Osteogenic Sarcoma: End Results Following Immunotherapy With Bacterial Vaccines, 165 Cases or Following Bacterial Infections Inflammation or Fever, 41 Cases

Helen C. Nauts

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INTRODUCTION

Osteogenic sarcoma is the most frequently seen primary sarcoma of bone. However, since the survival rate of patients treated by surgery and/or radiation has been only 5 to 19%, there has been little opportunity to study a large number of long term survivors. (54; 55; 56; 99; 106; 112; 127) Following conventional amputation and/or radiation most metastases become evident within one or two years and most deaths occur within two or three years after diagnosis.

Amputation has been the treatment of choice for this tumor for over 50 years, with little change in the survival rate. Massive preoperative radiation was tried between 1942 and 1972 in several centers here and abroad with little change in the survival rate. (13; 17; 70; 87; 100; 105)

Conservative Surgery:

W.B. Coley was the first to suggest that by utilizing "prophylactic" or adjuvant treatment designed to destroy incipient metastases, one could hope to improve the end results. (30) He also was the first to suggest that toxin therapy combined with conservative surgery (curettage or resection) might enable one to avoid amputation in certain cases of sarcoma of the long bones. (32) This was seldom attempted, but among the 17 cases so treated (six of which were inoperable), six patients remained well and free from the disease 6 to 50½ years after onset with a normal functioning limb: Table 1, Case 24, recurrent fibrosarcoma of the humerus, died 50½ years after onset of heart failure; Case 27, osteogenic sarcoma of the tibia, death over 5 years later of tuberculosis; Case 31, chondrosarcoma of the tibia, death from adenocarcinoma of the colon 24 years after onset; Case 38, parosteal fibrosarcoma of the tibia, traced well 16 years after onset; Case 38, osteogenic sarcoma of the clavicle, died of heart disease 23 years later; Case 39, inoperable osteogenic sarcoma of the scapula, traced well 15 years later.

Until quite recently very few other surgeons or roentgenologists have tried to save the limb in osteogenic sarcoma of the long bones. Although a few roentgenologists had reported small series of cases treated by irradiation alone, very few five year survivors were recorded.

W.B. Coley was the first to use radiation as a primary method of treatment at Memorial Hospital with discouraging results. (49) Higinbotham and B.L. Coley reported on 69 cases so treated between 1935 and 1941 and concluded: "In view of the small number of five year survivals, irradiation alone should not be relied upon in the treatment of osteogenic sarcoma." (87)

Doub reported a successful result in a case of osteogenic sarcoma of the clavicle treated by radiation combined with artificial fever therapy. (59). This patient recovered completely and remained well in 1974, over 41 years after onset. (16)

The concept that primary irradiation could be used to preserve a useful limb, either until death from early metastatic disease or until ablation at a time when the risk of metastatic disease was relatively small, was attractive to some physicians and remains a recommended approach in the United Kingdom. (92) The Westminster Hospital series of 92 cases so treated showed a five year survival rate of 21.8% by 1964. (100) Tudway reported that five of nine patients treated by radical radiation survived three to 14 years (one had metastases). He believed that radical radiation should be considered in place of amputation for osteogenic sarcoma of the upper extremities. (182)

McKenna et al reported their results in treating 130 children under 16 years of age with osteogenic sarcoma between 1925 and 1955, and noted that radiation was never "curative" when used as the sole method of therapy, and that treatment failure was higher in the group of patients treated by preoperative irradiation and then amputation, than in the group treated by amputation alone. (104)

To our knowledge, no surgeons since W.B. Coley have tried to save the limb in osteogenic sarcoma or other neoplasms involving the extremities until recently, when Stehlin tried perfusion combined with heat. (16) Most of his cases have been soft tissue sarcomas or malignant melanoma, but his procedure has tripled the survival time to date. (16)

An entirely new surgical approach designed to save the limb in osteogenic sarcoma of the extremities has recently been devised by Marcove at Memorial Hospital and the Hospital for Special Surgery in New York. The first patient so treated was a male, aged 50, with a low grade chondrosarcoma of the shaft of the femur. He had been treated unsuccessfully by curettage and cryosurgery, with recurrence. Marcove then resected the entire femur with a total prosthesis replacement by a metallic implant. Ambulation with weight bearing was started six weeks after the operation and the patient was able to use the artificial metallic knee joint. (115) Marcove states that the method is applicable to tumors which the surgeon feels may be completely removable surgically. Since this case was reported, 17 more such procedures have been successfully performed in patients 14 or more years of age with osteogenic sarcoma. (16)

Since many of these tumors occur in the pediatric age where optimal treatment is too frequently modified by emotional considerations of the parents and by an air of hopelessness on the part of the physician (105), new techniques or a combination of older ones such as Coley toxins plus more conservative resection of such lesions, should now be attempted. The recent use of interferon before

and after resection of such lesions by Strander and Nilsonne in Stockholm is of special interest and should be tried in other centers. (to be published 1975)

Metastases: Prevention, Treatment

Those surgeons who prefer to continue to amputate may wish to follow the suggestion of Kuehn, who in 1965 started tying the common iliac veins as well as the femoral vessels prior to amputation for osteogenic sarcoma, recognizing that one should treat these neoplasms as a form of infection to avoid dissemination. Eight of the first eleven cases so treated remained alive and well over three years later. (99)

A more aggressive attitude should also be encouraged as regards surgical resection of lung metastases. (16; 76; 77; 110; 113; 120; 162; 163) Since 75% of osteogenic sarcoma cases in the state of Connecticut have died of pulmonary metastases within one year (99) and other states within 10 months, these statistics suggest that blood stream metastases are extremely important. One of the first cases in whom pulmonary metastases were removed by B.L. Coley in 1941 (lobectomy), remained well and free from further evidence of disease 34 years later. Marcove and Lewis reviewed the literature in 1973. (113)

Another advance is being made in the chemotherapy of metastatic osteogenic sarcoma by using high doses of methotrexate with citrovorum factor, with complete regression of pulmonary metastases in some cases. (89)

McKenna noted that at least 75% of the autopsied cases of osteogenic sarcoma had demonstrable pulmonary metastases. (106) In planning more effective control of these neoplasms now and in the future, we must attempt to utilize host-stimulating forms of therapy that can help the patient destroy blood-borne tumor cells or incipient metastatic lesions. The cases listed as Table 2 suggest that concurrent infection, fever or inflammatory episodes can achieve this. Of the 41 cases with these "complications", 34% survived five to 43 years after onset.

In recent years immunotherapy of human cancer has begun to receive significant recognition. Those forms being used include BCG, various bacterial toxins such as Corynebacterium parvum (78; 142) and MBV (also known as Coley toxins). This last preparation consists of a heat-killed mixture of Streptococcus pyogenes and Serratia marcescens. Considerable data on the effects of concurrent infections and fever or of toxin therapy have been assembled in recent years, and many have been published. (66-69; 129; 133-142) The possible host-stimulating effects of concurrent bacterial infections, inflammatory or febrile episodes were never considered in evaluating factors affecting prognosis, until the present study was undertaken. (See Figure 1) The possible deleterious effects of prior removal of tonsils, adenoids or appendix then began to be noted. (108) We believe that all these factors should now be carefully considered and recorded on the patient's

history in all cases of neoplastic disease; so should the possible immunosuppressive effects of physical and psychic trauma prior to onset or during the course of therapy. Prior or concurrent administration of immunosuppressive agents or procedures should also be considered. (94; 95; 104; 146; 147) The routine use of antibiotics may also be questioned in these patients, since concurrent infections seemed to have a salutory rather than a deleterious effect when they occurred, and since antibiotics may have a deleterious effect on the immunological defenses of the patients. (68; 138; 139)

Of the 41 cases with concurrent infection, fever or inflammation, 14 (34 per cent) were traced well 5 to 46 years after onset. (see Tables 2 and 4) This was over three times the expected survival rate in the period in which these patients were treated. One other case was found which was not included in Table 2, which may be of interest to cite here: an extensive osteogenic sarcoma of the proximal half of the right humerus with pathological fracture in a female aged 9, who was treated at the Mayo Clinic in 1925, following incisional biopsy, by radiation alone (7000 r tumor dose). *A year later she developed scarlet fever.* This patient was alive and well when last traced in 1975. The radiation had caused considerable deformity of the proximal humerus and shoulder girdle and radiation dermatitis of the skin in this area. However, this did not prevent the patient from working for years as a laboratory technician. Since metastases usually develop at about the time this patient developed scarlet fever, it is possible that the infection may have exerted a favorable effect on her immunological competence. It is of interest to note that no other case of osteogenic sarcoma of the humerus is known to have recovered under radiation alone. In addition to attempting newer surgical techniques in dealing with osteosarcoma such as cryosurgery (111) or the replacement of entire bones as noted above, (115) Marcove has been administering an autogenous irradiated tumor vaccine (prepared following ablation of the primary by amputation) for a considerable period after surgery. The five year survival rate from this adjuvant therapy is approximately 40%, as compared to the present rate of approximately 17% with surgery alone in Memorial Hospital. (114)

Another immunological study was started about 1965 by Nadler and Moore at Roswell Park Memorial Institute, all cases selected for their study having been pronounced incurable by conventional means. Using volunteer patients with histologically similar tumors, they sensitized them to each other's tumor by subcutaneous implantation of a piece of tumor from Patient A into the thigh of Patient B and vice versa (or by incubating the tumor with leukocytes cultured *in vitro*). After 10 to 14 days when homograft rejection is thought to have taken place, leukocytes from Patient B are transfused into A and vice versa. The transfusions are repeated daily for three weeks. The leukocytes sensitized to tumor during culture *in vitro* are injected intraperitoneally in the original patient after 10 days. These injections are given daily or every other day. Several cases of

osteogenic sarcoma were among the 100 cases treated in this way, and in a personal communication (1973) Moore stated that two of these patients had remained well for over five years and the survival rate for the group as a whole was considerably better than in the controls. (132)

Enneking and his colleagues in Gainesville, Georgia, has recently almost doubled the expected survival rate in a small series of adolescent osteosarcoma cases using autogenous lymphocytes sensitized against the patients' tumor. The lymphocyte infusion was given after resection of the primary, i.e., these were operable cases, a stage of the disease which is far more amenable to immunotherapy. (116; 117) The use of the bacterial products such as Coley toxins is a less complicated and less costly form of immunotherapy. Although the first case of osteogenic sarcoma was treated by this method in 1894 (it involved the ilium), no attempt was ever made until recently to analyze the factors affecting prognosis with this form of treatment, and thus help us determine how the method could be used more effectively.

In recent years a number of end result studies of various types of malignant tumors treated by toxin therapy have been completed. (60-69; 129; 133-142) It was found that several factors played a significant role in determining success or failure with the method: a) the type of preparation of toxin used: 15 were available in Coley's lifetime, of which only 3 were reasonably stable and potent: Buxton VI, Tracy X and Tracy XI; (135) b) the technique of administration as regards site, dosage, frequency and duration of injections, especially the latter; c) the stage of the disease when toxin therapy was begun. (133-142)

Materials and Methods:

The present report comprises an end result study of all microscopically proven cases (failures as well as successes) of osteogenic sarcoma, chondrosarcoma and fibrosarcoma who received at least seven injections of Coley toxin (165 cases) or cases known to have had a concurrent bacterial infection, inflammatory or febrile episode (41 cases). All the cases treated by toxin therapy (Streptococcus pyogenes and Serratia marcescens) at Memorial Hospital from 1906 through 1941 were included. The infection cases at Memorial Hospital range from 1926 to 1949. Most of the patients receiving toxins were treated prior to W.B. Coley's death in 1936 (138 of the 165 cases). Of the 27 treated after his death only five were successes (18%) as compared to 36% in the cases treated during his lifetime. We believe this significant difference is due to the fact that the later cases received only brief courses of toxins, and a less potent preparation was then being used. Unfortunately, after 1936 those reporting on end results of these tumors failed to mention that at Memorial Hospital up to 1941, all but six of the five year survivors with osteogenic sarcoma had received Coley toxin therapy. (16; 123) In addition to the Memorial Hospital Series, we have included those treated by W.B.

Coley, B.L. Coley or N.L. Higinbotham at the Hospital for Special Surgery in New York, or those reported in the literature, if detailed histories were available as to technique of administration. (3-6; 15; 21; 24; 52; 88; 90; 121; 122; 123; 125-128)

Six successes treated at the Mayo Clinic and cited by Coventry and Dahlin were not included in Table 1, although the patients remained well 8-33 years after onset: two osteogenic, one chondrosarcoma and three fibrosarcoma (54). The Mayo Clinic undoubtedly had some toxin treated failures and these histories were also unavailable for detailed analysis of factors affecting prognosis when immunotherapy was given. Prior to 1935 all osteogenic sarcoma patients seen at the Mayo Clinic were advised to have irradiation and toxins post-operatively. (125)

The cases are listed in the various groups as follows, according to the bone involved, with the osteogenic sarcoma first, the osteochondrosarcoma second, and the fibrosarcoma cases last.

TABLE 1: Successes Treated by Immunotherapy (Coley Toxins) combined with surgery and/or radiation, traced 4 to 57 years: 45 cases:

34 primary operable (29%)
8 recurrent (32%)
3 inoperable or with metastases (12%)

TABLE 2: Successes Following Concurrent Infection, Fever or Inflammation: traced 5 to 43 years: 14 cases (34% 5-year survival)

TABLE 3: Failures Treated by Immunotherapy: 120 cases

Group 1, Primary operable: 83 cases
Group 2, Recurrent operable: 13 cases
Group 3, Inoperable, polyostotic and/or metastatic: 24 cases

TABLE 4: Failures following Infection, etc.: 27 cases

FIGURE 1 **END RESULTS IN OSTEOGENIC SARCOMA ACCORDING TO EXTENT OF DISEASE WHEN IMMUNOTHERAPY (COLEY TOXINS) WAS BEGUN**

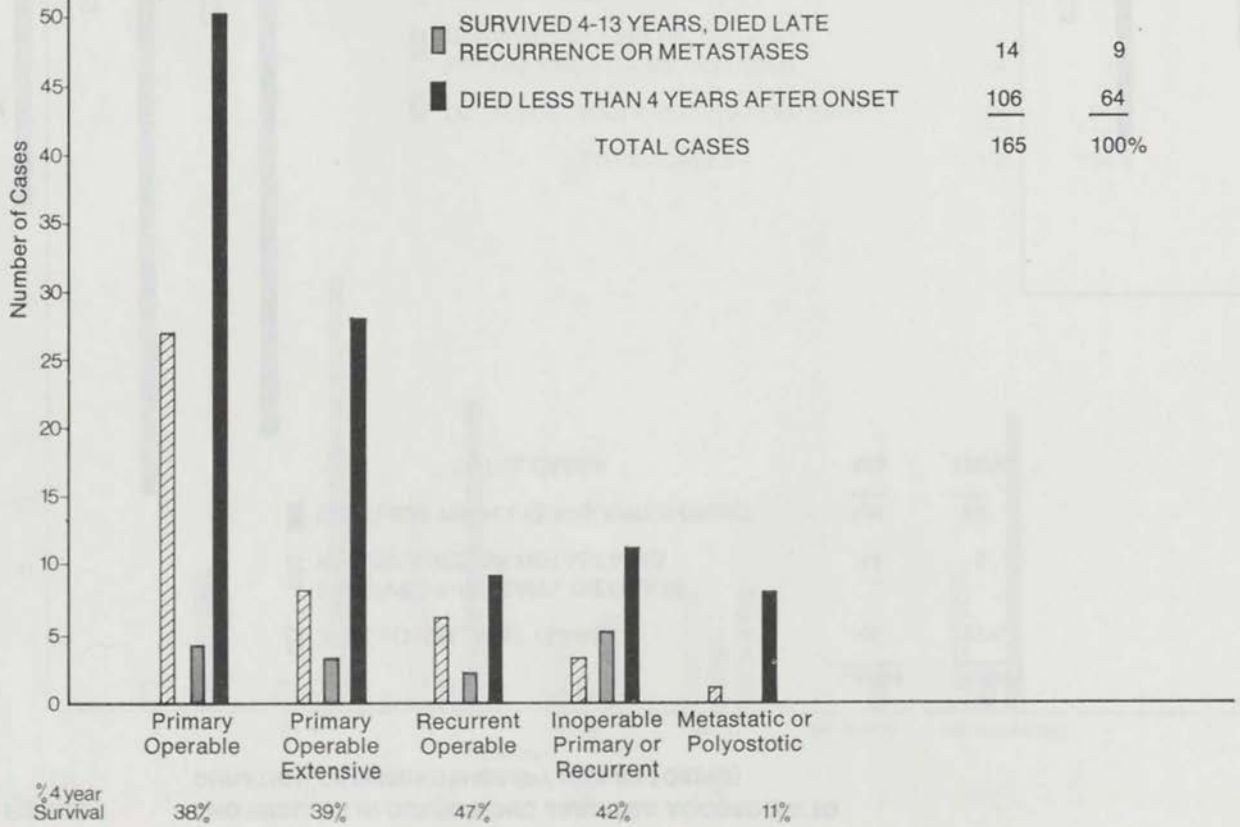


FIGURE 2 **END RESULTS IN OSTEOGENIC SARCOMA ACCORDING TO DURATION OF IMMUNOTHERAPY (COLEY TOXINS)**

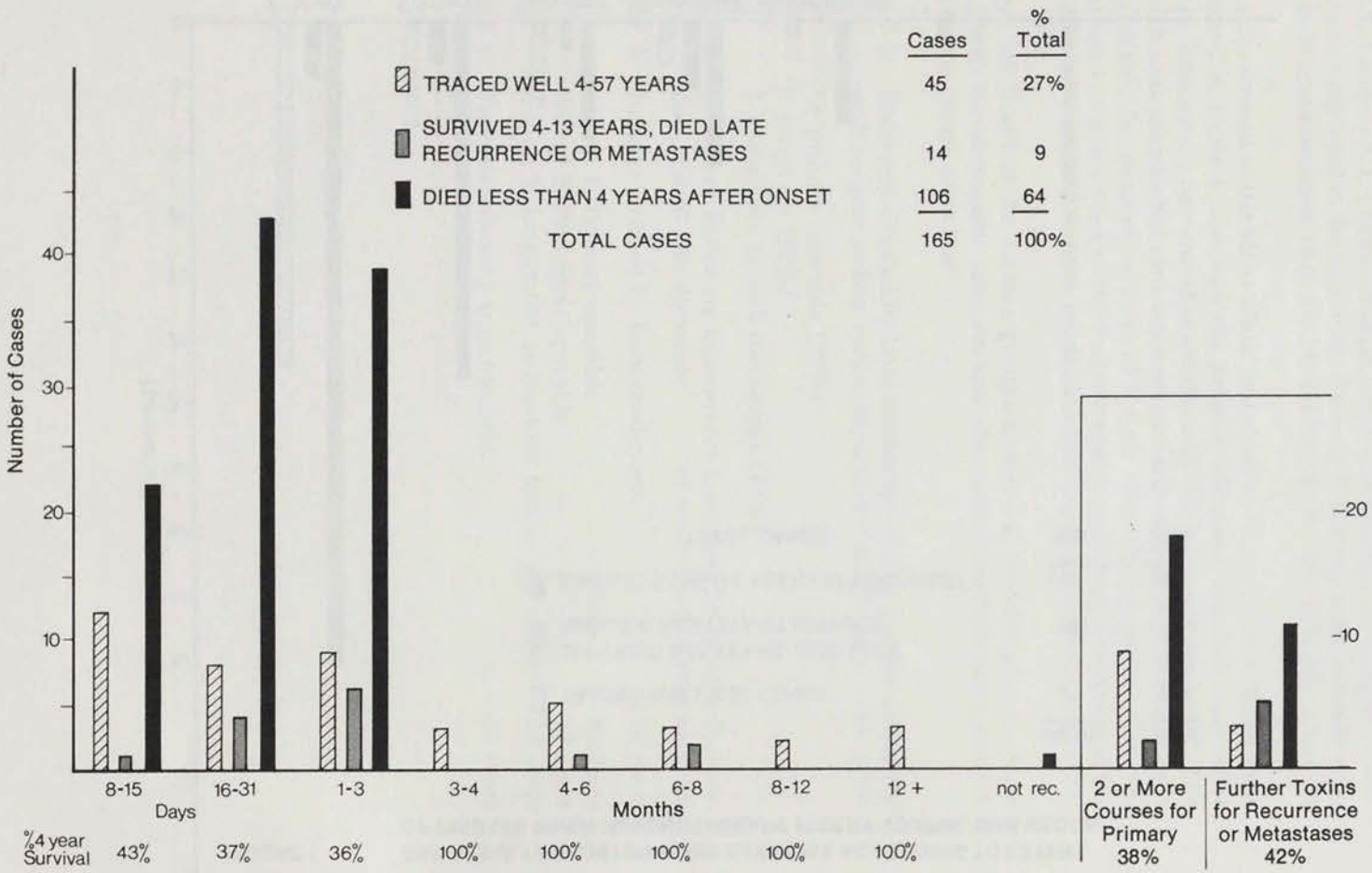
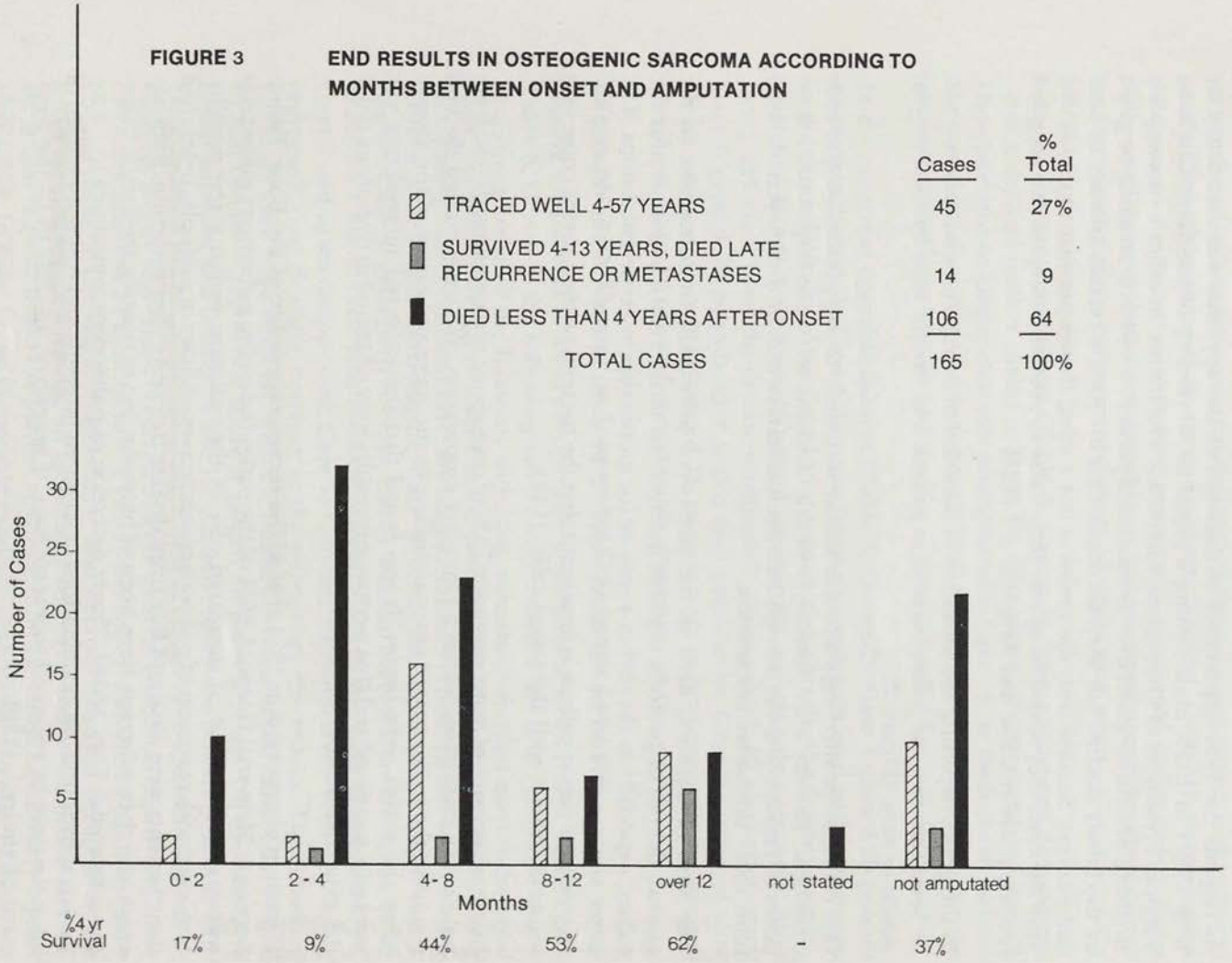


FIGURE 3 **END RESULTS IN OSTEOGENIC SARCOMA ACCORDING TO MONTHS BETWEEN ONSET AND AMPUTATION**



Factors Affecting Success or Failure with Toxin Therapy

As regards the vital importance of duration of therapy, this was mentioned by W.B. Coley in 1935, in discussing a paper by Meyerding of the Mayo Clinic on Surgical Treatment of Osteogenic Sarcoma: "The toxins, in order to accomplish anything, should be given over an extended period . . . (they) can easily be given by the family doctor, but they do require on his part, a certain amount of time and interest. Success with the toxins is not a thing that is peculiar to me. If that were the case, they would be of very little value to posterity. Anyone can get good results, *if they give time and thought to it.*" (125)

In the graph depicting the influence of duration of therapy on end results it will be seen that *very few failures occurred in patients who received toxin injections for four months or more.* (Figure 2)

One other factor affecting success or failure with toxin therapy is the *timing* of such treatment. Results were seldom favorable if toxins were not begun until large doses of radium or x-ray therapy had been administered, or if they were delayed until some time after amputation.

The sites of injection used in the past were principally intramuscular in the gluteal, deltoid or pectoral regions; intravenous (after 1930); and in or near the tumor, especially in the earlier years, or for inoperable or recurrent lesions. The latter site appears to be valuable, since to be most effective in increasing antigenicity of tumor cells, it is important that the bacteria or their toxins come into intimate contact with the target cells. (142)

In the experience of many surgeons 75% of osteogenic sarcomas usually die from pulmonary metastases within a year after amputation. We have studied the end results of the toxin-treated cases according to the stage and extent of the disease when the toxins were begun. It was found that the expected survival rate was markedly increased and that permanent results were obtained in over three times the expected number of patients.

Martini et al reported in 1971 that in the recent experience of the Bone Tumor Service at Memorial Hospital, 80% of the patients develop pulmonary metastases within two years and, if untreated, die of their disease within a few months. However, with resection of pulmonary metastases, solitary or multiple, nearly half their patients were alive and free from disease two years after resection. Radiotherapy and chemotherapy have been of limited value in treating metastatic osteogenic sarcoma. They added: "Early detection of pulmonary metastases by roentgenography follow-up examinations at frequent intervals and surgical excision of all metastases by repeated thoracotomies, if necessary, appears to be the treatment of choice." (120)

In this connection it may be of interest to note the effects of Coley toxins alone or combined with radiation on patients with pulmonary metastases in the present study. One of the successfully treated patients (Table 1, Case 21), an osteogenic sarcoma of the humerus with lung metastases, recovered under toxins alone, following interscapulothoracic amputation and remained in excellent health until sudden death from a coronary occlusion 18 years after onset.

Among the operable failures (Table 3, Group 1), lung metastases disappeared after x-ray and further toxins in Case 27; they almost disappeared in Case 70, chest pain due to lung metastases disappeared in Case 71. In these three patients the initial brief course of toxin therapy had been given with radiation for the primary tumor.

In the recurrent operable failures (Table 3, Group 2), Case 1 gained 20 pounds after toxin therapy. In Case 4 the growth was arrested, with marked improvement in the general condition. In Case 5, the pain ceased after the third dose of toxins, with slow, steady regression, 10 pound weight gain, and complete recovery. After being well eight years the disease reactivated, causing death 10 years after onset. Case 6 gained 20 pounds after toxins and amputation; Case 8 improved after toxins and x-ray; Case 11 gained 18 pounds with improvement in the general condition. Case 12 showed considerable regression in two weeks.

Effects of Toxin Therapy in Inoperable Osteogenic Sarcoma:

Among the patients that were inoperable or metastatic when toxins were begun, Table 3, Group 3, the following effects were noted: Case 2: an extensive osteochondrosarcoma of the humerus with lung metastasis showed marked hemorrhagic necrosis of the large tumor mass, and gained seven pounds despite lung metastases; Case 3: a similar case, the lung metastases remained stationary for 3½ months after toxins were begun; Case 4: metastatic nodules on thighs disappeared; Case 5: gelatinous necrotic tumor was discharged from the sinus in the humerus; Case 6: recurrent osteochondrosarcoma in the tibia disappeared, recurred and again disappeared; Case 7: recurrence disappeared, recurred, again regressed; Case 8: slight decrease in the pulmonary metastases. The following five cases were huge inoperable osteochondrosarcomas of the ilium: Cases 9 and 11 had complete regression (Case 9 gained 40 pounds); Case 10: the extensive tumor softened and drained; Case 12: marked regression occurred and the general condition was excellent (this patient died of infection 38 months after onset); Case 13: steady regression occurred and the general condition improved. These five cases survived 17 months to 4½ years after onset. In Case 14, an inoperable fibrosarcoma of the ilium, hemorrhagic and necrotic changes occurred in the groin metastases. In Case 15, an inoperable osteogenic sarcoma of the sacrum, the lesion regressed and the patient returned to work. Death occurred five years after onset. In Case 17, an inoperable extensive osteogenic sarcoma of the clavicle, there was much inflammation in the tumor area following toxins, with weight

gain, union of the pathologic fracture and improvement in the general condition. The patient survived two years. In Case 18, another clavicle case, marked regression and wound healing occurred, with a survival of 38 months. In Case 20, an osteogenic sarcoma of the rib, almost complete regression occurred. In Case 21, osteogenic sarcoma of the rib, marked decrease in size occurred. In Case 23, an osteogenic sarcoma of the occipital bone, complete recovery occurred and the patient remained well for many years; death did not occur until eight years after onset.

These effects, produced with little knowledge of the optimum technique of administration, suggest further use of bacterial toxin therapy in metastatic or inoperable osteogenic sarcoma, even if cure may not be effected in many of these cases.

Etiological Factors in Osteogenic Sarcoma

Viral: In recent years a number of reports have indicated that osteogenic sarcoma may occur in more than one sibling. Roberts was the first to report this in 1935. (158) Pohle et al noted the occurrence in two sisters the following year. (151) Robbins reported its occurrence in four siblings in 1966 and the fifth such case in 1967 (157), and Epstein reported a family in which six of 15 members over three generations developed seven malignancies. Osteogenic sarcomas appeared in successive generations. All these authors regarded the problem as one of heredity. Recent studies on viral oncogenesis have suggested that this may be due to exposure to a virus. Antibodies have been recovered from family members and other individuals who came in close contact with the patients in far greater titres than controls not exposed.

Radiation: In 1929 Martland and Humphreys were the first to report osteogenic sarcoma developing as a result of occupational exposure to radium in watch dial painters. (172) Among those who have reported cases of post-irradiation osteogenic sarcoma since then are Wolfe and Platt in 1949. (192).

Spitz and Higinbotham in 1951 found several patients with seminoma of the testis who had received radiation therapy who later developed osteogenic sarcoma of the bones in the area that had received excessive radiation. (174) Cruz et al reported on 11 new cases at Memorial Hospital by 1957, one of which occurred in the thumb of a dentist who had received x-ray therapy for Verruca vulgaris. The thumb was partially amputated and thereafter the stump was exposed to x-ray every time he took dental x-ray of his patients. Osteogenic sarcoma developed seven years after the radiation. They maintain that post-irradiation sarcoma evolves in areas of radiation osteitis of not too severe a degree. They found in these areas bizarre connective tissue cells that might be regarded as precursor cells of the sarcoma. (54a)

Waltz and Brownell reported the development of fibrosarcoma developing in the region of the sella turcica in two patients five and eight years after irradiation for pituitary adenoma. They found eight comparable cases in the literature. (187)

Tebbet and Vickery reported a case of osteogenic sarcoma that developed following irradiation for retinoblastoma. (180) Skolnik et al analyzed 10 collected cases. The three youngest had been treated for retinoblastoma. Two of their own cases were also reported. The first developed osteogenic sarcoma 3½ years after radiation of a postauricular keloid and was surgically resected. The second developed it in the frontal bone 10 years after irradiation for retinoblastoma. (167)

Meredith et al reported a case developing following irradiation for a benign pituitary tumor. This patient had also received cortisone continously for a prolonged period. (124) More recent studies of these cases include Phillips and Sheline (149); Soloway, in 1966 who reviewed 25 cases of radiation-induced neoplasms following curative therapy for retinoblastoma, most of which were osteogenic sarcoma or its variants. The prognosis of these tumors was exceptionally poor. (172) By 1971 Arlen et al were able to find 50 cases of radiation-induced osteogenic sarcomas seen at Memorial Hospital (2), (54a) 22 of which had previously been described.

Stature: Fraumeni had noted that children admitted to the Children's Hospital Medical Center in Boston with osteogenic sarcoma were found to be considerably taller at diagnosis than a hospital control group with non-osseous cancers. These findings are consistent with the known high incidence of canine bone sarcoma among larger breeds of dogs, and the demographic observations on human bone cancer which suggest that the origin of at least some of these tumors is a function of skeletal growth rates during childhood and adolescence. (73)

Paget's Disease: This condition has long been recognized as a predisposing factor in osteogenic sarcoma by many authors. (22; 55; 104; 153; 154; 164; 177) Coley and Sharp in reviewing 72 cases of osteogenic sarcoma in patients over 50 found Paget's disease was a predisposing factor in 28%. Multiple bones may be affected without metastases to liver, lung, brain or other viscera. Up to 1931 none of these patients at Memorial Hospital in New York or in the Bone Sarcoma Registry had been cured. (22) Paget's disease occurs five times more frequently in men than in women. These authors suggested the use of prophylactic constitutional therapy with the mixed toxins (Coley toxins) as a method worthy of trial in these cases. (22) This was done successfully in a case involving the right proximal humerus in a 49 year old woman in 1936: preliminary toxin therapy combined with x-ray (10 treatments) was followed by cessation of pain and gradual shrinkage of the palpable mass. (The patient had refused disarticulation) There was steady gain in weight and complete recovery, with marked regeneration of bone. Two more courses of toxins were given and 10 more x-ray treatments (1,675 r)

to prevent recurrence. The patient remained in excellent health until sudden death from a heart attack six years after onset. (Table 1, case 23)

Another case of osteogenic sarcoma arising in Paget's disease of the humerus, tibia and fibula, developed osteomyelitis of the tibia and fibula following open reduction of pathologic fractures. (164) The lesion in the humerus was resected, a bone graft inserted which lysed, and the patient remained well until death from congestive heart failure eight years later. (Table 2, case 10) The concurrent infection may have helped prevent reactivation of the disease in this case. (138) As Berger recently stated: "The state of natural resistance may be dependent on the availability and utilization of endotoxin." (9)

Summey and Pressly found the average age for sarcoma complicating Paget's disease was 49.5; the youngest 32, the oldest 78. The prognosis in women is better than in men, *but it is extremely grave*; 84% of their cases occurred in men, mostly the femur, 24, humerus, 20, skull, 15, and tibia, 13. They stated: "*There is no known cure.*" (177)

Price suggested that in persons over 40 years of age Paget's disease increases the risk of osteogenic sarcoma developing about thirty-fold. (154) Weinfeld and Dudley reported that in their experience 50% of all patients over 40 with Paget's disease developed osteogenic sarcoma and only one survived five years. (188)

Porretta et al noted that on 128 cases of osteogenic sarcoma arising in Paget's disease recorded in the English-language literature to 1957, the only five-year survival was that of Sherman and Soong. (165) This is the case described above which received three courses of bacterial toxins (immunotherapy) combined with a small amount of x-ray therapy.

Trauma: That injury may play a role in the development of all types of malignant tumors has been recognized by the laity for centuries. Popular beliefs of such long standing and so deeply rooted have almost invariably proved in the end to be founded upon facts. (33)

There is probably a strong predisposition to the development of cancer in persons who develop tumors following trauma. Such injuries prove harmless in patients with a strong natural resistance to cancer.

W.B. Coley made a special study of trauma and cancer, having become interested in the subject in 1890, the first year of his practice. At that time a girl aged 18 was referred to him with a history of having had her hand severely squeezed between two Pullman chairs while travelling. About a week later she began to have pain in the third metacarpal bone. The pain continued and grew worse daily, and within another week a slight swelling developed at the site of the injury, which

continued to increase in size. A number of physicians were consulted who diagnosed the condition as "rheumatism". About eight weeks after the injury the patient was referred to Coley. He performed a biopsy which was reported as "round cell sarcoma" (it would now be regarded as a Ewing sarcoma, or reticulum cell sarcoma of bone). Dr. William T. Bull was called in consultation, and an immediate amputation was advised. Six weeks after Coley performed the amputation (midforearm), metastases developed in both breasts and the patient died two months later of generalized metastases. Coley stated: "This case made a deep impression on me, and in my opinion, furnished convincing evidence that the local trauma was an important causative factor in the development of the sarcoma . . . From that time on I began to take careful histories of all the cases of malignant tumors that came under my observation, with special reference to antecedent local trauma." (8; 27, discussion appears in reprint only; 52) By 1910 Coley had observed 970 cases of sarcoma of which 225 (23%) had a definite history of trauma. The tumor developed within the first month after the injury in 117 cases of typical acute traumatic malignancy. (33) Coley's subsequent studies on this subject were reported in six further papers, the final one in 1933. (50) Campbell noted that trauma was associated in at least 50% of his 250 cases, many of which sustained injury to the bone itself. (14)

Krebs and Olsen (97) discussed the role of trauma in the development of malignant bone tumors in 1963. They stated that reparative processes with or without inflammation constitute a stress on the normal resistance of the organism, and surgical procedures may have a similar effect.

It would seem that injury may aggravate an incipient neoplasm, and this may be to the patient's advantage in that the patient may seek aid earlier than he would otherwise have done. These authors believe with Ewing that trauma *reveals* more malignant growth than it *produces.* (97)

The studies of Vaitkevicius et al have shown that by injuring the transplant site prior to transplantation, they could reduce the minimal size of the implant of a patient's viable tumor cells required to produce successful transplants. These transplants behave like spontaneous metastases. (185) It has been suggested that tissue injury may destroy or inhibit "host defense".

Riddle and Berenbaum studied the effects of operation on the lymphocyte response to phytohemagglutinin in patients undergoing a variety of surgical procedures. They observed a significant fall in the percentage of lymphocytes in the peripheral blood undergoing transformation and they attributed this observed depression to the effects of surgical trauma. (156)

These findings suggest some of the reasons why antecedent local trauma, surgical

trauma, pathologic fracture or injuries sustained during or following treatment, may affect the prognosis unfavorably.

In the present study it was found that trauma had occurred in 16 of the 45 toxin treated successes (35%). Of the failures, Group 1, operable when toxins were begun, 33 of the 83 cases had a history of trauma (40%); while 44% of the 37 cases in Group 2 and 3 (recurrent, inoperable or with metastases) had prior trauma. These statistics suggest that when immunotherapy is administered, the deleterious effects of trauma may be lessened.

Factors Affecting Prognosis and End Results:

Age at onset: Several authors have noted that younger patients have a lower incidence of survival. McKenna et al noted that between 1925 and 1955 no child under 16 had a long term survival at Memorial Hospital. (105) Phelan and Cabrera stated in 1964 that in young children and teenagers the prognosis was invariably fatal. (148) By 1970 Marcove et al reported a five year survival rate of 17.4% in 145 consecutive cases of osteogenic sarcoma of the long bones in patients under 21 treated at Memorial Hospital. (112)

Paget's disease has been recognized as a predisposing factor in osteogenic sarcoma, as noted above, and such cases have an almost universally fatal prognosis. To date only five cases are known to have survived five years: the first, cited above, received three courses of Coley toxin injections before and during x-ray therapy (small doses). The second, cited above had osteomyelitis. The other three were treated at the Mayo Clinic details unknown) as cited by Dahlin in 1967. (56)

Duration of symptoms prior to treatment is inversely related to prognosis: the shorter the duration of symptoms, the more likely an unfavorable result. Ferguson was the first to report this in 1940 (64). He reviewed 400 cases and noted that in 40 patients with symptoms of less than six months duration prior to treatment the average survival was two months after amputation, with eight five-year survivals (17%); of the 34 having symptoms for more than six months the average survival was 31 months and there were seven five-year survivals (23%).

McKenna et al reported that 90% of the treatment failures were treated within six months of onset, whereas 55% of those successfully treated had symptoms for longer than six months. (105)

Macdonald and Budd, in a study of the cases in the Bone Sarcoma Registry to 1943, noted that the mean period of delay from onset of symptoms to the time of treatment is considerably greater in the uncured cases of osteogenic sarcoma and fibrosarcoma, but that this did not seem so apparent in cases of chondrosarcoma. (109)

We have studied the end results according to duration of time between onset and amputation in the cases receiving immunotherapy, Tables 1 and 3: *see Figure 3.*

Pathologic Fractures: Coley and Sharp noted that these had occurred in 21.3% of cases of osteogenic sarcoma; that they are most likely to occur in patients past the average age for the tumor; that 75% occur in the lower extremities; and that the proximal humerus was the most susceptible region (12 of 16 cases) due to severe stress in this area. They believed that life expectancy of patients with osteogenic sarcoma is shortened 60% when pathologic fracture occurs. Fractures increase the difficulty of handling these cases, especially when using treatments which may be administered on an ambulatory basis, i.e., irradiation or immunotherapy. Pathologic fractures may be postponed or prevented by early and continuous support. Failure to immobilize a limb in which pathologic fracture occurs predisposes to early dissemination of the disease. (22)

In the present study four of the 44 successes involving the long bones had pathologic fracture (9.1%) as compared to 17 of the 113 failures involving these bones (13%). The period of survival in most of these 17 failures with fractures did not appear to be shortened the expected 50% as is usual in such cases not receiving immunotherapy.

Cell Type:

Parosteal or Juxtacortical Sarcoma: Geschickter and Copeland were the first to describe parosteal osteoma of bone. This rare lesion, made up of abnormal ossifying tissue, may give rise to sclerosing osteogenic sarcoma or fibrosarcoma. It usually progresses slowly for months or years. The distal femur is most often affected in young adults or adolescents. The lesion appears separated from the bone on x-ray but anatomically is attached along one surface. Microscopically there is a composite of atypical benign ossifying fibrous tissue which may be intermingled with areas characteristic of osteogenic sarcoma or fibrosarcoma in those showing frank malignant change. (74) The five-year survival rate appears to be better than 50%. Dwinnell et al reported on 15 cases at the Mayo Clinic to 1954. They concluded: "In the past this type of tumor has commonly been believed to be a benign one, such as atypical chondrosarcoma or a strange recurring form of myositis ossificans. It is the authors' opinion that the lesions are usually malignant from the beginning." (60)

Van der Heul and von Ronnen collected 64 cases from the literature and 16 from the Netherlands Committee on Bone Tumors. Excision of the primary was followed by recurrence in four of five cases so treated. Recurrences also occurred after segmental resection and disarticulation. None of the recurrences were cured by further excisions; all but one of these finally required amputation or disarticulation. Radiation therapy had no effect. After excision large tumors seem to recur more often than smaller lesions. (186)

Two cases of juxtacortical osteogenic sarcoma are included in this study. The first, involving the humerus, was treated by immunotherapy (Coley toxins): see Table 1, Case 20. This patient received two massive x-ray treatments prior to amputation and toxin therapy was given for six months after surgery. The patient remained free from further evidence of disease until her death from chronic mylogenous leukemia 34 years after onset of the sarcoma. The other case involving the proximal femur had concurrent infection following amputation and remained well in 1974, 29 years after onset, see Table 2, Case 9.

Fibrosarcomas of Bone also have a much better prognosis than the *osteogenic or osteochondrosarcoma of bone,* as recorded by all the authors who have analyzed end results. The following table indicates the end results according to the bone involved in these three histological types. Even among the 83 primary operable cases, many had very extensive lesions. If the 27 cases that were inoperable, polyostotic or metastatic before immunotherapy was given, had been deleted, the percentages of success would have been higher as only 11% of these 27 cases remained well four or more years. Two of the successes and one failure had parosteal or juxtacortical osteogenic sarcoma. Two failures and one success had developed in Paget's disease.

Site and Extent of the Tumors: The femur, especially the distal third, is the most frequent site, with the proximal tibia, humerus and fibula ranging in order. In the tubular bones osteogenic sarcoma occurs most frequently in the metaphysical region, tending to invade both the epiphysis and diaphysis secondarily. That it should appear in the regions of greatest growth is not surprising. Lesions occurring in peripheral sites have a better prognosis than those more centrally located, those in the forearm have a better than 50% prognosis. (23) Very few five-year survivors occurred in cases of osteogenic sarcoma arising in the proximal third of the femur, although two osteochondrosarcomas in this area recovered (see Table 1). The proximal third of the humerus also has very few survivors from surgery and/or radiation alone, but two such cases recovered who received immunotherapy as an adjuvant to such treatment (see Table 1, Cases 20 and 21).

Extension of the tumor for a considerable distance up the marrow cavity, invasion of the femoral or axillary vein, extensive infiltration of soft parts, tissues of a telangiectatic character, all are of extremely unfavorable significance. Conversely, their absence gives a more favorable prognosis. (23)

Survival:

It is surprising that only one of the 11 fibula cases survived and that was a fibrosarcoma. It is also surprising that 23% of the osteogenic sarcomas of the humerus survived but none of the seven osteochondrosarcomas of this bone. These failures and those in the inoperable cases involving the ilium were responsible for the low over-all cure rate in these 37 cases of osteochondrosarcoma.

SURVIVAL ACCORDING TO BONE AND HISTOLOGICAL TYPE

Osteogenic Sarcoma, 111 cases, 23% cure

48	femur (mostly distal)	10	successes	21%
22	humerus (mostly proximal)	5	"	23%
17	tibia (mostly proximal)	4	"	24%
7	fibula	0	"	0
6	clavicle (4 inoperable)	1	"	17%
4	ribs (all inoperable)	1	"	25%
4	skull (inoperable)	1	"	25%
1	scapula (inoperable)	1	"	100%
1	bones of foot	1	"	100%
1	sacrum (inoperable)	1	"	100%

Osteochondrosarcoma: 37 cases, 22% cure

13	femur	3	successes	29%
7	humerus	0	"	0
6	tibia	2	"	33%
2	fibula	0	"	0
2	bones of foot	2	"	100%
1	rib ⎫ all inoperable	0	"	0
6	ilium⎭ or recurrent	1	"	17%

Fibrosarcoma, 17 cases, 82% cure

6	femur	5	successes	83%
3	humerus	2	"	67%
4	tibia	4	"	100%
2	fibula	1	"	50%
1	ulna	1	"	100%
1	clavicle (inoperable)	1	"	100%

Site of Amputation:

Coley and Pool noted in 1940 that 35% of their series amputated through the involved bone had survived as compared to 21% of those disarticulated at the proximal joint, and 36% of those amputated in the proximal bone. They concluded: "Although some authors maintain that one should never amputate through the bone primarily involved, our figures would indicate that for at least low femur tumors, indiscriminate hip disarticulation was scarcely justified." (23) Dahlin and Coventry believe there is no proved advantage in having a joint between the site of amputation and the tumor. (55).

Pack et al (1942) reported on 15 cases of osteogenic sarcoma in which interscapulothoracic amputation had been performed for osteogenic sarcoma. The only two patients who survived had immunotherapy (Coley toxins) as an adjuvant, although Pack did not mention this point. (145)

The present series of cases include a few patients in whom amputation was *not* performed who recovered under radiation and toxin therapy alone. (See Table 1.) These data suggest that modern immunological techniques may enable orthopedic surgeons to preserve the limb in many more cases than was possible in the past. (115)

Adjuvant Therapy other than Immunotherapy

Chemotherapy: Copeland reported in 1967: "Our own experience and a review of the literature would indicate that the sarcomas of osseous origin respond very little or not at all to chemotherapy by perfusion or infusion. Stehlin found no response in six osteogenic sarcomas using HN_2-like compunds, actinomycin D and methotrexate in various combinations. (53)

Jaffe and Paed (1972) reported that high doses of methotrexate with citrovorum factor were administered to 10 patients with metastatic osteogenic sarcoma. A complete regression of pulmonary metastases was obtained in two patients and partial regression of tumor in two others. Side effects included nausea, vomiting, abdominal pain, stomatitis, bone marrow suppression, skin lessions and renal impairment responding to additional citrovorum factor. The duration of response varied from one to eight months with complete regression of tumor persisting in one patient. (89) Further studies are being carried out by several clinical investigators including Djerassi who was the first to use this combination as an adjuvant to amputation, in order to prevent metastases.

Nutritional Adjuvants: Krebs in Denmark reported on 25 years' experience in treating bone sarcoma to 1959. Between 1935-1949 x-ray therapy alone was used with 11.5% five-year survival, while between 1950 and 1959 this treatment was combined with the administration of large amounts of egg yolk and prolonged bed rest. In this later period the five year survival rate was 34.4%. He added that if the patients in the later period who had metastases when first seen were excluded, the five year survival rate in this group would be 38.1%. Krebs also noted that for the 54 patients who died between 1950-1959 the survival period was 554 days from admission as compared to the 354 days for the 78 patients prior to 1950 who did not receive egg yolk. Even in the terminal phase of the disease, the general condition of the patients given egg yolk appeared better than those in the first series.(97) To our knowledge, no one else has ever attempted this regime.

Recently there has been an increased interest in the possible beneficial effects of nutritional or vitamin supplements in the treatment of malignancy. We do not believe this has been tried in osteogenic sarcoma.

Treatment of Metastases

As noted earlier, prognosis may be improved by a more aggressive treatment of pulmonary metastases when they occur. Resection or lobectomy have produced significant numbers of permanent results, some now living over 25 years. (16; 76; 77; 110; 113; 120; 123; 161; 163)

Further study of high doses of methotrexate and citrovorum factor also seems warranted by the results obtained by Djerassi and others with this technique. (16; 89) The protective effects of bacterial toxins on normal tissues and their ability to potentiate the response of the tumor tissue to radiation and to chemotherapeutic agents also deserves much further study.

Concurrent Infections, Inflammation or Fever

For over 200 years physicians have observed dramatic regression of cancer following concurrent acute bacterial infections, principally streptococcal or staphylococcal. Most of these occurred in neoplasms involving the soft tissues. (135-142) Only five recorded cases involving osteogenic sarcoma were found in the literature (see Table 2). The other 36 infection cases in Tables 2 and 4 were all Memorial Hospital cases.

That such complications as infection and fever may increase the resistance of patients to their neoplasms is now becoming recognized as a result of the recent work of such investigators as Berger (9), Christensen (18), Everson and Cole (62), Fisher et al (65), Fowler (66-69); Halpern et al (78); Jakoubková (90, 91); Miller & Ketcham (128); Miller and Nicholson (129); Nauts (133-142b); Old (143); Stjernswärd (176); Weiss et al (189); Zweifach et al (194).

It is of interest that 34% of the 41 patients in Tables 2 and 4 with concurrent infection, fever or inflammation were apparently cured. This was over three times the expected survival rate from surgery and/or radiation alone in the period in which these patients were treated.

Since infection may play a protective role, it would seem much wiser to avoid using immunosuppressive antibiotics prior to or after surgery in cases of osteogenic sarcoma, but to rely instead on the enhancing effect on resistance to infection produced by bacterial vaccines(9; 67-69; 128; 129; 133-142b; 194)

Immunotherapy

W.B. Coley began using his mixed toxins (Streptococcus pyogenes and Bacillus prodigiosus, now known as Serratia marcescens) as an adjuvant to amputation in osteogenic sarcoma in 1906. His first bone tumor case, in December 1894, was a huge inoperable osteochondrosarcoma of the ilium the size of a child's head. This patient received toxins alone with complete regression. Unfortunately, the

disease later reactivated following an exploratory operation and the patient died (see Table 3, Group 3, Case 9).

Codman in analyzing the only 13 registered "five year cures" in the Bone Sarcoma Registry in 1926 stated: "If it had not been for Coley's enthusiasm and optimism we should have few (cured cases) to record. Coley has shown us at least that cases considered hopeless may be cured . . . Whether or not the evidence also justifies his faith in the use of mixed toxins is an academic matter compared with the bald facts that he can furnish evidence of the cure of apparently hopeless cases and that he has . . . nearly as many cures as all the other surgeons of the country together." (19)

Orthopedic surgeons such as Meyerding at the Mayo Clinic (125-127) or Campbell of Memphis, Tennessee (14; 15) advised Coley toxins as an adjuvant to surgery and/or radiation in osteogenic and other bone sarcomas. However, since no one understood the rationale for such treatment until very recently, and no one had made a study of the optimum technique of administration or the other factors which might affect prognosis unfavorably, the method never became widely used.

The results obtained in the 165 primary operable, recurrent and inoperable toxin treated cases in the present study are impressive when one recognizes that many of the patients had very extensive tumors when first seen, and many received the weaker preparations of Coley toxins for too short a period of time. For the first time a detailed analysis was made of the duration of toxin treatment as it may affect prognosis in these tumors. The results are astonishing. If toxins were given for three or more months *all patients survived four or more years.* However, four of these 22 patients died from 4 to 13 years after onset of further reactivation of their disease. If toxins were resumed when recurrence or metastases developed, 42% of the patients so treated survived four or more years; five of these died of their disease over four years after onset. *These results have never been duplicated by any other methods of treatment.* (See Figure 2)

It must now be recognized that onset of pain anywhere in a recovered case should be regarded as indicating possible metastases and toxin therapy should be resumed at once and given persistently for at least three or four months. With this technique it may be possible to salvage many more patients.

It was found that if large doses of irradiation (x-ray or radium) were given prior to toxin therapy, the resulting immunosuppression had an unfavorable effect on prognosis, as had been noted for other types of malignancy. (66-69; 129; 133-142) Two patients who had received two or three massive exposures to x-ray prior to toxin therapy developed chronic myelogenous leukemia 25 and 33 years later, (see Table 1, Cases 20 and 26).

Now that the protective effects of prior or concurrent bacterial toxin injections on radiation injury to normal cells or tissues are more fully recognized, one can prevent such effects by using this type of treatment when radiation is to be administered (1; 135-142; 194). One can also prevent the development of osteogenic sarcoma following irradiation for other conditions by judicious prior or concurrent use of microbial products in such cases as retinoblastoma, seminoma or various benign conditions, so that smaller doses of radiation may be utilized, due to the potentiating effects of bacterial toxins on radiation to the tumor, as well as their protective effect on normal tissues. (2; 54a; 124; 149; 167; 172; 174; 180; 187)

CONCLUSIONS:

The data we have presented suggests that if immunotherapy (bacterial toxin injections) were now given as a routine in all cases of primary osteogenic sarcoma prior to and following resection or amputation for at least four months (on an outpatient basis, by the family physician after the first week or ten days), it is probable that very few of the patients would develop pulmonary metastases.

If injections were *immediately* resumed in the cases that did develop metastases and were given both before and after pulmonary resection of the lesions, it would perhaps insure a permanent result in many more of these cases than is presently possible by surgery alone.

Surgeons should become aware of the fact that toxin therapy stimulates wound healing and bone regeneration (following pathologic fractures or resection of bone).

Patients receiving toxins before and immediately after amputation appeared to have little or no "phantom pain." The pain relief in patients not subjected to surgical ablation (i.e. inoperable or preoperative cases) was marked, and often evident within a few days after the first toxin injection.

Since tumor cells are more vulnerable to heat than normal cells, the febrile reactions elicited by the Coley toxins seem to be of value. The intratumoral or intravenous routes elicit fever with much smaller doses than the intradermal or intramuscular. Intramuscular or subcutaneous injections appear to be less effective than other sites.

It is hoped that the data assembled in this monograph will stimulate more extensive studies on the most effective use of various forms of immunotherapy in ostoegenic sarcoma.

TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION: 45 Cases

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
FEMUR: 18 cases: 10 osteogenic, 3 osteochondrosarcoma, 5 fibrosarcoma						
1. W.B. Coley (10, #408; 12; 16; 28, case 2; 41, case 10; 43, case 10; 47, case 16; 52)	F 18 (S.D.)	osteogenic sarcoma distal rt. femur; onset early 1905, pain in rt. knee; by Feb. 1906 bedridden, emaciated, extremely weak; (sections reviewed by Stewart, 1947)	medicines, cast applied for 7 mos., no improvement; explored, curetted April, 1906; 11 days later amputation 10 cm. below trochanter	none	Coley toxins (Tracy XI) 8 days after surgery; 0.5-8 minims, daily at first then every 2-3 days with 2 intervals of rest, for almost 6 mos., i.m. in buttocks; maximum reaction 104° F., caused inguinal lymph node enlargement	2 mos. after toxins were begun general condition had markedly improved (weight, hemoglobin, r.b.c.); gained 23 lbs. in 4 mos.; NED; obtained prosthesis Jan. 1908, returned to work; in very good health until Oct. 1953, then acute arthritis of lt. knee; given cortisone; within weeks scirrhus carcinoma of breast developed with axillary metastases; radical mastectomy Dec. 1953; well 5 yrs.; pulmonary metastases evident following bronchitis 1957; death at 71, Sept. 17, 1958, 53 yrs. after onset of osteogenic sarcoma, almost 5 yrs. after onset of mammary carcinoma

2. W.B. Coley (10, #582; 16; 41, case 6; 43, case 6; 52)	F 40 (R.W.S.)	osteogenic sarcoma distal femur, onset immediately after fall; of rapid growth	amputation over 6 mos. after onset	none	Coley toxins (Tracy XI) begun 2 wks. after surgery; daily i.m. then every 2 days, 0.5-5 minims; maximum reaction 104° F. continued by family physician for 15 mos.	some weight loss, practically bedridden at first, then complete recovery; in very good health thereafter; 1941 developed arteriosclerotic heart disease; death, coronary thrombosis May 27, 1946, at 78, 38 yrs. after onset of osteogenic sarcoma
3. W.B. Coley (10; # 172; 16; 41, case 26; 44, case 7; 46, case 7; 123)	M 19 (H.S.)	osteogenic sarcoma distal femur; onset Feb. 1920, immediately after fall; pain in popliteal space	local applications; small doses radium	July 1920: radium pack (20,958 mch); amputation August 1920, 6 mos. after onset	Coley toxins (Tracy XI) April 24, 1920 i.m. in buttocks for 3 wks, prior to surgery, caused definite decrease in size; continued 3-4 times weekly for 2½ mos.; toxins resumed after radium, maximum dose 24 minims, no marked reactions; improvement temporary	complete recovery after amputation and further toxins; in excellent health until death at 50, Dec. 1951, coronary occlusion, 31 yrs. after onset
4. B.L. Coley (10, #800; 16; 88; 123)	F 16 (E.R.)	osteogenic sarcoma distal rt. femur; onset Spring 1925, pain, then swelling	amputation Nov. 1925 (gross appearance osteochondrosarcoma)	excision of cicatricial area in center of stump May 1926; small bit of cotton found in draining sinus)	Coley toxins (Parke Davis XIII) 11 days after surgery; daily then 3 a week in buttocks but mostly i.v.; reactions 103°-104.5° F.; continued about 4 mos. (latter half as an outpatient); 5 more doses toxins May 1926	gained 10 lbs. in 9 wks.; obtained prosthesis; good function; worked as bookkeeper, in excellent health until 1954: profuse postmenopausal bleeding due to multiple fibroids, panhysterectomy; after being mugged & mother's death, severe hemorrhaging peptic ulcer, 5 transfusions; in very good health, NED,* working full time 1975, 50 yrs. after onset

*NED = no evidence of disease

TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
5. B.L. Coley (10, #1117; 16; 52)	F 37 (T.P.)	osteogenic sarcoma distal lt. femur, pathologic fracture; onset March 1928, swelling, intermittent pain, limitation of motion	none	radium packs (54,000 mch); mid-thigh amputation April 9, 1929, 13 mos. after onset (tumor 10 cm. in diameter; femoral marrow was hyperplastic); May 1929: x-ray (8) to chest	Coley toxins (Parke Davis XIII) June 12, 1928, 6 i.m., 6 i.v. prior to radiation; slight reactions except after 1st i.v. (103.6° F.); resumed Sept. 1928 (5 in 24 days); 3rd course April, 1929, 18 days after surgery: 7 i.v. in 27 days, reactions 101°-105.4° F.	complete recovery; 7th child born 1931; poverty prevented her obtaining prosthesis for yrs.; prior to 1950 developed Parkinson's disease, incapacitated by 1952; NED until death at 72, from coronary thrombosis April 18, 1964, 36 years after onset
6. W.B. Coley (52; 88; 123)	M 62 (S.K.)	huge telangiectatic osteogenic sarcoma distal lt. femur, with hepatomegaly; 50 lb. weight loss; marked emaciation; onset Feb. 1930, also had hypertension (240), pituitary dystrophy	heat, baking, massage; x-ray (7); tumor then grew rapidly; radium; amputation 7 mos. after onset (tumor 19 cm. in length many areas of necrosis)	none	Sept. 27, 1930: Coley toxins (Parke Davis XIII) begun 19 days after surgery, given 1 month i.m.; moderate reactions (to 102.1° F.)	complete recovery, but did not obtain prosthesis; pea-sized nodule excised from rt. leg 1936; "giant cell tumor of tendon sheath"; in good health, NED until sudden death heart attack Nov. 22, 1939, 9½ years after onset
7. B.L. Coley (10, #1767; 16; 23; 123)	F 15 (M.B.)	osteogenic sarcoma distal rt. femur; onset, Feb. 1934, pain in rt. knee, then swelling, limitation of motion	aspiration biopsy, high thigh amputation 6 wks. after onset	none	Coley toxins (Parke Davis XIII) April 1934, about 2 wks. after surgery, daily for 10 days i.m. reactions to 102.4° F., maximum dose 10 minims	complete recovery; obtained prosthesis, attended business school, worked as secretary; in excellent health except for hysterectomy for fibroids in 1956; fractured lt. hip 1965; cholecystectomy 1972; continued to work until 1974; NED March 1975, 41 yrs. after onset

8. B.L. Coley (10, #2065; 16; 123)	M 21 (A.L.)	recurrent osteogenic sarcoma distal rt. femur; onset July 1934	incisional biopsy Sept. 7, 1934; amputation refused; incomplete excision elsewhere October 1934; x-ray (8 in 8 days) December 1934; high thigh amputation February 1935	none	Coley toxins (Parke Davis XIII) March 3, 1935, 8 days after amputation; 5 i.m., 5 i.v. in 23 days; developed pleural effusion requiring several thoracenteses, considered due to pulmonary metastases	complete recovery; fracture rt. forearm November 1935; obtained prosthesis, married 1949, had 2 sons; in excellent health 1975, except for mild diabetes, 40½ years after onset
9. B.L. Coley (10, #2059; 16; 123)	F 6 (E.B.)	osteogenic sarcoma distal lt. femur; onset September 1935	aspiration biopsy, x-ray (2000 r in 2 weeks)	January 1936 x-ray (2000 r); curettage March 1936; cavity saturated with zinc chloride, Dakin's solution; high thigh amputation July 1936, 10 mos. after onset; blood transfusion	Coley toxins (Parke Davis XIII) Dec. 1935, 4 i.m. little or no reaction; resumed April 1936 (Special Lilly product) i.m. and i.v. daily for 6 wks.; in excellent condition until late June 1936 when wound broke down	regained strength; recurrent furunculosis in axilla due to crutches, persisted for over 18 yrs.; in excellent health working as a stenographer March 1975, 39½ yrs. after onset
10. B.L. Coley (10, #2062; 16; 123)	M 23 (W.R.R.)	osteogenic sarcoma distal lt. femur; onset October 1935, following a fall; weight loss, general condition poor	diathermy for 1 week, increased pain but aspiration biopsy negative; x-ray November 1935; some improvement but required crutches to ambulate; x-ray (2 more) March 1936, knee increased in size; 2nd aspiration biopsy May 30, 1936; cast applied June 1936; high thigh amputation August 1936, 10 mos. after onset	hip joint disarticulation for recurrence October 1937	fever 104.6° F. for 3 days after amputation with emesis and diarrhea; Coley toxins (Parke Davis XIII) begun 5 weeks after amputation; 8 i.m., 7 i.,v. in 16 days, reactions to 103° F.; pyocyaneous infection of part of wound after disarticulation; wound healed 2½ mos. later	in excellent health 1 yr. then recurrence in stump; no further evidence of disease, after disarticulation and wound infection; in excellent health when last traced October 1952, 17 years after onset
10a.C. Ford (10;16)	M 12½ (W.L.C.)	Osteogenic sarcoma distal rt. femur, onset folling severe bruise February 1921; in bed 8 weeks low grade fever, following scarlet fever summer 1920.	hot packs for 2 wks. Parents refused amputation. May 20, 1921 x-ray for 1 mo. prior to toxin therapy.	Radium needles (12,600 mch.) inserted in tumor weekly May 5-July 11, 1921. Amputation, Sept.9 1921 (7 mos. after onset.)	Parke Davis XIII March 26, 1921 for 6 wks. Chills, marked febrile reactions.	Tumor increased steadily in size and density until Aug. 17, 1921 to 24x12 cm. with extreme pain, general condition deteriorated markedly; Following amputation, rapid recovery, gained 10 lbs. in 10 days; obtained prosthesis. Studied medicine, then radiology. Married, 1934. Child born 1938. Retired at 70. Widowed; in retirement home 1983; remarried 1989. Alive & well at 85, 73 yrs. after onset.

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TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
11. W.B. Coley (10, #398; 16; 28; 41; 43; 46; 48; 52; 123; 168; 169)	M 22 (H.J.)	osteochondrosarcoma proximal lt. femur (originally regarded as Ewings sarcoma); onset February 1909 while working 10 hrs. a day as an engraver	physiotherapy; growth 10 cm. long chiselled away en masse August 1909	hip joint disarticulation Dec. 1909, 10 mos. after onset; tumor 12 x 7 cm., large areas necrotic, contained leukocytes (patient broke his engagement because of his amputation)	Coley toxins (Parke Davis XII - a very weak formula) Sept. 1909, 20 days after surgery; 14 i.m. no reactions; resumed November 1909 i.m. 1-14 minims, only 3 febrile reactions (100.6°-102.4° F.); toxins resumed after amputation (potent Tracy XI) for 4 wks. i.m., reactions 102°-104° F.	ineffective toxin therapy fall 1909 did not prevent recurrence; under further injections some temporary decrease in size; no further recurrence or metastases after amputation and Tracy toxins; obtained prosthesis, resumed work, in good health, married; diabetes 1937; cholecystectomy, appendectomy 1950; transurethral prostatectomy 1951 (benign hyperplasia); also had perineal fistula in ano (many) would become infected, drain & close; 1957 lumbosacral degenerative arthritis; 1958 coronary atherosclerosis, 1959 acute myocardial infarction, ischemic heart disease; death July 10, 1965, 56 yrs. after onset, from heart attack; post mortem: no evidence sarcoma

12. W.B. Coley (12; 16; 35, 37 p. 123; 43, case 22 in Table 7; 50)	M 24 (H.P.P.)	very extensive osteochondrosarcoma lt. proximal femur onset October 1910 2-3 wks. after trauma, severe pain caused insomnia, general condition markedly deteriorated, cachexia; affected limb 20 cm. larger than normal	hip joint disarticulation April 1912, 18 mos. after onset (patient almost moribund)	none	Coley toxins (Tracy XI) April 25, 1912, 25 days after surgery; 53 in 76 days i.m. in pectoral region, little reaction except twice (102°-103° F.)	complete recovery; gained 30 lbs., in perfect health; returned to work; in excellent general and local condition when presented at Memorial Hospital April 1914; died Oct. 12, 1914, "asphyxia from illuminating gas, 4 yrs. after onset
13. B.L. Coley (10, #1042; 16; 123)	M 19 (W.H.R.)	osteochondrosarcoma distal lt. femur; onset early 1929, after slight trauma in Navy	x-ray (3) elsewhere; amputation May 15, 1929	none	Coley toxins (P.D. XIII) 5 days after surgery; daily at first, i.m. and i.v.; 50 in 6 mos.	complete recovery; in excellent health 27 yrs.; 1956: hypertension; February 1957: intestinal obstruction; x-rays negative; death from "peritonitis due to multiple ulceration of large bowel" (autopsy), Feb. 28, 1957, 28 yrs. after onset
14. W.B. Coley & Graham (10, #184; 41, case 17; 123)	F 26 (G.T.)	fibrosarcoma lt. distal femur, onset February 1916, after 2nd fall on knee	explored June 1916: "chronic osteitis"; radium packs July 1916 (24,000 mch), no improvement	amputation August 20, 1916	Coley toxins (Tracy XI) July 5, 1916: 7 in 14 days, i.m., 0.5-4½ minims; mild reactions to 101° F.; no improvement; toxins resumed immediately after amputation, continued for "considerable period" by Graham	complete recovery; NED, in excellent condition, returned to Scotland; alive and well 1924, 8 yrs. after onset
15. W.B.Coley & Barrow (10, #586; 16; 41, case 18; 43, case 18); 123)	M 48 (J.H.F.)	fibrosarcoma rt. femur (had fractured it twice at age 4 and 11); onset June 1916; evidence of tuberculosis in lt. lung (?)	August 1916, curettage; x-ray (8); temporary improvement, then increase	3 radium packs (2000 mch) given during toxins Oct. 1916; hip joint disarticulation Oct. 31, 1916, 4 mos. after onset	Coley toxins (Tracy XI) Oct. 16, 1916; 6 i.m. & 3 in tumor in 12 days; little improvement; some suppuration in stump; November 1916 toxins resumed (Tracy XI F, filtrate) continued by Barrow 8 mos.	complete recovery; in good health, NED until sudden death, cerebral hemorrhage 1936, 20 yrs. after onset

TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
16. W.B. Coley (10, #2060; 16; 123)	F 11 (M.L.)	extensive fibrosarcoma lt. distal femur; onset November 1935	incisional biopsy January 1936; radium packs daily January 24-February 7, 1936 (60,000 mch)	amputation April 29, 1936, 6 mos. after onset; fatty tissue excised from stump, acetic acid dressings	February 7, 1936: Coley toxins (Special Lilly preparation) 10 i.m. & 2 i.t., reactions to 106° F.; large tumor became inflamed, fluctuant, tense, but no smaller; pyocyaneous infection of stump, considerable slough; profuse discharge; May 14, 1936, 10 more doses toxins in 10 days, reactions to [illegible] 104° F.	complete recovery; obtained prosthesis, NED, in good health, attended regular school, obtained job as secretary, bookkeeper, became general office manager; well until Nov. 1963 mammary carcinoma, radical mastectomy January 1964; panhysterectomy October 1964; alive & well, NED 1975, 39½ yrs. after onset of fibrosarcoma & over 11 yrs. after onset of breast cancer
17. B.L. Coley (10; #2272; 16; 123)	F 14 (M.S.H.)	fibrosarcoma distal rt. femur; onset November 1937	aspiration biopsy x-ray January 24, to February 12, 1938 (4,800 r.) each preceded by 15 minutes of diathermy; blood transfusion (600 cc); amputation February 1938, 3 mos. after onset (effects of radiation and heat apparent in specimen)	none	Coley toxins (P.D. XIII) begun 9 days after amputation; given daily, 8 i.m., 7 i.v., febrile reactions to 103° F.; few mild infections and dermatitis of stump	complete recovery; married; daughter 1944, son 1950; in excellent health, NED, until sudden death cerebral thrombosis, Oct. 28, 1965, 28 yrs. after onset, at age 42
18. Dodd (16)	M 64 (?)	recurrent fibromyxosarcoma distal femur	surgical excision of primary, reported as benign myxoma; recurred in 6 mos., amputation; reported as fibromyxosarcoma	none	Coley toxins (P.D. XIII) for 2 mos., gained weight during treatment	complete recovery, NED when last traced December, 1945, 4 yrs. after onset

HUMERUS: 7 cases: 5 osteogenic, 2 fibrosarcoma·

19. Mayo Clinic (16; 122; 127)	F 56 T.C.R.	huge recurrent osteogenic sarcoma proximal humerus; onset June 1915, 5 mos. after trauma	local excision	interscapulothoracic amputation at Mayo Clinic, July 1916	Coley toxins (Tracy XI) May 1916 by Thompson in Texas; 15 in 2 mos.; did not prevent recurrence, pathologic fracture; toxins resumed after amputation	complete recovery; in good health; became insane 1941; fell, fracturing hip 1946, died a month later at 87, April 19, 1946, 31 yrs. after onset
20. W.B. Coley (10, #1352; 12; 16; 123)	F 34 (K.C.)	large sclerosing juxtacortical osteogenic sarcoma proximal rt. humerus, extensive involvement soft tissues; onset March 1925, pain in both arms regarded as rheumatic; August 1925 upper rt. arm rapidly enlarged	x-ray August 25, 1925 (2 for 80 minutes each, anterior and posterior); amputation September 1925, 6 mos. after onset	none	Coley toxins (Tracy XI) Sept. 30, 1925, 2 wks. after surgery; i.m. for 6 mos., at 1st every other day, alternating shoulder and buttocks	complete recovery; in excellent health 33 yrs., then developed chronic myelogenous leukemia; repeated transfusions; death April 14, 1959, 34 yrs. after onset of osteogenic sarcoma**
21. B.L. Coley (10, #1860; 123)	M 23 (J.F.B.)	osteogenic sarcoma proximal humerus originating 10 yrs. after curettage and x-ray for cyst resulting in pathologic fracture, false joint, 15 cm. shortening; onset sarcoma June 1934, lost 38 lbs. in 9 mos., evidence lung metastasis April 1935	interscapulothoracic amputation March 1935; blood transfusion (400 cc.)	none	Coley toxins (P.D. XIII) April 2, 1935, 9 days after surgery, daily i.m. rapidly increasing doses, later i.v. (11 in 12 days, reactions to 103.2° F.)	lung lesion no longer apparent 3 wks. later; regained 38 lbs. lost weight; in excellent health until sudden death June 18, 1952, coronary occlusion, myocardial failure, over 18 yrs. after onset

** See below Case 26 for another case who developed myelogenous leukemia 25 years after receiving three massive x-ray treatments (two hours each)

TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
22. B.L. Coley (10, #1864; 16; 123)	F 12 (K.H.)	osteogenic sarcoma rt. proximal humerus 8x9x7 cm. with pathological fracture, arm markedly edematous glenoid fossa filled with tumor, cartilage completely destroyed, patient obese (169 lbs.); onset December 1933	massage for 1 mo. by midwife; x-ray spring 1934; radium October 1934 (15,000 mch); May, June 1935 further radium (30,000 mch); considerable healing; reactivation fall 1935; interscapulothoracic amputation Nov. 19, 1935, 23 mos. after onset	terminal neuroma excised 1938; superficial area of gangrene following this procedure, wound healed slowly; 1947 another neuroma (brachial plexus)	incision broke down (mild infection?); Coley toxins (P.D. XIII) 1 wk. after surgery; 15 in 18 days i.m. maximum febrile reaction 104.4° F.; wound then rapidly healed; pinch grafts took 100%; 1 year after surgery rheumatic fever following u.r.i. with fever and cervical lymphadenitis, no heart lesion developed	in excellent condition, complete recovery, only problem anxiety neurosis caused by long illness and deformity; gradually overcame this, studied typing, working regularly thereafter; in excellent health, NED October 1961, 28 yrs. after onset
23. B.L. Coley (88; 123; 165)	F 49 (F.C.)	osteogenic sarcoma rt. proximal humerus, developing in Paget's disease; onset November 1936	treated as arthritis for a year; x-ray (2), aspiration biopsy, disarticulation refused; 2nd aspiration biopsy May 1938	x-ray (10) March 1938; x-ray (10) Fall 1938 (1,675 r. tumor dose)	Coley toxins (P.D. XIII) Feb. 28, 1938, 9 i.m. in 9 days febrile reactions 102° -103° F.; 4 more i.m. (15 minims each) last wk. in March 1938 (reactions 104°-105° F.) 2nd course toxins May 1938; 5 i.m. in 5 days; reactions averaged 102°-103° F.; final course November 1938: 7 i.m. in 9 days, 1 i.v. (reactions 101°-104° F.)	pain ceased, gradual shrinkage of palpable mass over proximal humerus, steady gain in weight, complete recovery, *limb saved;* marked regeneration of bone, little restriction in use of arm; in excellent health, NED until sudden death heart attack, November 1942, 6 yrs. after onset

24. Gibbon (10, #413; 12; 14, case 7; 16; 52; 175)	F 17 (I.R.)	recurrent fibrosarcoma rt. distal humerus; slight trauma prior to onset, January 1908	iodine applied locally, causing severe irritation; growth removed surgically 5 wks. after onset (amputation refused)	several x-ray treatments	Coley toxins (weaker P.D. XII) Feb. 8, 1908 4 days after surgery i.m. near wound, no reactions for 9 days, did not prevent local recurrence apparent by March 6, 1908; potent Tracy XI preparation then used steadily for several months	recurrence disappeared, complete recovery, limb saved NED, married, had 4 children, in excellent health 1947; death Oct. 24, 1958 heart failure, cerebral thrombosis, severe hypertension, pulmonary edema, generalized arteriosclerosis; also had carcinoma rt. breast; survived 50½ yrs. after onset
25. B.L. Coley (10, #1774; 16; 123)	F 34 (C.T.)	medullary fibrosarcoma lt. proximal humerus, moderately anaplastic; onset November 1933; spontaneous abortion 4 wks. later	tumor incised, incompletely curetted, pathologic fracture, tumor then fungated; March 27, 1934 interscapulothoracic disarticulation	none	slight wound infection; Coley toxins (P.D. XIII) begun 9 days after surgery, 9 i.m.; reactions 101°-105° F. final i.v. 106.8° F.	complete recovery; patient again pregnant August 1934; pregnancy & confinement uneventful; in very good health when last contacted Oct. 16, 1959; returned to Italy, death July 9, 1964, over 30 yrs. after onset, cause unknown
TIBIA, 10 Cases: 4 osteogenic, 2 chondrosarcoma,4 fibrosarcoma						
26. Linder (12; 16; 123)	F 19 (E.B.)	twice recurrent osteogenic sarcoma proximal tibia onset July 1, 1914, 4 mos. after trauma	treated for rheumatism; local excision September 1914; 3 x-ray treatments (*2 hrs. each*) causing deep purple discoloration, 2nd operation for dermatitis; recurrence December 1914; 2nd recurrence by January 1915; amputation February 1915, 7 mos. after onset	none	Coley toxins (Tracy XI) February 1915, soon after amputation, continued several months	complete recovery, NED thereafter; well 23 yrs., then acute myeloblastic leukemia, death March 21, 1925, over 24½ yrs. after onset osteogenic sarcoma*

***NOTE:** See above, case 20 for another case who also received massive x-ray and 33 yrs. later developed myelogenous leukemia

TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
27. W.B. Coley (10; #181; 41, Case 27; 43, case 27; 52; 123)	M 16 (A.K.)	osteogenic sarcoma proximal lt. tibia onset July 1920, 2 mos. after trauma	3 casts applied for 8, 6 & 8 wks. respectively; incisional biopsy February 2, 1921, curettage next day	radium packs May-Nov. 1921 (96,554 mch)	Coley toxins (Tracy XI & P.D. XIII) begun a week after curettage, i.m. (reactions to 103.2° F.), toxins continued during radium therapy for 7 mos.	*limb saved*: wound healed, great improvement in tibia, calcification proceeded, by July 1922 no evidence of disease in tibia but had pulmonary tuberculosis; tibia continued to improve, lung condition worse, finally caused death November, 1925 over 5 yrs. after onset (no lesion in tibia at death)
28. W.B. Coley (10, #177; 16; 41, case 24; 43, case 24; 46, case 19; 88)	M 15 (J.C.)	osteogenic sarcoma rt. proximal tibia, onset 1 wk. after trauma, late July 1921	local applications; 4 electric treatments; Oct. 6, 1921, explored	radium (40,162 mch.) Oct. 21, 1921; amputation, Dec. 2, 1921	October 7, 1921: Coley toxins (Tracy XI) 15 hrs. after exploratory surgery; 8 in 14 days i.m. reactions to 101.8° F; toxins resumed Oct. 28, 1921, given 6 mos. by family physician	complete recovery, NED, well until July 1944; nephrectomy for renal stone; returned to work as engineer; 1926, shot in chest in hold-up, causing hemothorax, requiring thoracentesis; in excellent condition until December 1962, fell on ice fracturing femur also had developed hypertension; unemployed, became alcoholic, heavy smoker, fell downstairs 1963, cerebral concussion, compression of 3 vertebrae, fracture of T5; lost to follow-up thereafter; this was 43 yrs. after onset

29. B.L. Coley (16; 123)	F 16 (K.B.McN.)	osteogenic sarcoma proximal lt. tibia (osteolytic type); onset December 1939	incisional biopsy May 1940, curettage, mid-thigh amputation, May 16, 1940; transfusion (500 cc. whole blood)	December 1940 P32, 11 doses in 5 mos. causing leukopenia (3000 wbc)	Coley toxins (P.D. XIII) begun 5 days after amputation; 14 in 20 days (8 i.m., last 6 i.v.) reactions 100.6°-106.4° F., chills on 9 occasions, 3 severe, herpes labialis once	complete recovery; in excellent condition, obtained prosthesis Nov. 27, 1940; remained in excellent health, obtained job, but worked too hard (overcompensating); married, 1947, daughter 1949; NED 1975, over 35 yrs. after onset
30. W.B. Coley (10, #833; 16; 123)	F 8 (R.M.)	chondromyxosarcoma proximal half rt. tibia, onset osteitis fibrosa cystica Fall 1921; onset sarcoma early 1927	treated for osteitis fibrosa cystica for over 3 yrs., 2 or 3 operations, radium	amputation 1938 for recurrence	Coley toxins (P.D. XIII) June 11, 1927: 25 i.m. in 60 days	great improvement, bone regenerated, gained 13 lbs. well 10½ yrs., then recurrence; good recovery after amputation; obtained prosthesis; worked as bookkeeper, married 1957, several miscarriages; adopted 2 children; alive and well 1975, 48 yrs. after onset
31. B.L. Coley (16, 123)	M 38 (J.M.)	chondrosarcoma lt. mid-tibia, onset early 1928	surgical removal encapsulated growth 1932, 3 yrs. after onset	April 1932: radium needles in wound (2,000 mch); x-ray (2) wide excision; skin graft fall 1935	Coley toxins (P.D. XIII) 6 wks. after surgery 7 i.m. in 9 days reactions to 104°F; March 1933, mastoidectomy after influenza	complete recovery: summer 1935 irradiated area ulcerated, did not heal for 8 yrs., recurred during hunting season; well until 1950, then adenocarcinoma of sigmoid colon, grade III; partial colectomy; died Oct. 19, 1952, liver metastases from colon carcinoma, (no evidence chondrosarcoma) 24 yrs. after onset, limb saved

TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
32. Ashhurst (4; 5; 6; 60)	M 44 (A.K.)	fibrosarcoma rt. proximal tibia (parosteal in origin); onset March 1915, 4 mos. after severe local trauma	area "lanced" June 1915; proximal tibia resected September 1915, bone graft from other tibia	none	Coley toxins (Tracy XI) begun 3 days after surgery; given every 24-48 hrs. for several mos. i.m.	complete recovery, *limb saved,* NED 1931, 16 yrs. after onset
33. Campbell Clinic (10, #1177; 15; 16)	M 46 (A.L.M.)	fibrosarcoma distal rt. tibia; onset February 1926	incisional biopsy and amputation Feb. 18, 1927, 1 yr. after onset	none	Coley toxins (P.D. XIII) every 48 hrs. for 4 mos. i.m. (reactions averaged 99°-100° F.)	complete recovery; neuroma on stump prevented wearing prosthesis; developed diabetes 1950; some "prostate trouble"; NED until death July 5, 1958, at 77, 3 wks. after a bad fall, 31½ yrs. after onset
34. B.L. Coley (10, #1454; 16; 123)	F 19 (T.L.S.)	fibrosarcoma proximal rt. tibia, onset October 1929	December 1929 x-ray (2); January 1930 aspiration biopsy causing temporary regression; incisional biopsy April 1930	x-ray April 3; 4 radium packs April 4-7, 1930 (32,000 mch); incisional biopsy; May 1933 x-ray (1,500 r.) for local recurrence; amputation September 1933, almost 4 yrs. after onset	Coley toxins (P.D. XIII) March 31, 1930; 16 i.v. in 33 days, 12 caused chills; reactions to 102.6° F. gained 18 lbs. in 6 weeks; follicular tonsillitis May 1933, some regression then occurred; September 1933 toxins resumed i.v. & i.m. after amputation; 21 in 13 wks., no severe reactions	complete regression, gained 10 lbs; became pregnant, child born July 1931; well nearly 2 yrs., slight recurrence May 1, 1933; condition satisfactory until area traumatized August 1933, disease then reactivated, lost 7 lbs.; gained 20 lbs. during final toxin therapy; NED thereafter in excellent health 1975, 46½ yrs. after onset

35. Campbell Clinic (10, #1177; 15; 16)	M 16 (B.H.)	fibrosarcoma (grade II) proximal lt. tibia; onset early September 1931, several months after slight local trauma	incisional biopsy December 7, 1931; amputation 3 mos. after onset	none	Coley toxins (P.D. XIII) Dec. 12, 1931, shortly after surgery, 3 i.m. a week in courses of 6 wks. with intervals of 2-4 wks. rest, total 20 mos.; reactions 102°-104° F.	complete recovery; used prosthesis well, worked as accountant, married 1945, gained 20 lbs., in good health, NED 1975, 43½ yrs. after onset
SMALLER BONES: 10 cases						
36. B.L. Coley (10, #2069; 16; 123)	F 26 (M.W.W.)	recurrent fibrosarcoma rt. distal fibula, onset October 1934, 4 yrs. after trauma	local heat, considerable relief; March 1934, distal fibula resected 5 mos. after onset; recurred in 6 mos.; 2 aspiration biopsies (unsatisfactory)radium (40,000 mch), no benefit; amputation 15 mos. after onset	none	Coley toxins (P.D. XIII and special formula similar to Buxton VI) Feb. 3, 1936, shortly after amputation i.m. & i.v. 19 in 21 days, marked reactions	complete recovery; gained 30 lbs.; married 1944, 1 miscarriage, 1 pregnancy; NED; Pap smear 1959: squamous cell metaplasia: panhysterectomy; gained 20 lbs., well except for menopausal symptoms 1960-62: recurrent episodes angina pectoris; 1962, myocardial infarction; 2nd coronary fatal, April 1963, 28 yrs. after onset
37. W.B. Coley (10, #187; 16; 41, case 12; 43, case 12; 52; 123)	F 15 (C.W.)	fully malignant fibrosarcoma rt. distal ulna, with deformity and atrophy of radius, onset 1909, 1 yr. after severe trauma	brief x-ray; tumor increased in size; several operations, incisional biopsy;	amputation May 1913, 4 yrs. after onset	some form of vaccine therapy, type unknown; April 1913: Coley toxins (Tracy XI) subcut., i.m. & in tumor area; 22 in 47 days; little improvement, toxins resumed for considerable period after amputation	complete recovery, gained 30 lbs. in a year, NED thereafter; hysterectomy 1937 for uterine fibroids; in good health until death, heart attack, June 12, 1949, 40 years after onset

TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
38. Huntington (12; 16; 32, case 6; 36, p. 558; 40, case IV; 52)	M 40 (X.H.)	osteogenic sarcoma rt. clavicle, onset June 1908, 21 mos. after severe trauma	total excision clavicle September 1908, 3 mos. after onset	none	slight wound infection (3 mos. to heal); Coley toxins (Tracy XIII) begun 2 wks. after surgery, every 48 hrs. in region of wound for 6 mos., reactions to 106° F.	complete recovery, in perfect health, NED until 1926, then chronic valvular heart disease, death December 15, 1931, 23 yrs. after onset
39. B.L. Coley (21; 123)	M 35 (P.S.G.)	inoperable osteogenic sarcoma rt. scapula (low grade spindle cell); atrophy of shoulder girdle, 40 lb. weight loss; onset 1932	diathermy, insulin injections; September 1935: x-ray (1500 r); no regression; 2 aspiration, 1 incisional biopsies Sept.-Oct. 1935; radium implant Nov. 9, 1935 (5,000 mch)	none	Coley toxins (P.D. XIII) Nov. 11, 1935, 22 in 30 days 15 i.m., 11 i.v. & 5 in tumor, reactions to 105.4° F. from i.v.	regression occurred during toxin therapy also marked symptomatic improvement, palpable tumor much smaller, intense radiation reaction (vesication); gained 20 lbs. in 9 mos., last traced in excellent health, good function, NED 1951, over 15 yrs. after onset
40. Mayo Clinic & Family Physician (16; 37, case 100 in Table; 122)	M 34 (D.J.)	recurrent osteochondrosarcoma rt. ilium; onset early 1912; (2 of recurrences were reported as chondrosarcoma, rest as chondroma)	tumor size of fetal head removed at Mayo Clinic February 1912; toxins advised	2nd recurrence excised and cauterized May 1914; 8 more excisions for recurrences 1918-1935 (total of 12 operations)	Coley toxins (Tracy XI) begun 5 wks. after 1st operation by Dietz for recurrence: 78 i.m. in 1 yr.; toxins resumed for 3 mos. after 2nd operation (self-administered) using Tracy XI and P.D. XII	growth regressed, complete recovery; further recurrences 1918-1935; none after 1935; in relatively good health until Dec. 1, 1969, then congestive heart failure due to arteriosclerotic heart disease, and acute myelogenous leukemia; death Dec. 17, 1969 at 91 yrs. of age, over 57 yrs. after onset

41. W.B. Coley & Cook (10, #373: 16;43;51)	F 28 (K.F.)	inoperable osteogenic sarcoma 7th, 8th and 9th rt. ribs, onset 1922, 3 yrs. after fluoroscopy to this area	explored June 1922; x-ray (2), radium packs to axilla December 1922	none	Coley toxins (P.D. XIII) Dec. 6, 1922, continued by Cook for 11 mos. i.m. in buttocks	tumor regressed very slowly periodic chest films showed improvement; had 2 normal children 1925, 1931, nursed them both; extreme cystic mastitis next 7 yrs. bilateral mastectomy 1938; acute glaucoma 1957; in good health thereafter, NED April 1975, 53 yrs. after onset
42. Univ. Hosp. San Francisco (184)	F 16 (J.W.)	osteogenic sarcoma "bones of foot"	x-ray to chest and foot Oct. 9-24, 1929; amputation Oct. 29, 1929	none	Coley toxins (P.D. XIII) after amputation - "prolonged course"	complete recovery; married, well, NED 10 yrs. after onset
43. B.L. Coley (16; 123)	F 15 (D.B.)	very cellular chondrosarcoma (grade III) lt. os calcis; onset April 1932, 1 wk, after turning ankle severely	incisional biopsy, amputation Aug. 6, 1932	none	Coley toxins (P.D. XIII) 1 week after surgery; 10 i.m. in 14 days, reactions averaged 103°-104° F.; 2nd course October 1932, 8 i.m. & i.v., marked reactions (102°-105° F.)	complete recovery, married, 8 children in 16 yrs., husband died encephalitis prior to last child's birth 1957 (she was a mongoloid); peptic ulcer 1959; despite her problems remained in excellent health as did her children and 8 grandchildren until August 1974, then primary lymphosarcoma involving mediastinum; complete remission after chemotherapy; no evidence osteogenic sarcoma, 2nd primary quiescent 1975, 43 yrs. after onset

TABLE 1. OSTEOGENIC SARCOMA SUCCESSFULLY TREATED BY IMMUNOTHERAPY AS AN ADJUVANT TO SURGERY OR RADIATION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Years Traced After Onset
44 B.L. Coley (10, #1493; 16;123)	F 34 (L.W.)	osteochondrosarcoma metatarsal bones rt. foot, onset early September 1929	x-ray March 1930 (500 r tumor dose); radium pack, April 1930 (1400 mch); vesication, pain relief; May 1930, radium pack (7000 mch); total radium about 760 r. to dorsal margin	bulky, friable tumor excised May 14, 1930; wound swabbed zinc chloride; amputation May 24, 1930 8 mos. after onset	Coley toxins (P.D. XIII) May 5, 1930: 7 i.v. in 14 days moderate reactions	complete recovery, in excellent health thereafter; in later yrs. developed arthritis & poor circulation; NED 1975, 45½ yrs. after onset
45. W.B. Coley & Lund (10, #239;16;43, Case 53; 52)	M 14 (G.P.)	4-times recurrent osteogenic sarcoma mastoid; onset 1915	4 operations for primary and 3 recurrences December 1915 to June 1916; radium (2) January 1916	2 or 3 x-ray treatments August 1916	Coley toxins (P.D. XIII) begun by Lund, July 1916 (no reactions); Coley resumed injections, increasing dose to produce reactions of 103° F., continued at home by Lund for nearly 1 yr. (i.m.)	complete recovery, no further recurrence, in excellent health, NED when last seen 11 yrs. after onset, shortly afterward committed suicide in fit of depression

FIGURE 4

CAUSES OF DEATH IN SUCCESSFUL SERIES

Of the 45 successfully treated cases, 25 died from 4 to 57 years after onset of their osteogenic sarcoma. The causes of death are listed as follows:

a. **Other forms of neoplastic disease:** 5 cases

One patient developed scirrhus carcinoma of the breast following administration of cortisone for arthritis, causing death at 71, 53 years after onset of her osteogenic sarcoma of the femur. (Table 1, case 1).

One patient died of adenocarcinoma of the sigmoid colon with liver metastases 24 years after onset of his osteogenic sarcoma of the tibia (Case # 31).

Three patients developed chronic myelogenous leukemia causing death 24, 34 and 57 years after onset of their bone sarcomas. (Table 1, cases 20, 26 and 40). Case 20 (juxtacortical osteogenic sarcoma of the humerus) and 26 (twice recurrent osteogenic sarcoma of the proximal tibia) received two and three massive doses of x-ray prior to toxin therapy (lasting 80 and 120 minutes respectively). Case 40 had no x-ray therapy, but 12 operations for recurrent chondrosarcoma of the ilium, for which he had repeated x-ray examinations.

b. **Cardiovascular disease:** 13 cases

5 coronary thrombosis (case #2, 3, 5, 21, 36)
4 "heart attack" (#6, 23, 24, 37)
2 cerebral hemorrhage (#15, 17)
1 acute myocardial infarction (#11)
1 chronic heart disease (#38)

c. **Miscellaneous causes:** 7 cases

2 falls (case #19, 33)
1 peritonitis following multiple ulcerations of the colon 28 years after onset of osteochondrosarcoma of the distal femur (#13)
1 asphyxiation due to illuminating gas (accident) 4 years after onset (# 12)
1 pulmonary tuberculosis over 5 years after onset (#27)
1 suicide, 11 years after onset of osteogenic sarcoma of the mastoid (# 45)
1 cause unknown, over 30 years after onset (#25)

TABLE 2. OSTEOGENIC SARCOMA WITH CONCURRENT INFLAMMATION, FEVER OR INFECTION: 14 Successes

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Infection	Prior Therapy	Concurrent or Subsequent Therapy	Infection, Fever, or Inflammation	Immediate and Final Result Years Traced
FEMUR, 6 cases						
1. Speed (16; 173)	M 21 (J.D.)	osteoblastic osteogenic sarcoma rt. distal femur, pulmonary metasases, 30 lb. weight loss in 9 mos., insomnia due to pain, rt. knee twice normal size; excessive cigarette smoker; onset August 1928	none	amputation May 1929	stabbing pain on deep inspiration, cough, dustcolored sputum for 3 wks. prior to admission, also severe pains in rt. ilium & back; pain in chest, bloody frothy sputum persisted, uniform clouding of upper lobe interpreted as pressure atelectasis; 1930-1942: recurrent attacks dysnpea, cough, bloody sputum (repeated examinations negative for tuberculosis); 1942, wbc 14,000	obtained prosthesis; during 1930 chest films at intervals showed additional metastases & some enlargement of older lesions; later films showed scattered calcified masses; 1960 films: "no internal change in appearance of metastatic lesions throughout both lungs . . . doing very well last traced 1974, 46 yrs. after onset
2. Memorial Hospital (16; 123)	M 17 (I.L.)	osteogenic sarcoma rt. distal femur 4½ x 6 cm.; onset April 1942	aspiration, incisional biopsies; amputation September 1942	none	hemarthrosis rt. knee after biopsies, fever 100.4°-102.2° F. before & after amputation; moderate amount serous discharge for 10 days; small abscess on stump October 1943	prosthesis obtained 2 mos. after amputation, handled very well; gained 27 lbs. in 5 mos, in excellent condition, finished college, law school, married, 3 healthy children; in excellent health 1975, 33 yrs. after onset.

3. B.L. Coley (10, # 2260; 16; 123)	M 15 (D.H.S.)	osteogenic sarcoma distal rt. femur; onset, November 1938, 2 mos. after local trauma (deep pitch-fork wound 10 cm. above knee)	local heat incisional biopsy Feb. 1939, major portion curetted; 6 days later amputation (tumor 5 x 8 cm.)	Coley toxins (P.D.XIII) 4 days after amputation, 5 in 5 days i.m. (101.6° -104°F.) dose increased to 12 m.	had acne vulgaris; developed furunculosis of stump about 1 yr. after amputation, persisted for over 15 yrs. (staph.)	complete recovery; obtained prosthesis 4 mos. after surgery, returned to work as farmer, later as dairy inspector; basal cell carcinoma excised from neck 1962; in excellent health 1973, over 34 yrs. after onset
4. Memorial Hospital (16; 123)	M 10 (A.L.)	osteogenic sarcoma distal rt. femur, 5 x 8 cm.; onset July 1943; knee ankylosed, very markedly swollen, considerable weight loss, anemic, poor general condition (several enlarged lymph nodes in groin considered inflammatory)	x-ray for 3 wks. August 1943 (3600 r. tumor dose); severe radiation sickness; aspiration biopsy; mid-thigh amputation by Pack, September 1943	none	multiple erythema of arms, hands, legs, temperature 99° - 101.8°F. before and after amputation	complete recovery, obtained prosthesis; studied engineering; developed bilateral gynecomastia 1950; in excellent health when last traced August 20, 1959, 16 yrs. after onset
5. Memorial Hospital (16; 123)	M 12 (J.G.)	telangiectatic osteogenic sarcoma distal rt. femur; onset December 1942	February 1943 amputation, 2½ mos. after onset	2 transfusions whole blood (300 cc each) March 1943	fever 100°-104.6° F. on day of surgery, remained elevated 2 wks. (100°-104.6° F. septic type, no apparent cause)	complete recovery, obtained prosthesis, good psychological adjustment; in good health, NED until sudden death in auto accident, 1956, over 13½ yrs. after onset
6. Memorial Hospital (16; 123)	M 10½ (D.B.)	osteogenic sarcoma distal lt. femur, onset September, 1948 aggravated by football injury	aspiration, incisional biopsies; high thigh amputation October 1948	none	episode abdominal pain postoperatively, fever to 100.2° F. for 1 wk; throat cultures showed Streptococcus viridans and hemolytic Staph. aureus; later developed chronic otitis media	complete recovery; difficulty in adjusting to prosthesis at first, but good psychological adjustment, completed college, became a teacher, married; healthy daughter 1963; in excellent health 1975, 26½ yrs. after onset

TABLE 2. OSTEOGENIC SARCOMA WITH CONCURRENT INFLAMMATION, FEVER OR INFECTION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Infection	Prior Therapy	Concurrent or Subsequent Therapy	Infection, Fever, or Inflammation	Immediate and Final Result Years Traced
7. Rumel et al (162)	F 15 (at onset)	osteogenic sarcoma rt. distal femur December 1948; bilateral pulmonary metastases November 1949	mid-thigh amputation 2 mos. after onset; lung lesions seen 11 mos. later,November 1949; rt. middle lobectomy Nov. 22, 1949 for 5 cm. solitary lesion; Dec. 14, 1949, lt. lower lobectomy & lingulectomy with partial pericardectomy (3 lesions present 2-4 cm. in diameter)	none	after 2nd lobectomy critical period of hypotension with cardiovascular collapse and fever to 106° F.; followed by oliguria	complete recovery, normal, healthy; graduated from college, has worked steadily since - N.E.D. March 27, 1957, 8½ yrs. after onset
8. B.L. Coley (16; 123)	F 48 (M.D.)	very extensive osteochondrosarcoma proximal rt. femur (15 cm); onset April 1945, pathologic fracture Fall 1946	rt. hemipelvectomy November 1946 transfusion (2000 cc. whole blood, 1000 cc plasma)	penicillin, streptomycin; abscess incised 200-300 cc. heavy, purulent matter exuded; wet dressings for 3 wks; further penicillin for 2nd infection	postoperative infection 28 days later (hemolytic Staph. aureus) fever to 104° F.; large abscess in wound; another infection (sore throat, influenza, fever to 101.8° F.)	complete recovery, in excellent health; did own housework, ambulating on crutches; NED 1975, 30 yrs. after onset
9. B.L. Coley (16; 123)	F 42 (B.R.)	recurrent low grade fibrochondrosarcoma lt. proximal femur; (or juxtacortical osteogenic?); onset November 1944 (primary reported as osteogenic chondrosarcoma)	aspiration, incisional biopsies, tumor 11 x 7 x 5 cm. excised March 1, 1945; hip joint disarticulation November 27, 1947	penicillin; revision of stump, pinch grafts; sinus tracts excised, further penicillin	fell twice 2 days after amputation, hematoma on stump wound infected, foul odor; spiking temperature; atelectasis lt. distal lobe; deep pocket of pus in stump drained for 4 mos.; wound healed in 6½ mos.	well 1 yr. after primary was resected except for hysterectomy for fibroids May 1946; recurrence apparent November 1947; complete recovery; returned to work; in very good health March 1974, 29 yrs. after onset

10. Schatzki & Dudley (164, case 19)	M 46 1948	fibrosarcoma rt. humerus arising in Paget's disease which developed 22 yrs. previously	hospitalized for pathologic fractures of rt. tibia & fibula due to Paget's disease; open reduction; amputation of rt. leg; local resection 15 cm. of mid shaft rt. humerus & brachialis muscle; bone graft from fibula	none	sepsis and osteomyelitis after open reduction of fractures rt. tibia & fibula	despite lysis of graft, pseudoarthrosis & radial nerve palsy good function of hand; well to 1956, then urinary tract problem, congestive heart failure causing death 8 yrs. after resection of humerus
11. B.L. Coley (16; 123)	M 44 (M.B.)	osteogenic sarcoma rt. distal tibia; onset 1934, fractured tibia November 1934	aspiration, incisional biopsies; amputation September 1935	reamputation December 1935	post-operative fever, wound infection, osteomyelitis for 2 mos., fever to 103° F.	complete recovery, NED; obtained prosthesis; in excellent condition; benign bone lesion removed from sternum 1950; by 1972 had diabetes, cardiac failure; condition satisfactory until October 1974, then very ill, jaundice, ankle swollen, cause unknown; recovered without treatment, doing well March 1975 (age 84), 40 yrs after onset
12. Memorial Hospital (16; 123)	M 60 (J.diM.)	chondrosarcoma ischium; onset October 1944	hemipelvectomy January 1945, 3 mos. after onset	penicillin, digitalis, sulfadiazine, 5 transfusions, 500 cc. each; 2 of 250 cc. each	postoperative fever to 103.4 ° F., due to local infection; packing removed; 80 cc. bloody fluid evacuated	complete recovery; ambulated on crutches; did well until early 1963, then acute cholecystitis; cholecystectomy February 1963; further studies revealed adenocarcinoma sigmoid colon; reoperated March 1, 1963; large tumor resected, colostomy required; April 1963; metastases to throat from chondrosarcoma of ischium; progressive downhill course, death April 28, 1963, 18½ yrs. after onset

TABLE 2. OSTEOGENIC SARCOMA WITH CONCURRENT INFLAMMATION, FEVER OR INFECTION (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Infection	Prior Therapy	Concurrent or Subsequent Therapy	Infection, Fever, or Inflammation	Immediate and Final Result Years Traced
13. Jakoubková (16; 66; 67)	M 60 (J.V.)	osteogenic sarcoma proximal rt. ulna invading soft tissues; onset 1962 (weakness, fatiguability of rt. arm), tumor apparent early 1964	explored February 1964 amputation refused	drainage, antibiotics; 2nd exploratory operation; x-ray March 26-May 12, 1964 (4,000r tumor dose); no apparent benefit; antibiotics, temporary effect; amputation, June 27, 1964 (tumor size of man's fist)	postoperative phlegmona, drainage, Feb. 1964; cachetic, febrile during radiation due to necrosis & fistula over tumor area; (Staphylococcus & Achromobacterium); again febrile	lung metastases seen May 30, 1964, mainly in rt. lower lung; slight regression by June 18, 1964; general condition rapidly improved after amputation, gained weight; lung lesions at first increased, then disappeared by Nov. 1964; N.E.D. thereafter; died suddenly myocardial infarction Oct. 13, 1966, over 4 ½ years after onset
14. Doub (16; 59)	M 30 (J.T.)	osteogenic sarcoma clavicle; onset pain about December 1933 (mild injury mid-November 1933 with later some swelling which regressed and recurred several times; pathologic fracture January 15, 1934)	incisional biopsy January 18, 1934; x-ray (4 cycles 750 r. & about 500 r. posteriorly each time)	none	fever therapy in Kettering Hypertherm at weekly intervals (8) lasting 5 hrs., 105°-106° F. rectal	within 3 mos. x-rays showed partial recalcification, thickening of bone at fracture; pain-free, function of arm normal; fracture united in 5 mos., N.E.D., worked in large industrial plant, in excellent condition except for some discomfort in right shoulder; alive & well April 1973, over 40 yrs. after onset

Addendum, p. 48, case 14.

In 1959 subcutaneous lesion on back biopsied: mycosis fungoides; x-ray (2500 rads) n.e.d. thereafter; pathologist reviewed slides from primary lesion in clavicle 1976, not osteogenic sarcoma, felt it very possible that both lesions were manifestations of a type of lymphoma; last traced well 1976, 42 years after onset.

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TABLE 3, GROUP 1: OSTEOGENIC SARCOMA FAILURES, PRIMARY OPERABLE WHEN IMMUNOTHERAPY WAS BEGUN: 83 Cases

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
FEMUR: 49 Cases: (38 osteogenic sarcoma; 10 osteochondrosarcoma; 1 fibrosarcoma)						
1. Fabricius (42, case 8 in Table 7; 52)	F 21 (F.E.)	osteogenic sarcoma distal femur; onset July 1910	treated as t.b.; explored, excised January 1911	amputation 10 cm. above knee, early February 1911, 7 mos. after onset	Coley toxins (Tracy XI) January 1911, for 2 wks., probably i.m. (no details given) resumed i.m. in very small doses (1-2 minims) about March 1, 1911; 38 in 4 mos; average reactions 99.5°F.	no apparent effect from first course of toxins; in fair health until October 1912, then pulmonary metastases, death December 10, 1912, 26 mos. after onset
2. W.B. Coley (42 case 2 in Table 7; 52; 123)	M 19 (H.L.)	fungating, sclerosing central osteogenic sarcoma rt. femur; onset November 1915, shortly after trauma; inguinal, femoral nodes enlarged, limb very endematous, thigh to foot	physiotherapy; incisional biopsy x-ray (9) no benefit; referred to Coley; amputation Feb. 2, 1916; 3 mos after onset	none	Tracy XI, 13 in 19 days i.m. in pectoral & gluteal regions slight febrile reactions	good recovery; pulmonary metastases developed, causing death June 30, 1916; less than 9 mos. after onset
3 W.B. Coley (10, #100; 41, case 16; 42, case 16; 46, case 10; 52; 123)	F 23 (E.P.)	sclerosing osteogenic sarcoma distal rt. femur (18 cm); onset Dec. 1915; some weight loss	Oct. 23, 1916-Jan. 11, 1917, 7 radium treatments (total 9616 mc. in 56 hrs.) slight diminution after 1st dose, then began to enlarge, no further effect; early Feb. 1919 incisional biopsy in Baltimore	amputation July 9, 1917, 19 mos. after onset; small hard tumor excised from vulva 1926 "non-malignant"; 3 radium pack treatments to metastases late August 1928 (22,000 mch), no effect	Tracy XI & Parke Davis XIII Dec. 15, 1917, i.m. for 5 mos., mild reactions; following surgery prolonged course given	little benefit noted from preliminary toxins and radium; complete recovery after amputation; well 11 yrs.; June 1928: pain in ribs; 2 mos. later severe pain in spine on motion due to metastases in scapular region; involving ribs near spine; also in left lung; death Dec. 1928, 13 yrs. after onset

4. W.B. Coley (42, case 10 in table 7; 52)	F 14 (V.B.)	extensive osteogenic sarcoma rt. distal femur, oblique pathological fracture, rt. leg markedly enlarged almost to Scarpa's triangle; hemoglobin 25% (onset Feb. 1917)	plaster cast applied; hip joint amputation 3 mos. after onset	none	Tracy XI(?) given briefly after amputation	pulmonary metastases 4 mos. later; death Nov. 9, 1917, 9 mos. after onset
5. W.B. Coley (52)	F 12 (K.W.)	osteogenic sarcoma rt. femur involving distal half; onset June 1917	heat applied with some relief of severe pain; radium packs (11,700 mch) Sept. 7 & 20, 1917	3rd radium pack Oct. 3 1917; amputation Oct. 16, 1917, 4 mos. after onset	Tracy XI, Sept. 7, 1917 12 i.m. in 26 days; 101°-103° F.	thigh decreased 3 cm. in 1st 10 days of toxin treatment, then steadily increased; 3 mos. after amputation metastases to lungs, increased with great rapidity, death March 18, 1918, 9 mos. after onset
6. W.B. Coley (10, case 598; 46, case 9)	M 23 (J.A.L.)	osteogenic sarcoma distal rt. femur; Sept. 1923, struck leg against desk; onset Nov. 1923	Feb. 1924: x-ray for 2 mos. no benefit; explored May 9, 1924; amputation May 20, 1924, 6 mos. after onset	Feb. 1928: 2 radium packs (20,000 mch)	P.D.XIII May 27, 1924, a week after amputation; 13 in 25 days i.m., 1 marked reaction (104° F); toxins resumed for metastases Feb. 7, 1928: 9 i.v. in 4 wks., reactions to 104.4° F	very good recovery; well 3 yrs. until pleurisy August 1927 following another u.r.i.; December 1927 pulmonary metastases; gained 3 lbs; improvement temporary; death July 8, 1928, 4 ¾ yrs. after onset
7. B.L. Coley (10, #508; 42, case 47 in text; 123)	F 5 (P.S.)	fungating telangiectatic osteogenic sarcoma lt. distal femur; onset March 1924; almost moribund, growth 13 x 13 cm. when admitted to Memorial Hospital (trauma)	incisional biopsy; rapid growth; blood transfusion May 1924; amputation 2 mos. after onset; transfusion	none	P.D.XIII June 10, 1924 about 10 days after surgery; 21 i.m. in 41 days	general condition improved steadily; child grew remarkably that summer; well 1 yr.; July 1925 pneumonia; metastases to lungs, rt. shoulder; rapid downhill course; death Aug. 10, 1925, 17 mos. after onset

TABLE 3, GROUP 1: OSTEOGENIC SARCOMA FAILURES, PRIMARY OPERABLE WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
8. W.B. Coley (10, #512; 42, case 42 in Table; 123)	F 6½ (J.Z.)	osteolytic osteogenic sarcoma rt. distal femur, telangiectatic in areas; onset April 1924, about a week after trauma; pathologic fracture	plaster spica removed 2 days prior to fracture; a 2nd applied; x-ray June 1924(4)	amputation July 26, 1924, about 3 mos. after onset; x-ray to lungs	P.D.XIII June 13, 1924 26 i.m. in 37 days; slight reactions except twice (102° F. 103° F.)	no improvement following x-ray and toxins; metastasis to lung October 30, 1924; some improvement following x-ray; metastases to proximal humeri, rt. clavicle; death March 18, 1925, 11 mos. after onset
9. W.B. Coley (10, #784; 123)	F 15½ (L.F.)	densely ossifying osteogenic sarcoma distal femur; onset mid-June 1926	amputation Oct. 14, 1926, 4 mos. after onset	none	P.D.XIII begun immediately after amputation, i.m. continued at home by family physician (technique & reactions not recorded)	regained normal weight, in excellent health until June 1927 then lung metastases; death August 1927, 14 mos. after onset
10. W.B. Coley (10, #1104; 52; 88; 123)	M 20 (I.L.)	osteogenic sarcoma involving large portion of distal lt. femur; onset sometime after severe trauma (leg caught in subway door March 1921); date of onset early 1925(?)	osteotomy, curettage August 1923; osteomyelitis or productive osteitis; physiotherapy Oct. 1924, continued several mos.; incisional biopsy March 16, 1925; amputation refused	x-ray concurrent with toxins (3) May 1925; x-ray for recurrent pain Sept. 1926; x-ray to femur, abdomen Nov. 1926	P.D.XIII April 1, 1925 begun 1 month before x-ray; dose rapidly increased to 15 minims some i.m., some into tumor; little reaction continued 2 mos.; 2 more doses Nov. 1926; no reaction	immediate improvement apparent May 1925, pain-free, steady regression; local & general condition excellent gained 21 lbs; symptom-free 18 mos; then pain recurred, metastases to lungs & lower abdomen November 1926; definite decrease under x-ray and toxins; then rapid downhill course; death May 1927 2½ yrs. after onset
11. W.B. Coley (10 #836; 52; 88; 123)	M 15 (L.T.)	osteogenic sarcoma lt. mid-femur; onset May 1926, several weeks after straining knee (severe trauma)	incisional biopsy negative; amputation nevertheless advised but refused	radium; amputation 6 mos. after onset	P.D.XIII August 31, 1926, 13 days after biopsy; given in or near wound, no marked reactions; toxins after radium (11 more) 5 in tumor, better reactions until October 1926	pain diminished, clinical & x-ray evidence of regression; then no further decrease; metastases to lungs, scalp; death May 31, 1927, 13 mos. after onset

12. B.L. Coley (10, #1099; 52; 880);	M 16 (S.F.)	very malignant osteogenic sarcoma lt. distal femur; onset December 1926, 15 mos. after fall, striking knee	explored elsewhere Feb. 1927; radium (9000 mch) March 23, 1927; amputation March 24, 1927	none	sinus became infected: whole thigh edematous large pus cavity (25 cm) phlegmonous inflammation involved tumor; P.D.XIII April 2, 1927 10 days after amputation, 19 in 10 wks, 18 in rt. hip; marked reaction (104.2°F.) from 6 m. in lt. thigh near stump; further brief course toxins Nov. 28, 1928	in excellent condition, obtained prosthesis; evidence lung metastases November 1928; disease progressed, death July 1, 1929, 2½ yrs after onset
13. W.B. Coley (10 #863; 88; 123)	M 50 (R.C.)	osteogenic sarcoma rt. distal femur; onset June 1927	explored August 1927 by A. Whitman entire distal femur involved; curetted for 10 cm., cavity swabbed with phenol & alcohol	3 radium packs Sept. 3, 4, 5; (40,000 mch) amputation Sept. 28, 1927, 3 mos. after onset	P.D.XIII Sept. 3, 1927, 10 days after surgery 16 i.m. in lt. buttock in 17 days, slight reactions except for final dose (108° F.)	pathologist reported main tumor mass wholly necrotic, devoid of structure . . . chronic inflammation in periosteum; 5 mos. later metastases to chest wall; severe pain; death May 2 1928, 11 mos. after onset
14. B.L. Coley (123)	M 42 (A.S.)	osteogenic sarcoma involving proximal ⅓ of rt. femur with extensive infiltration of soft tissues; onset March 1927	"treated for sciatica"; incisional biopsy November 1927	7 radium packs Dec. 3 - 15, 1927 (16,000 mch); Feb. 1928 radium needles in tumor (89 mc); 8th radium pack July 21, 1928; 2 more Nov. 1928 (11,400 mch); palliative amputation 1930	P.D.XIIII Dec. 2, 1927 i.v. & i.m. 38 in 2 mos., slight reactions except from larger i.m. doses (102° F.-103° F.) and from i.v., (to 104° F.); fever from absorption; severe infection July 25, 1928 (4 days after radium); 2 more injections Fall 1928; further infection, fever, Oct. 1928 (105° F.)	slight improvement, then slow increase in size; tumor fungated with copious drainage (1 wk. after radium needles); condition hopeless, fever for 4 mos. (absorption: necrotic tissue?); began to improve and gain weight; 1929: progressive downhill course (no lung metastasis) death June 1, 1931, 4¼ yrs. after onset
15. W.B. Coley (10, case 810 52; 123)	M 43 (V.M.)	rather extensive osteogenic sarcoma involving lt. femur; onset October 1926	treated for rheumatism for 3 mos.; then amputation by Zadek	radium pack (10,000 mch) May 10, 1928	P.D.XIII March 11, 1928; 15 i.m. in 21 days 1 more i.v. May 16, 1928 (104.2° F.)	disease not controlled, death September 11, 1928, 25 mos. after onset

TABLE 3, GROUP 1: OSTEOGENIC SARCOMA FAILURES, PRIMARY OPERABLE WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
16. B.L. Coley (10, #1072; 123)	M 39 (E.R.)	osteogenic sarcoma lt. distal femur; onset September 1927 (trauma)	x-ray (18); curettage; bone transplants; in cast 2 mos.; alpine lamp treatments; 12 more x-ray early 1929; no apparent benefit, limb larger, pain more severe; amputation 13 mos. after onset	none	P.D.XIII October 28, 1929, 12 days after surgery; 26 in 30 days (8 i.m., 18 i.v.); no reactions from i.m., 101° F. or more from i.v.	obtained prosthesis, returned to work; symptom-free 4 yrs., then metastases to skull, lungs caused little pain or trouble till May 1934; death June 14, 1934, 6¾ yrs. after onset
17. W.B. Coley (10, #1072; 123)	M 40 (C.R.)	osteogenic sarcoma proximal femur (fibrous type)with pathologic fracture following fall downstairs, severe pain, whole neck of femur involved; onset December 1928	in cast 12 wks; incisional biopsy December 19, 1929, 9 radium packs (30,000 mch. in 2 weeks)	none	P.D.XIII Jan. 4, 1930, (13 mos. after onset); 37 in 60 days i.m. & i.v.; average reactions moderate (maximum 104.4° F.)	disease progressed; death May 30, 1930; 18 mos. after onset
18. W.B. Coley & Whitman (10, #1078; 12; 52; 88)	M 18 (A.K.)	osteogenic sarcoma distal lt. femur; onset July 1929; trauma (considered to be giant cell tumor at first)	(sinuses washed eraser removed from nostril, had been there 6 yrs) October 18, 1929; next day curettage of tumor of lt. femur; physiotherapy February 1930, no improvement (on crutches, fell); amputation 7 mos. after onset	x-ray given (technic unknown)	October 1929; concurrent bilateral sinusitis chronic tonsillitis; P.D.XIII, March 2, 1930 (3 i.m., 2. i.v., latter gave reactions, 102.4°-103.6° F.); 9 more 1 month later, no marked reactions	no improvement, required crutches early 1930; fell, striking knee, pain increased, considerable swelling; huge local recurrence, later pulmonary metastases; death April 1, 1931, 20 mos. after onset

19. W.B. Coley (10, #1247, 123)	M 11 (G.R.)	telangiectatic osteogenic sarcoma distal lt. femur; 5 x 7 x 6 cm.; onset mid-July 1930, 5 mos. after trauma	September 1930 radium pack (16,000 mch); then amputation	none	P.D.XIII, October 1, 1930, 1 wk. after surgery, 20 i.m. in 36 days, 5 moderate reactions	excellent condition, felt perfectly well until late February 1931 but lung metastases were present; stump recurrence, severe pain, generalized sarcomatosis with anasarca, death October 2, 1931, 19 mos. after onset
20. W.B. Coley (10, #1298; 52; 123)	M 26 (A.F.)	very cellular osteogenic sarcoma distal lt. femur; onset August 1930 (trauma) severe pain	none	x-ray (30) in 3 courses November 1930, February and April 1931; incisional biopsy, amputation by Coley August 1931; gold seeds, x-ray to chest, stump (12,500 r. in 3 mos.)	P.D.XIII November 1930 (25 i.m.) given in Scranton; pain relieved temporarily; 2nd course September 1931, 9 days after amputation; 30 in 75 days i.m., 2 marked reactions (103.4° and 103.8°F.)	April 1931 recurrence above stump; December 1931 metastases over lt. clavicle, lung; recurrence regressed, pain relieved, but clavicular mass increased; improvement temporary; edema of entire body, death June 5, 1932, 22 mos. after onset
21. B.L. Coley (10, #1294; 123)	F 32 (M.M.)	osteogenic sarcoma lt. distal femur, 33 lb. wt. loss in 9 wks., severe pain; onset May 1931	amputation August 1931 11 wks. after onset	x-ray to lungs April 1934 (3000 r), May (3200 r) July 1934 (3200 r)	P.D.XIII August 24, 1931, 12 days after surgery; 7 i.m. 2 i.v. in 15 days; latter caused reactions 103° - 105° F.; few more i.m. at home, November 1931 caused painful indurations in gluteal region; further toxins March 1932 for recurrence (8 in 15 days i.m. and i.v.) moderate reactions	in excellent health, obtained prosthesis; March 1932 recurrence in stump, pelvis; complete regression of recurrence regained lost weight, in excellent condition; April 1934 lung metastases, marked clinical & radiographic improvement from 1st 2 cycles x-ray, little benefit from 3rd; rapid downhill course; death August 27, 1934, 39 mos. after onset

TABLE 3, GROUP 1: OSTEOGENIC SARCOMA FAILURES, PRIMARY OPERABLE WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
22. B.L. Coley (10, #1375; 123)	F 17 (B.F.)	telangiectatic osteogenic sarcoma distal 1/3 lt. femur; (patient an orphan); onset October 1931	December 16, 1931; cast applied to lt. leg; x-ray (2100 r)	January 11, 1932 x-ray (2100r); amputation February 3, 1932, 3½ mos. after onset; revision of stump, June 1932	P.D.XIII December 21, 1931 (12 in 19 days, 9 i.m., 3 i.v.) 6 moderate reactions; Feb. 2-3, 1931: fever 101° - 102° F. for 36 hours (no apparent cause); infection, suppuration of wound, few more toxin injections after surgery; further infection (osteomyelitis)	improved; fell, injuring hip May 1932; lung metastases August 1932; felt well until terminal pneumonia September 1932; death October 18, 1932, 12 mos. after onset
23. Mayo Clinic (122; 125; 127)	F 30 (?)	sclerosing osteogenic sarcoma distal lt. femur; 40 lb. weight loss in 2 yrs.	refused surgery; x-ray (6 cycles in 6 mos., 18,960 r.)	Achilles tendon lengthened July 1933; amputation elsewhere over 3½ yrs. after onset	P.D.XIII January 1932 11 i.m.; reactions not recorded	in perfect health 18 mos., believed cured; died 3 mos. after amputation with lung metastases, almost 4 yrs. after onset
24. Mayo Clinic (16; 52; 122)	M 23 (B.D.)	osteogenic sarcoma distal femur, onset while in medical school (date not recorded)	amputation March 29, 1932	x-ray to back	P.D.XIII May 1932, 2 mos. after surgery (given by patient's father, a physician), several series of 10 i.m., caused febrile reactions, chills	good recovery; well until mid-October 1932, then back pain above hip joint; disease progressed rapidly after radiation; death April 12, 1933, 13 mos. after amputation
25. B.L. Coley (10, #1695; 123)	M 15 (J.F.)	osteogenic sarcoma lt. proximal femur; onset early September 1932	November 1932 explored, curettage in New Jersey (amputation refused); x-ray December 1932 (4800 r)	January 1933 2nd cycle x-ray (6000 r); x-ray to chest April 1933 (3000 r)	P.D.XIII December 29, 1932 5 i.m. in 10 days, 2 moderate reactions; 7 more injections in 12 days ending Feb. 11, 1933, 3 i.m., 4 i.v.; 3 caused reactions	well until April 1933, then lung metastases; improved briefly after x-ray, then recurrence in femur, weight loss; death November 1, 1933, 14 mos. after onset

26. W.B. Coley (10, #1693; 123)	M 17 (J.J.O'R.)	sclerosing osteogenic sarcoma distal 1/3 lt. femur; trauma; onset May 1933 (deplorable home, destitute)	August 1933; radium (159,000 mch); severe pain abated, tumor decreased	amputation Dec. 27, 1933 7 mos. after onset	P.D.XIII August 26, 1933; 21 in 27 days (11 i.m., 10 i.v.) very small doses, 3 moderate reactions	pain-free in 5 wks.; gained 15 lbs., February 1934, epileptic form attacks; March 1934 lung metastases; death June 10, 1934, 13 mos. after onset
27. W.B. Coley (123)	M 15 (L.E.R.)	extensive osteogenic sarcoma mid-shaft of rt. femur; onset June 1933 (had been run over by a car 4 times)	aspiration biopsy July 28, 1933; August 1-28 1933, x-ray (9600 r)	May-June 1934, x-ray to lungs (7900 r); to sacrum February 1935 (500 r)	P.D.XIII, August 29, 1933; (21 in 38 days, 8 i.m., 13 i.v.) 1 marked reaction (104° F.), 2 moderate; 2nd course August 28, 1934 after 2nd cycle x-ray; 17 in 31 days, 8 i.m. (average reactions mild to moderate, maximum 104.4° F.), 9 i.v. (average reactions 102° F.)	pain-free in 5 weeks; in excellent condition, gained weight until December 1933 lost 13 lbs. in next few mos.; March-April 1934 u.r.i.; lung metastases, recurrence in femur May 1934; *all regressed completely after combined therapy;* symptom-free until mid-December 1934 except for pain in lumbo-sacral region due to metastasis; January 1935 large radiation ulcer on thigh, further lung metastases February 1935; rapid downhill course after final x-ray, death March 4, 1935, 21 mos. after onset
28. Higinbotham (10, #1963; 123)	M 12 (J.S.)	telangiectatic osteogenic sarcoma lt. distal femur; child rejected by mother, very unhappy at home; onset July 1934	treated as rheumatism; tonsillectomy December 1934 (20 lb. wt. loss in 3 mos. prior, regained 10 lbs. in 3 mos. after this); 1st aspiration biopsy negative, March 3, 2nd March 9, 1935 positive; x-ray (3200 r) in 9 days; amputation March 31, 1935, 7 mos. after onset	none	P.D.XIII April 8, 1935 9 days after surgery; 16 in 18 days (11 i.m. & 5 i.v.), reactions averaged 100.6° - 103° F. (minimum 100°, maximum 103.6° F.)	stump healed quickly; child in excellent health but mother very difficult; sent to camp July 1935; gained 23 lbs. in 13 wks., continued in apparent very good condition, gained more weight, but asymptomatic lung metastases seen September 1935, did well till shortly before death, February 28, 1936, 19 mos. after onset.

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Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
29. B.L. Coley (10, #2264; 123)	F 18 (A.M.)	osteogenic sarcoma distal femur, 10 lb. weight loss in 2 mos., tonsils & adenoids removed mid-June 1937 trauma mid-July 1937, onset mid-August 1937	incisional biopsy, amputation September 13, 1937	x-ray to lungs for metastases seemed to accelerate their growth & spread	P.D.XIII September 20, 1937, 7 days after surgery: 16 in 19 days (9 i.m., 7 i.v.); moderate febrile reactions	gained weight, well 18 mos., began to feel poorly April 1939, lost weight, progressive anemia; lung metastases seen June 1939; skeletal lesions appeared after x-ray; death February 7, 1940, 2½ yrs. after onset
30. Higinbotham (123)	M 27 (J.P.O'N)	osteogenic sarcoma distal rt. femur, trauma in auto accident; onset late June 1937 (about 1 week later)	hot applications caused regression of swelling temporarily; September 29, 1937, amputation, hemorrhage from stump 4 days later (300-400 cc. in shock), 2nd hemorrhage (100-150 cc) October 7; 3rd next day; stump opened large hematoma evacuated, bleeding vessel in muscle sutured; transfusion	palliative x-ray March 29, 1939	spiking fever to 103.2° F. during week after amputation continued (low grade) for 4 wks.; November 10, 1937: P.D.XIII, 15 i.m. in 15 days, 7 marked reactions (maximum 106° F.)	gained 20 lbs., in good health, NED for 18 mos. then large metastases scapular region, ribs, lt. lung; death May 8, 1939, almost 2 yrs. after onset
31. B.L. Coley (10, #2251; 123)	M 15 (E.R.)	extensive osteogenic sarcoma lt. femur 18 cm. in length; possible trauma prior to onset; onset about March 1938	April 1938; x-ray (4000 r in 8 days) aspiration biopsy	May 16, 1938; incisional biopsy, amputation 2½ mos. after onset; (combined therapy had rendered tumor acellular)	April 26, 1938: P.D.XIII: 15 in 16 days, 6 i.m. 9 i.v. (maximum reaction 105°F.)	stump healed rapidly; metastasis seen in lt. lung, July 1938, widespread by October; continued in school to December; death December 19, 1938, 10 mos. after onset

32. Higinbotham (10, #2251; 123)	M 17 (L.C.H.)	telangiectatic osteogenic sarcoma distal lt. femur, sprained lt. knee prior to onset, early May 1938	wet heat applied; plaster cast for 10 days; aspiration biopsy July 9, 1938, x-ray (3750 r); amputation 2½ mos. after onset	none	July 27, 1938, P.D.XIII (7 days after surgery); 11 in 15 days (6 i.m., 5 i.v.) moderate reactions	felt fine, returned to college; chest pain late November 1938, due to widespread lung metastases; death December 24, 1938, 8 mos. after onset
33. Higinbotham (123)	F 18 (A.C.)	telangiectatic osteogenic sarcoma distal rt. femur with pathologic fracture, considerable wt. loss, early acromegaly(?); had fractured rt. tibia 3 mos. previously in fall; onset about September 21, 1938	aspiration biopsy October 13, 1938; then x-ray (2000 r.); Oct. 17, 1938, amputation, transfusion (1200 cc)	none	spiking fever to 104.6° F. October 3-18; P.D.XIII October 24, 1938, 7 days after surgery; 19 in 19 days: 7 i.m., little or no reaction until maximum dose (104.4° F.); 12 i.v. reactions averaged 102° - 103° F.	general condition excellent wound entirely healed in 2 wks.; gained weight, obtained prosthesis; in excellent health for a year; October 1940 cough due to lung metastases, morale good, death November 26, 1940, 26 mos. after onset
34. B.L. Coley (123)	F 13 (V.H.)	osteogenic sarcoma distal lt. femur 9x5x5 cm. involving knee joint; onset pain early October 1939, 7 wks. later kick in lt. knee caused exacerbation of pain	x-ray December 1939 (9600 r. in 4 wks.)	transfusion (500cc); amputation January 31, 1940 (areas of gelatinous degeneration and hemorrhage)	P.D.XIII December 29, 1939, 12 in 19 days, 7 i.m., 5 i.v. (50% gave reactions of 102°-103.6° F.)	January 1940, anemia, metastasis in rib & lung; stump healed slowly due to extensive radiation effects wt. increased slightly for 3½ mos., bedridden late June death July 15, 1940, 9 mos. after onset
35. B.L. Coley (123)	M 16 (?)	osteogenic sarcoma distal rt. femur 15x16x8 cm.; onset late October, 1939	diathermy; aspiration biopsy January 25, 1940 (no tumor cells) x-ray, preceded by diathermy each time (9000 r. in 16 days) caused decrease in size; amputation 4 mos. after onset	none	P.D.XIII February 28, 1940, 14 days after surgery; 9 in 9 days (6 i.m., 3 i.v.), reactions 101°-105°F.; 2nd course July 1940: 12 days, 6 i.m., 6 i.v. nearly all caused marked reactions	excellent general health, gained 20 lbs. in 4 mos; lost 9 lbs. during 2nd course of toxins; obtained prosthesis; by March 1941 weighed 200 lbs., bilateral lung metastases present March 26, 1941; general health not affected; severe grippe December 1941; led normal life; Fall 1942 condition began to deteriorate, lost 20 lbs. but morale good; death July 31, 1943, 3 3/4 yrs. after onset

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36. B.L. Coley (123)	F 10 (P.Y.)	osteogenic sarcoma distal rt. femur, onset late September 1941; child obese emotionally unstable	aspiration biopsy October 31, 1941; x-ray (9600 r)	2 transfusions late November, 1941; amputation December 19, 1941, 3 mos. after onset	P.D.XIII November 10, 1941, same day as x-ray for 9 days (8 i.m., 1 in tumor); 2 more i.m. December 19, 20; 2nd caused reaction 104° F., 9 more January 1942 (5 i.m., 4 i.v.); average reactions moderate; 3rd course February 26, 1942 13 in 19 days (7 i.m., 6 i.v.)	motion of knee, general condition improved considerably after x-ray and toxins; stump wound healed well, gained weight; March 7, 1942, lung metastasis seen, bilateral lesions by April 1942; May: rt. orbital metastasis, exophthalmos; remained fairly comfortable; death June 21, 1942, 9 mos. after onset
37. Memorial Hospital (123)	F 9 (M.E.R.)	telangiectatic osteogenic sarcoma distal rt. femur; had had intestinal worms (ascaris lumbricoides) with severe anemia for 5 yrs.; onset early December 1941; 6 lb. wt. loss in 2 mos., very weak	treated as rheumatism, sulfanilamide, liver injections; x-ray in Mexico (2400r) caused pain relief; aspiration biopsy negative February 24, 1942; incisional biopsy 2 days later, much bleeding; cast applied; further x-ray (1300r) March 2, 1942; transfusion March 5, 1942	2nd transfusion March 18, hip-joint disarticulation April 8, 1942, 4 mos. after onset ("destruction such that diagnosis . . . has to be made on gross specimen"); x-ray to lungs June 1942 in Mexico (4000r), also calcium, liver extract, vitamins	febrile reaction to transfusion, 103.2° F.; P.D.XIII, March 9, 1942 1st 3 given same day as x-ray; 14 in 25 days all i.t. marked reactions (averaging 102.4° -104.8° F., maximum 106° F.); toxins resumed 14 days after surgery: 7 i.v. in 7 days; reactions 102.4° - 103.2° F.	a week after toxins begun, tumor softer, smaller; pathologic fracture March 24, 1942, wound healed 16 days after amputation; lung metastases seen April 29, 1942; *these completely regressed* by August 1942, very well for 2 mos., then sudden hemorrhagic effusion, death late February 1943, 13 mos. after onset

38. B.L. Coley (123)	M 5½ (M.G.)	osteolytic osteogenic sarcoma lt. proximal femur; trauma prior to onset, September 1946	explored; amputation refused; x-ray November 27, 1946 for 3 wks.	none	Sloan-Kettering XIV & P.D.XIII December 19, 1946: 18 i.v. in 34 days; 2 wks. later 8 i.v. reactions 101°-105.6° F.; Jan. 4, 1947: concurrent mumps; febrile few days early January 1947 (due to necrosis of tumor?) February 1947 infected ingrowing toenail; 8 more i.v. injections Feb. 19, 1947 & first wk. of April 1947	April 1947 reactivation of growth; disease progressed death July 16, 1947, 10 mos. after onset
39. W.B. Coley (123)	M 15 (M.L.)	osteochondrosarcoma distal lt. femur; onset August 1915 shortly after trauma	none	October 1915, amputation 2 mos. after onset	P.D.XIII, Sept. 16, 1915, 12 in 15 days (8 i.m., 4 i.t.) latter caused reactions to 104°F.; 14 more i.m. in 36 days, begun 20 days after surgery, reactions mild except once (104.5°F.)	no apparent improvement after pre-operative toxins, discharged; disease not controlled; death June 1916, 10 mos. after onset
40. B.L. Coley (10; 123)	F 17 (R.R.)	advanced osteochondrosarcoma femur 11.5 x 14 cm.; onset October 1, 1929, severe pain	incisional biopsy Fordham Hospital; pain controlled during December by morphia; amputation by B.L. Coley Jan. 8, 1930, 3 mos. after onset	none	P.D.XIII January 15, 1930, 7 days after amputation; 14 in 21 days (4 i.m., 10 i.v.), latter caused only 1 marked reaction (102.2° F.); further injections by family physician March, April 1930	in excellent condition, gained 20 lbs.; asymptomatic though extensive metastases seen Aug. 20, 1930 especially in rt. lung; went to country, did wonderfully well until shortly before death Nov. 18, 1930, 13 mos. after onset
41. W.B. Coley (16; 88)	F 19 (C.W.)	sclerosing osteochondrosarcoma lt. distal femur; onset October 1929 (had broken lt. ankle 15 mos. previously while sledding)	none	incisional biopsy, January 18, 1930 reported as "adult bone"; amputation January 29, 1930; intensive x-ray to chest August & September 1930	P.D.XIII January 18, 1930; 6 i.m. in 11 days, mostly mild reactions (maximum 102.4° F.); resumed 9 days after amputation (2 more i.m. reactions 103° & 101° F.) then 1 a wk. by family physician	in very good health; wound entirely healed in 2 wks.; lung metastases seen August 1930; disease progressed during radiation; death November 7, 1930, 13 mos. after onset (patient up and about until 4 days before death)

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42. W.B. Coley B.L. Coley (10, #1242; 16; 88)	F 35 (C.D.)	osteochondrosarcoma proximal rt. femur; onset July 1929 (in 2nd month of 3rd pregnancy); fell September 1929 & January 1930; child born March 1, 1930; 40 lb. wt.loss	none	May 6, 1930: osteotomy; mass of soft gelatinous material curetted; 9 radium packs in 4 wks. beginning May 28, 1930 (98,709 mch); disarticulation of rt. hip, September 24 1930 by B.L. Coley; transfusion (500cc); revision of stump October 29, 1930, July & September 1931, x-ray to stump recurrence (2550, 2250r)	P.D.XIII May 2 & 3, 1930; i.m.; resumed June 5, 16 in 31 days, 8 i.m., 8 i.v.; (reactions mild from i.m., moderate from i.v. except one, 104° F.); gangrene of part of wound, profuse drainage; injections resumed 21 days after amputation 5 i.m., 5 i.v. in 27 days; February 2, 1931:13 i.m. in 32 days; no marked reactions; further i.m. injections by family physician, slight reactions; 4 more i.m. July 1931 (moderate reactions)	pain much relieved temporarily by combined therapy; increased in August; excellent course after disarticulation, complete healing in about 2 mos.; gained 7-8 lbs.; prosthesis obtained April 1931; recurrence in stump; gained 7 lbs. after final course of toxins; temporary decrease in size; radiation dermatitis, fungating tumor, metastases to spine, death March 1, 1932, 31 mos. after onset

43. B.L. Coley (10, #1355; 88; 123)	M 48 (C.W.C.)	osteochondrosarcoma rt. proximal femur, with pathological fracture October 1930; 25 lb. wt. loss, severe pain; onset September 1928; (also had lipoma in axilla); onset, September 1927	incision, drainage elsewhere: osteomyelitis; 2nd operation June 1929, area drained for several wks.; femur reopened August 1929, Dakin tubes; diagnosis osteochondroma with malignant changes; x-ray (1) to thigh October 1929; physiotherapy March 1930; lipoma in axilla excised April 1930; also osteotomy of femur by B.L. Coley; continued to have osteomyelitis; curettage November 1930; cast applied; foul odor, hospitalized 4 mos.	hip joint disarticulation January 30, 1931, 3½ yrs. after onset	P.D.XIII November 23, 1930, 10 in 24 days, 1 i.m., 9 i.v.; reactions averaged 101°-102° F.; January 1930 unexplained fever (104.6° F) after amputation; 13 days later 4 more i.m. (102° -104.8° F.)	very satisfactory stump; in excellent condition for 2 yrs., seen by Coley March 29, 1933, NED: became psychotic, marked personality change, rectal symptoms (urgency); suicide, July 14, 1933, almost 4¾ yrs. after onset
44. W.B. Coley (10, #1249; 123)	M 12 (J.T.)	extensive osteochondrosarcoma rt. distal femur; onset mid-October 1930, 2 wks. after trauma (fell from bicycle); severe pain	disarticulation at Hospital for Joint Diseases, January 10, 1931, 3 mos. after onset	none	January 24, 1930 P.D. XIII, 14 in 37 days 6 i.m., 8 i.v.; (reactions moderate, maximum, 103.8° F.)	excellent recovery, looked "picture of health" until fall, hurting knee early June; metastases to lung & lt. knee apparent shortly thereafter; disease progressed, death October 2, 1931, 12 mos. after onset

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45. B.L. Coley (10, #1293; 12; 88; 123)	M 31 (G.K.)	osteochondrosarcoma distal rt. femur, 9 x 9 cm., with marked inguinal adenopathy; onset March 1931, about 4 mos. after being hit in this region by a roll of zinc weighing 110 lbs.	treated as rheumatism (pills, ointment, ultra-violet light); plaster cast; knee aspirated, greenish fluid evacuated; referred to Memorial Hospital; 2 aspiration biopsies July 18, 1931; amputation July 22, 1931	x-ray to chest August 1932 (8000r.)	July 31, 1931, P.D.XIII 9 days after surgery; 14 i.m. & 5 i.v. in 5 wks., few marked reactions	in excellent condition, gained 25 lbs.; lung metastases seen January 24, 1932; also mass lt.temporal region; no improvement under x-ray; death October 15, 1932, 19 mos. after onset
46. Higinbotham (10, #1548 123)	F 19 (I.T.)	osteochondrosarcoma rt. distal femur (23 cm. long); onset November 1932; 20 lb. weight loss; hypertrichosis of lower extremities	osteotomy April 1932; suspected osteomyelitis; drainage for 5 wks.; 2nd operation July 9, 1933, incomplete removal elsewhere; hip joint disarticulation at Memorial Hospital, September 6, 1933, 10 mos. after onset	none	mucopurulent vaginal discharge (B. subtilis) late August 1933; febrile for 1 wk. after amputation (to 103° F.); P.D.XIII October 3, 1933, 4 wks. after surgery: 12 in 19 days (8 i.m., 4 i.v.), little or no reaction except twice (102°, 102.6° F.)	gained 40 lbs; stump & general condition excellent; October 1934 "cold", pleural effusion; lung metastases seen November 1934; rapid downhill course, death December 19, 1934, 25 mos. after onset
47. B.L. Coley (10, #1858; 123)	M 16 (D.G.)	osteochondrosarcoma distal rt. femur, onset July 1934; 18 lb. weight loss in 5 mos.	2 aspiration biopsies early December 1934; amputation December 20, 1934; thick, bloody *purulent fluid evacuated from stump*	sciatic exeresis; December 1940, massive doses Vitamin B.	P.D.XIII December 30, 1934, 10 days after surgery; 15 in 18 days (11 i.m., 4 i.v.) 1 marked reaction	prosthesis obtained September 1935; in excellent condition over 5 yrs.; November 1940 sciatic pain, stump numb; unable to void, December 1940; by January 1941 huge metastases to lumbar vertebrae, sacrum, also lungs; death June 17, 1941, 7 yrs. after onset

48. Higinbotham (10, #2260; 123)	M 28 (P.R.)	osteochondrosarcoma proximal rt. femur, 21x17x15 cm.; 15 lb. weight loss in 9 mos., markedly emaciated; onset March 1937	incisional biopsy; x-ray elsewhere; 9½ mos. after onset, Jan.19, 1938 hip joint disarticulation; blood transfusion (1500 cc); 2 days later another 500cc; 3rd Jan. 25, 1938 (no reaction)	4th transfusion, Feb. 12, 1938 (no reaction) x-ray to lung December 1938 (4000r), slight palliation	fever to 104.2° F. day after amputation, remained high for 4 days 102°-104° F., gradually declined; P.D.XIII Jan. 31, 1938, 12 days after surgery; 11 in 14 days (8 i.m., 3 i.v.), latter caused marked reactions	wound healed well; excellent general health, gained 35 lbs in weight in 6 mos., stump in excellent condition until October, then low back pain; lung metastases Nov. 30, 1938; weight loss; *disease progressed rapidly after x-ray,* death March 30, 1939, 2 yrs. after onset
49. W.B. Coley (43; 52)	M 12 (J.A.)	fibrosarcoma distal rt. femur onset January 1907, a week after being kicked in area, of rapid growth	incisional biopsy Jan.15, 1907	amputation Feb. 1, 1907	Tracy XI; Jan. 18, 1907 10 in 10 days (5 i.t., 5 i.m.) marked reactions (102.6° -104.8° F.)	lost 2½ lbs. in weight, growth decreased 3 cm. in circumference, overlying skin became loose and wrinkled; lung metastases developed very promptly, death about May 15, 1907, less than 4 mos. after onset
HUMERUS: 15 cases (14 osteogenic, 1 osteochondrosarcoma)						
50. W.B. Coley (10, #998;123)	F 60 (B.J.)	osteogenic sarcoma proximal rt. humerus (had 13 children, 6 living); onset, July 1928; 14 lb. weight loss in 6 mos.	none	January 1929: radium packs to humerus; (70,000 mch); May 1929 to femur (42,000 mch)	P.D.XIII Jan. 18, 1929 concurrent with radium; 5 i.m., 1 i.t., 21 very small doses i.v. in 56 days, no reactions; (concurrent tonsillitis during which toxin injections were not given); 1 final dose after tonsillitis, unusual reaction (cyanosis, pain in back, legs)	pain less, felt better by Feb. 6, 1929; April 1, 1929, shoulder softer, almost cystic; symptom-free 2½ mos; then asymptomatic tumor seen in x-rays of lt. distal femur; pathologic fracture getting into taxi, May 1929, disease progressed, death Sept. 28, 1929, 14 mos. after onset

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51. B.L. Coley (10; 88)	M 26 (J.McK.)	telangiectatic osteogenic sarcoma proximal lt. humerus; onset October 1928; wrenched arm 3 mos. later, causing pathologic fracture	strapped for 10 days, then in cast; shoulder joint disarticulation; Jan.4, 1929, fair amount of hemorrhage; shock	plastic operation May 27, 1929	P.D.XIII Jan. 14, 1929 10 days after surgery; 12 in 21 days (2 i.m., 10 i.v.); moderate reactions	wound well healed in 3 wks, general condition good; then ulceration occurred; disease reactivated, death March 22, 1930, 17 mos. after onset
52. B.L. Coley (10, #1215; 16; 52; 123)	M 19 (J.M.H.)	telangiectatic, mostly osteolytic osteogenic sarcoma lt. proximal humerus with pathologic fracture; onset Jan. 19, 1931 (had broken rt. ankle 2 yrs. before & thereafter had pain in rt. knee)	Feb. 23, 1931, explored; referred to Coley March 2, 1931, interscapular thoracic amputation 2 days later, 2½ mos. after onset	none none	P.D.XIII March 12, 1931, 8 days after amputation, i.m. & i.v. for 5 wks., reactions 102°-104.6° F. further toxins advised but not given	wound healed in 12 days; gained 9 lbs.; general condition excellent; July 1931 lung metastases; death Aug. 13, 1931, 8 mos. after onset
53. B.L. Coley (10# 1349; 123)	F 15 (J.O'B.)	osteogenic sarcoma lt. proximal humerus with pathologic fracture; onset mid-April 1931, 1 wk. after slight strain; pain intolerable	radium packs (96,000 mch) ending May 21, 1931 (pain increased); shoulder spica applied, then double sling; marked regression by July 1, 1931; incisional biopsy September 9, 1931	interscapulothoracic amputation October 16, 1931, 6 mos. after onset; excision of probable local recurrence in skin February, 1932	P.D.XIII September 21, 1931, 12 in 19 days (9 i.m., 3 i.v.), 1 marked reaction from 1st i.v.; toxins resumed 12 days after amputation, 8 in 16 days (1 i.m., 7 i.v.)	wound healed, keloidal scar; lung metastases seen March 7,1932, pain in hip; death July 21, 1932, 15 mos. after onset
54. B.L. Coley (10, #1358; 123)	M 35 (H.C.G.)	highly malignant osteogenic sarcoma rt. proximal humerus with pathologic fracture; onset April 1931 (trauma 2 mos. later)	aspiration biopsy October 14, 1931; radium pack; transfusion (200 cc blood, 300 cc saline); interscapulothoracic amputation November 4, 1931	radium packs	P.D.XIII November 11, 1931, 7 days after surgery; 4 i.m. in 4 days (no reaction) 7 i.v.(good reactions), duration less than 3 wks.	surprisingly little nerve pain, felt fine 8 mos., then large ulcerated recurrence, very foul odor; pain less after radium; some regression, then disease progressed; death December 21, 1932, 20 mos. after onset (autopsy showed no metastases)

55. B.L. Coley (10, #2250; 123)	M 15 (D.C.)	highly malignant sclerosing osteogenic sarcoma rt. proximal humerus; trauma by truck 3 yrs. prior to onset: developed septicemia, erysipelas on lt. knee & thigh, bedridden 5 mos.; palpable axillary & inguinal lymph nodes; May 1936, shortly prior to onset, sprained arm playing ball	massage by "bone setter" July 8, 1936, x-ray for 12 days (3000 r); 2 days later interscapulothoracic amputation, 2½ mos. after onset, profuse hemorrhage, transfusion 700 cc.	x-ray to metastasis in jaw (200r) Fall 1936	P.D.XIII July 31, 1936, 15 days after amputation, 8 i.m. in 11 days, 3 marked reactions (103°-105.6°F.)	rapid downhill course by October 7, 1936; metastases to mandible, chest; paralysis by January 25, 1935, abdomen distended, double vision, death March 19, 1937, 10 mos. after onset
56. B.L. Coley (123)	F 16 (S.E.S.)	osteoblastic osteogenic sarcoma proximal lt. humerus; had been in "run-down condition" 7 mos. but arm appeared normal at examination 1 wk. prior to pathologic fracture, December 25, 1936	received injections (vitamins?); gained 15 lbs.; x-ray (8100 r.)	interscapulothoracic amputation February 10, 1937; also blood transfusion (600 cc) pathologist reported "almost" complete necrosis had occurred	P.D.XIII January 12, 1937, 16 days after 1st x-ray, 24 in 27 days (10 i.m., 14 i.v.), latter gave reactions 100.2° -104.2°F.	growth regressed under combined therapy; gained 7 lbs., returned to work, symptom-free until July 1937, then lung metastases, death September 16, 1937, 10 mos. after onset
57. B.L. Coley (10, #2263; 123)	M 20 (F.R.)	sclerosing osteogenic sarcoma lt. proximal humerus (not very cellular), onset January 1937, 1 mo. after auto accident; symptoms worse July 1937 while in Army camp	interscapulothoracic amputation November 22, 1937	none	P.D.XIII November 29, 1937, 7 days after surgery, 14 in 21 days (8 i.m., 6 i.v.), latter caused reactions averaging 103°-104° F.	wound in excellent shape, felt well except for slight discomfort in lt. chest March 1938 (lung metastases), no other symptoms, in excellent condition, gained weight, no clinical evidence disease until July 1939 after swimming, then hemoptysis, chill, dizzy; hydrothorax, August 1939; death October 1939, 2½ yrs. after onset

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58. Higinbotham (123)	M 15 (S.V.)	osteogenic sarcoma lt. proximal humerus; onset pain December 24, 1939 while playing basketball, tumor present	aspiration biopsy January 17, 1940	x-ray January 18, 1940 (4200r); shoulder joint disarticulation February 15, 1940	concurrent strep throat (103.6° .) with cervical lymphadenitis; febrile 2 wks; fever after surgery (103° -105° F.) atelectasis; P.D.XIII February 23, 1940, 8 days after surgery; 12 in 16 days, 5 i.m., 7 i.v.; (reactions 102°-106.8° F. from 3 of i.v.)	stump in excellent condition, symptom-free; metastases to rt. lung September, to lt. ischium October 1940; lost ground rapidly, death February 7, 1941, 14 mos. after onset
59. B.L. Coley (123)	M 16 (J.K.C.)	fully malignant osteogenic sarcoma proximal lt. humerus; onset August 1940	salves, liniments, 2 aspiration biopsies; x-ray October 8, 1940 (5200r); 3 injections P^{32} (totalling 10.96 mc.); growth progressed; interscapulothoracic amputation, November 13, 1940; profound shock, transfusion (500cc), saline (100cc)	P^{32} injections resumed at intervals until June 1941	P.D.XIII November 22, 1940; 9 days after surgery; 13 in 20 days, 8 i.m., 5 i.v., (reactions averaged 102°-104° F. after half of the injections)	gained 12 lbs., stump in excellent condition; lung metastases seen May 1941, lost ground rapidly, death August 29, 1941, 12 mos. after onset

60. B.L. Coley (123)	M 6 (H.H.)	osteogenic sarcoma rt. proximal humerus, pathologic fracture onset mid-December 1940	aspiration biopsies January 20, 1941, x-ray: 5200 r in a month; 4 injections P^{32} in 3 wks. ending February 11, 1941	shoulder joint disarticulation March 27, 1941; x-ray to rt. pelvis November 1942, (2000 r) & to chest (6400 r)	concurrent varicella prior to radiation: February 9, 1941 P.D.XIII, 6 i.m. in 18 days, 3 reactions 104°-104.8° F. others 101°-101.4° F.; second course September 8, 1942: 12 in 13 days, 6 i.m., 6 i.v., reactions 100.2°-105° F.	good regression, gained 9-10 lbs in 15 days, remarkable change in bone, much calcification & regeneration, general condition excellent; lt. lung metastases seen September 9, 1941 though appeared symtom-free; continued to gain weight, only symptoms occasional pallor and nervousness; metastases to rt. ischium October 1941; pain in this area ceased after x-ray; multiple bone and lung metastases present at death March 7, 1943, 2¼ yrs. after onset
61. Higinbotham (123)	M. 11 (S.R.)	extensive osteogenic sarcoma lt. proximal humerus; with pathological fractures, onset shortly after trauma, May 1941	plaster spica for 4 wks.; aspiration biopsy July 18, 1941; x-ray (5600 r) in 1 mo. ending August 18, 1941; arm kept in sling	August 19, 1941: 1 dose radioactive strontium; interscapulothoracic amputation August 29, 1941; transfusion; in shock	P.D.XIII July 31, 1941; 12 i.m. in 24 days, (first 9 given on same day as x-ray); mostly moderate, 2 marked reactions	wound healed well: in excellent condition, symptom-free, gained 7 lbs in 5 wks. after surgery; asymptomatic lung metastases seen February 18, 1941; disease progressed rapidly, death June 16, 1942, 14 mos. after onset
62. B.L. Coley (123)	M. 10 (S.B.)	sclerosing osteogenic sarcoma rt. proximal humerus; onset November 1, 1941, 5 wks. ater tonsillectomy; child obese	aspiration biopsy January 2, 1942 x-ray January 5-28, 1942	January 31, 1942 shoulder joint amputation; (tumor *markedly hemorrhagic, cystic in areas and quite necrotic*) palliative x-ray November 1942 for 2 mos. (some regression lt. lung, marked increase rt. lung); 1 dose cobra venom January 1, 1943	January 16, 1942: P.D.XIII begun during x-ray; 8 in 11 days, 5 i.m., 3 i.v., moderate reactions; 2nd course March 1942, 10 in 15 days, 7 i.m., 3 i.v. average reactions moderate	physical recovery good, mental condition poor; gained 21 lbs, in excellent condition 6½ mos. then slight wt. loss, cough; October 28, 1942, large lung metastases; lost 17 lbs. in 3 mos.; death, terminal pneumonia, January 13, 1943, 14½ mos. after onset

TABLE 3, GROUP 1: OSTEOGENIC SARCOMA FAILURES, PRIMARY OPERABLE WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
63. B.L. Coley (123)	F. 10 (F.H.)	sclerosing osteogenic sarcoma rt. proximal humerus, 10 x 8 x 8 cm. with pathologic fracture; onset September or October 1941	incisional biopsy Dec. 26, 1941: fully malignant osteogenic sarcoma; January 1941, x-ray	interscapulothoracic amputation March 27, 1942: "central portion quite necrotic, some of it almost gelatinous in consistency"; November, December 1941 x-ray to lungs (1600 r)	special P.D. toxin using Buxton VI formula: 10 i.t. in 22 days, reactions averaged 102°-104° F., maximum 105° F.	wound well healed in 14 days; gained 5 lbs. in 2 wks., in excellent health NED for 7 mos., then pain in rt. distal chest, lung metastases seen, more marked in rt. lung, also to brain & cervical spine; death Jan. 19, 1943, 16 mos. after onset
64. W.B. Coley (43; case 89 in Table 7; 123)	M 50 (W.B.)	osteochondrosarcoma proximal rt. humerus; onset December 1913; lost 40 lbs. in 5 mos.	treated as inflammatory rheumatism at first; June 1, 1914, 5 cm. of rt. clavicle resected, sub-clavian artery ligated	interscapulothoracic amputation Aug. 17, 1914, 8 mos. after onset; x-ray postoperatively causing bad burn	Tracy XI June 10, 1914, 27 in 51 days, 20 i.m., 7 i.t.	some regression after toxins, *resected clavicle nearly regenerated during toxin therapy*, fairly well; jaundice October, severe pain in stump late November 1914; death from multiple metastases May 1915, 17 mos. after onset
TIBIA: 12 cases, 10 osteogenic, 2 osteochondrosarcoma						
65 W.B. Coley (43, case 57 in Table 7; 52)	M 30 (J.J.W.C.)	osteogenic sarcoma proximal lt. tibia, involving joint; general condition poor, very severe constant pain, extremely neurotic, at times irrational; onset October 1913	October 24, 1913 explored, incomplete curettage, profuse hemorrhage	amputation November 22, 1913	Tracy XI October 27, 1913; 24 i.m. in 26 days (maximum 102° F.)	pain disappeared in 2 wks. except at peak of reaction; recurred November 17, 2 wks. after amputation; became hysterical, but general health improved; NED until June 1915, then stump recurrence, metastases to ribs, death few mos. later, about 2 yrs. after onset

66. W.B. Coley (10, #478; 43, case 66 in Table 7; 52)	M 19 (M.L.)	osteogenic sarcoma rt. proximal tibia, onset December 1922 (2 injuries 5 & 2 wks. previously)	explored Dec. 14, 1922; amputation a week later	none	P.D.XIII Jan. 5, 1923, 2 wks. after amputation: 4 small doses i.m. in 5 days, 2nd course Mar. 21, 1923; 7 in 14 days (5 reactions 100° -102.8°F., little from other 2); 3rd course Aug. 9, 1923, 18 i.m. in 36 days (5 reactions averaging 101° -104° F.); 4th course Mar. 7, 1924: 21 in 7 wks. (101° -104° F.); final dose June 26, 1924	stump healed, regained lost weight, felt well; July 1923 metastases to rt. lung; *unchanged for 1 yr.*; disease progressed after toxins were stopped; death November 1924, 2 yrs. after onset
67. W.B. Coley (10, #569; 43, #152 in Table 7; 123)	F 13 (K.W.)	osteogenic sarcoma proximal lt. tibia several lymph nodes palpable lt. inguinal region; onset mid-April 1924	x-ray and ultra-violet therapy; amputation Nov.13, 1924	x-ray to chest over 5 areas after toxins; 4 more in April 1925	P.D.XIII Nov. 23, 1924 18 days after surgery; 17 i.m. in 40 days mild reactions (99°-101°F., maximum 103° F.)	lung metastases seen April 15, 1925, marked emaciation, dyspnea after 2nd cycle x-ray to lung; recurrence in stump; death Aug. 22, 1926, 16 mos. after onset
68. B.L. Coley (43; 123)	F 15 (R.B.)	osteogenic sarcoma proximal rt. tibia; onset early November 1924	January-February, 1925 neosalvarsan & mercury i.v. by family physician; explored Feb. 10, 1925; x-ray (30 in 2 mos., ending late May); amputation June 2, 1925	none	P.D.XIII June 15, 1925 13 days after surgery; 14 i.m. in 60 days	well 18 mos.; developed giant cell tumor (epulis) maxilla; excised January 1927; final course not recorded; died April 10, 1927, 2½ yrs. after onset
69. B.L. Coley (10, #1445; 123)	F 5 (M.D.S.)	atypical osteogenic sarcoma proximal lt. tibia; onset early December 1931	February 1932 explored; amputation April 6, 1932	none	low grade infection in wound after exploratory; P.D.XIII April 14, 1932, 8 days after amputation; reactions 102.4°-103°F., 14 i.m. in 22 days	local recurrence on stump; bedridden by August 1932; death October 16, 1932, generalized metastases, 10 mos. after onset

TABLE 3, GROUP 1: OSTEOGENIC SARCOMA FAILURES, PRIMARY OPERABLE WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
70. B.L. Coley (10, #1547; 123)	M 5 (E.D.)	osteogenic sarcoma proximal 1/3 rt. tibia; onset May 15, 1933, sudden severe pain, several mild chills, no fever	aspiration, incisional (2) biopsies May, June 1933	x-ray July 12-18, 1933 (2400r) repeated August & January 1934; x-ray to lung April 1934 (3200r); 4th cycle to tibia May 1934 (1200r) 5th cycle August 1934 (3600r)	P.D.XIII June 19, 1933: 13 in 33 days, 8 i.m. moderate reactions, 5 i.v., (101°-105° F., chills, local heat in tumor area); Jan. 30, 1934: 19 in 29 days, 9 i.m., 10 i.v. (average reactions 101°-103° F.); August 1934, 5 i.m. in 10 days	marked regression, excellent local & general condition, gained 10 lbs., lung metastases April 1934; almost disappeared after x-ray; fell, pathologic fracture, December 1934, disease progressed, death March 20, 1936, almost 3 yrs. after onset
71. B.L. Coley (10, #1770, 123	F 13 (M.E.H.)	osteogenic sarcoma mid-third rt. tibia; onset, spring 1934 following local trauma	explored June 21, 1934; amputation refused; x-ray July 11-12, 1934; amputation July 1934	x-ray to lungs (6000r) December 1934	P.D.XIII Aug. 1, 1934, 12 days after amputation; 23 in 41 days, 14 i.m., 9 i.v. (reactions averaged 102° -104° F., maximum 105.4° F., minimum 99.6° F.); 11 more i.m. after x-ray to lung; large doses i.m., reactions 105°-107° F.	stump & general condition excellent; lung metastases seen June 1935; chest pain ceased after toxins, symptomatic improvement, but no regression occurred; death April 4, 1936, 26 mos. after onset.
72. B.L. Coley (123)	F 16 (S.S.)	osteogenic sarcoma proximal lt. tibia; onset Dec. 11, 1938 (sharp, lancinating pain)	aspiration biopsy Jan. 12, 1939; incisional biopsy; amputation next day	none	P.D.XIII Jan. 18, 1939, 5 days after surgery; 14 in 24 days, 8 i.m. 6 i.v. (reactions 101°-104.2° F. from i.m., 102.2°-106° F. from i.v.)	stump and general condition excellent; obtained prosthesis June 1939; did well until December 1939, then slight cough, pain in shoulders; lung metastases seen February 1940, weight loss, death March 1940, 15 mos. after onset

73. B.L. Coley (123)	M 17 (A.A.K.)	osteogenic sarcoma proximal rt. tibia; 20 lb. wt. loss in 2-3 mos.; onset October 1940, sudden stinging pain after kicking football	aspiration biopsy Dec. 24, 1940; x-ray in next 5 wks. (8600r); P^{32} (8.24 mc in 7 doses)	none	P.D.XIII Jan. 10, 1941; 18 in 20 days; 7 i.m. (mild reactions), 11 i.v. (averaged 103.6°-104.8°F.)	intense skin reaction to radiation; felt fine 22 mos.; disease then reactivated, death April 24, 1943, 2½ yrs. after onset
74. B.L. Coley (123)	M 15 (P.H.)	osteogenic sarcoma proximal rt. tibia; onset October 1941, 8 mos. after fracturing tibia & fibula in auto accident	x-ray mid-November 1941 (1000 r); amputation Nov.17, 1941, 2 days after 2nd x-ray; transfusion	none	P.D.XIII March 14 1942, 4 mos. after surgery; 19 in 20 days; 8 i.m. (little or no reactions); 11 i.v.(averaged 102°-103° F., maximum 104° F.)	stump in excellent condition; gained weight, obtained prosthesis April 1942; lung metastases seen May 1942; death Aug. 16, 1942, 11 mos. after onset
75. W.B. Coley (10, case 1291; 123)	M adult (J.H.)	osteochondrosarcoma of lt. proximal tibia; onset April 14, 1931 (had repeated trauma to area weekly for a few mos.)	May 14, 1931 incisional biopsy; radium pack same day (1200 mch) amputation June 10, 1931	x-ray to lungs;May-June 1932 (5000r); another cycle Feb.-March 1933 (8500r) July 1933, x-ray to skull	P.D.XIII June 23, 1931, 13 days after surgery; 11 in 11 days, 3 i.m., 8 i.v. (latter gave reactions 102°-104.2° F.)	wound healed in 3 weeks, looked, felt well, gained 19 lbs.; prosthesis unsatisfactory; lung metastases seen February 1932 but remained symptom-free, gained 6 lbs. August 1932; *chest films clear July to October 1932;* gained 3 lbs. symptom-free though further lung lesions seen November 1932; held up surprisingly well until June 1932, then metastases to lt. parietal region; death July 27, 1933 pneumonia, 27 mos. after onset

TABLE 3, GROUP 1: OSTEOGENIC SARCOMA FAILURES, PRIMARY OPERABLE WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
76. B.L. Coley (123)	M 13 (S.D.)	highly malignant osteochondrosarcoma rt. proximal tibia; onset early August 1937, hemorrhage from fungating lesion October 1937	exploratory incision, intractable hemorrhage; hasty biopsy, packed with gauze elsewhere; Dakinization for infection; transfusion; amputation Nov. 4, 1937; transfusion	3rd transfusion November 22, 1937	wound badly infected after biopsy (99°-102.4°F.); P.D.XIII Nov. 15, 1937, 11 days after amputation; 15 in 16 days, 10 i.m. (3 reactions 104°F.) 5 i.v. (3 reactions 104°-105°F.); purulent discharge from stump after amputation	gained weight, well 8 mos. then multiple lung metastases; hemoptysis shortly before death July 1938, 11 mos. after onset
77. W.B. Coley (10, #577; 43, case 70 in Table 7; 123)	M. 18 (W.L.)	osteogenic sarcoma proximal lt. fibula, 5 lb. wt. loss; onset September 1924	incisional biopsy 1 wk. after onset, considered osteomyelitis	November 8, 9, 10, 1924 radium packs (30,000 mch, concurrent with toxins); amputation refused; resected by Albee December 1924	P.D.XIII November 1-15, 1924 few i.m. little reaction; resumed later, continued 1st 4 mos. of 1925 by family physician	in good health until August 1926 then metastases to pelvic bone & abdomen; death spring 1927, 2½ yrs. after onset
78. W.B. Coley (10, #1449; 88)	M. 21 (B.M.)	osteogenic sarcoma proximal lt. fibula (8 cm); groin nodes enlarged; onset April 1930 while bowling	liniment applied, aspiration; amputation September 26, 1930	slight revision of stump January 1931	September 23, 1930; P.D. XIII 1 i.m. 3 days prior to amputation; resumed 12 days after, no appreciable reaction from 1st 3 i.m., thereafter 28 i.v. in 60 days; 2nd course January 8, 1930, 17 in 6 wks., moderate reactions; March 27 1931, 7 i.v. in 13 days, moderate reactions	gained 4 lbs.; lung metastases seen mid-February 1931, (after stump revision); progressed rapidly, death August 11, 1931, 16 mos. after onset

79. B.L. Coley (6, #1241; 87)	F. 18 (C.C.)	osteogenic sarcoma proximal rt. fibula, 8 x 4 x 4 cm; onset, early January 1931, 2 mos. after trauma	March 7-10, 1931: x-ray (3600 r); March 11, 1931 amputation; considerable discharge necrotic material	thoracentesis December 12, 1931 (1300 cc aspirated) x-ray ending December 30, 1931 (4000 r to chest); 3 more thoracenteses (1800-2000 r each time)	P.D. XIII March 25, 1931, 12 in 25 days, 4 i.m., mild reactions; 8 i.v. (101°-103° F. 3 times)	excellent conditon that summer, obtained prosthesis, gained weight; late November 1931, chest pain, lung metastases seen December 2, 1931, death February 4, 1932, 13 mos. after onset
80. B.L. Coley (10, #1440; 123)	M. 17 (C.G.)	very cellular osteogenic sarcoma proximal rt. fibula, 8 x 5 cm.; onset March 25, 1932	aspiration biopsy; amputation refused	radium packs June 3, 1932 daily for 5 days (40,000 mch.); June 8, 1932: amputation	P.D. XIII May 28, 1932, 19 in 33 days, 10 prior to surgery; resumed June 15, 1932: 3 i.m., 6 i.v., moderate reactions (maximum 102.4° F.)	pain relieved in week after toxins begun; gained 16 lbs. in 3 mos., obtained prosthesis; fell February 2, 1933, bruising rt. buttock. then lost 28 lbs. in 6 mos. bad fall in February striking stump; pain severe; metastases to rt. iliac bone; disease progressed, death February 1934, 23½ mos. after onset
81. B.L. Coley (123)	M. 21 (L.H.)	osteogenic sarcoma proximal rt. fibula, onset, April 1937, about 1 mo. after 50 lb. case fell on back of leg; 20 lb. wt. loss	aspiration biopsy June 30, 1937; x-ray (1800 r) over rt. fibula July 2-9, 1937; amputation July 14, 1937	none	P.D. XIII July 22, 1934, 8 days after surgery, 12 in 12 days: 10 i.m., (reactions averaged 101.2°-102.4° F.); 2 i.v. (103.8°-104° F.)	*stump healed completely after 1 wk. of toxins; gained 15 lbs.;* mid-October 1937 pain in lt. back, metastases to lungs seen October 26, 1937; rapid downhill course, death January 6, 1938, 10 mos. after onset

TABLE 3, GROUP 1: OSTEOGENIC SARCOMA FAILURES, PRIMARY OPERABLE WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
82. B.L. Coley (10, #1769; 123)	M 29 (L.B.)	extensive osteochondrosarcoma proximal third rt. fibula; onset January 1933, 6 mos. after being knocked down by car, fracturing rt. distal fibula (as taxi driver, he often knocked proximal rt. leg against gear shift); also had rt. direct inguinal hernia, lipomas chest wall	aspiration biopsy, partial resection fibula Aug. 21, 1934; cast applied to prevent foot drop	excision of recurrence Mar. 6, 1935; 2nd very large recurrence excised July 22, 1935; amputation May 6, 1936; 3 lesions on chest wall aspirated (lipomas); 2 lung lesions resected Jan. 2, 1940; x-ray to chest, slight pain relief May 27, 1941	P.D.XIII Sept. 13, 1934, 22 days after surgery 10 i.m. in 16 days (mild reactions); resumed Oct. 12, 1934: 6 i.m. in 6 days, (100.6°-104° F.); May 18, 1936, 12 days after amputation: 23 in 27 days, 6 i.m. (100°-103.6°F.), 17 i.v. (101.2°-104.6°F.)	returned to work part time mid-November; local recurrence February 1935; again went back to work; another mass anterior to scar May 1935; well until March 1936 then another recurrence; prosthesis, Aug. 26, 1936; did exceptionally well with it; symptom-free till Nov. 24, 1939, then lung metastases, also 3 more lipomas on chest wall; December 1940 further lung metastases, bulky chest wall recurrence 30x20 cm. metastatic node lt. inguinal region; death June 21, 1949, 8½ yrs. after onset
83. W.B. Coley (43, #76 in Table 7; 52)	F 30 (M.K.)	extensive fibrosarcoma fibula; onset November 1894	none	amputation by Coley November, 1895, 1 yr. after onset	Buxton VI October 1894 for few weeks by family physician	growth decreased 2½ cm. in diameter; then remained stationary for 1 yr.; lung metastases, death, 2 yrs. after onset

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TABLE 3, GROUP 2: OSTEOGENIC SARCOMA FAILURES, RECURRENT (OPERABLE) WHEN IMMUNOTHERAPY WAS BEGUN: 13 Cases

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
1. B.L. Coley (123)	M 16 (G.S.)	osteogenic sarcoma distal rt. femur 15 x 16 x 8 cm.; onset late October, 1939	diathermy; aspiration biopsy Jan. 25, 1940 (no tumor cells); x-ray (preceded by diathermy each time) 9000r. in 16 days, caused decrease in size; amputation 4 mos. after onset	none	P.D.XIII Feb. 28, 1940, 14 days after surgery; 9 in 9 days (6 i.m., 3 i.v.), reactions 101°-105° F.; 2nd course July 1940; 12 days, 6 i.m. 6 i.v., nearly all caused marked reactions	excellent general health, gained 20 lbs. in 4 mos.; lost 9 lbs. during 2nd course of toxins; obtained prosthesis; by March 1941 weighed 200 lbs. bilateral lung metastases present March 26, 1941; general health not affected; severe grippe December 1941; led normal life; Fall 1942 condition began to deteriorate lost 20 lbs. but morale good; death July 31, 1943, 3 ¾ yrs. after onset
2. W.B. Coley (52; 123)	F 50 (F.deV.)	recurrent chondrosarcoma rt. distal femur; onset May 1907; recurrence November 1913, size of coconut extending to acetabulum	amputation elsewhere May 1908; resection of recurrence by Coley Nov. 28, 1913; wound fulgurated	Dec. 13, 1917 radium (31,300 mch); Jan. 5, 1918: incision drainage necrotic tumor tissue	Dec. 24, 1913: Tracy XI (5 wks. after surgery) 4 i.m. in lt. buttock; no reactions; injections resumed October 1917 by family physician, caused fluctuation, mucinous degeneration, Dec. 13, 1917, toxins by Coley (Tracy XIF) 14 in 6 wks., 1 in tumor, rest i.m., only 2 or 3 caused reactions (to 103.6° F.)	in excellent conditon until August 1917, then another recurrence in stump, of very rapid growth (58 cm. in circumference by December 1917); *third of tumor became necrotic*; disease progressed, death October 1918, 11 yrs. after onset

3. W.B. Coley (52)	F 23 (T.B.)	recurrent chondrosarcoma distal rt. femur, "highly cellular"; onset summer 1914 following injury (sprain); recurrence apparent 11 days after curettage; very anemic (3,900,000 hg. 20%, w.b.c. 20,000)	explored by Gibney December 14, curettage, swabbed with phenol, packed with gauze; 2nd curettage	Jan. 8, 1915 amputation by Coley	Tracy XI, January 1915, 4 i.m; 14 more i.m. after amputation, reactions to 104° F.	complete recovery, married; NED about 2½ yrs.; then chest symptoms; became pregnant; December 1916: metastases involving whole right thoracic cavity; rapid course, death December 18, 1916, almost 2½ yrs. after onset
4. W.B. Coley & Wilson) (52)	M 17 (H.S.)	recurrent osteogenic sarcoma lt. proximal humerus; onset Fall 1900 (recurred rapidly after amputation)	explored by Bull, interscapulothoracic amputation May 1, 1901	mass 5 x 7 cm. excised; wound healed completely	Buxton VI for 2-3 wks. directly into recurrence below axilla; resumed after excision, given at home every 48 hrs. by Wilson June 12 - August 1, 1901, reactions to 105° F., considerable cyanosis; resumed in 8 days, for a few more wks.	growth arrested, marked general improvement; did well until August 1901, then pain in sternum, lung metastases, weight loss; death November 30, 1901, 12 mos. after onset
5. W.B. Coley & Fisher (37; 38; 43; 51; 52)	M 14 (F.L.)	recurrent osteogenic sarcoma proximal third lt. humerus, very severe pain, affecting sleep; onset mid-January 1909, 2-3 wks. after spiral fracture, flail joint	explored by Finney June 1910, incomplete curettage	Fisher curetted recurrence late August 1910, amputation, Jan. 1911; incomplete removal recurrence July 1911; shoulder girdle removed 1912	Tracy XI, June 16, 1910, i.m. for about 2 mos. in pectoral region, every 3rd or 4th dose i.t.; resumed August 1911 for 6 mos. after incomplete removal	pain ceased after 3 injections; slow, steady regression; recurrence; gained 10 lbs. after toxins resumed; 3rd recurrence mid-December 1910; 4th recurrence July 1911 in pectoral region; regained weight, strength after toxins, 1911; well until April 1912; 5th recurrence after removal; *complete recovery after prolonged toxins, excellent health 8 yrs.*; lung metastases, death 1920, over 10 yrs. after onset

TABLE 3, GROUP 2: OSTEOGENIC SARCOMA FAILURES, RECURRENT (OPERABLE) WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
6. W.B. Coley (10,#1068; 123)	M 14 (D.M.)	recurrent osteogenic sarcoma proximal ½ rt. humerus, severe pain; onset mid-October 1929 after sprain, throwing snowball	November 1929 x-ray; rapid improvement in swelling; radium pack (12,141 mch)	November 21, 1929 2nd radium pack (12,141mch) after 2 doses toxins; interscapulothoracic amputation, January 24, 1930 3 mos. after onset; explored August 1930: inoperable	P.D. XIII November 11, 1929: 14 i.t. & i.v. in 4½ wks; 1 more after amputation; final course July 7, 1930: 28 in 60 days	improved for 2 mos., then became worse, gained 20 lbs. after amputation; local recurrence early July 1930; fungating tumor on shoulder, death, January 2, 1931, 14½ mos. after onset
7. W.B. Coley (43; 52; 123)	M 16 (M.P.)	recurrent osteochondrosarcoma rt. distal 2/3 humerus (18 cm.), intense pain; onset, September 1914	operated elsewhere 4 mos. after onset; then x-ray, March-April 1915; growth increased steadily	disarticulation June 1915 at Mt. Sinai Hospital	Tracy XI & XIF (Filtrate) May 4, 1915; 10 in 16 days i.m. & i.t., 3 reactions to 103°F.; 2 chills: pain relieved after these	tumor massive by June 1915; death, September 1915, 1 yr. after onset
8. B.L. Coley (10, #2259; 123)	M 42 (L.M.)	recurrent osteogenic sarcoma rt. proximal tibia, 10 lb. weight loss; onset September 1937	primary excised November 24, 1937; x-ray January 4-7, 1938 (1200r); amputation January 8, 1938	x-ray to lungs October 1939 (6300r), more January 1940 (6000r) concurrently with toxins; 3rd cycle April 1940 (3600r)	P.D.XIII January 14, 1938, 6 days after amputation: 14 in 14 days, 5 i.m. (101.2°-101.4°, average); 9 i.v. (average 101.4°-103.4°F.); 2 attacks pleurisy Fall 1939; further toxins Jan. 4, 1940: 12 in 12 days i.m. & i.v. (to 104°F. from i.v.)	pain & discomfort in stump so no prosthesis for 7 mos. March 1939, lung metastases seen; improved after combined toxins & x-ray; metastases to frontal bone July 1940; death August 1940, almost 3 yrs. after onset

9. W.B. Coley (43, case 72 in Table 7; 123)	M 20 (H.D.)	irregular infiltrating recurrent osteogenic sarcoma proximal rt. fibula involving joint & condyle of tibia; lymph nodes in groin enlarged; onset January 1918 after sprain	leg bandaged, cast applied; March 1918 growth excised elsewhere; fluid in joint thereafter	radium pack April 23, 1918 (9400 mch); next day silver tubes of radium in sinus; no improvement; amputation May 1, 1918, 4 mos. after onset, August 28, 1918 x-ray to lungs (8)	(bloody purulent discharge from incision); Tracy XI April 21, 1918: 6 i.m. in 1st 15 days, mild reactions; injections resumed 13 days after amputation: 18 in 41 days, little reaction except once (104.4° F.); resumed Aug. 27, 1918: 5 in 15 days, mild reactions	disease not controlled, progressed rapidly after final radiation, death November 1918, 11 mos. after onset
10. B.L. Coley (10, #1694; 123)	M 25 (J.H.L.)	recurrent telangiectatic osteogenic sarcoma proximal rt. fibula with pathologic fracture, 6 lb. weight loss; onset early November 1933; 2 severe injuries to rt. leg 2 yrs. & 2 mos. prior to onset	aspiration biopsy; radium packs Dec. 23-Jan. 3, 1934 (80,000 mch; April 1934, 81,000, pain relief, marked regression; symptomfree for several weeks, then reactivated; amputation Aug. 9, 1934, 9 mos. after onset	x-ray to lt. femur January 1936 (2000r) pain relieved; 2nd cycle April 29-May 11, 1936 (3000r)to lt. thigh; 3rd cycle to lt. femur February-March 1937 (2400 r); complete pain relief; bilateral thoracic cordotomy May 14, 1937, not a complete success; alcohol injections	P.D.XIII, August 16, 1934, 7 days after amputation; 21 in 46 days; 12 i.m. (5 reactions 103°-105° F.) 9 i.v., (averaged 101.5°-102.5° F.) October 1936 infected finger, burn on lt. elbow, lymphadenopathy of elbow & axilla	stump & general condition excellent, gained 7 lbs.; obtained prosthesis November 1934; condition satisfactory until November 1935, then metastasis to lt. femur; November 1936 asymptomatic lung metastases seen in lt. hilum; general condition remained excellent; pain in rt. hip April 1937, metastasis to rt. pelvis; disease progressed, death September 8, 1937, almost 4 yrs. after onset
11. W.B. Coley (10, #475; 43; case 73 in Table 7;123)	M 12 (C.S.)	twice recurrent cellular osteochondrosarcoma lt. fibula; weight loss, anemia; onset December 1919 after appendicitis, severe pharyngitis, unable to work after March 1920	curettage January 1920; March 1920 15. cm. fibula resected for recurrence; 3rd operation for 2nd recurrence August 1920 fibula removed, except for bit near joint	4 radium packs Aug. 28, 1920 (31,870 mch); explored, scar tissue excised Nov. 24, 1920, 5 radium tubes inserted in soft tissues; 2 more radium packs, Nov. 20, Dec. 6, 1920, (12,159 mch); radium burn early 1921; amputation April 6, 1921, 16 mos. after onset	Tracy XI, August 25, 1920, 8 i.m. in 14 days, little reaction; continued at home by family physician; December 1920, daily i.m.	gained 18 lbs., general condition improved after toxins & radium, but pain recurred intermittently due to metastases in tibia & femur (seen in amputated specimen); lung metastases, death September 1921, 21 mos. after onset

TABLE 3, GROUP 2: OSTEOGENIC SARCOMA FAILURES, RECURRENT (OPERABLE) WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
12. W.B. Coley (12; 31, Case VI; 40, p. 140; 123)	M 19 (G.M.)	extensive recurrent fibrosarcoma lt. clavicle; onset March 1908	treated as rheumatism for several mos.; total excision April 1909	none	Tracy XI, September 28, 1909, daily or every other day i.m. pectoral region about 9 wks., slight reactions except twice 102° -104.8° F.)	considerable decrease in size in 2 wks., increased mobility of various recurrent nodules; improvement then ceased, disease progressed, death March 25, 1910, 2 yrs. after onset
13. Treves & Hoffman (123)	F 34 (J.M.)	recurrent chondrosarcoma rib extending into pleura; onset July 1, 1931	resection Oct. 1931; 4 radium packs Nov. 1-5, 1931 (36,000 mch); some regression; 5 more radium packs Feb. 1932 & Oct.-Nov. 1934 (34,000 & 40,000 mch)	radical resection after pneumothorax, April 25, 1933; x-ray concurrent with fever therapy, August 4-10, 1933 (400 r each), caused radiation burn	P.D. XIII December 12, 1932: 17 in 36 days, 16 i.m., 1 i.v., little or no reaction till 8th dose, 1 very severe (107.8° F.); last reactions averaged 101°-103° F.; fever therapy by "super diathermy" August 1, 4 & 10, 1933 to 102.4° F.	some regression after radium very marked skin changes, general condition good; reactivated Fall 1932; slight regression after further radium; increase in size Feb. 1933; May 1933, hydrothorax; pain relieved, gained 6 lbs. in excellent condition; metastases rt. lung; no benefit from fever therapy & x-ray; downhill course, death January 16, 1934, 2½ yrs. after onset

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TABLE 3,GROUP 3: OSTEOGENIC SARCOMA FAILURES, INOPERABLE, METASTATIC OR POLYOSTOTIC WHEN IMMUNOTHERAPY WAS BEGUN: 24 Cases

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
1. B.L. Coley (10, #1245; 123)	M 48 (W.H.)	osteogenic sarcoma distal lt. femur, rt. tibia, arising in Paget's disease; onset April 1930, following herniotomy; increased after fall July 1930; (also had epithelioma lip from 1926)	physiotherapy, home remedies; January 1931 incisional biopsy; Feb. 1931, radium packs to tibia (5600 mch), to femur (7800 mch)	none	P.D.XIII Feb. 28, 1931: 14 i.m. in 38 days small doses, slight reactions (maximum 102° F., once)	unimproved; severe cold April 1931, bedridden thereafter, death Aug. 16, 1931, 16 mos. after onset
2. B.L. Coley (10, #1096; 123)	F 13 (R.B.)	osteochondrosarcoma rt. proximal humerus with pulmonary metastases by July 1928, some weight loss; onset immediately after forcible blow in area late May 1928	ultra violet & x-ray; severe pains in hand, disability of arm then occurred; July 1928, 4 more x-ray at Memorial Hospital; some decrease in swelling	plaster cast to arm, broke 3 wks. later, removed; shoulder joint disarticulation September 19, 1928, outer third of clavicle & bony prominence of scapula removed	P.D.XIII August 15, 1928; 1st i.v. gave reaction 103.8° F., pathologic fracture occurred during chill; 8 more i.v., 2 i.m. in 26 days (101.8°-103° F.); 2nd course Nov. 2, 1928; 18 i.v., 2 i.m. in 47 days (average reactions 100°-102° F., maximum 103° F. twice)	*amputated specimen showed marked hemorrhagic necrosis of much of the extensive tumor mass;* gained 7 lbs. in December 1928 despite lung metastases, general condition excellent; April 1929, rapid downhill course, death October 4, 1929, 16 mos. after onset
3. W.B. Coley (43, case 95 in Table 7; 52;123)	M 40 (B.F.S.)	cellular osteochondrosarcoma proximal lt. humerus; bilateral pulmonary metastases; onset November 1916	explored, curetted Feb. 7, 1917, radium pack (5472 mch)	radium (during toxins); interscapulothoracic amputation Feb. 28, 1917; wound irrigated with Dakin's solution; x-ray to lt. shoulder, mediastinum, rt. neck	Feb. 9, 1917, Tracy XI, 2 days after surgery, 12 i.m. in 15 days, 7 prior to radium; wound infection, purulent discharge; 11 more i.m. in 28 days	wound healed in 2 wks., gained 10 lbs., general health good; *lung metastases remained unchanged for about 3½ mos.;* June 1917 recurrence in scar, lung metastases very extensive by mid-July; death Aug. 15, 1917, 9 mos. after onset

4. B.L. Coley (10, #1342; 123)	F 9 (J.H.)	extensive osteochondrosarcoma mid-shaft rt. humerus (12 cm. long), metastases to thighs; onset September 1931, following trauma (obesity, precocious development)	aspiration biopsy Nov. 19, 1931; shoulder joint disarticulation 22 mos. after onset	incisional biopsy lt. tibia August 1933; x-ray August, October (3000r each); November 19 - December 4 (6000r); December 20 to parathyroids (300r); December 28-January 8, 1934 to lt. femur (4000r) January 1934, palliative, high thigh amputation, transfusion	P.D. XIII December 6, 1931, 9 days after surgery; 13 in 16 days (11 i.m. 2 i.v.) 50% caused reactions 102° -104° F.; January 20, 1932; 8 in 16 days; 3rd course November 3, 1933: 6 i.m. & 3 i.v.; latter caused reactions 103°-105.8° F.	wound healed in 12 days; *nodules on thighs disappeared,* excellent health, gained steadily, very active, rapid progress in school; NED 8½ mos.; July 1933 sprained lt. ankle; 2 wks. later metastasis to lt. tibia; recurred after x-ray, December 1933, metastases to lt. distal femur, to lt. occipital region, low back pain; no metastases to lungs; death September 6, 1934, almost 3 yrs. after onset
5. W.B. Coley (43, Case 88 in Table 7; 52; 123)	M 50 (G.M.)	inoperable recurrent fibrosarcoma proximal rt. humerus involving joint & scapula; onset spring 1910 (pain); swelling apparent 16 mos. later; general condition fair	curettage, cavity packed February 1912 by Guthrie; seropurulent discharge	wound washed daily with peroxide or iodine; incision & drainage 3 oz. necrotic tumor; sinus kept open & axillary region incised & drained	Tracy XI May 12, 1912; 15 in 19 days in pectoral muscles; reaction 102.6° F. from 1st dose only, febrile for 3 wks. June 1912 (to 105.2° F. due to wound infection & toxemia from absorption necrotic tumor tissue, profuse discharge) 2nd course toxins 6 wks. after 1st, i.m. every 48 hrs. for 4 wks.	*gelatinous tapioca-like material discharged from sinus,* disease ruptured into rt. lung; extreme emaciation, death October 12, 1912, 2½ yrs. after onset
6. W.B. Coley (10, #772; 123)	M. 68 (E.S.)	immunotherapy osteogenic sarcoma rt. tibia, rt. humerus, rt. ulna arising in Paget's disease; injured severely in auto accident 10 wks. prior to onset, tibial lesion April 1924; onset ulna lesion May 1927	March 1925 incisional biopsy of tibia; amputation rt. leg March 25, 1926; radium pack to ulna June 1927 (8000 mch)	x-ray (2) to humerus July 25-27, 1925	P.D. XIII July 4, 1927, 13 i.m. in 23 days, (little reaction, maximum 102.5° F)	unimproved; August 23, 1927, death 3½ yrs. after onset

TABLE 3,GROUP 3: OSTEOGENIC SARCOMA FAILURES, INOPERABLE, METASTATIC OR POLYOSTOTIC WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
7. Harmer (81, case 87; 121)	M. 20 (F.Mc.H.)	recurrent chondrosarcoma rt. tibia with lung & groin metastases; onset April 1911, recurred 9 wks. after surgery involved whole leg below knee, size of child's head, ulceration 10 cm. in diameter; lymph nodes in groin markedly enlarged	grapefruit-sized primary excised; amputation October 28, 1912, groin nodes biopsied	x-ray to chest	P.D. XIII, November 20, 1912; 3 wks. after amputation; i.m., 6 while in hospital, continued at home every 48 hrs., marked reactions from larger doses, given about 3 mos.	recurrence on stump soon after toxins were begun, *disappeared,* recurred, *again regressed* but during last month of treatment was unchanged; returned to Ireland, died June 1913, 26 mos. after onset
8. Pack (123)	M. 21 (R.C.)	secondary chondrosarcoma, rt. proximal tibia with lung metastases; 10 lb. wt. loss; jaundice, diarrhea, hepatomegaly September 1941; (enchondroma excised from lt. knee summer 1936; dislocated rt. knee at soccer spring 1939; torn semilunar cartilage removed July 1939); onset July 1940	explored July 1940; x-ray (14,000r)	x-ray to lungs December 8, 1941 daily for 1 mo. during toxins (3800r); 2nd cycle March 26, 1942 (4800r in 3 wks. during toxins to lt. chest)	P.D. XIII December 8, 1941, 23 i.m. in 30 days, no adequate reactions until 6th dose, thereafter averaged 102.6°-103.6° F. (maximum 104.2° F.); March 26, 1942 2nd course, 16 in 21 days 13 i.m. 3 i.v. (5 reactions, 103°-105° F.)	*slight decrease in lung lesions during combined therapy;* continued for about 1 mo. then pain in rt. forearm, numbness in fingers; recurrence of diarrhea; pain in arm; May 1943 diplopia, due to brain metastases; complete paralysis, death June 12, 1942, 2 yrs. after onset

9. W.B. Coley (24; 25; 26; 31)	M. 23 (B.M.)	extensive inoperable osteochondrosarcoma involving entire rt. ½ of ilium; fell 4 stories 10 yrs. before; fell striking rt. buttock 3 yrs. prior to onset; size of child's head by February 1894; extending from mid-sacrum behind nearly to edge of rectus muscle in front, filling much of rt. iliac fossa; rapid loss of wt.; emaciated	untreated	December 1894 portion of ilium removed: no evidence of sarcoma (this surgery reactivated the disease)	Buxton V (filtrates) March 1894; 19 in 28 days, marked reactions (some i.t.) *high fever for 1 mo. after toxins stopped due to absorption necrotic tumor;* injections resumed December 1894	*growth very rapidly broke down, great masses sloughed out,* condition critical for wks., then steady improvement, *regained strength, gained 40 lb. very rapidly, complete regression* by October 24, 1894; recurrence shortly after exploratory surgery December 1894; did not respond to further therapy; died July 1896, about 3 yrs. after onset
10. Hunter (52)	M. Adult	enormous recurrent inoperable chondrosarcoma involving crest of ilium & entire proximal thigh; severe pain required large doses morphine; onset late 1896	extensive radical operation February 1897 by Wyeth	none	Buxton VI February 1899 given deeply into tumor with aspirating needle; as tissues softened Coley gradually decreased the depth; reactions not recorded except that chills occurred after 6 or 8 injections lasting 15-40 min.) probably had over 30 injections	*in 3 wks. extensive tumor softened over area injected (15-20 cm.), felt like a cyst;* necrotic tumor tissue drained through needle puncture sites (50 cc. at a time); after toxins were stopped disease slowly progressed; died May 1901, about 4½ yrs. after onset

TABLE 3,GROUP 3: OSTEOGENIC SARCOMA FAILURES, INOPERABLE, METASTATIC OR POLYOSTOTIC WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
11. Bissell & W.B. Coley (12; 16; 52; 123)	M 37 (C.V.)	enormous inoperable chondrosarcoma lt. ilium (30 × 39 cm); onset 1 month after falling into manhole striking lt. hip on cable	untreated	excision of furuncles, poultices; purulent, necrotic material evacuated from tumor through several incisions; Feb. 5, 1914, drainage tubes inserted, irrigated with disinfectants; March & April 1914, radium (4), no local or general reaction; another, October 1914 caused burn; recurrence partially removed by Coley Feb. 1915, thick brownish material drained	Tracy XI January 5, 1914; i.m. in rt. buttock; next day furuncle on neck; 5 days later another i.m. in rt. buttock, next 3 i.t.; pain, tenderness of entire leg; tumor area infected (staph.), profuse discharge from 4 cm. sinus; febrile for 6 wks. (101°-105.5°); 7 more i.m. in February, 1 marked reaction	*tumor definitely smaller in 6 wks.;* lost much weight during infection; began to gain in late February, felt stronger; *enormous growth completely regressed in 2 mos., weight and strength normal, resumed work* as lineman; October 1914, small local recurrence, increased to 8 × 10 cm. in 4 mos.; disease slowly progressed 1915-1916, death February 25, 1917, over 4 yrs. after onset

12. W.B. Coley (88; 123)	M 46 (J.H.S.)	inoperable chondrosarcoma rt. ilium, sacrum and pelvis; onset August 1926, shortly after a fall, straining hip joint; increasingly severe pain, foot drop, crutches required	osteopathy for 2 mos.; winter 1927 Glover serum, mistletoe given; slow regression April-September 1927, general condition improved; October 1927, x-ray (4)	November 1927, 8 radium packs (42,000 mch); January 1928, physiotherapy; late June 1928, 4 radium packs (12,000 mch) November 1928 2 more radium packs (17,208 mch.); January 1929 final radium; May 1929 large trochar inserted in tumor, pint necrotic tissue removed, wound irrigated with saline; hot compresses to infected tumor summer 1929	P.D. XIII October 18, 1927: 10 i.m. in 21 days; received 93 in 18 mos. (courses of 4 to 17) all i.m. except 6 i.t., 1 i.v.; moderate reactions except twice 103° F.; spring 1929 Strep. viridans septicemia, E. coli infection in tumor area, fever to 106.8° F. May 1, during May 100°-102.3° F. average, maximum 103.4° F.; June, 99°-101° F., July 104.6° once, to 101.8° F. daily; infection, anemia increased August 1929	2nd° burns on feet (hot water bottles) Dec. 1927, healed in 16 days; *decrease in pain, marked tumor regression* by Feb. 21, 1928, *general condition excellent;* April 1928 *within 5 days of resuming toxins, further regression:* June July 1928 *further marked improvement after more toxins, radium;* growth then reactivated, pressing on rectum, bladder; better after more toxins & radium; tumor in ilium stationary Nov. 1928 to late Feb. 1929, then lung metastases; March 1929, *tumor softened at site of i.t. injections,* May 1929 *large recurrence broke down, became fluctuant;* after evacuation necrotic tumor tissue, nausea ceased, ate well; by August 1, 1929 tumor smaller, sinuses still discharging necrotic tumor; death October 1929, due to infection, 38 mos. after onset
13. W.B. Coley (123)	F 32 (B.F.)	extensive inoperable chondrosarcoma involving almost all rt. ilium & trochanter of femur, filling rt. iliac fossa; severe pain, could not walk; onset June 1932 (no trauma)	cast for 2 wks.; incisional biopsy April 6, 1933; radium packs April 6-17, 1933 (96,000 mch.)	May 1933, 5 more radium packs (40,000 mch)	P.D.XIII April 20, 1933, 16 in 47 days: 7 i.m., 2 slight reactions, 9 i.t., average reactions 103°-104° F., maximum 105° F.	*growth became softer, almost fluctuant during toxin therapy, general condition improved, steady regression, pain much less for some wks.;* after toxins were stopped tumor enlarged, disease progressed, death November 17, 1932, 17 mos. after onset

TABLE 3,GROUP 3: OSTEOGENIC SARCOMA FAILURES, INOPERABLE, METASTATIC OR POLYOSTOTIC WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
14. W.B. Coley (123)	M 21 (W.D.Jr)	inoperable fibrosarcoma rt. ilium 11 × 5 cm., lymph node metastases; 2 yrs. prior to onset fell 50 ft. breaking ligaments of rt. knee; August 15, 1927, 10 days prior to onset of pain, hit by car in rt. hip; 10 days later tumor size of grapefruit; nodes 5 × 4 × 2½ cm.	explored at Lahey Clinic December 2, 1927; x-ray, lead given January & March 1928	3 radium packs June 1928 (42,500 mch); large doses morphine for severe pain day of 2nd radium	P.D.XIII May 22, 1928, 16 in 27 days, 13 i.m. 3 i.v.; 3 reactions 103°-104° F.; June 25, 1928 6 i.v. in 33 days, little reaction	*toxins caused hemorrhagic & necrotic changes in groin metastases (no radiation was given to that area);* improvement temporary, then disease progressed, death September 30, 1928, about 15 mos. after onset
15. University Hospital San Francisco (183)	F 23 (D.M.)	osteogenic sarcoma sacrum, inoperable	incisional biopsy, February 1915	x-ray February to May 1915; menses ceased	P.D.XIII February to May 1915, during radiation (1 febrile reaction)	*decrease in size; patient returned to work;* disease later recurred, involving sacral region and back; death January 1, 1920, over 5 yrs. after onset
16. W.B. Coley (40, Case X; 52; 123)	M 47 (A.T.B.)	extensive osteogenic sarcoma rt. clavicle (20 × 6 cm.), shoulder ankylosed; metastases to lungs; 55 lb. wt. loss; onset December 1916, after influenza & pleurisy	treated as rheumatism for weeks	x-ray April 13, 1917, 9 days after toxins	Tracy XI April 4, 1917; 10 i.m. in 26 days, average reactions 100°-101.5° F., maximum 103°F.	temporary check in primary growth, no other apparent improvement; disease progressed, death September 1917, 9 mos. after onset
17. W.B. Coley (52; 123)	M 49 (B.F.)	inoperable osteogenic sarcoma rt. clavicle, pathologic fracture; 15 lb. wt. loss, great pain; onset, November 1917, few wks. after fall on sternum	fracture immobilized in plaster for wks., no union; July 1918, explored, biopsied; radium pack August 18, 1918.	none	P.D.XIII August 9, 1918, day after radium; 28 i.m. in 69 days, mild reactions (maximum 102°F.)	*no further extension of disease, much inflammation in tumor area, gained wt. general condition improved, fractured area regenerated;* later generalized metastases to abdomen, chest wall, lungs; death November 1919, about 2 yrs. after onset

18. W.B. Coley (10, # 1766; 123)	M 23 (W.E.H.)	inoperable osteogenic sarcoma rt. clavicle, pathologic fracture; onset July 1933 following chronic low grade trauma from heavy ice tongs (was an iceman)	complete excision November 1933; x-ray December 29, 1933; 4,800 r in 20 days	sinus area opened March 1934, discharged pus; palliative x-ray January 1935 (1500 r); furuncle poulticed; further x-ray September 1935 (2000 r); cautery, fungating tumor incised, zinc chloride, gradual debridement, cleansing	P.D.XIII January 18, 1934: 26 in 42 days, 8 i.m. (2 mild reactions) 18 i.v. (average 101°-103° F., maximum 104° F); June 1934 furuncle in affected shoulder caused pain relief; summer 1936 acute anterior urethritis (gonorrhea)	*marked regression, wound gradually healed;* in prison that summer disease reactivated, large fungating recurrence by December 12, 1934; improved considerably after x-ray; returned to work; lung metastases September 1935, but general condition unaffected; growth decreased over 50% that fall, little activity until spring 1936 then tremendous extension axilla, chest wall, death September 1936, 38 mos. after onset
19. Harmer (80)	M young adult (M.A.)	recurrent inoperable fibrosarcoma rt. clavicle, involving apex of rt. lung; onset late 1905; 10 lb. wt. loss (recurrence 5 mos. after surgery)	primary size of orange removed August 1910; partial resection recurrence June 1911; x-ray 3½ mos. ending early November; steady increase (14 cm); interscapulothoracic amputation November 18, 1911; (removal incomplete, apex of lung involved)	none	December 10, 1911 P.D.XII into recurrent egg-sized mass for a month; moderate reactions	no apparent effect; death March 25, 1912, 7 yrs. after onset
20. B.L. Coley (10, #1466; 123)	M 29 (C.W.)	inoperable recurrent osteogenic sarcoma rt. 8th rib (10 cm); onset December 1931, 9 mos. after injury to rt. chest in auto accident	February 1932 excision; aspiration biopsy of recurrence April 30, 1932; x-ray that day & May 9, 1932 (1500 r)	none	P.D.XIII May 11, 1932: 15 in 24 days, 5 i.m., 9 i.v., slight reactions except twice (103°, 105° F.)	*almost complete regression, felt fine during toxin therapy;* 4 wks. later greatly increased pain, disease progressed, death December 28, 1932, 12 mos. after onset.

TABLE 3,GROUP 3: OSTEOGENIC SARCOMA FAILURES, INOPERABLE, METASTATIC OR POLYOSTOTIC WHEN IMMUNOTHERAPY WAS BEGUN (con'd)

Physician or Hospital (References)	Sex Age (Initials)	Site, Extent, Duration of Disease Prior to Immunotherapy	Prior Therapy	Concurrent, Subsequent Therapy	Immunotherapy Site, Duration Reactions Elicited	Immediate and Final Result Period of Survival
21. Pancoast (183)	F 15 (M.G.)	huge inoperable osteogenic sarcoma lt. 4th rib, constant dry cough; onset March 1934 lt. chest pain; 12 more episodes in 3-4 mos.	incisional biopsy March 1, 1934	x-ray August 9, 1934, begun 5 days after toxins given concurrently	P.D.XIII August 4, 1934; 12 i.m. in 12 days, 3 reactions (103°F.)	*marked decrease in tumor;* u.r.i. fall 1934; lesion then greatly increased in size, low back pain; rib continued to improve, then downhill course, severe leg pain; death from terminal pneumonia, January 12, 1935 10 mos. after onset
22. W.B. Coley (54, case 1; 123)	M 18 (G.Z.)	extensive inoperable osteogenic sarcoma skull, 12 × 12 cm; onset early January 1924, 2 yrs. after sharp blow on temple; 14 lb. wt. loss; (at first regarded as myositis ossificans by 8 or 10 surgeons & pathologists, but Coley believed it to be osteogenic sarcoma)	Jan. 22, 1924 biopsy; 2nd incisional biopsy April 4, 1934 positive for sarcoma; radium packs 10 in 25 days ending April 19, 1934 (76,000 mch.)	none	P.D.XIII April 6, 1934, 2 days after 2nd biopsy; 3 i.m. in hospital in 11 days, resumed at home, details not recorded	slight temporary improvement then lost vision of lt. eye, death Aug. 30, 1934, 8 mos. after onset

23. W.B. Coley (10, #837; 44; 46; 60; 87)	M 28 (W.B.)	inoperable osteogenic sarcoma occipital bone extending into dura; onset, August 1, 1925 5 wks. after severe blow from heavy object on back of head	incision 3 days after injury, 2nd late September 1925; explored October 7, 1925, growth very vascular	3 radium packs during toxins fall & winter 1925; radium packs July & December 1930 (9,000 & 3,000 mch); March 1933 further radiation; July 1933 attempt to repair radiation ulcer; nerves bound down by fibrous tissue, excessive hemorrhage	P.D.XIII October 10, 1925: i.m. for 8 mos.; resumed for recurrence July 23, 1931: 9 i.m. in 21 days (100°-103° F.); 3rd course February & March 1933; 4th course May & June 1933, 3 i.m. weekly	*wound healed, complete recovery, well 4 yrs;* recurrence September 1929, headaches over entire head; lesion larger after radium, July 1930; severe frontal headaches 1st 6 mos. 1931; growth then size of orange; *pain disappeared after toxins; returned to work, symptom-free 10 mos.;* then pain from pulsating vein in occipital region; disease progressed May 1933, pain increased extending to mastoid *pain again decreased after toxins,* June 1933; rapid growth after surgery, July 1933; paraplegia, death September 13, 1933, over 8 yrs. after onset
24. Harmer (12; 37, p. 162; 80, Case 7; 121)	M 31 (J.T.)	inoperable chondosarcoma antrum, ethmoid & sphenoid sinuses, exophthalmos lt. eye; onset mid-September 1912, 2 wks. after trauma over zygoma	submucous resection under cocaine; 2 attempts to establish drainage via naris abandoned (hemorrhage); radical operation November 1912 (incomplete removal)	cavity dressed, repacked, slough or granulations curetted; paste applied 3-4 times; recurrence curetted free, molars removed February 13, 1913; 2 wks. later x-ray; lt. eye enucleated January 2, 1914	P.D.XII November 16, 1912, 4 days after radical surgery; about 15 in 35 days i.m., little or no reaction (maximum 100.2° F.)	recurrence 2½ mos. after radical surgery; well until February 1914; then another extensive recurrence involving orbit; death December 23, 1915, 39 mos. after onset

TABLE 4: OSTEOGENIC SARCOMA FAILURES WITH CONCURRENT INFECTION, INFLAMMATION OR FEVER: 27 Cases

Physician (References)	Sex Age (Initials)	Diagnosis Extent of Disease	Treatment Prior to Infection	Concurrent or Subsequent Therapy	Type of Infection or Fever	Immediate & Final Result Period of Survival
1. W.B. Coley (52)	M 20 (M.R.)	inoperable sclerosing osteogenic sarcoma femur 5 × 10 cm.; 25 lb. wt. loss; onset November 1925	incisional biopsy October 29, 1926; x-ray (9), November 1926; 9 small doses Coley toxins (Parke Davis XIII) concurrently, no reactions	incision and irrigation of furuncles	November 29, 1926, dizzy, weak; 4 days later furunculosis rt. auditory canal; fluid and pus discharged from leg March 1928	disease slowly progressed; mid-January 1928 leg enormously swollen (1½ times size of body); March 31, 1928 large vein ruptured, severe hemorrhage, death April 2, 1928, 2½ yrs. after onset
2. B.L. Coley (10, #1099; 52; 88; 123)	M 16 (S.F.)	very malignant osteogenic sarcoma lt. distal femur; onset December 1926, 15 mos. after fall striking knee	explored February 1927; radium (9000 mch) March 1927; amputation 4 mos after onset	Coley toxins April 2, 1927; 19 in 10 wks.; 18 in rt. hip, no reactions, 1 in lt. thigh near stump, marked reaction (104.2° F.); further brief course November 28, 1928	following exploratory (in another hospital) sinus became infected; whole thigh edematous, large pus cavity extending 25 cm. along bone; phlegmonous inflammation involving tumor	in excellent condition; obtained prosthesis; lung metastases November 1928; death July 1, 1929, 2½ yrs. after onset
3. B.L. Coley (123)	M 42 (A.S.)	osteogenic sarcoma involving proximal 1/3 rt. femur, extensive infiltration soft tissues; onset March 1927	treated as sciatica; November 1927, incisional biopsy; December 1927 radium packs (1600 mch) concurrent with toxins, P. D. XIII i.v. & i.m. 38 in 2 mos. slight reactions except from larger doses (102°-103° F) and from i.v. (to 104° F.); February 1928 radium needles i.t. (89 mc); 8th radium pack July 21, 1928; Fall 1928, 2 more toxin injections	none	fever from absorption; July 1928; severe infection 4 days after radium; further infection, fever for 4 mos, Fall 1928 (to 105° F.)	slight improvement after toxins and radium; July 1928 tumor fungated, copious drainage after radium needles; condition hopeless; began to improve, after fever & infection Fall 1928 gained weight (hospitalized 9 mos.); 1929, progressive downhill course, *but no metastases,* death June 1, 1931, 4¼ yrs. after onset

4. Adair (10, #1521; 52; 123)	M 39 (G.G.)	osteogenic sarcoma rt. femur (grade III) arising in a benign giant cell tumor, with pathologic fracture, autumn 1930; (onset of benign giant cell tumor early 1928)	curettage of benign lesion June 1928; x-ray April & May 1930, at intervals to February 1929; skin denuded, necrotic; operation December 1930 to correct deformity	amputation May 27, 1931; Dakin's solution September & October 1932; x-ray to metastases (1700 r) December 1932 & January 1933 (2400r); March 1933, thoracic hemilaminectomy	April 1931; staphylococcus & pyocyaneous infection of necrotic irradiated skin, copious suppuration; underlying bone became necrotic	metastasis to groin; no benefit from radiation; death May 11, 1933, 5 yrs. after onset of giant cell tumor, 2½ yrs. after onset osteogenic sarcoma.
5. B.L. Coley (123)	M 14 (A.C.)	osteogenic sarcoma rt. distal femur; onset early January 1941	wet boric acid compresses; aspiration biopsy, January 29, 1941; x-ray (16,800 r in 25 days); also P^{32} (7 i.v. in 21 days); March 5, 1941; amputation; 5 transfusions; revision of stump required due to radiation necrosis; skin grafts; Coley toxins (P.D. XIII) 5 i.m. in 11 days slight reactions	none	spiking fever after amputation, suppuration, fibrosis, mild pyocyaneous infection in stump May 1941; late October 1941, 2 attacks erysipelas, quite severe; April 1941, severe chest cold	no apparent benefit from heavy radiation or 5 doses toxins; hospitalized 5 mos; lung metastases, September 1941; death June 1942; 18 mos. after onset
6. Higinbotham (123)	F 18 (A.C.)	telangiectatic osteogenic sarcoma distal rt. femur, pathologic fracture, considerable wt. loss; had fractured rt. tibia 3 mos. previously in fall; (early acromegaly?) onset, August 1938	October 13, 1938 aspiration biopsy, x-ray (2000r); P^{32}, October 17, 1938, amputation, transfusion (1200r)	Coley toxins (P.D.XIII) October 24, 1938, 7 days after surgery 19 in 19 days, 7 i.m. little reaction until maximum dose (104.4° F.), 12 i.v. (average reactions 102° -103° F.)	spiking fever to 104.6° F. October 3-18, 1938	general condition excellent, wound entirely healed in 2 wks,; gained weight, obtained prosthesis; in excellent health 1 yr; October 1940, cough due to lung metastases; morale good; death, November 26, 1940, 26 mos. after onset

TABLE 4: OSTEOGENIC SARCOMA FAILURES WITH CONCURRENT INFECTION, INFLAMMATION OR FEVER: (con'd)

Physician (References)	Sex Age (Initials)	Diagnosis Extent of Disease	Treatment Prior to Infection	Concurrent or Subsequent Therapy	Type of Infection or Fever	Immediate & Final Result Period of Survival
7. B.L. Coley (123)	M 5½ (M.G.)	osteolytic osteogenic sarcoma lt. proximal femur; trauma prior to onset, September 1946	explored; refused amputation; x-ray November 27, 1946 for 3 wks; Coley toxins (S.K.I. XIV & P.D. XIII); December 19, 1946; 18 i.v. in 34 days; 2 wks later 8 i.v. (101°-105.6°F.)	8 more injections i.v. early April 1947	January 4, 1947, concurrent mumps; febrile a few days the next week (due to necrosis of tumor?); February 1947 infected ingrowing toe nail	disease reactivated April 1947, downhill course; death July 16, 1947, 10 mos. after onset
8. Memorial Hospital (123)	F 14 (E.K.)	highly malignant osteogenic sarcoma distal rt. femur (14 cm) involving overlying muscles and joints, intractable pain, anemia; onset, sudden sharp pain mid-February 1942 (awakened her at night)	put in traction; aspiration; March 1942, incisional biopsy, sulfathiozole; cast applied for fracture	amputation April 10, 1942 "extensive growth necrotic, extremely hemorrhagic..almost entirely destroyed"; June 1942 Vitamin B complex; July 18, 1942 x-ray to spine (700 r); 2 more to spine Sept. 9, 10, 1942; plaster jacket applied to support spine (not tolerated); x-ray to rt. femoral stump, rt. pelvis (1200 r), no pain relief	April 6, 1942; special P.D. made with Buxton VI formula: 2 i.t., "felt better after 1st dose". July 22, 1942 erysipelas rt. face neck, arm (no fever); P.D. XIII Aug. 20, 1942; 2 i.m., 2 i.v. in 8 days; (no appreciable reaction from i.m., 99.4° & 103° F. from i.v.); spiking fever for a month; 2 doses cobra venom November 1942 (fever to 105° F. daily for over a week) pain partially controlled in this period	slight cough May 1942; faint shadow in lt. base May 21, 1942; cough subsided; mid-July 1942 sudden low back pain due to metastasis to spine (10D); pain ceased after x-ray & erysipelas, but lung metastases increased (bilateral by mid-August); 1942 further collapse D11 & D12 vertebrae; pain recurred in spine Sept. 1942; pain in stump rt. ilium, October 1942: decubitus ulcer uncontrolled, but child showed "most extraordinary resistance"; death November 28, 1942, 9 mos. after onset

9. B.L. Coley (10, #1355; 88; 123)	M 48 (C.W.C.)	osteochondrosarcoma rt. proximal femur, pathologic fracture, 25 lb. wt. loss, severe pain; onset September 1928 (also had lipoma in axilla, developed a year before)	none	incision, drainage, 2nd operation June 1929, femur reopened August 1929, Dakin tubes; x-ray (1) to thigh October 1929; physiotherapy March 1930; lipoma excised April 1930, also osteotomy of femur; curettage November 1930, cast applied; November 23, 1930 toxins P.D. XIII 10 in 24 days, reactions averaged 101°-102°F.; hip joint disarticulation January 23, 1931, 3½ yrs. after onset; 4 more toxin injections i.m. (102°-104.8°F.)	osteomyelitis Spring 1929 area drained after 2nd operation for several wks., osteomyelitis continued 1930, foul odor, hospitalized 4 mos.; January 1930 unexplained fever (104.6° F) after amputation	very satisfactory stump, in excellent condition 2 yrs. (seen by Coley March 29, 1933); April 1933 became psychotic, marked personality change, rectal symptoms (urgency) suicide July 14, 1933, almost 4 ¾ yrs. after onset
10. Higinbotham (10, #1548; 123)	F 19 (I.T.)	extensive osteochondrosarcoma distal femur, 23 cm. long, 20 lb. wt. loss, hypertrichosis of legs; onset November 1932	none	April 1932, osteotomy; July 9, 1933; incomplete removal; hip joint disarticulation September 1933, 10 mos. after onset; P.D. XIII October 3, 1933, 4 wks. later 12 in 19 days, 8 i.m., 4 i.v. little or no reaction except twice (102°, 102.6° F.)	suspected osteomyelitis, April 1932, drained 5 wks. after osteotomy, mucopurulent vaginal discharge (B. subtilis) late August 1933; febrile for a wk. after amputation (to 103 °F.); October 1934 had a "cold", pleural effusion	gained 40 lbs.; stump and general condition excellent; lung metastases seen November 1934; rapid downhill course, death December 19, 1934, 24 mos. after onset

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Physician (References)	Sex Age (Initials)	Diagnosis Extent of Disease	Treatment Prior to Infection	Concurrent or Subsequent Therapy	Type of Infection or Fever	Immediate & Final Result Period of Survival
11. B.L. Coley (10, #1858; 123)	M 16 (D.G.)	osteochondrosarcoma distal rt. femur; 18 lb. wt. loss in 5 mos.; onset July 1934	2 aspiration biopsies early December 1934; amputation December 20, 1934	10 days after surgery P.D. XIII 15 in 18 days (11 i.m., 4 i.v.) 1 marked reaction; November 15, 1940; sciatic exeresis; December 1940, massive doses vitamin B1	thick bloody purulent fluid evacuated from stump	prosthesis, September 1935 *in excellent condition 5 yrs;* early November 1940 sciatic pain; numbness of stump; local pain relieved, phantom pain persisted after sciatic resection; in 2 mos. huge metastasis apparent sacrum & lumbar vertebrae, also lungs; death June 17, 1941, 7 yrs. after onset
12. Higinbotham (10, #2260;)	M 28 (P.R.)	osteochondrosarcoma proximal rt. femur, 21× 17×15 cm.; 15 lb. wt. loss in 9 mos, markedly emaciated	incisional biopsy, x-ray; January 19, 1938 hip joint disarticulation, 9½ mos. after onset, blood transfusion (1200 cc.)	P.D.XIII January 31, 1938, 12 days after surgery, 11 in 14 days (8 i.m., 3 i.v.) latter caused marked reactions; 3 more transfusions; December 1938, x-ray to lungs (4000 r)	fever to 104.2°F. day after amputation, remained high 4 days (102°-104° F.) gradually declined	*wound healed well, excellent general health, gained 35 lbs. in 6 mos. stump in excellent condition* until mid-October 1938, then low back pain; lung metastases seen November 1938; wt. loss, disease progressed rapidly after x-ray to lungs; death March 30, 1939, 2 yrs. after onset
13. Higinbotham (123)	M. 15 (S.V.)	osteogenic sarcoma lt. proximal humerus; onset pain December 24, 1939, while playing basket ball (tumor present at that time)	aspiration biopsy January 17, 1940	January 18, 1940; x-ray (4200 r); February 15, 1940, shoulder joint disarticulation; P.D. XIII 8 days after surgery, 12 in 16 days (5 i.m., 7 i.v.) reactions 102° - 106.8° F. from 3 i.v.	concurrent strep. throat (103.6° F.) cervical adenitis, febrile 2 wks., also febrile after surgery (103°-105° F.) atelectasis	stump in excellent condition, symptom-free; metastases to rt. lung September 1940, to. lt. ischium a mo. later; failed rapidly, death February 7, 1941, 14 mos. after onset

14. B.L. Coley (123)	M. 8 (H.H.)	osteogenic sarcoma rt. proximal humerus, pathologic fracture; onset mid-December 1940	aspiration biopsy January 20, 1941	x-ray 5200r in a month, also P^{32} 4 injections ending February 11, 1941; P.D. XIII, February 9, 1941; 6 i.m. in 18 days, 3 reactions - 104°-104.8° F., others 101°-101.4° F.; disarticulation March 27, 1941; September 8, 1942 P.D. XIII, 12 in 13 days, 6 i.m., 6 i.v. (100.2-103° F.); x-ray to pelvis, November 1942	varicella January 1941, prior to x-ray	good regression, gained 9-10 lbs. in 15 days, remarkable change in bone, much calcification & regeneration, general condition excellent ; lt. lung metastasis seen September 9, 1941. though symptom-free; continued to gain wt., only symptoms occasional pallor, nervousness; metastasis to rt. ischium October 1941; pain in this area ceased after x-ray; then multiple metastases to bones & lungs, death, March 7, 1943, 2¼ yrs. after onset
15. W.B. Coley (43, #95 in Table 7; 52; 123)	M. 40 (B.F.S.)	cellular osteochondrosarcoma lt. proximal humerus metastases to lungs; onset November 1916	explored, curetted February 7, 1917; toxins, Tracy XI, February 9, 1917; 12 i.m. in 15 days, 7 prior to radium (5472 r) interscapulothoracic amputation, February 28, 1917	wound irrigated with Dakin's solution; 11 more toxin injections i.m. in 28 days; x-ray to lt. shoulder, rt. neck, mediastinum	wound infection, purulent discharge, after amputation	wound healed in 2 wks.; gained 10 lbs., general health good; lung metastases remained unchanged for 3½ mos.; June 1917, recurrence in scar, lung lesions very extensive; death August 15, 1917, 9 mos. after onset

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Physician (References)	Sex Age (Initials)	Diagnosis Extent of Disease	Treatment Prior to Infection	Concurrent or Subsequent Therapy	Type of Infection or Fever	Immediate & Final Result Period of Survival
16. Craver (10, #809; 123)	F. 14 (R.W.)	extensive recurrent inoperable osteogenic sarcoma (atypical) proximal rt. humerus, severe pain, wt. loss; pathological fracture; cachexia, lung metastases, anemia; onset May 1926, after heavy "cold", fell 4 wks. later	x-ray (3) no benefit; colloidal lead injection September 1926; 2 radium packs (10,000 mch.); 2nd lead injection October 14, 1926, caused marked softening, some regression; October 1926, x-ray (2); pain returned	further lead injections, December 6, 21, 1926, 3rd cycle x-ray January 1927; 5th, 6th lead injections February 23, 1927; May 1927 2 more x-ray; further x-ray January-March 1928, cast applied; shoulder joint amputation July 1928: huge hemorrhagic tumor (19 cm.); sequestrectomy, April 1929; x-ray, radium; toxins, P.D.XIII June 1929, over 3 yrs. after onset, 15 i.v., 5 i.m. in 33 days, slight febrile reactions 7th lead injection July 1929; more radium packs	November 23, 1926; lt. follicular tonsillitis (101.4° F.); low grade pyocyaneous infection in wound after amputation	after x-ray, radium & lead local condition improved, general condition declined (cachexia, anemia); pain returned after x-ray fall 1926 & lung metastases seen; *6 days after tonsillitis tumor again very soft, cystic, decreasing in size;* remarkable regression after further lead injections shortly thereafter; fracture healed, tumor regressed during 6 mos.' hospitalization; well summer, fall 1927; 2nd pathological fracture after slight fall, November 22, 1927, another fall January 1928; no improvement from further x-ray January & March 1928 causing endarteritis of vessels; metastases to lt. rib & lungs June 1929; no regression, but growth check temporarily 1929 after lead, toxins & radium; then slow increase in size, bedridden April 1930, death August 5, 1930; 4½ yrs. after onset

17. W.B. Coley (10, #998; 123)	F 60 (B.J.)	osteogenic sarcoma proximal rt. humerus, 14 lb. wt. loss in 6 mos.; (had had 13 children, 6 living); onset July 1928	January 1929 radium packs to humerus (70,000 mch) during toxins (P.D. XIII, 5 i.m. 21 i.v. (very small doses) i.t., no reactions	1 more small dose toxins after tonsillitis caused cyanosis, dyspnea, severe pain in back, legs	March 16, 1929 tonsillitis, fever 101° F., rt. cervical lymphadenopathy	shoulder mass softer, almost cystic by April 1929, symptom-free 2½ mos. then asymptomatic tumor seen in x-rays of lt. distal *femur*; pathologic fracture getting into taxi May 1929; disease progressed death September 28, 1929, 14 mos. after onset
18. W.B. Coley (10, case 88 in Table 7; 52; 123)	M 50 (G.M.)	inoperable recurrent fibrosarcoma proximal rt. humerus involving joint and scapula; onset pain Spring 1910, swelling 16 mos. later;	February 1912; curettage, cavity packed by Guthrie	Tracy XI May 12, 1912; 15 in 19 days in pectoral muscles; (102.6° F. from 1st dose only; 2nd course 6 wks. later i.m. every 48 hrs. for 4 wks.	seropurulent discharge from wound; febrile for 3 wks June 1912, (105.2° F.) due to wound infection & toxemia from absorption of necrotic tumor tissue, profuse discharge	gelatinous tapioca-like discharge from sinus; disease ruptured into rt. lung; extreme emaciation, death; October 12, 1912, 2½ yrs. after onset
19. B.L. Coley (10, #1445; 123)	F 5 (M.D.S.)	atypical osteogenic sarcoma proximal lt. tibia; onset early December 1931	February 1932 explored	amputation April 6, 1932; 4 mos. after onset P.D. XIII 8 days later: 14 i.m. in 22 days (102.4°-103° F.)	low grade wound infection, after exploratory operation	in good condition for some wks. then recurrence on stump; bedridden by August 1932; generalized metastases; death October 16, 1932, 10 mos. after onset
20. B.L. Coley (123)	M 13 (S.D.)	highly malignant osteochondrosarcoma rt. proximal tibia, onset early August 1937	exploratory incision, intractable hemorrhage, hasty biopsy, packed with gauze elsewhere	amputation November 4, 1937, transfusion; P.D.XIII 11 days later; 15 in 16 days (10. i.m., 3 reactions to 104° F., 5 i.v. 3 to 104°-105° F)	wound badly infected after biopsy, fever 99°-102° F.; Dakinization; purulent discharge from stump after amputation	gained weight, well 8 mos., then multiple lung metastases; hemoptysis shortly before death, July 1938, 11 mos. after onset

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Physician (References)	Sex Age (Initials)	Diagnosis Extent of Disease	Treatment Prior to Infection	Concurrent or Subsequent Therapy	Type of Infection or Fever	Immediate & Final Result Period of Survival
21. B.L. Coley (123)	F. 57 (H.B.)	osteogenic fibrosarcoma rt. proximal humerus 11 × 7 × 6 cm. with pathologic fracture and diffuse swelling whole upper arm; onset September 1949	novocaine injections; osteopathy; x-ray; incisional biopsy; interscapulothoracic amputation, December 1, 1949, 6 wks. after onset	none	febrile several days after surgery, (to 103° F.), also disoriented, pulse irregular for 16 days; no infection found; 15th day small stitch abscess evacuated; warm compresses	in excellent health 2½ yrs., then rt. lower chest pain; death June 11, 1952, over 2½ yrs. after onset, apparently due to lung and liver metastases
22. B.L. Coley (123)	F. 18 (E.M.)	recurrent fungating osteogenic sarcoma rt. tibia, developing in giant cell tumor, with metastases in lt. lung; onset about August 20, 1927	curettage (profuse hemorrhage); transfusion; fungating recurrence curetted again, uncontrolled hemorrhage; referred to Memorial Hospital March 1928; radium packs (30,000 mch) x-ray; very marked rapid fungation; 2 biopsies	zinc chloride paste: amputation May 20, 1928	wound infection after curettage; tumor area again infected after biopsies April 1928, fever 99°-103° F. during May 1928, 103.6° F. after amputation	*tumor diminished in size, disappeared on surface May 1928 during infection;* gained weight looked better after amputation, but lung metastases increased rapidly, death August 18, 1928, 12 mos. after onset
23. Memorial Hospital (123)	M. 17 (J.G.)	osteogenic sarcoma distal lt. tibia; onset June 1948	aspiration biopsy; amputation August 23, 1948, 2 mos. after onset	incision of furuncle, drained for 1 wk.	furuncle on stump September 10, 1949, 11 mos. after surgery; bronchitis for 6 wks. January 1950; west Nile virus inoculations February 10, 1950; infection not produced but fever (103° F.); final inoculation July 1950	lung metastases seen February 1950; death day after 2nd inoculation West Nile virus July 18, 1950, 37 mos. after onset

24. B.L. Coley (10 #694; 123)	M. 25 (J.H.L.)	recurrent telangiectatic osteogenic sarcoma proximal rt. fibula, pathologic fracture, 6 lb. wt. loss; onset early November 1933; 2 severe injuries to rt. leg 2 yrs. & 2 mos. before; November 1937 metastasis to lt. femur	aspiration biopsy, radium December 23, 1933 to January 3, 1934 (80,000 mch); mid-April 1934 another cycle (81,000 mch); amputation, August 9, 1934, 9 mos. after onset: toxins, P.D.XIII 7 days later 21 in 46 days: 12 i.m. (5 reactions 103° - 105° F.), 9 i.v.; (averaged 101.5° - 102.5° F.); January 1936 x-ray to lt. femur (2000r); April-May 1936 2nd cycle (3000r) to lt. thigh; 3rd cycle to lt. femur February-March 1937, (2400r); bilateral thoracic cordotomy May 1937, alcohol injections	none	October 1936 infected finger, burn on lt. elbow, lymphadenopathy of elbow, axilla	pain relief; marked regression after radium, symptom-free several wks., then reactivation; stump, general condition excellent after amputation, gained 7 lbs.; prosthesis, November 1934; well a year; November 1935 metastasis to lt. femur; pain relief after x-ray; November 1936, asymptomatic metastasis in lt. hilum; general condition remained excellent; April 1937, severe pain in rt. hip due to metastasis to rt. pelvis, not controlled by cordotomy death September 8, 1937, almost 4 yrs. after onset
25. W.B. Coley (24; 25; 26, 37)	M. 23 (B.M.)	extensive inoperable osteochondrosarcoma involving entire rt. ½ of ilium, fell 4 stories 10 yrs. before; fell striking rt. buttock 3 yrs. prior to onset; growth size of child's head by February 1894 extending from mid-sacrum posteriorly to edge of rectus muscle anteriorly, filling much of rt. iliac fossa; rapid loss of wt., emaciated	Buxton V (filtrates) March 1894: 19 in 28 days, i.m. & some i.t., marked reactions	December 1894 portion of ilium removed from site of former growth: no evidence of sarcoma (this reactivated the disease); injections then resumed	high fever for 1 mo. after toxins were stopped, (absorption of necrotic tumor?); condition critical	growth very rapidly broke down, great masses sloughed out, condition critical for weeks, then *steady improvement regained strength, gained 40 lbs. very rapidly; complete regression* by October 24, 1894; recurrence shortly after exploratory surgery December 1894; did not respond to further therapy, death July 1896, about 3 yrs. after onset

TABLE 4: OSTEOGENIC SARCOMA FAILURES WITH CONCURRENT INFECTION, INFLAMMATION OR FEVER: (con'd)

Physician (References)	Sex Age (Initials)	Diagnosis Extent of Disease	Treatment Prior to Infection	Concurrent or Subsequent Therapy	Type of Infection or Fever	Immediate & Final Result Period of Survival
26. Bissell & Coley (12; 16; 52; 123)	M. 37 (C.V.)	enormous inoperable chondrosarcoma lt. ilium (31 x 39 cm.); onset 1 mo. after falling into manhole striking lt. hip on iron cable	January 5, 1914: 1 dose Coley toxins (Tracy XI i.m. in rt. buttock	2nd dose toxins 5 days later, 3 more i.t., incision furuncles, poultices; necrotic, purulent material evacuated from tumor; several incisions in tumor February 5, 1914: drainage tubes, irrigated; March-April 1914, radium (4); October 1914 final radium caused burn; recurrence partially removed February 1915; thick brownish material drained, 7 more toxin injections i.m. in 9 days (1 marked reaction)	January 6, 1914: furuncle on posterior neck; suppurated several days; pain, tenderness entire leg; tumor area infected (staph.) profuse discharge, sinus 4 cm. in diameter; febrile 1 mo. to February 20, 1914 (101° to 105.5° F.)	tumor definitely smaller by February 17, 1914 much weight lost during infection, began to regain it by late February: felt stronger; *tumor completely regressed in 2 mos., weight, strength normal resumed work as lineman;* October 1914, small local recurrence; increased to 8 x 10 cm. in 4 mos., disease progressed slowly, 1915-1916; death February 25, 1917, over 4 yrs. after onset

27. W.B. Coley (88; 123)	M. 46 (J.H.S.)	inoperable chondrosarcoma rt. ilium sacrum, pelvis; onset August 1926 shortly after fall, straining hip joint increasingly severe pain, foot drop, walked with crutches, lung metastases by February 1929, incontinent March 1929	osteopathy for 2 mos. early 1927, Glover's serum, mistletoe injections, slow regression April-September 1927, general condition improved; October 1927, x-ray (4) P.D. XIII October 18, 1927: 10 i.m. in 21 days, 93 in 18 mos. in courses of 4 to 17, all i.m. except 1 i.v. & 6 i.t. moderate reactions except twice (103° F.); November 1927 radium packs (42,000 mch); January 1928 physiotherapy; late June 1928, radium packs (12000 mch) November 1928 radium packs (17,208 mch), January 3, 1929 radium	May 5, 1929 evacuation of pint of necrotic tumor with large trochar	2nd degree burns from hot water bottles, December 6, 1927; healed in 16 days; late April 1929: strep. viridans septicemia, also E. coli infection in tumor area, febrile (to 106.8° F. May 1); remained febrile during May (100° -102.6° F. average, maximum 103.4° F; during June 99°-101° F.; July 10, 1929, to 104.6° ; next 3 wks. to 101.8° F.) infection, anemia increased August 1929, infection continued, (proved fatal)	decrease in pain, marked regression of tumor by February 21, 1928, general condition excellent; April 1928, 5 days after resuming toxins, further regression noted; June-July 1928, further marked improvement after further toxins & radium; growth then reactivated, pressing on rectum, bladder; symptoms improved after 4 toxin injections, 2 radium packs; disease in ilium stationary November 1928 to late February 1929; lung metastases then seen; bladder, rectal incontinence; March 1929 tumor softened at site of i.t. injections; May 1929 *during infection large recurrent growth broke down, became fluctuant; May 1929 after evacuation of necrotic tissue, nausea ceased, ate well, by August 1929 growth smaller, sinuses still discharging necrotic tumor*; death October 1929, due to infection, 38 mos. after onset

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March 26, 1921 Parke-Davis XIII

DIAGNOSIS: Osteogenic sarcoma of the distal right femur, confirmed by microscopic examination at the Bone Sarcoma Registry by Lent C. Johnson, M.D. (Case #53.) Also cited by Kolodny.

PREVIOUS HISTORY: W.L.C. male, aged 12 1/2. The family history was then negative for cancer except for his paternal grandmother who had gastric cancer. Later a sister died of bladder carcinoma at age 77. In the summer of 1920, the patient was in bed eight weeks with a low grade fever of unknown cause following an attack of scarlet fever which left him in bad physical and mental condition for the next six months. In mid-February 1921 he bumped his right lower thigh against a table causing a severe bruise, and "immediate swelling and dislocation." Dr. Charles Ford thought at first that this was due to a hematoma. He treated it with hot packs for two weeks. X-ray examination on March 10, 1921 revealed some reactive periostitis. Six days later further x-rays showed marked increase in new bone formation. Immediate amputation was advised but the boy's father felt that any treatment was preferable.

RADIATION: Beginning March 20, 1921 x-ray therapy (150 k.v.) was given for a month. No details are given as to dosage. It was given by Dr. Harold Thompson of Seattle.

TOXIN THERAPY: (ParkeDavis XIII) On March 26, 1921, six days after the first x-ray treatment, injections were begun by Ford, the family physician and were given for about six weeks causing chills and marked febrile reactions.

FURTHER RADIATION THERAPY: Radium needles were inserted into the tumor weekly for 24 - 30 hours between May 5 and July 11, totalling 12,600 mch. It was given by the same radiologist.

CLINICAL COURSE: During these treatments the tumor increased steadily in size and density until by August 17, 1921, it was 24 x 12 cm. in diameter, causing extreme pain. The general condition deteriorated markedly.

SURGERY: Amputation was therefore performed on September 9, 1921 in order to save the child's life. This was almost seven months after onset. Post-operative chest films were negative for metastases.

CLINICAL COURSE: The child recovered very rapidly and gained 10 pounds in 10 days while in the hospital. As the surgery had left 8 cm. of the femur he was able to use a prosthesis. He returned to school in January having missed a year. He remained in very good health thereafter, and was accepted for life insurance at 19. While attending Rush Medical School in Chicago in 1933 he visited the Bone Sarcoma Registry and "was honored as the only patient ever to show up." He interned in Chicago and also in Seattle, Washington and at his State Board examination there in 1935 he was presented with his own leg to diagnose as a gross specimen. The pathologist apologized saying, "Gee,

Bill, I didn't know you'd be here." He did general practice in Grey's Harbor, Washington until 1952. Then, having delivered 1,000 babies, felt he couldn't physically continue so he went to the University of Colorado for three years of radiology and continued as a radiologist until his retirement in 1981 at the age of 70. He married in 1934 and in spite of the radiation therapy he'd received he had one daughter born in 1938, with a slightly cleft lip. In 1979 he became somewhat depressed and his weight declined about 10 pounds. His wife died of a brain tumor in 1983 and he then entered a retirement community in Seattle. This place did wonders for him. He has remained in excellent health, able to take part in many activities, i.e. ride a tricycle, play the cello, paint, sing in the chorus, etc. His only complaint was low backache. "It's just tired of carrying my 6 feet 2 inches on a prosthesis for 65 years." He attributed his survival to the immunotherapy he received prior to surgery. "Metastases must be prevented by the body as happened in my case." He remarried July 25, 1989 and remained in very good health when last traced in April 1993, 72 years after onset.

REFERENCES: 1) Bone Sarcoma Registry Case #53. 2) Cancer Research Institute Records: Letters from the patient and the Bone Sarcoma Registry.

COMMENT: This case is another example of the deleterious effects of prior radiation in osteogenic sarcoma. The possible role of scarlet fever the previous summer is difficult to evaluate. Chronic infections are usually immunosuppressive and this episode left him in poor physical and mental condition. The Coley Toxins were begun six days after the first x-ray treatment and injections were given for six weeks combined with radium meedles inserted into the tumor. During radiation the tumor increased rapidly to 12 x 24 cm. and the general condition deteriorated markedly. However, the toxin therapy probably stimulated an immune reaction sufficient to prevent metastases. Amputation did not occur until 7 months after onset.

Prolonged Survival of Osteogenic Sarcomas Treated by Coley Toxins (Streptococcus pyogenes and Serratia marcescens)

Case #	Age at Death or last Follow Up	Period of Survival From Onset
Case 1	Died at 71, breast cancer	58 years
Case 2	" " 78, coronary	38 "
Case 3	" " 50, coronary	31 "
Case 4	Alive & well at 84	68 "
Case 5	Died at 73, coronary	36 "
Case 6	" " 73, heart attack	9½ "
Case 8	Died at 80, cancer of pancreas	63 "
Case 9	" " " " 64	58 "
Case 10a	" " " " 85	72 "
Case 11	Died at 78, heart attack	56 "
Case 13	" " 42, ulcerative colitis	28 "
Case 15	" " 68, cerebral hemorrhage	20 "
Case 16	Alive & well " 68	57 "
Case 17	Died at 42, cerebral thrombosis	28 "
Case 19	" " 87, after fractured hip	31 "
Case 20	" " 68, C.M. Leukemia	34 "
Case 21	" " 41, coronary	18 "
Case 24	" " 67, heart failure	50½ "
Case 31	" " 62, colon cancer	24 "
Case 33	" " 77, fell	31½ "
Case 34	" " 81, Parkinson's disease	62 "
Case 35	" " 66, coronary	50 "
Case 36	" " 54, coronary	28 "
Case 37	" " 55, heart attack	40 "
Case 38	" " 73, heart disease	23 "
Case 40	" " 91 heart failure; g.m.l.	57 "
Case 41	" " 86, cause unknown	58 "
Case 43	" " 58, lymphoma	43 "
Case 45	" " 25, suicide, depression	11 "

Note: Cases 1, 4, 16 and 24 later developed breast cancer.
Case 10a is not included in Figures 9, 10 and 11 as we had not heard of it in 1975. Case 8 developed pancreatic cancer.

Alive When Lost to Follow Up

Case 10	Alive at 42	17 years.
Case 14	" " 34	8 "
Case 17	" " 68	4 "
Case 32	" " 60	16 "
Case 39	" " 50	15 "
Case 42	" " 26	10 "
Case 44	" " 79	46 "