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ACUTE HEMATOGENOUS OSTEOMYELITIS

SENIOR THESIS 1932

HOWARD I. FRISBIE
INTRODUCTION

Osteomyelitis defined is inflammation of the bone marrow or of the bone and marrow. It may be either acute or chronic. The acute form which is usually a septic condition is marked by fever, chills and pain, and is attended with suppuration of the medullary cavity. In its most common form it is a blood-born infection, which presupposes that a primary focus must exist.

This paper is not intended to be an extensive symposium on the subject, nor is any claim made for originality as to any of the ideas expressed. By a review of the history, and a correlation of the anatomical structures involved with the pathology of the disease, together with a statement as to the mortality and morbidity resulting from the condition, we hope to call attention to the existing mechanisms and the importance of the subject. An attempt is made to include all the most recent methods of treatment with the opinions of some of the best men as to the proper course to pursue.
Osteomyelitis does not seem to have been recognized in its entirety until, historically speaking, quite recently. The explanation of this probably lies in the fact that the abscesses finding their way to the surface obscured the deep pathology, and the cases were regarded simply as grave attacks of boils. Treatment at this time consisted of the application of fomentations, blisters, poultices, cupping, and ointments, together with the free use of antipyretics and sedatives. (1)

It was not until the middle of the 19th. century that the real significance of the disease began to be recognized, and not until after general acceptance of the work of Pasteur was there rationality in the treatment of the condition.

In spite of the comparative recentness of the recognition of osteomyelitis as a clinical entity, there is good evidence that it is one of the oldest of diseases. The earliest known diseases to which prehistoric man was exposed were probably those which affected and perhaps helped to exterminate the mesozoic reptiles and later fossil animals. Definite evidence of osteomyelitis is found in fossil reptiles in the topmost strata of the palaeozoic. The spine of the Heidelberg man, 7000 B.C., shows signs of Pott's disease.
Professor W. A. Freund of Berlin is said to be the possessor of a remarkable painting by Simon Vonet, which represents a case of suppurative osteomyelitis in a woman whose handsome appearance is in sharp contrast with her repulsive-looking limb. (II)

In the literature of the early part of the 19th century occasional mention may be found of cases which were undoubtedly osteomyelitis. As early as 1798, Dr. Nathan Smith (London), trephined a bone which was the seat of an acute osteomyelitis for drainage purposes. There is no evidence of the universal employment of bone drainage in the treatment, however, until many years later. (III)

In the "Medical and Surgical Reporter of Philadelphia" (1881), mention is made of two cases which were reported by Viany in a work edited by him in the latter part of the 17th century.

1. "A man thirty years of age received a severe blow on the front side of the tibia. At first it appeared to be only an ordinary contusion, but on the 7th day he was suddenly attacked by rigors that returned at frequent intervals. His skin became icteric and he died. An abscess was found post-mortem and collection of pus in the spongy tissue of the tibia."

Another case was that of a gunshot wound in the lower leg by which the bone was shattered.

2. "The bone could not be extracated and he died. The autopsy discovered suppuration in the condyles of the tibia and an abscess of the liver."

After this very remarkable description, the author con-
cludes, "it can collect in the bone cells where the matter can have no outlet at all." (IV)

Stanley (1855) describes the condition as an inflammation of the medullary canal of bones, which is likely to arise in some individuals from "neglect and causes most trivial. No disease is so severe in its consequences, none so fatal to life as suppurating inflammation extending through the canal of bones." Two cases were reported by him, both of which had a history of trauma and were drained superficially. In each instance at a later date the limbs were amputated and the medullary canal found to be filled with purulent material. (V)

M. Jules Houx, a French military surgeon, had under his care some 2000 soldiers who were wounded in the Italian campaign of 1859, and who presented conditions which he describes as demanding frequent amputation. Purulent material would be present constantly, and this, as he describes it, would burrow upward and into the bone. He made the observation that in those cases in which a disarticulation was done instead of an amputation that there was a decreased incidence of this complication. Because of this observation, he gave the advice that, in treating gunshot wounds where the bone was involved and amputation necessary, disarticulation be done at the most proximal joint. This does not seem to have received the support of the majority of surgeons of the time, but aroused much adverse criticism. (VI)
During the 6th., 7th., and 8th. decades of the 19th. century, the pathology began to be well understood, and there began to be among the medical profession an acceptance of osteomyelitis as a separate and definite clinical entity. The literature of this period is voluminous, with the Germans taking the lead in experimental and observational work. It cannot be said of osteomyelitis as in many diseases that our present knowledge is the result of the work and discoveries of one man. It is, rather, the observations and experiences of many. As this is not primarily a historical paper, only a few will be mentioned.

(VII)

Kocher in 1870 made some of the most important contributions to the diagnosis and treatment of the disease. In 1879, he published the results of some of his experimental studies and clinical observations. Three very beautiful colored plates are included in his article. One shows a humerus in longisection with the medullary cavity filled with greenish-yellow pus. The entire structure appears hemorrhagic and contains many areas of necrosis. A second plate shows a femur with an extensive involvement of the medullary cavity and rupture above the epiphyseal line. The third is a longisection through the knee joint showing destruction of the diaphysis of the femur and rupture into the knee joint. This is extensively necrosed. The surrounding soft tissue is filled with purulent material, which, on the anterior surface about two inches above
the patella, has evidently found its way to the surface and ruptured through. It is evident that a very adequate knowledge of the pathology of the condition was possessed by Kocher. Amputation was usually resorted to in the treatment if the process continued to extend after primary drainage of the superficial tissues. (VII)

At this time there was a general discrediting among the medical profession of the experiments of Pasteur, that is, as to their application to the diseases of mankind. Kocher's work received much quicker recognition, possibly because he was a doctor, but probably more because of the fact that he was working with diseases of mankind. There is no mention in Kocher's article of his acceptance of the bacterial theory of disease. He recognized, however, that the condition might at times be hematogenous. He was evidently an exponent of the ideas of Hilton (1807-1873), and Thomas (1834-1891), who advocated the control of inflammatory processes by methods designed to conserve body resistance. It is typical of medical history that we are again using a method advocated a century ago which, in the light of subsequent and more startling developments, had been lost sight of.

After the work of Pasteur, the bacterial theory began to be generally applied to osteomyelitis. In 1884, Rodet produced without the aid of trauma an osteomyelitis in rabbits by the injection of staphylococcus aureus intravenously. (III) Lexer in 1897, found that while a large
dose of living organisms given intra-venously to a young rabbit would cause death in twenty-four hours, a smaller dose would cause abscesses in the muscles, joints, and bones, with death resulting in a few days. He found it to be impossible to develop a condition simulating osteomyelitis in older animals. Like older people they were apt to develop an arthritis instead.

As the mechanism of the disease became more clearly understood, the treatment became less radical, and amputations less frequent. Earlier diagnoses were made and adequate drainage gradually became accepted as the general principle of treatment. However, the treatment of osteomyelitis has never been considered a closed subject, and we still find much controversy as to the best methods and principles to employ.

Bone is developed from mesenchyme. Either fibrous tissue or cartilage may be formed as an intermediary step. If from the former, it is known as intermembranous bone, and if from the latter, as intercartilaginous bone.

In the intermembranous development, when the inherent organic power of the organism stimulates the fibrous tissue to become differentiated into osseous tissue, certain cells known as osteoblasts deposit calcium salts in the fibrous tissue matrix. Later, the cells of the mesenchyme condense and form a stout membrane. This membrane becomes the peristeum. A layer of osteoblasts arrange themselves in a more or less definite manner between the peristeum and
developing bone. They then deposit a lamella of compact bone.

Thus we see that bone is a highly developed form of connective tissue. There are two distinct varieties, namely, compact and loose. Dense or compact bone is always found on the exterior part of bone tissue. It differs from spongy bone only in its degree of porosity. It forms the shafts of long bones and constitutes the outer portion of their extremities. (IX)

All bone possesses two membranes, the covering or periosteum and the lining or endosteum. The periosteum is a dense tissue which is firmly attached to the bone by trabeculae of fibrous tissue.

The Haversian or concentric lamellae are circular layers arranged around a central space or canal and known as a "Haversian Canal". The layers of each system are parallel to one another, but the layers of different systems cross at various angles. The canal contains blood vessels and nerves.

Osteoblasts are found in great number in the deep layers of periosteum and in the endosteum. They are irregular, flattened, stellato masses of protoplasm possessing a number of processes. These osteoblasts constitute the sole regenerative reserve of the periosteum.

Inside of the gradually increasing mass of growing bone changes are constantly taking place. These consist of the formation of new lamellae by the osteoblasts, and
at the same time the destruction and digestion of the recently formed areas of bone tissue, the formation of other new layers and so on. This destructive process is carried on by multinucleated giant cells known as osteoclasts. The protoplasm of the osteoclast is thought to produce a substance which dissolves bone. Bone lamellae can be seen to dissolve or melt when touched by one of these giant cells.

"The reconstruction of bone is based entirely upon the activity of osteoblasts and osteoclasts. It is always coördinated with local mechanical conditions existing at the time and guarantees the maximum possible rigidity of the corresponding part of the skeleton. The direct causes which make adjacent cells in a growing bone become either osteoblasts which form the bone or osteoclasts which destroy it are unknown. (Maximow, X).

In this destructive and rebuilding process which is occurring during growth, possibly lies the reason for the increased incidence of osteomyelitis during this period of life.

The process of infection in acute hematogenous osteomyelitis is thought to be dependent upon the blood supply of bone. The blood vessels of bone are very numerous. Those of the compact tissue are derived from a close and dense net-work of vessels ramifying in the periosteum. From this membrane vessels pass into minute orifices in the compact tissue running through the canals. The cancellous tissue is supplied in a similar way, but by a less numerous
set of larger vessels, which, perforating the outer compact tissue, are distributed to the cavities of the spongy portion of bone. In the long bones numerous apertures may be seen at the ends near the articular surfaces, some of which give passage to the arteries of the larger vessels, which, perforating the outer compact tissue, are distributed to the cavities of the spongy bone. The medullary or nutrient artery usually accompanied by one or two veins, sends branches upward and downward to supply the medullary membrane which lines the central cavity and adjoining canals. The ramifications of this vessel anastomose with the arteries both of the cancellous and compact tissues. In all cancellous tissue the veins are contained and supported by osseous structure and have exceedingly thin walls. When the surrounding bone is removed, the veins remain adherent.

In the bone marrow are found peculiar thin-walled vessels known as sinusoids. Their wall is formed by very thin histocytes or littoral cells. Foreign particles circulating in the blood easily penetrate the thin walls of the sinusoids and gain access through it to the tissue. Innumerable cells continuously pass through it from the tissue into the blood. (XI)

Organisms brought by blood to bone find their first opportunity to rest at a point where they enter the interosseous circulation. Having multiplied to sufficient numbers, they excite a little inflammation in the cells lining the blood space. These cells swell and fibrin and leuco-
cytes accumulate shutting off the blood space from the remainder of the circulatory system. This is a most favorable situation for the growth and multiplication of bacteria. Temperature and media (blood) are both present, and body defense mechanisms are hindered by the decreased circulation. (I)

It may be said, however, that the exact mode of infection is still somewhat in dispute, some teaching that bacterial emboli lodge in the cortex of the bone close under the layer of periosteum and that subperiosteal infection may be regarded as a primary disease. Most surgeons hold that in a large majority of cases the bacterial emboli lodge deeper in the cancellous spaces of the bone. (iii)

 Lexer's studies show that the vessels of the shaft ending near the epiphyseal lines are end arteries. This region is very vascular because it is the region of most rapid growth, and this is particularly true of the diaphyseal side of the epiphysis. As has been previously stated, the chief nutrient vessels enter the shaft near its middle, and send branches toward each extremity of the bone, while the vessels supplying the epiphyseal line enter the bone from the periosteum. The original focus in osteomyelitis is usually near the epiphyseal line, which, when considered with the circulatory peculiarities of the region, is substantiating proof of its embolic origin. (XII)

The hematogenous form constitutes by far the greatest majority of cases of acute osteomyelitis. It results from
a bacteremia or general blood infection, the origin of which is, in the greatest number of cases, obscure. In these cases it is thought that the entry point of the infection must necessarily be some surface (skin or alimentary) tract of the body. It is assumed that with very few exceptions (genito-urinary infections, furuncular infections of the skin), this surface is a mucous membrane lining of the alimentary canal at points where collections of lymphadenoid tissue are especially prominent such as tonsils and Peyer's patches. In a small percentage of cases, the bacteremia accompanies or follows a definite entity such as typhoid fever, or a definite focus of infection is present somewhere in the body, such as a phlebitis, a postpartum sepsis, or a furunculosis, to which the bacteremia is subsidiary and through which the osteomyelitis originates. (XII)

The bacteremia through which secondary foci of infection become established is usually not demonstrable. It is well known or at least taken for granted that the presence of bacteria in the circulating blood, even for a short period, is sufficient to infect any local area. It is thought that temporary states of bacteremia are constantly occurring even in conditions of health, and that the natural forces of the body are amply sufficient to overcome these so promptly that no evidence of them is perceptible in any way.

Although it is usually impossible to obtain a positive blood culture in early cases, it is frequently possible to do so in the later cases. In most of these the osteomyelitis
acts itself as a primary focus, and pours the organisms into the blood stream. General septicemia is common. A large number of different bacteria have been obtained after culturing pus found at operation. Staphylococcus aureus has been found most frequently, while streptococcus hemolyticus and viridens occur in a small number of cases. The pneumococcus and typhoid bacillus are not uncommon. Each of these give rise to symptoms and general body reactions in proportion to their respective virulences. (XIV)

The shafts of long bones are the common sites of involvement with the scapula, clavicle, iliac crest, and spine coming next in order. In 942 cases reported by Hemonem, 380 were of the femur and 338 of the tibia. The circulatory peculiarities are usually given credit for this predilection.

The infection usually has its primary site in the medulla itself, but in some cases it may be so near the surface that a subperiosteal abscess alone is formed without notable involvement of the shaft. With this process, there is edema of the over-lying tissue. Reddening of the surface and even perforation of the skin occurs in much neglected cases. Only rarely does the joint become involved. (XV)

It is sometimes possible from the history of acute cases to form the deduction that the process begins in one end of the shaft and extends quickly throughout the length of it. In other instances more or less of the whole shaft seems to become simultaneously involved. Although a com-
pletely satisfactory explanation for the variance in this mechanism cannot be made, it is thought to be due to simultaneous or closely associated thrombosis of the two main arteries in the first case, and a primary blocking of the main vessel in the second. From a practical viewpoint, however, extension may be said to result from pressure of the pent-up pus.

When this pressure has been relieved, that portion of bone which is deprived of its nutrition becomes a foreign body. The "reactive forces" within the bone separate the dead from the living bone, and the periosteum begins to exercise its proliferative powers. This is known as the involucrum, and it encases the old bone, which is known as sequestrum. Between these two layers of bone a line of demarcation is formed by the production of granulation tissue. Three to six months are usually required for its formation. This process may either partially or completely surround the shaft. Huge sequestra have become a rarity with the modern practice of early drainage. It is due to these marvelous regenerative properties that the end result of osteomyelitis is often so good.

In the early cases, a hyperemia is the only change in the soft parts. The periosteum is elevated from the bone by a serous exudate. In later cases, the exudate may be purulent and the periosteum may become widely separated from the underlying bone. Very early the bone may appear redder than normal, but usually by the time the patient
comes to operation the bone vessels have become occluded and the exposed bone is dull white. This is not an indication of the extent of the disease but of the fact that there is pus beneath.

In the more advanced cases, the overlying soft parts may be infiltrated with pus. A straw-colored exudate may indicate either a mild infection or an early stage of a streptococcus infection. (XII)

After the involucrum is formed the extent of the diseased bone may be determined by x-ray. A discharging sinus is evidence of dead bone. Upon operation, the sequestrum is seen loose in a bed of granulation tissue. After its removal the granulation tissue proceeds to obliterate the cavity.

In general there are four distinct histological processes that occur in the osteomyelitic process. They are:

1. The acute reaction to injury, with the collection of polynuclear leucocytes about the site of infection together with increased filling of blood vessels. Marrow cells are replaced and the adjacent marrow may be partially infiltrated by leucocytes.

2. Abscess formation of leucocytes and the plugging of vessels.

3. The separation of the dead from the living bone, which may or may not be accomplished by the osteoclasts. There is round cell infiltration with the endotheliod cell and fibroblasts intermingling to make up the picture. There must be adjacent living bone to activate the process.
Osteoclasts aid in the separation of some spicules.

4. Repair. Reparative processes begin with bone absorption. Fibroblasts form granulations in the presence of dead bone. Outside of the dead bone, beneath the periosteum, energetic bone regeneration takes place. Beyond this, fibrous tissue is formed. After the dead bone has been removed, new bone is produced at the border of the medullary cavity. This process is dependent upon the blood supply which is usually sufficient. (XII)

Doctor Dean Lewis makes the following observations as to the pathology of the early stage. "Early the medulla is congested centering about the focus of infection. The overlying periosteum is pinkish in color and edematous. It feels tense and rubbery but there is no pitting; an extensive hyperemia exists in the cortex and subperiosteal tissue. The fat has an oily appearance. There may be no pus in the incipient stage, but in twenty-four hours the entire medulla may be filled. The epiphysis is involved in 12% to 15% of cases between the second and seventh day of the disease. Then this occurs, further growth of bone from the epiphysis may be arrested if actual separation has occurred."

He continues that the disease is, however, usually limited to the diaphysis due to the epiphyseal cartilage which acts as a block against extension into joints. The distention seen in the joint so commonly is lymph which is outpoured into the synovia. This is entirely a protective mechanism.
Sequestration is explained by the same author in the following manner: "After frank pus appears in the medulla, necrosis usually follows. The inflammatory pressure develops simultaneously with the pus, and causes a shutting off of the blood and nourishing lymph to certain parts. These parts die. Medullary sequestration may take place in two weeks while cortical usually takes from four to eight weeks. Sequestration is accomplished by the osteoclasts which destroy the new useless bone. Solution is a long and slow process which may be aided by chemical stimulation." (XVI)

At the start of the process the pus is thin and clear. This is true even of those caused by staphylococcus aureus. Later it becomes very heavy and thick, while in the later stages it is again thin and watery.

The formation of new bone beneath the periosteum is hastened by the inflammatory process. After three to four weeks the periosteum has the feel and crackling of tissue paper, and gradually the layer of new bone nourished by the periosteum assumes a definite thickness and gradually loses its property of being moulded until in eight to ten weeks a definite shell of new bone surrounds the dead bone. The new involucrum is poor in quality. It is honeycombed with spaces through which pus escapes so as to greatly resemble a piece of latticework. It is also imperfect in its reproduction of the original bone. This is particularly true when no orthopedic devices have been applied to hold it in its original position.
Robertson of Toronto (1927) conducted a series of exhaustive experiments with animals. He makes the following conclusions:

1. "Organisms introduced into the blood stream are deposited, among other places, in the long bones.
2. "In bone there is a very active phagocytosis, except in the metaphysis.
3. "Organisms produce inflammatory centers in the metaphysis independent of trauma.
4. "It is possible to produce a general infection of the medulla by simple inoculation of organisms into the blood stream.
5. "Trauma may determine a local infection.
6. "Growing bones develop abscesses of the type of osteomyelitis within them. Adult bones do so but rarely." (lll)

These simple but conclusive conclusions seem to coincide remarkably well with the generally accepted belief as to the mechanism of infection etiology and predisposing causes.

The effect of the spread of osteomyelitis as has been pointed out is both destructive and stimulative. Destruction is signified by the amount of necrosis. The stimulative action of infection, noticed frequently in fractures, is well exemplified in the construction of the new case or involucrum under the periosteum. This bony shell may ultimately house the fully matured sequestra. This, however, is seen only in neglected cases when the infection has spread far beyond the limits of the original focus.
Acute hematogenous osteomyelitis is mainly an affection of youth with its greatest incidence in the male sex between the ages of two and fifteen. The adolescent boy is the most frequent victim. In 104 cases at a Copenhagen hospital boys were affected three times more frequently than girls. The reason for this predilection is thought to be the more general exposure to trauma by boys. This is questionable, however, as a history of trauma can be obtained in only about 15% of cases. Dr. Hertzler in his book "The Pathology of Diseases of Bone", rather doubts this explanation, but does not offer a substitute. (IV) (XXII)

In general it may be said that the predisposing causes aside from trauma may be all included in "resistance lowering factors". Cold and exposure of a part, exhaustion from over-exertion, and weakness from a long period of illness may each play a part.

The symptoms of acute osteomyelitis in its most common form are marked. In the early stage, they are those of an acute infection, mild, severe or fulminating in type. A rigor may occur at the onset, and the temperature often rises to 103° or 104° F. The high fever, rigors, and general toxemia may precede any local symptoms. Local symptoms are intense pain, very very severe, and usually causes agonized cries upon examination. Redness and swelling over the affected area is present within a few hours in the typically acute case. The patient is unable to sleep. Lowering the limb by increasing the congestion causes pain. Tapping the bone at some dis-
tance will cause pain at the site of involvement. (XXI) (XXII) (XXIII)

In many cases there is a prodromal phase before the typical clinical picture is established. This insidious mode of onset may last from seven days to two or three weeks, and is more usual in older children or adolescents. The pain is of a less acute type and is described as an aching. Increased pain after use is symptomatic. Important symptoms are a vague feeling of "seediness", intermittent limp and fixed pain at the end of a long bone. Metaphyseal tenderness is often present upon examination. This clinical stage corresponds to the stage in which the juxta-epiphyseal focus has not reached the surface, and is the stage during which diagnosis should most often be possible. (XX) (XXI) (XXII)

Later considerable swelling, with edema and redness of the skin may be present, and where rupture of the periosteum has occurred, the fluctuation of an abscess may be detected. The joint may be swollen and tense after the first few hours, or there may be only a moderate effusion. Joint movements, however, remain free and painless.

In fulminating osteomyelitis, the clinical picture of acute septicemia may overshadow the local signs and in exceptional cases death may take place in two or three days from the onset. In the average case with severe toxemia, a blood count will usually show a marked leukocytosis, and a culture may demonstrate the presence of the causative organism. The symptoms of a systemic infection usually abate when
the pus escapes from tension, either spontaneously or after surgical drainage. (XXIII) (XIX)

The high mortality of acute osteomyelitis is due unquestionably to the fact that the diagnosis is rarely made in the early stage. Mistakes continually arise because the clinical syndrome bears a superficial resemblance to certain acute infective conditions, yet the diagnosis of osteomyelitis is comparatively easy if it is kept in mind. Why is it that the diagnosis is so often not made in its early stage? Dr. R. T. Condon has made some interesting observations in his contact with the disease. In emphasizing the importance of early diagnosis he writes:

"There is probably no septic process in which the consequences of delay are so serious as in acute osteomyelitis. Within the peritoneal cavity the extension of acute infection is limited by a potent defense mechanism. A large percentage of acute appendicitis cases in which operation has been delayed result in the formation of local abscesses. Infection in the medullary space is, to use the words of Crile, infection in a defenseless area. Here there is no walling off process, and the dangers of septic absorption and metastatic infection are imminent.

"How can we explain the fact that the diagnosis of acute osteomyelitis is not made as a rule until the disease has progressed for days or weeks? The literature repeatedly refers to the inability of the general practitioner to recognize the disease in the first stage. Acute osteomyelitis is compared to
other surgical emergencies very infrequently. Acute perforating peptic ulcers are seen more frequently. Acute suppurative appendicitis is from fifty to one hundred times as frequent as acute osteomyelitis. Failure to make a careful physical examination is also responsible for many delayed diagnoses. If the disease is kept in mind the diagnosis is easy." (XVIII)

Pain which is constant and increasing is the most common symptom. It is usually complained of as being in the joint. Rheumatic fever is the most common erroneous diagnosis made. This, however, is characterized by an early swelling of the joint, followed by a sinovitis in other joints. The pain of acute rheumatism is relieved by salicylates, which, of course, have little effect on osteomyelitis. Joint pain, joint tenderness, and muscular spasm seen in arthritis may be contrasted to the painful, tender, and thickened metaphysis of osteomyelitis. (XXI) (XXIV)

Acute cellulitis may be confused. In this condition, there is early swelling and induration of the soft parts, skin redness, and the complete absence of localized metaphyseal tenderness and thickening. Tapping on the bone will usually localize the pain in a distant spot. This is the most constant and reliable diagnostic method. (XXV)

Acute infective arthritis in superficial joints such as the elbow or knee does not usually offer much difficulty if the diagnostic measures mentioned are employed. The differentiation between acute suppurative arthritis of the hip
and acute osteomyelitis of the neck of the femur is, however, more difficult. In both conditions early exploratory measures are advisable.

Special difficulties arise in the diagnosis of acute osteomyelitis of the deeper bones, for example, the pelvis, where the local signs may be obscured by the character of the overlying tissue. It is due to this that pelvic osteomyelitis has an exceptionally high mortality. Suggestive signs of involvement of the pelvis are (a) referred pain in the lower limbs, (b) pelvic tenderness on rectal examination, and (c) deep tenderness over the affected bone. A radiographic examination is of no value in the early stages. Only later is a localized area of destruction visible. Case I, which will be reviewed later affords an excellent example of this. (XXII)

In doubtful cases it is agreed by most orthopedists that an exploratory puncture of the bone should be done without delay. A small incision should be made over the metaphysis, the periosteum incised, and the cortex drilled in several places. If pus appears, appropriate drainage should at once be established. If no pus is found, material extruded from the drill holes should be cultured. If the diagnosis is not confirmed, no harm has resulted. A more general use of this procedure would possibly save many lives. (XXVI)

As has been mentioned before, the onset may be insidious and still be included in the category of acute osteomyelitis. This onset may last for a week or more and only at the end of that time show signs of localized bone disease. These cases
are hard to diagnose, but if the signs are looked for each day, a diagnosis can be made before extensive damage has been done. Let us emphasize at this time that x-ray is of no value in the early diagnosis except to indicate other pathology such as periostitis. It is freely claimed that the general use of x-ray as a diagnostic procedure in orthopedics has greatly hindered the early diagnosis of osteomyelitis. It must not be forgotten, however, that it is an invaluable aid in determining the extent of sequestration. (XXVII)

It is in the treatment of the disease and management of the case that the greatest arguments arise. The literature of the past three decades is voluminous, with accentuation being placed on early diagnosis and treatment. The methods and principles of diagnosis before mentioned in this paper are pretty well agreed on by the majority, but in studying the methods of treatment advanced we find wide discrepancies.

After the advent of Listerism and the definite proof as to the bacterial origin of the disease, free drainage and sensis began to be employed. The mortality lessened as a result and there began to be the hope that it soon would be reduced to a negligible percent. Some thirty years, however, have passed since these methods first came into general use, and we find that we still have a mortality rate of 15% in the United States, and approximately the same rate in England.

Upon one principle of treatment there is a most univers-
al agreement. It is that of early incision and drainage. It has been pointed out, however, by one man that in a certain type of case even this is not advisable. This Dr. Frazer describes as a type known to pathologists as sero-albuminous. He has made the observation that this type is almost invariably caused by the pneumococcus. His clinical experience has shown that this type almost invariably subsides without operation. He even goes so far as to say that operation is distinctly harmful, as dissemination of the disease may result. This condition is found only in babies and young children, and is not accompanied by the prostration found in the acute suppurative type nor with the high temperature and pain. There is also a much lower leucocytosis. These cases he treats with fixation of the limb in splints and extension. Hot local applications are applied, and the pain relieved by chloral or bromide. In his hands, this procedure usually results in recovery, but if not, and the symptoms of toxemia increase, drainage is resorted to. (XXVIII)

Until quite recently (the past ten years) the favored method of procedure was early surgical drainage in which the periosteum was split and reflected over the entire diseased area and for a centimeter or two on each side. The medullary cavity was then opened freely on each side, and immobilization with splints accomplished. The wound was loosely sutured and drains inserted. Dressings were made frequently, and the favorite antiseptic preparation of the surgeon was used. (1) (XX) (XXIX)

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Wartime experiences revised the opinions of many men as to the principles of antisepsis. The Carrell Daykin method was used extensively at that time and came into general use in the treatment of infected fields after the war. It is still the favored procedure with many, and seems to have proven superior to other antiseptic solutions. (XXIX)

Whether or not the medullary cavity should be opened at the time of the primary operation has been and still is a much disputed question. Ochsner (1) believes that ultimate healing is hastened by doing so. Dean Lewis (XVI) advises primary incision of the periosteum and later if the fever does not subside, drainage of the cortex. He points out that the use of sharp instruments prevents the formation, to some extent, of secondary sequestra. Rast made a comparative study of 226 cases. In 70 of these the marrow cavity was opened. Ten of these cases died, giving a mortality of 14%. In 156 cases, the marrow cavity was not opened, and the subperiosteal abscess was merely drained by free incision into the periosteum. Of this series, 12 died, giving a mortality rate of 7%. In another series of 80 patients, incision into the periosteum only was done. The mortality here was 6%, 5 having died. The claim is made that complications are more frequent where the marrow cavity is opened. This would seem to be a reasonable observation in cases where there has been no extension of the infective process into the cavity, but would seem to be unavoidable in the late destructive cases. (XVI)

At present, then, it would seem that the weight of the
evidence was against the opening of the medullary cavity, at least, at the time of the first operation. If, however, this is found to be necessary, most men have found that the curetage should be as light and as inextensive as possible. Many deaths from osteomyelitis are the result of secondary foci which are of embolic origin. To roughly curet the medullary cavity is to court many of these secondary complications. (XVI)

Dr. H. T. Jones of the Mayo clinic gives the following indications for conservatism:

1. "Early adequate drainage indicated when examination shows localization, but a radical operation on the bone is not indicated.

2. "During the stage of atrophy of the bone and repair during the three to six months following the original drainage, one should wait for the normal repair on the part of the organism.

3. "The removal of the sequestra should usually be accomplished with as little damage as possible to the granulation bed in which the sequestra are formed, reserving radical plastic operations on the bone until time indicates will not take place otherwise." (XVIII)

Dr. J. Frazer of London, previously quoted, describes his method of operation in the October, 1924 "Lancet". He believes that the marrow cavity should be opened so that adequate drainage may be established. After separation of the periosteum, the cortical bone overlying is perforated
with a trephine or large burr. From this opening a large quantity of fluid escapes. A series of openings are then made along the line of the shaft at intervals of about two centimeters. These are continued until the red and apparently infected bone marrow is exposed. Curettage, he believes, should not be done, due to the dissemination of the infection caused by the process. The wound is left open throughout its length and a number of capillary tubes are passed into the interior of the infected medullary canal. The Carrell Daykin treatment is used postoperatively until suppuration has ceased. Usually at the end of three weeks a partial closure of the wound may be accomplished with secondary sutures. This method he has found very satisfactory, and reports a low mortality in an extensive series of cases (XXVII) (XXIX).

Apparently there are but few cases that do not require secondary operation. The sequestra formation mentioned previously may be followed by x-ray. Operation should be delayed until this is complete and the patient should not be subjected to frequent curettements, as this tends to destroy the regenerating bone marrow and usually fails to remove the sequestra.

Operation in the second stage is not an emergency measure, but rather a methodical and tedious undertaking, and to be successful, must be complete. The Esmarch enemia (rendering the limb bloodless) is frequently used. The venous channels in the limb are emptied by holding it aloft for three minutes, and a rubber band is applied. This makes rapid operating possible. (101)
The operation may consist merely in the removal of cortical sequestra which may be found lying loose on the surface of the bone or may be beneath a well-formed involucrum. This is composed at this stage of soft bone and can be reflected over the underlying sequestra without destruction of the periosteal covering of the involucrum. It may be advisable as soon as the sequestrum is removed, to combine this operation with planefaction, which consists of cutting off the roof and sides of the cavity in which the sequestrum lies, until only a posterior shell remains. This permits the over-growing soft parts to become closely approximated to the bone, thusobliterating the cavity. (111)

There are several therapeutic measures which may be used as valuable adjuncts to the postoperative treatment. One of them is heat. This may be applied in the form of wet dressing, or with a cradle and light bulb. It would seem to be very much indicated in these cases where there has been extensive destruction of blood vessels, and should aid in the revascularization of the region.

Several attempts at immunization have been made. In one series of cases an attempt was made to create passive immunity by the transfusion of immunized blood. It was unique in the fact that the donors and not the patients were immunized. At the time of operation, a culture of the pus was made, and an autogenous vaccine prepared. This was given to a suitable donor. Innovulations were given every third day, and transfusions given between twenty-four and forty-
eight hours after inoculation. Between transfusions, smaller amounts of the donor's serum would be given hyperdermically. The results of this experiment were apparently quite satisfactory, and it would seem to be deserving further work. The scope of the trial was too small, however, to justify any conclusions. (XXX) Rovsing does not think it advisable to add to the antibodies in the acute stage. He believes that the extensive tissue damage occurs within a few hours, and that vaccine therapy is impotent to prevent this. In the chronic state, he adds it may be more rationally used to reinforce the existing antibodies. (XXXI)

Physical therapy has an important place in the treatment of these cases. It must be emphasized, however, that it is only valuable after surgical intervention. Bacteria are, of course, present in all cases, and the short ultraviolet ray is bacteriocidal in its action. Bacteria absorb more ultraviolet energy than the tissue cell, and the time required for death does not materially affect the cells. Every cavity or sinus should be rayed every day for a period of time, commencing with a three minute exposure, and increasing the time gradually until it reaches a period of ten minutes. (XXXII)

The metabolic condition of the patient suffering with acute osteomyelitis is usually far from good. The calcium content is invariably low, in many cases as low as 4½ milligrams. In the more chronic cases there is a deficiency of red cells, and low hemoglobin. Ultraviolet radiation has been found to be effective in these cases.

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Usually, as has been mentioned, there is a destruction of blood vessels, and an impairment of blood supply and drainage of the part, thus leaving a tissue which is especially susceptible to invading bacteria. Here diathermy is thought to act as a stimulus to the growth of small arterioles and thus aid in the reestablishment of circulation. Pain is also relieved by its sedative action on nerve filaments. Metabolism is increased and the absorption of inflammatory products hastened by the opening up of blood and lymph channels. (XXXII) (XXXIII)

The attention of the public has recently been called, through the medium of the newspapers, to the use of the fly maggot in the treatment of osteomyelitis. Their use, however, is far from being a recent innovation, and especially during the war, when it was often necessary to leave wounds undressed for considerable periods or time, the presence of maggots in a wound was observed in many cases to have been beneficial. (XXXIV)

Doctors G. C. Weil, S. Neillour and Rolun of Philadelphia have used the fly maggot in a number of cases with considerable success. Sterile maggots are produced by sterilizing the fly egg and transferring the colonies to sterile food containers, which, when placed in the incubator at 98°F will permit the cultivation of sterile maggots within six to twelve hours. The maggots are transplanted into the wound using all the aseptic precautions possible. A guard of copper wire is placed over the wound with the edges protected.
with adhesive strips to prevent the escape of the maggots. The wound is then exposed to the light, sunshine or electric baker. A temperature of 96° to 98° F. is necessary to insure the continued activity of the maggots. Every third day the wound is cleaned thoroughly with warm saline and a new implantation is made. As soon as the wound secretions change from a purulent discharge to a thin, clear serum, the maggot ceases its activity and migrates to the surface. (XXXIV)

The results of this most unique and interesting experiment have been most gratifying, and it is possible that it may receive further recommendation when subjected to further use.

Perhaps the most radical departure from the conventional methods of treatment has been suggested and practiced by Dr. Orr of Lincoln, Nebraska. Dr. Orr believes that our modern method of treating wounds has gotten away from the principles of Lister, and that many times a great deal of harm is done in the way of destroying tissue cells and normal body defense mechanisms by the use of antiseptics. He believes that much of the trouble experienced postoperatively is due to secondary infection from frequent dressing. (XXXV)

Dr. Orr's procedure is as follows:

**Principles**

Primary drainage and cleaning up of the infected area, immobilization of the diseased part, and protection of the wound against secondary and mixed infection.

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Procedure

1. Primary asepsis or antisepsis to reduce the focal infection (at the point of acute disease or injury.) It is not attempted to remove all infected or diseased tissue. The patient is relied on to take care of part of his infection if properly assisted and protected.

2. Adequate drainage (wide open to the depths of the infected area.)

3. A postoperative dressing or method that will protect the wound and the injured or diseased part so that the wound and the part are at rest and there is no opportunity for re-infection.

4. Immobilize, so that movement, pain and muscle spasm are relieved.

Technique

1. Make a fairly large incision over the infected bone area. Spread apart the skin, muscles, fascia and periosteum just far enough to afford access to the diseased area and no farther.

2. Chisel a window into the affected bone area large enough so that all diseased bone may be removed and so that there are no overhanging edges of bone over the diseased area. This is to be less extensive in acute cases.

3. Clean out the diseased area gently with a curet or gouge, being careful to refrain from unnecessarily damaging the tissues undergoing repair.

4. Dry the wound and wipe out with 10% iodine followed
by 95% alcohol.

5. Pack the entire wound wide open, but not tightly, with a sterile petrolatum gauze. Cover this with a dry sterile pad, and bandage on.

6. Now perform any reasonable forcible manipulation necessary to place the parts in correct anatomic position for splinting.

7. Apply a plaster cast preferably, or a suitable splint so that the parts are thoroughly immobilized in comfortable or correct position. Additional weight and pulley traction, Balkan frame, or even ice tongs or bone pins may be used in these infected bone lesions associated with fracture deformities which are being corrected at the time.

8. Finally, the cast is not to be a splint, nor are windows to be cut in the cast until the wound dressing becomes necessary. The wound is not to be dressed at all unless there is a rise in temperature or other signs of acute sepsis. As a rule, no dressing is required at all except on account of odor, and this may not be required for several weeks. In a majority of cases, the patient treated by this method will go through to complete healing with a few dressings at intervals of ten days to four weeks." (XXXVI)

Dr. Orr's enthusiasm and extensive writings on his subject have attracted much attention and aroused much comment in the recent writings on osteomyelitis.

Dr. N. B. Bitting, who formerly used the Carrel-Daykin method, has found the Orr method to be more satisfactory. He
likewise believes that in open drainage, reinfection is bound to occur. He, however, offers a different opinion as to why such good results are obtained by infrequent dressings. Vaseline gauze and undisturbed retention of pus in the wound is an important factor in resolving the infection, he thinks. Decreased pressure plus an increasing concentration of bacteriophage accelerate dissociation and phagocytosis. Dr. F. H. Albee also believes that bacteriophage formation is responsible for the success of the method. (XXXVII) (XXXVIII)

It is our belief, after noting the comments by different authorities on osteomyelitis, that the Orr method is growing in favor, and is deserving of more general use. (XXXVIII) (XXXIX)

Case 1. A fatal case of acute osteomyelitis of the ileum.

A boy, aged 17, was admitted to the hospital October 24, 1931, complaining of pain, tenderness and swelling above the left iliac crest, of one week's duration. The pain developed suddenly, and caused inconvenience in walking, but was only moderately painful. He had been playing football, but did not remember having received a blow in this region. X-ray of the region was negative. He was operated Oct. 31, 1931, and a small amount of pus was found. Its relation to the bone was not established. The patient ran a septic course and died Nov. 22, twenty-nine days after admission. Acute osteomyelitis of the left ileum was found at autopsy.
This case is atypical in some of its features. It is not a common site for the location of the disease, and the findings did not apparently justify an early diagnosis as such. Perhaps an early diagnosis and operation with adequate drainage of pus lying below the periosteum would have prevented the septicemia.

Case 2. Acute osteomyelitis of the right tibia caused by staphylococcus aureus.

A male baby, aged 2½ years, was brought to the hospital August 15, 1931, complaining of pain in the right knee, restlessness, crying, poor appetite, and inability to walk. He had bumped his knee four days before, but gave no complaints at that time. Two days before admission, he refused to walk and held his knee in a flexed position. Pain was marked over the proximal lateral side of the tibia. He was operated Aug. 17, 1931, and a pocket of pus was found. The periosteum was somewhat roughened. Ten days later a second operation was performed. This time the medullia was removed, leaving the endosteum. Iodine was applied, and paraffin and vaseline introduced into the cavity. This was allowed to remain for ten days with no dressing. An uneventful recovery followed, and he was dismissed from the hospital September 8, 1931, three weeks after admission.

Here prompt operative intervention was used with a satisfactory result. The second operation might have been avoided if the periosteum had been opened at the time of the first operation.

Case 3. Fatal case of osteomyelitis of the femur.

A baby girl, aged 2, was brought to the hospital May 11, 1931. The
complaints were pain and swelling of the left thigh, and fever. Three days before, upon awakening in the morning, she was unable to walk. The leg started to swell the next day. Traction was applied by the local physician for two days before entrance. The child had maintained a high fever from the onset of the trouble.

Examination showed a swollen and painful thigh and a diagnosis of acute osteomyelitis made. The child was operated immediately, and a large amount of bloody-tinged pus was found exuding from the upper part of the femur. Eight holes were drilled into the shaft of the bone. There was no marked increase in pressure. The wound was packed with vaseline gauze and temporarily closed with silk-worm suture.

The postoperative pulse was 180, and temperature 105°. This increased until death occurred five hours later.

This case should undoubtedly have been diagnosed much earlier. The high temperature, pain, and swelling should have at least aroused enough suspicion of osteomyelitis to warrant an exploratory operation. In this case, the severe toxemia indicates the virulence of the infection as contrasted to a comparatively avirulent type in case 2.

Case 4 is presented in detail because of the characteristic history, course, and development.

Francis Freeman, aged 10, was admitted Feb. 19, 1931. Her complaints at that time were, 1, pain in left knee region medially and proximal to the joint; 2, tenderness in the left knee region; 3, fever; 4, nausea and vomiting; 5, pain on standing.
Two days previously, while playing, she fell, striking on the outside of the left knee. Noticed no pain at the time, but a few hours later, the medial side of the knee joint became tender and soon began to pain when she walked. On Feb. 19th., upon awakening, she was sick at her stomach and vomited. The temperature at this time was 104°. She was seen by an outcall student and diagnosed as acute osteomyelitis. The next day, Feb. 19th., she was brought to the hospital with the above complaints.

The history was essentially negative, and there was no indication of any recent septic process. Examination showed extreme tenderness of the left knee with pain on standing. There was very little swelling and some local heat. Complete flexion and extension was possible but at some pain. Her white count on admission was 18,400, with 87% polymorphs.

On the same day an incision was made on the medial surface of the thigh at its distal one-third. The tissue was very vascular. The bone was reached and five holes were drilled. Pus could be seen oozing through one of them. A rubber tissue drain was inserted, over which several silk-worm sutures were placed. Daykin's solution irrigations were used daily until March 20, 1931. The temperature gradually returned to normal. An x-ray on March 21 showed considerable involucrum surrounding the old cortex with an incomplete sequestrum formation.

On March 20, saucerization was done. A thin layer of involucrum was removed over the anterior surface of the femur. Pus was seen to be exuding through the previously made drill holes. The bone between these holes was removed, and the cavity
lightly curetted. The cavity was filled with ether and the wound packed open by vaseline gauze. A posterior moulded splint was applied. Crepitus was noted immediately above the knee joint while lifting the leg to apply the splint. The fracture was reduced and a hip spica plaster applied. On April 14, the original packing was removed.

Improvement was steady from this time on, and she was dismissed May 26, 1931.

A more classical case could scarcely be imagined. It is typical in the age of the patient, mode of onset, physical and operative findings, and gradual recovery. It presents a good example of the successful termination of the acute form when a prompt diagnosis is made and prompt drainage secured.

These cases are illustrative of the variance of the disease, and impress one with the great seriousness of the condition. They serve to emphasize to us the importance of early diagnosis and surgical drainage, and that the mortality could be considerably lowered if the recognized procedures in handling the cases were followed.

With the foregoing facts in mind, then, we make the following conclusions:

1. That osteomyelitis was probably one of the first diseases to afflict mankind, but has existed as a clinical entity only since the middle of the 19th. century.

2. A thorough comprehension of the pathology and mechanisms involved is necessary to a complete understanding of the disease.
3. That there are probably two distinct types of acute osteomyelitis which may be called insidious and fulmonating, and which are deserving of a separate form of treatment.

4. The high mortality of the disease is particularly due to the fact that the diagnosis is rarely made in the early stage, due to the infrequency of the condition, but that diagnosis is not difficult if the disease be kept in mind.

5. That early surgical drainage is essential in the acute fulmonating type and that the Orr method is definitely better than pre-existing procedures.

6. The high mortality and protracted morbidity, despite recent improvement in methods of treatment, force us to conclude that there is still much room for advancement in the methods of handling these cases. The opinions of numerous authors expressed in the literature of the past decade are so marked in variance that one is led to believe that the problems involved in acute osteomyelitis have not all been solved.

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