

NEW CONCEPTIONS CONCERNING THE TREATMENT OF
ACUTE OSTEOMYELITIS IN CONSIDERATION OF
THE PATHOLOGICAL FINDINGS AND THE ACQUIRED
RESISTANCE OF STAPHYLOCOCCI IN CONNECTION
WITH ANTIBIOTICS

By

J. MICHAIL, K. HOULIARAS, S. THEODOROU, N. SIATIS
and K. SPYROPOULUS

The general use of antibiotics in the treatment of acute osteomyelitis has reduced the relapse rate as well as the previously high mortality, to a negligible quantity. In a pre-war statistical study at the Toronto Sick Children's Hospital, there was a 20 % mortality among 670 cases of acute osteomyelitis (*Farmer* (1), 1948). In our own recent series, there has been no death among the 155 children treated during the last 6 years.

Nevertheless, the reduction of the complications in acute osteomyelitis has not paralleled the lessening in the mortality. This is mainly due to the fact that in the treatment of the disease insufficient attention has been paid to the pathological changes and the development of the new resistant strains of staphylococci. The recent basic work on the subject (*Trueta* (2, 3, 4, 5) and *coll.*) suggests that the pathological lesion is usually a thrombosis involving the bone and producing bone necrosis.

There have been many attempts to describe the pathogenesis of acute osteomyelitis. The best descriptions are given in the classical works of *Lalelong* (6) (1879) and *Trueta* (1953). With slight differences, they admit the initial localization of the infection deep in the bone matrix, spreading gradually to the cortex. Bone necrosis is a usual consequence of the ischemia. Some other authors among which are *Lexer* (7), *Grille* (8), *Leveuf et coll.* (9, 10, 11, 12, 13) believe that the initial localization

is found around the point of penetration of the cortex by the nutrient artery. The principal lesion is a thrombosis of the artery which gives rise to a necrosis of the bone extending from the cortex to the medulla. Our feelings are in keeping with the *Lanelong's* classical conception.

After a detailed study of the question, we consider that the pathogenesis of the disease goes through the following stages: after the staphylococcus has entered the circulation of the bone, it shows a predilection for those regions where the circulation is slowest. Such is the metaphysis of the long bones especially after trauma. *Lewis* (14) (1956) has shown that the blood supply of the long bones comes partly from the nutrient artery and partly from the periosteal vessels. This periosteal circulation increases as the person grows older, for then the bone is essentially supplied by this periosteal circulation. The numerous venous sinuses in the metaphysis slow the local circulation and in this way favour the development of the staphylococcal abscess.

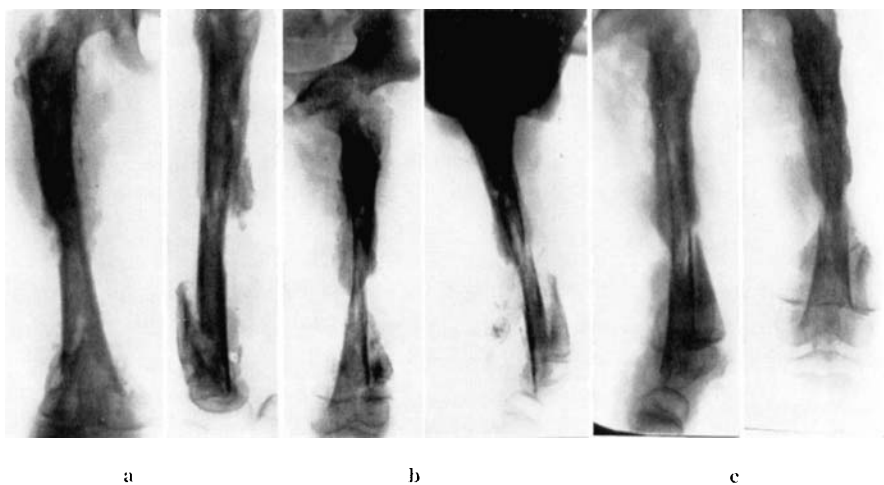
As a consequence of the bone necrosis a local inflammatory reaction is set up which leads to the development of a bone abscess. The pus spreads into the medulla and through the cortical channels to form a subperiosteal abscess. Since these bone constituents have their own arterial branches, the direct hematogenous infection of the periosteum (periostitis) and of the cavum medullae, is possible though not frequent. Pus collection tends to the enlargement of the necrotic areas. The rupture of the periosteum under growing tension is a dramatic development that may be avoided. We emphasize the great importance of the above pathological changes because we consider that the failure to understand this leads to insufficient or erroneous treatment. This loses precious time during which it would have been possible to avoid more extensive necrosis of the bone with the distressing sequelae outlined below:

1. large abscesses with one or more fistulae.
2. very large bone necrosis (pandiaphysitis) which may result in pseudarthrosis.
3. ankylosis of one or more joints. More frequently stiffness.
4. differential growth ending in anisoskelia.
5. in some rare cases an amputation may be the dread result.

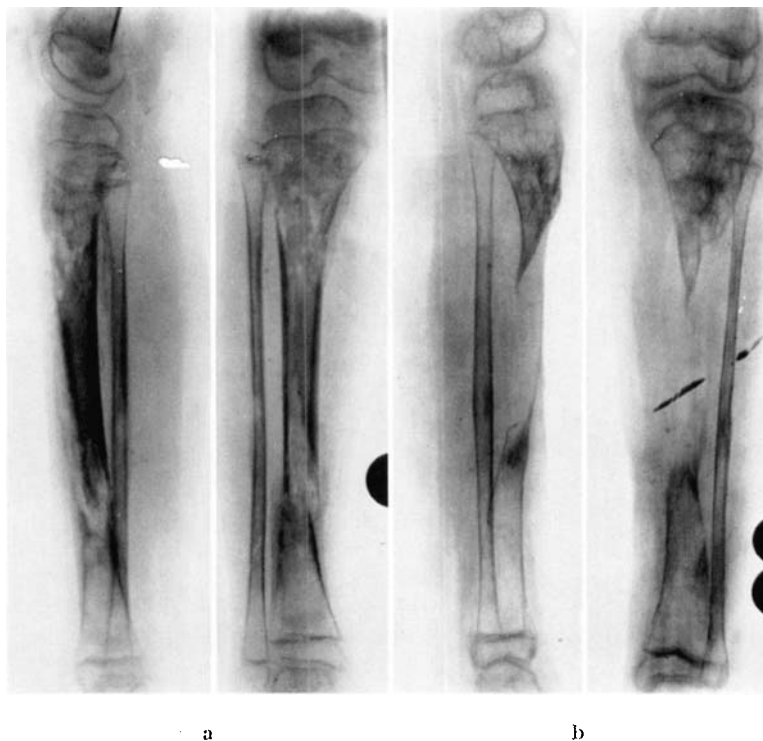
The treatment of all these complications necessitates a long period of medical control often with serious financial and physical consequences. Consideration of these principles led us to institute the method of treatment outlined below in a series of 45 cases of acute osteomyelitis.

*Fig. 1.*

- a. B. Theodoros, boy aged 3. An example of metaphyseal localization. Admitted after failure of conservative treatment.
- b. No doubt that he was late for suitable surgical treatment. The consequence was a pandiaphysitis. Prognosis will be in spite of this, good, but durable.

*Fig. 2.*

- a. The risk is greater in this case concerning K. Artemis, a girl aged 4. She was admitted, after prolonged conservative treatment, with extended necrosis including the diaphysis as a whole.
- b. Fracture and shortening ensued.
- c. Many plasters will be necessary before we can hope to remove fragments of the cancellous bone. Treatment will last months and even years.

*Fig. 3.*

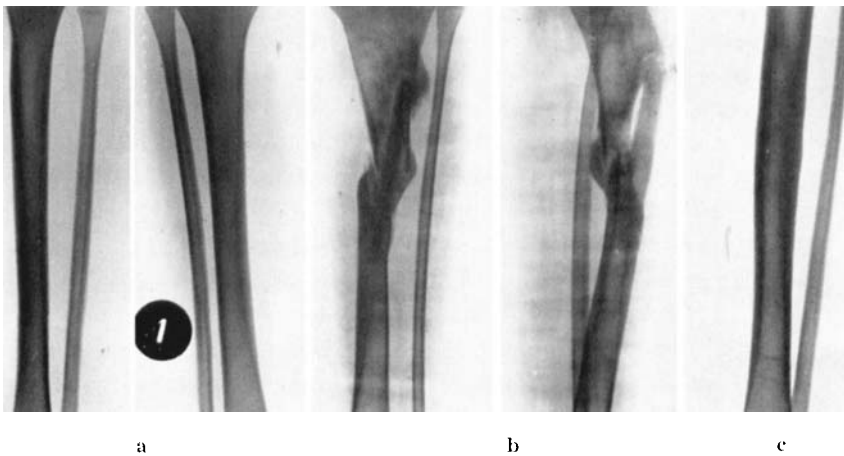
- a. G. Constantinos, aged 11. He was sent for operation after a very long period of conservative treatment. We noticed on admission a large necrosis either of the bone or of the skin.
- b. A large involucrum was taken out from the ulcerated skin. We had to wait a few months until grafting was possible. Series of plasters were necessary.

Altogether 155 cases of osteomyelitis were treated but 110 of the patients had the chronic form of the disease. We have not included them in this work as they have been the object of a previous paper already published (*Michail and coll. (15) 1951*).

As the principle object of this paper is then the study of the acute osteomyelitis, our remarks are related to the 45 acute cases. These patients were admitted into the Orthopaedic Clinic between 4 and 30 days from the onset of the disease. Almost all these patients had been treated elsewhere, before their admission, by antibiotics. So in the majority of the admitted cases, we had to face the development of resistant strains. Because of this and the established bone necrosis, our end results were not as satisfactory as we could hope when starting to treat our patients by the following method.

*Fig. 3.*

- c. The bone autograft was well incorporated.
- d. Now, 3 years later, the graft is thick enough, so the patient is allowed to walk with some precautions.

*Fig. 4.*

- a. No visible bone destruction when this boy, P. Georgios, aged 6 when admitted.
- b. But very soon a bone destruction became evident with loss of bone substance.
- c. Grafting ensued with perfect restitution.



Fig. 5.

- a. P. Dimitrios, aged 3. Early opening and fenestration of the bone. Evacuation of the subperiosteal and bone abscess.
- b. Excellent result. Healing without any late complication. It is clear that no conservative treatment was carried out.

As soon as a localization is perceptible, we open the soft tissues down to the periosteum. Hence we can drill the bone cortex. But this seemed to us insufficient, so we prefer now the fenestration of the bone, either at one or at both epiphyses simultaneously. Before doing this, as a routine procedure, we missed a second localization in two cases. We usually insert a drain before closing the soft tissues. Local and general antibiotherapy is continued for about 3 weeks after checking the sensibility of the staphylococci. In local antibiotherapy, we manage so that the drug is entirely introduced into the bone medulla through the cortical window.

Although the same procedure was carried out in all our cases, it was sometimes impossible to stop the bone necrosis, because this was already established before operative treatment began. It is important to realize that no radiological findings can be made before the third week (*Brailsford* (16)). It is therefore important to undertake the operative treatment in consideration of clinical symptoms without waiting for the appearance of radiological findings.

The picture of the evolution of acute osteomyelitis, varies with the patient's age. The younger the child, the more severe is the disease. Osteomyelitis is most frequent in children between 7 and 10 years old.

*Fig. 6.*

- a. J. Sotirios, aged 3. Admitted after a long conservative treatment. Puncture of the abscess followed by injections of penicillin. The result was the absorption of the head.
- b. After opening the hip joint and immobilization for a long time, the result was good enough, so we could hope to conserve movement and acceptable bearing.

Among our 155 cases, 50 are aged between 7 and 10. Males are more frequently affected than females. Localizations of the disease are divided according to their types as follows: 69 femurs, 51 tibiae, 14 humeri, 10 fibulae and 11 rare localizations. These figures appear from our own statistics. But they are somewhat different from those of *Trueta, Key* (17) and others, who found the tibial localization to be the most frequent one. The original source of infection is not as easy to discover as it may seem. We omit therefore to insert any statistical figure. The most frequent localizing factor may be a trauma, as we found this to be true in 45 among our 155 cases.

As a matter of observation, we believe that the staphylococcic infection goes through the following stages: a) primary infection (skin, nose, pharynx, ear); b) hematogenic septic infection with phlegmon and c) tertiary phase which results in multiple thrombosis causing osteomyelitis. When this last is attained, we may expect to have a relative immunity.

In order to know something more about the infective agent we performed systematic laboratory examinations of the pus. In 45 acute cases examined, we found staphylococcus 42 times and streptococcus 2 times; proteus was the infective agent of only one case.

Staphylococcus aureus and *micrococcus pyogenes* proved to be the most resistant to antibiotherapy, infective agents. *Marget* and *Richarz*

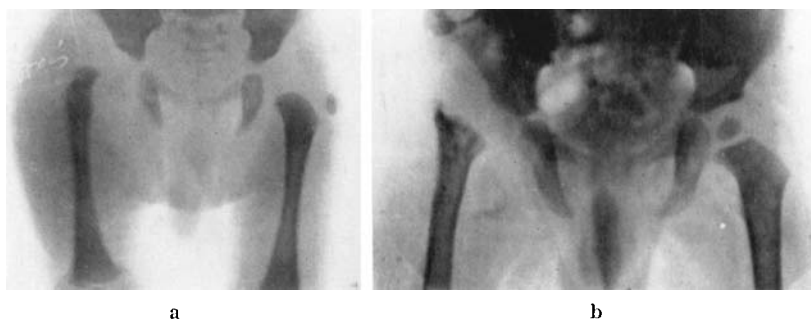


Fig. 7.

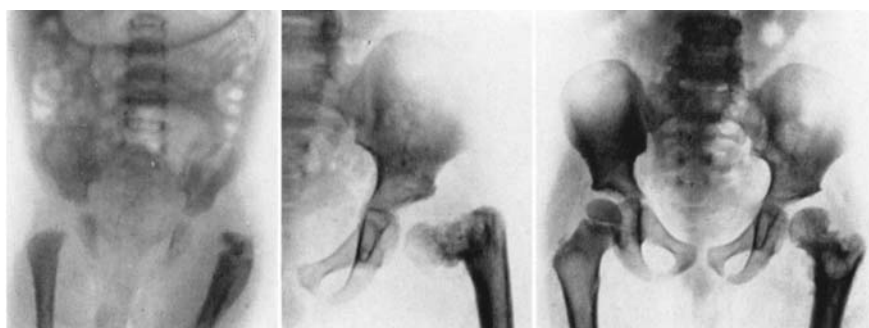
- a. S. Johannis, 3 months old. Conservative treatment lasted longer than in the preceding case, so the absorption of the head and neck was total with luxation.
 b. We hope to do something to improve this disastrous condition. But the boy is still too young.

(18) (1955) tried to explain the way these agents proceed by means of toxins and enzymes. Toxins are a) an exotoxin which has a necrotic and hemolytic power, b) a leucocidin which destroys the leucocytes and c) an enterotoxin which is rather a poison when ingested. Enzymes are a) coagulase and b) a fibrolysin; both are comparative to the hyaluronidase (spreading factor). Penicillin was found to be inactive from the beginning of the treatment in 21 acute cases. In 21 other cases, penicillin activity was moderate at first, then quickly diminished. The most active antibiotics were chloramphenicol, erythromycin, sigma-mycin, terramycin, novobiocin and kanamycin but each one became less effective with the lapse of time. In three cases, resistance was noted after short use. Streptomycin, seemed to have a resistance resembling that of penicillin (*Rauntree and Thomson* (19), *Linzenmayer* (20), *Arsenis* (21)).

To consider the respective value of our therapeutic results, our cases were divided in two groups. The time which preceded the admission of each patient after they had been infected, was taken into account.

Group I.

This group comprises 21 acute cases admitted after they had been treated elsewhere during a period of time varying between 5 and 10 days. The treatment already given had been inadequate. In exceptional cases, no treatment had been given. Penicillin or streptomycin was usually administered without any control. In all these cases the current



a

b

c

Fig. 8.

- a. T. Constantinos, 1 month. This infant came as soon as the physician realized that there was very little hope of improving the condition by conservative treatment. On the x-ray, partial destruction and luxation is evident.
- b. After opening and treating the local condition we noticed encouraging improvement. But immobilization was very long.
- c. The result was indeed good 4 years later after a successful high osteotomy.

operative treatment was indispensable and pressing; abundant pus was found inside the periosteum and in the bone matrix. In half of these cases, the amount of pus was so great that it had spread into the soft tissues. Suitable postoperative antibiotherapy was given after a resistance control had been carried out. The results of this combined operative and medicamental therapy are as follows:

In every case a striking improvement of the general condition of the patient was noticed. Temperature became normal 2 to 3 days after the operation. The sedimentation rate became gradually normal. But no parallel improvement was noticed on X-rays. This became evident in after-weeks.

After the 4th week, one could notice an important improvement of the local situation in 14 among the 21 acute cases of this group. But the X-rays still showed a few changes. In the other 7 cases repair of the bone was retarded; 3 of them were even more difficult to heal because of the wide spread of the infection and difficulty in obtaining adequate drainage. In similar cases we now prefer to open a window in the cortex of both epiphyses and more widely than before.

Group II.

This includes the remaining 24 acute cases admitted after the 10th day. Longer antibiotherapy without any control. This is the consequence

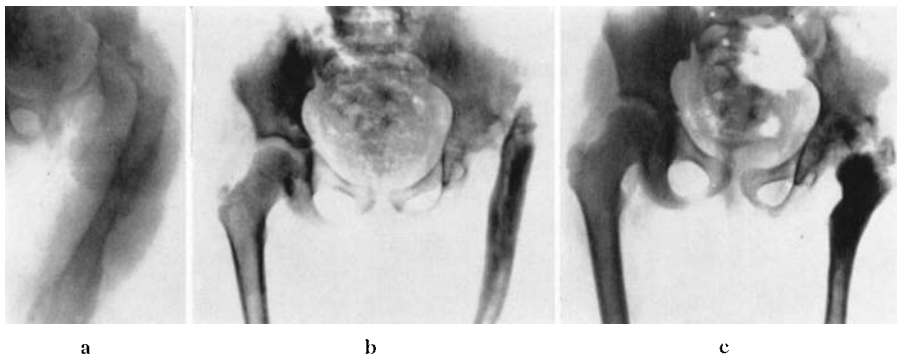


Fig. 9.

- a. B. Dimitra, 3 years old. She came with a partial destruction of the whole femur after a very long conservative treatment.
- b. After surgical treatment, it has only been possible to conserve the diaphysis with the inferior epiphysis. The upper epiphysis was completely absorbed and a luxation ensued.
- c. The result was very satisfactory 2 years later after a difficult osteoarthroplasty.

of a fundamentally wrong conception that one can surely heal a sub-acute osteomyelitis in using antibiotics for a long period. So they believe in discarding operative treatment. It then follows from this that the end results in this group are ordinarily disastrous.

In only 2 of these cases could the results be compared with those in the preceding group; in spite of their late admission (20 days since the beginning of the disease) a satisfactory result was obtained. But we had to evacuate a large collection of pus.

We had to face, on the other hand, a very serious situation in the following 2 cases. The persistence of the conservative treatment over a month caused the rupture of the subperiosteal abscess; the pus overflowed in the soft tissues. A large skin necrosis was noticed as well as a large bone necrosis. A huge sequestrum had to be removed leaving an extensive gap (pseudarthrosis). Five more cases were admitted in our Clinic with a dislocation of the femoral shaft because of the unjustified prolongation of the conservative therapy in cases of purulent arthritis of the hip. Parents were disheartened when informed of a certain degree of permanent disability. These patients having no fever, no pain and no swelling after a more or less long conservative treatment were supposed to be cured and therefore allowed to walk without any support or control.

It is then evident that the improper administration of antibiotics may

not only be ineffective but also be dangerous. Despite this, some authors, among them *Endler* (22) (1957), prefer aspirating and instilling abscesses. They persist in continuing conservative treatment until bone necrosis becomes obvious. This takes ordinarily a long time because of an illusive improvement. Inevitably these patients come in after weeks or months for operation. In such cases—those of group II—the end results will be unfortunate. The bone lesions are of such extent (usually pandiaphysitis) that it is necessary to wait several months until a sheath of new bone is formed before one can operate. If we do not wait long enough, we are apt to produce a pseudarthrosis. As it happens very often, more than one operation will be necessary. It is not always a simple thing to remove the diaphysis when necrosed. A fragment is very often ready to be removed before the whole is separated.

Acute osteomyelitis of the infant is to be considered separately because of the fast evolution of the phlegmon. Almost all of our patients showed a localization at the hip joint. So we are prone to consider this as the most frequently affected joint. Damage is usually great. When diaphysis was reached, we found the spreading or the pus in soft tissues to be in the infant less frequent than in children. The great elasticity of the periosteum, at this early age, favours the subperiosteal pus collection (*Blanche* (23)).

Among our 8 infant cases with acute osteomyelitis, 6 had an abscess of the hip joint, 1 of the femur and 1 of the humerus. In 3 of the 6 cases, where the hip was affected, the head of the femur was absorbed. But, in one of these cases, the head was partly absorbed, because we noted a regeneration of it 3 years later. In the remaining 3 cases, with an early operation in our Clinic, the final result was good. The result was the same with the femur and humerus acute osteomyelitis abscess.

As a rule, patients with purulent arthritis are brought to us very late. The results could be better and in a shorter time. This is to be put down, in certain cases, to the many diagnostic difficulties and errors. Symptoms may be lacking or may become manifest only after abscess formation. For this reason, the X-ray examination is valuable. A subluxation of the femoral head will be a frequent and in most instances, a very early radiological finding. When this is observed, it is necessary to evacuate the pus in an emergency arthrotomy. By doing this, one can expect to avoid the necrosis of the head. Local and general antibiotherapy will be useful, provided that the affected limb be kept in immobility.

CONCLUSIONS

Acute osteomyelitis, though now less frequent and less dramatic than before the antibiotherapy time, is nevertheless a serious and longlasting disease. All ages are affected, but children more frequently; males more than females.

The principal agent is staphylococcus (we found this in 42 among 45 pus cultures). Metaphysis is in children, the commonest localization. Trauma is an important fixative factor.

Conservative therapy, when carried out during the period of bacteriemia, may end in a complete arrest of the disease. But it has little likelihood of a cure when localization is established. Taking into account the fact that in very few cases intensive and effective treatment is practicable in the septicemic period we are prone to admit its inefficacy in the greater number of acute osteomyelitis. In many instances, it serves to produce new resistant strains. *Salz* (24) reviewing 101 cases of acute hematogenous osteomyelitis came to the same conclusion.

The early operation is undoubtedly the treatment of choice in all cases in which a localization is evident. The earlier this treatment is carried out the better the result will be, and in the shortest time. This average time is about 2 months in our cases of group I. It takes months for the cases of group II and years for some chronic patients. Our routine technique is based upon the very many pathological verifications that we have performed these recent years. If we are convinced of the existence of a central bone abscess in the presence of a phlegmon with bony inflammation, we look for it at one or both epiphyses. As early as possible, mostly before the appearance of the slightest radiological sign, we open the bone cortex as well as the soft tissues, even though a large abscess is amassed inside or outside the periosteum. The doubtful efficacy of the drilling of the cortex urged us to go on with the fenestration of the cortex. The fact that in the infant "the condition causes a severe and often permanent epiphyseal damage and joint infection" *Trueta* (25) makes incontestable the very early opening of a purulent joint.

The testing of the resistance was undertaken in all our acute cases in which staphylococcus was in the limelight. Penicillin is of little or no value, streptomycin scarcely effective. We recommend as among the most effective therapeutic agents chloramphenicol, erythromycin, sigmamicin, terramycin, novobiocin and kanamycin.

SUMMARY

Remarks and results concerning the study of 155 osteomyelitic children, among which 45 were acute cases, treated for several weeks or months in the Children's Orthopaedic Clinic of Athens, are reported. The main problem discussed is that of the treatment of acute osteomyelitis.

It appears from this study that conservative antibiotherapy, when continued for a long time—after the development of a phlegmon is of little or no value and, in many instances, increases the risks of an infirmity.

Combined with a methodical and rational antibiotherapy, our routine technique is more effective. This operative procedure is described including our personal modification. With this surgical treatment good results were obtained in 66 % of the acute cases of group I. Satisfactory results were obtained in only 8 % of the cases of group II. The patients of this group II, were mostly following—before their admission—a conservative treatment for a long period until an extensive bony destruction became obvious and therefore difficult to heal.

RESUME

Les auteurs font connaître leurs observations et résultats thérapeutiques après étude de 155 dossiers d'enfants atteints d'ostéomyélite, parmi lesquels 45 sont des cas aigus. Ces malades ont été en traitement chirurgical dans la clinique de Chirurgie Orthopédique de l'Hôpital des Enfants d'Athènes, durant quelques semaines ou quelques mois. C'est le problème thérapeutique de l'ostéomyélite aiguë qui a retenu spécialement l'attention des auteurs.

Il ressort de cette étude que le traitement conservateur par les antibiotiques, s'il est continué longtemps après la formation d'un phlegmon, non seulement est sans utilité, mais au contraire accroît les risques d'infirmité.

L'opération combinée à un traitement conservateur (par antibiotiques), systématique et rationnel, est plus efficace. Nous donnons un compte rendu de la technique opératoire que nous utilisons en y ajoutant notre contribution personnelle. Par ce traitement chirurgical, nous avons enregistré de bons résultats dans 66 % des cas en ce qui concerne le groupe I. Dans le groupe II, il n'y a eu de bons résultats que dans 8 % seulement des cas. Les malades de ce dernier groupe ont été soumis

pendant un temps plus ou moins long – avant leur admission dans notre Clinique – à un traitement conservateur pur et simple, jusqu'au moment où une destruction importante de l'os est devenue manifeste et par conséquent très difficile à guérir.

ZUSAMMENFASSUNG

Beobachtungen und Ergebnisse im Zusammenhang mit der Untersuchung von 155 an Osteomyelitis erkrankten Kindern, unter ihnen 45 akute Fälle, die während einiger Wochen oder Monate an der orthopädischen Kinderklinik von Athen behandelt wurden, werden berichtet. Das hier besprochene Hauptproblem ist das der akuten Osteomyelitis.

Aus dieser Untersuchung geht hervor, dass die konservative Behandlung mit Antibiotika, wenn eine lange Zeit hindurch fortgesetzt – nach der Entwicklung einer Phlegmone, nur geringen oder gar keinen Wert hat und dass sie in vielen Fällen die Gefahr eines dauernden Gebrechens erhöht.

Zusammen mit einer gründlichen und rationellen Antibiotikabehandlung ist unsere Routinetechnik wirkungsvoller. Das operative Vorgehen mit unserer persönlichen Modifikation wird erläutert. Mittels dieser chirurgischen Behandlung wurden gute Ergebnisse in 66 % der akuten Fälle der Gruppe I erzielt. Zufriedenstellende Ergebnisse wurden in nur 8 % der Fälle der Gruppe II erhalten. Die Patienten dieser Gruppe II, hatten meistens eine langdauernde konservative Behandlung vor der Aufnahme ins Krankenhaus mitgemacht, während der es zu ausgedehnter Knochenzerstörung gekommen war und die deshalb offensichtlich schwierig zu heilen waren.

REFERENCES

1. *Farmer, A. W.*: Journ. Bone & Joint Surg. (discussion) 30A: 679, 1948.
2. *Trueta, J.*: Bull. Hosp. Joint Dis, Vol. XIV: April 1, 1953.
3. *Trueta, J. & Morgan, J. D.*: Brit. Journ. Surg. Vol. XLI: No. 169, March 1954.
4. *Trueta, J.*: Practitioner Vol. 175: 613–618, Nov. 1955.
5. *Trueta, J.*: Bull. Hosp. Joint Dis. Vol. XIV: October 1953.
6. *Lancelong*: Quoted by *Lance & Mallet* in Encyclop. Medico-Chirurgicale II: 1952.
7. *Lexer, E.*: Archiv f. klin. Chirurg. 73: 481, 1904.
8. *Grille*: Quoted by *Lance & Mallet*.
9. *Leveuf, J., Laurence, G. & Mage, J.-J.*: Extrait et Rapport au Congrès Français de la Penicilline, Masson & Cie. Paris, 1946.
10. *Debré, R. & Leveuf, J.*: Presse Méd. No. 19: Mars 1939.
11. *Leveuf, J.*: Journ. Suisse de Méd. 39/40: 853, 1945.

12. *Leveuf, J. & Laurence, G.*: Journ. Intern. de Chirurgie 7-2: 77-104, 1947.
13. *Leveuf, J.*: Revue Franç. d'Orthop. 33: 179-216, 1947.
14. *Lewis, O. J.*: Journ. Bone & Joint Surg. Vol. 38B: No. 4, 1956.
15. *Michail, J. & Arzimanoglou, A.*: "Praxis" No. 39: 795-797, Sept. 1951.
16. *Brailsford, J. F.*: The Radiology of Bone and Joint. 4th ed. Churchill, London, 1953.
17. *Key, A.*: In *Lewis Practice of Surgery* Vol. II, Prior & Co, Hagerston, 1955.
18. *Marget, W. & Richarz, H.*: Deutsch. Med. Wochens. 80: 725, 1955.
19. *Rauntree, P. M. & Thomson, E. F.*: The Lancet 2: 262, 1952.
20. *Linzenmayer, G.*: Deutsch. Med. Wochens. 91: 956, 1957.
21. *Arsenis, A. & Marquetos, N.*: Personal Communication.
22. *Endler, F.*: Wiener Med. Wochens. Nr. 32/33: 653b, 658, Nr. 34: 689b, 694, 1951.
23. *Blanche, D.*: Journ. Bone & Joint. 34: 71, 1952.
24. *Salz, M. H.*: Journ. Bone & Joint Surg. 38B: No. 4, 1956.
25. *Trueta, J.*: Journ. Bone & Joint Surg. 41B: No. 4, 611-680, 1959.