THE REGISTRY OF BONE SARCOMA A HISTORY

Edward F. McCarthy, M.D.

There have been many national cooperative efforts led by panels of physicians, usually pathologists, to formulate nomenclature of particular diseases. Most of these efforts have dealt with neoplastic diseases, and their goal has been to correlate specific histologic features with a name and a prognosis. Examples of such panels are The Early Malignant Melanoma Panel, the Wilm's Tumor Study Group, and the Non-Hodgkin's Lymphoma Pathologic Study Group. These cooperative efforts to formulate nomenclature have their origin in the vision of one energetic surgeon, Ernest Codman, who, in 1921, established the Registry of Bone Sarcoma. Working under the auspices of the American College of Surgeons, Codman's goals were to record living patients with bone sarcoma, to revise inadequate existing nomenclature, and to learn the behavior of these neoplasms. The project lasted many years and was a great success. Not only did the Registry accomplish Codman's three goals, it achieved other further reaching effects. As the first national prospective study, it provided a model for studies of other diseases. Also, because many hospitals contributed to the Registry, it helped spearhead the movement toward hospital standardization. Finally, because the Registry depended on the working together of surgeons, pathologists, and radiologists, cooperative practice became fundamental to the treatment of bone diseases.

Ernest Codman (1869-1940) was a Boston surgeon with a special interest in bones (Figure 1). By 1897, only a year after Roentgen had discovered x-rays, Codman was emphasizing the importance of this tool in the clinical management of patients with bone disease[13]. In 1909 he had described the triangle of reactive periosteal bone adjacent to bone tumors that bears his name[2]. Codman was also a founding member of the American College of Surgeons, formed in Chicago in 1913[12].

In 1920 Codman had a patient with what he thought was a bone sarcoma. The family of this patient gave Codman a $1,000 gift to find out if any patients survived a bone sarcoma and, if so, what treatment they had. The treatments available at that time were amputation, x-rays, radium, and Coley's toxin. Coley's toxin, used from the early 1890s until World War II, was a sterilized suspension of streptococci cultures which, when inoculated into patients, was believed to enhance their resistance to neoplasms.

Figure 1. Ernest Codman (1869-1940). Courtesy of the National Library of Medicine.

Codman began his $1,000 study by writing a letter to every member of the American College of Surgeons, then about 4,000. The letter began as follows:

> Dear Doctor: Have you any living cases of bone sarcoma? I include in this question, recent cases which are now under treatment and also any cases which you may consider as having recovered[3].

The response was a surprise. One hundred and seventy one members responded immediately and wrote descriptions of patients they believed to have bone sarcoma. In

Correspondence to: Edward F. McCarthy, M.D.
Dept. of Orthopaedic Surgery
The Johns Hopkins Hospital
600 N. Wolfe St. Room 306
Baltimore, MD 21287
Telephone: (410) 614-3653
FAX: (410) 614-3766

Figure 2. James Ewing (1866-1943). Courtesy of the National Library of Medicine.

Figure 3. Joseph Bloodgood (1867-1935). Courtesy of the National Library of Medicine.

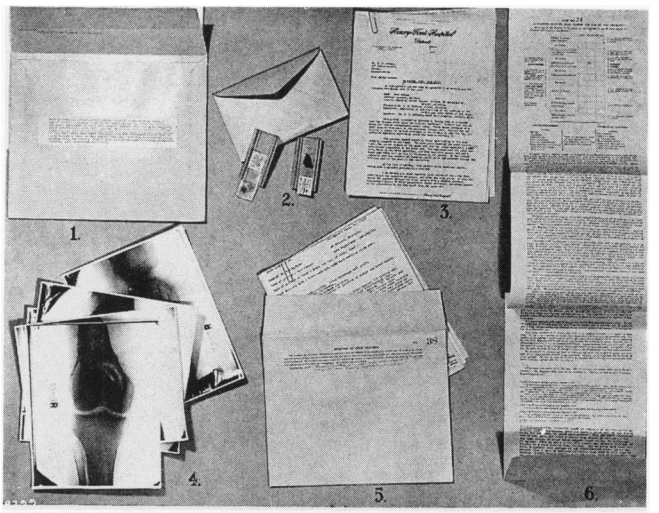
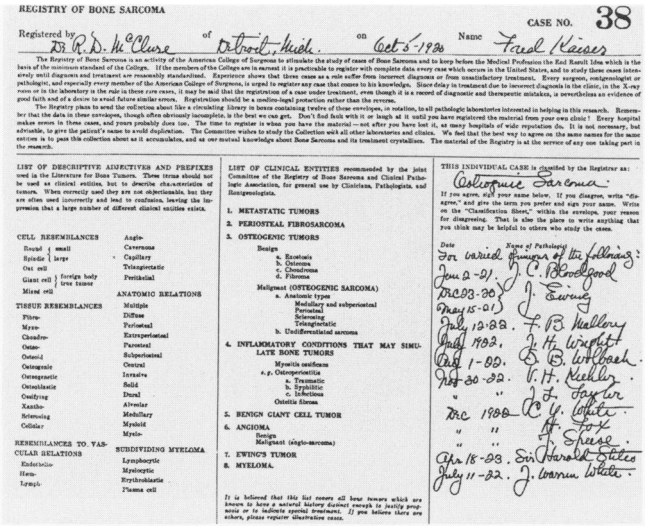


Figure 4. The various materials of one case. Reprinted with permission of Surgery, Gynecology & Obstetrics, now known as the Journal of the American College of Surgeons.

addition, 345 members also wrote to show their support of the study and suggested that such studies be made of other surgical diseases.

Because of this enthusiastic response, Codman was able to persuade the Regents of the American College of Surgeons to establish the Registry of Bone Sarcoma on June 7, 1921. Fifteen hundred dollars was appropriated by the College to continue the work[7]. Codman invited two other experts in bone diseases, James Ewing and Joseph Bloodgood, to work with him. James Ewing (1866-1943) was a pathologist in New York, at that time working at Cornell University (Figure 2). He had already published his book, *Neoplastic Diseases*[8], and he had just described the entity, diffuse endothelioma of bone, a malignant tumor which immediately (to his great protests) bore his name[9]. Joseph Bloodgood (1867-1935), a surgeon and director of surgical pathology at Johns Hopkins in Baltimore, also had an interest in bone tumors. (Figure 3). He had already published his observation based on his own cases and those he culled from the literature, that "giant cell sarcoma" behaved as a benign tumor[1]. Thus, the three physicians in charge of the Registry of Bone Sarcoma, were the country's most respected experts on bone tumors.

Codman continued to solicit cases of bone sarcoma from the members of the College. Only living patients could be registered. Surgeons sent the clinical history, details of the physical examination, radiographs, and histologic material (preferably wet tissue) to the Registry's headquarters at 227 Beacon St. in Boston[4]. The diagnosis and method of treatment was also submitted. The Registry sought yearly follow-up on each case and thus became the first national prospective study.



REGISTRY OF BONE SARCOMA

CASE NO. 38

Registered by Dr. R. D. McClure of Detroit, Mich. on Oct 5-1926 Name Fred Kaiser

The Registry of Bone Sarcoma is an activity of the American College of Surgeons to stimulate the study of cases of Bone Sarcoma and to keep before the Medical Profession the End Result Idea which is the basis of the minimum standard of the College. If the members of the College are in earnest it is practicable to register with complete data every case which occurs in the United States, and to study these cases intensively until diagnosis and treatment are reasonably standardized. Experience shows that these cases as a rule suffer from incorrect diagnosis or from unsatisfactory treatment. Every surgeon, roentgenologist or pathologist, and especially every member of the American College of Surgeons, is urged to register any case that comes to his knowledge. Since delay in treatment due to incorrect diagnosis is the clinic, in the X-ray room or in the laboratory is the rule in these rare cases, it may be said that the registration of a case under treatment, even though it is a record of diagnostic and therapeutic mistakes, is nevertheless an evidence of good faith and of a desire to avoid future similar errors. Registration should be a medico-legal protection rather than the reverse.

The Registry plans to send the collection about like a circulating library in boxes containing twelve of these envelopes, in rotation, to all pathologic laboratories interested in helping in this research. Remember that the data in these envelopes, though often obviously incomplete, is the best we can get. Don't find fault with it or laugh at it until you have registered the material from your own clinic! Every hospital makes errors in these cases, and years probably does too. The time to register is when you have the material—not after you have lost it, as many hospitals of wide reputation do. It is not necessary, but advisable, to give the patient's name to avoid duplication. The Committee wishes to study the Collection with all other laboratories and clinics. We feel that the best way to agree on the same names for the same entities is to pass this collection about as it accumulates, and as our mutual knowledge about Bone Sarcoma and its treatment crystallizes. The material of the Registry is at the service of any one taking part in the research.

LIST OF DESCRIPTIVE ADJECTIVES AND PREFIXES used in the Literature for Bone Tumors. These terms should not be used as clinical entities, but to describe characteristics of tumors. When correctly used they are not objectionable, but they are often used incorrectly and lead to confusion, leaving the impression that a large number of different clinical entities exists.

CELL RESEMBLANCES
Round { small / Spindle { large / Oat cell / Giant cell { foreign body / true tissue / Mixed cell
Angio-
Cavernous
Capillary
Telangiectatic
Pericanalicular

TISSUE RESEMBLANCES
Fibro-
Myxo-
Chondro-
Osteo-
Osteoid
Osteogenic
Osteogenetic
Osteoblastic
Ossifying
Xantho-
Reticuling
Cellular

ANATOMIC RELATIONS
Multiple
Diffuse
Periosteal
Extraperiosteal
Parosteal
Subperiosteal
Central
Invasive
Solid
Dural
Alveolar
Medullary
Myeloid
Myelo-

RESEMBLANCES TO VASCULAR RELATIONS
Endothelio-
Hemo-
Lymph-

SUBDIVIDING MYELOMA
Lymphocytic
Myelocytic
Erythroblastic
Plasma cell

LIST OF CLINICAL ENTITIES recommended by the joint Committee of the Registry of Bone Sarcoma and Clinical Pathologic Association, for general use by Clinicians, Pathologists, and Roentgenologists.

1. METASTATIC TUMORS
2. PERIOSTEAL FIBROSARCOMA
3. OSTEOGENIC TUMORS
   Benign
   a. Exostosis
   b. Osteoma
   c. Chondroma
   d. Fibroma
   Malignant (OSTEOGENIC SARCOMA)
   a. Anatomic types
      Medullary and subperiosteal
      Periosteal
      Telangiectatic
   b. Undifferentiated sarcoma
4. INFLAMMATORY CONDITIONS THAT MAY SIMULATE BONE TUMORS
   Myositis ossificans
   e.g. Osteoperiostitis
   a. Traumatic
   b. Syphilitic
   c. Infectious
   Osteitis fibrosa
5. BENIGN GIANT CELL TUMOR
6. ANGIOMA
   Benign
   Malignant (angio-sarcoma)
7. EWING'S TUMOR
8. MYELOMA.

It is believed that this list covers all bone tumors which are known to have a natural history distinct enough to justify prognosis or to indicate special treatment. If you believe there are others, please register illustrative cases.

THIS INDIVIDUAL CASE is classified by the Registrar as: Osteogenic Sarcoma.

If you agree, sign your name below. If you disagree, write "disagree," and give the term you prefer and sign your name. Write on the "Classification Sheet," within the envelope, your reason for disagreeing. That is also the place to write anything that you think may be helpful to others who study the cases.

Date — Name of Pathologist
For varied tumors of the following:
Jan 2-01. J. C. Bloodgood
Dec 03-30 J. Ewing
May 15-01 J. Ewing
July 12-22. F. B. Mallory
July 1902. J. H. Wright
Feb 1-00. H. B. Wolbach
Jan 30-22. V. H. Kelley
" " F. Taylor
Dec 1900 W. G. Lobitz
" " A. Fox
" " J. Speese
Apr 18-03. Sir Harold Stiles
July 11-22. J. Warren White

Figure 5. The face of the envelope used to package one case. Reprinted with permission of Surgery, Gynecology & Obstetrics, now known as the Journal of the American College of Surgeons.

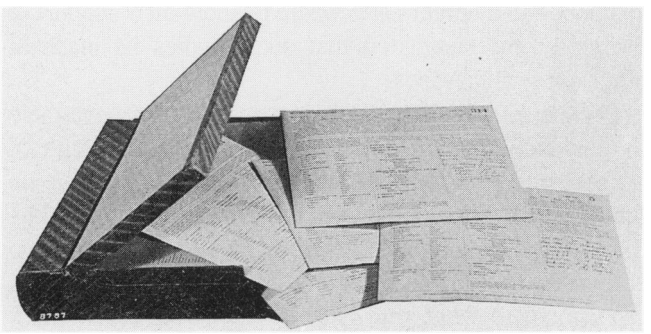
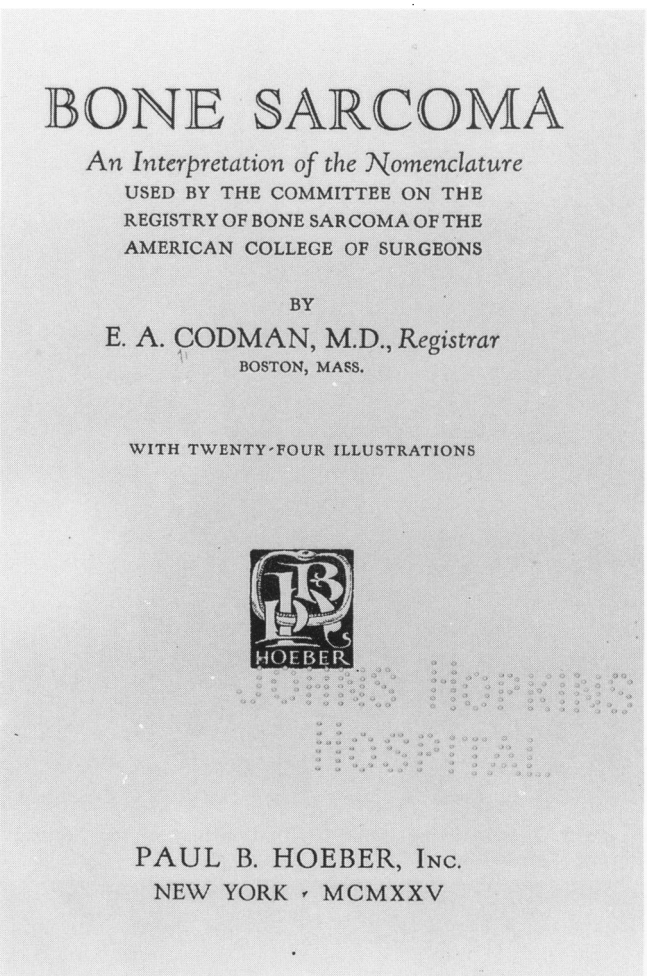


Figure 6. The box used to circulate groups of cases to consultants. Reprinted with permission of Surgery, Gynecology & Obstetrics, now known as the Journal of the American College of Surgeons.



BONE SARCOMA

An Interpretation of the Nomenclature

USED BY THE COMMITTEE ON THE REGISTRY OF BONE SARCOMA OF THE AMERICAN COLLEGE OF SURGEONS

BY

E. A. CODMAN, M.D., *Registrar*

BOSTON, MASS.

WITH TWENTY-FOUR ILLUSTRATIONS

HOEBER

PAUL B. HOEBER, INC.

NEW YORK · MCMXXV

Figure 7. Frontpiece of the Registry's monograph which explained the classification. Courtesy of the Johns Hopkins Institute of the History of Medicine.

Upon receipt, the Registry filed all the submitted material (Figure 4) in a numbered envelope. Data about the case was entered on the face of the envelope (Figure 5). Groups of cases were placed in boxes (Figure 6) to be circulated to other renowned pathologists like Mallory, Wright, or Wolbach, whom the Registry had enlisted to provide their opinion. Each case was then labeled with the consensus diagnosis.

By 1925, the Registry had collected the clinical history, radiographs, and histologic material on 560 cases. The results of the analysis of these cases were published that year by Codman in a small monograph (Figure 7). This monograph represents the first attempt to standardize and disseminate the nomenclature of a particular disease[5].

Earlier primitive attempts to classify tumors (including bone tumors) had generally been based on gross characteristics. However, in 1879, Samuel Gross published the first systematic study of 165 cases of bone sarcoma which included a histologic analysis[10]. Gross' classification, which influenced pathologists for many years, was based on two parameters. One was location of the tumor - whether the tumor was central or periosteal. The other was cell type — giant cell, spindle cell, or round cell. For example, in his classification there was a central round cell sarcoma and a periosteal spindle cell sarcoma. Other classification systems were based on the type of neoplastic tissue that predominated: fibro, myxo, chondro, or osteo. Thus, a sarcoma might be called a fibromyxosarcoma and another called a chondro-osteosarcoma.

Codman felt that these methods of classifying sarcomas were like classifying dogs according to the color of their spots. Moreover, observers rarely agreed on the classification of any sarcoma using these systems. Using the cases submitted to the Registry, Codman proposed a classification based on combined clinical, radiographic, and histologic features. Cases fell into only eight groups. The first six represented the primary bone tumors:

Periosteal fibrosarcoma
Benign and malignant osteogenic tumors

Giant cell tumor
Angioma
Ewing's tumor
Myeloma (what today are lymphomas and plasma cell myelomas)

The seventh and eighth groups were metastatic carcinoma and non-neoplastic disorders such as osteiitis fibrosa, myositis ossificans, and bone cysts. Interestingly, this system did not include chondrosarcoma. It was not until 1930 that Dallas Phemister suggested that this malignant tumor might be a distinct entity[14].

Today, we recognize at least twenty specific types of bone tumors. Some of these have many well-defined subtypes. However, the six categories of bone tumors proposed by the Registry would be the nucleus of all future classifications.

The Registry made an important observation very early —that many lesions submitted as bone sarcomas were, in fact, not primary malignant tumors of bone. Of the 560 cases collected by 1925, about one half were either metastatic carcinomas or non-neoplastic bone diseases. Fortunately, Codman had urged surgeons to submit cases even if they feared their diagnosis might be proved wrong. By means of publications and presentations, the Registry sought to raise the awareness that it was easy to misdiagnose a bone tumor. In 1926, Codman published a paper in which he defined 25 clinical, radiographic, and histologic features of osteogenic sarcoma[6]. It was the first effort by any physician to rigorously define a disease entity in order to avoid misdiagnosis.

By 1926, the Registry had also confirmed the suspicion that the prognosis for bone sarcoma was very poor. Of the approximately 250 cases which the members of the Registry agreed were bone sarcomas, only 17 (4 Ewing's tumors and 13 osteogenic sarcomas) were alive long enough to be considered cured. All but one of these cases had been treated by amputation. Some had had additional x-ray, radium, or toxin treatment. The members of the Registry then made a diligent attempt to define the features of the sarcomas of the 17 surviving patients. Although this attempt was unsuccessful, the members did conclude that x-ray treatment held great promise.

Codman suspected correctly that the Registry might provide some epidemiologic data. Because he repeatedly petitioned all the members of the American College of Surgeons, he believed the Registry was following almost all the cases living at any moment in the United States. He originally estimated this number to be no more than 500, but as the Registry grew he revised this number to 1,000. He also was convinced that all the surgeons in Massachusetts were contributing all their cases, and knowing the population of the state, he could calculate the incidence of bone sarcoma to be 1/100,000.

In addition to increasing the knowledge about bone tumors, Codman's project resulted in several broader benefits for medical practice. The first of these was hospital standardization. That many hospitals were substandard was evidenced by the frequent diagnostic errors submitted to the Registry and the often poor quality of the histologic slides, radiographs, and clinical histories. Codman believed that by participating in the bone sarcoma study, hospitals would be forced to improve—to produce only good quality radiographs and histologic specimens and to demand accurate and complete clinical histories. He even subtly hinted that a hospital's unwillingness to send cases to the Registry indicated inferior practices.

Codman was also interested in patient follow-up, another issue of hospital standardization. Many hospitals had inadequate follow-up systems. Codman had suggested mechanisms of patient follow-up to the American College of Surgeons as early as 1913[7]. He believed in the importance of the concept of "end-results" - that every hospital should follow a patient long enough to determine the final results of treatment. The "end result" concept was the foundation of the Registry of Bone Sarcoma. Codman believed that hospitals which submitted cases would have to be meticulous about patient follow-up.

In addition to hospital standardization, another lasting effect of the Registry was the model it provided for national clinical research. The Registry's success proved that, guided by a panel of experts, physicians across the nation could communicate and use their collective experience to benefit future patients. Patients with rare diseases would no longer be treated at the caprice of an individual surgeon who had never seen such a case before. Rather, each case would be backed by the collective experience of the entire medical world. Codman, Ewing, and Bloodgood also envisioned that the cases collected would be a library of information to be built on by future researchers.

The final effect of the Registry of Bone Sarcoma was to establish the principle fundamental to modern orthopedic practice - that bone diseases are not isolated radiologic or histologic entities. Instead, they are defined by a combination of clinical, radiographic, and histologic features. This was the principle of the Registry's classification system, and it demands close cooperation of surgeons, radiologists, and pathologists.

The Registry of Bone Sarcoma continued for many more years after the publication of its first classification system. By 1925, it had outgrown its facilities in Boston and was transferred to Chicago where, fully funded by the American College of Surgeons, Dallas Phemister was appointed to be its supervisor. In 1927, 700 cases were on file and were summarized by Anatole Kolodny of the University of Iowa[11]. The number of cases was so large by 1939 that Ewing requested that only unusual cases be

submitted. The collection was dormant during World War II, and in 1953 the entire collection, finally closed, was presented to the Armed Forces Institute of Pathology in Washington[15].

The patient whose family gave Ernest Codman $1,000 to start his project eventually died and was found to have metastatic carcinoma, not a bone sarcoma. But the gift has benefited bone tumor patients ever since.

BIBLIOGRAPHY

1. Bloodgood, J.C. The Conservative Treatment of Giant-Cell Sarcoma, with the Study of Bone Transplantation. Ann. Surg. ,56:210-39, 1912.
2. Codman, E.A. The Use of the X-Ray and Radium in Surgery. In W.W. Keen, Surgery, Its Principles and Practice by Various Authors. W.B. Saunders, Philadelphia. 5:1170, 1909.
3. Codman, E.A. The Registry of Cases of Bone Sarcoma. Surg. Gynecol. Obstet., 34:335-343, 1922.
4. Codman, E.A. The Method of Procedure of the Registry of Bone Sarcoma. Surg. Gynecol. Obstet., 38:712-721, 1924.
5. Codman, E.A. Bone Sarcoma: An Interpretation of the Nomenclature Used by the Committee on the Registry of Bone Sarcoma of the American College of Surgeons. Paul B. Hoeber, Inc., New York. 1925.
6. Codman, E.A. The Registry of Bone Sarcoma. Surg. Gynecol. Obstet., 42:381-893, 1926.
7. Davis, L. Fellowship of Surgeons. A History of the American College of Surgeons. American College of Surgeons, Chicago, 1988.
8. Ewing, J. Neoplastic Diseases. W.B. Saunders, Philadelphia, 1919.
9. Ewing, J. Diffuse Endothelioma of Bone. Proc. NY Path. Soc. 21:17-24, 1921.
10. Gross, S.W. Sarcoma of the Long Bones; Based on a Study of One Hundred and Sixty-Five Cases. Am. J. Med. Sci. 78:2-57, 338-77, 1879.
11. Kolodny, A. Bone Sarcoma: The Primary Malignant Tumors of Bone and the Giant Cell Tumor. Surgical Publishing Co., Chicago. 1927.
12. Obituary. Ernest Amory Codman. Trans. Am. Surg. Assoc. 59:611-613, 1941.
13. Peltier, L.F. Orthopedics, A History and Iconography. Norman Publishing, San Francisco, 1993.
14. Phemister, D. Chondrosarcoma of Bone. Surg Gynecol. Obstet. 50:216, 1930.
15. Stephenson, G.W. American College of Surgeons at 75. American College of Surgeons, Chicago. 1990.