1932

Acute hematogenous osteomyelitis

Howard I. Frisbie
University of Nebraska Medical Center

This manuscript is historical in nature and may not reflect current medical research and practice. Search PubMed for current research.

Recommended Citation

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 intendedto 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.

ACUTE HEMATOGENOUS OSTEOMYELITIS

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. (I)

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 paleozoic. 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 at-
> tacked by rigors that returned at
> frequent intervals. His skin be-
> came 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 Roux, 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 can not 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. (VIII)

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. Kochers 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(1807-1878), 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 staphlococcus aureus intravenously. (III) Lexer in 1897, found that while a large

-5-

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 osteo-myelitis 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 ampu-tations less frequent. Earlier diagnoses were made and adequate drainage gradually became accepted as the general principle of treatment. However, the treatment of osteo-myelitis 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 per-iosteum. A layer of osteoblasts arrange themselves in a more or less definite manner between the periosteum 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 par-
allel 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 ir-
regular, flattened, stellato masses of protoplasm possess-
ing 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

-7-

at the same time the destruction and digestion of the re-
cently 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 de-
stroy 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 oste-
omyelitis 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 por-
tion 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 branch-
es 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 can-
cellous 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 his-
tiocytes or littoral cells. Foreign particles circulating
in the blood easily penetrate the thin walls of the sinu-
soids and gain access through it to the tissue. Innumer-
able 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 inter-
osseous circulation. Having multiplied to sufficient num-
bers, 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 ali-
mentary 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. (XIII)

The bacteremia through which secondary foci of infect-
ion 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 per-
iod, 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 prompt-
ly 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

-11-

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 baccilus 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 predelection.

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-

-12-

pletely satisfactory explanation for the variance in this
mechanism cannot be made, it is thought to be due to sim-
ultaneous 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, how-
ever, 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 for-
eign 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 re-
sult 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

-13-

comes to operation the bone vessels have become occluded
and the exposed bone is dull white. This is not an indi-
cation 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 di-
seased bone may be determined by x-ray. A discharging
sinus is evidence of dead bone. Upon operation, the se-
questrum is seen loose in a bed of granulation tissue.
After its removal the granulation tissue proceeds to oblit-
erate the cavity.

In general there are four distinct histological pro-
cesses 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 to-
gether 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 endothelioid 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 innoculation 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 bonesdo so but rarely." (111)

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.

-17-

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 predelection 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. (1V) (XX11)

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 symtoms 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-

-18-

tance will cause pain at the site of involvement. (XXl)
(XXlll) (XlX)

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. In-
creased pain after use is symptomatic. Important symptoms
are a vague feeling of "seediness", intermittant limp and
fixed pain at the end of a long bone. Metaphyseal tenderness
is often present upon examination. This clinical stage cor-
responds to the stage in which the juxta-epiphyseal focus
has not reached the furface, and is the stage during which
diagnosis should most often be possible. (XX) (XXl) (XXll)

Later considerable swelling, with edema and redness
of the skin may be present, and where rupture of the perios-
teum has occurred, the fluctuation of an abscess may be de-
tected. 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 ex-
ceptional 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 leucocytosis, and a
culture may demonstrate the presence of the causitive organ-
ism. The symptoms of a systemic infection usually abate when

-19-

the pus escapes from tension, either spontaneously or after surgical drainage. (XXlll) (XlX)

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 practioner 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." (XVlll)

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 rhematism 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, tander, and thickened metaphysis of osteomyelitis. (XXl) (XXlV)

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 restal 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 1, which will be reviewed later affords an excellent example of this. (XXll)

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. (XXVl)

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 ortho-
pedics has greatly hindered the early diagnosis of osteomy-
elitis. It must not be forgotten, however, that it is an
invaluable aid in determining the extent of sequestration.
(XXVll)

It is in the treatment of the disease and management
of the case that the greatest arguments arise. The liter-
ature of the past three decades is voluminous, with accentu-
ation 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 dis-
crepancies.

After the advent of Listerism and the definite proof
as to the bacterial origin of the disease, free drainage
and sepsis 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 sub-
sides 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 temper-
ature 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 pro-
cedure usually results in recovery, but if not, and the symp-
toms of toxemia increase, drainage is resorted to. (XXVlll)

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 fav-
orite antiseptic preparation of the surgeon was used. (1) (XX)
(XX1X)

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. (XXlX)

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 (XVl) 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 periost-
eum. 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 un-
avoidable in the late destructive cases. (XVl)

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. (XVl)

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." (XVlll)

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 appar-
ently infected bone marrow is exposed. Curettage, he be-
lieves, 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 satis-
factory, and reports a low mortality in an extensive series
of cases (XXVll) (XX1X)

Apparently there are but few cases that do not require
secondary operation. The sequestra formation mentioned pre-
viously 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 regen-
erating bone marrow and usually fails to remove the sequestra.

Operation in the second stage is not an emergency meas-
ure, but rather a methodical and tedious undertaking, and to be
successful, most 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 pos-
sible. (lll)

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, thus obliterating 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. Innoculations were given every third day, and transfusions given between twenty-four and forty-

eight hours after innoculation. Between transfusions, smaller
amounts of the donor's serum would be given hyperdermically.
The results of this experiment were apparently quite satis-
factory, 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.   (XXXl)

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 ultra-
violet 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, com-
mencing with a three minute exposure, and increasing the time
gradually until it reaches a period of ten minutes.   (XXXll)

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 $4\frac{1}{2}$ milli-
grams.   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.

Usually, as has been mentioned, there is a destruction ~~time~~ construction
of blood vessels, and an impairment of blood supply and ~~construction~~
drainage of the part, thus leaving a tissue which is expec-
ially 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.
(XXXll) (XXXlll)

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, how-
ever, is far from being a recent innovation, and especially
during the war, when it was often necessary to leave wounds
undressed for considerable periods of time, the presence of
maggots in a wound was observed in many cases to have been
beneficial. (XXXlV)

Doctors G. C. Weil, S. Nellrour and Rolun of Philadel-
phia have used the fly maggot in a number of cases with con-
siderable success. Sterile maggots are produced by steril-
izing 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 cop-
per 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 elec-
tric 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.
(XXXlV)

The results of this most unique and interesting exper-
iment have been most gratifying, and it is possiblethat it
may receive further recommendation when subjected to further
use.

Perhaps the most radical departure from the conven-
tional 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 norm-
al 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.

-31-

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 reinfection.

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." (XXXVl)

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

Dr. N. B. Bitting, who formerly used the Carrell 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. (XXXVll) (XXXVlll)

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. (XXXVlll) (XXXlX)

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 ade-
quate 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, com-
> plaining of pain in the right knee, rest-
> lessness, crying, poor appetite, and
> inability to walk. He had bumped his
> knee four days before, but gave no com-
> plaints 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 medulla was removed, leaving the
> endosteum. Iodine was applied, and
> paraffin and vaseline introduced into
> the cavity. This was allowed to re-
> main 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 satis-
factory 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 swell-
ing 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 increas-
ed 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 con-

trasted to a comparatively avirulent type in case 2.

Case 4 is presented in detail because of the char-

acteristic history, course, and development.

Francis Freeman, aged 10, was ad-
mitted Feb. 19, 1931. Her com-
plaints at that time were, 1, pain
in left knee region medially and
proximal to the joint; 2, tender-
ness in the left knee region; 3,
fever; 4, nausea and vomiting;
5, pain on standing.

Two days previously, while play-
ing, she fell, striking on the
outside of the left knee. Not-
iced 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. 18th., upon a-
wakening, she was sick at her
stomach and vomited. The temper-
ature 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 neg-
ative, and there was no indication
of any recent septic process. Ex-
amination showed extreme tender-
ness of the left knee with pain on
standing. There was very little
swelling and some local heat. Com-
plete flexion and extension was pos-
sible 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 26, 1931. The tempera-
ture gradually returned to normal.
An x-ray on March 21 showed consid-
erable involucrum surrounding the
old cortex with an incomplete se-
questrum formation.

On March 26, saucerization was done.
A thin layer of involucrum was re-
moved over the anterior surface of
the femur. Pus was seen to be ex-
uding 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 ap-
plied. Crepitus was noted immed-
iately 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 mort-
ality could be considerably lowered if the recognized pro-
cedures 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 understand-
ing 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.

BIBLIOGRAPHY

I   Ochsner, A. J. & Crile, D. W.   Clinical Considerations of Osteomyelitis.
Surg. Gyn. and Obst., 1920, Vol 31, PP263-265

II Garrison, F. H.   History of Medicine.
Philadelphia, 1929, Saunders & Co.

III Ashhurst, A. P. C.   Clinical Lecture on Osteomyelitis.
International Clinics, June 1924, vol. 2, pp. 248-268

IV Boyland, G. H.   Practical Notes on Osteomyelitis Therapy as Allied to Ostitis and Periostitis.
Med. & Surg. Reporter, 1881, Vol. 45, pp63-66

V   Stanley, J. H.   Inflammation of the Medullary Cavity of Bone.
Lancet, 1855, Vol. 1, pp. 90-92

VI Roux, M. J.   Osteomyelitis Secondary to Amputation.
Med. Chir. Tr. Lond., 1865

VII Granley, H.   Osteomyelitis.
Lancet, 1876, Vol. 1, pp. 43-45

VIII Kocher, Theodore   Die Acute Osteomyelitis mit Besonderer Riccksicht ouf Ihre Ursachen.
Deutche Zeitschrift, 1879, Vol xi, pp.87-160

IX Geiger, C. M.   Modern Operative Bone Surgery.
1922, F. A. Davis CO., Phildelphia.

X   Maximow   Textbook of Histology.
1930, Saunders, Philadelphia.

XI Chatterton, C. C.   Osteomyelitis in Children
Minnesota Medical Journal, 1925, Vol. 8, pp. 91-96

XII Hertzler, A. E.   Surgical Patholoty of the Diseases of Bone
1930, Chicago. Lakeside Press

XIII Wilensky, A. O.   Mechanism of Acute Osteomyelitis.
Annals of Surgery, 1925, Vol. 82, pp. 781-802

XIV   Forbes, A. M.   Acute Osteomyelitis.
Canadian Med. Journal,1923,Vol. 13, pp579-582

XV   Wilensky, A. O.   Mechanism of Acute Bacterial Infection of a Joint.
Archives of Surgery, 1926, Vol. 13, pp.895-912

XVI   Lewis, D. Acute Osteomyelitis.
                      South. Med. Journal, 1923, Vol. 16,
                      pp. 861-870

XVII   Jones, H. T.   Indications for Conservatism.
                      Tr. A. Resid. and Ex-Resid. Physicians
                      Mayo Clinic, 1929, Vol. 10. pp. 164-166

XVIII Rosenberg, G. Differential Diagnosis of Osteomyelitis.
                      Journal of American Med. Ass'n., 1923,
                      Vol. 81, pp.14-79

XIX   Robertson, D. E. Acute Hematogenous Osteomyelitis.
                      Journal of Bone and Joint Surgery, 1927,
                      Vol. 9, pp. 8-23

XX   Billings, A. E. Acute Osteomyelitis.
                      S. Clinics N. American, 1923, Vol. 3,
                      pp. 233-241

XXI   Partis, B.   Acute Hematogenous Osteomyelitis in
                      Children.
                      S. Clinics North America, 1931, Vol. 2,
                      pp. 149-152

XXII Platt, H.   Therapeutic Measures in Acute Hematogen-
                      ous Osteomyelitis.
                      Lancet, 1928, Vol. 2, pp. 1305-1306

XXIII Payne, A. J.   Acute Osteomyelitis.
                      New Orleans Med. & Surg. Jr., 1931,
                      Vol. 83, pp. 797-798

XXIV Brickner, W. M. Considerations in the Treatment of
                      Osteomyelitis.
                      Journal Am. Med. Ass'n., 1924, Vol. 85,
                      pp. 1782-1788

XXV   Simon, M. M.   Acute Hematogenous Osteomyelitis.
                      American Medicine, August, 1931

XXVI Stollard, C. W. Acute Osteomyelitis.
                      West Virginia, 1929, Med. Jr., Vol. 25,
                      pp. 9-12

XXVII Cotton, F. J. Osteomyelitis with Special Reference to
                      Treatment.
                      New England Jr. Med., 1929, Vol. 201,
                      pp. 986-989

XXVIII Frazer, J.   Acute Osteomyelitis.
                      British Medical Journal, 1924, Vol. 2,
                      pp. 605-610

XXIX   Congdon, R. T   Acute Osteomyelitis and Its Relation to the General Practitioner.
Northwest Med., 1925, Vol. 24, pp.385-386

XXX   Travis, H. D.   Treatment of Acute Osteomyelitis by Transfusion with Immunized Blood.
Am. Jr. Surg., 1923, Vol. 37, pp.118-121

XXXI   Bennon, R.   Infective Osteomyelitis.
Surg. Gyn. & Obst., 1928, Vol.47, pp. 44-52

XXXII   Duval, E. C.   Physical Therapy in Acute Osteomyelitis.
Archives of Physical Therapy, 1928, Vol. 9, pp. 399-403

XXXIII   Garr, C. C.   Osteomyelitis, Acute and Chronic. Study of 58 cases.
Kentucky Med. Jr., 1927, Vol. 25, pp. 80-82.

XXXIV   Taylor, H.   The Problem of Acute Osteomyelitis.
South. Med. Jr., 1930, Vol. 92, pp 511-515

XXXV   Orr, H. W.   Treatment of Osteomyelitis and Other Infected Wounds.
Surg. Gyn. & Obst., Oct., 1927, pp446-464

XXXVI   Orr, H. W.   Treatment of Osteomyelitis by Drainage and Rest.
Nebraska Med. Jr. 1927, Vol. 12, pp. 222-224

XXXVII   Bitting, N. D.   Acute Osteomyelitis and Complications.
South. Med. Jr.,1929, Vol. 22,pp.580-583

XXXVIII   Albee, F. H.   Principles of Bacteriophage Applied to Osteomyelitis.
International Jr. Med. & Surg., 1929, Vol. 42, pp. 1-11

XXXIX   Henry, M. O.   Orr Method in the Treatment of Acute Osteomyelitis.
Lancet, 1928, Vol. 48, pp. 240-242