

UTERINE MYOMATA AND PREGNANCY WITH SPECIAL REFERENCE TO TUMOR NECROSIS¹

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WHILE uterine myomata, especially those of the submucous type and those located in such a way as to cause degenerative changes in the endometrium, generally are associated with sterility, it is well known that myomata in other situations may not act as barriers to conception. Pregnancy takes place in a certain percentage of cases and Giles finds that 30 per cent of women suffering with these growths do not conceive. This observation is quite in accord with the views expressed by the majority of writers.

Child states: "While it is true that many women grow myomata and babies indiscriminately and in large numbers, as a general rule these tumors promote sterility and retard fertility."

Olshausen, in studying the histories of 1,730 married women suffering with uterine myomata, found 30 per cent sterile, and Lynch, in 3,617 cases, found 31.5 per cent sterile.

Giles, in his outstanding work on sterility in women, states that myomata in the early years of married life do not play an important rôle in the etiology of sterility. The writer to whom we have referred cites 262 married patients—some married for not more than 5 years—in whom myomata were found in only one patient of every twenty, but in patients married for more than 10 years these growths were present in one of every three.

From carefully compiled figures, Giles further finds that up to the age of 30 the relation between myomata and sterility is quite unimportant since these tumors were found in only two of every one hundred sterile patients. After the age of 40, the relation is infinitely more striking and growths were found in two cases out of every five.

The proportion of married women suffering from myomata of the uterus who were found sterile was approximately one out of every three. To be exact there were found in 2,165 patients—reported by eleven different au-

thors—661, or 30.8 per cent, sterile. In 556 personal cases, Giles found that 395, or 71 per cent, had borne children and that 161, or 29 per cent, were sterile. Adding the personal cases observed by Giles to the number previously quoted we find a total of 2,702 married patients suffering with myomata, of whom 822, or 30 per cent, were sterile.

Giles believes that myomata must have some etiological relationship to sterility, but he is convinced that the influence of the growths upon conception is not very marked. This author also claims that there is a "converse aspect" of the subject that calls for consideration, namely, that myomata may not necessarily be the cause of sterility, but the result of sterility, or in other words, the result of the failure of the uterus to perform one of its assigned functions.

Giles endeavors to support this contention by citing the histories of 556 married patients of whom 60 per cent had never been pregnant, although at least 25 per cent of these women had been married for more than 5 years and 40 per cent for more than 10 years. Furthermore, the great majority had been married a long time before the fibroids developed and there were but few patients in whom the history of fibroids went back more than from 3 to 5 years. Giles claims, therefore, that these patients were not sterile because they had myomata, but that they developed the tumors because they did not conceive. This hypothesis has been considered and, at least partially, accepted by some, but by most writers it is looked upon with skepticism. Personally, this fanciful theory does not make an impelling appeal.

Irrespective of race and creed in this country, if not in most enlightened countries—I might say in most of the too enlightened countries—and even in the American born, regardless of parentage, there has been for a decade or two or longer a gradual diminution in multiple offspring. Large families are the

¹Presented at the Annual Meeting of the Waterloo Medical Society, Waterloo, Iowa, May 21, 1924.

exception rather than the rule. The gospel of personal comfort is more assiduously practiced than the rearing of large families. All in all, especially with the well-to-do and middle classes, families with three children and less are infinitely more frequent than families with three children and more. One-child, two-child, and three-child sterility, especially the first, is increasing because it has been selfishly so desired and so designed. A family of three children has often been regarded as the ideal, but even this ideal—if there still exists an ideal as to the family numerically—is not regarded with the same degree of favor as it was a decade ago.

How far the practice of contraception and the limitation of offspring will go, one cannot say. With the diminution in multiple offspring, it would seem logical and justifiable to assume that there should be a corresponding increase in uterine myomata while there has been an apparent increase in uterine cancer—though a disease of the multiparous largely—no striking increase in uterine fibroid has been noted.

Notwithstanding, the figures presented by Giles, we believe that uteri, the seat of myomata, especially those encroaching upon and deranging the endometrium, are influential in producing sterility to say nothing of the concomitant changes in the fallopian tubes which act as additional barriers to conception. Tubal changes of sufficient gravity to prohibit conception are found associated with 40 per cent of myomata. The ovaries, too, are variously affected in approximately 50 per cent of cases.

In 934 uterine myomata studied by Kelly and Cullen, the tubes were found normal in 482, but tubal inflammatory disease of varying degree was present in 423. In 496, or in over 50 per cent, the ovaries were similarly affected.

RELATION OF MYOMATA TO FERTILITY

Uterine myomata not only inhibit conception, but they are influential in diminishing fertility as well.

In 386 cases of uterine myomata Giles found a one-child sterility in 27.4 per cent. This is much greater than obtains ordinarily. Fifty-one and eight-tenths per cent of his

patients had two pregnancies and 70.7 per cent had had not more than three pregnancies.

T. B. Phillips, in his clinic in Amsterdam, found that the average number of children born to women who conceived was 3.21 per cent. Submucous and interstitial tumors are most commonly responsible for sterility. We observed a patient with a pedunculated submucous tumor blocking the cervical canal, who was sterile for several years. Removal of the growth was followed by conception and a full term labor. Subserous tumors do not, as a rule, hinder fertility nor, unless they be the seat of degeneration, or complicated otherwise, are they likely to cause abortion.

In 1,904 myomata, Scipiades found 814, or 75.5 per cent, occurring in married women and 244, or 29.9 per cent, of these patients were sterile; 264, or 24.5 per cent, were not married, so the relative frequency of myomata in the married and unmarried, this author believes, is about three to one. As regards productivity, the 814 married women had 1,805 children and 441 abortions. The number of children born to each mother was 2.25 and the number of abortions was 0.55 or excluding the nulliparous, 3.21 children and 0.8 abortions.

Kelly and Cullen, in 1,149 cases, found 842 married women and 307 single. All but 5 of the married women wedded before the age of 40. Of the total number, 584 (more than 50 per cent) were sterile, 75 had had miscarriages, but no full term labors and 490 had given birth to children. Of the sterile patients, 295 were married (187 white, 108 colored), and 298 were single. The length of married life of the 295 sterile patients was:

	Cases
Less than 6 months.....	5
2 months to one year.....	10
1 year to 5 years.....	55
6 years to 10 years.....	70
11 years to 20 years.....	94
21 years and over.....	43
Data not obtainable.....	18

In addition to the 72 women who had miscarried but who had never been delivered of full term children, there were 165 others, who, having given birth to children, had also miscarried, thus making a total of 240 patients who had miscarried. The majority of these

(153) had one miscarriage; some had several, ranging from 2 to 6, but these were rare. As to the term of gestation, abortion occurred at any time from the first to the seventh month, but the majority took place between the second and fourth month.

One hundred and seven of 130 miscarriages occurred between the first and fourth month; 7 in the fifth month; 11 in the sixth month, and 5 in the seventh month. In 110 the month of interruption was not mentioned. These figures show that one-half of all the patients had never conceived, and excluding the 307 single women, necessarily sterile, there were still 277 out of a total number of 842 who, though married, had never conceived. Kelly and Cullen in view of the frequent association of disease of the appendages, were unable to determine whether the myomata or the accompanying disease of the tubes and ovaries were responsible for the sterility.

INFLUENCE OF MYOMATA ON PREGNANCY

It seems logical to conclude that myomata uteri so often associated with manifold changes either in the growth itself, the uterine body, or the endometrium, would constitute a very barren field for the production of offspring. The majority of patients suffering with these growths, as we have already indicated, are sterile; but conception, while exceptional, may occur. In Kelly and Cullen's series, over 50 per cent of the married women did not conceive. However, sterility is not the rule. A certain number of patients conceive, but even if conception does occur, the soil still is unsuited for retention of the embryo, and interruption of the gestation is likely to occur. In a study of 188 specimens we found 6 complicated by intra-uterine gestation and 2 by pregnancy in the fallopian tube.

Scipiades claims that pregnancy complicating myomata often results in abortion and requires surgical interference in from 30 to 50 per cent of cases. However, in 8 cases under personal observation within the past 10 years we have observed only one instance of interruption. In this patient, abortion followed abdominal myomectomy. Scipiades believes that not more than 50 per cent of myomatous uteri will carry a pregnancy to full term.

The figures cited above show that uterine myomata predispose not only to sterility, but to interruption of gestation as well. This occurred, as mentioned, in 240 cases reported by Kelly and Cullen. Several factors, perhaps, are responsible for the interruptions of gestation. Uterine contractions set up by the tumor itself are probably influential in some cases. The changes in the endometrium, no doubt, are mostly responsible and hæmorrhage occurring about the gestation-sac favors premature separation of the placenta and subsequent abortion.

INFLUENCE OF MYOMATA ON LABOR

As a complication of labor at term, myomata are not frequently encountered. Pinard, according to Macfarlane, in 13,915 consecutive labors found only 0.6 per cent complicated by these growths.

A subserous tumor usually does not interfere with parturition, but a growth in the uterine wall may cause malposition of the fetus or placenta, and produce dystocia during labor. A neoplasm impacted in the pelvis may wholly prevent spontaneous expulsion of the fetus, but even a tumor low in the pelvis may rise during uterine contractions and allow fetal exit. A large tumor or multiple tumors may retard the progress of labor by interfering with uterine contractions. Postpartum hæmorrhage may also be favored by growths of this character.

However, in myomata complicating gestation, a certain number of both maternal and fetal deaths occur. Lafour, in 300 cases complicating pregnancy, in which delivery occurred through the vaginal canal, found the maternal mortality 53 per cent and the fetal mortality 66 per cent. In 20 per cent of the cases, forceps were used, with 8 maternal and 13 infantile deaths.

Johnston believes that myomata complicating pregnancy or labor will result in the death of one-third of the mothers and one-half of the babies. Crossen, in 84 cases, found that if the mothers were allowed to go to term 64 per cent delivered themselves without assistance and 36 per cent required forceps delivery. Veit had a maternal mortality of 33 per cent and a similar mortality for the children. In 87

version cases, this author had a maternal mortality of 64 per cent and a fetal mortality of 82 per cent. An adherent placenta was found in 21 cases, from which 13 of the women died.

INFLUENCE OF PREGNANCY ON MYOMATA

Increased nutrition usually favors increased development, so small tumors not previously recognized may become larger after the third, fourth, or fifth month of gestation. That they atrophy to a certain degree during involution is probable, and naturally to be expected, but that they completely disappear, as formerly thought, after the termination of gestation, is highly improbable. Necrosis of the growth, especially red necrosis, while rare, is not by any means an anomaly. We encountered eight instances of this type, and necrosis is most likely to occur in the subperitoneal and superficial interstitial growths. Our eight cases form the basis of this paper.

FREQUENCY OF RED NECROSIS

Fairbairn believes that 5 to 7 per cent of myomata, complicating pregnancy, are subject to this unusual form of degeneration. He bases this conviction on 88 myomata removed from patients in the Gynecological wards of St. Thomas' Hospital, London. Seven, or 8 per cent, of the tumors removed showed red degeneration. In another series of 105 specimens, 10 or 9.5 per cent, were affected by the degenerative process.

PATHOLOGY

Number of growths affected. As a pathological entity, red degeneration of uterine myomata was first described, according to Schiller, by Gebhard in 1899, but the first paper on the etiology, pathology, and treatment of the condition was presented by Fairbairn in 1903.

The term red degeneration or red necrosis has been applied to the condition because of the discoloration presented by the surface of the tumor on section. A peculiar feature of the pathology of red necrosis is that the disease is often limited to a solitary tumor, though sometimes two or three may be affected. This is true irrespective of how many tumors the uterus may contain. A specimen in which all

growths were affected has not been recorded. Occasionally, two or three or more may be involved. In three of our cases the alteration was limited to a solitary tumor. In two other cases two tumors were obviously affected and in two others two but not more than three were the seat of trouble. In one patient, though the uterus contained numerous growths, only two exhibited macroscopic evidence of the degenerative trouble.

Size of tumor. Tumors of large size are rarely, if ever, involved in red necrosis. This may be explained on the basis that pregnancy rarely occurs in uteri containing very large myomata. In most instances the disease seems to involve tumors of moderate size. In none of our cases did the growth exceed 3 inches in diameter and the majority did not exceed 2 inches. They were, for the most part, comparable in size to a large plum or lemon. Two were about the size of a baseball and these were the largest.

Site of tumor. The anatomical situation of the tumors seems to bear some etiological relation to the disease. In all our specimens, as well as all others the writer was able to study in the literature, the growths were either of the subserous sessile or superficial interstitial type. Most of the recorded cases are described as occurring in interstitial growths, but all of these were nearer the serous covering than the mucous lining.

The writer believes that the large proportion of specimens recorded can safely be placed in the category of the subperitoneal sessile or subperitoneal semi-pedunculated variety. None of our cases were pedunculated and all approached nearer the subperitoneal than the true interstitial type. This anatomical position renders conservative myomec-tomy possible without interruption of the gestation.

The anatomical relation of the growth may also play a rôle etiologically, brought about by mechanical pressure circulation. Mechanical pressure with obstruction of the blood supply may be provoked by impingement of the growth against the bony pelvis or against the abdominal wall. Why similar phenomena for similar reasons do not occur in truly pedunculated tumors the writer is unable to explain.

EXTENT OF NECROSIS

The extent of the necrotic process is variable. No two specimens will show the same degree or same type of disease. In describing the gross changes which occur it may be said that tumors exhibiting a state of red degeneration are more or less œdematous and, therefore, softer in consistence than an ordinary myoma. On section the surface of the neoplasm may show either localized or diffused degeneration. In the diffused process the whole tumor is involved in the disease. Widespread necrosis is said to occur in the majority of cases. This was not conspicuous in our cases. In these the process was circumscribed and appeared as multiple—three or four—localized necrotic areas in the center of the tumor mass. These did not exceed 2 centimeters in diameter and varied from 1 to 2 centimeters.

Bland-Sutton described a specimen in which the necrotic section appeared in streaks, involving only a few bundles of the fibers with normal fibers interposed.

In certain cases necrosis is seen as a shell near the periphery of the growth, leaving the central portion free. In most of the specimens studied the condition arose in the central section of the tumor. In none of our cases was there evidence of degeneration in the periphery. The relative frequency of central necrosis is explained on the basis that this portion of the growth is most remote from the blood supply.

The incised surface of the tumor mass is usually dry and listless—dull and lifeless—and but little fluid can be expressed from the tumor mass. In extensive cases, according to Lockyer, the surface on section resembles raw or partially cooked beef, hence the term "red degeneration." Indeed, even in myomata showing circumscribed necrosis, the only form we observed, the resemblance was striking and presented the appearance of moderately broiled beef. The color, however, was not red, but of a slate tinted or dusky gray hue.

The incised surface, it is said, emits a peculiar fishlike odor. This in our cases was not noted, at least not to the extent of attracting attention. The odor is attributed to the presence of amines because it is known that

these are one of the products of the destructive distillation of proteid.

Dilated vessels, with thrombosis, are observed both in the capsule and in the parenchyma of the incised tumor mass. These phenomena were not prominent in the specimens we removed, though free bleeding, because of the coincident pregnancy, was encountered.

It is pointed out that red degeneration is often, though not invariably, preceded by hyaline degeneration. This feature in our cases was conspicuously absent, at least macroscopically. It may be well to emphasize that the color of the necrotic tumor does not always harmonize with the term applied. It is not, as we have already indicated, invariably red, but ranges anywhere from red, reddish brown, mahogany, black, dusky slate, gray, yellow, and even white. In the cases herewith reported the color was rather characteristic and quite consistently of a listless dusky-gray slate hue. Whatever the original color may be it always becomes darker on exposure to the atmosphere. The discoloration is due to laking of blood through the necrosed tissue, by lipoids, and to the diffusion of blood pigment into the cells.

Schiller states: "It is most probable that this pigment becomes fixed in the tissue." Positive Prussian blue reaction was found twice, he says, in a case of Schueltze and Ahlstrom, though neither Murray nor Shaw found the positive iron reaction.

We have already pointed out that the color of the incised tumor is due to blood pigment which becomes laked by the action of lipid substances and hence the variation in the color of the necrotic areas is dependent upon the quantity of the lipid materials present. For example, according to Leith Murray, there is observed:

1. In red degeneration = lipid just sufficient to produce perfect hæmolysis.
2. In brown or brownish-black or gray degeneration = lipid in moderate excess.
3. In yellow degeneration = lipid in excess sufficient to cause bleeding.
4. In white degeneration = lipid sufficient to produce hæmolysis, the latter being restrained by blood plasma.

Here it is well to consider the relation of bacterial invasion—infection—to red necrosis. It is a common observation that in submucous myomata necrosis is almost invariably followed by infection and sepsis. Red necrosis, on the other hand, complicated by pregnancy, or occurring independently of gestation, is an aseptic process and infection rarely, if ever, occurs.

Schiller describes it as an aseptic necrobiotic change with hæmolysis and autolysis of tissue. Red necrosis, while it most frequently occurs as a complication of pregnancy, is sometimes observed, though rarely, in the non-pregnant. As a complication, independent of pregnancy, the process is not usually so pronounced nor complete.

Sometimes necrobiosis is used synonymously, though erroneously, with red degeneration. The term necrobiosis is used to imply partial death of tissue in contradistinction to true necrosis in which actual tissue death occurs.

Lynch claims that the term necrobiosis cannot be used interchangeably, because red degeneration may eventuate in complete recovery with restoration of tissue vitality, though there is abundant proof both clinically and pathologically that the process may continue in certain instances to liquefaction and total necrosis.

In none of our cases did complete necrosis occur. In three of our patients active symptoms indicating acute degeneration were present, but the symptoms subsided under simple expectant treatment. In these patients cesarean section with myomectomy or hysteromyomectomy was performed at term. In the specimens examined after operation the incised surface showed that complete restoration of tissue vitality had not occurred. They ostensibly received just sufficient nutrition to prolong life and prevent continuation of the necrotic process. The neoplastic tissue retained the grayish hue and was more or less dry and semilifeless. In respect to the term necrobiosis it may be stated that there is clinical evidence to show that in some of the tumors the active symptoms subsided, but this does not necessarily imply that tissue vitality has been wholly restored. Restoration is evidently only partial, but sufficient to

hinder further degeneration. Under the circumstances it does not seem to be proper to use necrobiosis synonymously with true necrosis. It should be looked upon simply as a feature or stage of the degeneration, continuing to actual death in certain cases and stopping rather short of death in others.

HISTOLOGY

The extent of degeneration is determined by the appearance of the cell nuclei and by the reaction of the cytoplasm when submitted to certain stains. Histologically, red necrosis has no distinguishing features and it cannot, therefore, be differentiated microscopically from ordinary necrosis of the tumor cell. The nuclei stain only moderately or do not take any stain at all. They seem to lose their capacity for taking up the stain, and because of this faint response to staining they have been described as "nuclear ghosts." Cell disintegration with pyknosis and karyolysis is always quite marked. Evidences of granular and hyaline alteration are nearly always present. The muscle cells seem to resist the necrotic process longer and their outline often remains well preserved.

In sections taken from the most active and advanced areas of the disease, the cells react to staining feebly if at all. In these sections the outline of cells may be lost and nothing but an amorphous mass of detritus may be found. The cells which respond to staining are probably those which are the last to succumb to the necrotic disorder.

Round cell infiltration is rarely found and this feature emphasizes the non-infectious nature of the trouble. Weigert's stain discloses fibrin in the smaller vessels, but in no place is there any proliferation of the vessel endothelium. Scattered throughout the sections small hæmorrhagic areas are usually observed. Hæmatoidin needles have been noted between the cells both by Hammerschlag and von Frankue. Fat is generally seen in the disintegrating fibers.

In a series of slides illustrating necrosis it would be impossible, then, to differentiate a specimen of red degeneration from a yellow or white type. In short, red necrosis does not represent a special histological form.

Lockyer says the microscopic features observed in necrotic fibroids is practically the same, irrespective of the color which the tissue may assume. The ordinary microscopic changes observed in hyaline degeneration are usually found coincident and these are looked upon as antecedents of red degeneration.

To summarize the histological features, they appear, as pointed out by Lockyer, as follows:

1. Irregular and scanty nuclear staining.
2. Granular and hyaline alteration.
3. Fatty material running in a line of the original direction of the muscle fibers.
4. Fat within wandering phagocytes, both outside and inside the lymphocytes.
5. Signs of vascular degeneration, engorgement, thrombosis and fibrin deposited within the vessels.

ETIOLOGY

Many hypotheses are advanced as to the cause of red degeneration. Owing to the outstanding work of Murray, most observers believe that the process is incited by hæmolysis from lipoids, because the lipoids in degenerating myomata are markedly hæmolytic. Murray claims that the hæmolytic action of the lipoids is restrained by the blood plasma or, in other words, that the blood plasma inhibits the hæmolytic influence of the lipoids. When the lipoids are greatly increased, hæmolysis occurs and oxyhæmoglobin can be demonstrated in the spectrum.

There is always observed more or less thrombosis of the blood vessels with the deposition of fibrin within the vessels and more or less degeneration of the blood cells. The theory of Murray has received quite general approbation though some authors, notably Ahlstrom, deny that the lipoids are increased. He records three cases in which they were decreased or wholly absent.

Some writers attribute the cause of red necrosis, as we have already indicated, to the scanty blood supply of myomata with thrombosis and hæmorrhage.

Lockyer, after a careful study of Murray's work, believes that hæmolysis and not thrombosis is the predominant change. Other observers believe that the necrotic process is inaugurated by the contractions of the uterus which normally occur during pregnancy.

This or some other cause may produce mechanical obstruction of the nutrient vessels and provoke necrosis. This theory would seem to have some bearing etiologically, since a uterus may contain multiple tumors, yet a single growth or only two, or at the most three, may be the seat of the degenerative change. Schiller assigned the cause in his personal case to a local disturbance in nutrition.

Obstruction of the nutrient vessels from mechanical pressure of the growth against the bony pelvis or abdominal wall appealed to the writer as a contributing factor, at least, and worthy of consideration in the 8 cases herewith recorded.

Vautrin, according to Schiller, believes that rotation of myomata in their capsular bed, resulting in disturbance in continuity, may be influential. Other writers look upon the toxins of pregnancy as causative. Some regard the trouble as due to increased coagulability of the blood and still others assign endarterial changes as provocative. Except in syphilitic subjects, endarteritis in the childbearing woman is rare. This would seem quite sufficient to exclude endarteritis as a cause. Finally, the elaboration of a proteolytic ferment must be kept in mind as possibly influential. From this array of theories, not one of which has been universally accepted, we are forced to admit that the cause of the trouble is still clouded in speculation, though the theory of Murray has received wider acceptance than any yet mentioned.

SYMPTOMS

The symptoms of necrotic myomata complicating pregnancy are variable. In most cases they are quite active and of sufficient intensity to enforce rest and recumbency. Pain, with localized tenderness, is the most distressing symptom as well as the most constant and prominent.

In the first two cases recorded in this series the onset of pain was most abrupt and most violent, resembling somewhat an acute appendicitis. Indeed, in these two cases, because of the pain being localized in the region of McBurney's point and associated with distinct circumscribed tenderness and a palpable mass, a tentative diagnosis of acute appendi-

citis was made. In the first case the true nature of the trouble was not disclosed until after the abdomen was opened. In the second case a positive diagnosis from knowledge gained by our experience with the first case, was determined before operation.

In 5 cases the onset of pain with tenderness was abrupt, but the cause of the distress was readily recognized in the degenerating myomatous nodules. The third patient in our series was treated expectantly and after a few days the pain and tenderness subsided. Four weeks, subsequently, the symptoms recurred with increasing violence, so much so, that immediate operation was decided upon and a conservative myomectomy was performed.

In the fourth case the patient had three or four mild attacks before operation was advocated and performed. In this patient we believe operation was deferred too long. Two weeks subsequent to operation she aborted a twin pregnancy.

In the fifth patient mild symptoms indicative of an oncoming necrotic process were experienced at about the fourth month. Two weeks subsequently, the symptoms returned with increasing severity and with such intensity, that immediate operation was considered. The patient was extremely anxious to carry her baby to term. She was, therefore, in accordance with her wish, placed in the hospital and under simple medical measures the symptoms subsided. During her residence of 14 days in the hospital she was extremely ill and at times her symptoms were indeed alarming. These ultimately subsided, however, and she was carried to term without further annoyance. She was delivered of a male child by cæsarean section, a conservative multiple myomectomy being performed at the same time.

The sixth patient experienced two or three relatively mild attacks which were controlled easily by rest and simple expectant means. She went to full term and was delivered of a female child by elective section. A conservative multiple myomectomy was performed at the same time.

The seventh patient of this series suffered several attacks of moderately severe pain which at times caused her family physician to

suspect a threatened abortion. With moderate care she was carried to term and was delivered of a female child by cæsarean section, followed by hysteromyomectomy.

Finally, the eighth patient in our series now is under our care and is approaching term. She has experienced several attacks of moderate pain, but never sufficient to cause alarm or cause one to think of interfering. At the present time, except for pressure of a myoma, comparable in size to a large orange and located in the lower left segment of the uterus, she is relatively free from symptoms. If our present plans do not go awry this patient will be delivered at term by an elective section and in accordance with her wish a conservative myomectomy will, if possible, be performed.

From the recital of the clinical histories of the foregoing patients it will be observed that pain, either moderate or intense, is the most constant as well as the most outstanding symptom. It will also be noted that, provided the tumor be localized in or near the right cornua of the uterus, the symptoms strikingly resemble an acute appendicitis. In some cases the symptoms have resembled, because of their severity, a ruptured tubal pregnancy and in others the condition was regarded as an ovarian cyst with a twisted pedicle. In Schiller's case a pre-operative diagnosis of a strangulated hernia was made. In certain cases, as indicated in the recital of our series, the symptoms may be mild or moderate and produce only moderate indisposition, but in acute cases the symptoms of an acute abdomen with peritoneal irritation are present.

Incidentally, I might add in this connection that in the non-pregnant red necrosis is not associated with severe or alarming symptoms. Pain and tenderness in the non-pregnant are infinitely less marked. When liquefaction takes place in the necrotic tumor the localized acute phenomena are succeeded by more or less general systemic symptoms expressed in the term "toxæmia." However, in all cases of red degeneration the symptoms, as in other pelvic conditions, may comprehensibly be divided into local and general. In acute red degeneration the predominant local symptom is pain. The predominant symptom is gastric irritation manifested by nausea and vomiting.

Ahlstrom in a collection of 74 cases of red necrosis and total necrosis found pain, moderate or intense, the most noteworthy local symptom in 54. Pain is most likely to appear abruptly and with intensity in those cases arising as a complication of pregnancy.

Systemically, there may be a mild febrile response due to absorption of fibrin, and with this there is the usual corresponding febrile acceleration of the circulation and respiration. Leucocytic reaction is present and the count ranges from fifteen to thirty thousand.

DIAGNOSIS

The diagnosis of the condition may be somewhat obscure, especially if the symptoms arise in a patient unsuspectingly harboring a myoma. This was the experience in 2 of our patients. The tumors in these patients were seated in the right anterior uterine wall. The pain and tenderness associated with a mass were referred to the region of McBurney's point, hence a provisional diagnosis of acute appendicitis was made.

In the first patient the true nature of the trouble was not recognized until after opening the abdomen, but in the second patient, from experience gained with the first, a positive pre-operative diagnosis was made. If, on the other hand, a patient has been under observation with a known tumor and acute symptoms later arise, no special difficulty should be experienced in determining their cause.

In certain cases the diagnosis may be determined only after operation, but with the recognition of myomata complicating pregnancy the possibility of red necrosis developing should always be kept in mind.

PROGNOSIS

If the cases herewith reported could be taken as a criterion, one could justly say that the prognosis is uniformly good. This in the main is true and even true irrespective of the acuteness of the symptoms. This is probably due to the necrotic process being non-infectious or aseptic. Death, resulting from red degeneration of myomata complicating pregnancy, is rare.

Schiller refers to 67 cases, 3 of which terminated in death. Two of these fatalities followed

operation, and here the part played by the operation itself in the mortality rate must be taken into account.

If one considers the remote possibility of total necrosis with liquefaction and secondary infection followed by rupture, the ultimate outlook would be less hopeful. Fortunately, total necrosis with liquefaction, while it occurs, is not frequent and rupture with infection still less frequent.

TREATMENT

From observations made in the 8 cases of red necrosis complicating pregnancy herewith reported, even though they be small in number, combined with a study of the cases recorded in the literature, one is able to formulate fairly definite rules regarding treatment. First, the writer believes that one can safely assert, as we do of myomata in general, that the simple presence of a myoma in the uterine wall is no indication for treatment at all. Even myomata in such a position ostensibly as to act as a barrier to parturition may rise out of the pelvis and permit of fetal exit. It is obviously not always an easy problem to decide which tumors may and which may not obstruct fetal passage during labor. However, these neoplasms are, as a rule, quite accommodating and they usually disclose their real intention several weeks before labor begins. Most of them rise out of the pelvis as the uterus increases in size and provide an unobstructive exit for the fetus.

The writer believes that during early pregnancy, unless the tumor excites acute symptoms, irrespective of its position, it should not be disturbed, but treated along simple expectant lines.

Tumors occupying persistently an obstructive position in the pelvis, provided they are agreeable to the patient, we believe, do not call for treatment until near term, when an elective cesarean operation may be performed and the tumor removed either by conservative myomectomy, depending upon the size of the tumor and the wishes of the patient, or a hysteromyomectomy depending again upon the wishes of the patient and the exigencies of the case. In three of our patients with quiescent tumors, conservative myomectomy was performed in two and a hystero-

myomectomy in one. With regard to therapy in those cases associated with necrosis and acute symptoms, one can safely say that this will depend upon the extent of the necrotic process and severity of the symptoms.

In most cases, if not all, we believe that a simple expectant plan may be instituted with the hope of carrying the patient to full term and then accomplishing delivery by section to be followed by a conservative operation or hysterectomy, as the case may demand. This course we believe wise, because it has been demonstrated that operation during the course of pregnancy is associated with abortion, according to Winter, in 17 per cent of cases.

In four of our cases early operation was demanded on account of the severity of the symptoms. In one patient the symptoms were most intense, but the patient was treated expectantly and the symptoms subsided. This patient had one exceedingly violent attack of pain with nausea, vomiting, mild febrile reaction, and leucocytosis. During this attack she was confined to the hospital and for a few days operation seemed inevitable. The symptoms, however, ultimately subsided and she continued to term. She was delivered by an elective section and the tumors, in accordance with her wish, were removed, conserving the uterus.

Finally, the problem of red necrosis of myomata complicating pregnancy with the symptoms, pathology, treatment, and results is further portrayed clinically in the following case histories.

CASE I. Mrs. J. T. D., Philadelphia, Pennsylvania; age, 39. The family history is negative regarding so-called "hereditary disease." At the age of 18 the patient suffered a severe attack of typhoid fever complicated by "double pneumonia." The menstrual period was established at the age of 14. The flow recurs regularly every 28 days and it lasts for 4 days. The discharge is moderate in quantity and it is not accompanied by clots or unusual distress. The last period occurred on April 24, 1924. The patient was married at the age of 27. She has had three pregnancies and she was delivered normally of female babies at full term. The first child was born on December 14, 1914. The second on January 5, 1917, and the third, on March 31, 1921. The three children are living and well. During the early weeks of her first pregnancy the patient suffered with severe nausea and vomiting. On July 11, or approximately 4 months after conception, the patient was

abruptly seized with an attack of acute abdominal pain. This was preceded, however, for 2 days with moderate "soreness" or a "dull ache" in the right pelvis. The pain was located in the right abdomen and in the vicinity of McBurney's point. The attack was accompanied with nausea and mild vomiting. The patient was seen 6 hours after the onset of the symptoms and examination disclosed the abdomen somewhat distended and moderately rigid. A circumscribed area of tenderness with rigidity was noted in the region of McBurney's point, and deep pressure disclosed an exquisitely tender resistant globular mass. At this time the temperature registered 100 degrees F., and the pulse rate was correspondingly accelerated. With the clinical symptoms presented plus the physical findings, a tentative diagnosis of acute appendicitis was made and immediate operation recommended. To this the patient consented and she was removed to Jefferson Medical College Hospital. Operation was performed at noon or about 12 hours after the onset of the acute symptoms.

After etherization and the customary preparation, a right rectus-Kammerer-incision was made. On opening the peritoneal cavity more than the usual quantity of clear serous fluid was encountered, but there was no evidence of peritoneal irritation. The enlarged uterine body was immediately exposed and there was found projecting from the right anterior fundal wall a myoma comparable in size to a tangerine orange. This, with the appendix, obviously free from disease, was regarded as provocative of the trouble and it was therefore removed.

After enucleating the tumor, a row of interrupted chromic catgut sutures were introduced with the view of obliterating the tumor bed and a row of similar sutures were used to approximate the superficial surfaces of the wound.

The appendix was also removed and the abdominal incision was closed in the usual manner. The patient was kept under the influence of sedatives for 48 hours subsequent to the operation and at no time thereafter did she exhibit any symptoms suggestive of an oncoming abortion.

Her convalescence, indeed, was in no way interrupted and she was discharged on July 31, or 20 days after operation. She went to term and was delivered normally of a female child on the date already mentioned, December 14, 1914.

Examination of the incised surfaces of the tumor revealed three areas of central necrosis of a dusky gray hue, ranging in size from 0.5 to 1 centimeter in diameter. The whole tumor, however, presented a dry, listless, gray appearance, indicating that the degenerative process, while pronounced in certain sections, was quite diffuse.

Subsequent history. Since the operation the patient has been remarkably well and, as we have heretofore stated, she has given birth normally to two more female children.

A pelvic examination made on April 20, 1924, revealed the uterus in good position, freely movable, normal in size, contour, and consistence.

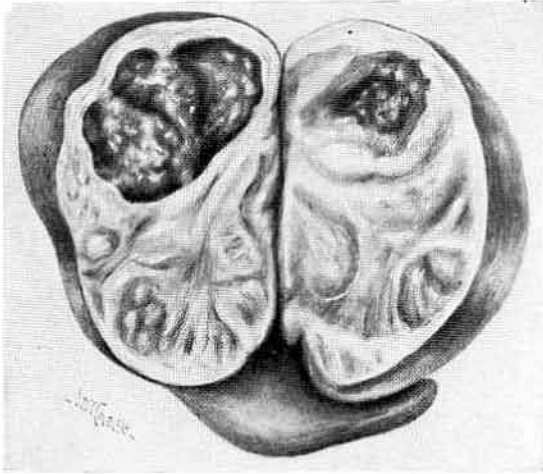


Fig. 1. Large subserous uterine myoma showing extensive necrosis with cyst formation. Removed from No. N-396.

CASE 2. Mrs. E. E. T., Philadelphia, Pennsylvania; age, 28; wife of a physician. The patient's father, three brothers, and one sister are living and well. Her mother died of "heart disease." The patient had measles and chicken-pox in early childhood. At the age of 21 she suffered with a severe attack of typhoid fever. The menstrual epoch was established at the age of 13. The periods recur regularly and are of the 28 day type. The duration of the flow is 3 days and the discharge is moderate in quantity. It is not accompanied by pain or clots. Prior to her admission to the hospital the last period occurred on September 28, 1913. The patient has been married 2 years, and she has not been pregnant hitherto. The patient was admitted to St. Joseph's Hospital on March 13, 1914, a date corresponding to the completion of the fifth month of her gestation. Twenty-four hours prior to admission the patient was suddenly seized with severe pain in the right lower abdomen. The attack, it was thought, followed rather violent exertion. The maximum point of distress was referred to McBurney's point and it was of such intensity as to enforce recumbency. Mild nausea with vomiting accompanied the attack. The abrupt onset of the pain with its location in the region of the right iliac fossa led her husband, a physician, to regard the trouble as appendiceal in origin. The patient was admitted to St. Joseph's Hospital on the date already mentioned.

Examination disclosed the abdomen somewhat distended and tender. The maximum area of tenderness was most marked in the region of McBurney's point, and here an exquisitely tender globular mass was palpable. The temperature of the patient on admission was 98.4 degrees F. and her leucocyte count was 13,000. The tender spherical mass was recognized as connected with the uterine body and a provisional diagnosis of a necrotic myoma com-

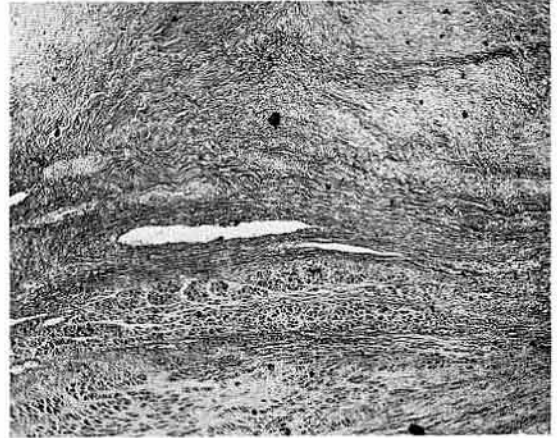


Fig. 2. Histological section of Figure 1. Light areas show necrosis.

plicating pregnancy was made. Immediate operation was advised and a conservative myomectomy was performed. The tumor was enucleated without difficulty and its bed was closed with a buried line of interrupted chromic catgut sutures. The superficial margins of the wound, including muscle and peritoneum, were approximated with a suture line of fine chromic catgut. The recovery of the patient was uneventful and she was discharged from the hospital on April 2, 1914, 19 days after operation. She continued to full term and was delivered normally of a female child on July 6, 1914. The tumor corresponded in size to the growth recorded in the preceding history, and on section it presented precisely the same characteristic necrotic features.

On October 3, 1914, 3 months after her delivery we operated upon this patient for acute suppurative disease of the gall bladder. Examination of the pus collected from the gall bladder revealed a pure culture of the typhoid bacillus. The attack of the typhoid fever antedated the gall-bladder disease by 7 years.

In August, 1916, the patient gave birth, normally at full term, to a second female child.

Subsequent history. Since the birth of her second child the patient has remained well and examination made on May 16, 1924, showed the uterus and its appendages to be normal.

CASE 3. Mrs. H. W., Philadelphia, Pennsylvania; age, 41. The patient has never suffered with any serious illness. Menstruation had its advent at the age of 14. The flow recurs regularly every 28 days and continues for 3 days. It is rather free, but not associated with the discharge of clots nor is it accompanied by pain. The last period occurred on April 14, 1924. The patient was married at the age of 34. She had one pregnancy and she was delivered, instrumentally, of a male child, at term, on July 2, 1918. During the fifth month of gestation the patient was seized with rather severe abdominal pain.

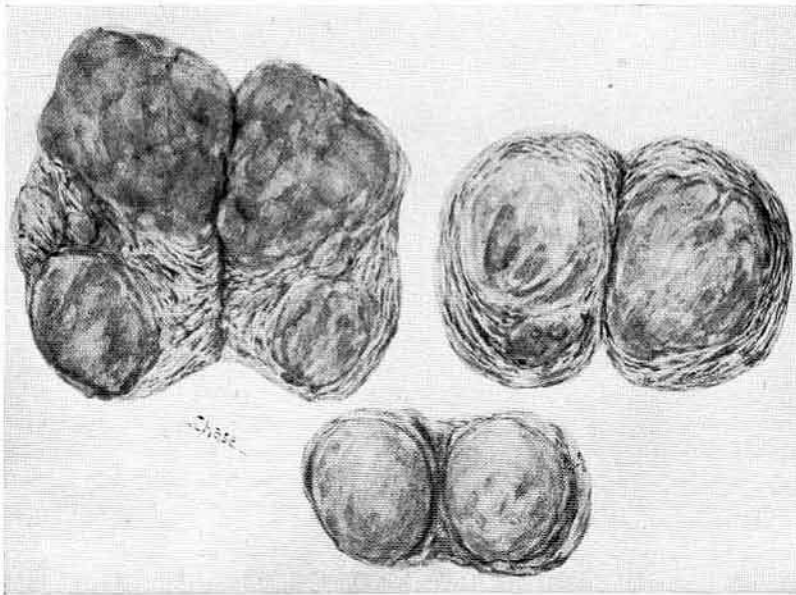


Fig. 3. Yellow necrosis of uterine myoma removed from patient described as Case 8. This patient was operated upon and was delivered by cesarean section of a normal male child. Multiple myomectomy was then performed and the tumors shown in this illustration were removed. Two of the growths show widespread yellow necrosis. The third and smaller tumor does not exhibit any necrotic change. The patient made an uneventful recovery.

There was no vomiting and no elevation of temperature. The pain was at times so severe as to confine the patient to bed. In February, 1918, an examination was made and the source of the trouble was found to originate in a superficial subperitoneal myoma. From the exquisite tenderness of the growth a diagnosis of red degeneration was made. The patient was placed in bed and treated along simple expectant lines. At the end of 3 days the symptoms had almost completely subsided. The patient was then free from distress for one month, when the trouble recurred with marked intensity and on March 2, 1918, the patient was admitted to Jefferson Medical College Hospital and a conservative myomectomy was performed. The patient remained in the hospital for 16 days. Her pregnancy continued without any sign of interruption and she was delivered instrumentally, as already mentioned, of a male child at full term. The tumor removed was the size of a lemon. The incised surface was dusky gray and lifeless. Three areas of slate colored necrosis, ranging from 0.5 to 1 centimeter in diameter, occupied the center of the neoplasm.

Subsequent history. Following the birth of the child the patient remained well. She has been seen by the writer from time to time. On April 28, 1924, an examination was made. This showed the pelvic organs in good condition. The cervix was free from disease. The uterine body was found in normal position, freely movable and, except for a small sub-

serous myoma in the anterior wall the size of a clay marble, the contour was normal.

CASE 4. Mrs. A. M., Vineland, New Jersey; age, 32. The mother of the patient died of cancer of the liver. The patient has never suffered with any serious illness. The menstrual epoch was established at the age of 13. The cycle is regular and recurs every 28 days. The menstrual discharge lasts for 4 days. It is moderate in amount and is not associated with unusual discomfort or the discharge of clots. The patient was married at the age of 27. She had one pregnancy and this terminated in an abortion in the latter part of the sixth month. Between the fourth and fifth month of gestation the patient was suddenly seized with pain in the lower abdomen. This at first was not severe and did not interfere with the patient discharging her household duties. During two or three of these attacks, she was seen by the writer and the origin of the pain was attributed to the incipient necrosis of three tumors occupying the uterine wall. Under rest and simple measures the attacks of pain subsided.

On May 9, 1921, the patient was abruptly seized with a violent attack of pain, and she was admitted to the Physician's Hospital, of Vineland, New Jersey. She was treated along simple lines without any relief and on May 10, operation was recommended and a conservative multiple myomectomy was performed. Five tumors ranging in size from a walnut to a small orange were removed. For 10 days subsequent to the

operation the convalescence of the patient was normal, and there were no impending signs of interruption of the gestation. After the tenth day a slight bloody discharge was noted. This continued intermittently but with increasing severity until the twenty-first day, when the patient aborted a twin pregnancy. The tumors removed exhibited the same features as were observed in those already described.

Subsequent history. Since the operation on May 10, 1921, and the premature interruption of the gestation, the patient has remained well. She has been anxious for children, but has not conceived. An examination made on March 14, 1924, showed the uterus and its appendages free from disease.

CASE 5. Mrs. L. S. M., West Chester, Pennsylvania; age, 27. Except for a rather severe attack of influenza, the patient has not suffered with any serious illness. Menstruation began at the age of 12. The flow recurs regularly every 28 days and it lasts for 5 days. The discharge is moderate in amount and is not associated with clots or pains. The last period occurred on April 8, 1924. The patient was married at the age of 34. She has had one pregnancy and she was delivered at full term by cesarean section, a conservative myomectomy being performed at the same time. About the fifth month of gestation the patient was seized with periodic attacks of pelvic pain. The pain would last for 2 or 3 days and then gradually subside. The patient experienced several mild attacks to which she did not pay much attention. Two attacks were extremely severe, during one of which the patient was admitted to St. Joseph's Hospital. She remained in this institution for a period of 2 weeks. While confined to the hospital the pain at times was most violent and interference seemed inevitable. The discomfort was accompanied by nausea and vomiting, but with no febrile disturbance.

Upon physical examination the cause of the distress was recognized as due to acute necrosis of a uterine myoma. The patient was extremely anxious to carry her gestation to full term and operation, in accordance with her request, was postponed. Gradually her discomfort subsided and the pregnancy continued to term. Delivery was then accomplished by cesarean section and a conservative myomectomy was performed at the same time.

The tumor removed corresponded in size to a large lemon. The growth was of the subserous sessile type. The bed from which it was removed, as well as the margin of the incision, was cared for as already described in the preceding histories. The neoplasm on section presented the same necrotic appearance as the tumors removed from patients one and two.

Subsequent history. On May 2, 1924, the patient was seen and she stated that she has not had any difficulty since her operative delivery. She has not experienced any disturbance in her menstrual cycle and an examination made on the date mentioned showed the uterus and its appendages to be free from disease.

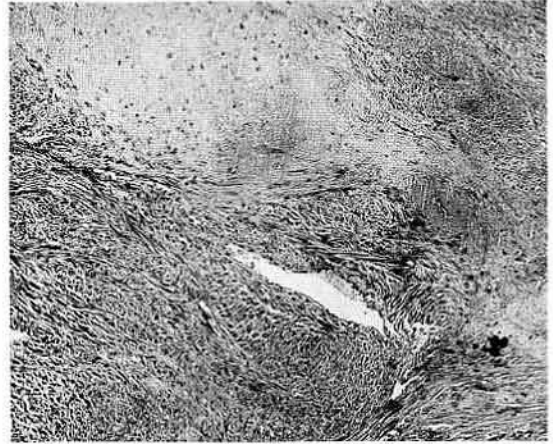


Fig. 4. Histological section of specimen shown in Figure 3. Right area in upper margin of illustration indicates site of necrosis.

CASE 6. Mrs. R. H., Buffalo, New York; age, 39. The patient suffered with diphtheria and "variloid" in childhood. She had typhoid fever in early adolescence and on seven occasions she has suffered with severe attacks of tonsillitis. The menstrual period was established at the age of 16. The flow is of the 28 day type and recurs regularly. It lasts for from 4 to 5 days. It is moderate in amount, and it is not accompanied by clots or unusual distress. The last period occurred April 10, 1924. The patient was married at the age of 31. She did not become pregnant until 4 years subsequently, or until her thirty-fifth year. She conceived in October, 1921, and was delivered of a female child by cesarean section followed by multiple myomectomy on July 1, 1922. After conceiving, the patient did not experience any discomfort until about the fourth month of gestation when she was seized by several attacks of abdominal pain lasting from a few hours to several days. These were never severe, although at times of sufficient intensity to enforce rest. In one attack the pain was quite violent and continued for 48 hours. These attacks were not associated with gastric irritability, nausea, or vomiting. After the sixth month the patient did not experience any discomfort except mild pressure symptoms. She was delivered by cesarean section on the date already mentioned. Two tumors, one as large as a baseball and the other the size of a small orange, were removed. These were of the sessile subserous type and protruded more from the uterine body than they did into the uterine body. The growths were enucleated without special difficulty. The surface of the myomata on section was dull and lifeless. This was quite diffuse, involving more or less all of the tumor substance. Dusky slate colored sections of red necrosis ranging from 0.5 to 1 centimeter in diameter were observed in the center of the growths, each tumor being the seat of three or four areas of this character.

Subsequent history. The recovery of the patient from operation was uneventful. She was able to nurse her child for the normal length of time. On May 8, 1924, she reported her health as being "very good." Although the patient is anxious to have more children she has not as yet conceived.

CASE 7. Mrs. G. M., Camden, New Jersey; age, 39. Menstruation started at the age of 14. The flow was of the 28 day type and recurred regularly. It lasted from 3 to 4 days and was moderate in amount. It was not accompanied by the discharge of clots or unusual distress. The last period occurred in October, 1918. The patient was married at the age of 26 and she has had two pregnancies. She was delivered at full term of a female child by cesarean section followed by a hysteromyomectomy on July 9, 1919. She was delivered normally of a male child at full term 15 years before. The patient was referred to the writer by Dr. Howard F. Palm, of Camden, New Jersey, when she was between the fourth and fifth month of her gestation. At the time the patient was complaining of periodic attacks of mild abdominal pain. These were more or less frequent and they were associated always with marked prostration. At no time, however, were her symptoms unbearable.

An examination was made and the symptoms were found to originate in multiple uterine myomata. The uterine body, indeed, was simply teeming with these growths. The patient was kept under observation and she continued to term and was delivered by cesarean section on the date mentioned above. The growths varied in size from a clay marble to a large orange and three of these showed the peculiar changes characteristic of necrosis.

Subsequent history. The patient reported on April 26, 1924, that subsequent to her operation she has remained well.

CASE 8. Mrs. H. F. C., Philadelphia, Pennsylvania; age, 33. The patient suffered with scarlet fever and diphtheria in childhood. Menstruation began at the age of 12. The flow recurs regularly every 28 days and lasts 5 days. It is moderate in amount and is not accompanied by clots or pains. The last period occurred on September 25, 1924. The patient was married at the age of 32. For several weeks the patient has experienced periodic attacks of pelvic pain. The pain in most instances has not been severe, but one attack was of such intensity as to enforce rest and require sedatives for relief. At this time the patient was examined by a colleague of the writer, and a diagnosis of myomata complicating pregnancy was made and immediate operation with hysterectomy was advocated. The distress, however, gradually subsided and the patient was seen by the writer on November 13, 1923.

Aside from mild discomfort from mechanical pressure the patient now is fairly comfortable. Pelvic examination on April 28, 1924, revealed several tumors occupying the uterine wall. These apparently are of the sessile subserous type. A large growth was found in the left lower uterine seg-

ment. A nodule the size of a large lemon was found in the right anterior uterine wall and a tumor of similar dimensions was observed in the left anterior fundal wall. The largest tumor is comparable in size to a fetal head and blocks quite completely the pelvic outlet. This, however, is gradually rising out of the pelvic cavity and at full term, 8 weeks hence, may permit fetal exit.

Because of the desire of the patient to give birth to a living child, a spontaneous delivery will be avoided and a cesarean section with multiple myomectomy will be performed instead. Since writing the above this patient was delivered by abdominal hysterotomy and at the same time a conservative myomectomy was performed.

Laboratory report, No. 16106 (Jefferson Hospital) by Dr. B. L. Crawford, pathologist. Clinical History No. N-440. Specimen: four fibroid tumors from uterus. Specimen consists of three nodular masses of tissue, together weighing 670 grams; each nodule is encapsulated and elongated. On section the largest measures 10 centimeters in its greatest dimension. The cut surface is yellowish gray in color. Some areas of the tissue are much softer and lighter in color. The other two pieces measure respectively 6.5 and 5 centimeters in their greatest dimension and on section are similar to the larger mass.

Zenker's fixation.

Histology: Sections from the masses are composed of interlacing fibers of muscle and connective tissue forming whorls and containing rather numerous endothelial lined spaces. Sections from different parts of the tumor show entirely different histological pictures. In parts of the tissue the muscle cells are much enlarged and the nuclei take the stain deeply, the tissue is rather cellular, while in other large areas there is extensive degeneration and necrosis. Areas of necrosis are rather sharply circumscribed.

Diagnosis: Multiple fibromyomata undergoing extensive degeneration and necrosis.

Laboratory Report No. 16099 (Jefferson Hospital) by B. L. Crawford, pathologist.

Clinical History No. N-396. Specimen: Uterus with pedunculated tumor attached thereto. Specimen consists of a large lobulated nodular mass weighing 570 grams. There are two portions of the specimen connected by a short thin pedicle, measuring 2 centimeters in length. The smaller portion of the specimen is the body of the uterus. The uterine wall is thickened, being 2.5 centimeters in thickness, contains numerous small circumscribed nodules in the wall. The uterine cavity is slightly irregular in shape. The mucosa is thickened and red.

The larger portion of the specimen is a firm, round, nodular mass measuring 10 centimeters in its greatest dimension. One area has definite fluctuation. On section a cavity is found which measures 4 centimeters in diameter. It contains bloody fluid and soft necrotic tissue. The tissue is adherent to the wall of the cavity. Portions of the lining of the cavity are perfectly smooth. The remaining portion of the mass is gray and lobulated.