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ACUTE HEMATOGENOUS OSTEOMYELITIS

BY

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INTRODUCTION

In attempting to deal with the problem of acute hematogenous osteomyelitis in this paper I have limited the majority of my efforts to consideration of the question of treatment of this disease. The etiological factors, pathological processes, diagnosis, etc., are important but for several reasons I am of the opinion that treatment is of utmost importance.

It is my belief that the treatment of bone infections is not perfected to the point to which the treatments of other infectious processes have been perfected. There are difficulties concerned with these infections such as the very nature of the tissue where they are localized but these difficulties could be met, I believe, more satisfactorily than our present methods do.

The number of cases of acute hematogenous osteomyelitis that have become chronic, with the course of the disease covering anywhere from two to as high as forty or fifty years, is surprisingly large. These patients with a hospitalization period that is longer than nearly any other infectious process present an economic problem that is serious, especially is this true in the larger cities. It is my belief that these patients could be afforded a greater chance for an
early termination of their infection, possibly with a less elaborate course of treatment, than is now quite generally true.

I also wish to discuss a new method of treatment that I was enabled to observe recently, not from the standpoint of the technic of the procedure but just to present the ideas upon which it is based.

This paper also presents an opportunity to evaluate, just from the point of view of impressions gained from the literature read, the present methods of treating osteomyelitis and to compare the different principles upon which these treatments have been developed. To give one a better understanding of the therapy a short time will be devoted to the factors involved in producing an osteomyelitic process, its symptoms, diagnosis and value of early diagnosis.
Osteomyelitis, in general, can be classified as an inflammatory, infective condition of the bone. (45) This classification would include osteomyelitic processes due to complications of a compound fracture, amputations, empyema, felons, abscessed teeth, metal bone plates and screws etc., all of which are disease processes with different etiology than is seen in acute hematogenous osteomyelitis. As this paper is dealing primarily with bone infections secondary to a bacteremia perhaps a more fitting definition would be that suggested by Hart (16) and Orr (37).

They define acute hematogenous osteomyelitis as a "local manifestation of a blood stream infection which is usually transient." This definition conforms to the picture in acute infections but excludes the conditions arising as a complication of a local process.

The most common organism found producing osteomyelitis are, in the order of their frequency, Staphylococcus Aureus, Albus, Streptococcus Pyogenes, Pneumococcus, Colon Bacillus, Tubercle Bacillus, Streptococcus Hemolyticus, and the Gonococcus. Any organism is capable of producing the disease but the aforementioned are the most frequent causative agents. (10, 16, 45, 36)
Even though acute hematogenous osteomyelitis is a blood borne disease it is not always possible to obtain a positive blood culture. In the cases in which blood cultures are positive there is a general septicemia and the case usually terminates fatally. In these cases the infecting organism is usually found to be Streptococcus Pyogenes, Streptococcus Hemolyticus, or Staphylococcus; the latter being five times more prevalent than the former two.

Acute osteomyelitis is a disease of children and occurs most frequently between the ages of two and ten and in addition shows a tendency to occur more frequently in boys than in girls. This last phenomenon is probably due to the fact that boys are more subject to trauma than girls, more apt to be exposed to disturbing climatic conditions, and also because of a greater prevalence of skin and mucosal infections in young boys. (16,45,15,32,23,24)

Trauma, according to Seybold, (45) plays such an important part in the development of an osteo and in the point of its localization because of the resultant edema, interference with blood supply, the pressure of blood, serum or tissue debris; all provide an ideal location for the development of pathogenic organisms.
This trauma may be so slight that no notice was taken of it at the time and no treatment required. It may have been diagnosed as a sprain or laceration of ligaments or a separation of the epiphysis. The real exciting cause may be anything from a mild passive congestion to a severe distention of the tissues by an effusion.

Other predisposing factors are those conditions which bring about a lowering of resistance to infection, such as diabetes, nephritis, malnutrition, exposure to cold, or any chronic debilitating disease. (45) Miller and Hobart, in a study of 108 cases of osteomyelitis, noticed that a history of preceding trauma directly to the bone involved, was obtained well over ninety per cent of the time. (18) This was interpreted by them as being an indication that trauma is the most important predisposing factor. This opinion is also shared by Key (22) and many others who have carried on exhaustive research in this field for years.

Acute hematogenous osteomyelitis has a tendency to occur at certain sites in the skeletal system with more regularity than others. These sites, in the order of frequency are; the upper end of the tibia, the lower end of the femur, the lower end of the tibia, and fibula, the upper end of the humerus, the
lower end of the radius, the lower end of the humerus, the upper end of the femur and the crest of the ilium. (45) This selectivity is occasioned by the greater incidence of trauma to these areas and perhaps influenced by the fact that there is a more abundant blood supply to the epiphyseal ends of growing long bones.

There has been, and still is, much discussion upon the question of the exact location of the first area exhibiting signs of infection. It has been thought that the diaphyses of the long bones are the original site (11) but in a very recent article strong arguments in favor of localizing the initial infection to the metaphyses of the involved bone have been advanced. Robertson believes that the medulla is never involved early and that it is impossible to obtain any evidence that would point that way. (44) He also is of the opinion that if a case can be made for the seat of the infection being in the metaphysis, the problem of diagnosis will be much simpler. Hart (16) agrees in this respect and advances many arguments to show that all the signs and symptoms point towards a primary metaphyseal involvement. Fraser states "I have a suspicion that in acute hematogenous osteomyelitis the bone disturbance is but a local evidence of a general infection, and that the reason why the local infection is so constantly localized to the
metaphysis is conceivably because we there encounter a concentration of reticuloendothelial tissue, and that the local suppuration which results from the defensive activities of the area is in some measure protective against the general disturbance. (14) Hobo (19) and Robertson (44), in their researches, have given us quite definite proof that the medullary cavity is much richer in phagocytic elements than the metaphysis which is more recently developed from the epiphysis and is therefore more vascular, more delicate, and less immune than the older bone of the shaft, which is dense and compact.

The observations of C. L. Starr also make one believe that the infection usually is located primarily in the metaphysis. (46) The cortex of the middle of the shaft is either slightly more or slightly less than one-fourth inch in thickness, while the cortex surrounding the metaphysis is much thinner, and near the epiphyseal disk it is paper thin. This is important in as much as it explains the ease with which infection with in the cancellous metaphysis may perforate into the Subperiosteal space and why the rupture is usually juxta-epiphyseal.

The arrangement of the blood vascular system in the metaphysis plays an important part in the localization of infection in the juxta-epiphyseal region of
growing bones. That the metaphyses, the epiphyses, and the cortex of the shafts have practically independent circulations was proved by Lexer, Kuliga, and Turk in 1904. (28) The metaphyses is abundantly supplied by the terminal branches of the nutrient artery. The fact that these arteries are end arteries is in itself important. The blood is necessarily slowed and infection is very likely to settle as a bacillary embolus. The nutrient artery also supplies the medullary cavity and endosteum and freely anastomoses with the periosteal vessels, through the haversian systems, which are the main sources of nutrition to the cortex of the entire shaft. Epiphyses receive their blood supply from articular and cortical arteries. The epiphyseal circulation is separated from the vascular system of the metaphysis by a practically avascular barrier, the epiphyseal disk. The extraordinarily rich capillary network of the metaphysis and juxta-epiphyseal region is gradually reduced with diminished physiologic activity of bone production of the epiphyseal disc. This explains why acute hematogenous osteomyelitis is essentially a disease of childhood and puberty.(10)

The studies of Haldeman on the pathological processes included in the development of a bone
infection are interesting. (15) He produced the disease in 33 rabbits by the infection of a tibia near its upper end. The development of infection in the bone was followed by the daily recording of the animal's temperature and by weekly x-ray pictures. The animals were killed at various periods from 1 day to 6 months following the operation. It was possible to make microscopic sections of the entire upper half of the tibia and thus to observe all the stages of infection and the defense processes called forth.

The changes which take place following the experimental introduction of infection into a long bone may be summarized in the following manner.

1- The blood vessels become engorged and the bacteria are walled off by fibrin, pus cells, macrophages, and fatty tissue forming definite zones in the order named, from within outward.

2- Newly formed bone (involucrum) which appears after 1 week comprises the outer shell of the defensive wall, and also replaces necrotic bone.

3- The separation of dead bone from the living cortex takes place after 2 or 3 weeks by means of a thrombosis of the vessels in the haversian
canals which in turn become enlarged and invaded by connective tissue and osteoclastic cells.

4- The bone marrow is replaced by fibrous tissue containing many fat cells.

5- In the chronic stage the contour of the bone is restored by involucrum, and the sequestra float unattached in an abscess cavity.

This is a rather typical description of all osteomyelitic processes that proceed from the acute stage to the chronic stage. It was thought by early observers that the spread of the infection was from the diaphysis to the medullary portion of the bone. It is now quite generally believed(15,45,1,40,23,44,) that the infection spreads from the primary abscess in the metaphysis, through the haversian system to the periosteum. On reaching the more resistant periosteum it dissects off large areas of this structure, the amount depending on the delay in opening the periostem and relieving the pressure that develops.

The problem of diagnosis in acute osteo is one that presents difficulties only in the early stages. The predominant symptom of acute osteomyelitis is the early, continuous throbbing and very severe pain, usually increased by the application of heat, (16,45,40,37,44) The pain is usually situated near a joint,
but not in the joint, in most cases one will get a history of some infection, either focal or general, about two or three weeks previously. (45) The objective sign of tenderness, limited and localized to the region of the metaphysis, with no tenderness on the bone surrounding this area, is quite constant. The neighboring joint is not involved and there is no fluid in, or swelling of, the joint. If the signs and symptoms point more to pathology in the joint, one thinks of tuberculosis rather than osteo.

The signs and symptoms thus far related may be the only signs of acute osteomyelitis for 24 to 35 hours or until the initial process has reached the periosteum, at which time there will be swelling, redness, edema, thickening of bone or, later still, fluctuation. When the periosteum ruptures and tension is released, the symptoms will become less severe and toxemia will lessen. The signs of toxemia present are, a temperature of 102-104 F. and the pulse rate rapid, from 120 to 130 per minute. A blood examination will reveal a polymorphonuclear leukocytosis, usually up to 25,000 to 30,000. Blood cultures should be done as a routine and the urine should be examined for the presence of Hedri's sign or the presence of lipuria. (16) It would seem then that the principal finding of signi-
ficance is point tenderness localized to a spot over the metaphysis. This point tenderness should not be elicited, according to Hart, until examination of the joint is finished. The increased pain results in a lack of cooperation, muscle spasm, etc., that make a thorough examination of the joint and surrounding tissues impossible.

The value of x-ray in early diagnosis of a bone infection is questioned by nearly all of the authorities consulted but the earliest time at which x-ray findings are positive has not been agreed upon. Haldeman is of the opinion that x-ray will show an area of rarefaction as early as the fifth day of the disease. He makes the provision that an earlier x-ray of the same extremity or of the opposite extremity is necessary for comparison. (15) Nearly all of the other writers expressed the opinion that x-ray usually shows nothing until about the tenth or twelfth day. At this time an area of rarefaction, cortical, will make it's appearance. (16,45,22,35, 14, 46)

Robertson states that x-ray is of no value until the abscess ruptures through the cancellous bone to a subperiosteal position. He is of the opinion that the first finding is an increase in density of an area,
subperiosteal which is followed sooner or later, depending on the virulence of the organism, by rarefaction. (44)

In considering the problem of treatment of an acute hematogenous bone infection, since all of the present methods of treatment include operative exposure of the infected field, it seems necessary to determine at what stage of the process most authorities deem surgery to be of the most value. This differs in some cases necessarily because of a failure to recognize the disease, but in other instances there is a difference of opinion because of clinical results obtained. Hart (16) is very strongly in favor of as early operative interference as possible. He bases his stand on the work done by himself and Starr (46). He believes that children with acute hematogenous osteo should be divided into two groups. The division depends upon whether or not the abscess has perforated the cortex of the infected metaphysis. In the first group the infection is confined within the metaphysis and the infection has not penetrated its thin wall or cortex. This phase is present during the first twenty-four, thirty-six or forty-eight hours of the clinical manifestations of the disease. Hart is of the opinion
that the disease can be recognized during this period and that a careful observer can operate at this time and anticipate the disease, saving the patient much bony destruction and time convalescing. It is at this time that he advocates exposing the shaft through a small opening. The incision through the periosteum is made over the infected metaphysis and a few small holes are drilled into the cancellous bone, being careful to avoid the medullary canal and the epiphysis. Seybold agrees in this manner of treatment (45) but he does not become so emphatic in limiting the exposure to just the metaphysis. He believes that if there is considerable pus under pressure that the medulla should also be exposed. Both men agree that there should be no exploring of the area in an attempt to curette away infected bone at this stage.

Albert Key holds another view. He believes in operation as soon as the surgeon has a reasonable suspicion of osteomyelitis but he states that if the operator is sure enough of the diagnosis to open the periosteum he should be willing to open it widely. For this reason Key gutters the cortex for about one-fourth of its length. (22)

Haldeman is another advocate of early operative
treatment. He does not believe that it is possible to diagnose the condition at an early enough stage so that it will be localized to a metaphysis. In operating then he recommends a long wide periosteal incision with drainage of the medullary cavity as well as the metaphysis. (3)

Crossan (11), in a study of 117 cases of acute hematogenous osteo, made some observations that are rather unusual. In the series studied, pus was found in the bone in 12 cases and in the medulla and the subperiosteal space in 24. In 39 cases the medulla was exposed and found free from pus. In the remaining 42 cases the bone was not opened. Pus was present beneath the periosteum in 105 of the 117 cases. "If this is not an argument against the intraosseous origin of the infection, it is evidence that the pus finds an exit, that decompression occurs, and that spread of the infection can be limited without surgical intervention"; these are his conclusions.

Of 4 cases in which operation was performed within forty-eight hours after the onset of the symptoms, pus was found in the subperiosteal space but not in the medulla. He believes that this is evidence for a subperiosteal origin following trauma rather than for
an intramedullary genesis.

In the reviewed cases the mortality was twice as high following early as following delayed operation. The author calls attention to the fact that the patient's margin of reserve is depleted by pain, insomnia, dehydration, the fright caused by his transference to a hospital, the shock of infection, and the shock of operation. Hasty operation is associated with danger of disseminating the infection and may result in embarrassment due to faulty diagnosis.

Crossan makes the following recommendations for treatment:

1- Delay operation until the patient's resistance has been improved by rest, transfusions, infusions, and adaptation to hospital surroundings.
2- Do not operate until local resistance of tissues has developed. According to the reviewed cases, the best time for operation is the second week of the disease.
3- Limit the operation to incision. Do not decompress at the first operation. In the few cases in which incision reveals pus in the medulla, pack the soft part for forty-eight hours before
opening the bone.

Hart, Key, Haldeman, in fact, all of the writers consulted, stated that the condition of the patient as to dehydration, nutrition, blood destruction etc., must be considered but I believe that holding a patient in the hospital for 7 to 14 days to get him in shape to open the periosteum is being too conservative. There is a great deal of resemblance between an acute metaphysitis and an acute appendicitis, as pointed out by Hart (16). I believe that early operation is necessary to obtain the maximum results. Due to the resistant structure of the bone, an accumulation of pus beneath it is going to force toxins into the system by lymph and blood channels. Release of this pus is going to result in a decrease of these toxic manifestations and also prevent spread of the infection subperiosteally by allowing it to escape and not build up a pressure intraosseously. In face of the observations studied, I would be of the opinion that early operation is essential, the extent of the operative measures depending on the extent of spread of the infection.
We know that osteomyelitis is an old disease in as much as there are pictures painted as far back as the fifteenth century depicting ladies with deformities of the extremities that could be caused only by an osteomyelitic process. There is no definite proof of any treatment extending as far back as this, however. The effect of maggots on infected wounds was noted at an early time but it does not state definitely if they were used in the treatment of bone infections.

Ambroise Pare (1509-1590) was the first, so far as is known, to note the beneficial effects of maggots in suppurative wounds. D. Hieronymus Fabricius (1634) Zachmann (1704), D. J. Larrey also are on record as having noticed the beneficial effects of maggots in wounds. J. G. Millingen and more recently in the United States Crile, Shafer, and Martin and W. W. Keen spoke of the disgusting infestation and noted its beneficial effects.

J. F. Zacharias, of Cumberland, Maryland, a surgeon in the Confederate army was the first to utilize maggots successfully in the treatment of suppurations. His findings were then forgotten until the work of William S. Baer. (13) Baer and Zacharias are to be complemented at least for their originality and daring in making use of what Baer spoke of as "a viable antiseptic".
In 1881 Hamilton packed the cavity with sea sponges. The idea being that these sponges should serve as a scaffold for growth of the granulations. This procedure follows operation for drainage or removal of sequestra.

In 1885 Keeting, of England, advocated sterilization by curetting the marrow cavity and swabbing the exposed tissue with carbolic and bichloride solution. He maintained drainage following this with a large rubber tube. (31)

This type of work was proved to be wrong by Nichols, of Boston, in 1904 when he showed that strong antiseptics and scraping destroyed some of the osteogenic properties of the bony structure. He solved the problem by removing all of the bone and suturing the opposing periosteal surfaces together. This removes bone that might sequestrate at a later date but has the hazard of causing a non-union.

From the time of the first operation for the purpose of drainage and removal of sequestra there have been a large number of materials used to fill in the cavity that surgery leaves. Bone chips have been employed but they usually sequestrate. Blood clots were tried but it was found they were a good media for the growth of bacteria.
Nearly all of the clinicians dealing with osteo have at one time or another concocted a paste that they used to fill the cavity left after operation. Most of these have failed due to their irritative properties which usually came from the antiseptic included. Iodoform was a common material used. In Starr's article Mosetig-Mochof paste, copper amalgam, Beck's paste, Morison's paste, are all mentioned but not recommended. Fat and muscle flaps have been used and are still considered to be of value especially to use close to a joint cavity. (27) Bipp paste, bismuth, iodoform and paraffin base, has been used quite a good deal.

At this time there were many variations introduced into the methods of therapy due to the observations of different men in the World War. Baer revived the idea of a "viable antiseptic" while Orr noticed that his patients improved more with adequate drainage and immobilization. It was at this time, also, that wounds were first irrigated with antiseptic solutions of the kind typified by Carrell-Dakin solution. There have been few different treatments of any value introduced since that time.
In discussing the Baer treatment the method of preparation of the maggots is one that is of the utmost importance but is such a detailed procedure that I am not including it in this article.

In discussing the actual treatment it might be well to give a few of the necessary physical signs before a patient is considered a good risk for the introduction of maggots. No case with a hemoglobin of less than 70 per cent or a red count of less than 4 million is considered for operation. A radical sequestrectomy is performed first and the wounds are not closed but are packed with plain sterile gauze for 48 hours to control hemorrhage. The gauze is removed at the first dressing, the wound is thoroughly irrigated with normal saline, and maggots 48 hours old are introduced. (23) Buchman & Blair don't believe irrigation with saline is necessary (23).

The number of maggots introduced depends on the size of the wound. At each dressing the wound is washed with saline and new maggots are introduced. At operation the skin is prepared with green soap and water and no other antiseptic measures are employed. The method of dressing to restrict the maggots to the infected field differs in most of the methods
employed but they are all of the same nature. Tightly fitting gauze bandages are applied around the wound with an open meshed material, such as crinoline, over the center to allow for drainage and light and air. The effect of the light, natural or artificial, for the first two or three hours is to cause the maggots to bury themselves in the wound and deeper layers of the gauze. There is said to be little pain except for small twinges occasioned by the crawling maggots touching an exposed nerve ending (32). This pain may become so annoying to the patient, especially at night, that it is necessary to remove the dressing or to give sedatives to the patient. The number of dressings or new introductions of maggots varies from five to thirty five with an average of eleven, and the cost of each application is placed at five dollars. (6) This together with the long period of hospitalization of the ordinary osteomyelitis case makes the treat­ment rather expensive. McKeever's method of preparing the maggots is designed to produce unsterile maggots and is some what cheaper although it is also more dangerous.

The first response to the maggots is a lessening of the odor and about twenty four hours later the
wound generates a brownish red offensive foam which wells through the dressing. (29) If the facilities for drainage are not adequate at this time the maggots will be drowned necessitating a new dressing. With the death of the maggots a still more offensive odor is generated. The amount of drainage is said to be five times the amount obtained under any other method of treatment. The discharge is made up of serum, bacteria, pus, and a healing secretion, the origin of which has not as yet been determined. With each successive application of maggots their life span is decreased. This is said to be due to an increased hydrogen ion concentration (alkalinity) and to the increased virulence of the active principle present.

The theory of this action as presented by Livingstone (29) is as follows:

1- Mechanical action. Because of scavenger activities of the maggots it is assumed that they seek, devour, and digest bacteria as well as the wound debris adherent to the surface.

2- Serum production. The reason for the increased wound secretion is not known, but it is probably due to local stimulation from the continuous crawling of the maggots and their persistent
attack upon the necrotic tissue in the wound, thus opening new channels for the free flow of fluid.

3- Active principal production. It is not thought that actions one and two in the foregoing paragraphs are entirely responsible for the healing of the wound. A series of experiments are now being carried out in the clinical laboratory and on the orthopedic service at Edward Hines Hospital which have revealed the presence of the afore mentioned active principle. This active principle when isolated has been effective in curing several of the cases treated.

This agent mentioned by Livingstone is now recognized as phage and will be dealt with under that heading.

Baer and Livingstone both were of the opinion that the scar resulting from this treatment was softer and less likely to become avascular and break down than the scars left by healing through any other type of treatment. McKeever differs in this respect and believes that after bony repair is accomplished the wound should be closed by secondary means of suturing. He states that this will result in a smaller scar and will also hasten the complete repair of the wound.
Albee(3) and Livingstone both agree that an active principle is generated by some mechanism, both obtaining it from a different source but both agreeing it is more important in the treatment than any other factor. Livingstone discovered that dead maggots in the wound seemed to do as much good as living ones and concluded that the scavenger action of the maggots was not as important as some unknown effect they produced. He has experimented with various extracts of the maggots and obtained good results in overcoming the bone infection.

In summarizing the Baer treatment it might be well to mention the type of bony repair that is obtained. According to Livingstone the bony repair in maggot therapy is almost entirely free from differences in density of the new bone. With the Orr treatment he reported that the bony repair showed areas of sclerotic bone intermingled with areas of rarefied bone, while in the same patient he was able to get a uniform bony structure with the use of maggots.

There are numerous objections to the maggot treatment however, the most important one being the danger from the maggots themselves. Baer himself(3) reported two deaths from tetanus in treatment of this kind before he resorted to preparing sterile maggots.
This necessitates elaborate equipment and entails much trouble in the preparation, making it impractical for small hospitals. Also "wild strains" of maggots have been produced that do as much damage to normal healthy tissues as they benefit the individual by devouring necrotic bone, bacteria, debris etc. McKeever (32) using a method of producing the maggots which is not sterile, gives all his patients tetanus anti-toxin routinely.

There is one more objection to this method of treatment that is very important in as much as it destroys the patients resignation to a long period of treatment (33) The actual experience of having the maggots crawling on exposed tissue constantly is usually very disgusting to the patient. If the dressings are not applied carefully each time they may escape and this is also very annoying to most patients.

The treatment of acute and chronic cases of osteo as practiced by Lohr is one that is not in use in this country as far as I can determine from reports in the literature. His treatment, carried out by the use of a cod-liver oil salve and plaster of paris dressing, has been used in cases of superficial burns, injuries to the extremities, and super-
ficial infection; but only recently has he been using it for bone infections. For this reason the case records on the results of treatment do not extend back over a period of five years. (30) In view of the fact that healing of a bone infection can take place so that it can again become active, this article is not conclusive evidence of complete cures. It is generally agreed that young bone tissue will heal without sequestration and sclerotic changes if it is allowed free drainage and is kept at rest and not stimulated to hyperactive proliferation by too frequent dressings. In his method of treatment Lohr makes use of all these facts and admits that they might have a great deal to do with the results obtained.

In general the method as outlined by Lohr is a skin incision over the affected area with just one incision into the periosteum. If there are any sequestra present they are removed but nothing radical in the line of bone surgery is attempted. He adheres to these principals because he thinks that in a young individual with adequate resources the infection can be taken care of by the patient with a minimum of aid. After the periosteum is opened and all the pus removed the wound is packed with cod-liver oil paste and the
wound is sutured loosely to permit drainage. The cod-liver oil is chemically practically non-irratating and dissolves at the edges, because of the body temperature, to permit free drainage. The principle of drainage is therefore maintained. The external wound is then covered with a thick layer of salve and then by a circular plaster of paris dressing. When this type of treatment is employed the patient can be immediately discharged. The day following the operation there usually appears a considerable secretion so that the plaster of paris dressing becomes moist and permeated by pus. This dressing is left in place from 14 to 31 days. The dressing may be changed when the secretion is excessive. With the progress of healing the amount of secretion decreases. When the plaster cast is removed for the first time the wound is more or less healed. When a roentgen picture is taken shortly afterward one finds a picture of a sequestrum resulting from the periosteal proliferation. In these cases however one must not be very hasty in regard to the second operation because a striking restoration of bony tissue, especially in young patients, frequently occurs. If however a sequestrotomy should be necessary 6-8 weeks after
the onset of the disease it must be carried out very radically. Among the patients reported by Lohr this was necessary in about 15 per cent of the cases. Following this operation healing takes place rapidly again.

Altogether in the last 5 years the author has treated 30 cases of acute osteomyelitis. Seven of these cases died, giving therefore a mortality of 34 per cent. Four died after three days from meningitis and multiple abscesses, one died after 30 days from general sepsis, and pulmonary abscesses, and one died after six months from an osteo of the entire thigh, the knee and hip joints. Five of the cases which died belong to those severe types with multiple foci which are no longer amenable to local therapy. The remaining cases responded by a prompt fall of temperature.

Cod-liver oil by mouth and vitamin-containing fresh fruits are given in conjunction with the treatment. In all the patients the gain in weight is very satisfactory. Of all the 33 cases only in one the removal of a small sequestrum was found necessary some later.

The cod-liver oil salve is sterile because of the properties of cod-liver oil. Now and then a
patient may complain of a maceration of the skin below the cod-liver oil plaster of paris dressing. Maceration of this type occurs when the secretion of the wound is excessive. They are easily controlled by waiting a few days before reaplying the dressing and by the application of a zinc paste to the margins of the wound. All of the patients treated by this method four years ago have remained free of new attacks, of fistulae or similar affections and roentgenologically the bony tissue revealed a good regeneration, a clear structure and no signs of transition to the much feared sclerotic form.

This same method is applied to chronic cases of osteomyelitis with the exception that in chronic cases the operator attempts to remove all infected and dead bone and open the area widely before applying the oil and plaster.

The advantages the author claims for this treatment are the absolute painlessness, the elimination of repeated change of bandages, the afebrile course and the satisfactory general condition of the patients, expressed in a considerable gain in weight.

I am not particularly impressed with the clinical record of the patients treated by this method. The mortality rate of 15 per cent is not at all good
but then as Lohr pointed out, it may have been that he was able to obtain only some of the worst possible risks. His principle of drainage, rest, infrequent dressings, supportive measures are just about what all the other authorities are trying to do. It is hardly possible to judge this method because of the small amount of literature that is available as to results obtained and the cases on record do not cover a long enough period to determine the length of the cure claimed.

Dolman (13) has done some rather original investigation in the effect of staphylococcus toxoid in osteomyelitic processes both in the acute and in the chronic stages. He has not published very complete reports, his work emphasizing just the laboratory aspects of the results obtained. The group of patients treated by this means consisted of children with chronic or recurrent migratory osteo to a great extent. The first two injections of toxoid, 0.05 c.cm. and 0.1 c.cm. respectively, were usually followed by an increased discharge of pus from the osteomyelitic focus, but the discharge later tended to diminish. These injections were followed by four injections graduated to amount to 0.5 c.cm. at the sixth dose.
In a few children with several years history of chronic osteomyelitis, one or more discharging sinuses healed over for the first time during or soon after administration with no recurrence since. In other instances sinuses healed following toxoid treatment but broke down again after a few weeks. The general health of all the children appeared to be definitely improved.

In a few adults with chronic osteo of long standing the toxoid seemed definitely to speed convalescence but in other cases there was no apparent improvement in their condition.

The sera of patients in this group showed some remarkable high staphylococcus antitoxin titres. Almost invariably the initial titre was above normal, and children with osteomyelitis with metastatic lesions showed an especial ability to develop high titres.

With the material at hand it is difficult to judge this type of treatment but the principle of the treatment is sound as far as the early hematogenous stage of osteo is concerned. While the infection is in the blood stream and there is very little, if any, bony destruction present; the use of measures designed to build up the patients immune reactions should be of value. It would not seem to be the
primary issue in the later stages when the focus becomes suppurative, but should deserve to be investigated more extensively to determine its possibilities.

Like the Baer method and Orr method the idea of treating osteo with irrigations of Carrel-Dakin solution was evolved during the World War. This sort of treatment is based on the principle of actually destroying the invading organism by the use of a strong antiseptic. (27) Advocates of this method depend on the patient to overcome the blood stream infection but attempt to rid the host of the localized aspect of it by the use of the Carrel-Dakin solution. To do this they irrigate the wound as many times a day as is thought advisable with the solution. This is done through a number of rubber tubes, varying with the size of the wound, that are introduced into the depths of the cavity after it has been saucerized and extend out of the dressings so that the solution can be injected into the tubes without disturbing the dressings. The part affected is supported by a cast with a window or splints as in most other methods.

This "antiseptic" method of treating osteomyelitis is not in very good repute with the majority of authorities on the subject. The principal objection
is due to the fact that the drug is too irritating to the tissues to permit the regenerative powers of the bone to function at their best, resulting in a long hospitalization. Some observers claim that even the normal tissues are injured. There is also the frequency of dressings to further disturb the granulating surfaces and retard healing processes. Orr also states that with the number of dressings and irrigations required, it is impossible to properly immobilize the part and there is greater danger of pathological fractures. "Eusol" is another drug that is essentially Carrel-Dakin solution and possesses the same disagreeable features.

Brockway has published reports on treating cases of osteomyelitis by the use of warm salt water bath. (5) This is in use almost exclusively in chronic cases and really has no place in the treatment suitable for acute osteo. It is carried out by placing the involved extremity in a warm salt solution for a certain length of time every day. The time element is determined by the degree of pathology present. The part is supported by a splint if necessary to prevent a spontaneous fracture. There is not a great deal of material in the literature on this method and it doesn't enjoy much popularity with the authorities.
on bone infections, making it difficult to say that it is or is not good therapy.

Max Thorek has exclusive use of a method of treatment that has not received very much attention. He packs his cavities with aluminum-potassium-nitrate paste, which he believes promotes the growth of the bacteria, thereby attenuating its virulence; and stimulating bodily defense by its irritant action tends to overcome the infection. He states it is not antiseptic, is non-toxic, and does not interfere with normal tissue metabolism. He makes claims for his method, that it is very beneficial, but so far has no followers among the recognized authorities.

In considering the Orr treatment of Osteomyelitis we should first attempt to understand the rational of the principles upon which it is based. Orr believes that, in view of the fact that there are no known antiseptics that are strong enough to destroy bacteria in bone infections we must look elsewhere for methods of combatting this problem. He believes that the use of antiseptics which dates back to the time of Lister and was especially developed, at that time, by Thomas H. Markoe, has only delayed the progress that should be made in the treatments of osteomyelitis. (37)
Orr states: "the application of the methods of Lister to the treatment of wounds has by no means yielded such fine results as when applied to the performance of aseptic surgical procedures. This suggests that primary asepsis is the fundamental and important thing and not antisepsis in the presence of infection." (7,43) Proceeding from this assumption Orr outlined his program of treatment roughly as follows.

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

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

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

4- Immobilize (not simply apply a splint) so that movement, pain, and muscle spasm are entirely relieved, and all the parts are in correct position for recovery with a minimum of deformity.
and disability.

Orr arrived at these conclusions after observing a great many cases during the World War and has to offer as proof of the correctness of his observations many clinical results obtained with these principles governing the treatment.

The exact technic of the operation as laid down by Orr in his first papers is followed with a few minor alterations, by many surgeons treating this disease today. These principles are as follows: (36,40)

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

2- Chisel a window into the affected bone area large enough so that all diseased bone may be removed and so that there are no overhanging edges of bone over the diseased area. (Less extensive in acute cases)

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

4- Dry the wound and wipe out with 10 per cent
iodin followed by 95 per cent alcohol.

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

6- Now perform any reasonable forcible manipulation necessary to place the parts in correct anatomic position for splinting (abduct the arm to 90 degrees in humerus cases; dorsiflex and supinate the hand in forearm and wrist cases; dorsiflex the foot to a right angle with the leg, in leg and foot cases, etc.).

7- Apply a plaster cast or a suitable splint so that the parts are thoroughly immobilized in comfortable and correct position. Any measures necessary for the correction of deformities may also be employed.

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

Since Orr first started his work he has changed his opinion on the matter of employing antiseptics following operation. He does not use iodin and alcohol any more but merely dries the wound and applies the cast. This change has been occasioned by the recognition of "phage" as a factor in healing and the belief that any sort of antiseptic measures tend to destroy or at least retard the development of this aid. Kulowski (24) using the Orr method with a few variations still believes in the use of iodin and alcohol. He uses it merely to exclude any possible secondary contamination at the time of operation, and does not think that it plays any important part in the treatment of the disease. This writer also thinks that the antiseptic has some hemostatic value, and places emphasis on the need for leaving the area dry and bloodless. The presence of blood clots forms a perfect media for the growth of bacteria. (41)

The use of hot packs following operation are also employed by Kulowski to be sure of hemostasis.
He also differs in detail from the Orr Method in that he believes that the bone should be removed down to and including a small amount of the healthy bone to insure a sound base for the repair process. Orr does not insist on saucerization if adequate drainage can be obtained with a window contending that small sequestra will be extruded through this window but Kulowski does a complete saucerization. These differences are merely technicalities and do not seem to occasion much difference in the clinical result.

The points in favor of this method are numerous. With such infrequent dressings the surgeon himself can keep in touch with the treatment of the wound and the patient. There is a great saving of labor and materials, and finally, and most important, the patient is spared the suffering attendant upon frequent dressings and makes more rapid and more satisfactory convalescence.

Many observers are of the opinion that long periods of immobility cause an ankylosis of the joint proximal to the diseased area. Kulowski states that he has never found this to be the case in a patient where the joint is not involved. He has observed temporary stiffness which disappears after the patient becomes ambulatory and in cases where the joint is
involved ankylosis is to be sought and not avoided.

In a series of 130 unselected cases of osteo reported by Kulowski (23), 99 were completely healed. The average time of healing was seven and fifty-eight hundredths months. The patients who were operated on primarily by the Orr method, without previous treatment, healed in six and twenty-one hundredths months. The cases treated secondarily by the Orr method healed in eight and ninety-five hundredths months. All conditions favoring secondary infection, such as the presence of sequestra or chronic sinuses, prolonged the healing time as did the presence of multiple foci of infection or joint involvement. The duration of the disease or the age of the patient did not seem to influence the regenerative healing power of the bone.

There were three deaths and six secondary amputations in this series. Only one death could be definitely attributed to the operative procedure. Of the amputations three were of mixed tuberculous infection. There were 154 lesions in the cases studied upon which 194 operations were performed. There is some degree of shock observed in the operative cases, especially where the femur is involved. For this reason Kulowski does not advocate operation on more than one site at a time in a case with multiple foci.
In the post operative care of patients treated by this method it is further emphasized that the vaseline dressings that are placed in the wound at each change of dressing should be placed in carefully and not packed in so as not to injure or disturb the granulations that are present on the healing surface of the area. The wound should be kept wide open so that healing from the bottom with good bony structure is obtained. Orr claims that the "antiseptic method" of treating osteomyelitis with frequent change of dressings, irrigations with strong antiseptics, etc., brings about more secondary infections, interference with the reparative processes, and by disturbing the wound produces more signs of a generalized sepsis than a policy of rest and "let alone".

In discussing bacteriophage it is not my purpose to attempt to present all the technical problems involved in the artificial preparation of a "phage" but just to try to explain the action it has when used in treating osteo, how it is used to best advantage, and a relative idea of what to expect from its use. There are several ideas as to why bacteriophage is beneficial when used in treating any infectious focus.

Boder believes that his experimental investigations support the theory that the therapeutic action of a bacteriophage is due only for the smallest part to a destruction of the bacteria in the sense of a
bacteriolysis, but is based essentially upon an alteration of the inciting organism, rendering it more accessible to the defensive forces of the body, in the case of osteomyelitis to phagocytosis. (20) Larkin (25) is of another opinion in as much as he thinks the action seen with the use of "phage" is due to the increased production of anti-toxins. In a series of experiments, using rabbits as the testing agent, he noticed hemolysis of the rabbits blood with either a staphylococcus toxin or a bacteriophage prepared from the organism. When the animal was with bacteriophage, hemolysis of the red cells following the introduction of the staphylococcus toxin was very noticeably diminished indicating that the host was producing anti-toxins at an increased rate and neutralizing the hemolytic effect of the toxins.

There is much other work done by investigators to prove both theories but this aspect of "phage" is not of primary importance here. It is overshadowed by the actual clinical uses and results.

A stock bacteriophage contains the antigen of a specific organism, metabolic products of this organism, the nutrient medium used in the preparation of the phage and a "lytic principle". (21) It is universally conceded that a specific bacteriophage
usually gives better results than a stock bacteriophage. No results at all can be expected with the use of, for example, a coli "phage" in a staphylococcus infection.

The use of bacteriophage is necessarily dependent on surgery to render the infected area accessible to the phage. In this respect Albee has agreed with Orr that the area should be opened widely and sauced to allow drainage and a better approach to the area. (2) After the primary operative procedure Albee takes a culture. If he has already found a specific bacteriophage, from a culture previously taken from a draining sinus, he pours two thirds of a test tube of this phage into and over the wound, so that the whole surface is bathed. He then packs the wound with a mixture of paraffin and petrolatum, either heating and pouring it in or forcing it through a syringe. He inserts one end of a rubber catheter through the paraffin-petrolatum wound tampon to the bottom of the cavity. He allows the other end to project through the dressing and cast with a sterile gauze or cotton dressing over the end. A laboratory phage is developed that is specific for the organism present and about 10cc. of this phage is injected through the rubber catheter once or twice a week,
Should the bacteriophage appear spontaneously in the wound, injection of the laboratory bred phage is still of advantage in that it accentuates the action of the native phage and may be a more specific one. As the catheter is firmly embedded in the paraffin-petrolatum tampon, the injected phage fluid cannot flow backward between the catheter and the tampon. It must therefore make its way inward between the tampon and the wound granulations and this, by reason of its bulk, spreads widely. At the end of 8 weeks the cast, applied nearly as Orr advocates, is removed and the wound dressed. Great care should be taken not to traumatize the granulating surfaces. If the wound is not entirely healed when the cast is removed, he again bathes it with a test tube of the prepared specific phage fluid and inserts a catheter or catheters to the depths of the wound. He again applies a paraffin and petrolatum tampon and a cast and repeats the treatment as before. Another culture is taken at this time to determine if the bacterial flora of the wound has changed and whether a more specific bacteriophage can be obtained. Albee has observed an average healing time of six months under this treatment which is somewhat less than the healing
time under the Orr treatment.

The procedure as outlined above is nearly the same as the rest of the clinicians use in a treatment by phage. Orr, since he first developed his own method of drainage and rest, believes that the cure seen in his cases is due in a large measure to the development of an autogenous bacteriophage. He is very interested in the development of bacteriophage therapy at this time and will very likely combine the two treatments as outlined by himself and by Albee. Livingstone (29) was originally interested in the development of the maggot treatment but since he observed that just as good results were obtained with the use of dead maggots in the wound he has abandoned his original ideas and begun to develop the use of a maggot extract in the belief that it stimulates an autogenous phage to develop. All of the writers who have had a lot of experience in this type of treatment give a very high percentage of cures, the average being about ninety percent of complete cures with no recurrence, but there are some reports that do not confirm these high results.

Bagley and Keller reported a study of ten cases of osteo that were treated with bacteriophage. They did not make use of the tampon method as developed by
Albee but used gauze packs wet with the phage and intramuscular and intravenous injections. (4) The use of gauze packs seems to be opposed to the ideas of most other investigators in that it causes too much disturbance with the granulations developing in the healing wound. The Gratia H. Strain was used in all but one case and gave lysis in vitro as well as in vivo which is a requirement, according to Hauduroy, (17) before good results can be expected. In this series, however, only three cases were pronounced cured with no recurrence to date while two died and the rest of the cases became chronic. The phage was used intravenously in three cases where a septicemia was discovered and toxic symptoms were very pronounced. Two of these cases died while one is still living. They concluded from their studies that the bacteriophage used in cases of osteomyelitis due to staphylococcus gave quite satisfactory results but were hesitant to endorse its use where other organisms or mixed infections were demonstrated.

In summing up advantages and disadvantages of the phage treatment of osteo it is first necessary to realize that the treatment is only as good as the maker of the phage. By this statement I mean that there is so much technical knowledge and skill in
the production of a "pure" phage and one that is specific for the organism infecting the patient that anyone not acquainted with the procedure of developing a phage or with the eccentricities of bacteriophage is not very likely to obtain any startling clinical results. It seems to me that Albee's method of treatment is somewhat better in as much as with the use of the tampon reinfection of the wound and undue disturbance of the granulating tissues is practically eliminated. Until the production of autogenous phages is made possible it doesn't seem that uniformly good results will be obtained. It seems from the literature reviewed that a phage developed from the patients own organism is much more likely to be specific and since this is technically so difficult to develop it seems that this method of treatment of bone infections will not be of practical value until facilities are available to nearly all the practicing physicians for its production.

D'Herelle has stated in his work on the subject that phage does not have any beneficial effect in a septicemia and since an early osteo is accompanied by a septicemia (16,45), this would not seem to be of any help in an early acute stage. The writers who are most impressed with the use of bacteriophage
don't use it for its systemic effect but for the effect in the localized tissue abscess so they are still within safe limits in claiming the results they do.

It would seem after studying a large number of reports of case histories that the best clinical results are obtained from the Orr method of treatment, that is very open drainage with complete immobilization and rest for the infected part. The various modifications of his treatment seem to get as good results but they are the same treatment as far as basic principles are concerned. There seems to be a very good reason to suppose that at least part of Orr's results are due to a combination of his principles with the effect of the development of an autogenous bacteriophage. He is of this opinion himself as revealed in some recent work of his. It was possible to culture or demonstrate the existence of a phage in almost ninety per cent of the cases that he had treated by saucerisation and immobilization. With this in mind one would be inclined to think that a combination of the Orr operative procedure and the use of phage would be even a better treatment than either one alone.

An aspect of the problem of treatment of osteo that I believe is even more important is that of making an early diagnosis of the condition. By an earlier
Diagnosis the amount of destruction of tissues is greatly reduced, the pain and discomfort to the patient is lessened, the number of acute cases becoming chronic is definitely lessened which is a very important consideration from the economic standpoint. With the average physician more familiar with the early signs of a bone infection, the number of cases of osteomyelitis diagnosed before there is extensive injury to the diaphyseal portion of the involved bone should increase very markedly.

Grossly, we can not tell the difference between diseased bone and healthy bone. At some point the bacteria are just invading and the bony changes that take place are not discernible. This is similar to the condition seen in an acute osteo in which we have only the inflammatory stage with no x-ray evidence of gross changes demonstrable. The bone that has undergone necrosis and is decalcified can be recognized but what is attempted in the surgical approach in osteomyelitis is to remove the bone beyond the limits of the infection. This limit can be reached by surgical means only after the entire field has been contaminated, since we carry our instruments from healthy to unhealthy tissue. It is evident then that by any surgical procedure the infection is disseminated more
or less and a certain amount of healthy tissue is sacrificed.

If it was possible to demarcate (form sequestra) the healthy bone from the diseased bone, operative procedures could be carried out more effectively and with more economy as far as healthy tissue is concerned. Due to the nature of the tissue in a bone infection, the metabolism is such that this is not an ideal site for such a process to take place. It would then seem very beneficial if there was some drug that could be carried by the blood stream that would aid the natural defenses of the tissues enough to enable them to accomplish this healing process and thereby save the healthy bone from destruction by surgical means or by a further spread of the infection.

At present the aseptic technic in surgical procedures is almost beyond reproach. Our surgical technic itself in relation to anatomy and the mechanics of the parts involved has reached perfection in the hands of the skilled specialists, yet there are diseases that we have not conquered, osteo being one of them. The approach in treating osteo that has not been developed is that of "antisepsis". If the surgical technic could be applied to an asep-
tic and also an antiseptic technic then it would seem that we are taking the next and most important step in surgery. The antiseptic that could be employed in such a role would have to be such that it would destroy the bacteria in the tissues without having any injurious effect on the tissues themselves. The antiseptic technics in use at this point in the treatment of osteo are all too strong to be used without effecting harmfully the normal tissue.

The solution to this problem would seem to be a mild germicide plus a cell stimulant of such a nature that phagocytosis would be increased and the healing processes in the tissues would be stimulated to more rapid and complete cell production. Such a drug is in existence but since there are no papers on record, I have nothing but the actual clinical results that I have seen obtained with its use on which to base my statements.

The answer to the specifications of such a drug seems to be in the application of certain groups of sulphur combined with heavy metals. Sulphur in combination with other elements (in certain radicals) possess peculiar properties such as the action on the growth of cells. The introduction of such a drug into the surgical procedures already at hand would seem to
be the answer to the treatment of osteomyelitis as well as many other infectious conditions.

Our knowledge of sulphur, the role it plays in metabolism and the part it will play in the future in the treatment of disease is most problematical. The molecular structure of the sulphur radical and the manner in which it enters into cell processes is not known but in view of recent work it seems that the solution to such problems as osteo lies in a chemurgic approach to augment surgery.
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