Osteomyelitis: Historical review

Abulfotooh M. Eid, M.D.

I. EARLIEST OCCURRENCE:

Osteomyelitis seems to have been a frequent occurrence not only in man, but also in fossil animals. Moodie described gross and microscopical features identical with those of osteomyelitis following fracture of the posterior dorsal spine of a Permian reptile.[1] This denotes that the disease has been encountered at such an early period of history of the earth, long before the advent of man.[2]

Associated with trauma, as it is, it must have affected early man frequently as his wild life exposed him to frequent open injuries. The proofs of its existence should have survived over the years. The paleopathology of soft tissues may not have but a limited material to illustrate it and only in well conserved mummies. On the other hand, bone is well preserved by its own nature and any disease that has affected it will leave its impression on it. As a matter of fact, the bones of dawn man, of which thousands of skeletons have reached us, being unearthed from the caves and buried grounds of Europe, Asia and Northern Africa, tell us that a common disease was inflammation of the bones, involving a joint and producing a deformity.[3]

The word pus has appeared quite early in the medical terminology. The Edwin-Smith Papyrus, "the earliest surgical treatise"[4] mentions the word "ryt" (pus) five times in its hieroglyphic text. Of course osteomyelitis is not clearly denoted as such in this Papyrus. However, those cases of wounds communicating with bones and pouring ryt (pus) were, most probably, cases of osteomyelitis. Although the author of this treatise described these wounds pouring pus to be "inflamed", it is not clear whether or not he knew that this inflammation could have involved the underlying bone.

Sequelae of Osteomyelitis in the skeletons and mummies of ancient Egyptians were met with. Elliot-Smith and Dawson in 1924 stated that mastoiditis and alveolar abscesses were frequently met with in the ancient Egyptian mummies.[5] Aboubakr and Abadir in 1955 mentioned that cases of periostitis and periostitis ossificans have been found and that osteomyelitis and mastoiditis were frequent in Nubia and Egypt.[6] As a sequel of open fractures evidence of bone infection was extremely rare.[7]

As a result of acute haematogenous infection, not a single case has been described. Apparently, these cases of osteomyelitis whether primary haematogenous or secondary to open fractures, could not live long enough for the pathological process to leave its imprints on the bone. This is because the mortality of these cases was regrettably high. [8]

II. TERMINOLOGY:

Various terms have been used by different authors to denote inflammation of bones. They have all been based on the pathogenic theories held at the time they started to be used. *Cold* "زكام"of the bones was the term used by Albucasis (Abulquasim Ez-zahrawy) in the eleventh century.[9] Cold was considered the aetiological factor of the disease by many authors prior to the discovery of bacteria[3].

Corruption "فساد" of the bones, was the term used by Avicenna (his real name is Ibn-Sina) and most Arab authors.[10]

Necrosis was the term used by Gross in 1830[11]. In his opinion the disease was mainly the result of necrosis. This was believed to be either due to local causes, such as blows, wounds, fractures and burns, or to general causes.

Typhus of the bone was the term used by Chassaignec in 1853, recognizing only the fulminating cases in which the patient quickly falls into "typhoid state".[12]

Carbuncle of the bone, was the term coined by Pasteur in 1860.[13] He noticed that the organisms were the same, both in the ordinary abscesses and bone infection.

Osteitis was the term used by Nowicki in 1931[14] and preferred by Dennison in 1948.[15] They believed that the inflammation involved mainly the bony tissues and that the bone marrow played only a small role in the suppuration.

Periostitis, osteitis and myelitis were terms applied by some authors to denote inflammation of the separate bone structures: periosteum, cortex or medulla respectively. The term *Osteomyelitis* was reserved to the combination of infection of the cortex and

Emeritus Professor of Orthopaedics and traumatology Faculty of Medicine, Alexandria University, Egypt.

medulla.[16] *Osteoperiostitis* was the term commonly used by other authors denoting that the main lesion was found to affect the cortex and periosteum.[15]

Periosteomyelitis was the term used by Starr in 1922[17] denoting that all the bone structures are affected in the process.

Osteomyelitis is the term more universally employed nowadays in relation to any bone inflammation. It was the term coined by Nelaton in 1846.[18] Wilensky in 1934 stated that this term was not in use before Nelaton..[19] According to leveuf in 1947, Lannelongue was the first to use this term in 1879 because he thought that the initial infection took place in the bone marrow.[20]

III. HISTORY OF THE PATHOLOGICAL KNOWLEDGE:

The first specialized treatise on bone was the Edwin-Smith surgical papyrus (1600 B.C.), translated by Breasted.[4] This accurate and systematized compilation of cases told us that the ancient Egyptians expected a fracture to communicate with the exterior of the body when it was overlied by a wound. They wisely avoided probing of wounds, accusing it for causing pus formation. They were afraid of pus, though they had no knowledge of bacteriology as far as we know. They noticed that a wound over a fracture could remain open and discharge pus. They then expected the extrusion of small pieces of bone.[21,22,23]

The Greeks derived a great deal of their knowledge from the Egyptian civilization.[24] Hippocrates in the fifth century B.C. described osteomyelitis of the skull and long bones especially after wounds. He recognized the extrusion of sequestra and that the scar resulting became depressed, and attached to the underlying bone.[25]

When Rome came to rule the World, about the third century B.C., the name of Celsus became famous for his classical description of inflammation. Galen (130-210 A.C.) described infections in bones after open fractures. He maintained that suppuration was essential to healing and insisted that the right kind of pus was the laudible pus.[23]

Medicine entered a static period of its history after the decline of Rome and Alexandria. The rise of Islam in 622 A.C. resulted in rapid revolution of all sciences, including medicine. This was part of the Islamic notions in the Holey Quran and the instructions of Prophet Mohammad, who urged all Moslems to search for therapy "as God did not create a disease without creating a treatment for it", so He said.[26]

«تداووا عباد الله فإن الله لم يخلق داءا إلا وله دواء»

Such names as Rhazes (860-932), Haly Ben Abbas (994), Avicenna (980-1037), and Isaac Judeus (955) became famous.[23]

Here is the instructive text of Avicenna quoted from his Canon[10]: "Section on the manifestations of foul bones: If bones are affected by corruption you will see that the flesh over it has become redundant and lax. It putrefies and forms pus. A probe passes through it easily and reaches the bone. When the bone is touched it does not feel smooth and slippery. It gets slightly stuck to it as if it finds in it something unstable. It may crepitate or soften especially if corruption is not at its start. If it is at its beginning this is not seen. If you expose it you will find that its colour has changed. It is commonly preceded by swelling and corruption in the flesh, which is then transmitted to it (to the bone). The original Arabic text reads as follows:

فصل: فى علامات فساد العظام: إنه إذا عرض للعظم فساد رأيت اللحم فوقه ترهل ويسترخى ويأخذ طريق النتن والصديد وينفذ فيه المرود إلى العظم أسهل ما يكون. فإذا وصل إلى العظم لم يجده أملس يزلق بل يلصق به قليلا وكأنه يجد شيئا غير ثابت فى نفسه. بل قد تفتت أو تعفن وربما تخشخش ولان وخصوصا إذا لم يكن الفساد فى الابتداء فإنه فى وقت الابتداء لا يظهر ذلك وإذا كشفت عليه وجدته متغير اللون وكثيرا ما يتقدمه ورم وفساد من اللحم وفساد ثم يدب إليه ....

The eleventh century witnessed Albukasis (Abulquasim Ez-zahrawy). This eminent man wrote the only surgical treatise over this period. He gave full description of cases of osteomyelitis and advised for their treatment in a detailed manner[8,27] [Vide infra].

In a law suit for medical fee in Massachusetts in 1660, there was an interesting description of a case of chronic osteomyelitis diagnosed as the king's evil.[2]

Alexander Monro in 1740 remarked the grave prognosis when the disease affected the vertebral column.[28]

Hunter in 1786 was the first to describe the mechanism of sequestrum formation. He pronounced the importance of the periosteal blood supply in calling for early incision of subperiosteal abscesses, "to prevent as much as possible the separation of the periosteum".[29]

Dorsey in 1818 wrote at length on necrosis of bone.[30] Ten years later, Nathan Smith noted that the disease was almost confined to young patients.[31]

Full description of the disease was given by Liston in 1837 in his "Elements of surgery".[32]

The cause of osteomyelitis remained obscure until Pasteur in 1860 demonstrated the presence of living microorganisms that could cause osteomyelitis.[13,33] Before him, the disease was thought to be caused by a "severe cold". Soon the common offending organism became known and named "Staphylococcus",[34] that was derived from two Greek words Staphyle which means bunch of grapes and Kokkos which means grain.

The differentiation of chronic osteomyelitis from tuberculosis of bone was not possible except after the isolation of the tubercle bacillus by Koch in 1882.[35]

The haematogenous route of infection in osteomyelitis was proved experimentally in animals by Rodet in 1889.[36]

Lexer in 1894 clarifying the haematogenous lesion stressed the effect of trauma as a focus of lowered resistance in the localization of the circulating microorganisms.[37] The importance of the presence of such an area of lowered resistance was much appreciated later on. It has been found that neither the local injection of staphylococci[38] nor their intravenous injection[39] alone were able to produce osteomyelitis. Osteomyelitis occurred only after injection of sodium morrhuate into the metaphysis, producing local necrosis, thus allowing bacteria to settle and initiate the disease.[38]

The first detailed description of localized abscess formation in long bones came by Benjamin Brodie in 1819.[40] He considered it a residuum of a previous low-grade osteomyelitis.

In 1864 Ollier[41] described a special type of bone necrosis which was reported by Poncet under the name periostitis albuminosa.[42] He considered it a local cortical and subcortical involvement by organisms of low virulence. This entity was later traced by Kuth in 1938 who was able to report 66 cases.[43]

By the year 1890, Chyne described a case of osteitis in the radius in which at operation a sequestrum was removed without a trace of pus being encountered.[44] Garre's description of similar cases came in 1893 after which the condition became known by his name.[45] He named it "Sclerosing non suppurative osteomyelitis".[46] Osteoid osteoma was considered a localized form of this entity, although Jaffe and Lichtenstein considered it neoplastic.[47]

The occurrence of malignant degeneration in the osteomyelitis sinuses was first described by Caesar Hawkins in 1833.[48] The second case was reported by Dittrich in 1847.[49] It was called the warty tumour.[50] Later on, reports followed classifying this condition into superficial and deep tumours.[51] Sarcomatous formation is more rare than carcinomatous degeneration.[52,53]

The nature of the disease was completed by the discovery of X-rays, by Roentgen in 1896 which facilitated the understanding of the bone changes.[54] Tomographic studies were used to demonstrate deep-seated small cavities.[55] Planographic studies helped to demonstrate small sequestra.[56] Diagnosis of the bone changes in the early stages of acute osteomyelitis did not benefit from Roentgen discovery except recently when the soft tissue changes occurring early in acute osteomyelitis became understood.[57,58] Advances in imaging have added much to the understanding of the pathology and diagnosis of different stages of osteomyelitis by scintigraphy,[59] ultrasonography,[60,61] Isotope bone scan,[62] computed tomography[62,63] and MRI.[64] New imaging modalities have improved the diagnostic and differential diagnostic criteria of bone infection such as fluorine-18-fluorodeoxyglucose- positron emission tomography[65] and sequential radionuclide bone- marrow and bone scans[66].

Phemister in 1924 described the silent foci of osteomyelitis which may remain silent for variable lengths of time and be discovered only by chance.[67] The danger of these foci is that they can be reactivated at any time. Gallie in 1951 described the flare up of a case of osteomyelitis after 80 years of quiescence.[68]

The mechanism of bone destruction in this disease was and still is controversial. At first it was thought to be a lytic effect of the toxins of the invading organisms.[69] Axhausen in 1914 advanced the hypothesis that necrosis was due to septic infarction, that is the collection or deposition of organisms in the lumina of the smaller branches of the vascular network which interfered with the regional circulation of the bone.[70] Starr in 1922[71] and Wilensky in 1927[72] and many others emphasized the fact that acute osteomyelitis is a metastatic lesion occurring during the course of bacteraemia. To them the retardation of the circulation as it passes through the tissue spaces of the bone, especially at the metaphyseal level, explained the tendency of blood born microorganisms to settle in this area.

Larsen in 1934 offered a different opinion.[73] He suggested that suppuration and the products of its tissue reaction caused an increased intramedullary pressure which produced ischaemia leading to necrosis. In his experiments, Larsen stressed that the amount of necrosis resulting is in direct proportion to the extent of intramedullary pressure and its duration.

Hobo (1921 - 1922) ascribed metaphyseal localization to the lack of active phagocytosis in the metaphyseal ends of long bones[74].

Many predisposing factors of the acute stage were known and mentioned in many textbooks. These included debilitating diseases, malnutrition and others. Genetic and immunological factors including certain tissue factors have also been blamed.[75,76,77]

IV. HISTORY OF MEDICAL TREATMENT:

Very early in history, the ancient Egyptians treated suppurations of bone by poultices of ground snakes, incinerated toads and puppies and by decoctions of various herbs, even sprayed perfumes and soft music were used.[78]

The ancient Chinese treated

bone inflammations by the application of small pieces of slow burning wood over the painful area. The Hindus followed their old dogma "The fire cures diseases which cannot be cured by the knife and drugs".[3]

In the fifth century B.C. Hippocrates turned Greek medicine into science. His writings were under the effect of one basic rule "diseases which are not cured by medicines are cured by ironing; those not cured by ironing are cured by fire; those not cured by fire are incurable". These principles were adopted by his followers, Celsus, Antyllus and at last Galen[3].

The ninth century A.D. witnessed Avicenna and his Arab successors. They revolutionized the lines of treatment with more interest in the medical aspect of the problem.[23]

Hunter in 1786 preached that immobilization and rest constituted the basic treatment of bone inflammation.[29]

Liston in 1837 advised, beside surgical treatment, "the administration of purgatives and nauseating doses of antimony, encourage the patient to move the neighboring joints, support the patient's strength and give the limb support and rest".[32]

The introduction of antiseptics by Lister in 1867 was a real achievement,[79] but soon it was realized that those agents can damage human tissues in the same way they can inflict death to the bacterial cells.[80]

World War I gave surgeons a tremendous experience in the treatment of open fractures and to some extent osteomyelitis. It must be emphasized, however, that to all practical and therapeutic purposes, haematogenous and post-traumatic osteomyelitis were appreciated to be different lesions.

Baer in 1931 in the period just following World War I, made the interesting observation that wounds which were contaminated with maggots " the larvae of the brown fly" healed with apparently greater ease than many of the wounds which had remained uncontaminated.[81] Other authors reported on the success of the method in the same era.[82-85] Maggot therapy was applied in the acute as well as the chronic stage of the disease.[84] This observation has been made long before by Pare in the sixteenth century,[86] Larry in 1882,[87] and Pirogoff in the mid nineteenth century.[88] During the American civil war, surgeons mentioned that maggots were actually more efficient at digesting necrotic tissues than the scalpel or nitric acid[89],- and advised their use to debride wounds of the soldiers.[90] However, 14 centuries earlier Prophet Mohammad of Islam has emphasized the curative effect of flies. He said:

«إذا وقع الذباب فى إناء أحدكم فليغمسه كله ثم ليطرحه، فإن فى إحدى جناحيه داء وفى الآخر شفاء»

Here is the English translation:

"If flies fall in one's dish, he should immerse "it" completely, then throw "it" away, as in one of its wings there is "something which causes disease" and in the other there is "something which causes cure".[91]

Recently there is an increasing interest in maggot therapy inspite of the advanced surgical technology and antibiotic therapy. The spectrum of conditions which responded to maggot therapy include skin and soft tissue wounds, pressure ulcers, ulcers due to venous stasis, neuro-vascular ulcers and diabetic foot infection.[92-95]

The biological and bacteriological backgrounds of this sort of treatment were investigated, so also were the methods of cultivation, sterilization and application of the larvae[81-85].

Baer applied maggots to gaping wounds left after thorough cauterization of the bone; the wounds healed remarkably well with astonishing clarity. He believed that maggots removed necrotic tissues and microorganisms by actual ingestion.[81]

Buchman and Blair in 1932,[96] and Buchman in 1934,[97] believed that the efficacy of the method depended on the action of the proteolytic enzymes secreted by the maggots on dead tissues, the physical removal of the microorganisms by the maggots and the minimal irritation of the wound caused by their activity.

Livingstone and Prince in 1932 believed that the value of the method depended on an active principle which they have obtained from maggots' extract and recommended its use.[98]

Stewart in 1934 believed that calcium carbonate was the active principle of the maggot treatment and suggested a chemical technique whereby this salt was diffusely precipitated in the cauterized wound.[99]

Robinson in 1935 discovered that allantoin was present in the excretions of maggots. He suggested its use as the active principle of maggot's therapy without the actual presence of maggots.[100]

Hall in 1995[101]believed that the effect of maggots was due to washing out of bacteria by serous exudate caused by the irritating effect of maggots in the wound, where as Thomas et al [102] related this to the secretion of various therapeutic and antimicrobial agents. The advantages of this method of treatment are believed to be efficacy, safety, simplicity and low cost. [95,101]

A main disadvantage of the method ,however, was the irritation to the skin by the action of the migrating larvae. For this reason the skin had to be protected by applying adhesive tape, rubber plastic or collodion on the skin around the wound.[81] Jewett in

1933 used the Unna's paste for the same purpose[103].

Albee and Patterson in 1930,[104] following the bacteriological work of d'Herrelle, suggested adding stock bacteriophage to the vaseline pack of an Orr dressing "vide infra". They claimed that the effect of the Orr treatment was due to the development of bacteriophage in the wound.

Brockway in 1932 introduced the method of treatment of osteomyelitis in the warm-salt-water pool. This, he believed, came more in indication if the disease process was near or involved a joint. He stated "it is a well recognized fact that the best stimulation to healing in the chronic stage of osteomyelitis is physiological motion. Also by means of the difference in the osmotic pressure between the solution (6-7 %) and that of the body fluids; the latter being higher, drainage from the infected tissues was accelerated. This, in turn, induces a regular and efficient washing and cleansing of the wound from its inner most depths".[105]

Benians in 1933 recommended using benzol by mouth.[106]

Terrel Gray in 1934 abandoned operations altogether,and treated his patients with mercury chloride in doses of 0.10-0.25 gm. given intravenously every day or every other day.[107]

Humpharies in 1936, believing that the disease is due to intestinal poisoning which lowers the germicidal properties of blood, treated his patients by means of liquid diet and immobilization with no operation[108].

Antitoxin has been used as an auxiliary to bone drainage, but with variable results.[109,110] Doliman in 1932 recommended the use of toxoid as well as antitoxin. He believed that the antitoxin was primarily antitoxic, indirectly bactericidal and definitely antileucocidic.[111]

All these methods were cut short by the birth of chemotherapy which rapidly took a firm clench on the disease.

Early before World War I Salvarsan was developed by Ehrlich.[112] Its use, together with other arsenic compounds such as neoarsphenamine, in the treatment of osteomyelitis, was tried and gave good results.[113] The sulphonamides followed. These were rapidly welcomed by the medical profession, as they realized the dream that long filled the imagination of surgeons to have a substance which will halt the multiplication of bacteria. Sulphanilamide was the first member of these agents and was synthesized by Gilmo in 1908.[114] Domagk in 1935 used the combination of Sulphanilamide and hydrocuparine and found that it was bactericidal in vivo. He called this compound Prontosil.[115] The other members of sulphonamides followed in succession. Good results were reported for these drugs in the treatment of osteomyelitis.[116-120] However, Bick in 1941

concluded that though these drugs saved life and shortened the duration of the disease, yet the local abscess had still to be drained and, in general, sulphonamide therapy in acute haematogenous osteomyelitis could not be a substitute for surgical treatment.[121]

The contamination in 1878 of a plate of Staphylococcus aureus by the spores of the species of penicillium was the beginning of the study of penicillin by Fleming.[122] The existence of penicillin was known to Fleming in 1929.[123] However it was not until 1940, that the Oxford Group of investigators reported its effectiveness against pathogenic organisms. In 1943 Florey and Florey prophesized that "one might anticipate the time when osteomyelitis treated early and intensively with penicillin should not require surgical intervention".[124] This prophecy was about to be fulfilled, as by the late forties and early in the fifties of the twentieth century, penicillin used to give magic results; it was called the miracle drug.[112] By its use, mortalities due to osteomyelitis fell to very low levels. Metastatic abscesses were almost unknown. Many reports followed announcing that osteomyelitis was about to disappear.[125-127] Unfortunately this did not stand the test of time and fell once again nearly to the zero level. The cause was the rapidly developing resistance of the microorganisms to penicillin.[128]

The other members of the antibiotic group followed in succession; streptomycin in 1944, bacitracin in 1945, chloromycetin in 1947, the tetracyclines (1948-1953), neomycin and allied drugs (1950-1959), the erythromycin group (1953-1957), the synthetic penicillins (1957)[129], the cephalosporines (1957), and at last (so far) are the quinolones.[130] However Staphylococcus aureus developed resistance to these drugs in direct proportion to the frequency these drugs were used.[128]

This depressing fact made surgeons try different methods of administration of antibiotics and modify the ways of their use in order to overcome this rapidly developing resistance.

They first resorted to "the multiple or combined antibiotic therapy", but the benefit was debatable.[131]

The carriage of the antibiotic through the tissues was facilitated and its destruction by the bacterial enzymes minimized by the use of detergents.[132,133]

The addition of anticoagulants to the antibiotics for the same reason and to diminish thrombosis was tried by Kortilla et al.[125]

Application of antibiotics in closed extracorporeal circulation was tried. The aim was to face the diseased area and hence the

infecting organisms with high concentrations of antibiotics which could not be delivered by the blood stream in the usual way. This high concentration of the antibiotic was believed to be able to knock out the infecting organism.[133-135]

Methods to improve the general resistance of the patient were resorted to, of course, in combination with antibiotics, to build up good defense mechanisms. This included, beside the general supportive treatment, the injection of gamma globulin[136] and the local injection of autogenous blood.[137]

Bingham in 1947 introduced the refrigeration treatment of acute osteomyelitis.[138] To him, refrigeration of the limb reduced signs of systemic infection, reduced fever, relieved painful swellings and diminished both local and systemic spread of infection. It did not interfere with the action of the circulating antibiotics. In the same time, it inhibited bacteria, made them more susceptible to the action of antibiotics, diminished the output of bacterial toxins and reduced tissue necrosis and autolysis. The author stressed that no harmful effect resulted from refrigeration which could be applied for periods as long as 75 days.

Inspite of all these trials, much has been left to be done by the surgeon. And as Trueta said, "Penicillin can never do what surgery can do" In many cases these conservative methods have to play only supplementary role in the problem.[139]

V. HISTORY OF SURGICAL TREATMENT:

A-The acute stage:

The ancient literature was very poor in describing cases of acute osteomyelitis, probably due to its high mortality rate. This led to the bad reputation of the disease, which together with the associated bad general condition, prohibited surgeons to attack the acute form.

John Hunter in 1786 stressed that as soon as ever it is known that suppuration has taken place, it should be drained to prevent as much as possible the separation of the periosteum[29]

Nathan Smith in 1827 knew that there was increased tension in the early stages of bone infection and that it was necessary to incise the periosteum and drill the bone to avoid interference with the blood supply[31].

Subsequently the advance in the clinical and bacteriological methods of diagnosis encouraged surgeons to proceed in this respect. Just before the twenties of the twentieth century surgical treatment was nearly the routine approach in every case of acute osteomyelitis. Mortalities of such treatment was however common. Apparently they were related to surgery although other factors, such as electrolyte imbalance, the bad general condition, the poor post-operative care etc. were equally effectively responsible. As a result surgical treatment was to a great extent halted.[3]

With the advance in general care and antibiotic therapy, surgical treatment of the acute stage took the priority again. However to operate early or to wait for localization remained an issue of controversy.

John Murphey (1916) advocated operating even before the diagnosis was certain.[140] He claimed that early incision would not hurt, while a late incision was an invitation to a fatality. To this school belong many authors. Waiting for localization flourished in the period of the forties of the twentieth century, and Wilensky seems to be the father of this school.[19,72] There is even a third school recommending not to operate at all; to this school belong many authors too.[141,142]

B- The chronic stage:

The first piece of knowledge available on the surgical treatment of chronic osteomyelitis is mentioned in the Edwin-Smith Surgical Papyrus (1600 B.C). The Ancient Egyptians knew that when a wound over a fracture site failed to heal and purulent material began to flow from it in increasing amounts, a small fragment of bone would eventually be extruded: a raspatory was then employed to scrape out the necrotic pieces of bone.[4]

Antyllus in the third century (260 A.C), described the removal of necrotic bones and diaphysectomy.[143]

Avicenna in the ninth century (980-1037) wrote a very comprehensive chapter on the treatment of chronic osteomyelitis and in particular of saucerization in his "Canon of medicine". Here is the translation of the original text of Avicenna.[10]

"Section on its treatment: The treatment of corruption of bones is by curetting "it", stopping "it", or cutting "it" or sawing "it" whether there is a sinus or not. It is essential to curette and expose it. Or by cauterizing the bad portion, so that the corrupted pellicles fall away and the healthy parts remain. Some drugs may make the bony pellicles fall away, just as the scalp pellicles fall away. If the corruption of bone is deeper, it has to be excavated. If the corruption has reached the bone marrow, it is imperative to remove the bone with its marrow. If the corruption can not be cured except by cutting the whole bone or sawing it, or of a big portion of it, this has to be done unavoidably". The original Arabic text is as follows:

"وفصل فى علاجه. علاج فساد العظم هو حكه وإبطاله أو قطعه ونشره سواء كان ناصورا أو لم يكن، فإنه لابد من كه وجرده أو كيّ المبلغ الفاسد منه لتسقط القشور الفاسدة ويبقى الصحيح. وقد تسقط قشور العظام بأدوية مثلما تسقط قشور الرأس... وإذا كان فساد العظم أغوص من ذلك فلابد من تقويره، وإن كان الفساد بلغ المخ لم يكن بد من أخذ ذلك العظم بمخه، وإن كان الفساد لا يبرئه إلا القطع أو النشر لكل عظم أو لطائفه كبيرة فلابد منه...".

Albukasis (Abulquasim Ez-

zahrawy) in the eleventh century described the treatment of chronic osteomyelitis, laying stress on sequestrectomy and diaphysectomy in his book (AI-Tasreef): the following is the translation of the original text of Albukasis.[9] "I introduced the probe into one of these sinuses, it reached the bone. I examined all the sinuses, I found that all were communicating with each other from all sides of the leg. I incised at once one of these sinuses until I exposed part of the bone, I found it corrupted, eaten, blackened, putrefied and perforated to the marrow. I sawed off all what I could of the exposed corrupted bone, thinking that there was no more corrupted bone and that I have removed it. Then I treated the wound with healing drugs for a longer period, but it did not heal. I then exposed the bone again, above the first exposure, I found more corruption in the bone. I sawed what has appeared from this corruption. I wanted to heal it but it did not heal. I examined it again, and I remained cutting from the bone bit by bit, wishing to heal, but it did not heal, until I have removed about hand-palm from the bone with its marrow. After this it healed and recovered quickly. Repetition of the operation was necessary because of the weakness of the patient, his inability to tolerate the operation and my fear that he might die. This was because he had occasional attacks of vomiting followed with bad drowsiness; he recovered completely". It is clear that Albucasis was aware of the bad general condition of the patients in this disease.

The following is the original Arabic text :

أدخلت المسبار فى أحد تلك الأفواه، فأفضى المسبار إلى العظام، ثم فتشت الأفواه كلها، فوجدتها يفضى بعضها إلى بعض من جميع جهات الساق، فبادرت وشققت على أحد تلك الأفواه حتى كشفت بعض العظم، فوجدته فاسدا قد تآكل واسود، وتعفن، وتثقب حتى نفذ إلى المخ، فنشرت ما تكشف لى وتمكن من العظم الفاسد، وأنا أظن أن ليس فى العظم غير ذلك الفساد وأنى قد استأصلته. ثم جعلت أجبر الجرح بالأدوية الملحمة مدة أطول فلم يلتحم، ثم عدت فكشفت عن العظم ثانية؛ فوق الكشف الأول، فوجدت الفساد متصلًا بالعظم، فنشرت ما ظهر لى أيضًا من ذلك الفساد، ثم رمت إجباره فلم ينجبر ولا التحم، ثم كشفت عليه أيضًا فلم أزل أقطع العظم جزءًا جزءًا وأرم جبره فلا ينجبر، حتى قطعت من العظام نحوًا من شبر، أخرجته بمخه، ثم جبرته بالأدوية فالتحم سريعًا وبرأ، وإنما وجب هذا التكرار فى عمله وشقّه لحالة ضعف العليل، وقلة احتماله وخوفى عليه من الموت، لأنه كان يحدث له فى كل الأوقات - من إفراط الاستفراغ - عشى ردىء، فبرئ تمامًا.

Before Avicenna and long after him, cautery was a very essential mode of treatment. In the fourteenth century, Pare (1510-1590) was probably the first to denounce cautery[86] and together with Aderne of England, recommended removal of free sequestra.[144]

Samuel Sharp (1739) prohibited cautery saying that the cruelty that attends its use should entirely banish it out of practice.[145]

Sparrow (1740), described diaphysectomy for osteomyelitis of the tibia by sawing the bone into two in its middle and extracting the two parts.[146]

William Hey (1803), was among the first to advocate drainage of the infected bone itself. He recommended enlarging the spontaneous fistulae which formed following the acute stage and removing the diseased bone.[147] Resection of the diseased bone was recommended in the nineteenth century by Heine, Langenbeck, Larghi and many others.[148]

In 1813, McCreary excised a clavicle,[149] in 1833, Massy excised a radius, ulna, Os-calcis and other bones.[150] This technique of bone resection was discussed in detail and popularised by Ollier, depending on the principle of regeneration following resection[151] and subsequently studied further by Nichols (1904).[152] Gurd in 1947 recommended excision of certain parts of the skeleton, which he called surplus bones to shorten period of disability.[153] Dorsey (1818) preferred amputation to the painful, difficult and hazardous operation of sequestrectomy.[30]

Liston (1837) advised "opening" the abscesses and removing sequestra when loose.[32]

Esmarch (1873) advised removal of free sequestra. The presence of a free sequestrum was proved by inserting sounds in the sinuses overlying it; by moving the upper sound, the remaining ones will move if the sequestrum is free. He described the Esmarch rubber tourniquet to avoid the massive haemorrhage which could occur otherwise when operating on cases of chronic osteomyelitis.[154]

Lister (1867) applied Pasteur's bacteriological discoveries to surgery.[79] He used carbolic acid in disinfecting open fractures and was able to minimize the incidence of osteomyelitis in these cases. In this way antiseptics entered the field in conjunction with the surgical regimen indicated. Soon other antiseptics were used for the same purpose, for example the strong solution of bichloride of mercury (Kettling 1885),[155] iodoform, spermacete and oil of sesame (Mosetig-Moorhoff 1903),[156] tincture of iodine (McCurdy 1907),[157] gutta percha (Moore 1905)[158] and bismuth paste (Beck 1909).[159]

On the other hand, Nichols (1904), demonstrated that the bone marrow and endosteum were as important as the periosteum in the regeneration of bone. He showed that thorough scrapping or the application of strong antiseptics delayed healing.[152]

The Carrel-Dakin irrigation treatment of septic wounds and compound fractures was known prior to the World War I.[160] It was a step forward in the therapeutic techniques. This technique depended in its action on thorough surgical debridment first, then the Carrel-Dakin solution (Soda Chlorinata Chirurgica, B.P.) was to circulate in the wound in a manner allowing contact of every

part of the tissues with it.[161] The method was claimed to give very good results by many authors.[162]

Some authors related the effectiveness of the Carrel-Dakin technique to the action of the chlorine atom present, thus producing chemical sterilization of the surgically prepared wound.[163] This was denied by Buchman.[160] He thought that similar results would be obtained with inert solutions used with the same meticulous surgical technique. He stated that the value of the treatment arouse out of the physical removal and possibly the chemical dissolution of the wound discharges.

However, this method caused severe pain and discomfort to the patients. Reinfection with nuisant organisms incidental to the frequent dressings occurred and was the cause of worsening the condition of the patient. In addition the method was tedious and time consuming. Because of these disadvantages the method lost its popularity and was replaced by another, which was completely opposite to it, namely the Orr treatment.[3,150]

Winnet Orr (1927),[164] feeling that infection was prolonged by inefficient immobilization in Carrel-Dakin treatment, resorted to his world known method. This was originally complete surgical debridment, subsequent packing of the wound with vaseline gauze and encasement of the limb in closed plaster. After this Orr followed his dictum "leave the wound alone. Each time you touch it, you stir up troubles".[165]

The plaster was changed scarcely, every 3 weeks or so, and especially when the odour and the softening of the plaster made its change imperative, or if there was pain underneath, or the patient became toxic and feverish which denoted accumulation of pus in newly formed pockets in the wound.[165]

Experiences with this method showed that although it held good for open fractures, it gave less gratifying results with haematogenous osteomyelitis. Anyhow, this method was a great advance. The vaseline pack acted as a drain and ,by its resistance, induced an evenly distributed formation of granulation tissue from the depth of the wound. The non-adherence of the pack allowed it to be pushed out of the wound by the newly forming granulations. It avoided reinfection by the infrequent dressings. A sort of autovaccination was thought to occur, between the body and the organisms present in the discharge. This was held responsible for the sterilizing effect of the method. It also provided rest which soothed the patient's pain, induced healing and avoided spread of the infection. In general the method excelled all other methods known at those days including the Carrel-Dakin treatment.[166]

Nevertheless, the method has some disadvantages: the patient lost appetite and weight, the plaster had foul odour and the prolonged immobilization produced joint stiffness and fibrosis of the adjacent soft tissues. Albee (1933), objected to the vaseline gauze pack used by Orr. He believed that the gauze was apt to become adherent to the bone at the bottom of the wound and so would resist extrusion and delay healing. In the same way, the wound granulations were likely to strangulate through the meshes of the gauze. For this reason, Albee used instead a paraffin- vaseline tampoon together with irrigation of the wound twice weekly by a bacteriophage[78].

Hawk (1933) criticized the method on the basis that bone is a viable tissue, which increased its vitality by use and that immobilization rendered the circulation sluggish and thus interfered with healing. For this reason, he preferred to make the excavation long and narrow, thus retaining the strength of the bone and allowing for quicker healing of the resulting cavity, because the granulating surfaces were not separated too far.[167]

Stewart (1934), objected the Orr treatment because it resulted in the formation of a mass of scar tissue.[99]

Various modifications have been introduced on the Orr treatment. In the Bipp method, the vaseline gauze dressing was replaced by liquid paraffin, bismuth and iodoform (Bismuth-Iodoform-Paraffin paste). Its aim was to institute "curtain drainage" by means of a film of liquid paraffin adherent to the surface of the wound. Its advantage was said to be the elimination of the disagreable odour characteristic of the Orr technique. But it had the disadvantage of the possibility of toxic symptoms incidental to the use of excessive amounts of the paste.[160]

Trueta, in the Spanish war, noticed that the skin in the vicinity of the wound got sodden by the vaseline pack, and used a dry pack instead. Later, after the introduction of the sulphonamides, Trueta added sulphonamides to the dressing. He called the technique "the closed plaster technique".[168]

Lohr (1934) replaced the vaseline pack by a cod-liver oil pack aiming at the benefit of adding vitamins to hasten healing.[169]

Fraser (1936) packed the wound with gauze soaked in liquid paraffin, acriflavine and 2% sodium citrate: the citrate kept the discharge in solution, the acriflavine was an antiseptic and the paraffin permitted easy removal of the pack.[109]

The Orr treatment and the other similar techniques owed their existence to the discovery by Mathijsen in 1852 of plaster-of-Paris.[170] Nevertheless, this invention did not become popular until published by Sayre in 1876.[171] In

reality it was the invention which paved the way for the Orr treatment of osteomyelitis 70 years later and encouraged surgeons to attack bones by different techniques.

When chemotherapy and antibiotics entered the field of therapy, they found their utmost indication in osteomyelitis. They came to supplement surgery both in cases of acute and to a lesser extent in chronic osteomyelitis. Surgeons became more bold to operate on bones and the surgical techniques improved since that time. However, vagaries of osteomyelitis continued and it seemed that the subject became a subspecialty of Orthopaedics. In big centres, such as Massachusetts General Hospital in America in the forties of the twentieth century, there existed "The Osteomyelitis Service". [172]

Systemic and local antibiotics were administered ; the latter was either in the form of local injection or intra-osseous instillation[172-174] or in a closed - irrigation-suction technique.[173-175] More recently an extracorporeal circulation was created; as in cases of chemotherapy for malignant tumours. The blood circulating in this system was to carry antibiotics in as a high concentration as the local tissues can tolerate.[176,178] Heparinization is needed and the system worked for half an hour after which the limb was washed with saline and the vessels reconnected. The method was to be applied once, after which a "radical" local surgery was applied.

The poor permeation of antibiotics into bone made some authors try to combine antibiotics with a "vehicle" to facilitate its carriage through the osseous tissues. This was done by addition of some detergents such as aerosol wash or alevaire.[12,133] Similarly permease[174] and some enzymes,[174] such as trypsin and pepsin were combined with antibiotics to promote proteolysis of bacterial toxins. Deoxyribonuclease was applied locally or administered intramuscularly to produce liquefaction of pus and facilitate its discharge from the sinuses.[179]

Until the thirties of the twentieth century the general consensus of opinion was that to leave the wound open, after whichever procedure was done. The aim of this was to allow drainage of the exudate and purulent discharges. However reinfection and superinfection occurred which together with other factors, such as the repeated injury to the newly formed granulation tissue, markedly retarded the closure of the wound. For this reason Lord (1935) recommended early closure and obliteration of any dead space.[180] He recommended the use of skin flaps as early as 1902 to achieve this purpose.

Smith-Petersen et al (1945) stressed that the fundamental principle in the treatment of deep sepsis was the creation of a path or avenue of escape for the accumulated products of infection. In those days "packing the wound open" was the method generally used to accomplish this purpose, but it had many draw-backs. Making a wound close from the bottom meant a prolonged period of healing during which there was bound to be considerable loss of serum from the granulating surfaces. This has been estimated for one case in 24 hours to be 39.1 g and in the average it was 11.9 g daily. This fact alone was a serious objection to drainage by packing the wound open.[172] Relatively frequent dressings are painful to the patient and time consuming to the surgeon, constituted another objection to the method. Partial primary closure of the wound was the logical answer to the problem. This was feared at first, but aided by a system of closed irrigation suction, or even closed suction alone, the fears of collection of the infected exudates, restarting a new focus, was over.[175]

Researchers on chronic osteomyelitis were, and still are, confronted with a major problem, that is the filling of the cavities resulting from operations of sequestrectomy and or saucerization. The success of any operation depends wholly on the absence of any dead space left after, as this will allow haematoma formation which becomes readily infected, as blood is the best culture medium. Thus a vicious circle will be established. Extensive trials have been made to overcome this obstacle either by saucerization if the site of the lesion permits,[181] exteriorization of the cavity using a skin graft either split thickness.[182-184] or pinch graft[185] or obliteration of the cavities by the use of various filling materials. The latter include a flap of fat or subcutaneous tissue,[186] free fat transplant,[187] a pedicle of living muscle,[188] moist blood clots,[189] autogenous blood and antibiotic blombage,[137] preserved amniotic membrane,[190] vazeline-wax-parafin-iodform-sulfonamide paste,[191] oxycel and gelfoam,[192] cancellous bone chips,[193-198] either as a -one stage procedure[196] or a- two stage one,[194] autoclaved pieces of plaster-of-Paris,[199-200] or bone cement.[201] A real contribution for eradication of bone cavities by bone transport was described by Ilizarov and good results were reported by different authors.[202,203]

Bridging bone defects secondary to osteomyelitis, too, remained a challenging problem. Preliminary control of infection seems mandatory. The methods used include direct cancellous bone grafts,[204,205] open cancellous papineau grafting,[206,207] cancellous insert graft,[208] fibular bypass,[209,210] tibial-fibular synostosis,[211] ipsilateral direct fibular transfer,[212,213] free vascularized or other composite trans-

plants,[214,215] internal bone transport,[216-218] bone graft substitutes such as morphogenic protein,[219] free fibular graft with intramedullary fixation,[220] cancellous and cortical bone allograft,[221,222] ceramics,[223,224] demineralized bone matrix,[225] bone marrow,[226] composite bone graft[227] refrigerated homogenous bone[228] or boiled cadaveric bone.[229]

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