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TUBERCULOSIS OF THE ENDOMETRIUM

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Reprinted from the Johns Hopkins Hospital Reports,



TUBERCULOSIS OF THE ENDOMETRIUM.

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Tuberculosis of the endometrium is found with a moderate degree of frequency at autopsy, but heretofore has rarely been noted at operation. The reason for this, in part at least, will be found in the fact that there are many cases of recognized tuberculosis of the appendages in which the tubes and ovaries have been removed, but in which the uterus has either been left behind or has not been subjected to a minute histological examination. During the past eighteen months Dr. Kelly has removed the uteri in all cases in which the tubes and ovaries have been found diseased, and we have thus been enabled to study the coincident changes in the endometrium. The mucous membrane of the uterus was in each case examined microscopically independent of its macroscopical appearance. In the eighteen months we have met with three cases of tuberculosis of the endometrium, and to these we append two observed at autopsy.

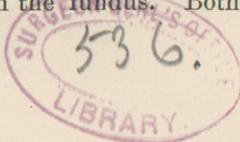
Tuberculosis of the endometrium may be divided into two classes :

a. Miliary.

b. Chronic diffuse tuberculosis.

The former is rare, being only met with in a certain percentage of those dying of miliary tuberculosis ; we have not met with such a case.

Chronic diffuse tuberculosis in its very early stages is not recognizable by the naked eye examination, as is shown by Cases I and IV of our series. Here the mucosa presented the usual yellowish-white appearance and was smooth and glistening. When the process is a little farther advanced the mucosa may still be intact (see Case V), but just beneath the surface a few yellowish-white nodules can be seen ; these vary from 1 to 2 mm. in diameter and are usually situated near the top of the fundus, as it is there that the process commences. Otto v. Franqué recently reported a case of epithelioma of the cervix in which, 2 cm. above the internal os, a soft reddish nodule the size of a cherry was found projecting from the mucosa. A similar nodule was detected farther up in the fundus. Both of these were



supposed to be metastases from the epithelioma, but on microscopical examination were found to be dilated glands, around the margins of which were typical tubercles. The mucosa between the tubercles will in the early stages appear normal, unless there has been a coincident or previous endometritis. When the disease has made farther progress the tubercles become larger and more prominent, giving the mucosa an uneven and roughened appearance. Some of these nodules have in the meantime broken down and formed ulcers. The ulcerated areas may be shallow and present a worm-eaten appearance or have undermined edges. If the tubercle has been quite superficial a shallow ulcer may be looked for, as the surface presents an area of necrosis greater than that found in the depth. If the tubercle be deeply situated an ulcer with undermined edges is likely to result. The ulcers are at times surrounded by small yellow tubercles. The process gradually extends, the areas of caseation increase and become irregular, and eventually the entire endometrium is converted into caseous material. Should the cervix uteri become occluded an accumulation of this caseous material may take place, giving rise to a condition resembling pyometra. The tuberculous process gradually extends to the muscle, sometimes reaching as far as the peritoneum, when rupture of the uterus may occur.

HISTOLOGICAL EXAMINATION.

In the early stages the mucosa over the lower portion of the fundus is normal. In passing toward the upper part of the fundus the surface epithelium is found to be intact, but here and there is swollen and stains poorly. As will be seen later, it is beneath the epithelium at these points that the tubercles are found. The surface epithelium has at various points proliferated, forming little teat-like prominences or delicate gland-like spaces. The uterine glands are small and round on cross section and have an intact epithelium; a few, however, may be dilated and partially filled with desquamated epithelium. With the low power pale-staining areas are seen scattered throughout the stroma of the mucosa. These are readily recognized as clusters of epithelioid cells. With the high power it is sometimes possible to make out all transitional stages between the stroma cells and epithelioid cells, as is well shown by Case V. The epithelioid nests are surrounded by small round cells which are sharply defined

from the normal stroma cells. Some of the tubercles, especially those at the top of the fundus, contain giant cells which are irregular, oval, or round in contour (see Plate XXI, Fig. 1), and which contain oval vesicular nuclei, arranged either around the margin of the cell, at one or both poles, or scattered promiscuously throughout the protoplasm.

From Case IV we are inclined to believe that at least some of the giant cells are formed by the coalescence of several epithelioid cells, the protoplasm of all of the cells fusing into one protoplasmic plaque, while the nuclei remain distinct. The centres of many of the tubercles show a tendency to become infiltrated with polynuclear leucocytes. Where the process is more pronounced the gland epithelium may have proliferated. This is seen in Case I, where the epithelial cells had proliferated, forming a typical tubercle which contained a giant cell and which projected into the gland cavity. Franqué has been able to make out precisely the same changes in a case which he recently reported. The tubercles continue to enlarge and soon merge one with the other; the surface epithelium disappears; the greater part of the mucosa becomes invaded by tuberculous material which undergoes caseation; this caseous material then breaks down, giving rise to areas of ulceration. Should a section be made through an early ulcer the following may be seen: the surface of the ulcer is covered by necrotic material in which the fragments of a few nuclei or some polynuclear leucocytes are visible; the underlying tissue consists of epithelioid cells and many small round cells. Scattered throughout this zone are typical tuberculous giant cells. On passing outward toward the muscle the small round cells increase in number, while the epithelioid cells gradually diminish until the normal muscle is reached. The tuberculous process continuing to advance, invades the muscle, the entire thickness of which may be occupied by tuberculous tissue. Tubercle bacilli are found on the surface of the mucosa, in the glands, epithelioid nests, and in the giant cells. They are especially numerous in the caseous areas.

CONDITION OF THE TUBES AND OVARIES.

In four of the five cases here described the tubercular process in the tubes was recognized with the naked eye, there being not the slightest doubt as to the diagnosis. In the remaining case only the uterine scrapings were obtained. In Case IV the left ovary was

converted into a tuberculous abscess. The ovaries in the remaining cases were normal.

ORIGIN OF THE TUBERCULOSIS.

Tuberculosis of the endometrium is usually secondary to that of the tubes, and is accordingly in the early stages confined to the upper segment of the uterus. In a certain number of cases it undoubtedly extends upward from the vagina and may then be due to infection through coitus. In Cases I, IV and V it was undoubtedly secondary to tuberculosis of the tubes. In Case II we had only the uterine scrapings to examine and are accordingly not in a position to give the probable seat of origin. The tubercular process in Case III was too far advanced to say whether it originated from the tubes or was primary in the uterus.

SYMPTOMATOLOGY.

There are no fixed symptoms in this disease, and if there were, these would probably be masked by those due to tuberculosis of other organs. The menstruation in the three cases where histories could be obtained was irregular; two had a slight leucorrhoea, the third had no vaginal discharge. Two of the patients were white and two were black; the color of the fifth is unknown. The ages of four of the patients were 3, 17, 26 and 33 respectively.

DIAGNOSIS.

Microscopical examination of the scrapings will usually prove the existence of the tuberculosis, as is shown by Case II. (See Plate XXI, Fig. 2.) In the very early stages, however, the tuberculous process may be confined to the cornua, when it is improbable that the diseased tissue will be removed by the curette.

TREATMENT.

Tuberculosis of the endometrium is rarely suspected until the abdominal cavity is opened, either for the purpose of exploration or for the removal of diseased appendages. Should the tubes prove to be tuberculous it will be advisable to remove the uterus at the same time, as it also may be tuberculous. Sippel reports a case where the right tube was removed and found to be tuberculous; the

left tube, which was apparently normal, had to be removed seven months later, as it also had become tuberculous. The uterus was curetted at the second operation. Weigert examined the scrapings and found them to be tuberculous. Sippel thinks in this case that with the atrophy of the mucosa following the removal of the appendages the tuberculous process will be checked. Curetting of the uterus has been advocated. We have several times examined the uterus which, before removal, had been thoroughly curetted and found that a good deal of the mucosa was still intact; this was especially noticeable near the top of the fundus, and it is here, as will be remembered, that the tuberculous process is most advanced. It would be scarcely possible to entirely remove the tuberculous tissue by curetting; therefore removal of the uterus is to be recommended.

CASE I.

Tubercular peritonitis; double tubercular salpingitis; tuberculosis of the endometrium, probably secondary to that of the tubes.

M. L., æt. 17, admitted to service of Dr. Kelly on November 20, 1894. On entrance she complained of enlargement of the abdomen associated with abdominal pain. Her menses commenced at fifteen and were very irregular, occurring at intervals of from two to eight weeks. About two weeks before each period she would have sharp shooting pains in the lower part of the abdomen. With the appearance of the menstrual flow the pain would cease. The flow was moderate in amount and lasted from two to four days. Date of last menstrual period, May, 1894. Her family history is unimportant. The patient had "la grippe" in December, 1893, and has not felt well since then. In March, 1894, she had "malaria," having chills every other day. In May of the same year she developed pleurisy, which lasted until the first week in June.

Present Condition. About three weeks ago her abdomen commenced to enlarge and she has had occasional sharp abdominal pain. This has not been confined to any one locality. She has had no nausea and no vomiting. The patient at present is fairly well nourished, her mucous membranes are pale, her tongue is coated, her appetite is good, but her bowels are somewhat constipated. She has neither urinary difficulty nor leucorrhœa. The abdomen is slightly and symmetrically prominent. By palpation nothing can be detected; on percussion a distinct wave of fluctuation can be elicited.

Operation by Dr. Kelly, November 21st. An incision 10 cm. long was made in the median line, and about four litres of a pale greenish transparent fluid escaped. This had a specific gravity of 1.019. The peritoneum was markedly injected and everywhere studded with small tubercles. It averaged 2.5 mm. in thickness. The ovaries and tubes were liberated from adhesions to the rectum by means of the fingers and a sponge. The left tube and ovary were tied off, the broad ligament opened and the left uterine artery ligated. The same procedure was carried out on the right side and the uterus amputated without any hemorrhage. The anterior and posterior flaps of the stump were approximated by silk sutures; the peritoneum from the vesico-vaginal pouch was united with that from Douglas' cul-de-sac, thus hiding the uterine stump completely and making it extra-peritoneal. On November 30th the stitches were removed, and in the lower part of the incision slight suppuration was noticed. On December 3d the lower angle of the wound broke down, discharging a large quantity of thick yellow pus. Six days later the patient was discharged feeling well, a small fistula, however, still remaining. Her temperature for the first nine days after the operation fluctuated between 100° and 103.5° . The highest point reached was 104.2° , which was on the eighth day. On her discharge the temperature was normal.

Pathological Report. The specimen consists of a portion of the uterus with the tubes and ovaries intact; also of a small piece of peritoneum. The portion of the uterus present is 4 cm. long, 5.5 broad, and 3.5 in its antero-posterior diameter. Both the anterior and posterior surfaces of the uterus are covered by a hemorrhagic, somewhat shaggy membrane 2 mm. in thickness. This membrane, besides covering the uterus, is continued laterally over the surface of the tubes. The membrane can be stripped off, leaving a white, somewhat roughened surface beneath. The uterine walls average 1.5 cm. in thickness and are pale pinkish in color. The uterine cavity is 2.5 cm. in length, its mucosa is pale yellowish-white in color, is slightly corrugated, but smooth and glistening. Near the internal os a few dilated glands can be seen, the largest of which is 2.5 mm. in diameter. The uterine mucosa varies from 2 to 3 mm. in thickness.

Right appendages. The tube is 10 cm. in length and somewhat convoluted. It gradually increases in size and at the fimbriated

extremity is 2.5 cm. in diameter. The tube is, as above mentioned, covered by a thick vascular membrane. The folds of the fimbriated extremity are everywhere visible and appear somewhat thickened. On pressure the tube is firm, but slightly yielding, and from its fimbriated extremity a small amount of milky fluid can be squeezed.

The ovary is 5.5x2x2 cm. in its various diameters; is grayish-white in color, smooth and glistening, except in a few places where it is attached to the tube by delicate adhesions. It contains a few Graafian follicles and is soft and yielding.

Left appendages. The tube is 12 cm. long and at the uterine extremity 1 cm. in diameter. On passing outward it increases in size, becomes bent on itself and terminates in a fimbriated extremity 2.5 cm. in diameter. The tube is covered by the membrane, which also covers the uterus. The folds of the fimbriæ are everywhere visible, are thickened and deep red in color. Scattered here and there over the surface of the tube are yellowish-white nodules, varying from 1 to 2 mm. in diameter. The parovarium is obliterated.

The ovary is 4x1.5x1.2 cm. in its various diameters. It is smooth and glistening and contains a few dilated follicles.

The piece of peritoneum removed is vascular, and is covered by minute whitish nodules.

Histological Examination. The glands of the uterine mucosa in the vicinity of the internal os are for the most part normal; some of them, however, are dilated. The epithelium of these dilated glands is cuboidal. About 1 cm. from the top of the fundus the surface epithelium is found to be intact, the glands are small and round on cross section and have an intact epithelium, but the stroma just beneath the surface epithelium contains tuberculous nodules, some with, others without giant cells. The giant cells are large, irregular in contour, and are partially filled with elongate, oval, deeply staining nuclei. Surrounding these cells are epithelioid cells, the nuclei of which are club-shaped, oval or semilunar. The stroma in the vicinity of such nodules is infiltrated by lymphoid cells. The deeper portions of the mucosa are perfectly normal.

On passing a little farther upward toward the top of the fundus a dilated gland is seen, the epithelium of which is partially intact. Where the epithelium has disappeared the walls are seen to be invaded by epithelioid cells. The cavity of this gland contains

epithelioid cells, also a giant cell. Near the top of the fundus the process is still more advanced. The surface epithelium becomes somewhat wavy, its individual cells more cuboidal, while just beneath the surface at these points are delicate glands lined by cuboidal epithelium. Where the process is most advanced the surface epithelium has disappeared, and nearly the entire thickness of the mucosa is occupied by epithelioid and lymphoid cells. Scattered throughout this newly formed tissue are numerous large irregular giant cells. These are most abundant along the advancing margin of the growth. There is no caseation. Tubercle bacilli can be demonstrated on the surface of the mucosa, in the lumina of the glands, and also in the giant cells. We are dealing with *tuberculosis of the endometrium limited to the upper half of the uterine cavity and most pronounced at the top of the fundus*.

The membrane covering the uterus is composed of newly formed connective tissue rich in blood supply. This tissue is everywhere studded with masses of epithelioid cells. The centres of some of these masses are occupied by giant cells. In some of the giant cells the nuclei are situated in the centre of the protoplasm, in others they are arranged around the entire outer margin of the cell or are confined to one pole. This newly formed tissue is everywhere infiltrated by lymphoid cells. The uterine muscle just beneath the membrane is infiltrated by lymphoid cells, but contains no tubercles.

Right appendages. The tubal mucosa at the uterine cornu is infiltrated by lymphoid cells, but is otherwise normal. The tube 1 cm. from the uterine cornu is markedly altered. Its lumen is partially filled with necrotic material in which nuclear fragmentation is visible. The folds where present are covered by masses of epithelioid cells intermingled with lymphoid cells. The greater part of the mucosa is transformed into a solid tissue composed of epithelioid and lymphoid cells. The epithelioid cells tend to arrange themselves in clusters, many of which contain giant cells in their centres. Scattered here and there throughout this new-formed tissue are small round, oval, or irregular gland-like spaces lined by cylindrical or cuboidal epithelium. A few of them contain desquamated epithelium. These spaces are the remains of the tubal mucosa. The muscular coat has in a few places been invaded by epithelioid elements and is everywhere infiltrated by lymphoid cells. The outer surface of the tube

is covered by a thick membrane, the histological characters of which are identical with those of that covering the uterus.

At the outer end of the tube the caseation is more advanced. The ovary is near its hilum covered by a membrane 2 mm. in thickness. This contains numerous tubercles. The greater part of ovary is, however, devoid of adhesions. It contains many ova and several Graafian follicles and is practically normal.

Left appendages. The tube at the uterine cornu has an intact epithelium. The process in the left tube is similar to that in the right. Here, however, the muscular coat shows more involvement, and both the mucous and muscular coats show some infiltration with polynuclear leucocytes. Tubercle bacilli can be demonstrated in both tubes. They are found in the centres of the giant cells, in their margins, or in between the epithelioid cells.

The adipose tissue in the mesosalpinx is infiltrated by numerous tubercles. The left ovary is comparatively free from adhesions, contains numerous ova and Graafian follicles and is normal. The piece of peritoneum cut out for examination is studded with tubercles.

CASE II.

Tuberculosis of the endometrium, diagnosed from scrapings.

H. J., æt. 26, colored, was admitted in the service of Dr. Kelly, Dec. 11, 1894. The patient has never had any serious illness, but has always been rather frail. Her menses commenced at 16 and were regular for the first three years. She was married at 19, but has had no children and denies any miscarriages. For the last seven years the menses have been very irregular. At first they were profuse and the patient passed clots of blood; at another time they ceased for one year. Her mother died of cancer of the breast; brothers and sisters healthy. Present condition: The patient's general condition is good; her heart and lung sounds are negative. In one breast are a few small nodules. She has considerable vaginal discharge, also painful micturition. The urine is amber-colored, has a sp. gr. of 1022 and is acid. It contains neither sugar nor albumen. On vaginal examination the uterus is found to be anteposed, normal in size and freely movable.

On December 13th the small nodules of the breast were enucleated by Dr. Clark, and on microscopical examination Dr. Bloodgood

found them to be fibromata. The uterine cavity was curetted on the same day that the nodules were removed.

The patient was discharged on December 21st. The examination of the scrapings is as follows:

Histological Examination. The surface of the uterine mucosa presents a wavy outline. The epithelium covering its surface is of the high cylindrical variety and everywhere intact; between the individual cells, however, are a few polynuclear leucocytes. The glands are small and round on cross section and have an intact epithelium. The stroma of the mucosa is rather dense, and with the low power numerous pale-staining areas are seen scattered throughout it. These are composed of epithelioid cells. In the centre of most of these clumps of cells giant cells are found. (See Plate XXI, Fig. 2.) These contain a large number of nuclei, arranged principally at one pole. The stroma is everywhere infiltrated by lymphoid cells. One of the tubercles contains many polynuclear leucocytes. No caseation can be seen. Tubercle bacilli are demonstrable in the giant cells.

CASE III.

L. B., a patient, the inmate of an insane asylum. Autopsy by Professor Welch, February 3d, 1886.

Tubercular salpingitis, and caseous tuberculosis of the endometrium following tubercular peritonitis, which apparently originated from ulcers in the ileum. There was tuberculosis of both lungs.

Our specimen consists of portions of the uterus and of one tube.

Histological Examination. The piece of the cervix present is perfectly normal. The greater part of the uterine mucosa is necrotic, while scattered throughout the necrotic material is a moderate number of polynuclear leucocytes. Some of the uterine glands are visible in the depth of this necrotic material. They are moderately dilated and have a partially intact epithelium which is either cylindrical or cuboidal in form. Surrounding the glands is a moderate amount of stroma, which is markedly infiltrated by polynuclear leucocytes and shows considerable nuclear fragmentation. The muscular tissue just beneath the mucosa has here and there a very rich blood supply, while between the individual muscle fibres are large numbers of polynuclear leucocytes and young connective tissue cells. The infiltration extends about 6 mm. into the muscle and then entirely

disappears. Scattered here and there throughout the muscle, especially in the vicinity of the caseous material, are numerous giant cells, most of which are surrounded by zones of epithelioid cells. A few giant cells are seen around which no epithelioid or lymphoid cells are found. No tubercle bacilli could be demonstrated; this may be due to the length of time since the specimen was obtained.

The tube is apparently free from adhesions. Near the uterine extremity its lumen is much altered. The epithelium of the folds is in some places intact, in other places has entirely disappeared. There is a marked increase of connective tissue cells throughout the muscular coat. Scattered freely throughout it are giant cells, the nuclei of which are elongate oval and deeply staining, and are arranged either at one pole of the cell or extend all the way around it. Most of these cells are surrounded by zones of epithelioid cells. Sections through the middle of the tube show that the folds of the mucosa have almost disappeared, while the stroma beneath is necrotic and infiltrated by polynuclear leucocytes. Scattered throughout this stroma are numerous gland-like spaces which are lined by cylindrical or cuboidal epithelium. The muscular coat is much altered and shows considerable amount of small round cell and polynuclear infiltration. There are numerous tubercles scattered throughout the tissue, some of which have undergone caseation and show nuclear fragmentation.

CASE IV.

Commencing tuberculosis of the endometrium, double tubercular salpingitis; tubercular abscess of the left ovary.

A. M., æt. 33. Admitted in the service of Dr. Kelly, Feb. 1st, 1895. On entrance she complained of pain in the lower abdomen and of frequent, prolonged and painful menstruation.

Twelve years ago she had an attack of "pelvic inflammation," the chief signs of which were great pain and tenderness in the lower part of the abdomen. At that time she had profuse leucorrhœa. Since this illness she has never been strong, and any exposure to cold would bring on a severe attack of pain in the lower abdomen. This was accompanied by slight fever, swelling of the abdomen and painful defecation. Two months ago she had a severe attack, the pain being in both ovarian regions and radiating to the lower extremities. For the last five weeks she has had constant pain in the region of the

left ovary; this has been much aggravated on exertion and at the menstrual period. The patient has been married four years, but has had neither children nor miscarriages. She began to menstruate when twelve years of age and was regular until two years ago, when the periods were only three weeks apart. The duration of menstruation has increased, lasting from eight to ten days. Last menstruation about Jan. 15th. She has slight, non-offensive, non-irritating leucorrhœa. Her family history is unimportant and none of her relatives have died from tuberculosis.

The patient at present is debilitated and appears somewhat anæmic. On vaginal examination the uterus is found retroflexed and adherent, and on the left side a distinct mass can be felt; this is about 10 cm. in diameter.

Operation Feb. 2d, by Dr. Kelly. Abdominal incision 11 cm. long was made. The omentum was adherent to the anterior abdominal wall over a large area. The left side was examined and its enucleation found to be impossible; the right side was then freed from adhesions to the broad ligament, was elevated and the ovarian vessels ligated; the right round ligament was then tied and severed; the left round ligament was tied off, the vesical peritoneum dissected away from the uterus and pushed forward; the right uterine vessels were then ligated and the uterus amputated, the left uterine vessels being in the meantime controlled by artery forceps. The ovarian abscess was then enucleated without difficulty by working in behind the cervical stump and stripping the sac from below upward. The abscess ruptured over an area 3 mm. in diameter and a small amount of fetid yellowish-green pus escaped; this was, however, prevented from touching the peritoneum. After the structures had been removed the general oozing from the pelvic floor was controlled by persulphide of iron. The flaps of the cervical stump were then united and the peritoneum from the anterior pelvic wall sutured to that of the posterior wall. The pelvic cavity was irrigated with salt solution and a gauze drain inserted in the lower angle of the wound. On Feb. 5th the gauze was removed, there having been very little discharge; a fresh piece of gauze was introduced and removed on Feb. 7th. During the first three days the pulse would at times drop down to fifty, but the patient's condition was good. She was discharged March 5th, feeling perfectly well.

Cover-slips made from the ovarian abscess at the time of operation gave a moderate number of pus cells, numerous red blood corpuscles, and several curved irregularly stained bacilli, some of which looked like diplococci. Cultures on agar and glycerine agar were, however, negative.

Pathological Report. The uterus is 6x5.5x3.5 cm. Anteriorly and on the top of the fundus are a few delicate adhesions, some of which contain fat and are apparently omental in origin. The posterior surface is practically free from adhesions. Two cm. of the cervical canal is present. The mucosa of this is whitish in color, smooth and glistening. The uterine walls average 2 cm. in thickness and are whitish-pink in color. The uterine cavity is 3 cm. in length, and at the top of the fundus 2 cm. in breadth. The mucosa is whitish-yellow, smooth and glistening; here and there it presents a few ecchymoses. It averages 2.5 mm. in thickness.

Right appendages. The tube after passing outward 4 cm. forms a gentle curve inward and backward, and gradually dilating, terminates in an occluded fimbriated extremity 1.5 cm. in diameter. The upper surface of the tube is comparatively free from adhesions. The under surface, however, is adherent to the ovary throughout the greater part of its course. The ovary is 4x3x2 cm., is covered by numerous vascular adhesions, and is soft and yielding.

Left appendages. The tube and ovary are matted together, forming a mass 7x5x5 cm. This is pinkish in color, covered by numerous adhesions and firmly adherent to the uterus. On section the greater portion of the mass is found to be filled with pus.

Histological Examination. The epithelium covering the cervical mucosa is intact; the underlying stroma, however, shows a moderate amount of small round-celled infiltration. The surface of the uterine mucosa is for the most part smooth and glistening, but here and there presents a wavy outline. The surface epithelium is everywhere intact, but in a few places it is somewhat swollen and stains very lightly. Between the individual epithelial cells are a moderate number of polynuclear leucocytes. Here and there the surface epithelium has proliferated and forms small finger-like projections. The glands are few in number, are small and round on cross section, or are slightly dilated. The gland epithelium is everywhere intact. The cavities of the dilated glands contain a moderate amount of

desquamated epithelium and granular material. The stroma of the mucosa is of the usual density.

About 1 cm. from the top of the fundus a cluster of epithelioid cells can be seen, in the centre of which many polynuclear leucocytes are visible. One or two similar nodules are seen near the top of the fundus. These contain large giant cells in their centres. The nuclei of the giant cells are elongate oval and vesicular, and are arranged either along the margin of the cell or are situated at one pole. It is over these nodules that the surface epithelium is swollen and stains poorly. The stroma of the mucosa in the vicinity of these nodules is very rich in small round cells. The deeper portions of the stroma are unaltered. It may be mentioned that one of the giant cells is composed of a large irregular plaque of protoplasm, scattered irregularly, throughout which are typical epithelioid nuclei. It looks as if the protoplasm of the different cells had coalesced, forming one large mass; the nuclei, however, appear to have been perfectly preserved.

The uterine muscle is unaltered. The interesting points in connection with the endometrium are that the tuberculous changes have been confined to the upper segment, that the surface epithelium is everywhere intact, but stains poorly over the points where the tubercles are present; also that all of the tubercles are situated in the superficial portions of the mucosa. Tubercle bacilli are to be seen scattered throughout the tuberculous areas. Both tubes show advanced tuberculosis. The left ovary is occupied by an abscess, the walls of which are composed of typical tuberculous tissue.

The tuberculosis of the endometrium is undoubtedly secondary to that of the tubes.

CASE V.

E. W., æt. 3, colored. Admitted in the service of Dr. Osler. Died April 22, 1895. Autopsy by Dr. Flexner.

Anatomical Diagnosis. Tuberculosis of the lymph glands, lungs, pleura, pericardium, peritoneum, liver, spleen, kidneys, Fallopian tubes and endometrium.

A description of the generative organs is as follows:

The vaginal mucosa is transversely corrugated, is bright bluish-white in color, smooth and glistening. The uterus is 2.3 cm. in

length, 9 mm. in breadth and 5 mm. in its antero-posterior diameter. Anteriorly and posteriorly it is smooth and glistening. The cervix is 7 mm. in diameter and projects 6 mm. into the vagina. The cervical lips are exceedingly delicate, in some places not being more than .2 mm. in thickness. The cervical canal is 1.5 cm. in length. Its mucosa is yellowish in color, smooth and glistening, and presents shallow longitudinal furrows. The uterine walls average 2 mm. in thickness. The uterine cavity is 1 cm. in length. Its mucosa is bluish-white and longitudinally furrowed. Just beneath the surface of the mucosa a few minute pin-point whitish-yellow dots can be seen.

Right side. The tube is 6.5 cm. long, and at its uterine end 2 mm. in diameter; after passing outward 3 cm. it becomes tortuous, having a corkscrew-like arrangement. It terminates in a partially occluded fimbriated extremity 5 mm. in diameter. On section it presents a yellowish-white somewhat cheesy appearance. The parovarium is intact. The ovary is 2.2x.5x.3 cm. It is whitish-pink in color and everywhere smooth and glistening. No Graafian follicles were to be made out.

The left tube presents the same appearance as the right, and the left ovary also resembles that of the opposite side.

Histological Examination. The vaginal mucosa is normal. The vaginal portion of the cervix is unaltered; the cervical portion is covered by cylindrical epithelium which conforms to the usual type. Opening on the surface of the cervical mucosa are the shallow glands, which are but slightly convoluted. The junction of the cervical with the uterine mucosa is sharply defined. The uterine mucosa near the internal os is covered by cylindrical epithelium, the nuclei of which are elongate oval and rather deeply staining. The uterine glands are few in number, but appear to be perfectly normal. On passing up toward the top of the fundus the surface epithelium is seen to have disappeared, and small masses of epithelioid cells are scattered throughout the stroma. The stroma cells themselves are swollen and slightly separated from one another. All transitional stages between the stroma cells and the epithelioid cells can be seen, indicating that the epithelioid cells themselves are nothing more than altered stroma cells. Near the top of the fundus the process is more marked; the superficial portions of the mucosa have

here and there undergone complete necrosis. Between this necrotic material and the normal stroma is a zone of epithelioid cells intermingled with small round cells. In one or two places giant cells can be made out in the epithelioid nests. The tissue, however, is characterized by its lack of giant cells. Tubercle bacilli are easily demonstrable both in the caseous areas and also in the nests of epithelioid cells. The uterine muscle is not involved. It has, however, an exceptionally rich blood supply. The mucosa of both tubes has undergone almost complete caseation; in this caseous material many bacilli can be found. Both ovaries are normal.

From these appearances it is probable that the tuberculous process in the endometrium is secondary to that of the tubes; first, because the process is much farther advanced in the tubes; and secondly, as only the upper part of the uterine cavity is involved.

RECAPITULATION.

I. Tuberculosis of the endometrium may be divided into two varieties: (a) Miliary tuberculosis; (b) Chronic diffuse tuberculosis.

II. Chronic diffuse tuberculosis usually begins near the top of the fundus. In the earliest stages it cannot be recognized macroscopically. Later the small yellowish-white nodules can be seen beneath the surface; these gradually increase in size, give the mucosa an uneven appearance and go on to ulceration. The endometrium is eventually transformed into caseous material, while the uterine cavity may, if the cervix be occluded, become filled with caseous material, giving rise to a condition simulating pyometra. From the endometrium the process extends to the uterine muscle.

III. *Histological Examination.* In the early stages the epithelium covering the surface of the mucosa is intact; over the tubercles, however, it is pale and somewhat swollen, and in some places it has proliferated, forming small teat-like projections or delicate gland-like spaces. The uterine glands are normal, but the stroma is infiltrated by tubercles, some with, others devoid of giant cells. Many of the tubercles show a tendency to break down, their centres being filled by polynuclear leucocytes.

All transitional forms between the stroma cells and the epithelioid cells can be seen, indicating that the epithelioid cells originate, at least in part, from the stroma cells.

The glands are affected later. Their epithelium proliferates, forming first masses of epithelioid cells. These masses of epithelioid cells soon contain giant cells in their centres, and typical tubercles are then seen springing from the gland walls and projecting free into the gland cavities. In this way the glands are soon obliterated, being transformed into tuberculous tissue.

In the later stages the superficial portions of the mucosa are transformed into caseous material, while the deeper portions consist of tuberculous tissue, scattered throughout which are numerous giant cells. The line of junction between the tuberculous process and the uterine muscle is sharply defined by a zone of small round-celled infiltration.

IV. The Fallopian tubes are usually first involved, and by the time that the endometrial tuberculosis has commenced they have undergone such caseation that there is no difficulty in making out the tuberculous process with the naked eye. In four of the accompanying cases the tuberculosis of the tubes could be made out macroscopically.

V. The ovaries are usually normal, but in some cases are involved.

VI. Tuberculosis of the endometrium is generally secondary to that of the tubes, but may be caused by infection from without.

VII. There are no fixed symptoms. Those present will to a large extent depend upon the coincident tuberculosis of the tubes. There may or may not be irregularity of the menstruation.

VIII. *The diagnosis can be made by microscopical examination of the scrapings* except in the very early stages where the tuberculosis is confined to the cornua and is beyond reach of the curette. To the naked eye the scrapings may appear perfectly normal.

IX. As tuberculosis of the endometrium is usually only detected when associated with tuberculosis of the tubes, it is better to remove the uterus with the tubes, as the process is likely to advance in the former.

DESCRIPTION OF PLATE XXI.

Fig. 1. 250 diam. Is a photomicrograph of a section taken from the fundus of the uterus in Case I. Three uterine glands can be seen. These are recognized by their epithelial lining, also from the fact that they contain cavities in their centres. The gland nearest the centre contains some desquamated epithelium. To the extreme left is a dilated gland, along one margin of which the epithelium is still faintly visible. Near the centre of the field three tubercles can be seen. In the centre of each is a giant cell. The nuclei of these cells are arranged principally around the margin. Surrounding the giant cells are pale-staining epithelioid cells, while scattered throughout the stroma everywhere are small round cells. To the left of the centre a small pale-staining area can be seen in the stroma. This is a cluster of epithelioid cells.

Fig. 2. 250 diam. Is a photomicrograph of the uterine scrapings from Case II. To the left are two uterine glands. On the right side is a typical tubercle, the centre of which contains a giant cell. The stroma of the mucosa is everywhere infiltrated by small round cells.

I here wish to express my sincere thanks to Dr. A. G. Hoen, who kindly made the photographs for this plate.

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FIG. 1.



FIG. 2.

TUBERCULOSIS OF THE ENDOMETRIUM.

