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FURTHER OBSERVATIONS ON THE CONSERVATIVE TREATMENT OF SARCOMA OF THE LONG BONES *

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THE present paper consists chiefly of a report of the cases of sarcoma of the long bones that have come under my personal observation during the past five years, with a brief review of cases previously published.

In a previous paper on this subject I have strongly advocated the conservative treatment of sarcoma of the long bones, and the cases observed during the past years, I believe, furnish further evidence in justification of conservative treatment. It might seem unnecessary to present this evidence, were it not for the fact that the majority of surgeons at the present time, including many men with wide surgical experience, have not fully accepted the principles of conservative treatment, and are now sacrificing many limbs which might be saved under conservative treatment.

In a paper read before the Southern Surgical Association in December, 1917, I published 200 cases of sarcoma of the long bones personally observed. Since that time 50 cases have come under my observation.

In the former papers I have discussed at considerable length the question of diagnosis. In the present paper I only wish to emphasize certain points which, larger experience has convinced me, deserve special note.

First, the element of pain. Pain, especially of a deep boring character, steadily increasing in severity, is often one of the earliest and most important signs of sarcoma of the long bones. Many of these patients are first treated for some rheumatic condition, until the disease has progressed sufficiently to produce a palpable tumor. Persistent pain is often present for weeks or months before there is a palpable tumor or the X-ray discloses any evidence of a new growth.

Pain is a more important symptom in periosteal growths than in the central tumors. The latter often attain considerable size, with little or no pain. I recently had under observation a case of periosteal sarcoma of the upper portion of the femur, in which severe pain was not only the earliest symptom, but required quite large doses of morphine before a swelling could be detected. Later on, a slight swelling was noticed in the outer aspect of the left femur, just over the trochanter. The X-ray

* Read before the American Surgical Association, June 16, 1919.

at this time showed a slight thickening of the periosteum which, in conjunction with the clinical symptoms, made the diagnosis of periosteal sarcoma probable. Under the toxin treatment alone, the pain ceased almost immediately; later a local application of massive doses of radium was made. Four weeks later the pain returned and increased in severity. An exploratory operation was done, showing an extension of the disease downward and marked involvement of the periosteum, of the extent of which the X-ray examination had given little evidence. The tumor apparently started in the under-layers of the periosteal covering of the bone, causing some roughening of the bone and great tension of the periosteum, which easily explained the agonizing character of the pain, since a condition was present not unlike a subperiosteal abscess, which produces such excruciating pain. The periosteal tumor in some places began to infiltrate the overlying muscle and fascia. A considerable portion of this tissue was removed; macroscopically it was perfectly characteristic of sarcoma. In fact, with the clinical history and macroscopical appearance, one could easily make a positive diagnosis of sarcoma. In spite of this the tissue removed for microscopical diagnosis did not show any characteristic tumor tissue, so that Doctor Ewing stated that he could not make a diagnosis of sarcoma. If the patient had continued to improve and made a complete recovery, there would always have been some doubt as to the diagnosis. A few weeks later another exploratory operation was performed in order to facilitate the use of bare tubes of radium. This time some of the tumor tissue was removed and examined microscopically. The histological structure was that of a typical small round-celled sarcoma. In very far advanced cases, the clinical signs, combined with the X-ray picture, may be sufficiently clear to definitely establish the diagnosis, and too much weight should not be given to a negative pathological report upon a specimen removed.

I still believe that in cases in which there is any reasonable doubt of the diagnosis, the advantages of an exploratory operation greatly outweigh the disadvantages. If the tumor is a periosteal sarcoma, it is extremely important to make the earliest possible diagnosis. It would certainly be unwise to sacrifice the limb, without a positive diagnosis, and it would be equally unwise to subject the patient to the discomforts of prolonged toxin or radium treatment, unless the diagnosis was reasonably certain. In the great majority of cases the clinical signs, confirmed by X-ray pictures, render the diagnosis practically certain. If the disease is far advanced, there will be no doubt. Even in these cases, particularly in tumors of central origin, it may be wise to make an exploratory incision, remove as much as possible of the tumor tissue and, in the central tumors, curetting to bare bone in order to facilitate the use of conservative methods, particularly the introduction of bare tubes of radium into the cavity. The histological type of tumor found may give us great help in making a prognosis.

The danger of metastases resulting from such exploratory operations is, I believe, extremely slight, and the advantage of knowing exactly the type of tumor one is dealing with, far outweighs the risk.

Giant-celled Sarcoma or "Giant-celled Tumors."—Great confusion has long existed in regard to the malignancy of the so-called giant-celled sarcoma of the long bones. Within the last few years several admirable papers have been published throwing much light upon this difficult subject, the most important of which are the contributions of Platou, of Christiania(ANNALS OF SURGERY, March, 1918), and Bloodgood (ANNALS OF SURGERY, April, 1919). Bloodgood reports 47 cases of benign giant-celled tumors (43 of the long bones) in which the ordinary features of malignancy were absent. A study of these cases has induced Doctor Bloodgood to make a repeated and even stronger plea than hitherto in favor of conservative treatment of these conditions.

My own experience, based upon a study of 250 cases of sarcoma of the long bones, would justify me in going even further than Bloodgood, and I would urge the employment of conservative methods, not only to benign giant-celled tumors, osteitis fibrosa and the like, but to actual sarcomas of the long bones, both of central and periosteal origin.

Platou, of Christiania, bases his paper on a histological study of nine cases that have come under his observation, and which he has reported in full.

He takes the position that the so-called giant-celled sarcoma is not a malignant tumor at all, but is properly classed as "giant-celled tumor." Although he states that the microscopic picture, which he describes in detail, usually shows a peculiar structure which is easily recognized, he further states that it is not possible to give any decisive distinguishing features between sarcoma and giant-cell tumor. According to Platou, "if the resorption of the osseous substances can be shown to take place in connective tissue with few cells (if, in other words, fibrous marrow is found), then that fact would indicate that the bone-destroying process is not of a malignant character." He adds, "The most striking feature of the disease is the enormous giant-cells with 50 to 100 nuclei in one cell. The picture on the whole shows a varied structure with regions rich in cells and bands of connective tissue, often showing hyaline degeneration; between them every variety merging into tumor-like tissue, also bone substance in the process of formation, resorption, and once in a while islands of cartilage. The cells are mainly round or oval, their protoplasm most often clear and well defined in outline; frequently no intercellular substance can be traced.

"On the other hand, a giant-cell sarcoma under the microscope shows a more homogeneous tissue, with no such extensive spots where cells are few. The shape of the cells is more like a spindle, the intercellular substance more abundant, and besides the giant-cells we find all intervening stages down to cells with 2 to 4 nuclei—a thing rarely seen in the case of

giant-cell tumor. We have been told that if giant-cells are seen in clusters this fact would be an indication that the tumor tissue is part of ostitis fibrosa, whereas in the case of sarcoma the giant-cells would be more evenly distributed throughout the tissue."

Platou's series of 9 cases further confirms the opinion long held by Bloodgood and others that a certain number of giant-cell tumors of the long bones, particularly of the tibia, are benign in character, and while easily cured by conservative operation, the limb should seldom, if ever, be subjected to amputation.

Platou after a careful study of his own cases and those reported in the literature has reached the following conclusions:

"It is deplorable that microscopical examination sometimes permits only a probable diagnosis. The interpretation of the preparation in question will always depend on a personal opinion. There has not yet been discovered any test whereby the diagnosis may become absolutely certain either way when the cases are doubtful.

"The operator, therefore, must take upon himself the responsibility of deciding whether to take the usual consequence of a diagnosis of sarcoma, when he is aware of the fact that the original disease may be ostitis fibrosa, or whether the clinical facts of the case justify a conservative treatment—nay, even demand it."

This is practically the position which I personally have held for a long time, although I believe that resection and transplantation of bone are seldom necessary.

If we could always be sure we were dealing with a benign giant-celled tumor of the long bone, such as Bloodgood describes, simple curetting, which he advocates, or in more advanced cases, resection, would suffice. But we must admit that in many instances it is difficult to determine whether a case in question is a giant-celled tumor of benign type, or an actual sarcoma with malignant features. In my own list of giant-celled sarcomas of the long bones, 40 in number, the diagnosis of giant-celled sarcoma was made by a number of leading pathologists. Yet the fact that out of these 40 cases 8 died of metastases proves that in certain cases, at least, the tumor was of a very different type from that described by Bloodgood and Platou.

Perhaps in the light of more recent study of these tumors it may be possible to differentiate, in a larger number of cases, the malignant giant-celled tumors from the benign. But at the present time, we must admit there are few that are able to make the distinction positively.

That the myelogenous or mixed giant-celled sarcomas, particularly of the lower end of the femur, are, for the most part, true malignant tumors, is well brought out by the statistics of the Bruns Clinic, reported by Kocher in the *Beitr. f. klin. Chir.*, 1906, Bd. 50, Hft. 1, p. 118. In 33 consecutive cases of central myelogenous sarcoma, 4 were too far advanced for amputation or the patient refused it (it is assumed that these ended fatally); of

11 cases in which amputation was performed, 1 died of the operation, 8 died of metastases, and only 2 were known to have been well beyond the three-year period. As no microscopic sections were published it is impossible to state how many were of the "giant-celled type" described by Bloodgood and Platou. If none were of this type it only confirms my own opinion that the benign giant-celled tumor of the femur is comparatively rare, especially when accompanied by the clinical signs of malignancy, rapid growth and extensive invasion of the surrounding tissues, especially the knee-joint.

My own series of cases shows that in a small number of cases of periosteal and highly malignant tumors of the long bones, the limb as well as the life of the patient can be saved by the prolonged use of the mixed toxins of erysipelas and bacillus prodigiosus, and even a larger number of cases with tumors of central origin of unmistakably malignant type, can likewise be saved.

If the tumor appears almost certainly benign, curetting alone will probably prove sufficient to effect a cure, but my own experience, covering 250 cases of sarcoma of the long bones, with 40 of the giant-celled type, shows that this type of tumor of the long bones is comparatively rare. I should hesitate to place complete reliance on the microscopical examination alone, unless fully supported by the clinical history and the X-ray pictures. Bloodgood's report of 43 cases of benign giant-celled tumors of the long bones, gives one, I think, a mistaken impression of the relative frequency of the condition—an impression which might be corrected by remembering that Bloodgood's interest in this subject dates back many years and his frequent reports of cases have influenced surgeons all over the country, to send him special cases, resulting in his being able to report a personal observation of 43 cases of what may still be regarded as a comparatively rare type of tumor.

In dealing with periosteal tumors we have an entirely different proposition. Here there is no longer any doubt about the malignancy of the tumor, and all agree that even the most radical operation rarely saves the life of the patient. The hopelessness of the condition warrants us in trying almost any method of treatment that offers the slightest prospect of saving the limb, and this very hopelessness justifies us, I believe, in making an exploratory operation in order to definitely establish the diagnosis at the earliest moment. The microscopical diagnosis of periosteal sarcoma is, in most cases, much less difficult than in the tumors of central origin, but in certain rare cases one also encounters similar difficulties. In a few cases it may be entirely impossible to make a positive diagnosis(histologically), yet the clinical history and physical signs leave little doubt that we are dealing with a periosteal sarcoma. Formerly I advised amputation in these advanced periosteal cases, until I found that in a number of cases in which the patients absolutely refused amputation I was able to save the limb as well as the life of the patient by the use of

the mixed toxins. In one of these cases recovery took place after metastases had developed.

The result in these cases, I believe, justifies us in treating even periosteal sarcomas by conservative methods. The question naturally arises: should we limit the treatment to the mixed toxins or to radium alone, or a combination of both. We know that the toxins, without any other agents, have cured the disease, saved the limb, and the patients have remained well for many years afterward. This is true of every type of sarcoma, both periosteal and central. As far as I know, few cases have been cured by radium alone. The only case reported in which the patient remained well five years, is that of Pinch of the London Radium Institute, 1918. No details of the case, however, have so far been published, nor do we know the nature of the histological structure of the tumor.

I have had under observation a case of periosteal sarcoma of the femur which failed to improve under a month's toxin treatment, and I then advised amputation followed by toxins. The patient later placed himself under the care of the late Dr. Joseph Bissell, who gave him repeated radium treatments. The tumor apparently disappeared and he remained well nearly two years, when he had a local recurrence which was not controlled with massive doses of radium. I then amputated below the trochanter, but lung metastases soon developed, and spinal metastases, causing death in a few months.

We have had two cases at the Memorial Hospital during the last year in which the tumors have apparently disappeared under the use of radium alone. One was a large tumor of the upper end of the humerus, pronounced chondroma from tissue removed at exploratory operation, but in view of the large size and rather rapid growth it was believed by Doctor Ewing to be chondrosarcoma. This tumor showed remarkable disappearance under radium treatment administered by Doctor Janeway, in the form of bare tubes introduced into the tumor substance, supplemented by massive doses of radium in the form of a pack. The sinus, however, persisted, and an examination of a recent curetting in May, 1919, showed the presence of a " degenerating chondrosarcoma." No active chondrosarcoma was found in this curetted material but only broken-down fragments of necrotic tumor tissue. The other case was a small giant-celled sarcoma of the upper end of the tibia which is still well a little less than one year. In view of these results it would seem that the interest of a patient suffering from sarcoma of the long bones may be best served by giving him the benefit of combined treatment, *i.e.*, the systemic effect of the toxins with the local action of radium. If the tumor does not show marked improvement in the course of four or five weeks under this treatment, I would advise amputation followed by the use of the toxins as a prophylactic against recurrence, that is, if the disease is not too far advanced for amputation.

Resection with or without bone implantation is, I believe, seldom indi-

cated. The cases I have reported in full, especially the tibia case with complete destruction of the upper five inches of the tibia, treated conservatively by curetting, toxins and radium, with almost complete restoration of the destroyed bone and the patient well nearly four years, shows how much Nature can do if the sarcoma has been completely controlled.

It is difficult to estimate the definite percentage of cases in which one may succeed in saving the life and limb in sarcoma of the long bones. It depends largely upon the stage of the disease at the time conservative treatment is begun; the percentage will be much higher in the cases treated at an early stage than in those treated at a later stage.

Nevertheless, my series of cases shows several cures in which the disease was so far advanced as to be entirely beyond hip-joint amputation. These cases show that few, if any, should be regarded as so desperate as not to warrant an attempt to save the limb as well as the patient's life. In a very large number of my cases the disease has been too far advanced for amputation, so that this series does not give a fair idea of the results which might have been obtained had the disease been treated at an earlier stage. However, they give some idea as to the number of recoveries that may be looked for in advanced cases. If we are able to cure a considerable number of patients with the disease too far advanced for amputation, we certainly have a right to expect a much larger number of recoveries in cases seen and treated in the early stages of the disease.

As the earlier cases have already been reported before the Southern Surgical Association, I think it may be of interest to give a brief analysis of the cases treated within the last five years. During this period I have had under treatment 60 long-bone cases, classified as follows: Femur, 32; humerus, 14; tibia, 9; fibula, 3; clavicle, 2. Of the 32 femur cases, amputation was performed in 13 cases after conservative treatment had failed (there was no mortality from operation); in 4, amputation was strongly advised but refused by the patient. Eleven of these patients are still living, 2 being recent cases still under treatment, with a reasonable prospect of saving the limb. One of the patients who refused amputation had a large central sarcoma of the lower end of the femur, which was treated with toxins and radium, with slight temporary improvement; metastases later developed in the lung and the patient lived but a few weeks. One periosteal sarcoma had toxins followed by amputation; well three years when a recurrence developed. One central sarcoma of the lower end of the femur with extensive involvement of the knee-joint, refused amputation, and recovered under the toxins alone; well five years. One extensive sarcoma of the lower end of the femur involving the knee-joint and upper end of tibia, in which amputation was refused, was treated with toxins supplemented by radium, and is well now three years, walking without support of any kind. One very large inoperable sarcoma of the upper half of the femur, quite beyond hip-joint amputation, recovered under toxins and radium and is well at present without any evidence of

the disease two years later. Two cases of periosteal sarcoma of the femur treated with radium and toxins during the last six months in the hope of saving the limb, result still doubtful. In three cases of sarcoma of the femur, amputation was performed followed by the use of the mixed toxins as a prophylactic against recurrence; two cases are still well three years later, and the third died of metastasis nearly three years after amputation.

NOTE.—Recurrence has taken place in one of these cases in October, 1919.

Following is a brief report of cases containing points of special interest:

Cases I and II have been reported in Transactions of New York Surgical Society with microphotographs of tumors in ANNALS OF SURGERY, March, 1917.

CASE I.—*Central Sarcoma of the Lower End of the Femur with Extensive Involvement of the Knee-Joint, Successfully Treated with the Mixed Toxins.* L. G., female, twenty-one years of age, was first seen in consultation with Dr. V. P. Gibney, at the Hospital for Ruptured and Crippled, in October, 1914. Family history negative, Wassermann negative; no history of antecedent trauma.

Eight months previously patient first noticed pain in the left knee, while walking up and down stairs. This gradually increased in severity and shortly after was present even while walking on level surfaces. She consulted a physician who made a diagnosis of tubercular disease and applied Buck's extension to the knee, with slight temporary relief. A little later she entered a hospital where a plaster-of-Paris splint was applied, which she wore for five weeks. No improvement was noticed; thereupon several teeth were removed, on the ground that she was suffering from ostearthritis due to pyorrhœa. Later on she was placed upon specific treatment. In spite of these widely varied therapeutic measures, the swelling and pain increased, and the patient was unable to bear the weight of her body upon the limb. She was admitted to the Hospital for Ruptured and Crippled (Doctor Gibney's service) on October 24, 1914, at which time physical examination showed general condition good; heart and lungs normal, patient wearing a plaster splint. She had lost considerable in weight. There was marked swelling and infiltration of the whole lower end of the left thigh and anterior aspect of the left knee. The knee was completely extended, with very greatly increased abnormal lateral motion, showing destruction or extreme laxity of the tissues. There was marked infiltration of the popliteal space, and moderate atrophy of the limb.

Measurements.—Left, 15, 15½, 12; right, 14¼, 14, 12.

The X-ray showed very marked expansion of the lower extremity of the femur; cortical substance thin and apparently on the point of breaking through; structure of bone has disappeared.

In view of the extensive involvement of the knee-joint, accompanied with great tenderness and extreme mobility, after careful examination and study of the X-ray plates, I concluded that the

disease was undoubtedly a central sarcoma which had pierced the cartilage of the joint, causing joint involvement and effusion. This condition is extremely rare and I had never, up to that time, seen a case similar to it with such extensive joint involvement. Doctor Gibney and Doctor Whitman also believed the condition to be sarcoma. All of us considered it too far advanced to justify conservative treatment, and strongly urged immediate amputation. This, however, was refused by the patient and her family. On November 6, 1914, an exploratory operation was made to obtain a piece for microscopic examination. On cutting down to the periosteum, a mass was found which occupied the entire lower end of the femur, the central portion of which was greatly expanded and occupied by a tumor having the typical clinical appearance of a sarcoma. It was quite vascular and penetrated into the joint; there was considerable effusion in the joint. As much of the tumor as possible was curetted and the wound packed. Hemorrhage, which was severe, was fairly well controlled with tight packing, and the limb was put in a plaster-of-Paris splint. After microscopical examination Dr. F. M. Jeffries reported it as a " mixed-celled sarcoma."

A further examination was made by Dr. J. Ewing, who reported as follows:

> The material consists of several broken portions of tumor tissue, each about 1 cm. in diameter.
>
> On section the masses are composed of dense fibrous tissue, in many places hyaline, covered with a fringe of sarcomatous tissue of the type of giant-cell sarcoma. The giant cells are of the epulis type. There are a few trabeculæ of bone which are separated by spindle tumor cells and are undergoing absorption. In several places the dense fibrous tissue is infiltrated by strands of tumor tissue in which the cells are spindle in form, with slightly hyperchromatic nuclei, but without admixture of giant-cells.
>
> In the absence of full data regarding the anatomy of the tumor and its clinical course, it is impossible to give any positive opinion of the clinical malignancy of the case. The giant-cell areas belong in a group which generally pursues a benign course. The spindle-cell areas seem to possess greater growth capacity.

X-ray examination, November 11, 1914, showed an attempt at formation of a new joint; shaft of femur resting on the outer articular surface of the tibia. Over the inner articular, to correspond with the inner condyle, is new bone formation, making a contour of a fairly good joint; no ankylosis between femur and tibia. Lateral view shows new bone formation, anterior to the patella; appears to be some ankylosis with the patella; no evidence of metastasis.

A few days after the exploratory operation the patient was put upon the mixed toxins of erysipelas and bacillus prodigiosus, and the doses were carried up to the point of giving a severe reaction. The toxins were begun on November 11, one minim, and increased daily by ½ minim, until December 27, when 8½ minims (the highest dose) was reached, which produced a temperature of 104°. After this, a short interval of one week's rest was given; the toxins were

then resumed, and kept up for one year with occasional brief periods of rest, seventy-three injections in all being given.

On December 2, 1915, Doctor Gibney reported that there was no deformity; the limb was straight with little, if any, motion. Two days later, December 4, the patient was discharged from the Hospital for Ruptured and Crippled wearing a brace on the right leg.

Inasmuch as the sinus had failed to heal the patient was given an anæsthetic and through-and-through drainage was established; curettings carefully examined by Doctor Ewing failed to show any evidence of malignancy. Rubber tubes were inserted and kept in for a number of months.

Patient was readmitted to the Hospital for Ruptured and Crippled on March 7, 1916, for infection of the old sinus. Just before admission, she developed pain and slight fever. Examination revealed what was apparently an inflammatory enlargement of the knee with a boggy swelling of the popliteal region. These symptoms continued and later fluctuation developed. In March, under local anæsthesia, an incision was made in the popliteal opening and a small abscess was found which apparently communicated with the old sinuses. One of these was opened and curetted and both openings were drained. Examination of curettings again failed to show evidence of malignancy. She was shortly treated with "Dakin's fluid" and rapid healing followed. The toxin treatment was resumed for a brief period.

The patient was shown before the New York Surgical Society in November 22, 1916, and again in January, 1919. She was also presented at the meeting of the American Surgical Association on June 16, 1919, at which time she was in good health with no trace of a recurrence, over four years later. She has 2½ inches of shortening and walks with a brace, without crutch or cane. (She is still well October 25, 1919.)

CASE II.—*Extensive Sarcoma of the Upper End of the Tibia Involving the Fibula.* C. M., female, seventeen years of age, was admitted to the Hospital for Ruptured and Crippled on July 22, 1915, with a history of having first noticed trouble in the upper part of the right leg, just below the knee-joint, six months prior to her admission. This consisted of a small swelling on the inner side of the upper portion of the right tibia, slight amount of pain, increasing disability, and moderate loss of weight; no enlargement of glands in the groin. At the time of her admission to the hospital she presented a symmetrical enlargement of the whole upper portion of the right leg, most marked below the patella. The limb could be flexed to about a right angle; no muscular spasm. Over the inner portion, the tumor was extremely soft on palpation, having the "feel" of semi-fluctuation.

Measurements.—Right, 11½, 12, 12¾; left, 11½, 11⅝, 11½, 10¾. X-ray showed a tumor involving the entire upper extremity of the tibia, the bony structure of which was practically destroyed except on the outer and upper aspect; other bones not

affected. The disease was so extensive that amputation was strongly advised, but refused by the patient. In view of the successful results obtained with the toxins in the case of sarcoma of the femur, already detailed in this paper, conservative treatment was advised in the present case, *i.e.*, curetting for a microscopical section, to be followed by toxin treatment. In this opinion Doctor Gibney concurred.

On August 2, 1915, a four-inch vertical incision was made below the knee. The tumor was curetted out, and found to involve the whole upper part of the tibia for a distance of four inches, and nearly the same length of the fibula, with the exception of the outer wall; a thin layer of cartilage which was perforated in curetting was all that was left of the upper end of the tibia. The wound was packed with gauze, and a roller bandage tightly applied and the limb put up in plaster-of-Paris before removing the tourniquet. Pathological examination was made by Dr. F. M. Jeffries (pathologist to the Hospital for Ruptured and Crippled), who reported the tumor to be "giant-celled sarcoma."

Dr. James Ewing also examined a section microscopically and reported: "Tissue composed of typical giant-cell sarcoma of epulis type and of very moderate malignancy."

A third examination was made by Dr. George Barrie, of the Post-Graduate Hospital, who pronounced it "fibrosarcoma with giant-cells." He stated it was a true sarcoma and not a benign tumor. The clinical history of rapid development and extensive involvement and recurrence after operation furnish sufficient evidence of the malignant nature of the tumor. Blood examination August 10, 1915: Red blood-cells, 4,700,000; hæmoglobin, 85 per cent.

Four days after curetting, the patient was put upon small doses of the mixed toxins of erysipelas and bacillus prodigiosus (no other treatment). The initial dose, ½ minim, was increased daily, by ½ minim, until a decided reaction temperature of 102°, 103°, 104° was obtained, after which four injections a week were given.

The cavity gradually filled up with healthy granulations, and a note by Dr. V. P. Gibney, dated November 15, 1915, reads: "Open sinus over inner head of tibia; no infiltration about knee. Small range of motion allowed, not fully tested. General condition excellent. On high road to recovery."

The leg and thigh were kept in a plaster splint and the sinus treated through a window in the splint. By December 1 the sinus had closed and there was no evidence of any tumor either by physical or X-ray examination. X-ray pictures were taken regularly every two weeks. Marked new formation of bone could be noticed in the upper end of the tibia, which was completely destroyed at the time of operation. The patient also gained in weight and strength. On December 27, 1915, she was shown before the Alumni Association of the Hospital for Ruptured and Crippled, at which time there was no evidence of any lesion present.

On January 9, 1916, the patient suffered from an attack of grippe and the toxin treatment was discontinued for two weeks. On January 26, the plaster cast was removed and a recurrent tumor the size of a pullet's egg was found at the upper and inner end of the right tibia, at the site of the old sinus. An X-ray picture also showed the growth. The toxin treatment was again administered and given both locally and systemically. The tumor diminished somewhat in size but did not disappear, and on March 3, 1916, a portion of the growth about the size of a hen's egg was removed by curette and the wound was packed. A microscopical examination of the mass removed was made by Doctor Ewing, who pronounced it "giant-cell sarcoma." Blood examination, March 5, 1916: Red blood-cells, 4,856,000; white blood-cells, 7800; hæmoglobin, 82 per cent.

On March 10, 100 mg. of radium emanations were applied over the site of the tumor, and allowed to remain for twenty-four hours. The toxin treatment also was resumed, the doses being increased every day up to the point of producing a temperature of 102°–103°. The soft tumor-like area slowly increased in size and by April 1 it measured 1 by ¾ inch; it was non-fluctuating. On April 8, 150 mg. of radium emanations were applied to the lower and ulcerated portion of the swelling, and kept on for seven hours, after which it was moved two inches higher over the articular surface of the tibia. On July 22, 240 mg. of radium were applied over the same site, for fourteen hours. Her local condition continued to improve, the sinus gradually healed, and the patient's general condition returned to normal. The toxins were continued during the summer with occasional intervals of rest.

On October 4, 1916, when she left the hospital, there was no sign of a tumor and she was in good physical condition. By November 22, 1916, she had gained twenty-four pounds in weight.

This patient also was shown before the New York Surgical Society on November 22, 1916, and again in January, 1919, and was presented at the meeting of the American Surgical Association on June 16, 1919, at which time she was in good health with no evidence of local recurrence or metastases. She now walks with a brace without the aid of a crutch or cane. The recent X-ray pictures show almost complete restoration of bone. (Well October 25, 1919, over four years.)

CASE III.—*Periosteal Sarcoma of the Tibia with Metastases in the Inguino-femoral Glands; Disappearance Under Toxin and Radium Treatment; Well at Present, Nearly Two Years.* Mr. S., thirty-nine years of age, was referred to me on April 27, 1917, by Dr. John H. Gibbon, of Philadelphia. Family history negative.

Personal History.—The patient's general health had been very good, and he had practically never been ill. Ten years before he was struck by an automobile and suffered a compound fracture of the right leg, four inches above the ankle. There had been no injury to the left leg as far as known. Three weeks before he was referred to Doctor Coley the patient had noticed a swelling about two inches

above the left ankle, extending upwards and involving the inner and anterior portion of the leg for a considerable distance. It was at first believed to be a periosteitis of inflammatory origin. In the latter part of April Doctor Gibbon was called in consultation and pronounced it a sarcoma. This opinion was strengthened by an X-ray examination.

Physical examination at the time of my first observation (April 27, 1917) showed a man in robust health. Examination of the left leg revealed a marked swelling occupying the lower third, apparently originating in the periosteum and extending nearly around the leg. It began about an inch above the internal malleolus and extended upwards five inches anteriorly, and 4½ inches on the outer side of the fibula. There was marked œdema of the whole lower third of the leg extending to the ankle. The swelling, which was most prominent over the inner and anterior part, was soft, almost semi-fluctuating, and markedly tender on deep pressure; the skin was slightly discolored. T. = 99.5°.

To definitely settle the diagnosis on April 27 an exploratory operation was made. A portion removed was examined microscopically by Doctor Ewing, who reported: "Section shows a tumor composed of small spindle cells consisting chiefly of nuclei. They are very numerous, with no visible stroma. The cell masses are very compact. The tumor is quite malignant in structure."

The patient was immediately put upon the mixed toxins of erysipelas and bacillus prodigiosus, which were continued four or five times a week in doses sufficient to produce a temperature of 102°–104°.

MEASUREMENTS

April 30, 1917:
1 inch above the internal malleolus = 9⅝ inches.
4 inches above the internal malleolus = 10⅝ inches.
6 inches above the internal malleolus = 10¾ inches.
The tumor itself, anteriorly = 5½ x 5 inches.

May 5, 1917:
4 inches above the internal malleolus = 10⅜ inches.
6 inches above the internal malleolus = 10⅜ inches.
The tumor itself = 4 x 3 inches.

May 11, 1917:
4 inches above the internal malleolus = 9¾ inches.
6 inches above the internal malleolus = 9¾ inches.
The tumor itself = 4 x 3 inches.

On May 1, 1917, the patient was treated with radium emanations 12 by 85 mc. (1020 mc.) through 2 mm. lead filter, 6 cm. distance, applied to the anterior surface of the leg for twelve hours.

On May 8, he received the following radium emanations: 660 mc., 2 mm. lead filter, 10 cm. distance, applied to the inner aspect of the leg for twelve hours, and on May 23 the same amount of radium emanations, 2 mm. lead filter, 6 cm. distance, applied to the external aspect of the leg for twelve hours.

MEASUREMENTS

May 21, 1917:
Circumference of leg across centre of scar = 9¼ inches.
May 25, 1917:
Circumference of leg across centre of scar = 9¼ inches.
Circumference of leg across upper end of scar = 9 9/16 inches.
Circumference of leg across lower end of scar = 9 9/16 inches.

On May 26, 1917, the patient returned to his home, where the toxins were continued three times a week by Dr. R. G. Gamble, his family physician, and on June 19 he was again admitted to the Memorial Hospital for further radium treatment, at which time he received 1200 mc. emanations, through 2 mm. lead filter, 10 cm. distance, applied to the internal surface of the leg for eight and one-half hours. The toxins were then continued at home during June and July, but in view of the fact that all evidence of the disease had disappeared and he was in such fine general condition it was thought safe to discontinue the treatment for four weeks during the extreme heat in August and September.

The patient returned to Doctor Coley for observation on September 15, 1917, stating that he had recently discovered a swelling in the left groin, which was increasing in size. A physical examination showed the leg to be apparently normal. The left groin was occupied by several large glands involving the femoral, inguinal, and iliac regions, the largest of which was about the size of a big hickory nut. Doctor Coley removed one of these under general anæsthesia and forwarded it to Doctor Ewing for microscopical examination, who reported: "Actively growing sarcoma. Cells large polyhedral. No pigment. Nature of origin uncertain."

RADIUM TREATMENTS

(Oct. 1, 1917).—Radium emanation pack, 600 mc. for 7 hours, 2 mm. lead filter, applied at a distance of 10 cm. to the left inguinal and femoral regions.

(Oct. 2, 1917).—Radium pack, 480 mc., lead filter for 29 hours, at a distance of 10 cm. to the same region, making a total of 18,000 mc. hours.

(Nov. 8, 1917).—Radium pack, 1400 mc. (2 mm. lead, 0.5 mm. German silver), applied at a distance of 8 cm. over the left inguinal region for 6¾ hours.

(Nov. 9, 1917).—Radium pack, 1420 mc. (2 mm. lead, 0.5 mm. German silver), applied at a distance of 8–10 cm. over the left inguinal region for 6 hours.

(Dec. 7, 1917).—Radium pack, 1800 mc. for 6 2/3 hours (2 mm. lead, 0.5 German silver), applied over the left inguinal region at a distance of 8–9 cm.

The toxins have been continued for nearly two years with occasional intervals of rest. The doses have been comparatively small, not sufficient to interfere with his regular occupation, and his general health has remained perfect throughout the entire time. A recent physical and X-ray examination showed apparently no trouble remaining in the tibia and no evidence of metastases in any other part of the body.

This case, I believe, illustrates the advantage of combining the

local effect of the radium with the systemic effect of the toxins; it also shows the importance of keeping up the toxin treatment in certain cases for a considerable period. It is too early yet to say that the patient is permanently cured, yet more than two years have elapsed since the disappearance of the primary tumor, and one and one-half years since the secondary. This patient was shown before the American Surgical Association June 16, 1919, at Atlantic City.

NOTE.—The patient was shown before the Clinical Congress of Surgeons of America in New York October 23, 1919, without trace of recurrence, in two and one-half years.

CASE IV.—*Central Sarcoma of the Femur with Extensive Involvement of the Knee-joint and Upper End of Tibia. Amputation advised, but refused; recovery under conservative treatment, curetting followed by systemic toxin injections and radium treatment; well at present, three years later.* C. S., female, twenty-nine year of age; married; family history good. Referred to me November 10, 1916; first noticed swelling over the inner condyle of the right femur seven months previously; the swelling was associated with a moderate amount of pain; admitted to St. Vincent's Hospital a few weeks before I saw her. An X-ray picture was taken and the diagnosis of sarcoma made; amputation strongly advised, but refused.

Physical examination Novmber 10, 1916, shows a tumor occupying the whole lower end of the femur, most prominent over the anterior and inner portion, apparently involving the knee-joint. The tumor is soft and semi-fluctuating over most of the area, consistence varied in different portions. On the inner side the swelling extends down to and apparently involves the upper end of the tibia; it is smooth and globular in appearance; superficial veins dilated. Measurements of tumor—6½ inches on the inner side; 7 inches on the anterior side; 5½ inches on the outer. Measurement over most prominent part of the tumor, 16¼ inches, 2 inches more than on the normal side. The popliteal space is partially filled up with a new growth of bone. The patient has been unable to walk for five months, and has lost 25 pounds in weight. Clinical diagnosis: Central sarcoma of the femur with extensive involvement of the knee-joint. X-ray examination shows a tumor occupying almost the entire lower end of the femur, apparently involving the knee-joint as well. There seems hardly any of the femur left, except the lower portion of the outer condyle. Amputation was strongly advised, but the patient absolutely refused. I finally decided to make an exploratory operation and to treat the patient with large systemic doses of the toxins of erysipelas and bacillus prodigiosus, possibly supplemented by radium. Operation, November 15: A tourniquet was applied at the upper and middle third of the right thigh and an incision 4 inches long made over the inner condyle along the inner border of the patella. A tumor, soft and semi-fluctuating, about the size of an orange, was found underneath the muscular layers. It had broken entirely through the periosteum, and while not actually infiltrating, had pushed to one side and outward the muscles and fascia.

By means of a curette and gauze sponges a large mass of soft grumous material of grayish-red color, macroscopically typical of sarcoma, was removed. The semilunar cartilages had been apparently entirely destroyed. The upper portion of the tibia for a distance of about 2 inches was almost completely destroyed and the whole joint was disorganized and occupied by a tumor which extended nearly through the outer condyle of the femur. The fibula was apparently not involved. Only a small shell of the outer side of the femur prevented spontaneous fracture. The tumor was finally curetted down to hard bone on the outer side and to the muscle and fascia overlying the popliteal vessels below, and to the upper end of the tibia until bare bone was reached. A cavity fully the size of an orange remained, which was packed tightly with gauze to prevent hemorrhage, and the limb put in a plaster splint. A pathological examination was made by Dr. James Ewing, who reported as follows: "The tumor has the general features of a giant-celled medullary sarcoma. Several areas are unusually cellular, which indicates a guarded prognosis." In a later report made on basis of examination of further sections, he states: "While the tumor shows certain areas of typical giant-cells, there are other areas in which the giant-cells are comparatively few in number and bunches of spindle- and round-cells are present."

This report taken in conjunction with the clinical history of the case, the very rapid growth of the tumor, perforation of the periosteum, complete destruction of the knee-joint and involvement of the upper end of the tibia, leave little doubt in my own mind that the tumor was a sarcoma of marked malignancy and could not be regarded as a giant-celled growth of benign character.

The packing was not completely removed until the end of a week, and the large cavity was kept clean by the use of Dakin's solution. Three days after the operation the patient was put upon systemic doses of the mixed toxins, the injections being made into the buttocks; the initial dose was ½ m., and this was increased by ½ m. daily up to the point of obtaining marked reactions. The highest dose was 14 minims. The patient was not very susceptible, and severe reactions did not occur until very large doses (10–12 m.) were reached. The large cavity gradually filled up with apparently normal granulation tissue. At the end of about two months the wound had practically closed without the slightest infection. Frequent X-ray pictures taken showed steadily increasing reproduction of bone at the site of the tumor.

The patient was shown before a conference at the Memorial Hospital on January 24, 1917, with the sinus healed, and able to get about on crutches. Just before the sinus had entirely closed, the toxin treatment was supplemented by the introduction of steel needles containing 100 mc. of radium, through the sinus at the bottom of the cavity; the needles were allowed to remain in place for three hours on three occasions. Later a radium pack treatment was given externally.

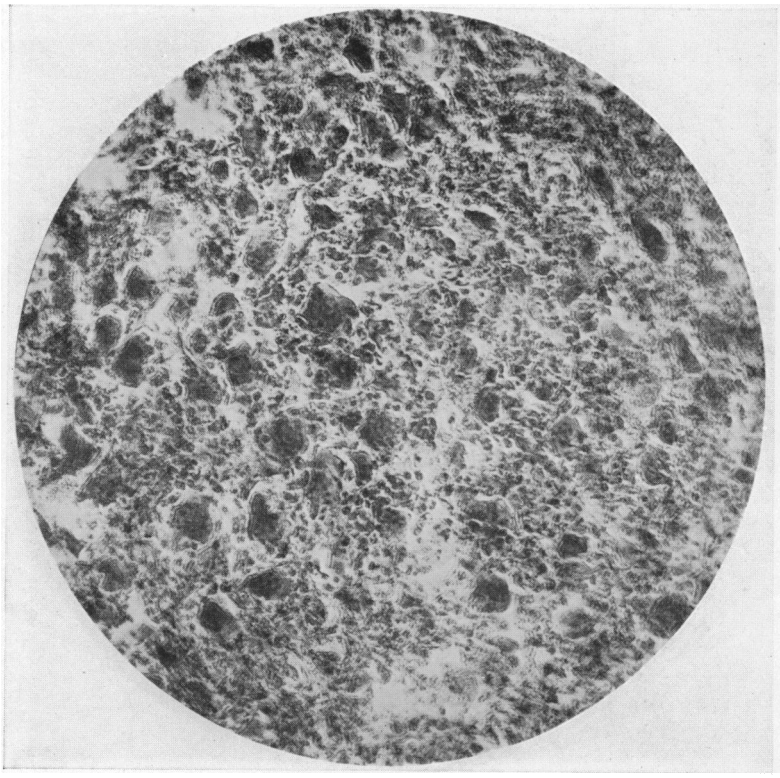

FIG. 1.—Giant-cell sarcoma of the femur, epulis type, recovering under simple curetting. Amputation advised and refused. Well in two years. Example of typical giant-celled tumor of low degree of malignancy.

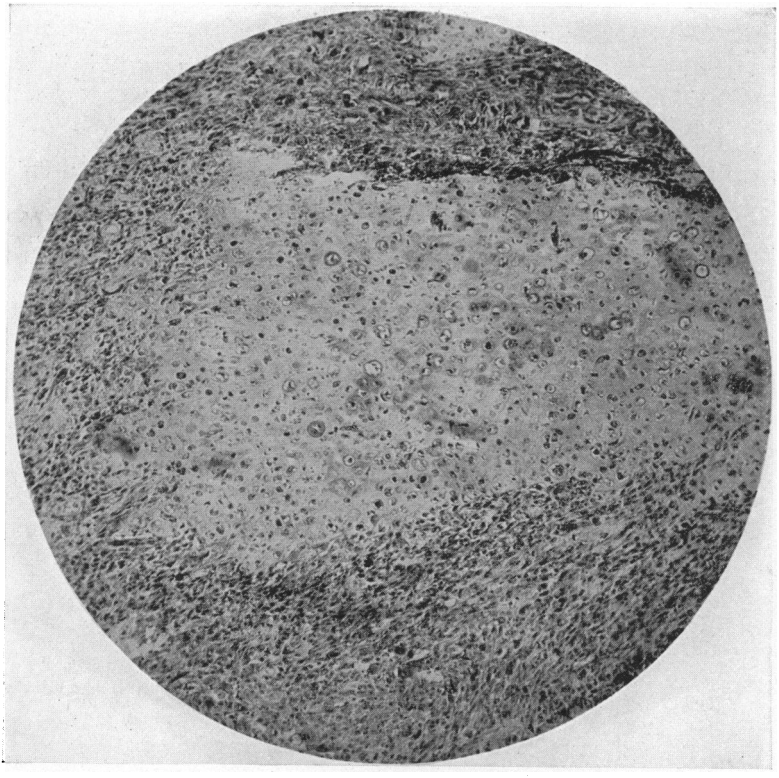

FIG. 2.—Spindle-, round-, and giant-cell chondrosarcoma. Death from metastasis in lung three years after amputation.

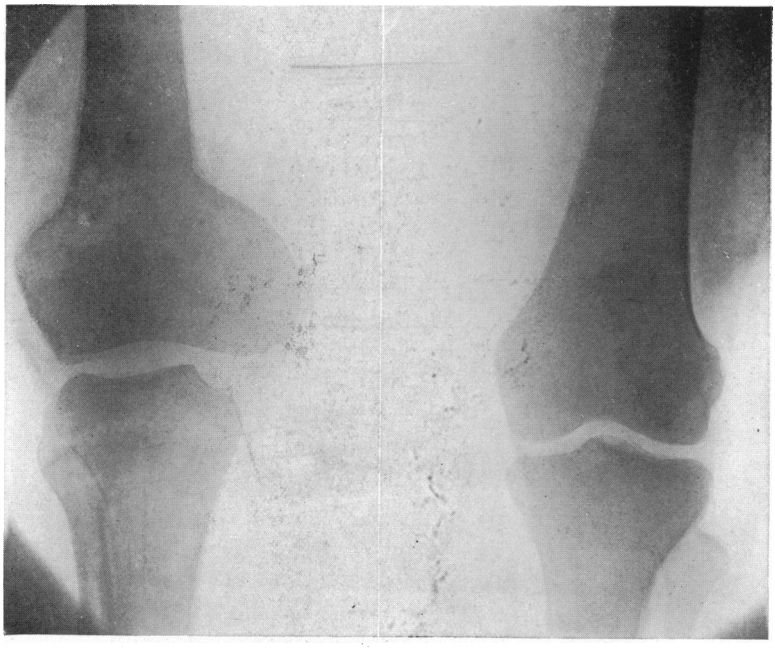

FIG. 3.—(Case I.) Central sarcoma of femur before treatment, involving knee-joint and upper end of tibia. Treated by curetting, toxins and radium. Complete recovery—well and walking with scarcely any limp three years later.

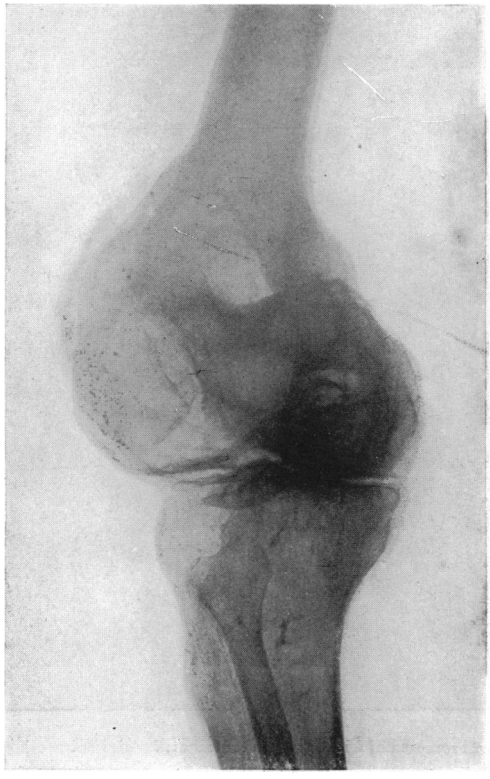

FIG. 4.—(Case I.) Sarcoma of lower end of femur with extensive involvement of knee-joint. Amputation advised and refused. Recovered under systemic treatment with mixed toxins alone. Patient is walking without crutch or cane at present (four years and eight months). This photo, showing extensive growth of new bone, was taken four years and eight months after beginning of treatment. Patient still wears a brace.

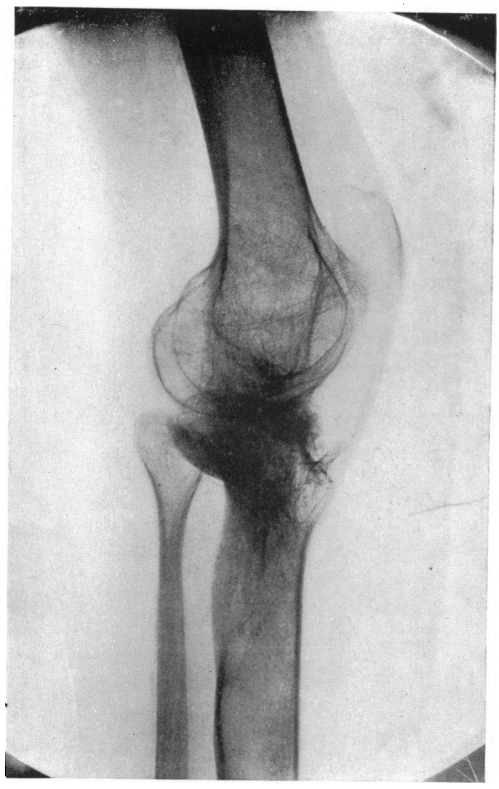

FIG. 5.—(Case II.) Sarcoma of tibia three years and ten months after toxin and radium treatment, showing reformation of upper five inches of tibia without bone grafting and after complete destruction by sarcoma. Treated by toxins and curetting, August, 1915, after amputation had been strongly advised by other surgeons. Patient well, in four months. Then sarcoma recurred and grew rapidly. Second curetting. Rapid recurrence. Disappeared under toxins and radium. Well October 26, 1919, more than four years. This picture taken three years and ten months after treatment. For photographs and microphotographs taken before treatment see ANNALS OF SURGERY, March, 1917.

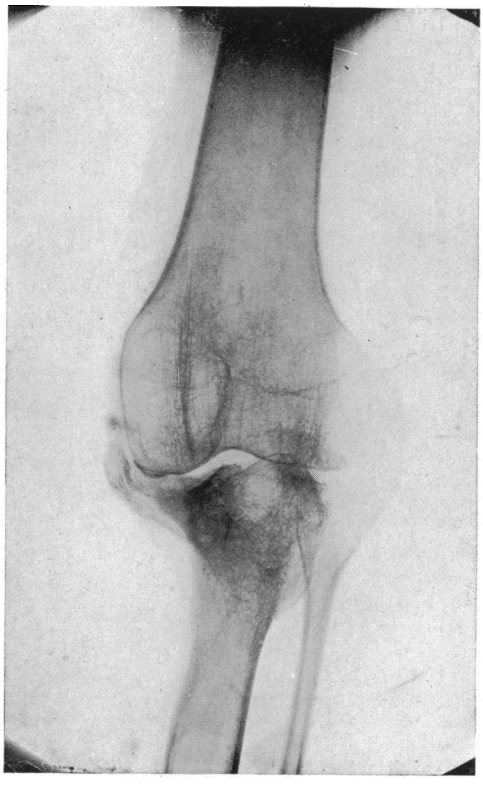

FIG. 6.—Same case as Fig. 5, three years and ten months after treatment.

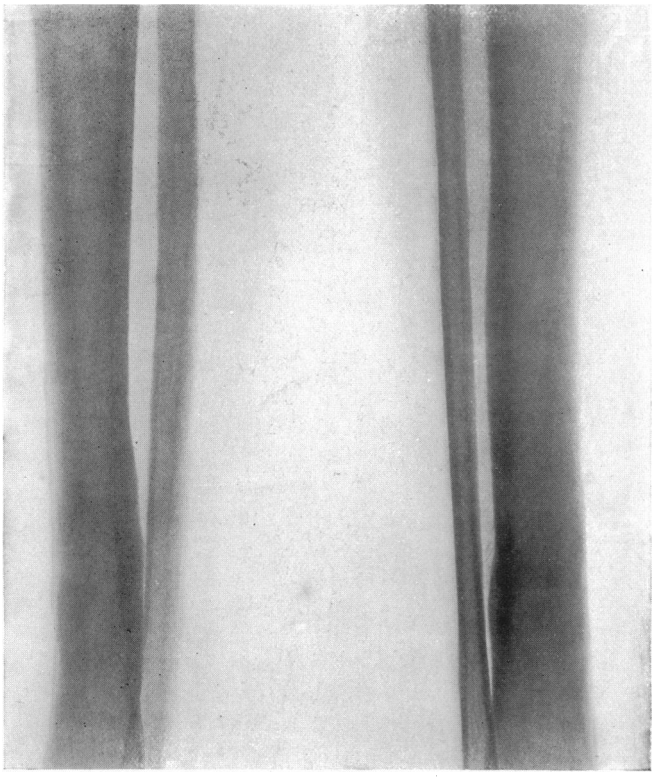

FIG. 7.—(Case III.) Periosteal sarcoma of tibia, spindle-celled.

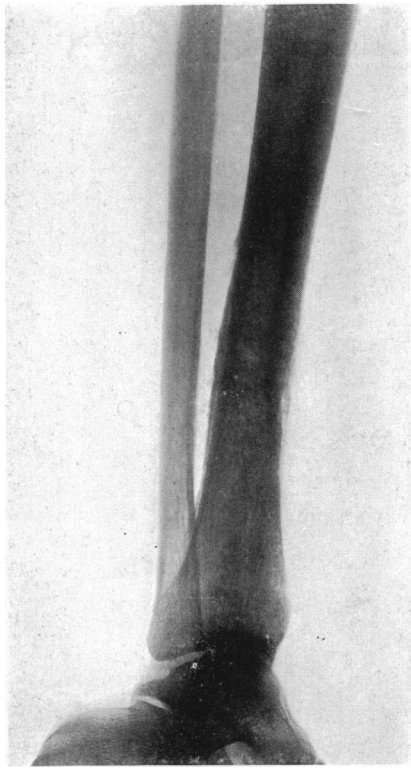

FIG. 8.—(Case III.) Two years later spindle-celled periosteal sarcoma of tibia. Very rapid development.

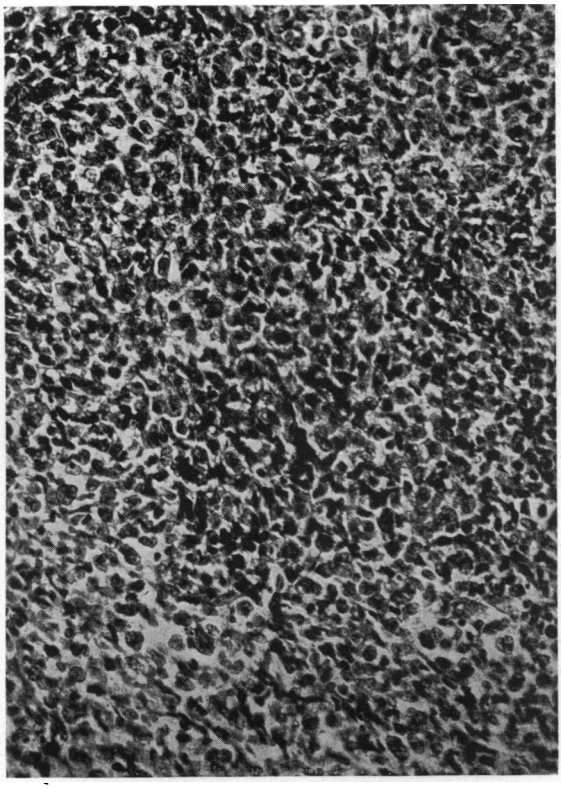

FIG. 9.—(Case III.) Periosteal sarcoma of the tibia. No giant-cells. Entire disappearance followed the use of toxins and radium, April, 1917. Recurred in glands of groin (femoral, inguinal and iliac) September, 1917. Diagnosis was confirmed by microscopic examination. Disappeared under further treatment but toxins were continued for two years. Patient well (January 16, 1919) without trace of disease. Microscopic examinations both made by Dr. Ewing. Diagnosis: Malignant spindle-celled sarcoma, no giant-cells.

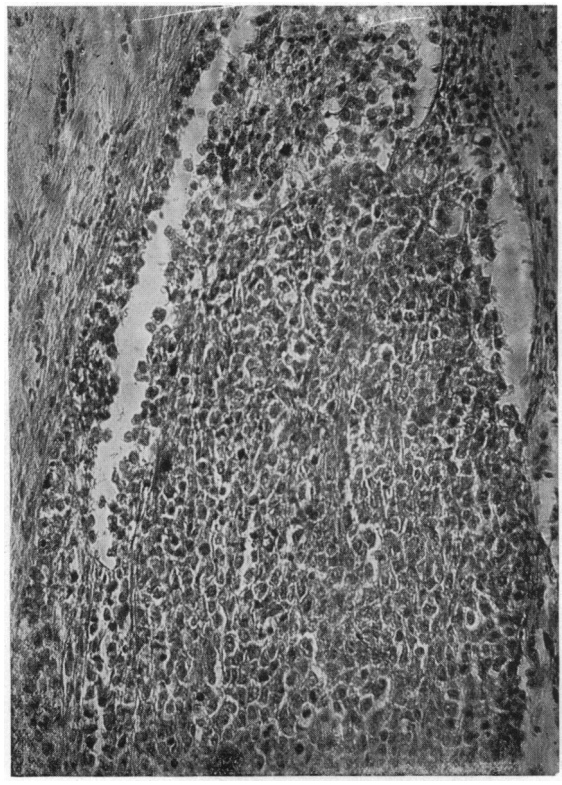

FIG. 10.—(Case III.) Section from metastatic tumor removed from inguinal region. Metastatic tumor six months later in groin, which disappeared under toxin and radium treatment. Again disappearance under same treatment and patient well and free from recurrence October 26, 1919, over two years from time treatment was begun.

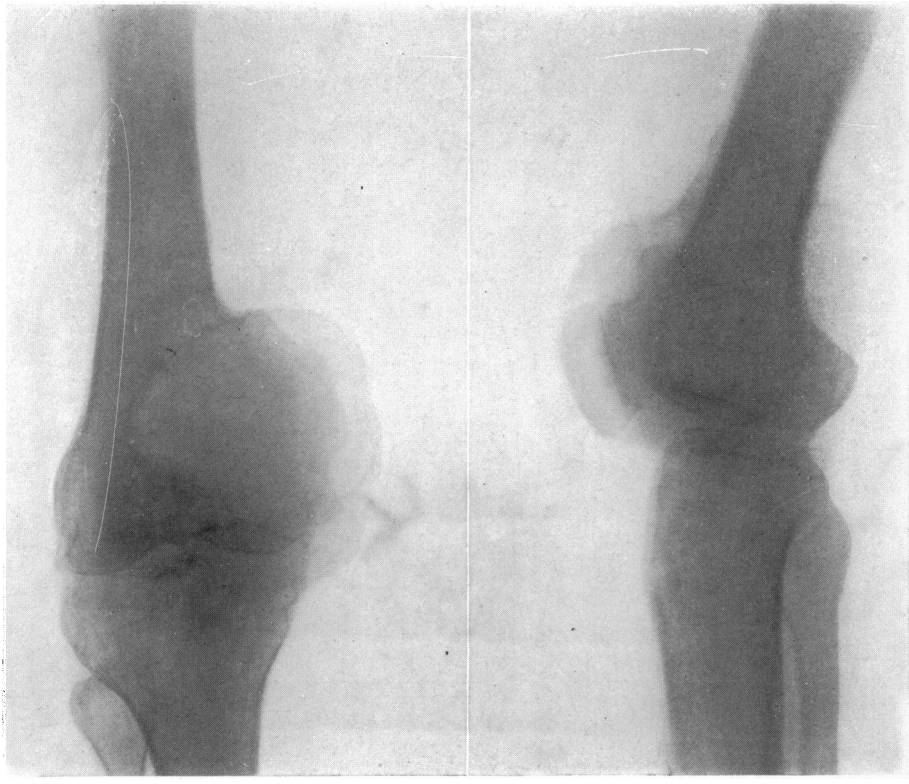

FIG. 11.—(Case IV.) Central sarcoma of femur. Giant- and spindle-celled. Rapid growth, involving the knee-joint and upper end of tibia.

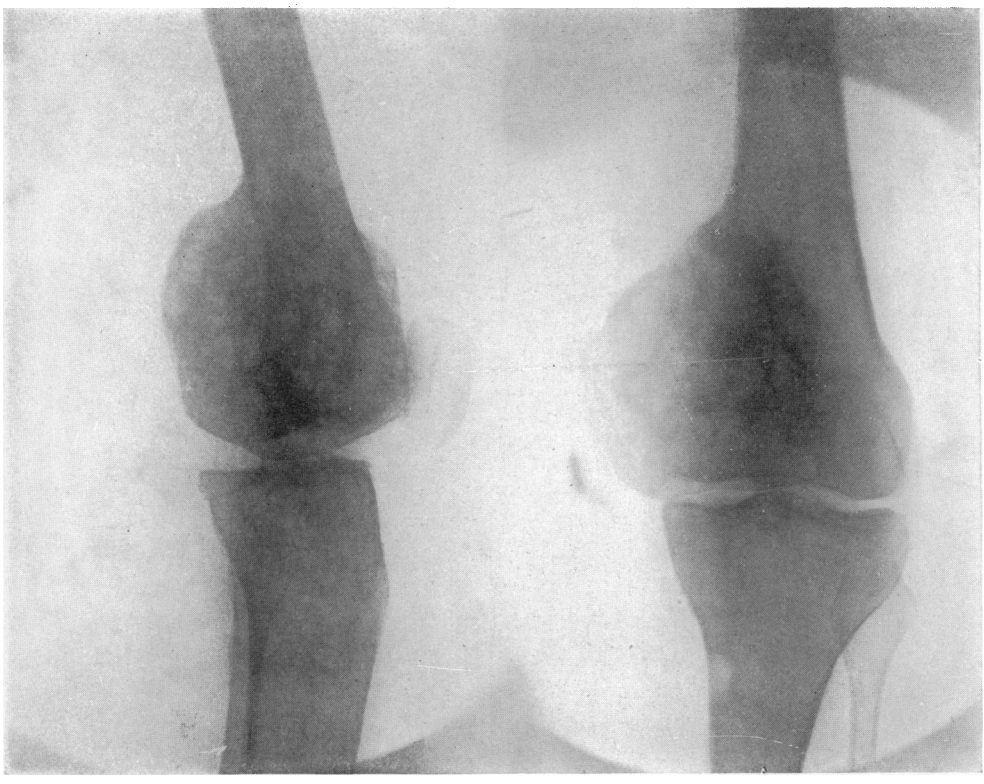

FIG. 12.—Same case as Fig. 11 two and one-half years later.

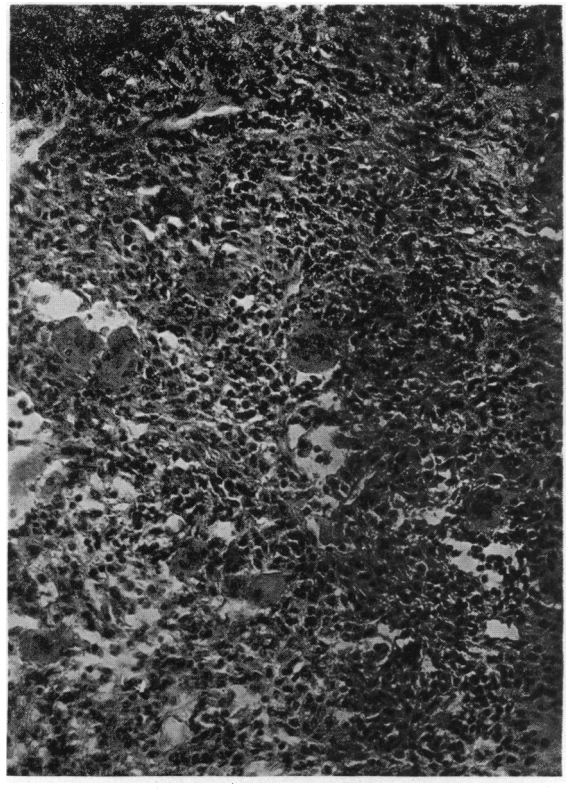

FIG. 13.—(Case V.) Spindle- and giant-celled sarcoma of femur involving knee-joint and upper end of tibia. Amputation advised by several surgeons and then at Vincent Hospital, but patient refused and was discharged. Amputation strongly urged by Dr. Coley and refused. Patient then treated by Dr. Coley by exploratory operation—curetting—followed at once by large doses of toxins. Cavity size of an orange healed by granulation. 100 mc. of radium inserted in sinus by means of steel needle and radium pack used externally. Patient well October 26, 1919, nearly three years.

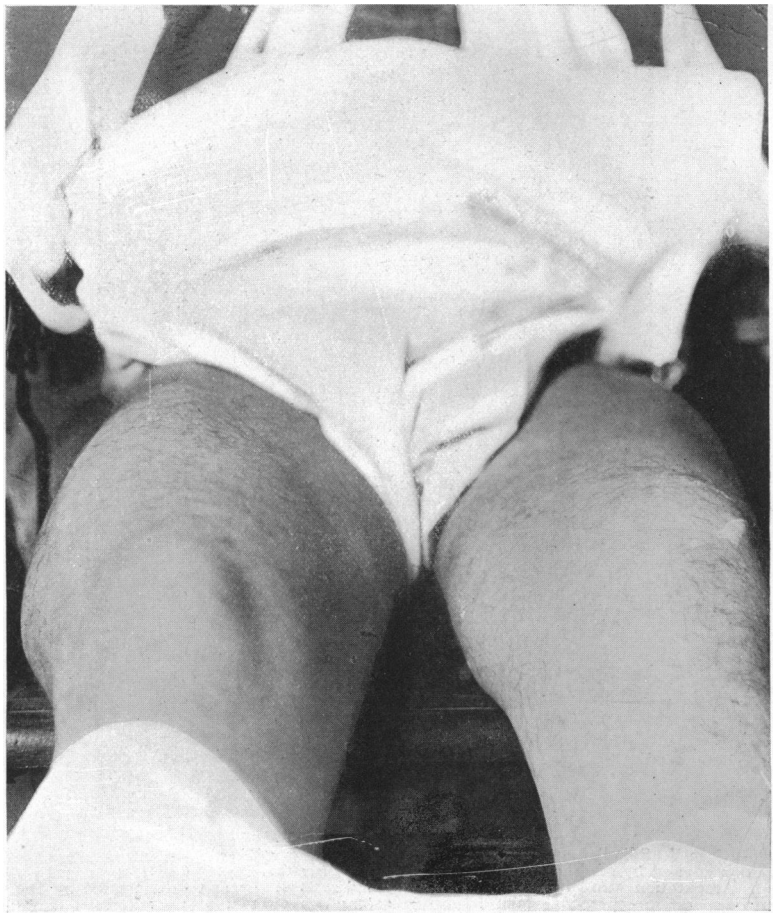

FIG. 14.—(Case V.) Inoperable periosteal sarcoma of femur. Disappearance under large doses of toxins and radium. Treated at Memorial Hospital, October, 1917, to July, 1918. Picture taken on admission. Entire disappearance of tumor and patient well October 26, 1919, two years.

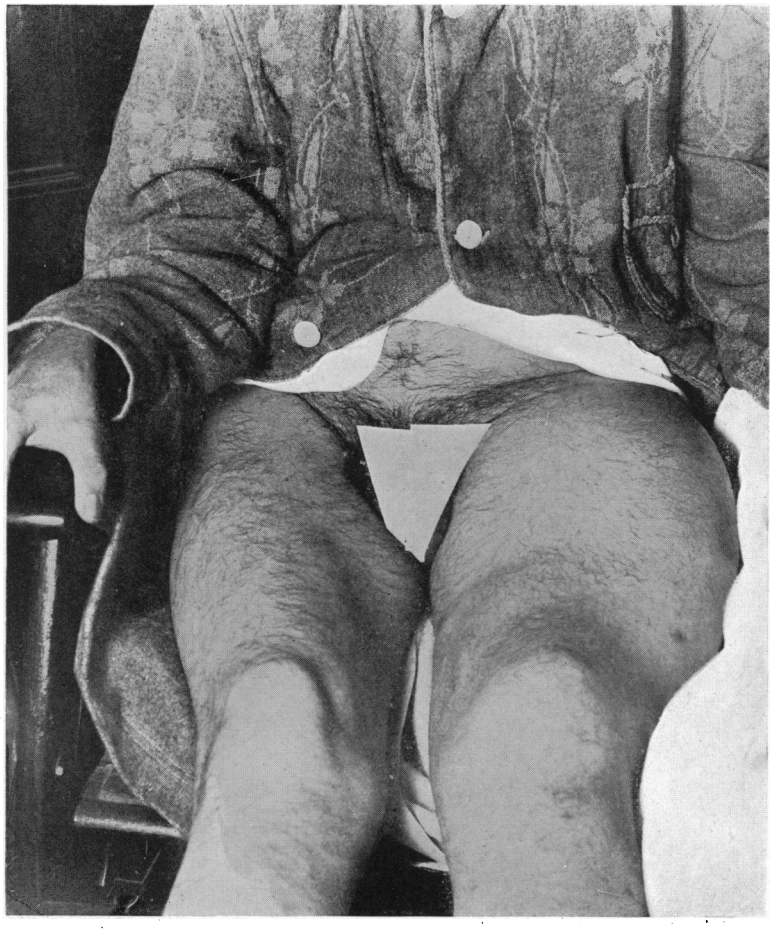

FIG. 15.—(Case V.) Inoperable periosteal sarcoma of the femur. Disappearance under large doses of toxins and radium. Treated at Memorial Hospital from October, 1917, to July, 1918. Picture taken one year after entering hospital, October, 1918.

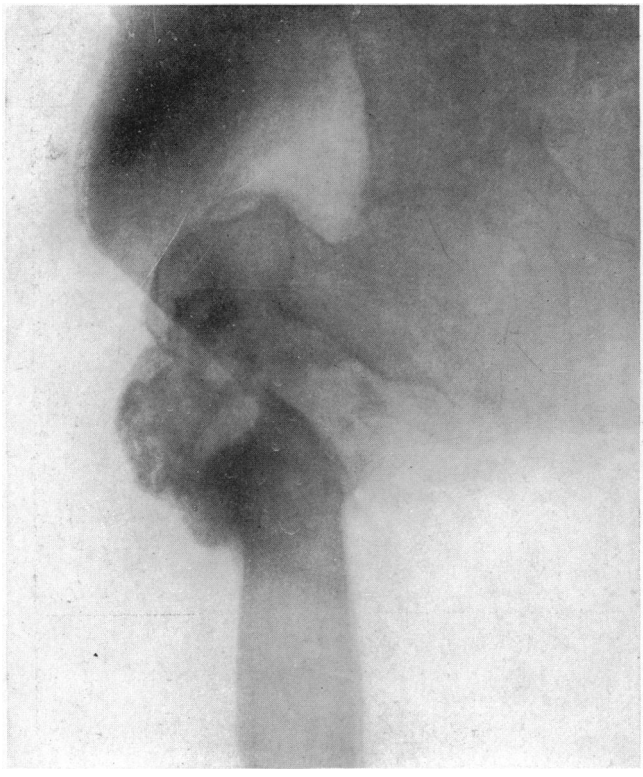

FIG. 16.—(Case VI.) Sarcoma of femur. X-ray taken one year after beginning treatment with toxins and radium. Entire disappearance of very large sarcoma involving upper two-thirds of femur under eight months' treatment by massive doses of radium, and large doses of mixed toxins injected systematically into tumor. Patient well October 26, 1918, two years later, with five and one-half inches of shortening.

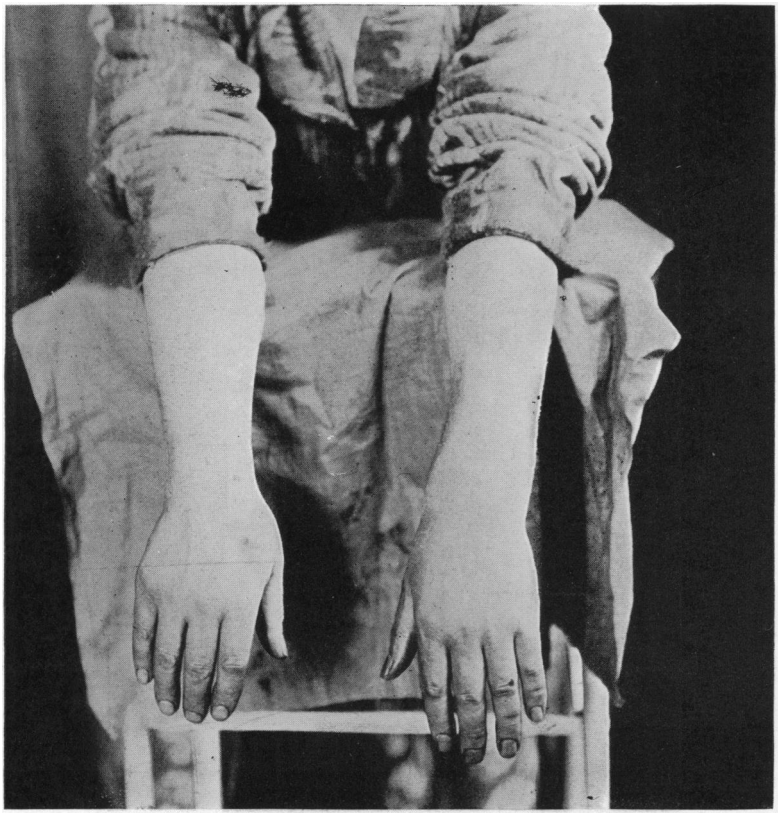

FIG. 17.—(Case VI.) Sarcoma of lower end of radius. Entire disappearance under toxin treatment alone in four months. Patient well at present, eighteen months later. See Fig. 19, taken seven months after treatment. Complete destruction lower three inches of radius. Rapid growth. Amputation advised by several surgeons.

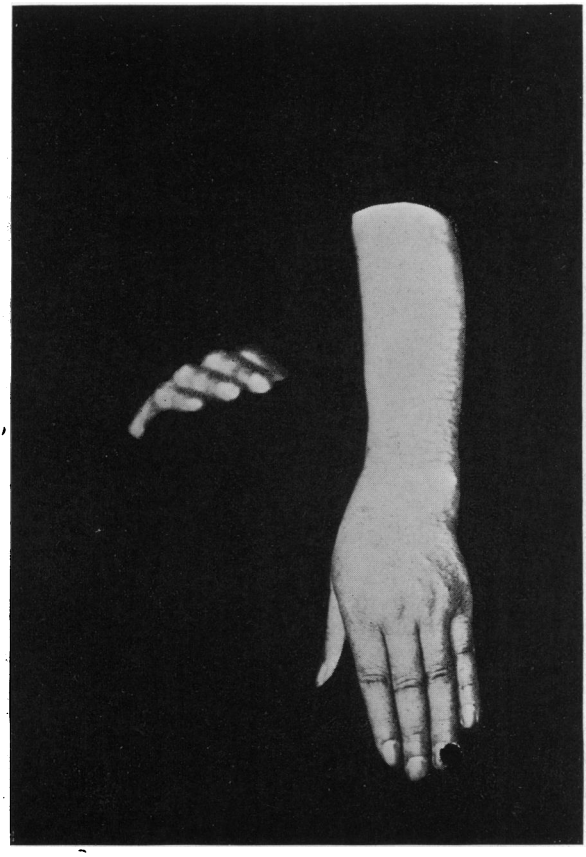

FIG. 18.—(Case VI.) Seven months after treatment. Entire disappearance of tumor under toxin alone. Patient now well with useful arm, eighteen months after beginning of treatment.

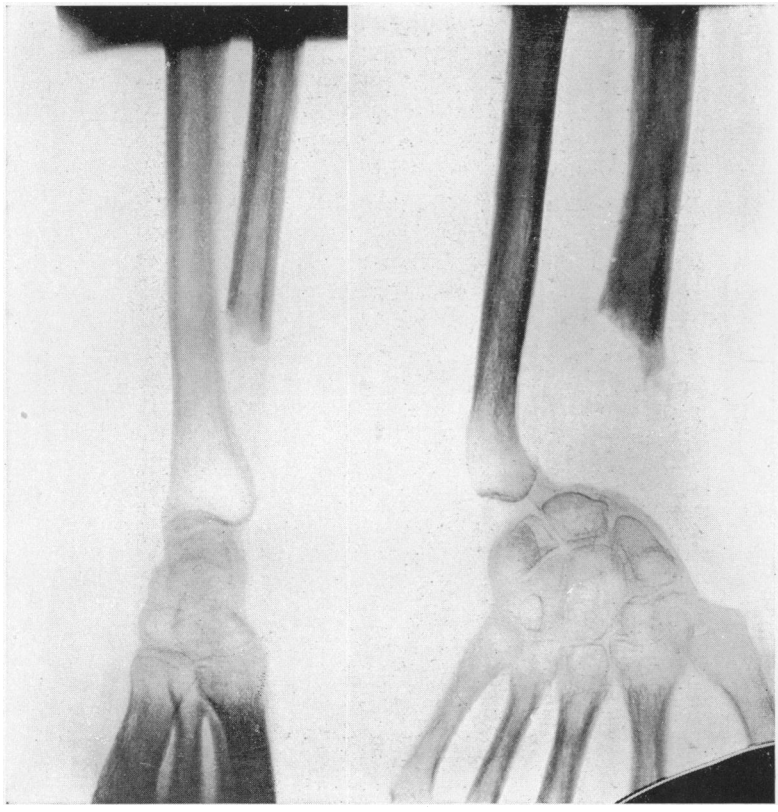

FIG. 19.—(Case VI.) Sarcoma of radius before treatment. Cured by toxins alone. Patient well October 25, 1919. Toxins injected into buttocks systematically one year and four months. No other treatment.

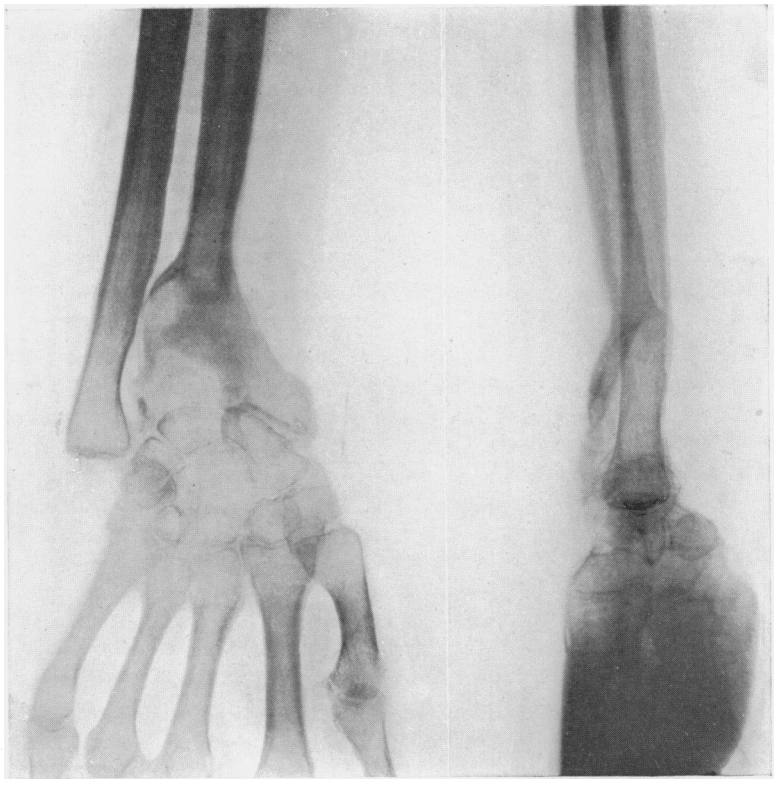

FIG. 20.—Same case as Fig. 19, seven months after treatment. Splint removed, and patient returned to work. Perfect function.

The patient made an uninterrupted recovery. For the last two years she has been attending to her household duties without the use of crutch or cane. She was shown at a clinic given for the Clinical Congress of Surgeons of North America, October 23, 1919, three years after treatment, and walked with only a slight limp and was apparently in normal health. The X-ray picture shows that the original tumor area has been almost entirely replaced by new bone, and the limb is apparently as strong as it ever was. X-ray picture of the chest shows no evidence of metastases.

CASE V.—*Very Large Inoperable Sarcoma of the Upper Portion of the Femur, Following a Recent Fracture; Disappearance Under Combined Toxins and Radium Treatment. Reunion of Pathological Fracture; Well at Present, Two Years After Beginning of Treatment.* R. H., male, thirty-six years of age, had been entirely well up to January, 1917, when he slipped on the ice, causing a fracture of the left femur, a little below the trochanter. He was taken to St. Vincent's Hospital in Bridgeport, Conn., where he was treated by Dr. Geo. W. Hawley. X-ray pictures had been taken at the time, but owing to Doctor Hawley's having been engaged in military service, I have been unable to see the pictures as yet. The hospital report, however, mentions nothing more than an oblique fracture below the trochanter. If there had been a pathologic fracture due to a tumor already present, it probably would have been discovered at the time of the first X-ray picture. The patient did well for nine weeks, at the end of which time a swelling appeared at the site of the fracture, and steadily increased in size.

NOTE.—I have later been over the case personally with Colonel Hawley, and he states there was no evidence of tumor in the first X-ray pictures at the time of the fracture.

He remained at St. Vincent's Hospital for twenty-seven weeks. The tumor steadily increased in size, and on October 3 the patient was sent to the German Hospital, New York City, where he came under the care of Dr. Herman Fischer. On October 20 Doctor Fischer referred the patient as an inoperable sarcoma of femur to Doctor Coley's service at the Memorial Hospital. He was examined at the clinical conference of the hospital staff, and both Doctor Downes and Doctor Coley regarded the case as entirely beyond hip-joint amputation. At this time the middle and upper portion of the left thigh measured 68 cm., and the right thigh 51 cm., and there was a complete pathologic fracture at the upper and middle third of femur. Longitudinally the tumor extended for a distance of 17 cm. The mixed toxins were begun on October 30, and continued three or four times a week, alternating the systemic with local injections, and producing severe reactions. On November 5 and 6 he was treated with very large doses of radium, by means of a pack, applied at 10 cm. distance, and remaining for a total of sixty-one hours (total dose, 40,000 mc. hours). An X-ray picture taken at the time of his admission to the Memorial Hospital showed complete destruction of the bone, involving the neck of the trochanter and

upper five inches of the shaft. An X-ray picture of the chest showed "chronic diffuse bronchitis, both apices (cloudy plates) suggestive of tuberculosis—probably metastases from the tumor in the femur." By December 10 there had been a decrease of 4 cm. in the circumference of the thigh. The radium was again applied on December 25, 1917. Examination on April 8, 1918, showed a still further decrease in the circumference of the thigh. The toxins were kept up without further radium treatment. On June 23 the patient was sent home to Bridgeport, Connecticut, to remain there during the hot weather and return in the fall. At that time his general health was good; the tumor had decreased in circumference from 68 to 60 cm., with a corresponding decrease in the vertical dimension; there was still marked mobility at the site of the fracture. The leg was put in a Thomas splint. He received no treatment during the summer.

On October 8, 1918, the patient was readmitted to the hospital, at which time his general health was good, and clinical examination showed apparently complete disappearance of the tumor. The length of the left leg was 33 inches, and the right, 38¼ inches, showing a shortening of 5¼ inches. The circumference 5 inches below the trochanter, left side, was 21 inches, and the right, 23¾ inches. Circumference 5 inches above upper border of patella, left side, 19½ inches; right, 20 inches. The patient had had no treatment since leaving the hospital in June. X-ray pictures taken at the time of his readmission showed apparently no tumor tissue left. The proximal portion of the femur at the site of the pathologic fracture had been drawn upwards to the region of the trochanter, and there was an attempt at union due to formation of new bone. X-ray examination of the chest was negative.

At the present time the patient is still wearing the Thomas splint adjusted by Doctor Gibney. This patient was kept under frequent observation during the fall and winter of 1918–1919, and was shown before the American Surgical Association June 6, 1918. He is still wearing a Thomas splint, but the pathologic fracture has united and is sufficiently firm to permit him to raise his leg without support. Recent X-ray photographs show no evidence of tumor and his general health is quite normal.

NOTE.—He was also shown at the Clinical Congress of Surgeons in New York October 23, 1919, two years after treatment.

CASE VI.—*Central Sarcoma of the Radius; Clinical and X-ray Diagnosis; Inoperable; Entire Disappearance Without Sacrifice of the Arm, Under Toxin Treatment Alone.* L. D. G., male, twenty-nine years, was referred to me by Dr. V. P. Gibney on April 25, 1918, with the following history:

Eight years ago had sprain of the wrist, but apparently completely recovered. In November, 1917, or five months prior to my first observation, he noticed sharp pain like the prick of a needle; two months later loss of power in hand; at the same time he noticed an enlargement of the lower portion of the left wrist, which enlargement increased rapidly. Physical examination showed enlargement of the

lower portion of the left forearm, extending down to the wrist. The tumor was apparently primary in the radius, involving the lower three inches. The whole wrist was markedly enlarged, the circumference being 2½ inches greater than on the normal side; there was apparently some thickening of the ulna as well. There was a pathologic fracture of the radius and almost complete fracture of the ulna as well. The skin was normal, not adherent; the tumor was soft, semi-fluctuating in consistency. The clinical diagnosis of sarcoma was made and confirmed by X-ray examination. The X-ray picture showed complete destruction of the radius over 2 inches; the tumor had apparently broken through the outer shell of bone and extended outward, involving the soft parts which were pushed to one side. On the left side the tumor extended beyond the ulna, which was apparently involved. The X-ray picture did not fully show the damage to the ulna, but the clinical examination showed almost complete pathologic fracture. Amputation had been advised and the patient was willing to sacrifice the arm, if necessary. He was admitted to the Hospital for Ruptured and Crippled on April 25, 1918, and put upon the systemic injections of the mixed toxins of erysipelas and bacillus prodigiosus. Only one injection was made directly into the tumor, ⅛ minim. This was followed by a very severe reaction, a temperature of 104°, nausea and vomiting and marked herpes of the lip. The systemic injections did not produce any marked chill or severe reaction until the dose had been increased up to 6 m.

At the time the toxins were begun the measurement over the most protuberant part of the tumor, 2 inches above the lower end of the radius, was 10½ inches; normal side, 8 inches. I at first intended to use both radium and the toxins in the hope of saving the limb. During the first two or three weeks of toxin treatment there was very little improvement, and in the early part of June, when I was out of town for a week, Dr. J. P. Hoguet came very near amputating the arm, believing that there was little or no hope of saving it by conservative treatment. The patient was quite willing to submit to the operation.

When on my return on the 10th of June there seemed to be appreciable improvement, we decided not to use any radium and the injections were kept up systemically, every other day, in doses sufficient to produce a temperature reaction of 102° to 104°. By the end of June the swelling had nearly disappeared, and by the end of July it had entirely disappeared. The arm had been kept in splints during the early part of the treatment and later, after the tumor had disappeared, was kept in plaster-of-Paris with the hand in an abducted position, to avoid deformity while the new bone was forming. The patient left the hospital and the treatment was kept up two or three times a week until the last of January, 1919. Frequent X-ray pictures were taken of the wrist, and these showed gradual increase in new bone taking the place of the 3 inches of radius and ulna which had been completely destroyed. The patient wore a short palmar

splint for six months; the new bone which has replaced the lower end of the radius is not entirely solid yet, but I believe it will soon be completely restored and the arm will be quite as useful as ever. I feel some confidence in this prognosis for the reason that in two similar cases in which the tumor had disappeared under the toxins without other treatment—both confirmed by microscopical examination—there has been complete restoration of the function of the respective limb; one of these patients is now well more than ten years.

NOTE (October 23, 1919).—The patient has been using his arm since January, 1919, and is doing his regular work as a grocer. He has normal functions and little deformity. This patient was shown before the Clinical Congress of Surgeons October 23, 1919.

The following case shows the difficulty sometimes experienced in determining in what cases to make use of conservative treatment and in what cases to amputate:

CASE VII.—*Sarcoma of the Radius and Ulna.* C. R., male, twenty-two years of age, was referred to me on September 22, 1914, with the following history: In May, 1913, he had first noticed a slight swelling in the lower end of the right radius; this was accompanied by pain which rapidly increased in severity. In September, 1913, the lower third of the radius was resected by Dr. Howard Lilienthal. The pathologic examination of the tumor showed it to be a round-celled sarcoma with no giant-cells. Four months later there was a return of the growth in the lower end of the ulna, with spontaneous fracture. Doctor Lilienthal then referred the patient to me for the toxin treatment. Physical examination at this time showed the lower half of the forearm enlarged, the skin purple in color; there was marked protuberance of the dorsal surface of the forearm extending down to the metacarpal bone. The swelling was soft, almost fluctuating, spontaneous fracture of the ulna, egg-shell-like crackling on palpation and some tenderness. The whole lower third of the ulna has apparently become disorganized and false motion is elicited almost at any point. There is marked silver-fork deformity of the wrist, and absence of the lower end of the radius. The X-ray taken on September 23, 1914, showed sarcoma of the radius with marked osteoporosis of post-operative remnant of radius; spontaneous fracture of ulna, marked sarcomatous involvement of ulna with some attempt at periosteal proliferation. Diagnosis: Osteosarcoma. The patient went out on a pass before treatment was instituted, and failed to return until October 13, 1914. During this short interval of three weeks the tumor had increased very markedly in size; it had attained the size of a small fist, involving the lower part of the right forearm and extending up a distance of two-fifths on the ulnar side and two-fifths on the radial. He remained in the hospital until October 31, 1914, and received nine doses of the mixed toxins, ranging from $\frac{1}{6}$ to $2^{1}/_{22}$ m., the highest temperature reached being 102.5°. The injections were made locally into the tumor. No marked change was noticeable from the treatment and the patient was

referred back to Doctor Lilienthal for amputation, who operated upon him on November 2, doing a circular amputation of the humerus in its lower third. A little more than four weeks later, about the middle of December, the patient died of metastases of the lungs. A letter from Doctor Mandelbaum, who had again carefully gone over the sections in this case, states that there were found no giant-cells in either specimen. The X-ray picture in this case closely resembles the picture of the preceding case that recovered under toxins alone.

CASE VIII.—*Sarcoma of the Fibula of Marked Malignancy, Trauma.* H. D., male, twenty years, referred to me by Dr. E. J. Mitchell, of Memphis, Tennessee, on April 18, 1918. The patient had been perfectly well until ten weeks ago when, while wrestling at school, he sprained the right leg just below the knee. Two weeks later he began to have slight pain; a little later lameness developed, but no appreciable swelling, and frequent X-ray examinations showed nothing abnormal. About two weeks ago the patient was examined by Doctor Mitchell, who detected a slight swelling in the outer upper aspect of the right leg. An exploratory operation was performed by Doctor Mitchell on April 14, an incision 5½ inches long being made over the fibula from the head downward, and a tumor was found involving the entire upper four inches of the fibula, extending into the knee-joint. The report of the microscopical examination made by Doctor Kraus, of Memphis, reads: "Endothelioma with some areas of rapid growth, round-celled type and others of slower development with central mucoid; the proliferation around pre-formed spaces is typical." The wound was drained and the patient referred to me for advice and treatment.

Physical examination at this time showed a 6-inch cicatrix beginning over the upper end of the fibula and extending to the upper and outer aspects of the knee; the exploratory wound was packed with gauze and there remained a good sized rubber drainage tube. There was very little swelling of the knee or leg and but slight tenderness over the knee, apparently little effusion of the joint. An X-ray picture taken showed extensive involvement of the upper portion of the right fibula, also evidence of involvement of the knee-joint. The patient has lost 20 pounds in weight and motion of the joint is extremely painful. The patient was put upon the mixed toxins of erysipelas and bacillus prodigiosus in doses to produce a slight chill. On the 21st of April the patient was given 6000 mc. hours of radium over the outer aspect of the tumor, and on April 25, a rubber tube containing 99 mc. of radium and four silver tubes were inserted into the sinus left from the exploratory operation covering the upper four inches of the fibula. It was left in place for six hours.

April 30: The tumor has steadily increased in size, in spite of the treatment; the effusion of the knee-joint is much more marked and there has been considerable swelling of the whole lower portion of the leg. At the site of the drainage tube in the upper portion of the wound there is beginning to appear a fungoid growth of tumor, bleeding very readily. The disease is progressing very

rapidly in spite of the treatment and immediate amputation is advised.

The toxins were given systemically for a considerable period after amputation; about four months later metastases developed in the chest. The disease ran a very rapid course, causing death six months from the time of amputation.

As regards the advantages and disadvantages of resection, I personally have never employed resection and bone-implantation in any of my cases. The end-results in the group of cases shown before the American Surgical Association—(*a*) extensive sarcoma of lower end of femur, well four years and eight months; (*b*) extensive sarcoma of upper end of tibia, well three years and ten months—show that Nature unaided is able to restore large defects in the long bones if the tumor tissue has been destroyed. Also in these cases recent X-ray pictures taken show in one case almost complete restoration of five inches of the upper end of the tibia, and in the other case a very successful attempt to reconstruct the lower end of the femur with formation of a new condyle in place of the one destroyed. If we can cure the disease and keep the limb at rest for a long period of time in plaster-of-Paris, very satisfactory results can be obtained without resection. In the cases that have come under my observation in which resection of the upper end of the humerus was performed by other men, the results have been so unsatisfactory that I hesitate to recommend this method of treatment. In one of these cases, rapid generalization of the diseases prevented an opportunity to judge of the end-results as regards the usefulness of the arm, and in the other, now six months after operation, the arm is entirely useless. I doubt if it will ever have any functional value even if the disease is cured, which at present is doubtful.

CASE IX.—*Sarcoma of the Humerus Treated by Resection.* E. D., male, twenty-eight years old, always well until September, 1917, when he received a series of vaccinations preparatory to entering the army. All the vaccinations were given in the muscles in the upper part of the right arm. A few weeks later, he began to have soreness at the site of inoculations and also loss of function of the arm. A swelling appeared and slowly increased in size until January, 1919, when he was operated upon by Doctor Hitzrot at the New York Hospital. A portion of the humerus was resected and grafts from the tibia implanted. On February 28, 1919, Doctor Hitzrot referred the patient to the Memorial Hospital for radium treatment. From that time up to the present, he has had a total of 75,000 mc. given at various occasions, varying from 9000 to 40,000 in a single application. The treatment has been given by Doctor Janeway. X-ray examination shows the absence of 3½ inches of the right humerus. The pathological diagnosis made at the New York Hospital reads as follows: "Osteochondrosarcoma; diffuse, infiltrating growth, involving the entire bone, extending into the surrounding muscle and fascia; extensive infiltration of muscle tissue. Diagnosis: osteogenetic sarcoma."

X-ray examination of the chest shows considerable infiltration about the right hilum, extending up into the apex; no definite glands.

July 1, 1919: The patient is still under treatment. A recent X-ray picture taken failed to show any evidence of a tumor either in the bone or soft parts, and chest examination is negative. It is too early to regard the disease as under control, but it is almost certain that the arm will be of little use, even if the patient is cured of the sarcoma.

The following case of periosteal sarcoma of the humerus is interesting from the fact that there are few recorded cases in which the patient has been well over three years. Of 54 cases of sarcoma personally observed, only 2 are known to be well beyond three years.

CASE X.—Mr. L., aged thirty-five years, was referred to me by Dr. J. M. T. Finney, of Baltimore, nine years ago. The tumor developed within two weeks after a spiral fracture of the humerus, and Doctor Finney believed that amputation offered no hope of saving the patient's life. In this case a large, rapidly growing tumor apparently disappeared under the toxin treatment alone; six months later it recurred and I performed a shoulder-joint amputation. This operation was followed by a very large recurrence in the pectoral muscle, which was only partially removed, and then prolonged toxin treatment given. The disease finally disappeared and the patient is now in good health, eight years later. A microscopical examination had been made by Doctor Bloodgood and also by Doctor Ewing; both pronounced it a highly malignant spindle- and round-celled sarcoma, no giant-cells.

This case has already been reported in full in the ANNALS OF SURGERY.

The following history illustrates the difficulties often associated with the early diagnosis of malignant tumors of the long bones. It plainly shows that in some cases it is practically impossible to make an early diagnosis, even with the aid of the X-ray and exploratory operation and microscopical section.

CASE XI.—*Spindle-celled Sarcoma of the Radius with Metastases.* W. T., aged twenty-six years, referred to me by Dr. David Felderbaum on March 26, 1919, with the following history: The patient, a college man, has always been very active in athletics; played much foot-ball, but does not remember any particular injury to the arm. Two years ago he first noticed what was believed to be rheumatic pain in the left arm, but there was absolutely no swelling. Three months later he had another severe attack of local pain, without swelling; physician could feel no tumor whatever. The first X-ray was taken in September, 1917, and showed the condition to be probably osteomyelitis. First operation in October, 1917, at the Mt. Sinai Hospital, by Dr. Alexis Moschcowitz. An incision was made and the bone scraped. The tissues removed were examined by Doctor Mandlebaum, who reported "no evidence of sarcoma." A month later the

pain returned and Doctor Moschcowitz, suspecting sarcoma, again operated. At this time pathological examination of the tissues removed showed sarcoma of the small spindle-celled type. In March, 1918, a third operation was performed by Doctor Moschcowitz, who resected the upper half of the radius. The pathological examination again showed small spindle-celled sarcoma. The patient remained perfectly well until November, 1918, one and one-half years later, when he began to feel pain in the right hip. A few weeks later a soft swelling developed over the occipital protuberance; this has been increasing in size steadily up to the present time (March, 1919). He also has had severe pains in the lower side of the right thorax, accompanied by some cough, but without loss of weight. The X-ray pictures revealed a large spherical mass replacing the entire root of the left lung and small numerous masses in the lower part of the right lung, apparently mainly pleural. There is a small amount of fluid in the right chest and numerous small nodules along the root of the lung. The picture of the skull shows a cystic condition eroding the occipital bone. The patient was referred to me for radium and toxin treatment. In view of the advanced condition of the disease and the marked generalization, it was decided to try the effect of intravenous injections of the active deposit of radium, together with a radium pack over the tumors of the skull. There was considerable decrease in the size of the tumor of the skull, and slight improvement in general condition. At the present time the pain is returning and the tumors are increasing in size and generalization of lesion progressing.

END RESULTS IN A SERIES OF 250 CASES OF SARCOMA OF THE LONG BONES OBSERVED FROM 1890 TO 1919

The serious and almost hopeless prognosis of sarcoma of the long bones from a surgical standpoint was well brought out at a symposium on Sarcoma of the Long Bones before the Royal Society of Medicine in London, November, 1912. Of a series of 61 cases observed at St. Bartholomew's Hospital during the preceding ten years, all were treated by amputation, with the following results:

Of 25 cases of periosteal sarcoma of the femur not a single patient was alive over three years later; of the myeloid type, 4 in number, only 2 survived the three-year period. Of 8 humerus cases, not a single patient reached the three-year limit. Of 2 radius cases, 1 died and 1 remained well over three years. Of 11 periosteal sarcomas of the tibia, 1 remained well over three years, and of 3 myeloid type, 1 remained well over three years. Of 61 cases of sarcoma of the long bones only 5 were well over the three-year period.

The statistics of St. Thomas's Hospital, covering the same period, show 28 periosteal cases and 17 myeloid. Of the former, not a single patient remained well over three years; and of the latter, only 5 (all of the giant-celled type) remained well for that length of time.

It is worthy of note that conservative treatment was not employed in any one of these cases, all having been treated by amputation.

Personal Cases.—An analysis of cases personally observed from 1890 to 1919 shows:

Femur	117
Humerus	54
Tibia	40
Fibula	8
Radius	12
Ulna	7
Clavicle	11
Metacarpal	2
Total	251

Of 117 femur cases, 21 were alive and well over three years. Of these amputation was performed in 15 cases, preceded or followed by a course of toxin treatment, and in no less than 6 cases the limb was saved by conservative treatment. Of these 6 cases, 3 were of the periosteal type and 3 central mixed, giant- and spindle-celled.

CASE I.—A small round-celled periosteal sarcoma involving two-thirds of the shaft of the femur, with extensive metastases in the ilium. Patient was treated with X-rays in February, 1902, for the tumor of the femur. Later a very large metastatic tumor developed in the ilium and was treated with toxins alone. The disease entirely disappeared, and he remained well for ten years, and then died of carcinoma, which developed in an old X-ray burn of the thigh.

CASE II.—Extensive periosteal sarcoma of the femur, clinical and X-ray diagnosis. Amputation advised by several surgeons, but refused. Treated with toxins alone. Well eight years.

CASE III.—Extensive periosteal sarcoma of the femur, small round-celled, no giant-cells; diagnosis confirmed by microscopical examination at the State Laboratory of North Dakota. Case pronounced beyond hip-joint amputation by Dr. Wm. J. Mayo. Toxins advised and carried out by Doctor Williamson, of North Dakota. Limb saved, patient in good health ten years later.

CASE IV.—Extensive central sarcoma of the upper portion of the femur, pronounced inoperable by Dr. A. P. Gerster. Diagnosis (giant-celled sarcoma) confirmed by microscopical examination. Pathologic fracture; curetting, followed by toxins; complete recovery, reunion of bone, useful limb. Patient well when last observed eight years later.

CASE V.—Central sarcoma of the femur, with extensive involvement of the knee-joint, believed to be too far advanced for conservative treatment and amputation recommended by Doctor Gibney and myself, but refused by patient. Entire disappearance of the disease under toxins alone, and patient well at present with a useful limb four years and nine months later.

CASE VI.—Sarcoma of lower end of femur, with extensive involvement of knee-joint and upper end of tibia. Amputation advised by several surgeons, including myself, as the condition was regarded too far advanced for conservative treatment. Complete recovery under curetting and long continued toxin treatment, supplemented at the end of two months by radium in the form of a pack, and 100 mc. of radium emanations introduced into the sinus in a steel needle. Patient well and walking about with scarcely any limp three years later.

Another case might be included, inasmuch as, while there was no microscopical

examination made, the clinical and X-ray findings pointed very strongly to a periosteal sarcoma of the femur. The tumor disappeared under the toxins alone and the patient was in good health ten years later; and still another case of periosteal round-celled sarcoma of the femur successfully treated with the toxins by Doctor Runyan, of Little Rock, Ark., under my direction. An exploratory operation was made in February, 1913; microscopical examination, small round-celled osteosarcoma; complete disappearance under four months' toxin treatment; patient in good health with a useful limb four years later.

Of 40 tibia cases, 8 were known to be well for a period of more than three years after operation. Of these cases amputation was performed in 4, and in 4 the limb was saved. The cases in which amputation was done are as follows:

CASE I.—Giant-celled sarcoma of tibia; amputation of the thigh; patient remained well for seven years and then died of lung metastases.

CASE II.—Central sarcoma of upper end of tibia; amputation alone; patient well ten years.

CASES III AND IV.—Both periosteal sarcoma, well over three years; amputation, followed by toxins as a prophylactic.

CASE V.—Periosteal sarcoma of tibia, well five years after amputation, died with metastasis of skull.

The 4 cases in which the limb was saved are as follows:

CASE I.—Periosteal spindle-celled sarcoma of tibia; entire disappearance under toxins; patient well at present, twenty years.

CASE II.—Central sarcoma of upper end of tibia; mixed-celled (round-, spindle- and giant-celled); disappearance under toxins; patient well eight years.

CASE III.—Mixed-celled sarcoma (spindle and giant cells) of upper end of tibia; twice recurrent; disappearance under toxins and radium; patient well three years later.

CASE IV.—Sarcoma of lower end of tibia. Giant-celled and spindle-celled. Three times recurrent. Disappeared under toxins and X-ray, 1905. Well at present, fourteen years.

Sarcoma of the humerus has long been regarded as the most malignant of all types of tumors of the long bones, and my own series of cases supports this view. Of 53 cases of sarcoma of the humerus, only 2 survived the three-year period, and both of these cases can reasonably be regarded as cures. In the other cases the patients have all died with the exception of 2, who are under treatment at present with only a moderate chance of getting control of the disease. In the 2 successful cases, 1 was a sarcoma of the upper end of the humerus, involving the portion of capsule; exploratory operation done by Dr. J. Bapst Blake. The disease was found to be quite inoperable, too far advanced for shoulder-joint amputation. The toxin treatment was carried out under my direction. The tumor entirely disappeared and the woman completely regained the use of her arm, and remained well for twelve years, when she died from some independent trouble. The diagnosis was round-celled sarcoma.

NOTE.—Doctor Bloodgood says he has never seen a giant-celled tumor of the humerus.

CASE II.—A very malignant periosteal, round- and spindle-celled sarcoma, no giant-cells, starting in the middle of the humerus, following a recent fracture. The tumor

apparently disappeared under toxins alone; pathologic fracture reunited; recurrence in the head of the humerus six months later; amputation; large recurrent mass in the pectoral region; incomplete removal followed by toxins; final recovery; well eight years.

Of 12 cases of sarcoma of the radius, 4 remained well beyond the three-year period. They are as follows:

CASE I.—Large giant-celled tumor of the radius, treated by another surgeon by simple curetting; observed by myself; perfectly well eight years later.

CASE II.—Extensive sarcoma of the radius, involving the ulna; amputation, followed by toxin treatment; well ten years.

CASE III.—Giant-celled sarcoma of lower end of radius; curetting by Doctor Hartley; amputation advised but refused; complete recovery under toxins; patient well eleven years.

CASE IV.—Giant-celled sarcoma of lower end of radius; small portion removed for microscopical examination; no curetting; disappearance under toxins alone; well three years later.

CASE V.—Extensive sarcoma of lower end of radius, with involvement of the ulna. Clinical and X-ray findings permitted no doubt as to the correctness of the diagnosis; amputation advised by several surgeons but refused; complete disappearance under toxins alone in May, 1918. Patient well at present with a useful arm.

This may have been a giant-celled tumor, although the bony shell has been destroyed, and the tumor was of rapid growth.

Of the 6 ulna cases, one spindle-celled sarcoma in which amputation was done remained well for seven years and then died of abdominal metastases.

Of the 8 cases of sarcoma of the fibula, not a single patient is known to have remained well beyond the three-year period.

Of the 11 cases of sarcoma of the clavicle, a total excision was done in 3, followed by the use of the toxins. This group is as follows:

CASE I.—Sarcoma of clavicle; total excision three weeks after noticing a rapidly growing tumor, which followed immediately after an injury; toxins given; local and metastatic recurrences within three months; death shortly after; whole course of disease was less than five months.

CASE II.—Total excision of clavicle for a rapidly growing periosteal sarcoma (round-celled, no giant-celled), followed by a long period of toxin treatment; patient in good health at the present time, with perfect use of arm, nine years later.

CASE III.—Total excision of clavicle for a round-celled sarcoma, periosteal, which Dr. Maurice Richardson referred to me for toxin treatment as a prophylactic. Toxins given for six months; patient in good health nine years later.

These cases are of particular interest inasmuch as the high malignancy of sarcoma of the clavicle is well known, there being few cases of cure on record—except the Valentine Mott case, in which the diagnosis is now believed to be " chondroma " instead of " sarcoma."

A brief summary of the cases that have remained well over the three-year period:

Patients remaining well more than three years, 35. Of these the disease recurred and proved fatal after three years in 5 cases. One tibia, seven years; 1 ulna, seven years; 1 femur, five years; 1 tibia, five years; 1 femur, five years.

TYPE OF TUMOR IN CASES WELL OVER THREE YEARS

Periosteal

Femur	8
Clavicle	2
Radius	1
Ulna	1
Humerus	1
Tibia	1
Metatarsal	1
Total	15

There were no giant-celled tumors in this series of cases. One case was pronounced a chondroma at the time of the first operation (hip-joint amputation performed by another surgeon); he remained well for five years, after which the disease recurred locally; I performed a second extensive operation, followed by a course of toxin treatment; the disease recurred again three years later, involving the pelvic bones; condition inoperable; failed to respond to large doses of radium; hopeless when last seen. This case proved to be a chondrosarcoma.

One patient with a spindle-celled sarcoma of the ulna remained well for seven years after amputation, and then developed an inoperable abdominal recurrence, causing death in less than a year. Another case, a periosteal ossifying sarcoma treated by amputation, later followed by toxins, remained well for about three years and then died of metastases.

In this series of cases the diagnosis was confirmed by microscopical examination, with the exception of one case, and in this, the rapid growth of the tumor in a young adult, combined with the very definite evidence of the X-ray picture, left little doubt as to the correctness of the diagnosis. The tumor disappeared under the toxins and the patient remained well for seven years.

In this group of periosteal tumors, amputation was performed in 9 cases, followed by toxins in 7. (For a more detailed history, see the preceding notes.)

Central

Femur	7
Tibia	5
Radius	3
Humerus	1
Total	16

Cases in which the Limb was Saved.—In this series of cases it has been found possible to save the limb in 17 cases; 11 by the use of the toxins alone; 4 by a combination of toxin- and radium-treatment; 2 by curetting (the latter 2 were giant-celled sarcomas, or giant-celled tumors). Of the 17 cases in which the limb was saved, 6 were of periosteal origin and 12 of central origin. Fourteen have remained well more than three years.