

# AN APPARENT RECOVERY FROM MULTIPLE SARCOMA\*

WITH INVOLVEMENT OF BOTH BONE AND SOFT PART TREATED BY THE TOXINS OF ERY-  
SIPELAS AND BACILLUS PRODIGIOSUS (COLEY)

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THE patient, Captain G. B., whose age upon admission on June 27, 1925, was 31 years, occupation master mariner, gave the following history: Sustained a bruise of left shin bone February 25, 1918, by being thrown against a hatch. The bruise soon healed and the leg appeared normal within six weeks. Thirteen months later he began to have severe pain at the spot where the skin had been bruised. This pain was accompanied by swelling and fever. The pain, but not the swelling, temporarily disappeared in about one week, followed by recurrent attacks of pain every two or three weeks, for a period of three months, during which time he was making a long voyage from Australia to New York. Shortly after his return to New York a roentgenogram of the leg revealed osteomyelitis of the tibia, and an operation was performed at St. Joseph's Hospital, Paterson, N. J., August 18, 1919. He remained in the hospital until November 23, 1919, and was still suffering pain at the time of discharge and walking on crutches.

He was admitted to U. S. Marine Hospital No. 21, New York, March 31, 1920, and remained until July 26, 1920, during which time he was treated by physiotherapy which relieved the pain. He went back to sea until March, 1921, and then came back to the hospital for two weeks, again back to sea off and on until March 3, 1924, when he was re-admitted to the Marine Hospital, New York, for operation for

chronic appendicitis and bilateral inguinal hernia. He was discharged March 28, 1924, recovered of these conditions but still having occasional attacks of pain in the leg.

He was readmitted to the hospital May 10, 1924, and remained under treatment until September 25, 1924, during which time he received baking and ultraviolet rays to the affected leg. After discharge this time all pain had gone; there was no swelling and the patient appeared to be cured.

Figure 1 taken October 2, 1924, shows marked corticle thickening and irregularity of the middle third of the tibia with greater density of the cortex, obliteration of the medullary cavity in the middle third, and marked periosteal roughening with bony projections, especially anteriorly. At this stage the diagnosis was osteomyelitis.

On April 24, 1925 he noticed swelling in the shin bone a little higher up than the site operated on in 1919. He was readmitted to the hospital and operated on in May. Osteomyelitis was found with free pus in the marrow and a sequestrum of dead bone. About two weeks after this operation the bone began to "swell" and ache just below the knee.

Figure 2, taken June 30, 1925, shows marked decalcification of the upper third of the left tibia with only part of the skeleton of the bone remaining, appearing like a bone desolving under corrosive fluid in the anterior upper third of the tibia. Shortly afterwards injections of sodium

\*This case was reported in *Military Surgeon*, July, 1927 (Lxi, 42-47), but in view of the fact that it is of such unusual interest, we have decided to republish it in full with the important roentgenograms and microphotographs which were not included in the original report.

iodide were begun and given every third day intravenously until a total of fifty grams were given. Figure 3, made September 13, 1925, shortly after the sodium iodide treatment, shows further advance

of bone was removed which was reported by the laboratory as myelosarcoma, very cellular, with slight fibro-sarcomatous structure: Figure 4 is a section through tumor of tibia. Fixation is in formalin 10



FIG. 1. October, 1924. Marked cortical thickening and irregularity; obliteration of medullary cavity; periosteal roughening. Diagnosis at this time: osteomyelitis.

of the erosion, with pathological fracture at the junction of the upper and middle third of the tibia, anteroposterior and lateral views.

On September 11, 1925, a small piece

per cent. The growth is composed of a mass of cells without regular arrangement. The cell units are small, polyhedral, with indistinct borders, often appearing as a syncytium. They are very uniform in size.

The cytoplasm is clear and stains poorly. The nuclei are generally oval, with one, two or three distinct chromatin granules. Mitotic figures are frequent. Strands of fibrous tissue pervade the growth, in some areas more conspicuous than in others. Blood vessels are not numerous.

was reported by the laboratory as myeloid sarcoma metastatic. Figure 6 shows section through lymph-node in mid-line of abdomen, just above umbilicus. Fixation is in formalin 10 per cent. The normal structure of the lymph-node is entirely broken down replaced by the irregular masses of invad-

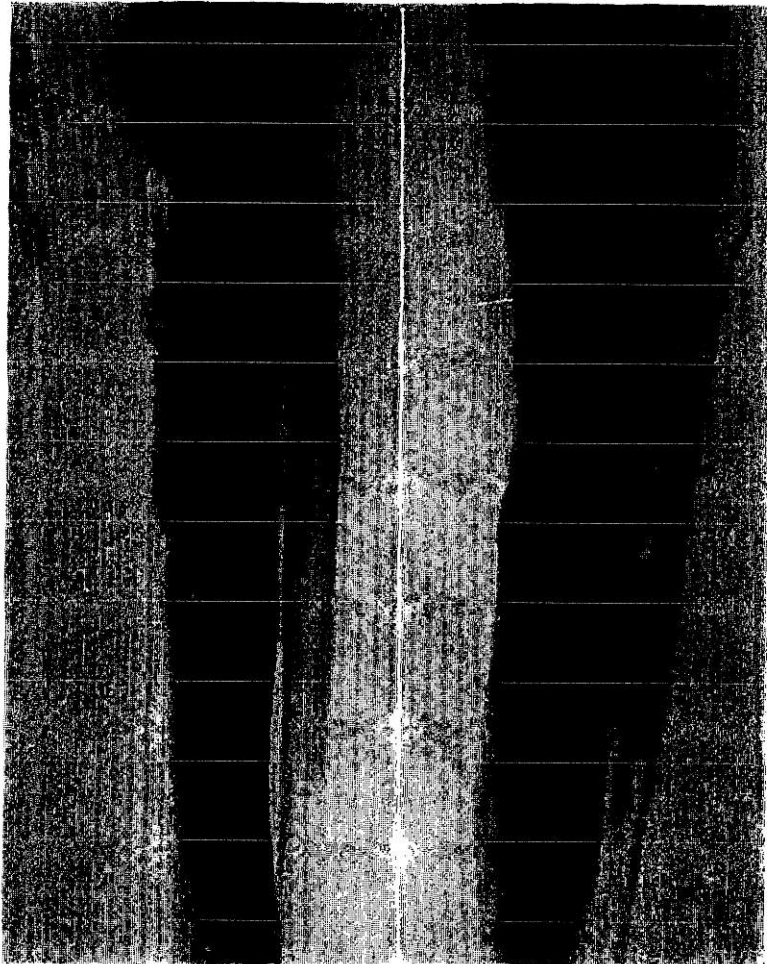


FIG. 2. June 30, 1925, shows marked bone destruction or loss of calcium; condition now begins to resemble a sarcoma rather than an inflammatory process.

Amputation of thigh in middle third was performed September 21, 1925. The wound healed in two weeks.

The pain in the stump continued. Figure 5 of the stump of the left femur 60 days after amputation, shows the periosteum intact, the cortex and medulla sharply demarcated. On December 12, a nodule was noticed beneath the skin just above the umbilicus, a specimen from which

ing tumor cells which resemble those of the growth on the tibia. Lymphocytes are intermingled in places with tumor cells. Ewing Taylor was the pathologist.

January 5, 1926, the patient presented the following conditions: The end of the femur-amputated stump had a tumor mass about the size of a man's fist on its inner aspect, with an additional growth about the size of a lemon, over its outer aspect.

The skin of the stump appeared quite healthy. There was a mass of new growth in the left inguinal region which was about 2 inches long, 1 inch wide and 2 inches thick. There was a supraumbilical mass which involved the skin. This mass was about  $\frac{3}{4}$  of an inch in diameter. The

quite severe (Chart A). Subsequent series of injections after the patient had established tolerance for Coley's toxins, did not produce such reactions, even with large doses (Chart B).

On January 22, the circumference of the stump was  $17\frac{1}{8}$  inches. The mass in the



FIG. 3. September 13, 1925, shows rapid extension of the process with pathologic fracture; and now the evidence in favor of a neoplasm is unmistakable. The picture is quite characteristic of the endothelial myeloma type (described by Dr. Ewing).

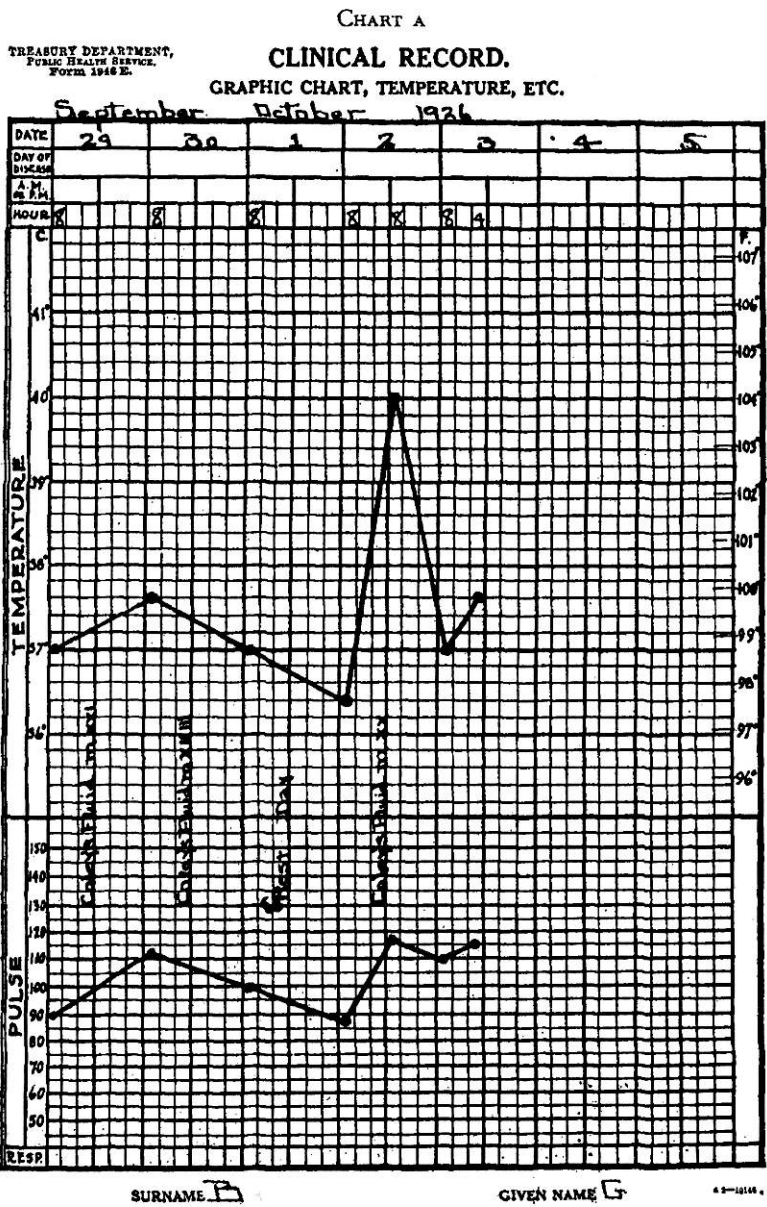
circumference of the stump was 19 inches.

Injections of Coley's toxins were begun, the dose  $\frac{1}{4}$  of one minim. This dosage was increased  $\frac{1}{2}$  minim daily until the patient was receiving  $6\frac{1}{2}$  minims. Temperature reactions following injections were

groin had disappeared. The supraumbilical mass was decidedly smaller, softer and lighter in color. The patient looked paler no doubt due to severe reactions following injections. His weight was  $117\frac{3}{4}$  pounds. The injections were held at  $6\frac{1}{2}$  minims from January 25 to February 2, 1926, when

they were increased 1 minim a day until the patient was receiving 18 minims daily. On February 20 they were discontinued because of extreme weakness of the patient. At this time the stump had taken on new growth, associated with considerable edema of both good leg and stump.

of Coley's toxins were injected directly into the tumor mass on the stump. The dosage was gradually increased each day until April 7, at which time he was receiving five minims directly into the tumor.



growth, associated with considerable edema of both good leg and stump.

On March 17 there were three small vesicles on the end of the stump. The supraumbilical growth had increased considerably in size and was now the size of a large lemon. On March 27 two minims

Each injection was followed by considerable temperature reaction. Figure 7 taken February 23, 1926, shows the stump of the femur undergoing dissolution. There is hardly a skeleton of the cortex seen with the bony substance, primarily the calcium, disseminated into the soft structures in all



directions, as if transported by the lymphatics and veins.

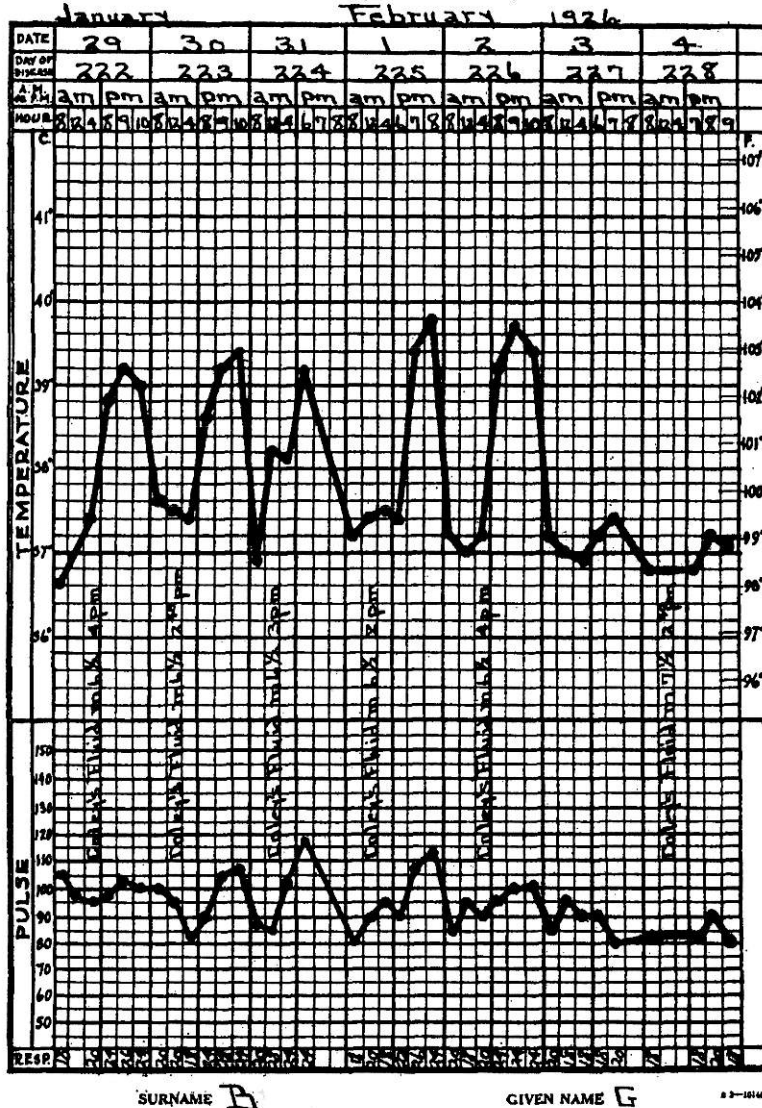
On May 5, 1926, several small nodules were felt under the skin of the abdomen. During May and June the patient grew

the circumference of which was 31 inches. The end of the stump had broken down over an area about 5 inches in diameter, from which there was a foul, profuse, ichorous discharge.

CHART B

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steadily worse with metastatic growths appearing in many parts of the body, among which was considerable involvement of the right clavicle and multiple tumors in the scalp, cranial bones, and cervical vertebrae.

About this time the maximum growth of the tumor in the stump was attained,

On August 5, 1926, Coley's fluid was again begun with a dosage of two minims and increased a minim a day until he was receiving 17 minims at a dose. The dose was held at this point until September 4. By this time improvement was marked; edema of the good leg and the stump had

decreased very much and the stump had almost healed. The supraumbilical mass had practically disappeared; areas of involvement of the scalp had disappeared, the clavicular tumor had decreased considerably in size.

An additional series of injections was begun September 19 and continued for three weeks.

On November 22, the general condition

in the scalp and skull could no longer be discerned. There was still present some degree of thickening and roughening of the right clavicle.

The pathological diagnosis of sarcoma was concurred in by Drs. Ewing Taylor, James Ewing, and E. A. Codman. The roentgenological diagnosis was made by Dr. Frank Liberson.

The patient was discharged from the

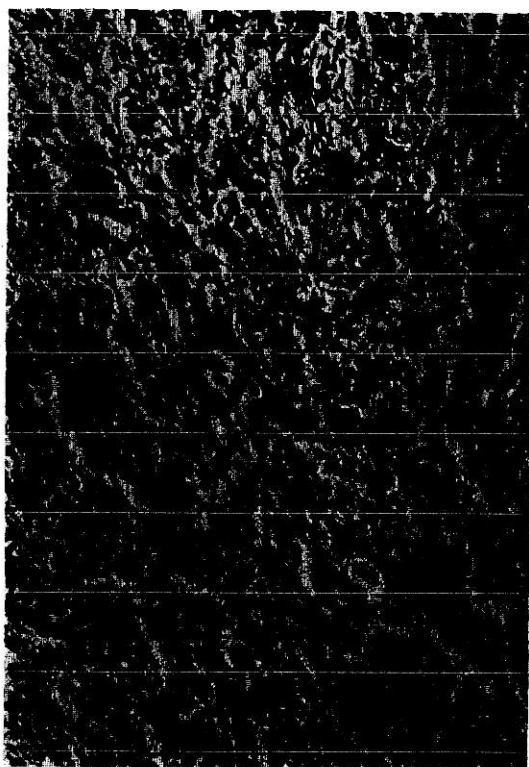


FIG. 4. Microphotograph of specimen of bone removed at exploratory operation on Sept. 11, 1925.

of the patient was excellent, weight being 147 pounds. The stump was 17 inches in circumference, a reduction from 31 inches in May. The old discharging wound of the stump was entirely healed, the skin quite leathery and underlying it was a tough fibrous mass believed to be scar tissue. Growths on the abdomen had disappeared. Just above the umbilicus there was an area of pigmentation of the skin which was  $3\frac{1}{2}$  inches long by  $2\frac{1}{2}$  inches wide and corresponded to the site of the former tumor. Areas of involvement

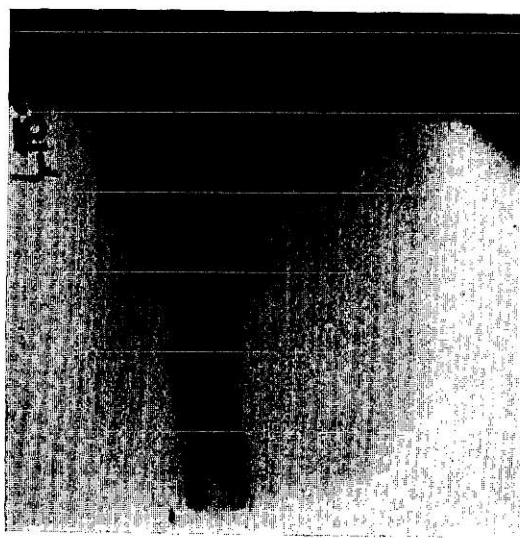


FIG. 5. Stump of femur on Nov. 25 or sixty days after amputation. No evidence of recurrence.

hospital apparently recovered, December 5, 1926.

At our suggestion the patient returned to the hospital February 13, 1927, for further treatment. Every third day he was given injections of Coley's toxins, beginning with 3 minims and the amount doubled each time, until 30 minims were given at a time. He was discharged March 27, 1927, in good condition.

He again returned to the hospital, according to suggestion, from October 23, to December 7, 1927, and was given Coley's toxins every third day up to 30 minims.

The patient was last examined January 9, 1928, at which time there was no evidence of disease present. There still remained as evidence of former disease, scarring, discoloration and slight thickening of skin over stump and abdomen (in

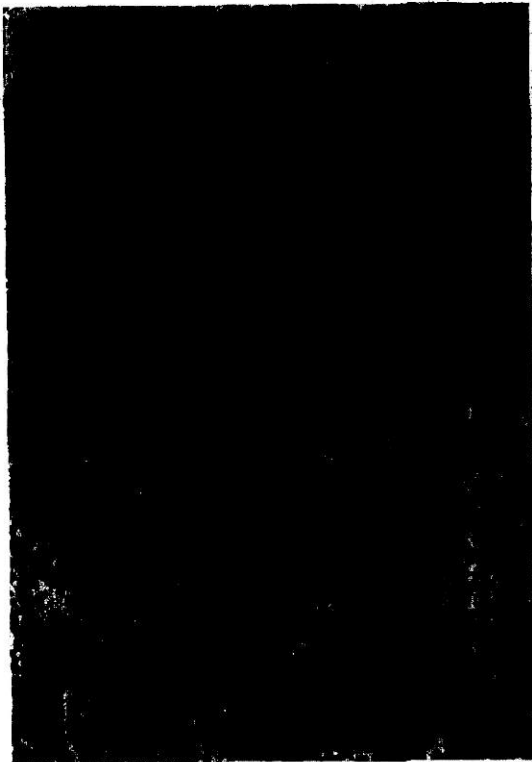


FIG. 6. Microphotograph of section from a metastatic tumor beneath the skin just above the umbilicus, removed on Dec. 12, 1926. Diagnosis: myelosarcoma, metastatic.

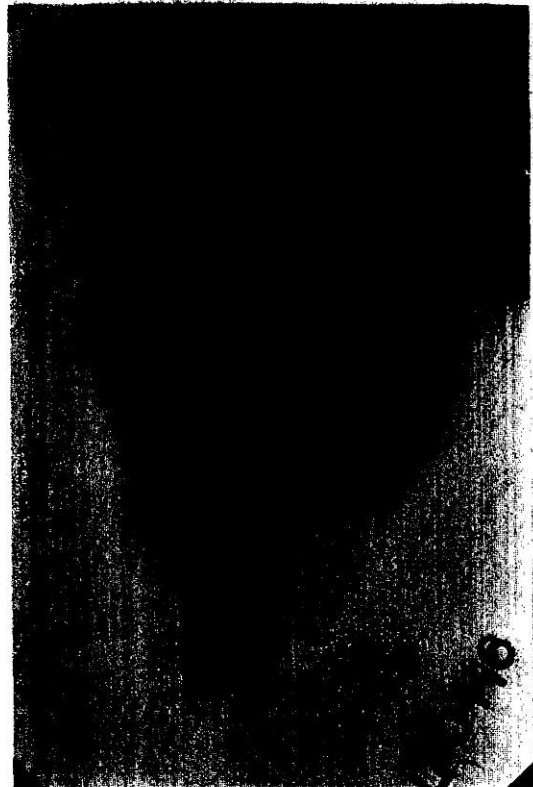


FIG. 8. Shows the condition of the femur and stump at present, Jan. 8, 1928, two years after the beginning of the toxin treatment and fourteen months after the disappearance of the metastatic tumors. Shows the marked new bone formation replacing the bone destroyed by the tumor.

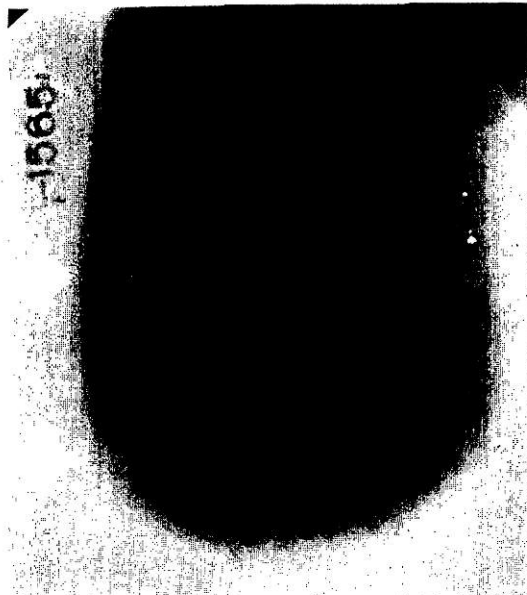


FIG. 7. Feb. 23, 1926, shows very extensive recurrence in stump and femur, with marked destruction or dissolution of bone extending nearly to the trochanter.

areas corresponding to former tumors) and slight thickening and roughening of the right clavicle, all of which appeared to be scar tissue and was essentially the same as conditions above reported November 22, 1926. His weight was 143 pounds.

Figure 8, taken January 9, 1928, shows the appearance of the stump at the present time. The photograph of the patient was taken January 9, 1928. (Fig. 10.)

On December 1, 1927, the patient was presented at the clinical conference at the Memorial Hospital, New York. The discussion at this conference by Dr. Coley follows:

COMMENTARY BY DR. WILLIAM B. COLEY OF NEW YORK

I am greatly indebted to Dr. Christian and Dr. Palmer for permitting me to present their patient at the staff-conference



of the Memorial Hospital on December 1, 1927. At this time the patient was apparently in the best of health; he had gained more than forty pounds in weight; and careful examination failed to reveal any evidence of the numerous metastatic tumors that were present in the bones and soft parts when the toxin treatment was

am almost certain that I should not have continued the treatment after three months when not only no improvement had been noticed but marked increase had taken place in the metastatic tumors and especially in the recurrent tumor of the stump (an increase of from 17 to 31 inches). In the second place, I am quite sure that



FIG. 9. Condition on Jan. 8, 1928, or two years after beginning toxin treatment. Stump entirely normal; and roentgenogram shows no evidence of disease.

begun. More than a year has elapsed since the last follow-note was made in the original report.<sup>1</sup>

I believe this is one of the most remarkable cases of malignant tumor of the long bones that has ever been published, and I am quite willing to admit that, had the patient been under my care, he would probably not be alive today. In the first place, I



FIG. 10 showing condition of patient on Jan. 8, 1928, two years after beginning treatment and fourteen months after disappearance of multiple metastatic sarcoma of stump of femur, skull, clavicle and soft parts of various regions.

I should not have dared to increase the dose to such a large amount (30 minims). However, it was not until these large daily doses were given that the improvement was noted, which improvement continued until all the tumors had disappeared. I have learned more from this one case than from any other that I personally have treated, and I feel that many of the past failures might have resulted otherwise had larger doses and more frequent injections of the toxins been given.

In view of the roentgenogram findings, the microphotograph and the type of multiple metastases that involved both bones and soft parts, I believe we are warranted in placing this case in the group of endothelioma or endothelial myeloma (so fully described by Dr. Ewing).

This case of Dr. Christian and Dr. Palmer together with the remarkable case of Dr. Howard Lilienthal, presented at the meeting of the New York Surgical Society in December, 1926,<sup>2</sup> prove that it is possible to cause the complete disappearance of a far-advanced inoperable sarcoma with extensive multiple metastases, by systematic injections of the mixed toxins of erysipelas and *Bacillus prodigiosus*, without radiation or any other form of treatment.

While too short a time has elapsed in the first case to permit it being classed as a "cure," Dr. Lilienthal's patient is well now three and two-third years since the treatment was begun. This case is almost as remarkable as the one under discussion. While Dr. Lilienthal describes it as an inoperable mediastinal tumor, on exploratory operation he found extensive involvement of the ribs and spine; and from these findings, as well as the clinical history, I am inclined to believe it to be, more probably, a primary sarcoma of the spine and ribs with secondary metastasis in the mediastinal glands. At any rate, the child had a large, inoperable

tumor of the mediastinum with involvement of the ribs and spine, resulting in complete paraplegia. At the time the treatment was begun, the case was regarded as entirely hopeless by every surgeon who had seen it. Under a very short course of toxin treatment covering a period of three weeks during which only eleven injections were given, the child made a complete recovery and is well at the present time. In this case, no radiation or other form of treatment but the toxins was given.

It is very fortunate that in both of these cases the diagnosis was confirmed by a number of eminent pathologists, including Dr. James Ewing.

I believe that these two cases, published within a few months of each other, furnish sufficient answer to the criticism often made in the earlier years and not infrequently in recent years that other surgeons have been unable to obtain the same results from the method (toxin treatment) as I have. Those who are interested in the results obtained in various types of bone sarcoma, are referred to my paper recently published in the *Archives of Surgery*.<sup>3</sup>

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