FROM THE DEPARTMENT OF ORTHOPEDICS AND SURGICAL TUBERCULOSIS
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CHEMOTHERAPY AND SURGICAL TREATMENT IN BONE AND JOINT TUBERCULOSIS

By

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At the State Medical Meeting in Stockholm, in Nov. 1949, I gave a preliminary account of our experiences at St. Görans sjukhus in connexion with chemotherapy in bone and joint tuberculosis, and afterwards published this lecture in the Svenska Läkartidningen. We began at an early stage to test the various chemotherapeutics, at first the sulfonamides and then, among other things, penicillin. Para-aminosalicylic acid, hereafter referred to as PAS, pyolipin acid and streptomycin were also employed, primarily in the most difficult fistular cases. At first these medicaments were generally of no apparent benefit, but there were surprisingly good results in occasional solitary cases. In a case of severe, prolonged fistulous coxitis, that had been active since 1910, a speedy healing occurred with intramuscular penicillin treatment. Another similar coxitis case, in which fistulae developed after arthrodesis in 1938, and where the patient also suffered from amyloidosis, an exceedingly poor general condition, SR 135 mm., and Hb 41 %, general nephrotic edema and signs of cardiac decompensation, healed quickly in a few weeks. She was dismissed from the hospital in a much improved condition, SR 59 mm., and Hb 70 %, with the heart well compensated and with no signs of edema.

In a number of other cases, as already mentioned, the results were not as favorable, and one had to grope one's way forward and try first one and then another of the drugs. Occasionally the fistulas were gradually mastered after a patient had had a trial of several of the above-mentioned drugs.

The case which came to form a notable point in our tests, and which allowed the formation of a definite principle of therapy, was one of coxitis. The patient, a woman, born 1903, had tuberculous

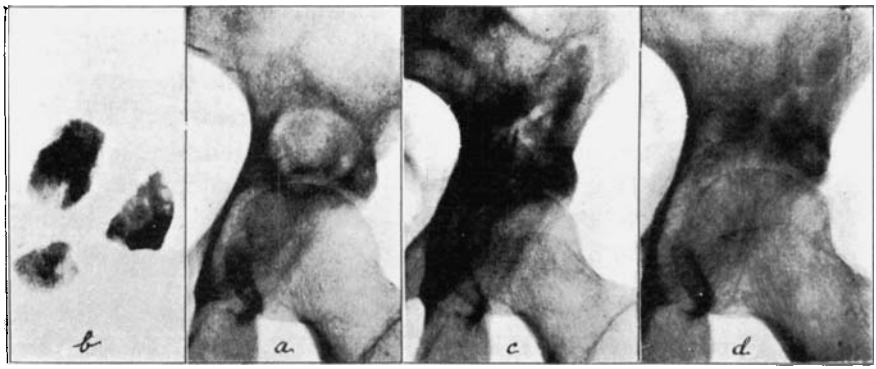

Fig. 1.

Tbc-coxitis (acetabular foci with penetration to the joint). KT 35/49. Female born 1903. Roentgen pictures: (a). 6.12.1948: Walnut-sized destruction in the acetabulum. (b). Removal of sequestrated bone by *operation 2.3.1949.* (c). 2.5.1949, 61 days after the operation. The evacuated cavity in the bone is very distinct, and filled with implanted cancellous bone. (d). 21.11.1950: Healing with growth of new bone tissue; height of joint cavity is maintained.

coxitis with a focus in the acetabulum, adjacent to the joint. In 1945 she had undergone osteosynthesis for tuberculous spondylitis of L II and L III. Pains with strain appeared in the hip in 1948. On 8.2.1949, she was admitted to the orthopedic department and from 17.2., was treated with PAS. Elimination of an acetabular focus, 2.3., revealed a walnut-sized cavity containing sequestered bone and granulations. The acetabular focus had perforated the joint, occupying an area of about 1.5×1.5 cm. The sequestra were removed and 1 g. streptomycin and 200,000 units of penicillin were placed in the cavity. Cancellous bone was also implanted in the defect in the acetabular roof and the defect was closed by primary suture. Streptomycin, 1 g. and 200,000 units of penicillin were administered intramuscularly daily, for 9 days. PAS was temporarily discontinued for several days after the operation, but readministered until the patient was dismissed, 18.5. The SR never exceeded 20 mm. The patient was discharged in a plaster cast for convalescence elsewhere. She was readmitted on 27.6. for a hip plaster. A roentgenogram revealed signs of healing, SR was 5 mm., and the hip showed no irritation. She was allowed to get up successively. The hip continued to be free from irritation, and repeated X-ray observations revealed good healing and retained cartilage height. She left the hospital on 16.7., is still free from trouble, has good hip mobility, and is able to perform all of her housework.

American and French experience of chemotherapy in bone and joint tuberculosis, partly associated with surgical intervention, our Swedish

lung specialists' recommendation of combined PAS and streptomycin (clinically investigated here by Westergren and Stavenov), the animal tests at the Mayo Clinic et aliia, together with our own clinical experience, have resulted in the following plan of treatment. The treatment begins and terminates with PAS administered by mouth in a daily dosage of 10-14 g. For a period of 14 days, commencing 3 days prior to the operation, 1 g. streptomycin in 2 doses daily is administered together with 500,000 units of penicillin with each dose, 300,000 units

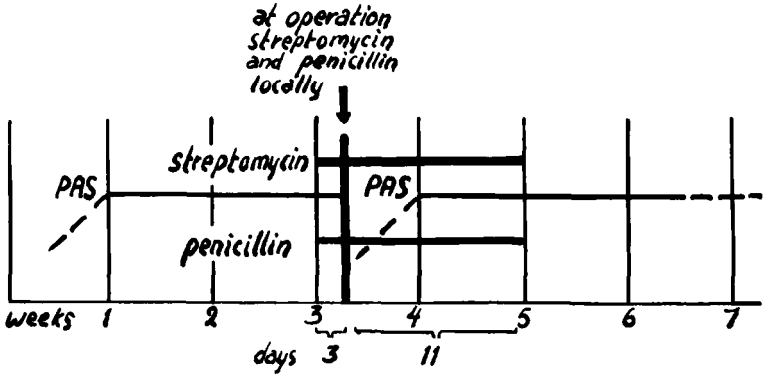

Fig. 2.

Dosage scheme for PAS and streptomycin-penicillin treatment.
The treatment began and ended with PAS per os in daily doses of 10-14 grams. For 14 days, beginning 3 days before the operation, 1 gr. streptomycin in two doses and 500,000 units of penicillin also in two doses or 300,000 units of penicillin-procain in one dose, were administered intramuscularly daily. The PAS dosage had frequently to be reduced or omitted during the operation period. In addition streptomycin-penicillin powder was applied locally to the wound at operation (1-3 gr. streptomycin + 200,000 units of penicillin according to the size of the wound). More recently, in isolated cases, we have employed Conteben simultaneously with PAS, as basic medicament.

of penicillin-procaine in 1 dose. The PAS dosage must frequently be decreased or entirely discontinued in connection with the operation. Moreover, streptomycin-penicillin as dry powder is placed locally in the wound at operation (1-3 g. streptomycin + 200,000 units of penicillin) according to the size of the wound. In order to avoid resistance it is essential, in this scheme, that the streptomycin-penicillin period be made as short as possible and that it coincides with the time of the operation. More recently we have employed in solitary cases Conteben simultaneously with PAS as the basic medication.

A closer study of the literature indicated that Americans combine

chemotherapy and operation in the treatment of fistulas and paravertebral abscesses, as a rule, without excavating the original foci. Their results are reported to be satisfactory.

Our procedure, as out-lined here, has also been applied in another group of our cases at St. Görans sjukhus, with good results. The tuberculous abscess is opened widely by means of a large incision or by costotransversectomy, the abscess and granulations are evacuated with a scoop and, when necessary, down to the vertebrae. The abscess membrane loosens easily, as a rule, with the aid of dry gauze compresses. Bleeding is then controlled. Streptomycin and penicillin are placed in the wound which is then primarily closed. Should the bleeding be abundant, a tampon powdered with streptomycin-penicillin can be inserted. After several days the tampon is removed and the wound is secondarily closed. It frequently occurs that the primary focus, in the vertebrae for instance, is inaccessible to exploration.

Primary healing has taken place in almost every case and there has been considerable improvement of the general condition, especially when the abscesses have been large. As a completion of this treatment, stabilization operations in joints or between the vertebrae have subsequently been performed.

By surgically and chemotherapeutically attacking the foci, abscesses and fistulae in this way, better reaction is manifested on the part of the patient. With the possible exception of one case, there was no sign of tuberculous spread or exacerbation. Chemotherapeutics and antibiotics serve as a protection against bacteria in the wound. Personally, I consider that the tissue exterior to the abscess membrane, which has previously reacted against the bacteria, is of great value and significance. For this reason, this tissue should be treated with care, and it is important to employ a blunt scoop rather than a sharp one. The intramuscular streptomycin treatment probably has a favorable effect on tissue which is injured at the operation, but the course need not proceed longer than the end of the first phase of wound healing, that is to say about 10-14 days. Another reason for not prolonging the streptomycin treatment is, as mentioned before, primarily to avoid the risk of resistance and also the risk of other complications to the patient.

A third group of our cases of bone and joint tuberculosis is that in which the tuberculous bone changes are small, and where there are no pronounced abscesses. These are frequently not suited to surgical intervention but are treated in a conservatively orthopedic manner and with stabilization operations and chemotherapy. In these cases, PAS and eventually Conteben, or both, have been employed, depending on

the reaction of the patient. The results of this treatment are very difficult to estimate and it will take a long time before this is achieved with any degree of certainty, for the reason that it is difficult to judge the value of chemotherapy in the treatment of lung, urogenital or organic tuberculosis in general. The stabilization operation makes the treatment more complicated.

From a surgical point of view it is obvious that the radical treatment, (excision of the original foci) is preferable, provided there is no risk of spreading the tuberculosis or of reactivation in other infected organs. With these methods, which have been employed in treating some 100 cases, neither spreading nor any reappearance of the processes has hitherto occurred, although in some instances the general infection was serious and the local processes were active. On the contrary, soon after the intervention, a very apparent improvement in the general condition took place.

There has been one death, an elderly man, with spondylitis and a paravertebral abscess, who had been ill for a long time and had been treated at another hospital for elbow and glandular tuberculosis, with great quantities of streptomycin. Because his general condition became increasingly worse, costotransversectomy to empty the abscess was decided upon. The wound healed primarily. His general condition improved during the 14 days following the operation, but a change for the worse occurred and he died of cachexia. His organisms were probably streptomycin-resistant and his power of reaction was not sufficient. Autopsy revealed that the abscess had partly reformed and had spread to the pleura. An abundance of granulations were present in the walls of the abscess.

In some cases, in which bleeding during the operation was abundant, and where primary suture had been made, abscesses recurred, but, on renewed operation, under the "streptomycin umbrella", healing occurred.

At the evacuation of the acetabular focus in the case of coxitis which had perforated to the joint, the capsule must have been affected. The joint tuberculosis healed however, and the joint mobility was restored. The result is explained by the fact that, after the elimination of the necrotic original focus in the bone, the joint capsule healed, owing to the effect of the chemotherapeutics and the orthopedic treatment of the joint. On the other hand, in cases of primary tuberculous synovitis treated only with local and general chemotherapy, improvement is tardy and the joint mobility returns slowly to its former state. That the healing is slow is undoubtedly due to the fact that the diseased tissue is so diffuse and abundant, that the chemotherapy and

antibiotics are not carried to the infected tissues in sufficient quantities to destroy the infecting organism. For this reason the healing process would be considerably hastened, if the synovial membrane was operatively removed to the greatest possible extent, to allow the chemotherapy to have the greatest possible effect. The Americans, *Smith* and *Yu* have made similar experiments (J.A.M.A.—Jan. 1950) with the joints of 3 knees and 2 elbows, and their results were excellent. They succeeded in restoring a certain mobility in the first 3 cases, and ankylosis in the latter 2.

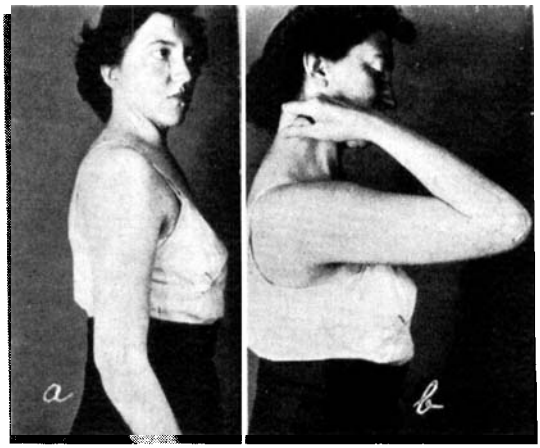

Fig. 3.
Tbc-synovitis in the elbow joint of a woman aged 29. KT 43/50. On 24.2.1950 *total synovectomy.* Severely swollen synovia with hydatidelike indentions in the joint. Delimited bone caries at the capsular attachment. The picture illustrates the joint mobility two months after operation.

We have endeavored, from the very beginning, both to heal the tuberculosis and, as far as possible, to preserve or increase the mobility of the joint.

At first, an attempt was made to treat the joints conservatively with chemotherapy, and no operation. The joints remained swollen so long, however, that movement could not be allowed for a considerable time. Then the swelling gradually subsided, but the mobility of these joints returned only to a limited extent.

The cases treated with the combination chemotherapy and synovectomy seem encouraging, especially those of the elbow joint, of which we have 3. Not only has the healing of the tuberculosis been excellent but, moreover, through early active movements, good mobility has been restored to the joint. Should the tuberculosis not heal, and

movements involve pain, resection can still be performed later. Judging from the results hitherto obtained, one should endeavour by all means to secure a mobile joint.

Prior to the chemotherapeutic era, the surgeon tried to evacuate the tuberculous bone foci lying near the joints before they penetrated the joint and infected the capsule. In this way it was possible to pre-

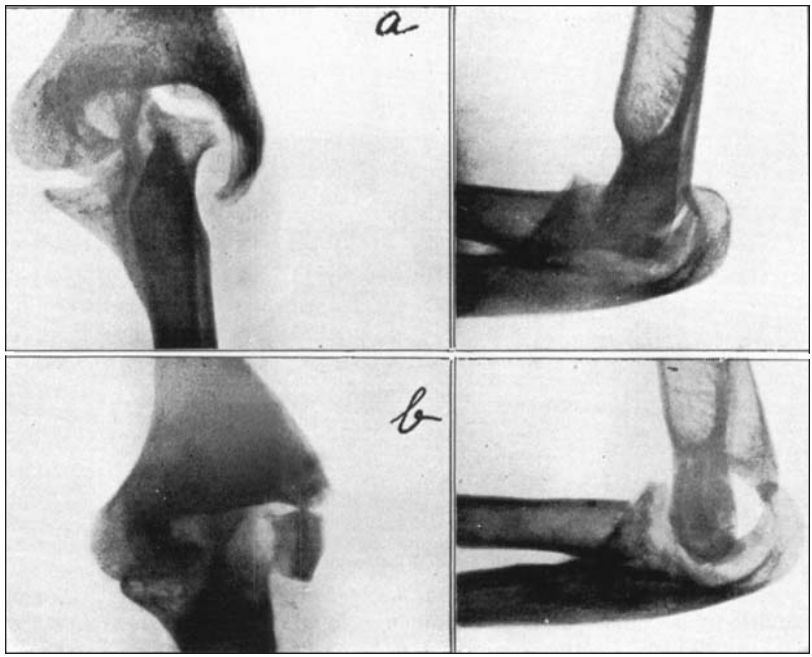

Fig. 4.

Destructive tuberculous arthritis in the right elbow joint of a man aged 30. KT 62/50. Roentgen before the operation (a) shows much bone destruction. On 22.3.1950: Synovectomy + resection of the capitulum *radii*. Thickened synovialis. Greater part of joint cartilage is destroyed or missing. Abundant granulation. Hollows at the attachment of the capitulum radii et humeri. (b). X-ray after the operation.

serve the function of the joint. With the aid of chemotherapy the prospect now exists of successfully being able to assail the foci near the joints, even when they have attacked the capsule and invaded the joint. By a combination of chemotherapy and synovectomy it is possible to master the primary synovial tuberculosis effectively.

Less severe forms of synovial tuberculosis should accordingly heal with internal local and general treatment, short streptomycin periods and basic medication with PAS, and possibly Conteben. If healing does not take place, and swelling remains or returns, or roentgenologic

signs of progress are manifest, it is best to perform a synovectomy, and, if cold abscesses and diffuse bone foci exist, resection may be necessary. It is expedient therefore to make contrast X-rays of the joint, in order to get some idea of the expansion and severity of the process. The joint cavity can be rendered more accessible to the contrast or eventual streptomycin-penicillin, by releasing the fibrin and purulent exudate with fibrinolytic ferments such as streptokinase and streptodornase. These procedures are going on in collaboration with Dr. Hedlund at Statens' Bakteriologiska Laboratorium. Children under 15 years of age should undoubtedly be treated with conservative measures as before.

With regard to operative complications, attention should be focused primarily on wound-hemorrhage. When operating on extremities an exsanguinating tourniquet or blood-pressure cuff should be applied in order to ensure focal blood vacuity. To offset the reactive hyperemia, this bandage or cuff should not be removed until the extremities can be elevated at the end of the operation. In cases where elevation is out of the question, for instance, when evacuating psoas abscesses or in costotransversectomy for paravertebral abscesses, one must be content with the customary but meticulous surgical hemostasis. As already mentioned, there have been recurrences in cases where there was profuse wound bleeding and where a hematoma developed.

We have not met any clinical resistance in any case since we introduced the above scheme with short streptomycin-penicillin periods. Hypersensitivity reactions have occurred now and then but they disappeared after the therapy was stopped and there have been no residual manifestations.

Contrast X-rays performed by paracentesis of the abscess or joint, are of diagnostic importance. In making these one often finds that existing granulation and detritus hinder the flow of the contrast medium. As a rule the contrast shadow is much smaller than it appears to be with the ordinary X-ray picture. Sometimes the shadow which appears to be an abscess is formed only by granulations, free from pus. This is found in the creeping tuberculosis which granulates along the vertebrae, and would seem to be identical with the "Hellstadius secondary spondylitis". Radiographic investigation with contrast medium facilitates the incision. The surgeon must know whether he should go to the right or left of the spinal column in cases of paravertebral abscesses. If it is a question of subcutaneous abscesses, he must know where they originate and where the communication with the deeper lying abscess or original focus is situated. It is necessary to take the roentgen pictures in two planes. Obviously, the better the

localization, the easier it will be to drain the abscess with minimum injury to the tissues. Contrast X-rays also give valuable information as to the contiguous spreading of the tuberculous foci.

The inclusion of the orthopedic department in the general hospital of St. Görans with its great diagnostic resources has made possible rational accomplishments in surgical interventions. There has been no difficulty in consulting other specialists, particularly those dealing with the lungs; in referring to the bacteriologic and pathologic institutions; or in obtaining the assistance of doctors for narcosis, etc.

When the diagnostic and operative treatment has been completed at the general hospital, further treatment could conceivably proceed at a nursing or convalescent home, at less cost, and in a more suitable environment, so situated that the doctors of the general hospital could follow and superintend the care. It is essential that those patients who must, as a rule, be taken care of for a fairly long time, have the same doctor throughout the whole period of treatment. Interest in the patient's illness slows down when the case is taken over by another doctor. By way of a suggestion, assistant doctors at the general hospital might superintend the care of patients at the said after-treatment hospital or sanatorium, as, for instance, Ljunggren and Obrant did with urogenital tuberculosis in Gothenberg, or like the arrangement made in 1922 for children with bone and joint tuberculosis at St. Görans sjukhus with after-treatment at *"Guldbröllopsminnet"* in Nynäshamn.

Formerly, the incision of a tuberculous abscess was looked upon as a professional error. By employing the streptomycin-penicillin umbrella this intervention is nowadays risk-free on the whole and can therefore be justified. As streptomycin has the same effect as antibiotics on ordinary pus-bacteria, it is probable that streptomycin alone, in many cases, is sufficient protection. Moreover, in consideration of the fact that of late years tuberculosis has been of an ever increasingly benign character here in Sweden, it is conceivable that such abscesses might be evacuated with local application alone. This is a subject to which attention should be paid. (My collaborators, *Felländer* and *Hiertonn,* are at present investigating the absorption and excretion of streptomycin.) Obviously, in some cases the secondary infection is of greater actual significance than is the primary tuberculous infection.

In cases of abscesses and fistulae which contain an abundance of granulation, detritus and pus, and perhaps necrotic and sequestrated bone in bone foci, chemotherapy may frequently fail to reach its specific goal, with resultant therapeutic ineffectiveness. Not until these substances and the abscess membrane have been removed will the

immediate tissue, containing plasma cells and other cell elements expressing the body's reaction, work toward healing the tuberculous disease. This is especially the case when the original focus is cleaned out or evacuated. If tuberculous processes inaccessible to surgical therapy, are active in other parts of the body, then, as in the treatment of organic tuberculosis, one must rely on the sanatorium treatment and general chemotherapy.

Chemotherapy in bone and joint tuberculosis is still at an early stage of development. It is fairly certain that in the near future other and more effective chemotherapeutics will be at our disposal and perhaps once again change the indications for surgical intervention. What is of most importance in all tuberculous treatment is, and will continue to be, prophylaxis. It should be observed that the new treatment routines contribute toward diminishing the spread of infection.

Accordingly, through the application of chemotherapeutics, and particularly streptomycin, bone and joint tuberculosis has become more accessible to rational surgical treatment comparable to the treatment of septic osteomyelitis achieved through the administration of sulfonamides and penicillin.

SUMMARY

The employment of chemotherapy in the treatment of about 100 cases of bone and joint tuberculosis at the orthopedic department of St. Görans sjukhus in Stockholm has apparently shown that the disease can be approached surgically in a specific therapeutic scheme, at an earlier stage than previously. The orthopedic methods of treatment and stabilization operations are employed as hitherto. If an original focus is surgically accessible, it should be eliminated. The risk of operative measures spreading and activating the tuberculosis would seem to be slight with the application of chemotherapy, if the streptomycin is administered for such short periods as 14 days in order to make the risk of developing bacterial resistance and complication, due to toxicity, minimal. Consequently, (1) when the primary bone focus, perforating the joint, has been eliminated, healing takes place with good joint mobility, and the primary synovial tuberculosis, after synovectomy and eventual excision of secondary bone foci, heals with good and serviceable mobility. This is especially true in elbow tuberculosis. In destructive arthritis and trochanteritis, bone foci are radically excised and abscesses drained. Bone foci can sometimes be radically treated in spondylitis, by means of costotransversectomy and evacuation of the abscesses. (2) If the original focus is inaccessible, fistulae

and abscesses are surgically removed, whereupon the general reaction of the body to the disease is mobilized, and thus the original foci heal more readily. (3) If the original foci are surgically inaccessible, and no large abscesses exist, orthopedic methods and stabilization operations with subsequent chemotherapy are employed during the patient's stay at the sanatorium, as in the treatment of urogenital tuberculosis. When surgical measures in foci and abscesses can be carried out *radically, with the "streptomycin umbrella"*, it will be possible to reduce the period of treatment considerably, in comparison with the conservative methods, and to diminish the risk of recurrence.

RESUME

L'utilisation de la chimiothérapie au traitement d'environ 100 cas de tuberculose des os et des articulations dans le Service Orthopédique de S:t Görans sjukhus, à Stockholm, a montré de toute évidence que la maladie peut être traitée chirurgicalement d'après un schéma spécifique à un stade plus précoce qu'antérieurement. Les méthodes orthopédiques du traitement et les opérations de stabilisation sont appliquées comme jusqu'à présent. Si un foyer primaire peut être opéré, il doit être éliminé. Le risque de propagation et d'activation de la tuberculose par l'opération semble très faible avec l'appui de la chimiothérapie, si la streptomycine est administrée pendant une période de 15 jours seulement en vue de rendre très minime le risque de voir se développer une résistance pathogénique et de complications dues à la toxicité. En conséquence: 1) lorsque le foyer osseux primaire qui perfore l'articulation a été éliminé, la guérison s'effectue avec une bonne mobilité de l'articulation et la tuberculose synoviale primaire guérit après synovectomie et excision éventuelle des foyers osseux secondaires, avec une mobilité bonne et utile. Ceci est vrai notamment dans la tuberculose du coude. Dans les arthrites et trochantérites destructives, les foyers osseux sont radicalement excisés et les abcès drainés. Les foyers osseux peuvent parfois être traités radicalement dans la spondylite par costotransversectomie et évacuation des abcès; 2) si le foyer primaire est inaccessible, les fistules et les abcès sont chirurgicalement éliminés, après quoi la réaction générale du corps à la maladie est mobilisée, ce qui fait que les foyers primaires sont plus disposés à guérir; 3) si les foyers primaires sont inaccessibles à l'opération et qu'il n'existe pas de larges abcès, des méthodes orthopédiques et des opérations de stabilisation avec chimiothérapie subséquente sont appliquées pendant le séjour du malade au sanatorium, comme dans

le traitement de la tuberculose urogénitale. Lorsqu'une intervention chirurgicale radicale peut être appliquée à des foyers et des abcès, accompagnée de streptomycine, il est possible de réduire considérablement la période du traitement, par comparaison avec les méthodes de traitement conservateur et de diminuer aussi le risque de récurrence.

ZUSAMMENFASSUNG

Die Anwendung der Chemotherapie in der Behandlung von ungefähr 100 Fällen von Knochen und Gelenkstuberkulose an der orthopädischen Abteilung des St. Görans sjukhus in Stockholm hat scheinbar gezeigt, dass die Erkrankung nach einem spezifischen therapeutischen Schema zu einem früheren Zeitpunkt chirurgisch angegriffen werden kann, als vorher. Die orthopädischen Behandlungsmethoden und Stabilisierungsoperationen werden wie bisher angewendet. Wenn ein ursprünglicher Herd chirurgisch zugänglich ist, dann sollte er ausgeschaltet werden. Die Gefahr der Aussaat und Aktivierung der Tuberkulose durch den operativen Eingriff scheint bei Anwendung von Chemotherapie gering zu sein selbst wenn das Streptomycin nur für einen so kurzen Zeitraum wie 14 Tage gegeben wird, um die Gefahr der bakteriellen Resistenz und toxische Komplikationen auf ein Minimum herabzusetzen. Daher, (1) wenn der ursprüngliche, in das Gelenk durchbrechende Herd ausgeschaltet worden ist, kommt es zur Heilung mit guter Beweglichkeit des Gelenkes, und die primäre Synovialtuberkulose heilt nach Synovektomie und eventueller Exzision von sekundären Knochenherden mit guter und gebrauchsfähiger Beweglichkeit aus. Das ist besonders der Fall bei der Ellbogentuberkulose. In Fällen von destruktiver Arthritis und Trochanteritis werden die Knochenherde radikal entfernt und die Abszesse drainiert. Knochenherde können manchmal bei Spondylitis mittels Costotransversektomie und Ausräumung der Abszesse radikal behandelt werden. (2) Wenn der ursprüngliche Herd unzugänglich ist, werden Fisteln und Abszesse chirurgisch entfernt, so dass die Allgemeinreaktion des Körpers gegenüber der Erkrankung mobilisiert wird, und auf diese Weise die ursprünglichen Herde leichter ausheilen. (3) Wenn die ursprünglichen Herde chirurgisch nicht zugänglich sind und keine grossen Abszesse bestehen, dann werden orthopädische Methoden und stabilisierende Operationen mit folgender Chemotherapie während des Aufenthaltes des Patienten im Sanatorium verwendet, wie bei der Behandlung der Urogenitaltuberkulose. Wenn chirurgische Eingriffe an Herden und Abszessen *mit Hilfe des Streptomycin-Schutzes* radikal ausgeführt

werden können, dann wird es möglich sein die Behandlungsdauer im Vergleich mit der konservativen Behandlung bedeutend abzukürzen und die Gefahr des Rückfalles zu vermindern.

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