I.	M.	3 M.	R.	1½ yrs.	Primary vaginal.
152.	Schmit, 2.	Ab.	7 W.	R.	22 M.	Primary vaginal.
157.	Schultze,	Ab.	5 W.	R.	6 W.	
158.	Sanarclens,	M.	5½ M.	D.	5 M.	Recurrence in Lungs.
159	- do - 2.	Tubal	3 M.	D.	2 days	Very severe operation.
165.	Steinhaus,	Ab.	A few weeks.	D.	A few days.	
166.	Sticker,	M.	18 M.	R.	6 M.	Very chronic case.
167.	Tannen,	M.	8 M.	R.	8 yrs.	
168.	Teacher, (Edgar)	Ab.	12½ M.	D.	9½ M.	
169.	Teacher, (Kerr)	Ab.	10 M.	D.	same day	Haemorrhage.
170.	Teacher. (Pace)	M.	2½ M.	R.	2½ yrs.	
172.	Tedenat, 2.	M.	2 M.	D.	11 M.	Recurrence in 7 months.
174.	Trantenroth,	B.	4½ M.	D.	12 days	Cardiac failure.
176	Ulesco-Stroganowa,	M.	15 M.	R.	Soon.	Slow case.
177.	Veit,	Ab.	4 M.	R.	4 yrs.	
179.	Voigt.	M.	10 W.	R.	Some mos	
180.	Wehle,	B.	A few days	D.	1 M.	Very rapid recurrence.
181.	Wehle.	B.	A few days	D.	1 M.	Very rapid recurrence.
186	Zagorjanski-Kissel.	Ab.	2 W.	R.	15 M.	Metastasis had occurred.
187.	Zondeck,	M.	2 M.	R.	Soon.	

Plate. I. Tumours.

Fig. 2a.

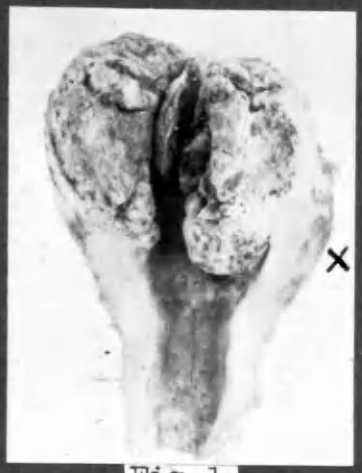

Fig. 1.

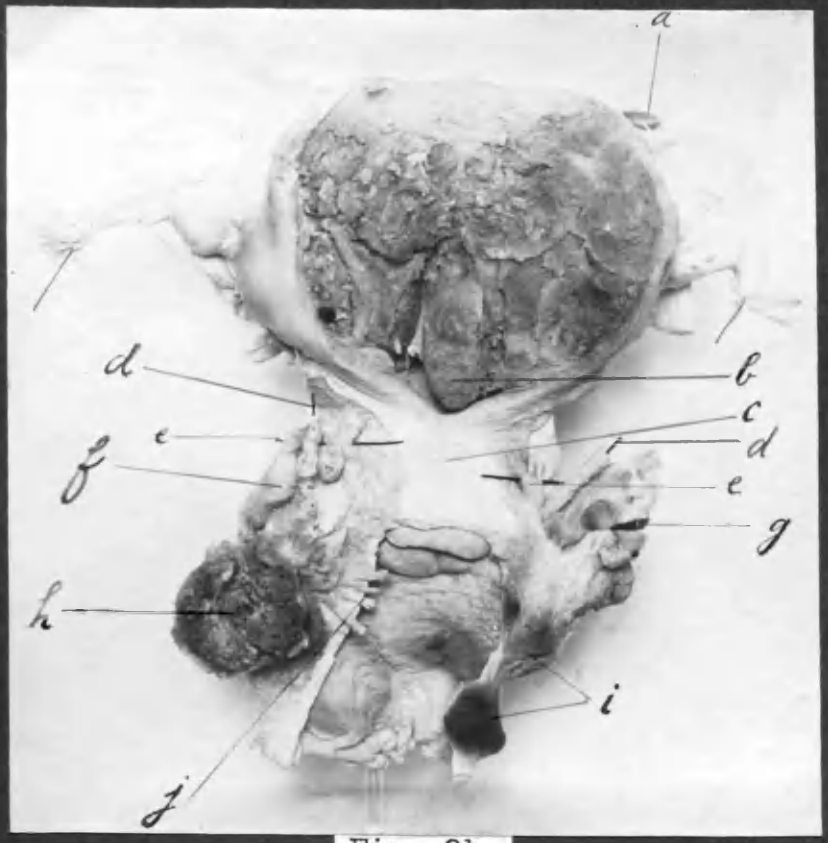

Fig. 2b.

Fig. 2.

Plate II. Placenta.

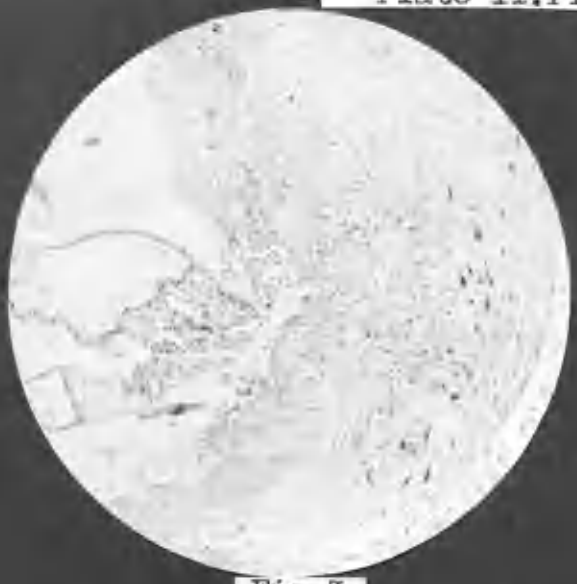

Fig. 3.

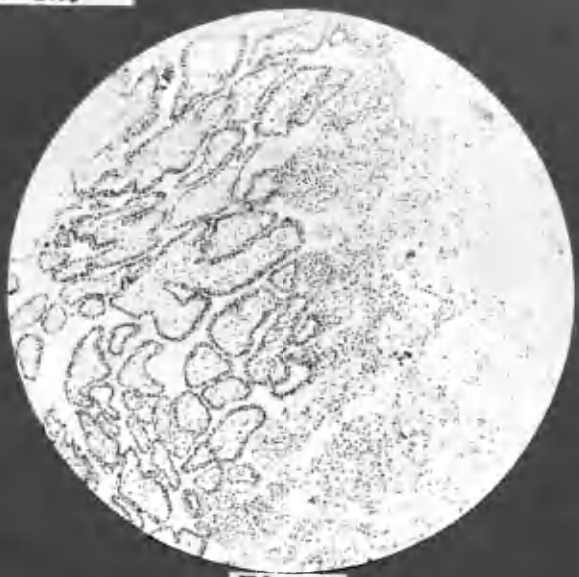

Fig. 4.

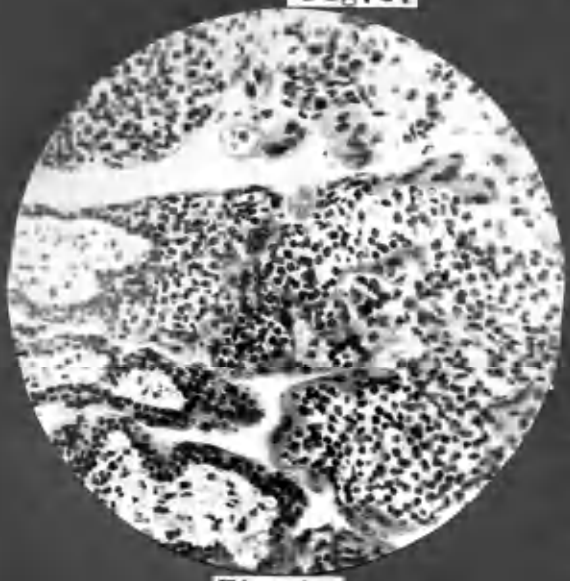

Fig. 4a.

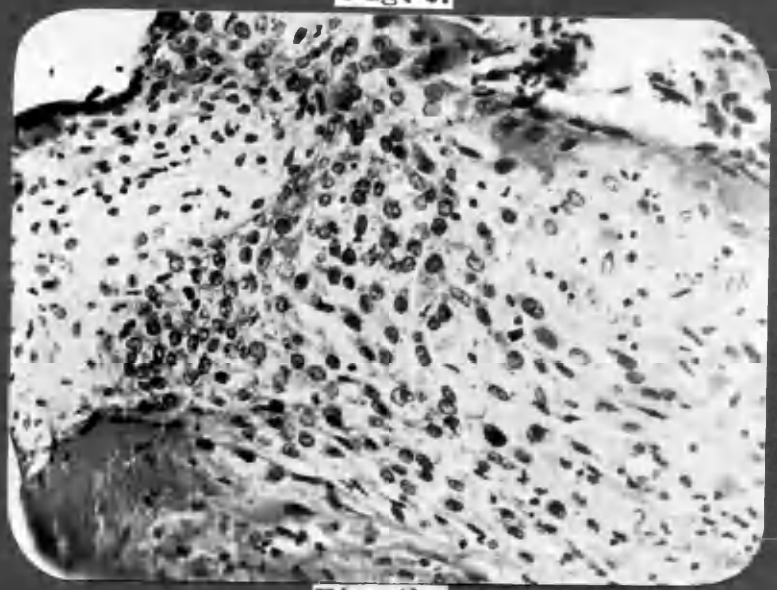

Fig. 4b.

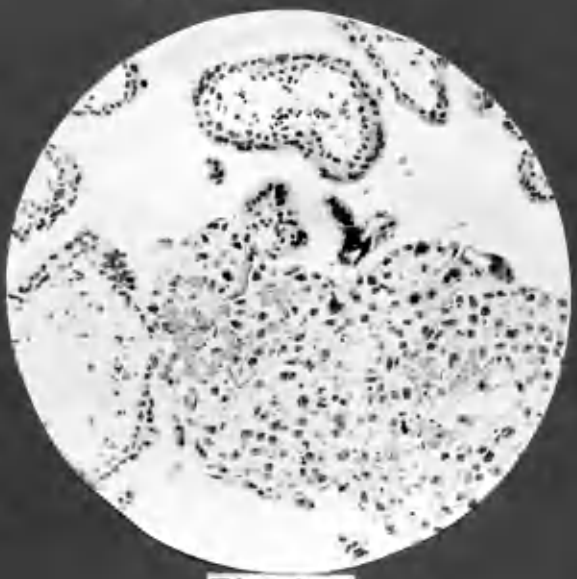

Fig. 4c.

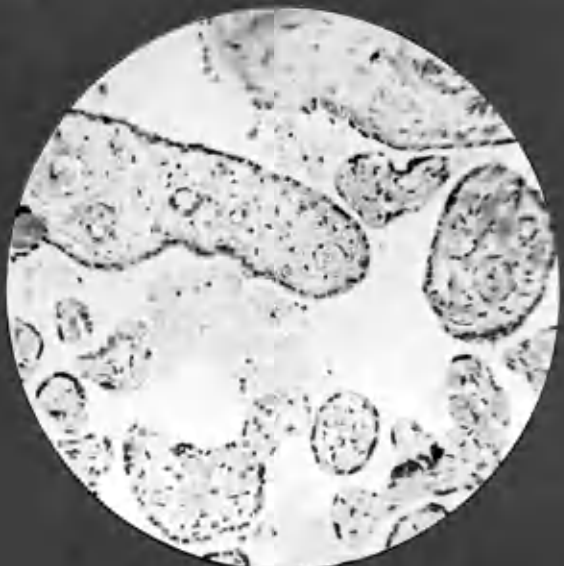

Fig. 4d.

Plate. III. Peters' Ovum.

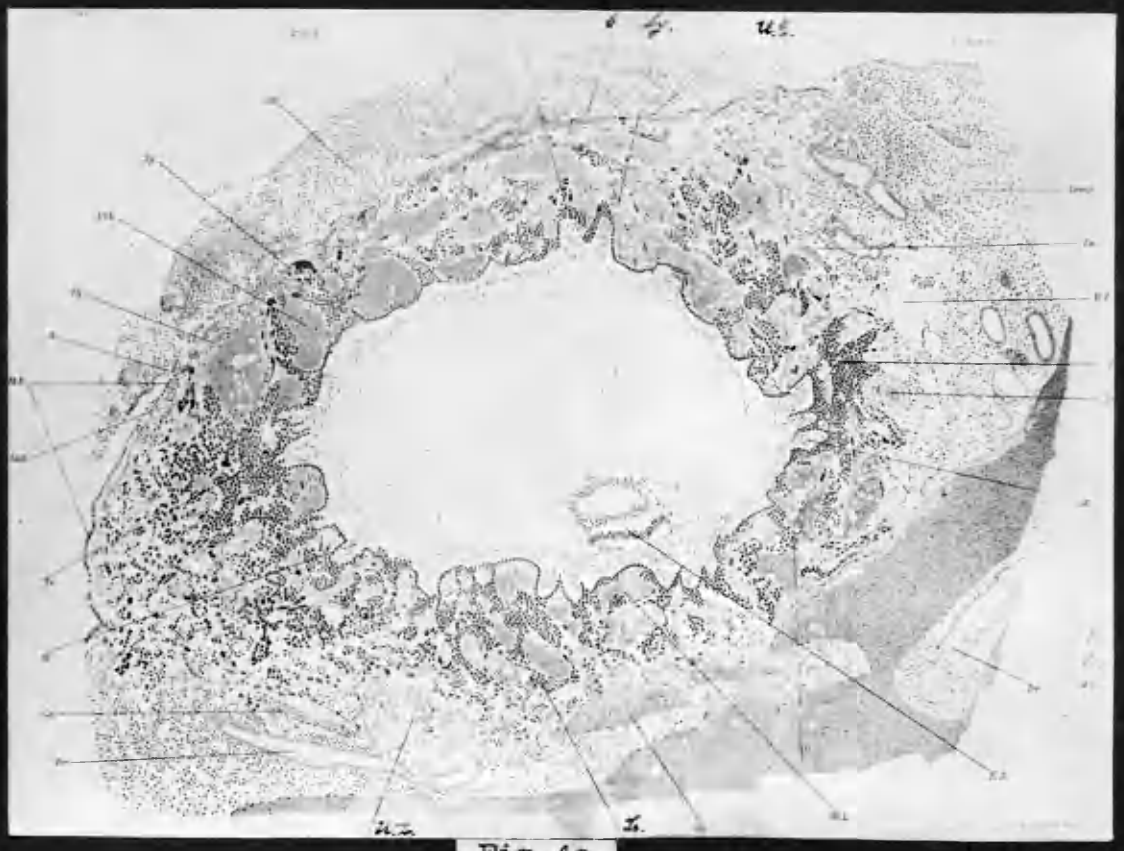

Fig. 4e.

Fig. 4f.

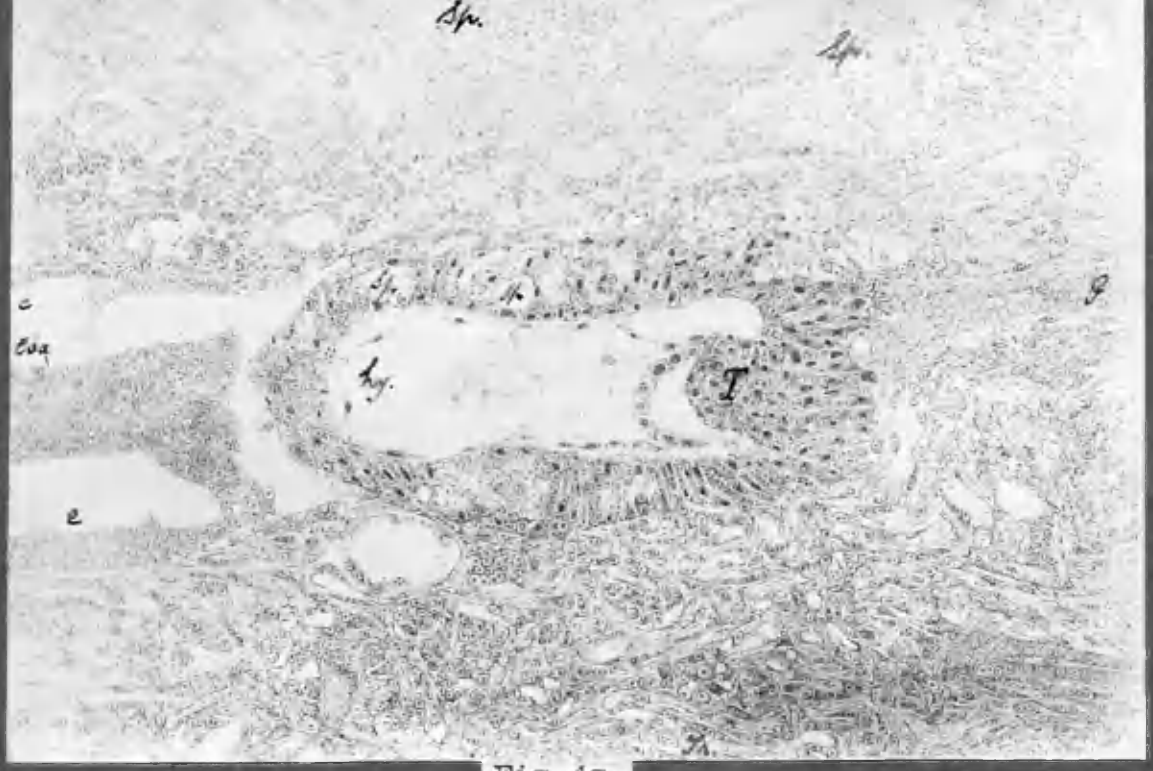

Fig. 4g.

Fig. 4h

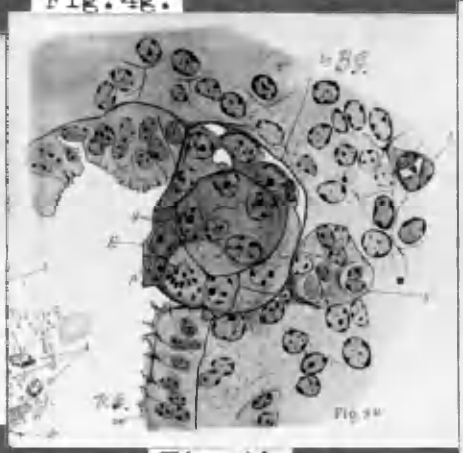

Fig. 4i.

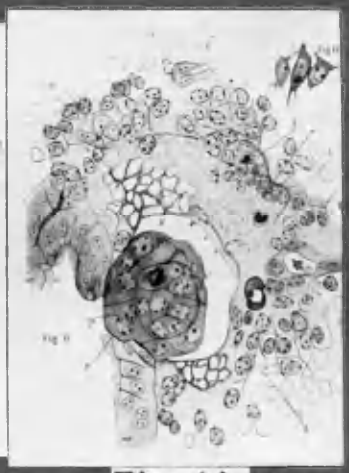

Fig. 4j.

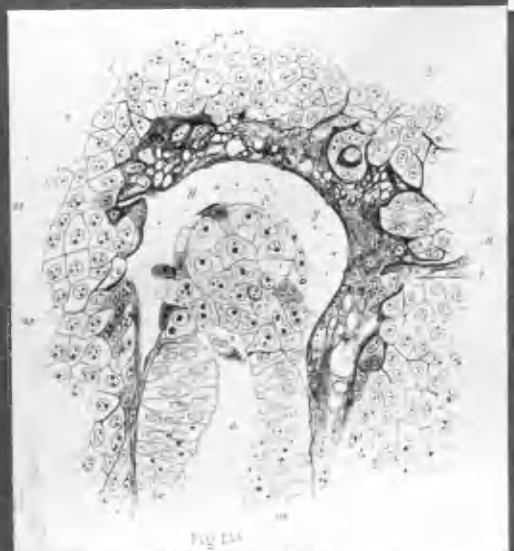

Fig. 4k.

Fig. 4l.

Plate IV. Imbedding of the Ovum.

Plate V. Trophoblast and Hydatidiform Mole.

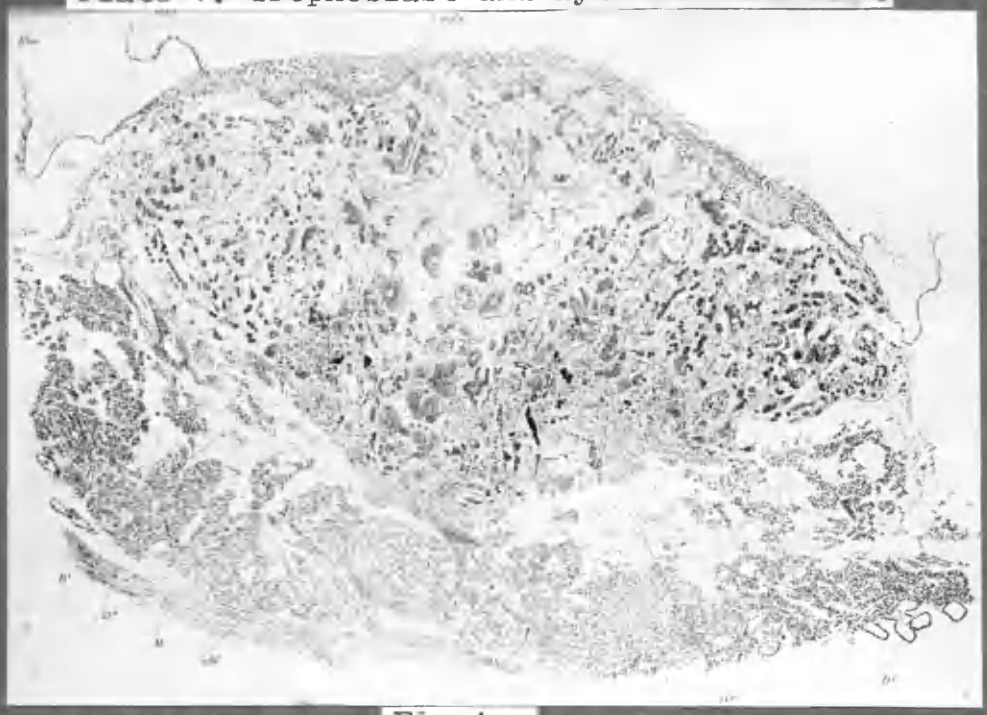

Fig. 4m.

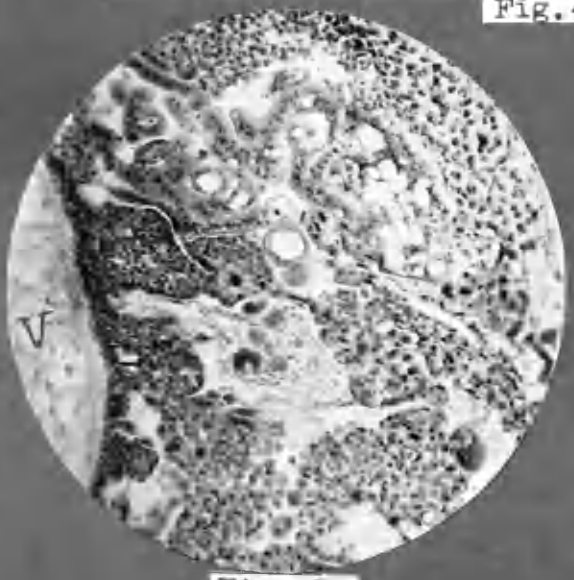

Fig. 5.

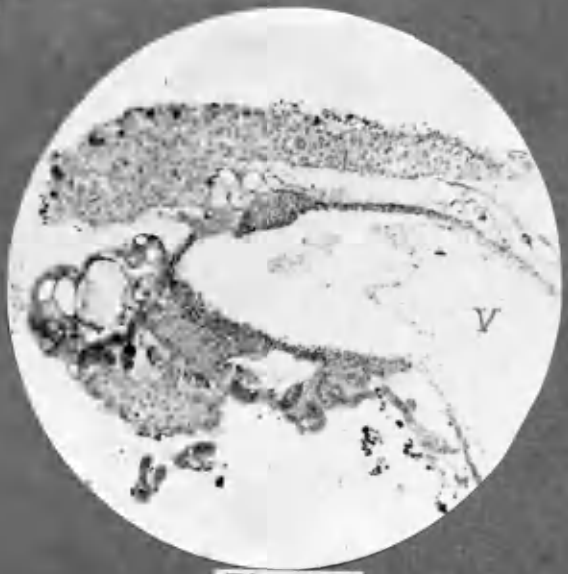

Fig. 5a.

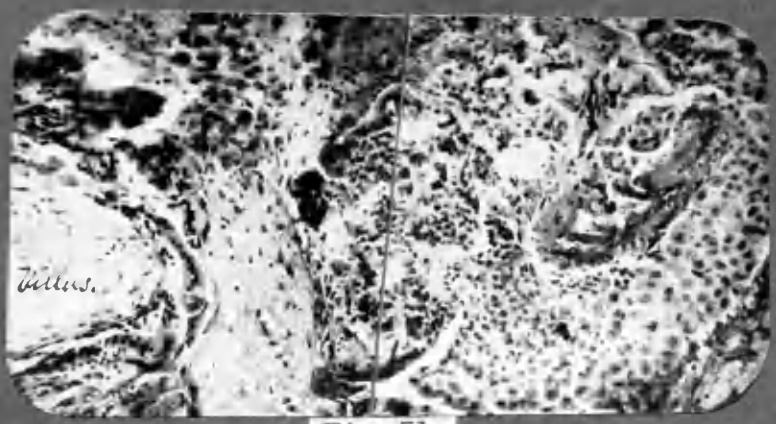

Fig. 5b.

Plate VI. Chorionepithelioma.

Fig. 6.

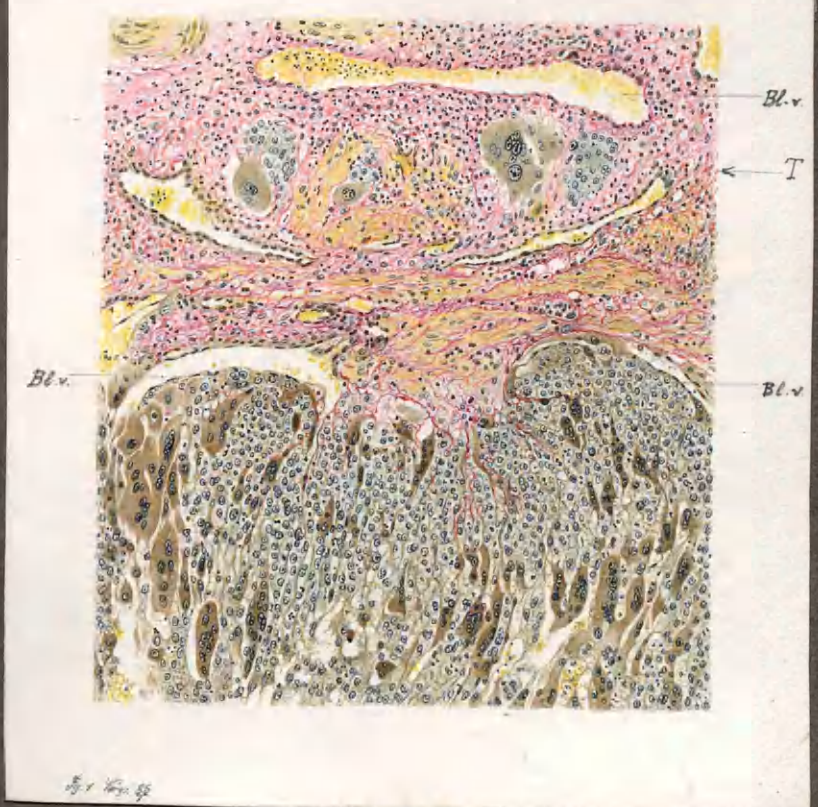

Fig. 7.

Plate VII. Chorionepithelioma with presence of villi.

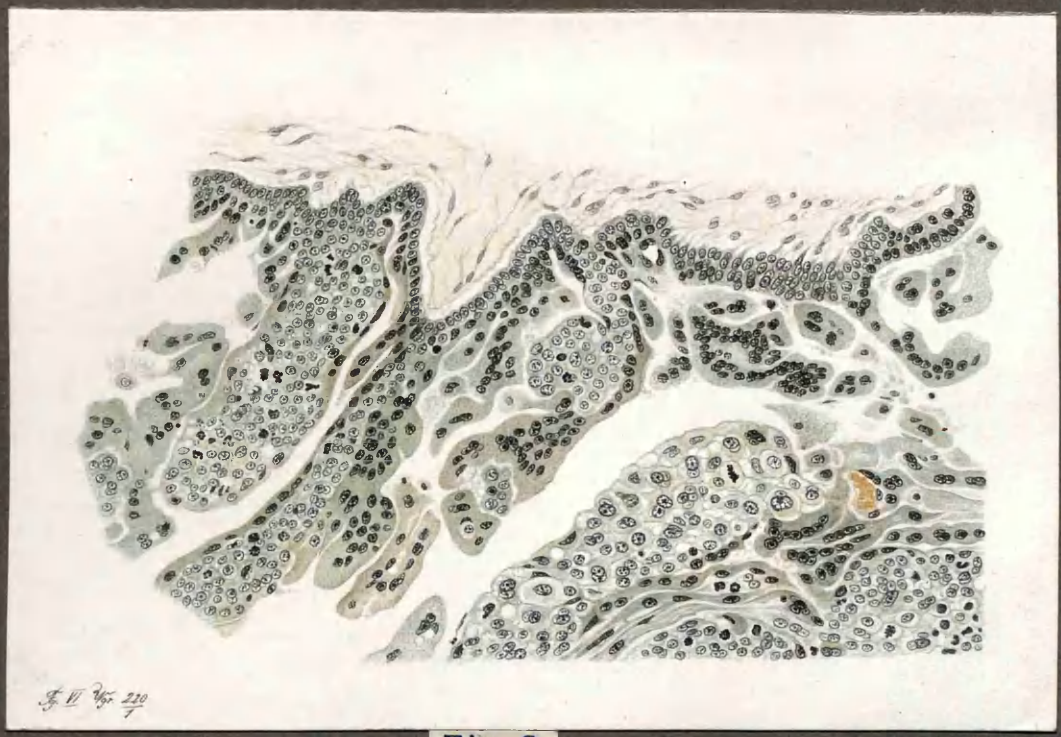

Fig. 8.

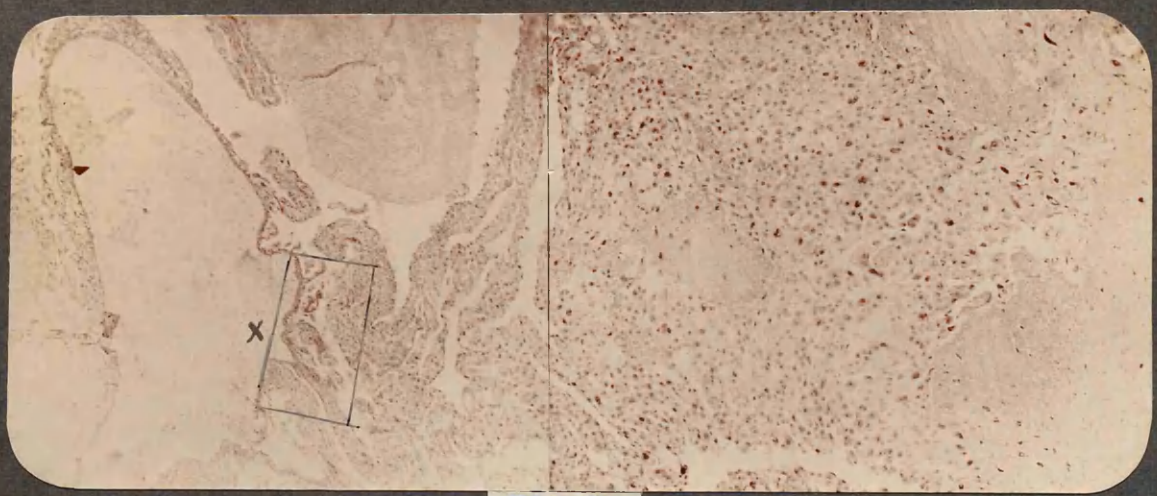

Fig. 8a.

Plate VIII. Chorionepithelioma.

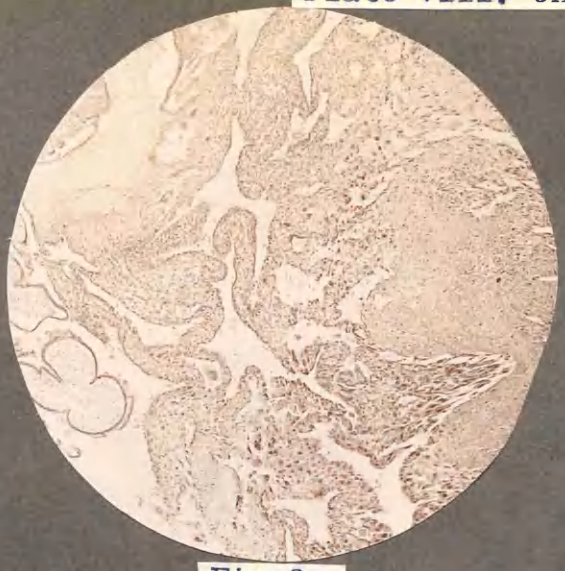

Fig. 9a.

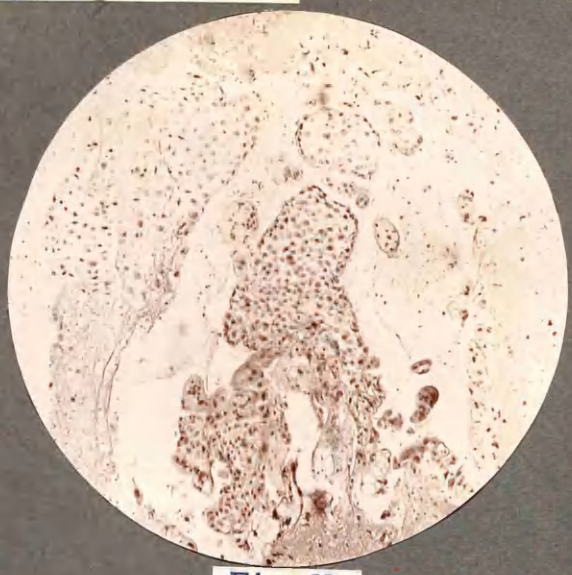

Fig. 9b.

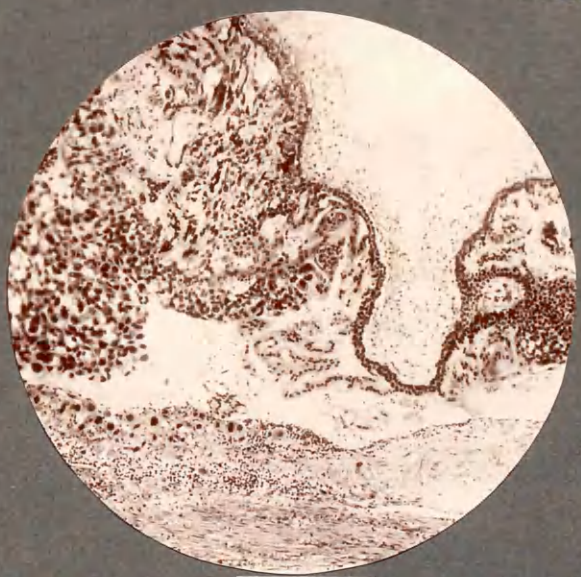

Fig. 9.

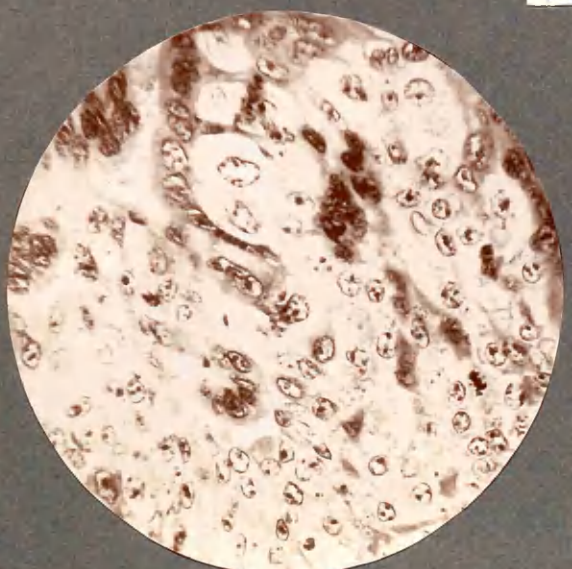

Fig. 9d.

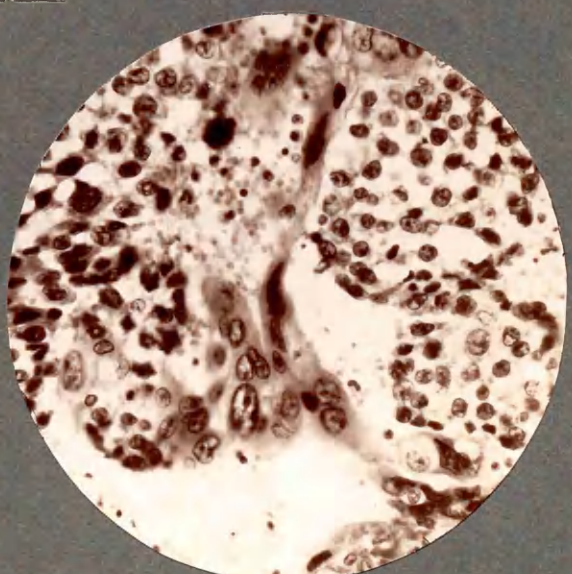

Fig. 9c.

Plate IX. Chorionepithelioma.

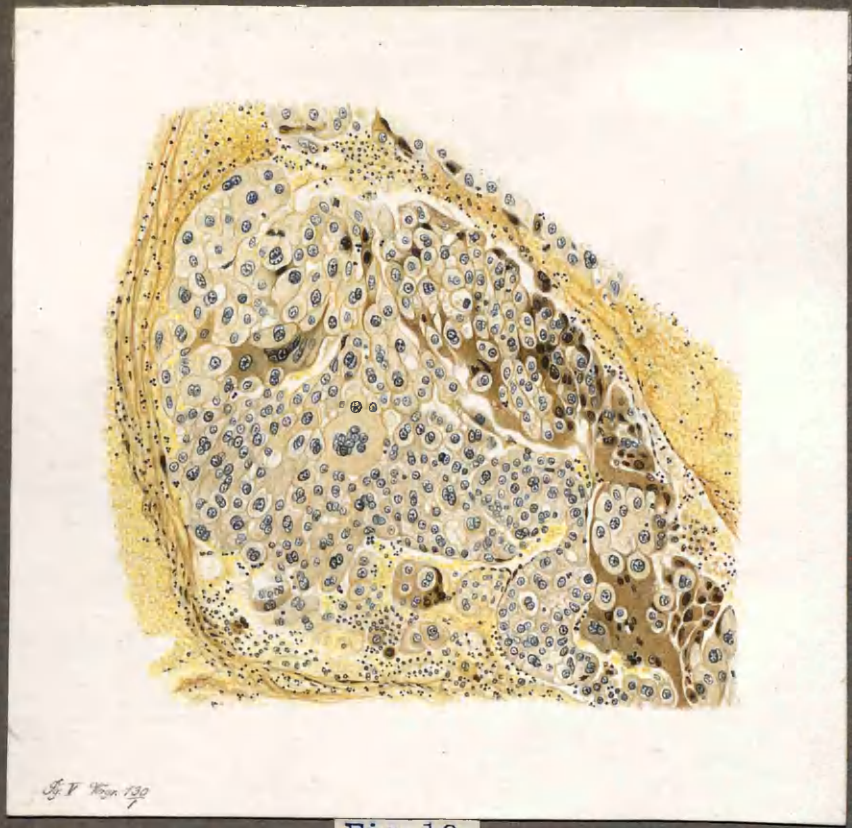

Fig. 10.

Fig. 11.

Plate X. Chorionepithelioma and the blood-vessels.

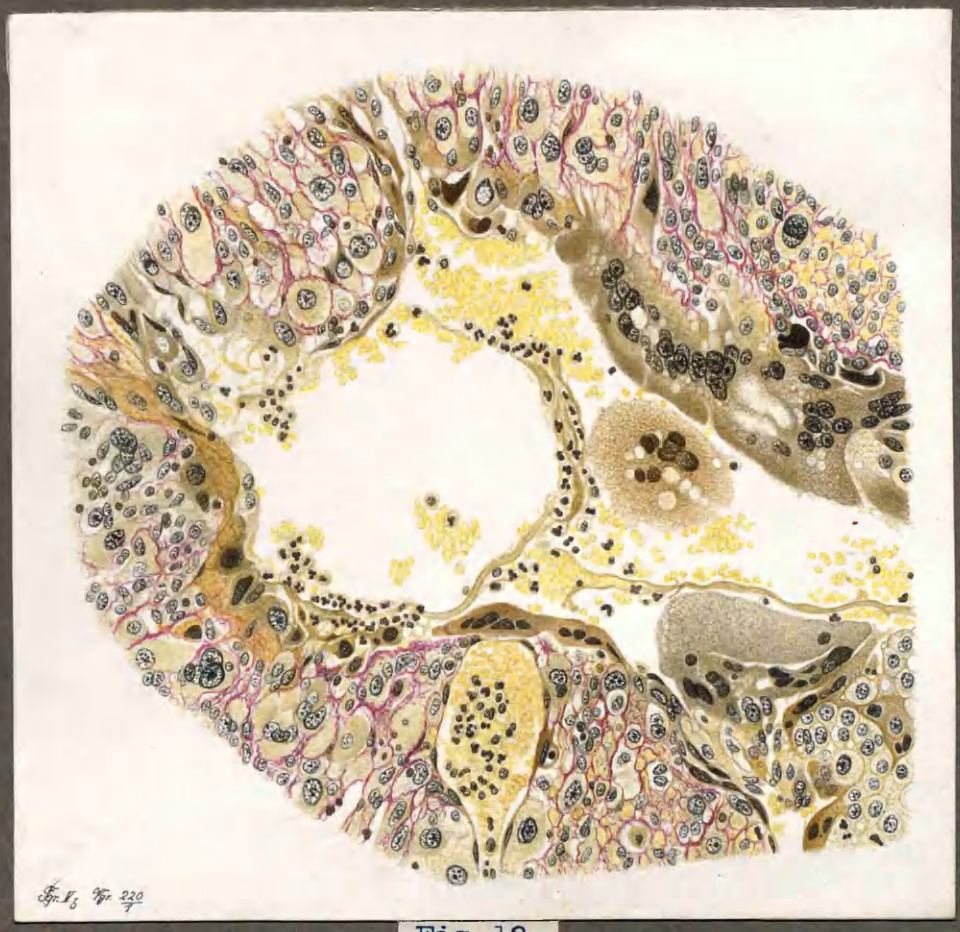

Fig. 12.

Fig. 15.

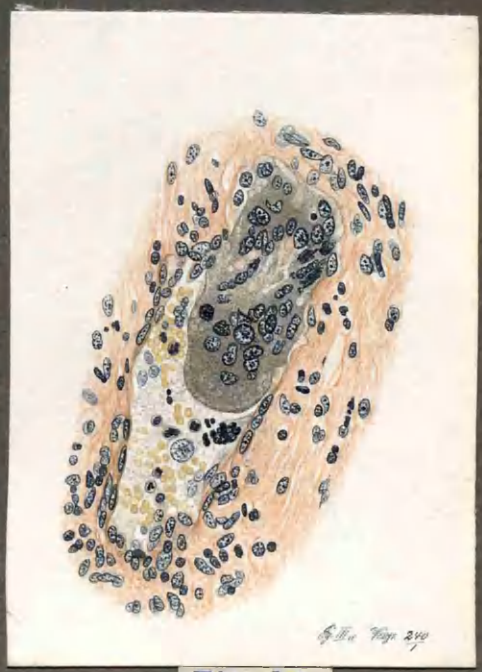

Fig. 16.

Plate XI. Chorionepithelioma and the blood-vessels.

the blood-vessels.

Fig. 13.

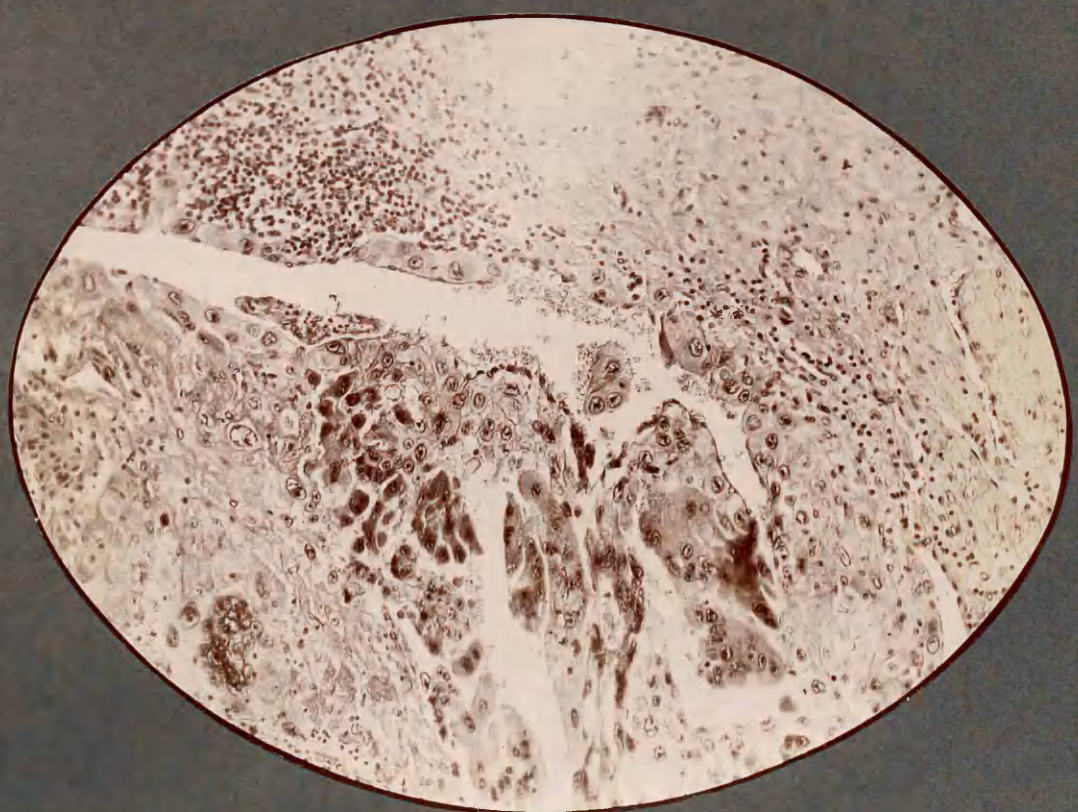

Fig. 14.

Plate XII. Chorionepithelioma.

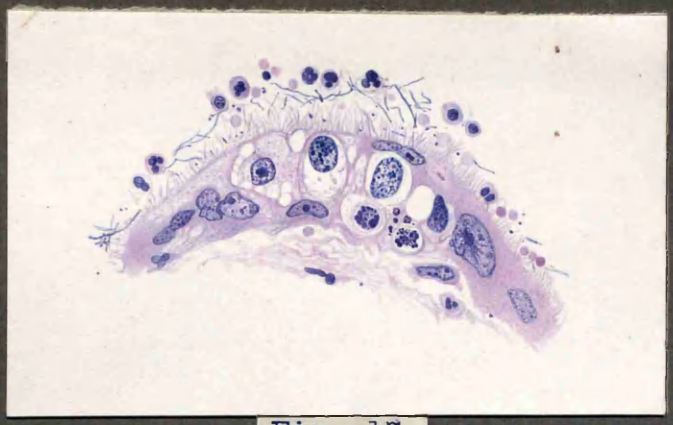

Fig. 17.

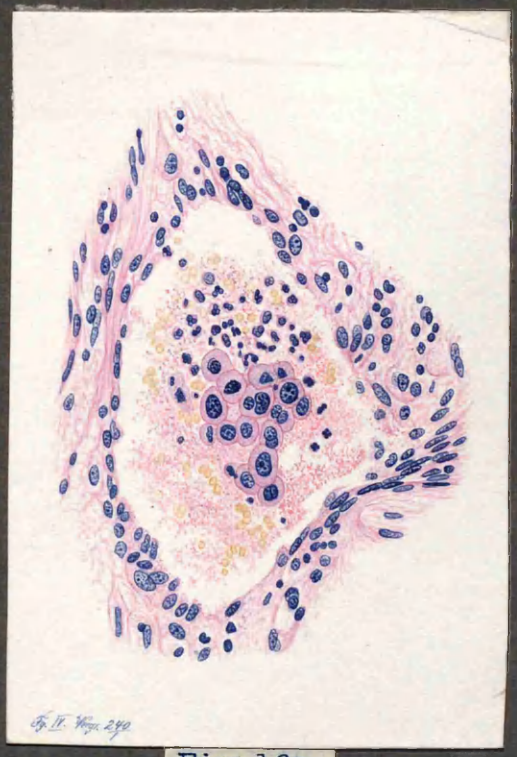

Fig. 16a.

Fig. 18.

Plate XIII. Chorionepithelioma. (high power.)

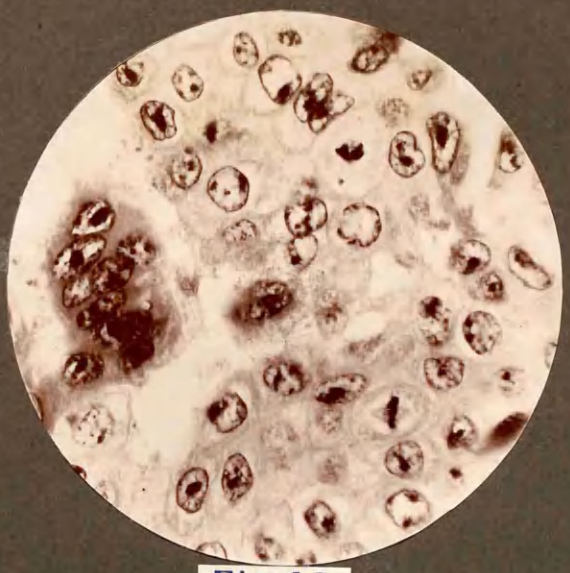

Fig.19.

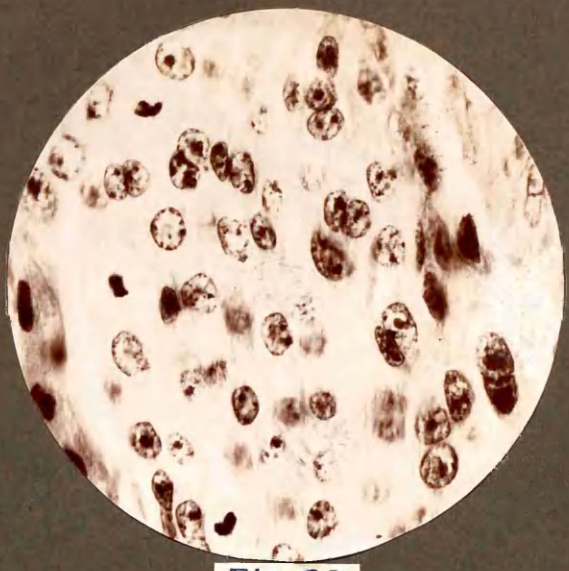

Fig.20.

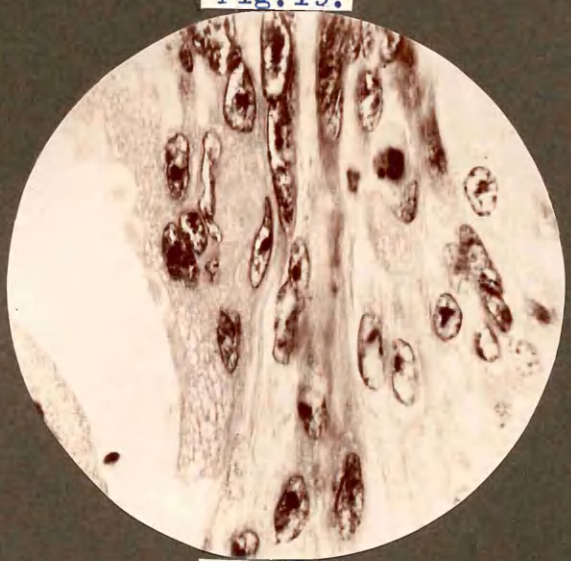

Fig.22.

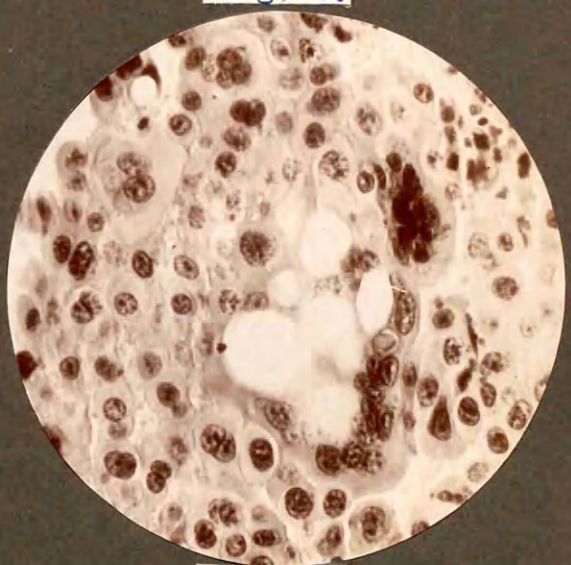

Fig.21.

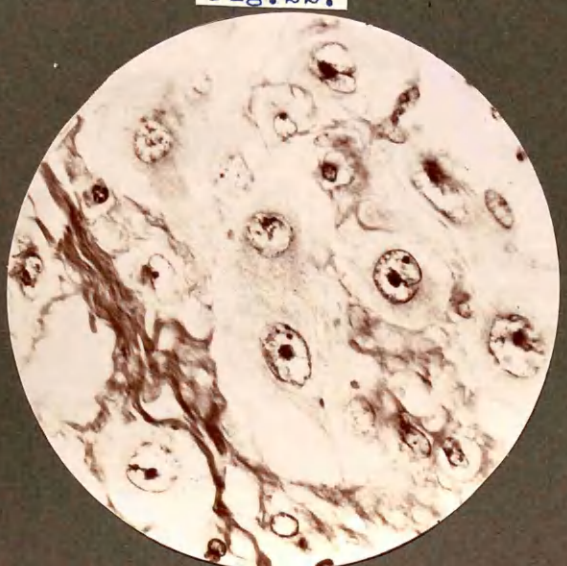

Fig.23.

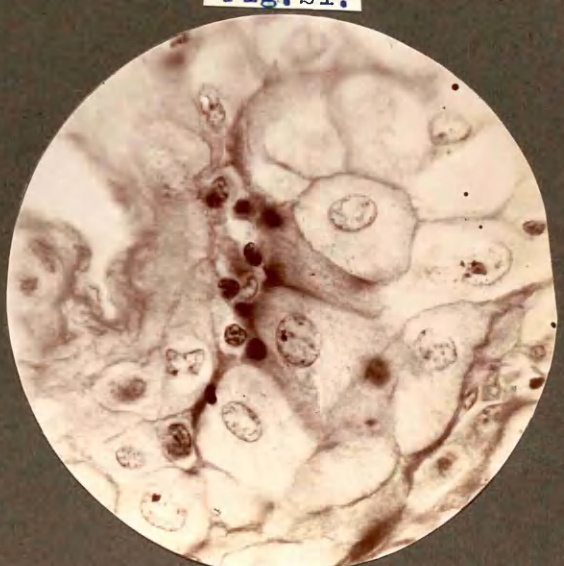

Fig.24.

Plate XIV. Chorionepithelioma and other tumours.

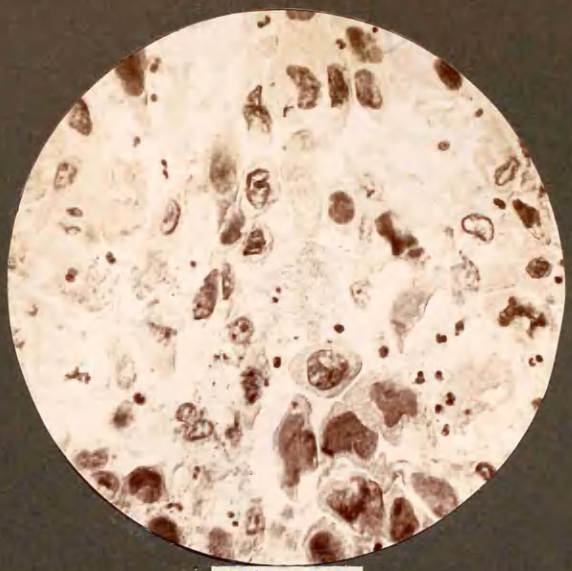

Fig.25.

Fig.25a.

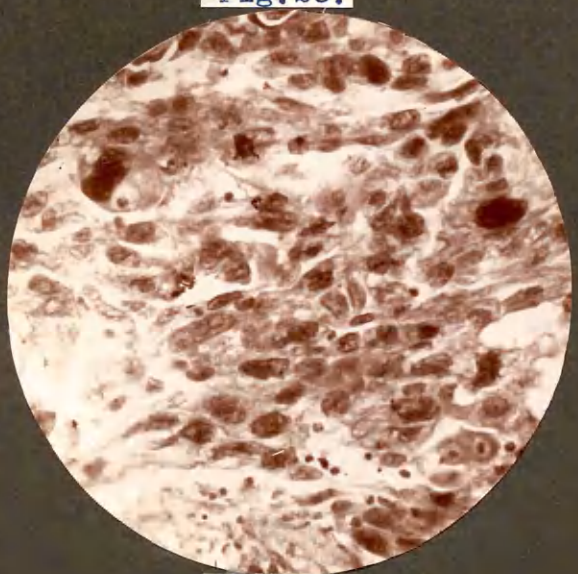

Fig.25b.

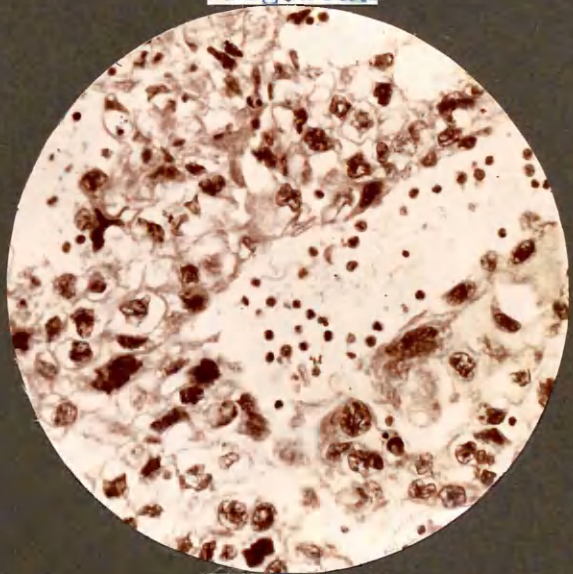

Fig.25c.

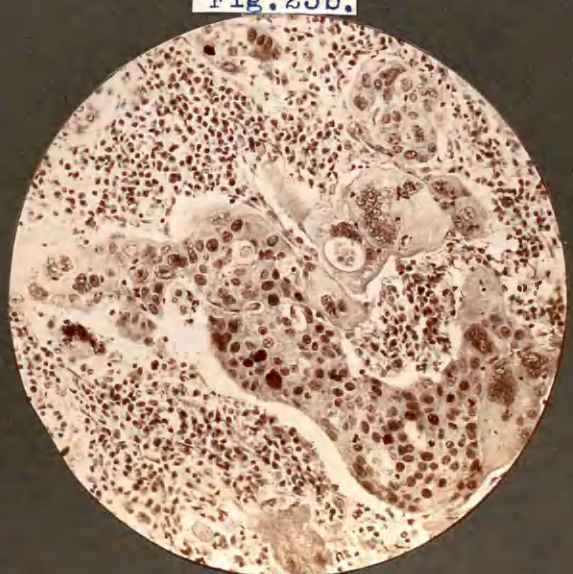

Fig.26.

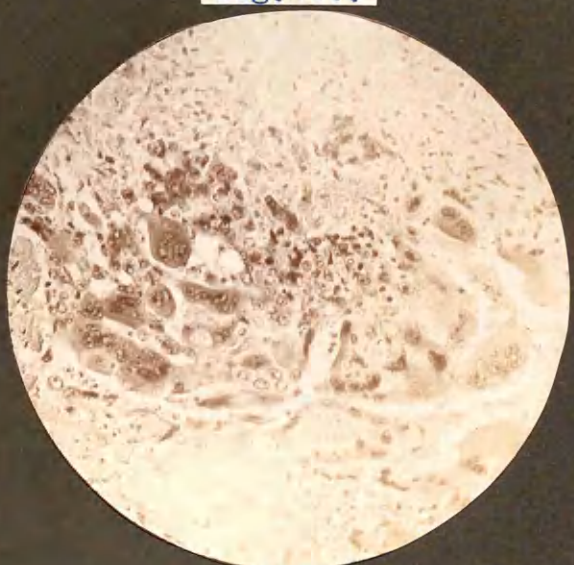

Fig.26a.

Plate XV. The chorionepithelioma of teratomata.

Fig.26e.

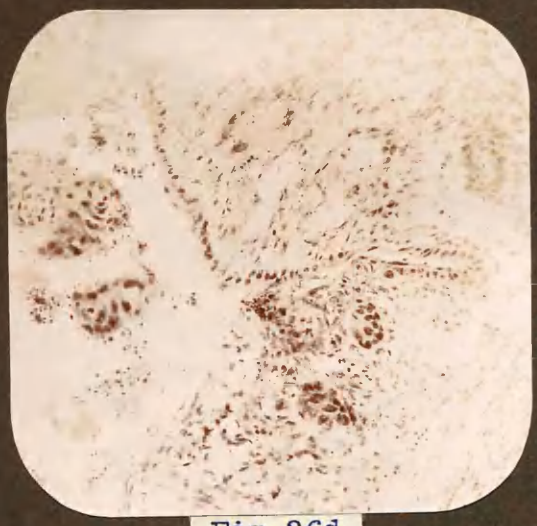

Fig.26d.

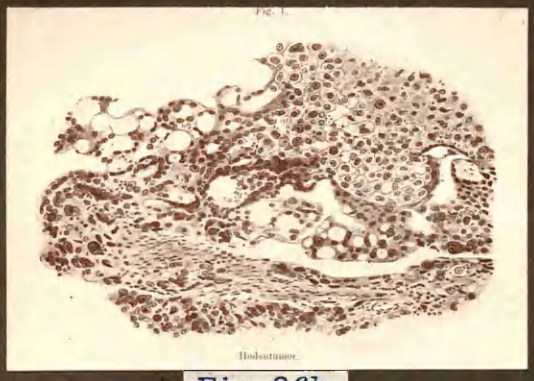

Fig.26b.

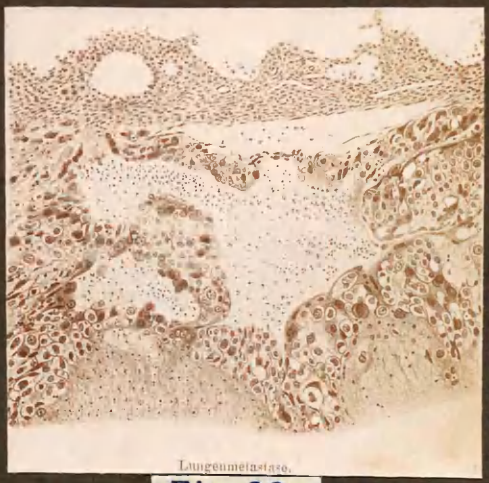

Fig.26c.

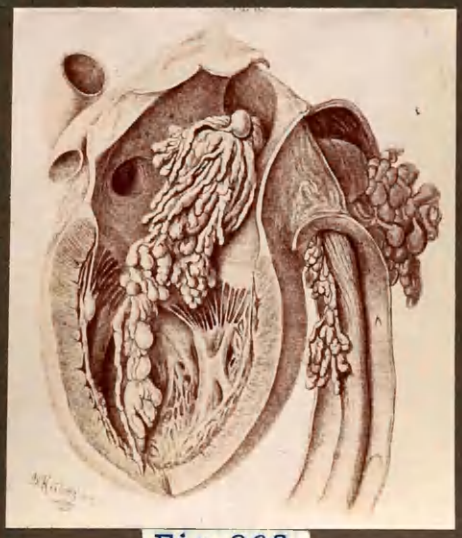

Fig.26f.

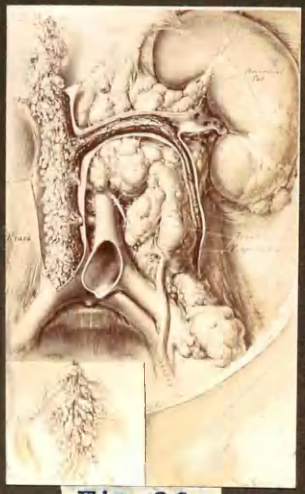

Fig.26g.