Chronic osteomyelitis: with special reference to treatment

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CHRONIC OSTEOMYELITIS WITH SPECIAL REFERENCE TO TREATMENT

by

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INTRODUCTION

The object of this paper is to review rather generally the problems facing the physician in patients with bone infections, especially chronic bone infections. The main problem in chronic osteomyelitis is the treatment of the condition. In order to consider the problem properly it is necessary to take up all phases of the disease including acute bone infections. It is important in discussing treatment to know the possible etiologic agents, predisposing causes, incidence, pathology, symptoms, and complications and these will be considered briefly here.

Etiologic agents will be discussed here rather extensively (for the size of the paper) for the reason that in most instances in discussion of osteomyelitis they are not considered as a group but singly or not at all.

Treatment of osteomyelitis, both acute and chronic, as it appears in the literature has in the past been rather confusing. There are almost as many methods as there are physicians and surgeons treating the disease. For this reason an attempt will be made to gain the consensus of opinion and the trends toward present day treatment.

A general review of previous methods of treatment and their effectiveness in the past will be presented as
will also the most widely accepted present day methods of treatment and their results.

Complications and statistics regarding them will be presented to gain an idea of the problems yet to be overcome in treatment of this important disease.
ETIOLOGY

There is no sharp line of demarcation between acute and chronic osteomyelitis. Just where an acute hematogenous osteomyelitis becomes chronic depends more or less on the individual surgeon. Therefore in many cases the organism involved in the acute hematogenous osteomyelitis is the same when the infection becomes chronic. There are some bone infections which have no acute course and are considered subacute or chronic when first recognized.

Common Causes Of Osteomyelitis

Infection reaches the bone in three ways: by the blood stream; by direct extension from soft parts; by open wounds of the bones.

Infection by blood stream——. Hematogenous osteomyelitis is by far the most common form of infection. The hemolytic staphylococcus is the cause of the blood born infection in about 90 percent of the cases (69). The staphylococcus aureus is found twice as often as staphylococcus albus (69), and is present in about 75 percent of cases (75). The skin is the most frequent portal of entry for this organism. In the first month of life, infections such as folliculitis are the most common cause of osteomyelitis. It may develop also from infection of the umbilical cord and occasionally from
an infected cephalematoma. Later in life boils are the most frequent predisposing lesions. Others less common are: paronychiae, acne mustules, blisters arising from friction, burns, freezing, impetigo, eczema, chickenpox, smallpox, and vaccination. In adults a carbuncle is occasionally a cause. Small wounds apparently produce osteomyelitis more often than do large deep ones.

Infection by direct extension from soft parts—.

In comparison with hematogenous osteomyelitis this occurs rather rarely. According to Kulowski (47) these comprise about 25 percent of all cases of osteomyelitis. It is seen most frequently as a result of infection of accessory sinuses, staphylococci, streptococci or pneumococci being the most common organisms involved, and the middle ear with the pneumococcus and the streptococcus being the causative organism here. The phalanges of the fingers may be infected from the adjoining soft parts and also osteomyelitis may develop from a primary arthritis by direct extension.

Decubitus ulcers and extensive chronic varicose ulcers may extend down to bone, the staphylococcus, streptococcus, and the colon bacillus being the most common organisms. Simple fracture, with a non-communicating wound of soft parts may become infected by direct extension.
Infection by open wounds of the bones---. Osteomyelitis may develop in several types of fractures: I. Open wounds in which there is a fracture. This infection usually remains localized but may become diffuse. 2. Osteomyelitis following operation on a simple fracture in which the simple fracture is made compound. Cleveland (2I) feels that entirely too many chronic suppurative bone and joint infections "are due to ill-advised original surgical treatment, where superimposed on vascular and infectious trauma is the insult of improperly placed incisions, too wide removal of uninvolved bone and failure to immobilize the damaged part." 3. Skeletal traction producing osteomyelitis at sites of introduction of tongs, pins, and wires.

Also should be mentioned here, the importance of proper transporting of a patient with a simple fracture in order to prevent compounding of the fracture. Too many patients are subjected to a long drawn out disabling disease because of neglect or ignorance in handling a simple fracture at the time of the accident. Gunshot wounds involving bone especially when produced by shell fragments are particularly apt to result in osteomyelitis. Extraction of teeth, block anesthesia, or curettage of apical abscesses may lead to osteomyelitis of the jaw. (69, 75, 36, 40, 2I, 47).
Unusual Causative Agents In Osteomyelitis

The more uncommon and rare organisms causing osteomyelitis will be considered here because of their infrequent mention in textbooks and because they are usually so lightly skimmed over generally. Every attempt should be made to recognize the causative organism in osteomyelitis because of the importance in prognosis and treatment. (7).

I. The streptococcus as a cause of osteomyelitis--.
The hemolytic streptococcus is the causative organism in about 3 to 5 percent of cases of osteomyelitis. The usual known portal of entry is the respiratory tract. Predisposing conditions are acute otitis media, acute rhinitis, tonsillitis, bronchitis, influenza, pneumonia, lung abscess, and empyema. Very often the portal of entry cannot be determined. The streptococcus is considered the most frequent secondary invader in those debilitated from chronic bone infection. (75, 49).

Hemic infections due to streptococcus behave differently from those due to the staphylococcus as is shown by both the general reaction and the local reaction. (7). There are many cases of streptococcus osteomyelitis reported in the literature. Hosmer, Burnham, and Davis '40 (32), report an unusual case resulting from sinus disease due to a hemolytic streptococcus, and associated
with particularly severe diabetes and with recovery
from the bone infection. In 1926, Phemister and Gordon
(23) reported two cases of solitary bone cyst in which
streptococcus viridans was isolated. Few attempts have
been made to culture organisms from the solitary bone
cyst, benign giant cell tumor, or osteitis fibrosa.
Day (23) reported two cases in which streptococcus
viridans was found in bone cysts but in eight other cases
no etiological agent was found. Compere (23) reported
a case of localized osteitis fibrosa without cyst
formation in which streptococcus viridans was recov­
ered. Another similar case was negative as to an et­
iological agent. Phemister and Gordon do not believe
there is as yet enough evidence to consider the benign
giant cell tumor as a chronic inflammation caused by
a bacterial agent.

2. The pneumococcus--is a less frequent cause of
osteomyelitis than the streptococcus and usually prod­
uces the disease as a complication of either pneumonia
or otitis media. (23).

3. The typhoid bacillus--. In 1835 Maisonneuve
first recognized osteomyelitis as a complication of
osteomyelitis. According to Winslow (39), .45 percent
of all osteomyelitis cases are caused by the typhoid
organism. This organism is considered to be practically
always associated with subacute or chronic osteomyelitis from the beginning. (75).

There are an interesting group of cases reported which yield pure cultures of typhoid bacilli after the sinuses have remained open months and years. Bunts (89) reports the recovery of a pure culture of typhoid from a tibial abscess 17 years after the appearance of the attack. Fogh (89) mentions their existence for 13 years in the ulna; Gere (89) for 11 years in the frontal bone and a number of observers for periods ranging from a year upwards.

4. The colon bacillus is probably next in frequency but apparently is quite rare judging from the fact that Cooperman and Leventhal (24) found only eight cases reported in the literature. It may be that others have not been recognized or that they have been seen and not reported. Wilensky (87) is of the opinion that except for direct infection colon-bacillus osteomyelitis is secondary to a lesion in the gastro-intestinal tract through which the bacillus gains entrance to the blood stream.

Cooperman and Leventhal (24) report a case of osteomyelitis of the femur caused by the colon bacillus and thought to be secondary to a pathological gall-bladder. Dickson, Lively, and Kiene (26) report one case of
osteomyelitis caused by this bacillus and found sulphathiazole had no effect on it.

5. The influenza bacillus has been isolated in a very few cases. Zweig has reported one case.

6. The tubercle bacillus--. Infection of the bone by this organism is usually secondary to some tuberculous focus elsewhere in the body. It is considered most likely to be blood borne. (6).

Basom (6) of the Mayo Foundation states that tuberculous lesions of long bones are rare. In the records of the Mayo Clinic a series of 18 completely studied cases were found. 75 percent of the patients were male. Two-thirds had no history of trauma.

7. The gonococcus--. Gonorrheal infections of bone are quite rare few cases ever being reported. Bardenwerper (5) reports one case in a young female of 20 years. He states that the infection is particularly rare in females. Still rarer is a case of gonorrheal osteomyelitis in the infant. Palew (65) reports a case in a two week old infant. He claims no other similar case has been reported in the literature. The infection was in the left tibia and the causative organism was checked twice because at first it was thought a mistake had been made. (28).

8. The spirochete of syphilis--. Syphilis of bone
is more common than most of the previously mentioned infections. It may be congenital but is more often a disease of adults between the ages of 20 and 40 years. It is a secondary or tertiary phenomenon and is seldom seen before two years following the infection. (81). Mendelbaum and Saperstein (54) report a case of acute gummatous osteomyelitis in which syphilis was acquired through the medium of blood transfusion.

9. The organism of paratyphoid fever--. Osteomyelitis is a rare complication of paratyphoid fever. Jetter (37) reports a case due to S. schottmulleri with unusual widespread involvement of bone and ending fatally. According to Jetter there are only 18 other cases reported in the literature.

10. The organism of Malta fever--. Osteomyelitis complicating Malta fever is uncommon but Kulowski (48) feels that the diagnosis is often missed simply because the possibility is not thought of. He reports osseous and joint lesions in five adult males in which the infecting organism was Brucella melitensis.

11. The smallpox virus--. Bone infection during or as a sequel to smallpox is a comparatively rare condition. There are two distinct forms of osteomyelitis in this disease. One type is the ordinary pyogenic metastatic osteomyelitis that occurs in other infectious diseases.
The other type is a distinct form of necrosing non-suppurative osteomyelitis probably due to the specific virus of smallpox. It is of course most frequently seen in children. (14). W. L. Brown and C. P. Brown reported two cases in 1923. (14).

12. The anaerobic bacteria--. These organisms are rarely observed in osteomyelitis. (49). Baer (3) in treating his first cases of osteomyelitis with maggots sometimes found secondary infections by the tetanus bacillus and Cl. welchii.

13. The mycotic organisms--. Mycotic lesions are often widespread infections but in general are rather uncommon causes of osteomyelitis. Actinomycosis most frequently involves the vertebrae, ribs, sternum, and jaws, but rarely is an independent lesion. The spirithrix produces a suppurative osteomyelitis with abscess formation and pathological fracture. (49).

Coccidiodal osteomyelitis is caused by a specific fungus Coccidiodes immittis. The exact classification of the organism is still unsettled. McMaster and Gilfillan (56) report 24 cases of bone and joint involvement by this organism and there are numerous other reports in the literature on the disease.

Osteomyelitis following frost-bite--. There are few cases of osteomyelitis complicating frost-bite reported
in the literature according to Scott and Pigott (72) and modern textbooks do not give it as a complication of frost-bite. These men report a case of osteomyelitis in the small bones of the extremities following severe frost-bite of these members and associated with marked gangrene of the fingers and only very small areas of gangrene on the toes. The infection was probably favored by both vascular and nerve damage in this case and not by mere chance infection. (72).

Osteomyelitis complicating infections of the gastrointestinal tract--. Osteomyelitis secondary to genitourinary pathology is rare. Kretschmer and Ockuly (45) report three cases each one occurring in a male of more than 50 years. They state that only one other case is reported in the literature and that by Pederson; an osteomyelitis of the humerus secondary to abscess of the prostate. In their cases the head of the tibia head of femur, and the bodies of the sixth and seventh dorsal vertebrae were involved.

Predisposing Causes

General lowered resistance of the body frequently precedes the development of infections of bone. Trauma apparently is a common predisposing cause. (69). Schmidt (73) found a history of trauma in two-thirds of the cases analyzed in the surgical clinic at Bonn.
McCarrol and Key (55) reviewed 200 cases of chronic osteomyelitis admitted to the St. Louis unit of the Shriner's Hospital for Crippled Children between the years 1924 and 1938. No patients were admitted in whom the disease had resulted from a compound fracture or from extension of an infection from neighboring tissues. 25 percent of the patients gave a history of a definite injury during the preceding week and 40 percent during the month preceding the development of the disease. These men believe it probable that in a considerable percentage of the cases trauma played a part in inaugurating the disease or in determining the site of the primary focus. It is their opinion that most of the patients were apparently normal healthy children in whom the disease developed suddenly and for some unknown reason.

Osteomyelitis, as mentioned previously, is occasionally a complication of infections of lungs or pleura such as pneumonia. Lung abscess, bronchiectasis, and empyema are rarely complicated by bone infection. Also lesions of the gastro-intestinal tract other than typhoid such as cholecystitis, appendicitis, and colitis, are rarely complicated by osteomyelitis. Contagious diseases such as measles, diphtheria, whooping cough, and scarlet fever are rarely complicated by osteomyelitis. (69)
In the McCarrol, Key series preceding illness and foci of infection were not mentioned with sufficient frequency to be of etiological significance according to them. (55).

There is some variation in the frequency of osteomyelitis with the seasons. Tichy (84) claims that cold or damp weather predisposes to its development presumably by increasing the liability to skin infections. Boils which are common predisposing lesions are most prevalent during the warm weather. According to Van Oordt there is a rapid increase in the number of organisms in the skin during foggy weather as a result of the shutting out of ultraviolet rays. (69).

Incidence

The onset of the majority of cases of osteomyelitis is in the first or second decade of life. (47). Probably children from 2 to 12 years are most often affected. (75). McCarrol and Key (55) found the ages ranged from 10 months to 14 years, the average being 7.7 years.

Hematogenous osteomyelitis affects male children twice as frequently as female. (47). McCarrol and Key found in their series, 123 or 64 percent were boys and 72 or 36 percent were girls. (55). Shipley (75) says the proportion is three or four boys to one girl. This is probably due to the fact that boys are more
exposed to injury and infection. (69).

The following is a table which appeared in an article by Kulowski in the Journal of the Missouri Medical Association in 1935 (49) on "Unusual Pyogenic Osteomyelitis".

The Anatomical Distribution of 1484 Cases of Pyogenic Osteomyelitis

<table>
<thead>
<tr>
<th></th>
<th>Males 1130</th>
<th>Cases</th>
<th>Females 441</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower extremity</td>
<td>1064</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper extremity</td>
<td>220</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Spine and pelvis</td>
<td>138</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Head bones</td>
<td>42</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Chest wall</td>
<td>20</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Unusual localizations</td>
<td>595</td>
<td>40%</td>
<td></td>
</tr>
</tbody>
</table>

The primary lesion in the McCarrol, Key series was in the lower extremities in 83.5 percent and there were no instances in which the primary focus was in the spine or cranium.

There is some disagreement as to whether the femur or tibia is more frequently involved but these two bones and the humerus comprise by far most of the cases of osteomyelitis. Nathan Smith (76), in a report on osteomyelitis in 1827 states that in his own experience he found the tibia to be the frequent site of the disease, next, the femur, and then the humerus. Phemister states (69),
that the femur, tibia, and humerus are most often affected and published a report by Klemm of 385 separate lesions in 320 cases of osteomyelitis in his chapter on pyogenic osteomyelitis in Nelson Loose Leaf Surgery Vol. III Chapt. VII. Klemm's distributions were:

<table>
<thead>
<tr>
<th>Bone</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>111</td>
</tr>
<tr>
<td>Tibia</td>
<td>101</td>
</tr>
<tr>
<td>Humerus</td>
<td>27</td>
</tr>
<tr>
<td>Os ilii</td>
<td>26</td>
</tr>
<tr>
<td>Fibula</td>
<td>23</td>
</tr>
<tr>
<td>Calcaneus</td>
<td>19</td>
</tr>
<tr>
<td>Skull</td>
<td>11</td>
</tr>
<tr>
<td>Radius</td>
<td>8</td>
</tr>
<tr>
<td>Ulna</td>
<td>8</td>
</tr>
<tr>
<td>Metatarsus</td>
<td>8</td>
</tr>
<tr>
<td>Talus</td>
<td>8</td>
</tr>
<tr>
<td>Clavicle</td>
<td>7</td>
</tr>
<tr>
<td>Sacrum</td>
<td>6</td>
</tr>
<tr>
<td>Vertebrae</td>
<td>4</td>
</tr>
<tr>
<td>Sternum</td>
<td>3</td>
</tr>
<tr>
<td>Ribs</td>
<td>3</td>
</tr>
<tr>
<td>Scapula</td>
<td>3</td>
</tr>
<tr>
<td>Os pubis</td>
<td>2</td>
</tr>
<tr>
<td>Os ischii</td>
<td>2</td>
</tr>
</tbody>
</table>
Os cuboideum..............1
Phalanx digiti pedis.......1
Phalanx digiti manus.......1
Metacarpus.................1

According to Phemister the frequency of involvement of phalanges, metacarpals, jaw bones, and ribs in this series is lower than that of the average series of cases.

Kulowski (47) believes that lesions of the spine and pelvis are more common than has previously been suspected.

The etiology of osteomyelitis seems to have little to do with the distribution. In cases of tuberculosis of bone reported by Basom (6) from the records of the Mayo Clinic, the tibia was involved most frequently and the femur and humerus were next in order. In typhoidal osteomyelitis, Winslow (89) reported the tibia, femur, and ribs in the order named as the bones most frequently attacked but stated that no bone is immune. Kulowski (48) , in a report of five cases of osteomyelitis caused by Brucella melitensis found two instances of spondylitis, one of a humerus, one of the wrist joint, and one instance involving the skull and ribs.
The true pathology of osteomyelitis has not been until rather recently realized. Nathan Smith (76) in 1827 in an article on "Observations On Pathology and Treatment of Necrosis" wrote as "the etymological definition of necrosis" -- "the death of some part of the bony structure." In the same article he wrote of osteomyelitis or "necrosis" as it was called, "Medical men while humoral pathology prevailed, probably would have explained it in the following manner: The fever to expel the morbific matter from the system, throws it on the part affected, which causes the inflammation and subsequent collection of matters." Surprisingly, though Smith did not have the correct concept of the pathology involved, his surgical treatment of osteomyelitis was quite modern.

Acute and Chronic Osteomyelitis

The course of osteomyelitis is divided pathologically into three stages: 1. the acute stage which is the stage of infection, necrosis, suppuration, and general intoxication; 2. the subacute stage which begins with the evacuation of the purulent exudate and the cessation of toxic absorption; 3. the chronic stage which is characterized by formation of sequestrum,
involucrum, and sinuses. (58).

The usual pathologic picture of hematogenous osteomyelitis is that of a thrombo-embolic process attended by suppuration and necrosis and based in part upon the locally induced anemia. The majority of osteomyelitic lesions and especially in children seem to be on the diaphyseal side of the epiphyseal cartilage. (74,13). Siegling (74) attributes this to the fact that the blood supply at this site consists of terminal arteries in which infective emboli lodge and multiply.

Hobo (55) found that bacteria and carbon particles injected into the blood of experimental animals tended to localize in dilated capillary loops in the metaphysis adjacent to the epiphyseal cartilage plate where the blood stream was slowed. McCarrrol and Key (55) do not believe Hobo's work explains the predilection of the disease for this area. They point out the fact that in the large sinusoids of the spleen and red bone marrow the blood current practically stops at times and wonder why these areas are not affected if the localization is due to a slowing of the blood stream.

After localization in the metaphysis near the epiphyseal line, the infection usually breaks through the bone at this point and reaches the periosteum. It was formerly thought that the usual method of spread
was along the medullary canal but in 1922 Starr (78) showed that the infection spread outward from within the metaphysis broke through the bone beneath the periosteum and if not drained at this point went on to detach the periosteum over a large area and travel through the Haversian canal system to the medulla. In these severe cases where the infective process is not stopped by adequate treatment there is widespread necrosis with large areas of detached periosteum and extensive involvement of the medulla. The periosteum may be broken through later and pus found in the medulla, in the cancellated bone, under the periosteum, and in the soft tissues outside. As a rule a portion of the infected marrow and cortex becomes necrotic over a greater or less extent, depending on when the process is stopped, and persists for a time as a sequestrum. If, on the other hand drainage is established within a few hours of the onset, recovery may take place before there is much detachment of the periosteum or extensive damage to cortex and medulla. (58).

Microscopically, dead and dying bone cells in large and small areas are found surrounded by bacteria and leukocytes in the cortex and medulla. Beneath the periosteum in the diseased area, the same bacteria and toxins which destroyed bone deeper, are here stimulating the
formation of new bone. The same factor which produces the sequestrum by destroying the life of the bone, causes the periosteum to generate involucrum. A cross section through the subperiosteal areas shows budding capillaries growing from the detached periosteum toward the diseased cortex. There are new bone cells seen in large numbers everywhere among the loops of minute blood vessels. Bacteria and leukocytes are in great numbers in the new granulation tissue. Thus the separated portion of the periosteum begins to produce a shell of new bone or involucrum which surrounds the necrotic shaft. (83).

Ollier (61) in 1867 was the first to demonstrate by experimental work the regenerative power of the periosteum and its ability to regenerate an entire bone. He did not however recognize the ability of the endosteum to regenerate bone. (58).

Nichols (58) in 1904 demonstrated that the bone marrow and endosteum were as important in the regenerative power of bone as the periosteum.

The invading granulation tissue described above furnishes food for the osteoblasts and newly formed bone cells. The bone cells proliferate, displace the granulations and form normal bone tissue. The bacteria
and leukocytes are meanwhile eliminated and healthy bone is left. Concavities that are too deep do not heal because the granulations become choked off by scar tissue formation before they have spread to the depths. (83).

In general repair within the shaft is brought about by the formation of granulation tissue which arises from the reticulum of the bone marrow and of new bone which arises from the endosteum.

**Brodie's Abscess**

This is considered a primary chronic lesion and it occurs typically in the ends of long bones. It is a localized area of reduced density which is lined by a membrane and surrounded by a reactive zone of sclerosis. (49).

**Sclerosing Non-suppurative Osteomyelitis**

Kluppel (38) first described the condition in a boy of 12 years in 1879 but Garre (32) in 1891 described it as a definite clinical entity, and the disease is also known by his name. There is a spindle form thickening of the cortex of the long bones. It occurs in children and there is not much local or general disturbance and usually ends in recovery. The etiology is unknown. There is a permanent osseous enlargement remaining after all signs and symptoms disappear. (38).
The mode of tissue response in this condition suggests to Klein (43) an attenuated infection. He believes either the bacteria are not highly virulent or else the body is more resistant than in the classical type of osteomyelitis or possibly the infection first localizes in an atypical part of bone; cortex instead of diaphysis.

There is also a mysterious form of non-suppurative osteomyelitis called "quiet necrosis" described by Paget. The sequestrum is eroded on all surfaces by caries rather than by the usual gross process of necrosis in ordinary osteomyelitis. The separation is not complete and there is no line of demarcation. It is apparently induced by an anemia of the deeper portions of the compact bone and not by the sudden blocking of its circulation by an acute and virulent inflammatory exudate as in acute osteomyelitis. The disease is usually seen in elderly individuals. (49).

It is interesting to note that tuberculosis of bone is not always characterized by destruction of bone. Proliferation of bone may occur if the compact or cortical areas are involved. It is the reaction of the bone to the etiologic agent rather than the specific type of invading organism present which determines the gross pathologic picture. Most of these bone infections show both. (6).
SYMPTOMS AND DIAGNOSIS

Acute osteomyelitis--. The onset is sudden. Most children are very ill from the beginning of the infection. Sometimes there is such rapid progress of the disease that delirium and coma supervene before localizing signs and symptoms are evident, though this is not usually the case. The face is florid and there is profuse sweating, restlessness and anxiety. The outstanding symptom is local pain which is continuous, deep, boring, and severe and the outstanding sign is exquisite tenderness on pressure over the bone, with increase indiscomfort brought out by tapping along the shaft of the affected bone.

The patient shows high fever, rapid pulse, dehydration, exhaustion from pain, lack of sleep, and infection. Very often there is vomiting.

Roentgenograms are of no positive value in the early diagnosis of acute osteomyelitis.

If a child complains of pain over the end of a bone and does not want to move it, if there is tenderness on deep pressure over a bone, as well as symptoms of an acute infectious process, if the onset of these signs and symptoms has been abrupt and if the evidences of infection are rapidly on the increase, a diagnosis
of acute osteomyelitis should be made. (75).

Chronic osteomyelitis-- is usually readily diagnosed by the existence of a sinus either spontaneous or from previous operation on an acute case. The X-ray usually clears up the question of diagnosis in these cases. (25). Chronic diffuse osteomyelitis is nearly always a sequela of acute diffuse osteomyelitis.

Chronic localized osteomyelitis begins with slight pain in the involved region slowly increasing in severity and may be nocturnal. Localized swelling and tenderness may be present. (69).

Occasionally an extensive primary infection of low grade develops with few or rarely no acute manifestations. The patient develops pain in the region of the bone, which is slight at first and is apt to be painful only at night or when the extremity is used. Swelling and tenderness may be absent or may slowly develop. General symptoms are usually absent or when present are slight. (69).
HISTORY OF TREATMENT

Infection of bone has been recognized for many ages by man, in fact it dates back to paleolithic times. (35). One of the earliest known works on osteomyelitis is the English translation of Ambrose Paré's Surgery Book 19, Chapter 26 (21) published in London in 1634 entitled "Why Bones Become Rotten and By What Signs It May Be Perceived." This was nearly 250 years before Pasteur's experiments established bacteriology and afforded the possibility of studying the infections.

Wounds were treated by primitive man by dressing them with moss, fresh leaves, ashes or natural balsams, and when poisoned treated by sucking and cauterizing with red hot irons. (21).

In Homer's time the spear and arrow wounds were treated with healing ointments, pounded root, astringent, and anodyne. Appropriate incantations were then fervently recited in order to help the wound heal. Religious influence was strong in the pre-Christian era in medicine. Celsus, who was a famous Roman surgeon in the reign of Tiberius used emollient salves in wounds and called on the gods to help. The Greeks called on the aid of Apollo and Aesculepius. (1).

In 1100 there was more faith in sucking wounds than
HISTORY OF TREATMENT

Infection of bone has been recognized for many ages by man, in fact it dates back to paleolithic times. (35). One of the earliest known works on osteomyelitis is the English translation of Ambrose Pare's Surgery Book 19, Chapter 26 (21) published in London in 1634 entitled "Why Bones Become Rotten and By What Signs It May Be Perceived." This was nearly 250 years before Pasteur's experiments established bacteriology and afforded the possibility of studying the infections.

Wounds were treated by primitive man by dressing them with moss, fresh leaves, ashes or natural balsams, and when poisoned treated by sucking and cauterizing with red hot irons. (21).

In Homer's time the spear and arrow wounds were treated with healing ointments, pounded root, astringent, and anodyne. Appropriate incantations were then fervently recited in order to help the wound heal. Religious influence was strong in the pre-Christian era in medicine. Celsus, who was a famous Roman surgeon in the reign of Tiberius used emollient salves in wounds and called on the gods to help. The Greeks called on the aid of Apollo and Aesculepius. (1).

In 1100 there was more faith in sucking wounds than
in dressing them. Sybella, beautiful wife of the Duke of Normandy sucked the poison from a terrible wound in his thigh and as a result saved his life but sacrificed her own.

In the middle ages repulsive remedies were in great favor in treatment of wounds. Crushed body lice, incinerated toads, Egyptian mummy powder, and heron imported from the Orient were used.

In Pare's time (1509-1590), it was common for maggots to breed in a wound and the favorite precaution against wound infection was to pour boiling oil or molten pitch in which elderberry bark had been dissolved into the wound. He also took considerable pains to give a good diet and keep the patient comfortable. In one case which had been treated by other physicians Pare ordered the patient's linen changed, he made three openings in the thigh, took out the bone splinters, cleaned the wound with boiling oil, put in drains, and applied plaster with a window. He then ordered the patient to eat a list of delectables, smell flowers of herbane and water lilies bruised with vinegar and rose water with a little camphor, for hours. Music was provided and a comedian to make the patient happy. In one battle Pare ran out of boiling oil in treating wounds and as a last resort used a cold mixture of yolk
of egg, oil of roses, and turpentine instead. The next morning those treated with the yolk of egg etc. were so much better than those treated with boiling oil that Pare thereafter used the cold dressing. (1).

In the 1700's Heister, a German Army Surgeon and others of this time, used salves, plasters, vitriol, nitrate of silver, and lint. Gooch used a wax sheath to cover his wounds and left them alone.

The early German school probed the infected wounds unmercifully and filled them with lint. This persisted for nearly 200 years.

Richter later adhered to the principle that Nature accomplished the healing and all the surgeon had to do was to remove grave obstacles. (1).

Bell insisted on the free and unobstructed flow of pus and introduced lead tubes.

Debridement, probably the most important advance in treatment of wounds was first described by Petit in the first half of the eighteenth century. However it probably even originated long before this (40).

To the end of the eighteenth century the dogma of the injurious effect of atmospheric air on wounds prevailed. (1).

Before the period of Lister in the nineteenth century, surgeons were unable to cope with infections
and they had to resort to amputation frequently, in bone infections and infections of all kinds. This operation in itself carried a high mortality. Up to Lister's time any patient who recovered after a compound fracture, no matter what the deformity and disability was considered to have done well. (40).

On August 9, 1867 Lister, then professor of surgery at the University of Glasgow, spoke before the British Medical Association at a meeting in Dublin "On the Antiseptic Principle In the Practice of Surgery." This was the beginning of a revolution in the practice of surgery which, however, progressed slowly. Eight years later, in 1875 at Edinburgh, Lister again, before this same association, gave his address "On the Effect of the Antiseptic Upon General Salubrity of Surgical Hospitals." In this address he brought together his own observations and clinical experiences, and those of a number of other distinguished teachers of surgery as to the clinical value of asepsis and antisepsis. When Lister became professor of King's College, London in 1877 there were not more than three or four surgeons in London employing the antiseptic method. Since that time and up to the present there has been less regard for the original antiseptic principle in treatment of most cases of osteomyelitis of compound fractures.
and other infected wounds than there would have been by Lister himself in 1870. (63).

In 1874, Sir W. Howes advocated a method of treatment that was very close to the modern method. He opened the bone cavity from end to end, lifted out the sequestrum and allowed the wound to granulate. (52).

In 1881, Hamilton advanced the idea of hastening healing by packing the cavity with sea sponges to furnish a scaffolding for the new bone formation.

In 1885, the first number of the Annals of Surgery contained an article by Keetling of England, in which he advocated sterilization of the bone by scraping out the marrow completely and swabbing with carbolic acid and strong bichloride of mercury solutions, followed by thorough drainage with a large rubber tube. (52).

Neuber in 1886 was the first to describe a method of treating bone cavities, following operations for osteomyelitis, by turning flaps of skin and other soft tissues into the cavity. This principle has since been widely employed. (71).

John Hunter enunciated the employment of the natural forces of repair in surgery practice. John Hilton set forth the protection of the patient against irritation, motion, and muscle spasm. Hugh Owen Thomas of Liverpool and Sir Robert Jones advocated the use of
mechanical apparatus to secure immobilization and rest in correct position. (63).

The earliest mention of operations undertaken on the principles laid down by Ollier, 1867, (the regenerative power of the periosteum), in this country are in the Medical and Surgical Reports of the Boston City Hospital. However these cases were undertaken because of special indications in the individual cases and the general principles underlying the operation did not seem to be recognized and no attempt was made to formulate any general operative procedure. (58).

Nichol's principles of treatment of osteomyelitis were based on a theory he formulated while working on the pathology of bone lesions in Sear's Laboratory of the Harvard Medical School in 1895. From a study of a considerable number of cases of osteomyelitis he thought it might be possible to remove the necrotic shaft of bone early and approximate the inner surface of the periosteum and in this way obtain a shaft by proliferation from the periosteum, which would serve the function of the removed necrotic shaft. He reasoned from anatomical and pathologic facts that the time to remove the necrotic bone was, not during the acute stage because of the intense infection and difficulties in manipulating the periosteum, but later when the acute
suppuration and infection was no longer present and the membrane just rigid enough to manipulate. This idea was first publicly stated in a paper read before the Massachusetts Medical Society June 7, 1898, although it had previously been taught in the class rooms for three years. (58).

Dr. Hayward W. Cushing of Boston was the first to perform the operation based on this theory. It was a complete success and the results obtained by various other surgeons were uniformly good. (58).

Later, in 1904, Nichols demonstrated that the bone marrow and endosteum were as important in the regeneration of bone as the periosteum, and that thorough scraping and strong antiseptic as previously employed in treatment delayed healing. (52).

From 1917 to 1919 in the military hospitals there was constant use of chemicals of all kinds in compresses, fomentations, drainage tubes, irrigations, and frequent dressings. Neither the wound nor the patient had protection or rest. Wounds were constantly contaminated by all sorts of organisms carried by the surgeon and his assistants. S tints were loosely applied and even removed so dressings could be put on. Plaster of Paris bandages were fenestrated, split, or bivalved so that they never were or soon ceased to be efficient.
for immobilization which is now known to be so important in treatment of osteomyelitis. (63).

During the first World War, Baer (3) made an observation which led to his investigation of the treatment of chronic osteomyelitis with maggots. At a certain battle in 1917 two soldiers with compound fractures of the femur and large flesh wounds of the abdomen and scrotum were taken to the hospital. Both of these men had been missed when the wounded were picked up and had lain for seven days in the brush on the battlefield without food or water and exposed to the weather and insects. On their arrival at the hospital they were fever free and there was no evidence of septicemia. Their condition was remarkably good and if it had not been for their starvation and thirst they would have been in excellent condition. On removing the clothing from the wounds there were thousands upon thousands of maggots swarming in and about them. The sight was very disgusting to the surgeons and they immediately washed out the maggots with normal saline. Instead of the pus which they expected to find, healthy looking granulation tissue was seen. There was practically no bare bone and the internal structures of the wounded bone, as well the surrounding parts were covered with granulation tissue which filled the wound. Bacterial
they destroy that tissue they do in time what the surgical operation does." Dr. Edward Martin of Philadelphi, said before the same session of the Clinical Congress of Surgeons of North America that they had "been advised by one eminent member of the profession to take all the antiseptics and throw them into the sea and another had advised them to raise a brood of tame maggots to take care of the wounds." (3).

However, no mention had been made of any experimental or voluntary use of the maggot in wound treatment in time of peace before Baer's time.

Before the war the surgeon gave most of his attention to aseptic methods, his great object being to exclude microbes from the wound. He was not interested in how to deal with the bacteria after they were in the wound. The wounds were dressed once or twice a day with various antiseptics like carbolic acid, mercury salts, and boric acid. (28).

In 1914 at the beginning of the war all the old antiseptics; carbolic acid, perchloride or bichloride of mercury, boric acid, and hydrogen peroxide, were poured into septic wounds once or twice daily. Soon campaigns were started for particular antiseptics and early in 1915 pure carbolic acid and 20 percent iodine came into use. A short time later antiseptics in packs
were advocated. The wound was plugged and it was soon found that this interfered with drainage and gas infections developed in many cases. (28).

The first real advance in the use of antiseptics for treatment of wounds was the introduction of the hypochloritic solution. Lorrain Smith introduced a solution of hypochlorous acid, Dakin a solution of sodium hypochlorite. New surgical procedures were also introduced at this time and the importance of thorough surgical cleansing was recognized. Carrel introduced his system of intermittent irrigation with antiseptic solution and the Carrel-Dakin treatment came into being. (28).

After the Carrel-Dakin treatment, came the era of B. I. P. P., a paste of iodoform, bismuth, and paraffin. It was, however, combined with thorough surgical cleansing of the wound and also, after treatment of the wound with the paste, it was not touched thus obtaining complete rest for the part. B. I. P. P. was not in itself an antiseptic. (28).

After B. I. P. P. came the dye-stuffs. Flavine became popular but it was soon found that when a wound was treated with flavine 1:1000 for more than a few days all the reparative processes stopped, while the flavine did not sterilize the wound. It was discontinued
as treatment for septic wounds. (28).

In 1923 Orr introduced his method of vaseline dressing with germicidal powder and cast for weeks without disturbing the wound. (1).

Albee, after using the Orr treatment for a time, decided there was something besides the rest, immobilization, non-interference, and avoidance of reinfection that was making this treatment successful. He concluded there was some relation between what d'Herelle, a French Bacteriologist at Yale University found in 1923 and in a phenomenon in treatment of osteomyelitis. d'Herelle found an ultramicroscopical parasite of pathogenic bacteria which had markedly beneficial results in certain acute intestinal diseases. He called this bacteriophage. Albee claimed that a bacteriophage was formed in cases of osteomyelitis treated by the Orr method and this was what made it effective. He developed a phage in the laboratory which he used in treatment of osteomyelitis. (5).
TREATMENT

The discussion of treatment here will be limited mostly to the various accepted methods of treatment used today in chronic osteomyelitis and their comparative effectiveness.

As in other infectious processes the most effective treatment of chronic osteomyelitis is preventative. Since most cases of chronic osteomyelitis are a continuation of an acute process, it is important to consider the prevention of acute osteomyelitis.

First of all, simple fractures must be properly immobilized to prevent them from becoming compounded while transporting the patient. Patients with simple fractures of long bones should not be moved at all until proper traction has been applied. The compounding of a simple fracture by performing an open operation on it frequently leads to osteomyelitis. Kennedy (40) says, "We should never subject a patient with a simple fracture to the compounding of an open reduction unless we have confidence in the capability of our entire team and the perfection of all our apparatus."

In a compound fracture of the long bones it is even more important to apply a fixed traction splint before moving the patient. It does not matter whether or not
the bone is projecting for it is more important to get the fracture in traction than it is to prevent a projecting fragment from re-entering the wound. The wound has to be handled at the hospital as a potentially infected one regardless. The excess dirt however should be wiped away from the wound and a sterile dressing if available put over it. Also someone should see that the surgeon is told that the bone had been exposed.

Early attention to compounded fractures is a very important point in preventing bone infection. These are emergency cases. Treatment for shock should be begun immediately upon arrival at the hospital whether or not the patient is in shock at the time so that treatment of the fracture can be carried out as soon as possible. A thorough and prompt debridement of the wound is indicated in compound fractures and simultaneously traction is maintained on the extremity. In fractures compounded from the outside all foreign bodies, blood clots, tissue with ground in dirt and all tissue which seems too badly damaged to live are removed. The wound is left open after debridement unless it is not contaminated from outside dirt and then it often can be closed primarily. Reduction of the fracture is attended to at the same time as the debridement. Some type of fixation is
chosen, whether internal or external which is permanent and adequate so that there is no disturbance of the bony relationships during change of dressing. This is a potentially infected wound and any continuous slight change in position will increase the chances of a bone infection so gradual reduction by traction is dangerous. Complete immobilization of the fracture until union has taken place is essential. (40,21).

Early and adequate drainage of nearby soft tissue abscesses diminishes extension to nearby bones. Other measures of prevention are the eradication of etiologic and predisposing causes discussed previously under those headings.

Treatment of Acute Osteomyelitis

The exclusive treatment of acute osteomyelitis will be dealt with only briefly in this paper. However in some methods of treatment acute and chronic osteomyelitis are not differentiated since the principles are essentially the same. Also if for example, certain forms of treatment are instituted in the acute stage the infectious process may go into the chronic stage without change in treatment. These methods will be considered under treatment for chronic osteomyelitis.

Although there are numerous methods and much controversy over the treatment of acute osteomyelitis,
it is quite generally agreed that early adequate drainage and immobilization are the important principles. (40,22).

All osteomyelitis cases should be hospitalized immediately. Measures should be directed against the systemic infection at once, sedation, chemotherapy, immunotherapy, oral and parenteral fluids, and repeated small transfusions being advocated. (47).

The bone should then be drained as soon as possible provided the patient is in a condition to stand the operation. "Operation within the first week is considered early but not early enough." Incision is made in the overlying soft parts down to the periosteum. If there is pus beneath the periosteum a number of small holes are made in the cancellous portion of the bone and the medullary canal because it is involved by this time. If there is no pus beneath the periosteum, it is incised and a small hole is drilled into the bone near the epiphyseal line in the metaphysis. (75). Pus is almost always found here and the medullary canal is not yet involved. A curette should never be used at this stage to gouge out bone for cells upon which regeneration depends are destroyed. (7).

According to Cohn (22), after free drainage is established it is immaterial whether dichloramine T
or vaseline or anything else is used.

Starr, in 1922, advanced the treatment of acute osteomyelitis by drainage of the abscess early through small openings. Orr, in 1929, further improved treatment by adequate drainage, packing of the wound in the soft parts with vaseline gauze, and instituting complete rest of the part through immobilizing the limb within a plaster cast, and infrequent dressings. (7).

Early and adequate drainage, then, tends to prevent or limit the extent of the chronic bone infection and to decrease the number of instances in which joints or other bones are involved. (55).

Recently much work has been done with sulfanilamide and sulfathiazole in osteomyelitis. Their effect on chronic osteomyelitis will be considered later but here it can be said that these drugs are advocated for use in contaminated wounds and clean operative wounds in which infection is feared or undesirable. (41).

The administration of the sulfonamides in acute osteomyelitis is especially effective and very definitely indicated. Death from acute osteomyelitis is usually due to a septicemia and since the sulfonamides are more effective in the blood stream than elsewhere, the mortality has recently been greatly reduced in this disease.
Treatment of Chronic Osteomyelitis

The first and most important treatment of chronic osteomyelitis is operative. This is generally agreed; it is the after-treatment which is in constant controversy.

When is the proper time to operate a case of osteomyelitis? A bone should not be entered for the purpose of removing necrotic bone and establishing free open drainage until there is a sharp demarcation of the devitalized tissue from the living tissue. This can be determined largely by X-ray examination. Following the acute stage of osteomyelitis there is a period of time when the condition should be considered inoperable (with the exception of establishing drainage in the acute stage which is advocated by some men) but eventually may become operable. During this time the disease is diffuse and roentgenograms show no distinct outline between necrotic and living bone. An operative procedure at this time is absolutely contraindicated for much good bone might be removed and necrotic or diseased bone left. Also considered inoperable are those cases in which the whole shaft and medulla are replaced by diseased bone which may even obliterate the medullary canal. All the diseased bone could not be removed in this case without complete excision of the
shaft, a procedure which is inadvisable. When the
disease extends into an adjacent joint the problem is
more complicated and often is considered inoperable. (83).

The cases considered operable are those in which a
complete sculptural operation can be done removing all
sequestra and penetrating bone sinuses without too
greatly endangering the continuity and strength of the
remaining healthy bone. Thornton (83) gives the follow­
ing as the indication for radical operation; "When it
is learned from roentgenographic study that the process
of repair has progressed to such a stage that the line
of demarcation between the dead and the living bone has
become well defined, and when enough new bone has
formed to insure strength of the shaft of the bone,
then radical operation is indicated."

The object of the radical operation is to remove
all devitalized bone completely and to change the
contour of the remaining bone so that natural healing
may occur.

The operation briefly---; A tourniquet is applied
above the operative area so that a comparative blood­
less field is obtained. The periosteum is then de­
flected from the portion of bone to be removed and
left intact elsewhere. The sculpturing is done with
sharp chisels and a mallet. It must be done boldly
but with great care. All bone sinuses have to be completely destroyed even at the expense of a good deal of good bone because an infected penetrating bone sinus will not remain healed. It is very important to make deep cavities shallow and rough areas smooth so that soft tissue will fall into them. There is very little loss of blood and the shock if any is usually slight. When a complete operation has been performed a permanent cure can be expected for this is the crux of the cure of chronic osteomyelitis. (85, 26, 40, 62, 71).

Occasionally in a case extensive osteomyelitis with or without non-union an amputation may be more advisable than prolonged hospitalization with possibly a limb of slight usefulness when healing has been obtained. (40).

With the exception of a few minor variances in technique, the treatment of chronic osteomyelitis up to this point is generally agreed. But from this point on there are almost as many procedures as there are surgeons treating these cases. The methods most widely accepted and used will be considered first.

Common of Methods of Treatment

Orr Treatment

This is probably the most widespread method of treatment in use today. (26). Kulowski (46) in a study
of the literature found that Henry, Johson, Hey Groves, Albee, Kleinberg, Chu, and Kreuscher and Huepper report favorably on Orr's method. It is known as the method of immobilization and rest. (63). It embraces sound surgical and pathological principles by adequate drainage and adequate immobilization until the wound has completely healed. In this method there is only one primary operation because no distinction is made between the acute and chronic stages of the disease. (46).

Orr (62) lists the points to be considered in treatment of osteomyelitis as, "a. drainage b. removal of dead tissue, c. protection of the infected area against reinfection or mixed infection, d. to place the patient in such a position and under such conditions as will enable him to make the most efficient natural resistance to his infection, e. to have the patient recover with all the affected parts and other parts in the vicinity in such relation to each other as will make for avoidance of deformity, a minimum disability, and therefore the best possible function. All these points must carefully be considered in each case."

Technique---; 1. A fairly large incision is made over the infected bone area. The skin, muscle, fasciae, and periosteum are spread just far enough apart to afford access to the diseased bone area.
2. A window is next chiseled in the affected bone area large enough so that all diseased bone tissue can be removed and so that no overhanging edges of bone are left over the diseased area.

3. The diseased area is then cleaned out gently with a curette or gouge. Care must be taken not to damage tissues undergoing repair any more than is absolutely necessary.

4. The wound is dried and wiped out with 10 percent iodine followed by 95 percent alcohol.

5. A sterile vaseline gauze pack is put into the entire wide open wound but is not packed tightly. This is then covered with a dry sterile pad and bandage.

6. Any manipulation necessary to place parts in correct position is now carried out but with not too much force.

7. A plaster cast is applied so that the parts are thoroughly immobilized in a comfortable and correct position. Traction if needed can also be applied at this time.

8. Finally no windows are to be made in the cast and no splitting of the cast is done until it is necessary to dress the wound. The only indications for dressing the wound are rise in temperature and signs of acute sepsis. Usually no change of dressing is
needed unless the odor becomes so bad that it is very objectionable to the patient and staff. (62,46).
Orr (62) states that "in a majority of cases the patient treated by this method will go through to complete healing with a few dressings at intervals of from ten days to four weeks." There is usually little or no drainage present but even if profuse the wound will continue to heal without ill effects. (62).

If small sequestra form with the Orr method, they are extruded easily and spontaneously usually at the first post-operative change of plaster.

Secondary infection is prevented in this treatment by the principle of non-interference with the post-operative wound. Under these conditions the wound takes care of itself without the superfluous use of antiseptics. (26,63,29).

The Carrel-Dakin Treatment

This is probably the next most popular treatment followed today in the treatment of osteomyelitis. (26). The method of treatment came in during the first World War. It is a combination of the use of Dakin's solution with a special technique devised by Carrel.

It consists first of preparation of the wound with strict aseptic precautions. The wound is thoroughly disinfected and all foreign material, necrotic
bone, etc. are removed as in the other operations described.

Tubes are then placed in the wound so that the Dakin fluid will be able to reach every part. In the care of the wound the strictest care must be taken to preserve asepsis. Dakin's solution, which is a solution of sodium hypochlorite, is then made to flow into the wound every two hours. The object is to maintain an antiseptic of definite chemical concentration in constant contact with every portion of the wound.

The treatment is continued day and night and the wound is inspected once every day to make sure the apparatus is working correctly. Bacterial counts are made regularly. When three successive bacteriologic examinations have failed to reveal microbes, the wound is considered sterile. This usually occurs within from five to nine days. After the wound has been found to be sterile it may be closed by suture or elastic traction again observing careful asepsis. (64).

There are many modifications by numerous surgeons of all methods but there is a special modification of the Carrel-Dakin treatment which should be mentioned. This calls for the use of dichloramin-T, a synthetic chloramin. The method is simpler than the Carrel-Dakin and calls for only daily dressings. It also permits
dependent drainage. (1,28).

The Maggot Treatment of Baer

Although Dr. Baer was not the first to observe this principle of treatment, he was the first to use and advocate it in civilian practice. He first tried this method in private practice in 1928. It has been largely discarded in treatment of osteomyelitis at present. (26).

Baer's method in 1928 was as follows: The infected bone was exposed and the medullary cavity laid wide open. All granulations and sequestra were completely removed but a complete saucerization was not done. No antiseptics were used; the wound was simply cleaned by debridement. The wound was then packed with plain sterile gauze to check any hemorrhage. The pack was left in 24 to 48 hours. The pack was then removed and the wound entirely filled with maggots. Adhesive plaster was put on the edges of the wound to prevent tickling and to act as a base for the "cage" which prevented the maggots from getting out of the wound. The cage was made of edges of soft sponge rubber over the top of which was sewed a fine wire mesh. The cage could be cut in any size to fit the wound. Finally sunlight and air were necessary for the existence of the maggots. The cage was removed and the maggots washed out and
replaced every five days. The entire operation was done with the bare hands. After about six weeks the wounds entirely healed in his first cases not only in the deeper structures but also up to the skin. (3).

However in these early cases secondary infection often developed from lack of sterilization and anaerobes were frequently found. Later, Dr. Baer found it was necessary to use sterile maggots and also that it was necessary to cultivate the maggots so that there would be constant production of larvae summer and winter. It was found that the best method was to sterilize the egg instead of the maggot because there were bacteria in the gastro-intestinal tract of the maggots. (3).

The action of the maggots is to clear away the minute fragments of bone and tissue sloughs caused by operative trauma. This according to Baer (3) can be accomplished in a way not attained by other methods. Also maggots cause the wound to be alkaline and in this way diminish growth of pathogenic bacteria.

Baer, (3) in his article, states, "Maggots seem to have other more subtle biochemical effects within the wound itself and perhaps cause also a constitutional reaction inimical to bacterial growth. This is under investigation."
The Sulfonamides In Treatment of Chronic Osteomyelitis

Key, Frankel, and Burford (42) in 1940 were the first to report impressive results obtained by implantation of sulfanilamide in contaminated wounds. They found that the drug diffuses from the bloodstream into the body fluids but that it is in a lower concentration in the fluids than in the bloodstream and that most of its effect is on generalized infections having little effect on localized infections. When introduced directly into a wound, they found that sulfanilamide inhibited only slightly the primary healing of the wound this not being enough to contraindicate its use in clean operative wounds. They also discovered that the drug could be used in open infected wounds without seriously interfering with the healing of such wounds. They concluded that when sulfanilamide is implanted in a wound, the drug exerts a neutralizing effect on the toxins present, thus minimizing the amount of tissue breakdown, and that the drug converts bacteria into a static or non-pathogenic phase in which they do not invade the surrounding tissues and do not multiply. The normal body mechanisms then are able to destroy the bacteria.

They advocated the use of the drug in contaminated wounds and in clean operative wounds in which infection
is feared. (26,42).

Impressed with the results these men obtained, Dickson, Lively, and Kiene '41 (26) decided to try sulfathiazole by mouth and in the wound in the treatment of subacute and chronic osteomyelitis. They used sulfathiazole because it is more effective against staphylococci.

The following is the method of treatment they used: Sulfathiazole is administered for at least three days before operation in sufficient quantity to assure an average blood concentration of 4.7 percent (1 gm. q 4 or 6 hrs.). This is for the purpose of securing whatever benefit possible from the presence of the drug in the blood stream. Next the operative treatment is carried out. A tourniquet is applied to the extremity. Any sinus tracts are injected with methylene blue for the purpose of staining and outlining all necrotic material in the soft parts and in the bone. They are then completely dissected out. The dead and necrotic bone stained by the methylene blue is removed, the cavity saucerized, and the rough edges smoothed with an electric burr. All scar tissue in the soft tissue is also dissected away so that healthy tissue can be brought in contact with the bone cavity. Next 1 to 2 gms. of sulfathiazole powder is put in the wound by
means of a nasal insufflator.

The deep parts are sutured with interrupted suture in such a way as to bring them into close contact with the denuded bone. More sulfathiazole powder is put in the wound and the superficial structures closed. The skin is closed with cotton thread and a firm dressing applied. Finally a plaster cast is put on the extremity without drainage. Sulfathiazole is also administered by mouth, usually four to five days, following surgery. (26,41).

This method of treatment is coming more and more into widespread use by orthopedic surgeons and although it has not been in use long enough to accurately judge the results it will probably continue to gain favor.

Less Widely Used Methods of Treatment

Bacteriophage Treatment

This method of treatment was fostered by Albee (1) who reported it in the literature in 1932. After using Orr's treatment for a short time Albee decided the beneficial effects were due to an ultramicroscopic parasite of pathogenic bacteria somewhat like that discovered by d'Herelle (1) in 1923. This parasite is called bacteriophage. Albee claims that a bacteriophage develops at the wound site in Orr's treatment of
osteomyelitis in about 94 percent of the cases. In 3 percent of the remaining cases the laboratory can supply phage specific for the organism in question. In the other 3 percent it is unable to do so. Further there is hope that with the perfection of laboratory methods and more knowledge about the phage, it will be possible to isolate races of phage for each bacterium. (1).

Method of treatment—; After thoroughly cleaning up the diseased bone surgically as in the previous methods, bacteriophage is placed in the wound. Sterile vaseline gauze soaked in bacteriophage is then packed in the wound. The packing is allowed to overflow the wound so that it covers an inch or more of skin on either side. It is then covered with a gauze dressing and cotton padding after which the limb is in plaster and the joints above and below thus immobilized. No window is cut in the cast. The dressing is left intact for eight to ten weeks at which time it is changed and reapplied unless the wound is healed. This process is continued until healing is complete. (1,79).

Active Principle of Maggot Therapy

Livingston and Prince (51) first reported treatment of cases of chronic osteomyelitis using an active principle isolated from maggot filtrates. They mentioned
that the substance was undergoing chemical analysis and animal experimentation to determine its nature. In treating their cases they used the active principle and vaccine with and without the additional use of live maggots. (51).

Then Stewart (79) in 1934 published the findings of a series of experiments to attempt to determine how maggots effect a cure in cases of osteomyelitis. (79).

It was discovered previously by Heig (79) that maggots exude calcium carbonate through their body walls. In 1929 Beckhold (79) found that calcium ions stimulate phagocytosis. Then Stewart found that the maggots probably absorb leucocidin, which is excreted by the bacteria, through their intestine or body walls and render the leucocidin non-toxic. Also at the same time the exuded calcium carbonate increases phagocytosis. In early experiments Stewart used picric acid alone and found it undesirable in the treatment. He also used calcium carbonate alone and likewise found it ineffective. However when he used the picric acid solution and the calcium carbonate suspension together progress was marked and rapid. (79).

Method of treatment---; The necrotic bone is removed the excavation being made long and narrow so that the strength of the shaft can be retained as much
as possible and so the cavity will close more quickly.

The wound is then packed for 24 hours with vaseline gauze to allow the trauma to subside somewhat. The vaseline gauze is removed and the wound is thoroughly irrigated with picric acid glycerine solution by means of a syringe. In a few seconds an aqueous suspension of calcium carbonate is sprayed into the wound by means of a nasal atomizer without attempting to remove the picric acid solution. The picric acid gets an opportunity to go deep and act on the greater quantity of leucocidin and apparently does this immediately. When the calcium carbonate is added calcium picrate is formed and the calcium ions are rendered available to simulate phagocytosis. Also, dead protoplasm being acid, the wound suffers from diminished oxygen tension in the granulation tissue cells and this stimulates the autolytic enzymes contained within these cells to dissolve the surrounding protoplasm. The calcium carbonate is alkaline therefore controlling the dangerous acidity. The rate of drainage is increased rapidly which is also beneficial. Calcium carbonate has very definite analgesic properties which gives relief to the patient. The wound is next packed with dry gauze in order to prevent closure.

Usually these treatments are given three times a
week unless the case is a very severe acute one, then they are given daily for the first week or two and then three times weekly. Stewart advises getting the patient on his feet as soon as he has recovered from the mechanical part of the operation provided enough bone has left to support the limb. This increases the blood flow, mobilizes calcium, and stimulates the part to meet demands placed upon it. (79).

X-Ray Treatment

Tait (80) published a report in 1941 of a number of cases of osteomyelitis which had received various forms of treatment previously over long periods of time and were doomed for amputation. As a last resort he used heavy X-ray dosage with the idea of producing, not a stimulating reaction but a destructive germicidal effect on the invading organisms. The infections cleared up with excellent results. The osteomyelitis in these cases had involved bones of the hands and feet. Some had draining sinuses, some had been opened surgically and one was an acute infection which was not draining and had been opened surgically. (80).

Intravenous Injections of Hydrochloric Acid

Chronic osteomyelitis can be symptomatically relieved in certain cases by intravenous injections of hydrochloric acid. The rationale for the use of the
acid in dilutions of 1:1500 and 1:1000 was first described and practised by Burr Ferguson of Birmingham Alabama (2). The beneficial results are attributed to the stimulation of leukocytes with a resultant increase in defensive forces inherently present in the human organism. (2).

Backenstoe (2) reports good results in one case in which the patient always was able to get relief from pain, swelling, and tenderness with repeated intra-venous injections of hydrochloric acid.

Its use seemingly is amply justified in carefully selected cases. (2).

Toxoid Treatment of Recurrent Infection

Valentine and Butler (85) reported in 1940 a method of treating patients with recurrent staphylococcal infection following osteomyelitis and war wounds. These people are given injections of toxoid in the hope of preventing or of limiting further trouble. The injections are continued for a period of years to maintain a high level of antitoxic immunity.

The treatment probably is of value in cases with symptoms of persistent toxemia, for example war wounds, but there has not yet been time to evaluate the treatment in preventing further recurrence.

Large Reverdin Grafts in Chronic Osteomyelitis
There have been, for a long time, various methods for treating bone cavities following operations for osteomyelitis. Soft tissues, bone, skin, and fascia, various filling materials like Schede's moist blood-clot, Mosetig-Moorgof paste, and pieces of fat and muscle have been used in the attempt to obliterate cavities. (71). Lord (53) in 1902 used a Thiersch graft for this purpose.

Reid (71) in 1922 reported use of large Reverdin or pinch grafts for epithelializing the walls of bone cavities following operations for chronic osteomyelitis.

Technique---; The bone cavity is irritated with Dakin's solution until it becomes lined with firm granulations. Two hours after the last irrigation large thick pinch grafts one-half cm. in diameter are placed closely together upon the surface of the cavity. The wound is then exposed to the air for six to eight hours. This serves to fix the grafts firmly to the granulation tissue. The grafts are then covered and held in place with a single layer of gauze which is firmly secured to the normal skin so that the moistening and changing of saline compresses during the next two days will not displace the grafts. After two days the grafts have taken and the use of Dakin's instead of salt solution is begun. This is applied by laying
wet compresses against the wound every two hours during the day and every four hours at night. After about five days the Dakin's is discontinued and the wound is dressed with rubber or old linen. The grafts grow quickly and cover the granulation tissue with epithelium usually in ten days to two weeks.

This method is to be used when the other simpler methods mentioned above are not effective in treating bone cavities. (71).

Reid lists the following advantages of this treatment:

1. Epithelial covering is thicker and more durable than that obtained with Thiersch grafts.

2. The grafts are certain to take if the surface is properly prepared with Dakin's solution.

With such a method of treating chronic osteomyelitis bone cavities the time required for curing the most stubborn cases is usually from four to six weeks. (71).

Glycerol and Magnesium Sulfate Packs

Hawk (33), in 1933, proposed the packing of osteomyelitis wounds with gauze well impregnated with a paste made of one part glycerol and two parts magnesium sulfate. His treatment is based on the principle of increasing the exudation from the wound by
the high osmotic pressure action of the magnesium sulfate and of using a solute, magnesium sulfate, having a high valence and active ionization for the precipitation of colloids and destruction of bacteria. (33).

Stewart (79) claims that magnesium sulfate acts as a narcotic upon tissue cells and thereby retards phagocytosis; that the high osmotic pressure seriously dehydrates phagocytes and granulation tissue; bacteria are not eliminated from the wound by an increase in the exudate as Hawk implies. Also magnesium sulfate is not an effective bactericide.

Factors For and Against the Various Methods of Treatment

The factors considered in favor of and against the various methods of treatment by the orthopedists will be discussed here with reference only to those methods in popular use today. The various men do not always agree upon the advantages and disadvantages of any one treatment, therefore, a factor considered favorable by one man for a certain treatment may be considered unfavorable by another man for the same treatment.

The Orr method of treatment will be considered first:

Factors in favor of: Kulowski (46) lists the
advantages as follows:

1. It is a painless, economic, universal method and is applicable in any stage of osteomyelitis.
2. The period of hospitalization is greatly decreased with this method.
3. Transportation of the patient is simplified.
4. The method prevents sequestration.
5. The general condition of the patient is improved.
6. Only one primary operation is necessary.
7. Secondary infection is prevented by non-interference with the postoperative wound.
8. The wound takes care of itself without the "superfluous" use of antiseptics.
9. There is an absence of postoperative pain and temperature.
10. A good functional end result is obtained.
11. It minimizes loss of limb by amputation.
12. The death rate is insignificant.
13. It is the only treatment that satisfies all the tenets of orthopedic surgery.
14. It is a procedure suitable for the rank and file of the profession.
15. It shortens the postoperative course of a condition which previously to the advent of this treatment was in many cases intractable.
Kulowski (46) states, "Orr's treatment is based on sound surgical and pathological principles."---Also, "The seemingly initial radicalism is entirely compensated by the absolute postoperative conservatism."

Orr (63) says of his method of treatment, "A minimum of pain, inconvenience, expense, and with much less than the usual incidence of acute complications, infectious sequelae, and ultimate deformity and disability." Other advantages claimed by Orr (7) are: increased local resistance of tissues; further spread of infection is prevented; and a state of complete muscular relaxation is obtained.

Factors against:

1. Dickson, Lively, and Kiene (26) claim with Orr's treatment there is a long period required for healing and healing is largely by scar tissue "a real disadvantage in many locations."

2. Kulowski (46) although highly in favor of the Orr method admits there is occasional atrophy and stiffness resulting.

3. The Orr treatment does not seem to Cohn (22) to meet surgical principles. The secretions which accumulate, he claims, irritate the skin and the odor becomes nauseating after a time. He states, "With more frequent change of dressing there is less likeli-
hood of concealed damage occurring."

Orr (62) in retaliation to this and other similar objections claims there is usually little or no drainage. That when there is a lot a drainage the wound continues to heal and the drainage in his experience, with the exception of one instance, was not irritating to the surrounding skin.

4. Stewart's (79) opinion of Orr's method of treatment is in direct disagreement with Orr and his followers. He claims that the duration of treatment is usually long; the incidence of recurrence is too high; a great deal of scar tissue forms which causes a high degree of loss of function; the theory of the action of bacteriophage upon the pathogenic organisms in this treatment does not hold because of the necessity of oxygen by the bacteriophage and a wound that is "tightly" packed with vaseline respire very little. He quotes (79) Hawk (1933) as writing "But for adequate drainage to be secured in a rigid bone plugged with vaseline, a substance non-miscible with water, and the part then enclosed in a plaster cast for an indefinite period is more than the writer's imagination can encompass." Hawk also writes, "We have emphasized that bone tissue is rigid to the nth degree, the only alteration that an enclosing plaster case can accomplish
is to render circulation more sluggish and thus to interfere with healing."

Stewart (79) states," Orr's method has been widely used in the treatment of osteomyelitis for several years and every observer must admit that the results have been far from satisfactory."

The Carrel-Dakin treatment:
Factors in favor of:
1. Results are good if the proper technique is strictly adhered to.
2. Perfectly aseptic and satisfactory healing results if the wound is sterile and a careful aseptic procedure is used in closing with suture. (64).

Factors against:
1. Usually requires long period of hospitalization. (26).
2. Meticulous care in the daily dressings is necessary.
3. Frequency of irrigation and dressings are distressing to the patient, arduous for the surgeon, and increase the risk of re-infection. (1).
4. The cast is softened by fluid and the necessary windows in it for drain tubes weaken it and make immobilization imperfect. (1).
5. Keen (39) lists three disadvantages:
1. The treatment is likely to irritate the skin which must be protected by vaseline and by careful attention to the strength of solution which is ineffective below .45% and too irritating above .50%.

2. The treatment is too exacting and expensive, requiring a large staff of nurses.

3. Basin-like cavities must be made in the wound, and all dependent drainage avoided in order to get maximum efficiency from the solution being in contact with all parts of the wound.

6. Orr (64) adds to this:

1. The method interferes with rest.

2. There is practically always enough disturbance to destroy the correct position of healing parts.

3. The method is so complicated that it requires special training of surgeons using it.

4. With all precautions and in the best hospitals there is a possibility of secondary infection.

7. It might be mentioned here that the dichloramine-T method which is similar to the Carrel-Dakin treatment is much simpler but the other objections to it are much the same as the above.

The Maggot Treatment:

Factors in favor of:

1. Maggots, raised and sterilized as Baer describes
may be used in any wound without risk to the patient. (3).

2. The post-traumatic or post-operative general condition is better in the maggot treatment than in the older forms of treatment when infection was combatted by chemicals or other types of dressing. There is also less absorption and less toxic reaction. (3).

3. Stewart (79) lists the following as advantages:

   1. Recovery is more rapid than in Orr's treatment.
   
   2. There is little scar tissue formed in comparison to that formed in Orr's treatment.
   
   3. There seems to be very little danger of a recurrence of the condition.
   
   4. The patient need not always be placed in a circular cast and thereby decrease the circulation and invalid the patient to a high degree.

Factors against:

1. The method is cumbersome and time consuming. (75).

2. It is essential to have a constant supply of maggots from the proper kind of meat fly for some maggots will attack granulation tissue. (75).

3. The maggots must be carefully fed, cleansed, and sterilized in order to prevent infection of the wound and it is not always easy to obtain absolutely sterile maggots. (79).
4. A feeling of disgust is frequently created in the mind of the patient when he contemplates living maggots working in his body tissues. (75).

The Bacteriophage treatment:

Factors in favor of:

1. Satisfactory results are obtained in cases of osteomyelitis in which only the staphlococcus organism is present.

2. In the hands of certain men the results are apparently satisfactory.

Factors against:

Stewart (79) objects to Albee's treatment because:

1. Lysis of bacteria is a secondary phenomenon which may or may not follow the accumulation of phage depending on the conditions of the environment.

2. Phage can be present for months without manifesting itself or becoming active, because the bacteria are for some unknown reason resistant to it during this period of time.

3. Phage introduced into the body is usually entirely eliminated in 24 to 48 hours.

4. Repeated administration of moderate amounts of phage over a long period of time as Albee advises, is inadvisable because of the development of antiphage which abolishes all phage action.
Results of Treatment

Let us now consider the results obtained in recent years with some of these methods of treatment. Only the most common methods will be discussed. No attempt has been made to completely cover the literature or to obtain a complete statistical study; rather a few results on comparatively large series of cases will be quoted in order to gain some idea of the effectiveness of the individual methods in use in recent years.

Acute osteomyelitis---. Because of the importance of the treatment of acute osteomyelitis in the ultimate outcome of the chronic disease it will be considered first.

In a clinical review of 180 cases which Brown (15) reported in 1939, he found that in 59 toxic patients upon whom immediate operation had been performed, 37 lived and 22 died, a mortality of 37.7 percent.

In 18 toxic cases operation was delayed. Of these 13 lived and 5 died, a mortality of 27.7 percent.

Of the non-toxic patients, 25 were operated upon immediately; 24 lived and one died. Operation was delayed in 40 non-toxic patients. Of these 39 lived and one died, a mortality of 2.5 percent.

Brown concludes from this that immediate operation with opening of the bone, whether by gouge or drill
upon diagnosis of acute osteomyelitis in an acutely
toxic patient is accompanied by an unjustified high
mortality.

Burns (17) in a study of 162 cases of osteomyelitis (1931) found 9 cases to be acute when admitted to
the hospital. Four of these patients died, two from
septicemia, one from sepsis, one from amyloid disease.

In 1933 Pyrah and Pain (70) published a review of
262 cases of acute infective osteomyelitis. Of this
number, 71 patients died, giving a mortality of 27.1
percent. In their paper they listed the mortality fig-
ures "in other recent series."

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Deaths</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrah &amp; Pain.....1932</td>
<td>262</td>
<td>71</td>
<td>27.1</td>
</tr>
<tr>
<td>Gwynne Williams..1932</td>
<td>91</td>
<td>18</td>
<td>19.8</td>
</tr>
<tr>
<td>Lloyd, E. I.......1932</td>
<td>40</td>
<td>13</td>
<td>32.5</td>
</tr>
<tr>
<td>Ogilvie, W.......1928</td>
<td>51</td>
<td>11</td>
<td>21.6</td>
</tr>
<tr>
<td>Mitchell, A.......1928</td>
<td>70</td>
<td>10</td>
<td>14.3</td>
</tr>
</tbody>
</table>

Garr (31) in 1927 reported 58 cases of osteomyel-
itis of which 20 were classified as acute osteomyelitis.
Six of these patients had septicemia. Three died fol-
lowing operation and one without operative intervention.
Two were considered cured.

Since the advent of the sulfonamides the mortal-
ity from septicemia with bone infections has been
markedly reduced.

Pemberthy and Weller (67) in July 1941 reported their mortality rate in acute osteomyelitis since 1934 as follows:

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of pts</th>
<th>Expired</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1934.....23</td>
<td>5</td>
<td></td>
<td>21.7%</td>
</tr>
<tr>
<td>1935.....29</td>
<td>7</td>
<td></td>
<td>24.1%</td>
</tr>
<tr>
<td>1936.....15</td>
<td>3</td>
<td></td>
<td>20.0%</td>
</tr>
<tr>
<td>1937.....32</td>
<td>3</td>
<td></td>
<td>9.3%</td>
</tr>
<tr>
<td>1938.....22</td>
<td>1</td>
<td></td>
<td>4.5%</td>
</tr>
<tr>
<td>1939.....12</td>
<td>0</td>
<td></td>
<td>0.0%</td>
</tr>
<tr>
<td>Jan.1 to Dec.1 1940.....7</td>
<td>0</td>
<td></td>
<td>0.0%</td>
</tr>
<tr>
<td>Total</td>
<td>140</td>
<td>19</td>
<td>13.5%</td>
</tr>
</tbody>
</table>

The early administration of sulfapyridine or sulfathiazole apparently controls the bacteremia and evidently plays a prominent role in the prevention of secondary metastatic foci in other bones. In the Pemberthy and Weller series of 19 cases treated by chemotherapy none of the patients developed evidence of other bone involvement. Only two of their cases showed evidence of later sequestration. From these results these men believe that chemotherapy combined with early surgery even in the presence of a bloodstream infection, reduces mortality and lowers the
incidence of secondary bone involvement.

Finally they conclude that the mortality from septicemia with bone infections can be considerably reduced by sulfapyridine or sulfathiazole therapy employed in conjunction with relatively early and adequate surgical drainage of the local lesion.

Although reports in the literature are as yet few, the mortality rate in future years will undoubtedly differ greatly from that of the past with the use of the sulphonamides.

Results with Orr treatment: Kulowski (46) in 1931 reported a study of 130 cases of osteomyelitis treated by the Orr method. These were not divided into acute and chronic types. Briefly the end results, not considering reoperation, metastasis etc. occurring, were:

- Healed 99 cases or 76.15%
- Unhealed 22 cases or 16.92%
- Amputated 6 cases or 4.6%
- Deaths 3 cases or 2.3%

He states in his paper, "The results shown by this statistical study (which is much more complete in his paper) warrant our confidence in the Orr treatment."

Burns (17) reported in 1931 on results obtained by the Orr method in 162 cases. 131 of the cases were hematogenous osteomyelitis, 31 were non-hematogenous.
As mentioned previously 9 cases were admitted to the hospital as acute osteomyelitis; 4 of these patients died. Among the 122 cases of chronic osteomyelitis there were five deaths. The period of hospitalization was longer in the hematogenous cases; an average of 171 days, whereas the average for the non-hematogenous cases was 153 days. Also the plaster of Paris cast was worn longer in the hematogenous cases; an average of four and one half months as against four months in the non-hematogenous. Of 104 patients followed he considered 89 cases or 86 percent healed. Six drained intermittently but closed after a time. Four were draining intermittently at the time he published his results. Five patients reported no benefit from treatment at all. Ten patients or 9 percent received treatment after dismissal from the hospital. Thirty patients or 29 percent had deformities as a result of the disease.

Ninetyone or 87 percent of the 104 patients were able to follow a useful occupation. 96 or 91 percent regarded their condition as satisfactory. 99 or 95 percent of the patients expressed satisfaction with the treatment received.

Diebert (27) treated 100 unselected cases by the Orr method. These included 57 cases of chronic osteomyelitis involving the various bones. Practically all
of the chronic types were healed but there were six deaths in the non-chronic cases treated.

Orr (64) in his book on "Osteomyelitis and Compound Fractures" published in 1929, gives numerous case reports on chronic osteomyelitis treated by himself and other men by the Orr method in which results were very satisfactory. He mentions thirty cases of acute osteomyelitis which he had treated at this time by his method. In this series there was only one death and two or three instances in which secondary complications occurred.

Beekman and Sullivan (7), 1940, consider Orr's method as "one of the greatest advances so far made in the treatment of acute inflammatory lesions of bone." They showed an improvement in their mortality by using this method.

Results with Carrel-Dakin treatment: Albee (1) adopted the Carrel-Dakin method in 1918 when he was Chief Surgeon at a large Army Hospital. He states, "Of the 6000 serious bone cases which came under my care at this Army Hospital, I can safely say that half owe useful extremities to conquest of wound infection by this method before reconstruction surgery was attempted." Albee later changed to Orr's treatment and still later advanced the bacteriophage method of treatment.
Wilensky (88) in 1922 wrote that in his experience the Carrel-Dakin method was useful only in the simplest of the acute cases of osteomyelitis. That it was useful in chronic cases only when the conditions approximated those of simple uncomplicated acute cases. He states, "The method is not successful in any case either acute or chronic, in which the infection is not entirely eradicated, in which there are adverse mechanical conditions (bone cavities, sinuses or canals) in which complications (joint infections) coexist which are not properly cared for, or in the presence of acute and chronic blood infections."

In the proper hands of specially trained men this method is apparently satisfactory although it has been largely discarded in present day treatment.

Results with chemotherapy: Results obtained in acute osteomyelitis have already been considered under that section.

Dickson, Lively, and Kiene (26) in July 1941 reported results obtained in treatment of 22 cases of chronic osteomyelitis in about one year with operation and sulfathiazole. 18 of their cases were hematogenous osteomyelitis. The duration of the osteomyelitic process varied from 19 years to 37 days with an average of 4.8 years. 14 cases or 78 percent healed by primary
union; 2 or 11 percent did not heal; and 2 or 11 percent had been too recently treated to report.

The average length of time from day of operation to healing was 21 days.

Four cases followed compound fracture. In all four, healing was complete. Average time between surgery and healing was 26 days.

Of the wounds in the 22 cases, 18 or 82 percent healed; 2 or 9 percent failed to heal; 2 or 9 percent were too recent to report.

Average time for healing was 23 days.

Results with Baer's Maggot treatment: Baer's first cases treated by this method were four children each of whom had been operated upon three or four times before he started treatment. He states that at the end of about six weeks the wounds had entirely healed. (3).

According to Thorek (82), Baer reported 21 cases of from four to ten years standing, all of which were said to have recovered within six weeks following treatment.

In 1932 Livingston and Prince (51) reported 100 cases of chronic osteomyelitis, infected wounds, and compound fractures which were treated by the maggot active principle and vaccine with or without the use of live maggots. 88 percent of their cases healed.
However they discussed numerous conditions occurring in osteomyelitis in which the treatment was not effective.

In another series of 100 cases of chronic osteomyelitis reported by Livingston (50) in which only maggots were used, he claims 95 percent cures. Two cases failed to respond to treatment; there were two recurrences; and there was one death.

Results with bacteriophage treatment: Ten cases of osteomyelitis were studied by Bagley and Keller in 1932 (4) to test the therapeutic value of staphylococcus bacteriophage. Three cases had wounds which were infected with several types of organisms. These did not respond to the bacteriophage treatment. Four patients having a pure culture of Staphylococcus aureus were treated by subcutaneous and intramuscular injections as well as by dressings, and three of these showed good results. One died of meningitis due to osteomyelitis of the skull. The three remaining cases were complicated by Staphylococcus aureus septicemia and were treated by intravenous injections of the bacteriophage. Two of these patients died, one survived.

They concluded that the best response to bacteriophage therapy is obtained in cases of Staphylococcus aureus uncomplicated by other organisms or by septicemia.
McCarrol and Key (55) reported 200 consecutive cases of chronic osteomyelitis admitted to the St. Louis unit of Shriner's Hospital for Crippled Children between the years 1924 and 1938. In the treatment of these cases standard surgical procedures and prolonged hospitalization with adequate after treatment was used. No mention was made of any specific method.

They considered end results poor in 35.5 percent of cases, fair in 28 percent, good in 25.5 percent, and unknown in 11 percent. Healing was obtained in 61.3 percent of 98 cases which were followed for three years or longer.

Kulowski (77) reports one percent of all admissions to the University Hospitals at Iowa City are due to pyogenic osteomyelitis. Eighty percent of these patients had been affected for from six months to seven years. He states, "This situation does little credit to accepted methods of treatment in the past." (1940). According to Kulowski recent studies show that the mortality is lowest in those cases which are subjected to operation during the second week of the disease.

Stewart (79) made the statement in 1934, "No single treatment is effective in all cases and most of them offer little hope of successful results in any case."
COMPICATIONS

Kulowski (47) writes, "The high mortality, morbidity, chronicity, and crippling effects of pyogenic osteomyelitis are dreaded alike by laymen and physicians. This has led to an erroneous, hopeless attitude."

The common complications of osteomyelitis are provoked by bone localization, but in general they are metastasis, sinus formation, pyemia or septicemia, extension into neighboring joints, and chronicity. (49).

Death of course is the most serious complication of osteomyelitis if it can be considered a complication. It results from a septicemia or a pyemia which is probably due to a sudden injection of subperiosteal pus under tension into a torn and gaping vein (29,7). In acute fulminating types of osteomyelitis the mortality may reach 50 percent (47). However this has undoubtedly been reduced greatly since the advent of the sulfonamides. Ninety percent of all deaths from acute osteomyelitis occur in the first two weeks of the disease. According to Kulowski (47), 75 percent of osteomyelitis infections occur through the blood stream and are accompanied by a general septicemia.

In a review of 217 cases of pyogenic osteomyelitis at the University of Chicago Clinics by Bisgard, (13)
there was associated arthritis in 51 cases or 23.5 percent. Forty two cases of 19.3 percent arose by direct extension from an adjacent diaphyseal infection; 9 cases or 4.1 percent became involved by blood borne infection. The importance of this is the end result on the joint. 13.2 percent regained good function, 65.2 percent became ankylosed, and 22.6 percent suffered varying degrees of functional limitation.

In the McCarrol and Key series (55) mentioned before there was involvement of the joint adjacent to the focus in the bone in 50 percent of the cases. Also in this same series secondary foci developed in other bones in 25 percent, of cases.

Draining sinuses may persist over a period of many years. (86). Insufficient operations may lead to this. (89).

Acute exacerbations—-Even after years, the osteomyelitis may flare up. (86). Only a minority of cases of osteomyelitis show recurrence of infection however. (85).

Unusual complications are non-union, deformities, pathologic fractures and dislocations, epiphyseal separations, pseudo-arthrosis, erysipelas, vascular disturbances and accidents, nervous system involvement, malignant degeneration, epithelization of the sinus tract, myositis ossificans, and skin defects. (49).

Non-union—-. There has been much discussion as
to whether fractures heal in the presence of infection. White (40) states that in the majority of cases union takes place despite the continuance of an infectious process and "in fact the infection produces an irritation which is a potent factor in the production of union." Starr (40) says that infection and sequestration does not prevent union of fractured bone. "Even if the sequestrated area involves the whole thickness of the shaft, if the remaining ends of bone are brought into apposition, union usually results."

Carcinoma in osteomyelitis—. Carcinoma developing in old sinuses and ulcers in osteomyelitis is a rare complication but none the less one to be considered. It occurs in long standing cases of osteomyelitis (usually 30 years or more) in old sinuses or ulcers and more often in the tibia than in any other bone. It seems to be almost entirely confined to males. (8,16).

"The incidence of carcinomatous degeneration of the skin associated with chronic osteomyelitis has recently been called to the attention of the medical profession by the papers of Benedict and Henderson."---Hobart and Miller. (35). This association has been seen in 12 of 2400 cases reviewed by the first author and 5 of 2396 cases seen by the latter author at the Mayo Clinic. At the Cook County Hospital this condition was seen in
7 of 400 cases (35).

Epithelization of bone cavities--- from epithelial cells reaching the cavities along persisting sinuses in osteomyelitis prevents healing and makes for an extremely long duration of the disease if not eradicated. (16).

Eighth nerve involvement---. Hobart and Miller (35) report two cases of toxic deafness of the eighth nerve as a sequelae of bone infection.

Growth deformities---. In review by Siegling (74) of cases of osteomyelitis seen at the University of Chicago Clinics, the growth deformities of greatest significance were found to be either shortening of an extremity due to complete arrest of growth, or deformity resulting from arrest of one part of an epiphysis with continuation of growth of the remainder. This review and others show a high incidence of partial or complete arrest of longitudinal growth of long bones although the incidence was formerly thought to be relatively low.

When growth arrest occurs the ultimate deformity depends upon the age at which the arrest occurred and the rapidity of growth of the particular epiphysis. (74).

Disability from locomotor disturbances---. Local and widespread paralysis is not uncommon after in-
Involvement of such specific sites as the upper end of the fibula, lower end of the humerus, or spine in which situations the peripheral and central nervous systems are particularly vulnerable. (49).

Shaft deformities. These are for the most part almost all of purely mechanical and static origin, on the basis of more or less extensive destruction of bone. The extreme of this type is the pathological fracture which occurs most frequently in the femur. (49).

Silent foci. Silent foci usually arise as complications or sequelae of diffuse staphylococcus osteomyelitis. Localized osteomyelitis may develop painlessly and may be present for weeks or months before producing local symptoms. (68).

Butler (18) in a follow up of 223 cases out of 500 admitted to the London Hospital during the years 1919 to 1937 found that about 50 percent of patients can be expected to make a perfect recovery, but the remainder will be subject to either deformity, pain, discharge, or recurrent infection.

In a series of treated cases from the Surgeon General's Report of the first World War on compound fractures of the femur, 8 years after injury 2669 of 5138 patients were less than 50 percent disabled; 2469 of 5138 patients were more than 50 percent disabled.
Of the latter 789 were more than 80 percent disabled. About one-half of the patients were found eight years later to be still over 50 percent disabled; 15 percent of the total were over 80 percent disabled. (40).
CONCLUSIONS

As far as etiology is concerned the staphylococcus organism is agreed to be by far the most common agent involved in both acute and chronic osteomyelitis, whereas infection by way of the blood stream is the usual route of involvement. It is important to know the type of organism one is dealing with in bone infections if possible. Other etiologic agents are uncommon but nevertheless are to be watched for and considered in approach to treatment.

Trauma seems to be a fairly common predisposing cause to osteomyelitis but apparently not nearly so common as formerly supposed. The general condition of the individual is important here as in all other infections. The predisposing cause is unknown or cannot be determined in many cases. The acute infection may be considered an important predisposing cause to chronic osteomyelitis.

The disease occurs in the greatest number of instances in childhood and early adult life being more predominant in early childhood before puberty.

The bones of the lower extremity are involved much more often than those of the upper extremity. The incidence is greatest in the femur, and tibia, the
humerus being next in order.

Treatment of acute osteomyelitis has been until recently, simply early drainage and immobilization. The results when septicemia or bacteremia did not occur were fairly satisfactory if the treatment was instituted early enough. However the high mortality from septicemia overshadowed all other results. Now, with the use of the sulfonamides in the acute process, in the past few years the treatment has made tremendous progress, especially in greatly lowering the mortality. The accepted treatment of this condition at present seems to be early operation combined with administration of one of the sulfonamides, and immobilization.

As far as any one method of treatment is concerned, whether it be for acute or chronic osteomyelitis, the Orr method is probably the preferred. The results are as good or better than in any of the other methods and the method is comparatively simple. The results with the Orr treatment can be quite good in almost any surgeon's hands, whereas results in most of the other methods are fairly good only if the procedures are carried out by specially trained men or there is special equipment at hand.

The present trend of treatment of chronic osteomyelitis seems to be toward Orr's principles, surgery
drainage, and immobilization, combined with the use of the sulphonamides in the wound and by mouth.

It is important in both the acute and chronic stages to give the patient support: sedation, oral and parenteral fluids, and blood transfusions besides chemotherapy.

The present war will undoubtedly give chemotherapy treatment of osteomyelitis a good test as it is being used in other countries and will probably be used by the armed forces in this country.

The future for the treatment of osteomyelitis holds much more promise today than it did a few years ago before the advent of the sulphonamides.
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