

EXPERIENCES OF STREPTOMYCIN TREATMENT IN ORTHOPAEDICAL DISEASES

*Paper given at the Congress of the Scandinavian Orthopaedical
Association 17.6.50*

By

L. O. NYBERG

We have been in a position to use streptomycin in Finland since the end of 1948. Its supply has been extremely limited, however, and this has affected our opportunities of benefiting from it. Partly for this reason, partly owing to a conscious conservatism we have refrained from carrying out any radical operative interference in association with streptomycin treatment. Abscesses have not been opened and fistulas and tuberculous foci have not been scraped out; consequently streptomycin has only been used as a supplementary aid in an otherwise conservative programme of treatment. Both streptomycin and dihydrostreptomycin have been employed alongside each other and we have not been able to observe any distinct difference between the effects or toxicity of the two.

Streptomycin has been partly used in tuberculous conditions both with and without abscesses and fistulas, for osteites, and in some operations which prevented the otherwise probable inflammation of a tuberculous affection, and also in some infectious conditions in which normal antibiotics had no effect.

The series comprises 32 men and 18 women with tuberculous affections, 6 men and 3 women with osteites, and 1 man and 2 women with other troubles, altogether 62 persons.

The cases which received streptomycin were given hospital treatment under the following diagnoses:

6 of the cases described here were kindly placed at my disposal by Doctor G. Wallgren of the Diakoniss Hospital, Helsingfors.

Tuberculosis of the vertebrae	19
" " " wrist	1
" " " hip	11
" " " clavicle	1
" " " scapula	1
" " " os pubis	2
" " " acetabulum	1
" " " oss. pedis	8
" " " talocrural articulation	1
" " " knee joint	3
" " " peritonitis	2
	50

Osteitis of the tibia	1
" " " pubis (Proteus)	1
" " " femur (")	1
" " " knee joint	3
" " " vertebrae	2
" " " radius	1
Proteus wound infection after cup arthroplasty	1
" infection in wounds with large skin defects	1
Infection of the urinal passage in paraplegia after vertebral fracture	1
	12

A classification of the results gives the following table:

	No.	Good	Some Impro- vement	No Impro- vement	Under Treatment
Prophylaxis in operations on the.					
cases	5	1	2	—	2
Tbc. fistulas	29	14	11	4	—
" abscesses	7	5	1	1	—
" others	9	4	1	2	2
Total	50	24	15	7	4
		48 %	30 %	14 %	8 %
Osteites	9	3	5	1	—
Large wound areas or wounds with proteus inf.	2	1	—	—	1 (good)
Infection of the urinal passage after paresis	1	—	—	1	—
Total	12	4	5	2	1

The above-mentioned 29 cases of tuberculous fistulas made up a total of 39 fistulas, 29 of which closed, while 18 remained open. After the streptomycin treatment was finished, an average of 7.8 months passed in the case of the good results while in those cases which showed either some or no improvement the average was 6.7 months.

The average amount of streptomycin given per patient was 32.7 grams administered in two daily doses, either 0.25 or 0.5 gr. per dose, i.e. 0.5 gr. and 1.0 gr. per day respectively. On comparison of the results of these dosage schedules no definite grounds can be seen for concluding that the larger daily dosage would be more effective; on the contrary it appears as if the lesser dosage would give a better result over a longer period. If the results are expressed on a percentage basis, a daily dosage of 0.5 gr. shows an incidence of 60 % good results while the corresponding figure for 1.0 gr. per day is only 27 %. In this connexion it ought not to be forgotten that a lesser daily dosage involves a longer period of rest in hospital but nevertheless one cannot help thinking that the lesser daily dosage is to be preferred, at least if the total amount of streptomycin at one's disposal is limited. On comparing the effect of a larger total dosage with that of a lesser, with 25.0 gr. as the limit, an incidence of 45-50 % good results is obtained in both groups.

Owing to force of circumstance it often happened that streptomycin was repeatedly given in lesser dosages, usually 15 or 30 grams and often with considerably long intervals in between. If any definite resistance should have developed in connexion with such a schedule, it was not observable. In this series there were only two patients who received 90.0 gr. and only one who was given 120.0 gr.; all three had had their courses of treatment in repeated dosages of 15-30 gr. and only at the end of the whole period of treatment did their tuberculous affections show signs of healing. The average dosages for those tuberculous patients who made good improvement were 34.4 gr., for those with some improvement, 37.6 gr., and for those with no improvement 35.7, that is, almost similar amounts. As a rule both the general condition and the subjective wellbeing improved during the course of the treatment, also the weight, S. R., and hemoglobin.

The toxic symptoms of streptomycin were insignificant in this series; on the whole only 28 patients reported any bad effects at all, and of these there were only 3 who had direct objective, noticeable trouble. After 9 grs. of streptomycin, given at the rate of one gr. a day, one of these 3 suffered from sight disturbances, dizziness, and nystagmus, so that the course had to be broken off; after 14 grams another patient suffered from a neuritis optica, demonstrable in the ophthalmos-

scope, with swollen pupillae and enlarged blood vessels in the eye ground, accompanied by double images; this patient too received one gr. a day. Now, half a year after the treatment, no bad effects remain. After 60 gr. of streptomycin a third patient had a rash which still remains, 9 months afterwards. Except for these, the patients' complaints consisted of rapidly diminishing subjective troubles, as is evident from the following classification:

Buzzing in ear	6	Lowered appetite	5
Itching	6	Deafness	1
Swollen joints	1	Dizziness	9
Insomnia	1	Rash	1
Palpitating heart	3	Shortness of breath	2
Sight disturbances	5	Headache	3
		Sickness	1

The total number of patients who experienced troublesome effects was 28, out of 62.

No manifestations of allergy were observed amongst the hospital staff.

It is almost impossible to draw any definite conclusions concerning the results from such a small series as this, when in addition the observation time was so short. I prefer therefore to describe some special cases. We obtained one of the best results with a total dosage as small as 15 gr. The patient in question was a 46 year old woman who had walked about for 19 years with a tuberculous fistula of the spine, arising after an Albee operation. This fistula had already healed up after 2 weeks treatment with 0.5 gr. a day and is still good now, 15 months after the completion of the course of treatment. So far as I have been able to see from the literature, Streeten¹ is the only one who,—after first instilling an NaOH solution into joints attacked by tuberculosis in order to obtain a PH value of 9, at which the effect of streptomycin is optimal,—then injected streptomycin into the joints attacked and achieved good results with amounts totalling as little as 5 grs.

Another case was a patient with a 6 year old spondylitis and complicating tuberculous peritonitis who progressed from a bad general condition and a sedimentation rate of 108 to a sedimentation rate of 16 and a condition in which his weight increased 13 kg. in 4 months; this patient is the only one who received 1000 gr. Pas concurrently. A further patient showed scars of tuberculous manifestation over almost the whole of his body and had at that time a particularly active tuber-

¹ Streeten, D.: South African Med. J. 23: 777-782. Sept. 1949.

culous infection in the bones of the foot; for this reason amputation had already been decided upon, but after being given 60 gr. of streptomycin he became well again and now performs heavy standing work as an electric fitter. 9 months have passed since he was discharged from hospital. A 16 year old girl, already operated upon on the spine (Albee) and on the one hip (Brittain), had an inflammation here after the latter operation and probably miliary tuberculosis also, according to the roentgen photographs. The course of the disease was halted and remission obtained with a dosage of only 30 grams; since then 10 months have passed and the girl's condition is satisfactory. The only patient who died was a small 10 year old boy who had originally had tuberculous spondylitis and coxitis. Tuberculous meningitis set in afterwards and while in an extremely bad condition he was given 15 gr. of streptomycin, but died a couple of days after the medicament was discontinued. Perhaps after all the good results obtained in a number of *Proteus* infections have provided the most remarkable recoveries due to streptomycin. As an example I may mention a soldier in the war who suffered from a bad osteite of the femur after being injured by a grenade. He was operated upon on 19 separate occasions; on 4 occasions trepanations were performed at the Invalid Foundation's Hospital but neither wound nor fistula healed. After he had been given streptomycin for 3 days, however, the wound secretion lost its repulsive odour and after one week the wound had healed. The other cases in which *Proteus* was cultivated from the wound secretion recovered in the same rapid way.

As has already been pointed out it is impossible to draw any definite conclusions on the basis of this material since the cases are too few and the observation time too short. It seems, however, as if considerably lesser amounts of streptomycin than those generally reported in the literature can lead to good results. A more active therapy in tuberculous bone affections than that which we have employed may also be regarded as justified. In addition it appears as if a daily dosage of 0.5 gr. streptomycin is to be preferred to a larger dosage over a shorter period.

S U M M A R Y

An account is given of 62 cases of orthopedical disease, chiefly tbc. of the bone, which have received streptomycin and been treated conservatively in other respects. 48 % of the cases made good improvement, 30 % only some improvement, 14 % did not at all improve and in 8 % the treatment was still in progress. In some *Proteus* infections

the results were excellent. The writer considers that a lesser daily dose (0.5 gr.) over a longer period is to be preferred to a larger one over a shorter period, and also recommends an active operative therapy in bone tuberculosis.

RESUME

Il est rendu compte de 62 cas de maladies orthopédiques, notamment de tuberculose osseuse traités à la streptomycine et soumis par ailleurs à un traitement conservateur.

Sur les cas tuberculeux, 48 % ont été sensiblement améliorés, 30 % quelque peu améliorés, 14 % sans amélioration et chez 8 % le traitement était encore en cours. Dans quelques infections de proteus, on a obtenu un très bon résultat. L'auteur estime qu'il est préférable d'administrer une petite dose journalière (0.5 g.) pendant longtemps plutôt que de donner de fortes doses pendant peu de temps. Il recommande aussi une thérapie opératoire active dans les cas de tuberculose osseuse.

ZUSAMMENFASSUNG

Ein Bericht über 62 Fälle von orthopädischen Erkrankungen, meist Knochentuberkulose, die Streptomycin erhalten haben und im übrigen konservativ behandelt wurden, wird gegeben. Von den tuberkulösen Fällen zeigten 48 % gute, und 30 % etwas Besserung, 14 % keine Besserung und 8 % der Fälle sind noch unter Behandlung. Bei einigen Proteusinfektionen war das Resultat ausgezeichnet. Der Verfasser ist der Ansicht, dass kleine Tagsdosen (0,5 gr.) und eine längerdauernde Behandlung einer kürzeren Behandlung mit grösseren Dosen vorzuziehen ist und er anbefiehlt ausserdem ein aktiv operatives Vorgehen bei der Knochentuberkulose.