SELECT CLINICAL REPORTS.

(Under this heading are recorded, singly or in groups, cases to which a special interest attaches either from their unusual character or from being, in a special sense, typical examples of their class).

I.**A Case of Chorionepithelioma complicated by
Hæmatometra.***

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THE patient was a lady forty-two years of age, who had borne four children, the last in 1897.

Menstruation commenced at the age of eleven, the periods were never quite regular, the intervals varying from three to five weeks, and the bleeding was usually profuse. In 1903 for a term of three months menstruation was suppressed; there was no evidence of pregnancy and at the end of this time the menstrual flow was re-established and continued of the usual type until May, 1905. The last period commenced on May 20th and ceased on May 25th, 1905; shortly afterwards pregnancy ensued.

The pregnancy ran a course apparently normal until August 9th. On that date a blood-stained vaginal discharge was noticed and at the same time aching pain was felt in the pelvis over the whole area from pubes to sacrum. Between August 9th and November 17th there occurred numerous small hæmorrhages, but the amount lost was never sufficient to cause alarm.

On November 17th the patient's medical attendant, Dr. Sharman of Rickmansworth, brought her up to consult Dr. Griffith.

Although there had been six months' amenorrhœa, the top of the uterus was only six inches above the pubes; its characters, however,

* Read before the Obstetrical Society of London, June 5th, 1907, with exhibition of the specimen, microscopic sections, and drawing.

resembled those found in a normal pregnancy. Dr. Griffith suspected that the embryo was dead, and advised a delay of one month and the termination of the pregnancy at the end of that time if the uterus had not increased in size.

The patient was seen again on December 15th when the following note was made: "The uterus presents no change in size or characters, but behind it can be felt a small tumour, probably the left ovary enlarged."

On December 29th, Dr. Sharman induced abortion by inserting a laminaria tent into the cervical canal, and on the following day a mole was spontaneously expelled. The mass presented the general characters of a carneous mole but, later, Dr. Sharman informed us that he noticed on the surface a few small vesicles.

On January 28th, 1906, Dr. Griffith was again asked to see the patient on account of persistent hæmorrhage and the passage of clots. The uterus was of almost the same size as at his last examination, and the cervical canal was patent, admitting the finger easily. Under anæsthesia a large quantity of inoffensive blood-clot was removed by the finger, the uterus then contracted well; the curette was introduced and "a considerable quantity of decidua with adherent clot brought away." Hæmorrhage ceased and the patient's progress was regarded as satisfactory until February 16th, when a small quantity of dark blood escaped; after this date there was no further bleeding but aching pain in the epigastrium and hypogastrium persisted, and for this reason Dr. Griffith was again consulted on February 28th. He found the uterus as large as upon his first examination; the fundus reached to six inches above the pubes, and the organ was unusually broad from side to side. A diagnosis of chorionepithelioma was made, but it was difficult to explain the fact that for the last month there had been hæmorrhage on one occasion only and then slight in amount.

The patient was suffering from a troublesome cough, and from pain in the right side of the thorax. On March 1st Dr. Garrod examined the chest, but could detect no signs which led him to suspect the presence of new growth in the lungs.

On March 3rd the operation of abdominal hysterectomy was performed. When the abdomen was opened a quantity of thin blood-stained fluid escaped—this resembled closely the fluid contained in the cysts of the ovaries. A tumour, which proved to be the uterus, was seen rising out of the pelvis; its colour, size and general characters corresponded with those of the uterus at the end of the fifth month of a normal gestation. The ovaries presented a remarkable appearance, both were enlarged by the presence of multiple cysts and were of a curious dark plum colour. The right was the larger of the two and formed a tumour equal in size to a goose's egg. The

enlargement was due to the presence of a number of cysts, some with serous contents, others filled with a deep-red jelly-like material; some of these cysts ruptured during the process of removal. The left ovary was rather larger than a billiard ball, the cysts on its surface were smaller but of similar appearance. The uterus, together with the uterine appendages, was removed, the vessels were secured and the body amputated at the level of the os internum; as soon as the cavity was cut across a quantity of dark, semi-fluid blood escaped, the walls shrinking and contracting. The cervix was removed separately. A nodule was felt in the posterior vaginal wall; this was enucleated, but on investigation it proved to be a small cyst and to contain no chorionepitheliomatous tissue.

The patient made a good recovery, the convalescence being interrupted by no untoward symptoms.

Immediately after removal the condition of the uterus and cervix was investigated; the cervical canal was occluded by a quantity of coagulated blood; a probe could be passed without difficulty but, apparently, the clot had been sufficiently firm to prevent the escape of blood, and to lead to distension of the cavity by hæmorrhage from the surface of the growth. As soon as free exit was given, the uterus contracted, forcibly expelling a large quantity of blood.

A puzzling feature in the clinical aspect of the case had been the rapid increase in size of the uterus associated with complete cessation of vaginal hæmorrhage. The explanation was now quite clear; coagulated blood completely occluded the cervical canal, the hæmorrhage previously external, had become converted into the concealed variety and led to the formation of a hæmatometra.

We have read no account of the association of this condition with chorionepithelioma, and one of our reasons for recording this case is to draw attention to the possibility of such a complication. The rest of the history is soon told. On August 18th, five months after the operation, Dr. Sharman wrote as follows:—"The condition is not quite satisfactory although Dr. Griffith, Dr. Garrod and I have been unable to find anything suggesting a recurrence. The patient has had a series of attacks of neuritis and myalgia in different parts of the body and especially the chest, back and front, simulating pleurisy and pleurodynia, at first accompanied by slight evening rise of temperature. Recently she has been breathless with some palpitation but nothing definite to account for it." A fortnight later, Dr. Garrod detected signs of new growth in the lung. Death ensued in the latter half of November.

No post mortem examination was performed.

Description of the specimen.

After removal, fluid and clotted blood escaped and the walls of the uterus contracted, actively expelling most of the clot. At the

close of the operation the uterine cavity was packed with cotton-wool soaked in a ten per cent. solution of formalin.

As seen at the present time the dimensions of the organ are:—

Length, 8 inches.

Transverse diameter at the level of the point of entrance of the Fallopian tubes $6\frac{1}{2}$ inches.

Circumference at the same level 15 inches.

In appearance it closely resembles a uterus enlarged by pregnancy. The surface is smooth and peritoneum-clad throughout the greater part of its extent, beneath the peritoneum are numerous small dilated vessels; the shape is pyriform and the Fallopian tubes are attached two inches below the highest point of the fundus. The lower part of the body is devoid of peritoneum on both its anterior and posterior aspects, from these areas the peritoneum has been stripped during the course of the operation. A short distance above the level of the os internum amputation of the corpus uteri has been performed, the cervix was removed subsequently and the two parts have now been stitched together as nearly as possible in their natural position. The length of the cervix is $1\frac{1}{4}$ in.; its canal is patent, a large probe can be passed through its whole extent. The condition of hæmatometra did not depend upon any structural change in the cervix but resulted from occlusion of the canal by blood clot.

The posterior wall of the uterus has been removed by a longitudinal coronal section. The cavity is greatly dilated, the walls are thickened but unequally so, and measure $\frac{5}{8}$ of an inch in thickness at the fundus.

On the inner aspect of the anterior wall nearer to the fundus than the cervix is an irregular area of ulceration three inches in length and two inches in breadth; its long axis corresponding roughly with that of the uterus. The edges of the ulcer are raised, hard and everted; the base is depressed below the level of the surrounding tissues. The ulcerated surface is covered by a number of papilliform projections to which adhere portions of blood clot and debris.

Nearer to the fundus, one inch above the upper margin of the ulcer, are two large patches of pale yellow material resembling masses of coagulated lymph. Sections cut through these show them to be composed of growth similar to that which forms the floor of the ulcer.

The points of entrance of the Fallopian tubes are situated two inches below the summit of the fundus. The abdominal ostia are patent but deeply congested; in other respects the tubes appear to be healthy. On the surface of each are some small sessile sub-peritoneal cysts (dilated lymphatics) and attached in the neighbourhood of the infundibulum on the right side are three small accessory tubes, two of these are fringed by miniature fimbriæ, the third is

occluded at its distal extremity and forms a small cyst (hydrosalpinx of an accessory Fallopian tube).

Both ovaries are enlarged but have shrunk and undergone changes in the process of hardening. As seen immediately after removal the right ovary formed a tumour the size of a goose's egg, composed of a mass of thin-walled translucent cysts; some of the cysts ruptured during removal, their fluid contents escaping into the peritoneal cavity. A section through the organ discloses three main cavities filled with dark-red gelatinous material.

The left ovary is smaller—the size of a golf-ball; its deeply corrugated surface is raised here and there into rounded eminences by the projection of small cysts. At one spot on the peritoneal aspect was a small yellow plaque measuring a third of an inch in diameter and raised slightly above the level of the surface, this was removed for microscopical examination and will be described subsequently. On section, the ovarian stroma is of an almost jelly-like consistence and of a red colour.

Macroscopical Examination.

Sections have been cut in such a manner as to include the edge of the growth and a part of the adjacent uterine wall. The growth is a typical chorionepithelioma, composed of Langhans's cells and syncytium. The fibro-muscular stroma of the wall is seen in part of the section; the tissues of which it is composed take the stain badly, many of the nuclei are fragmentary and details of a chromogen network cannot be determined. The fibrillæ of the muscle bundles can still be seen but the outlines of individual fibres are very indistinct.

The nearer we approach the edge of the growth the more marked is the degeneration of the muscle and finally when we reach the growing edge of the tumour the maternal tissues are represented by an almost homogeneous fibrinous material closely resembling Nita-buch's fibrin layer. In it, however, we can still trace the remains of degenerate nuclei, and scattered through it are a few round cells possibly of an inflammatory nature.

In the normal ovum the trophoblast exhibits destructive properties, in virtue of which the highly differential tissues of the decidua are, in its immediate neighbourhood, reduced and converted into an almost structureless fibrin-like mass; the same destructive action is exhibited by the tongue-like processes which form the vanguard of the growth.

In a specimen of chorionepithelioma—probably the oldest in existence, for the patient died in the year 1872—studied by Dr. Williamson and described in "The Journal of Obstetrics and Gynæcology of the British Empire," Vol. iv., page 306, he was able to

demonstrate in the neighbourhood of the growth a number of blood channels in the uterine wall, and to show that around these blood-spaces the cells which formed the out-posts of the tumour were grouped. This mode of invasion we cannot trace in the present case; we find no constant relation between uterine vessels and the tumour out-growths.

Cells of various forms are seen in the deeper parts of the uterine wall. Those of one variety are small and possess a central vesicular nucleus surrounded by a scanty cell substance which stains faintly with eosin. In others the cell substance is granular and stains more deeply, the nuclei are denser and not clearly vesicular, in this respect resembling the syncytium.

These various cellular elements are found in the tissues at some considerable distance from the tumour; the smaller cells first described are the most numerous; in their characters they differ markedly from the round cells so familiar to us in inflammatory processes and are evidently derivatives of the foetal epiblast. They are most numerous in the neighbourhood of the vascular spaces but are not confined to these areas.

The tumour may be described as consisting of a sponge-work of syncytium, the interstices of which are occupied by large rounded or oval cells each possessing a single centrally situated nucleus. From the growing edge, tongue-like processes project into the uterine stroma; the maternal tissues in the neighbourhood of these projections have undergone necrosis, they do not persist to form a stroma for the tumour but disappear completely, first becoming converted into a structureless substance resembling Nitabuch's layer of canalized fibrin. As the result of the destructive action of the invading tissues, many of the processes are surrounded by spaces containing red blood corpuscles; it is from these vascular channels that the growth derives its principal blood supply.

Two distinct varieties of tissue can be recognized in the growth:—

(1) Syncytium present in the form of irregular masses, in the form of the so-called multinucleate giant cells and in the form of ribbon-like strands so united as to constitute a sponge-work; in the spaces of this sponge-work are groups of tightly packed cells. Between the masses of syncytium on the one hand, and the well formed discrete cells on the other, all stages of gradation are found. The protoplasm of the syncytium stains well with eosin; it is finely granular, opaque and vacuolated. The nuclei show no constant arrangement; in some parts they lie in rows, in others they are scattered irregularly throughout the protoplasm; in form and structure they exhibit marked differences, some are small round darkly-staining bodies, others are larger and vesicular and possess a distinct chromogen network.

(2) *The Langhans' Cells* are rounded, with a clear defined outline, the nuclei are large, centrally-situated, and vesicular, the cell-substance is granular and vacuolated, differing from the protoplasm of the syncytium in that it exhibits a reteform structure and stains less deeply with eosin.

The syncytium forms a sponge-work of interlacing strands and in the interstices of this sponge-work lie groups of Langhans's cells packed closely together.

Microscopical examination of the ovaries reveals:—

(1) That the organs are unusually vascular.

(2) That lutein tissue is present in three situations. (a) In the walls of the cysts. (b) In the ovarian stroma. (c) On the surface of the ovary.

(3) That the stroma-cells have undergone modifications.

The *blood-supply* of the organs is a rich one, in addition to well-formed vessels there are vascular channels possessing little more than an endothelial lining. The red jelly-like appearance of the ovaries is due to the presence of blood extravasations into the œdematous stroma.

The Lutein Tissue.

The various cysts scattered through the ovaries are lined by a pale yellow membrane composed of lutein cells, this membrane is thrown into wavy folds. In most instances the lutein cells are in direct contact with the cyst contents, occasionally a lining of fibrinous almost structureless material lies within the lutein layer. A stratum of similar material is constantly to be seen in the normal corpus luteum separating the lutein cells from the central blood-clot and, in our opinion, is to be regarded as the membrana propria of the normal Graafian follicle greatly hypertrophied.

The lutein tissue is formed of rounded and irregularly-shaped cells with opaque cell-substance and a centrally situated vesicular nucleus. Karyokinetic figures are seen in some of the nuclei and furnish evidence of rapid cell proliferation; such figures are rarely found in the mature corpus luteum. Groups of lutein cells are scattered through the stroma and, at one spot on the surface of the left ovary, a mass of the tissue projects.

We have already drawn attention to a small yellow plaque one third of an inch in diameter attached to the surface of the left ovary. The mass is composed of rounded cells with a central vesicular nucleus and opaque cell-substance; between the cells is a scanty inter-cellular stroma. Two explanations of the origin of this group of cells suggest themselves. (1) That we may have here a "decidual nodule," one of those small masses of decidual cells described originally by Schmorl and Kinoshita which are so often to be found scattered over the peritoneum of the uterus and of Douglas's cul-de-sac

and upon the surface of the ovaries, in women dying soon after childbirth. (2) The nodule may be composed of lutein tissue. The yellow colour of the plaque and the characters of the cells have led us to adopt the latter view. Dr. F. W. Andrewes and Dr. Cuthbert Lockyer, who have been good enough to examine the sections, agree with our conclusions.

The ovarian stroma has become modified; in many parts it is oedematous and degenerate, the cells possess oval or rod-shaped nuclei and the elongated cell-processes unite to form a network whose meshes are sometimes occupied by red blood-corpuscles. In this degenerate stroma are groups of lutein cells. In other places the stroma-cells are no longer of the embryonic type but are oval or rounded with large clear vesicular nuclei some of which show karyokinetic figures; it is possible that these may represent the earlier stages of the lutein cell. We possess no differential stain for lutein tissue and we are not in a position to state with certainty that these modified stroma-cells are of this nature.

In a paper read before the Obstetrical Society of London in 1905, Dr. Cuthbert Lockyer accepted the theory of migration of lutein cells; there is no positive evidence available in favour of the existence of such a phenomenon. The origin of the lutein cell cannot be regarded as definitely settled. We are, however, firmly convinced that it arises by modification of the cells of the theca interna and not from the membrana granulosa. The cells of the theca interna are merely modified stroma cells, and we find no difficulty whatever in believing that lutein tissue may arise directly from the connective tissue cells of the ovarian stroma. The specimen before us furnishes no clear proof of the truth of this theory, but the marked modifications in the form of the stroma and the presence of the groups of lutein cells scattered through it are very suggestive.

The study of chorionepithelioma is still in its infancy and it is important that every case presenting unusual features in either its clinical or pathological aspect should be reported. In its clinical aspect this case was unusual in that a month before operation there was cessation of vaginal hæmorrhage although the uterus continued to enlarge.

In its pathological aspect it presents three points of special interest.

First, in the excessive formation and wide distribution of lutein tissue throughout the ovaries.

Secondly, in that it supports the theory that lutein cells may arise by modification of the connective-tissue cells of the ovarian stroma.

Thirdly, in the presence of a layer of necrosed tissue, closely resembling Nitabuch's layer of canalized fibrin between the uterine wall and the tumour out-growths.