prolonged at one side. In all cases the cytoplasm was markedly eosinophilic, and suitable staining revealed well-marked cross-striations (Fig. 3) in some cells, with longitudinal striations in others. In the multinucleate forms the striations tended to be concentric. There were numerous mitotic figures.

The vascular supply was rich and tended to be sinusoidal. The supporting stroma was scanty, and there was a rich reticulum arranged around columns of cells as well as around individual cells. The histological appearance was that of a rhabdomyosarcoma. Sections of the metastases in the liver showed an identical appearance.

Comment

This tumour was typical of its kind in that it presented itself as a cause of acute retention in an infant (of 11 cases reported 8 have occurred in infants) and that it proved fatal within 5 months (average 6½ months).

This case is unusual in that distant metastases were found. Their structure was identical with that of the tumour. Distant metastases have been described in only one preceding case—that of Mackenzie and Chase (1928).

I wish to thank Mr. J. W. Riddoch, honorary surgeon, in whose charge this patient was treated, for encouragement to publish this case; Dr. A. G. Marshall, pathologist to the Corbett Hospital, who performed the necropsy and supplied the histological report; and Dr. W. Whitelaw, Birmingham, who kindly provided the micro-photographs, and who permits me to say that he agrees with the diagnosis.

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STREPTOMYCIN IN NON-TUBERCULOUS INFECTIONS

SUMMARY OF A REPORT TO THE MEDICAL RESEARCH COUNCIL

BY

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In December, 1946, the Medical Research Council appointed a committee* to arrange clinical trials of streptomycin in non-tuberculous infections, in parallel with the trials in certain forms of tuberculosis which have been organized by another committee of the Council. The trials in non-tuberculous infections began at five centres in London and later were extended to eleven centres throughout the country. This report summarizes the pooled results of the investigation; more detailed results will be published by individual observers. Because of the small amounts of streptomycin available, the relative rarity of suitable cases, and the wide diversity of conditions treated, experience of most infections in which streptomycin therapy may be effective is still limited. Even when, as in *Haemophilus influenzae* meningitis, a reasonably large series has been studied, the distribution of cases over so many centres has led to unavoidable variations in case selection, therapeutic procedure, and bacteriological control. For these reasons present claims must be guarded. Nevertheless, some clear-cut results have been obtained and profitable lines for further inquiry have been indicated.

These trials have been restricted to infections resistant to other forms of therapy in which bacteriological control of treatment has been possible. With few exceptions the infecting organism has been proved streptomycin-sensitive before treatment has been begun; occasionally—e.g., in infective endocarditis—when penicillin treatment has failed, subsequent attempts to isolate the organism have been unsuccessful.

The chief value of streptomycin (apart from tuberculosis) lies in the treatment of penicillin-resistant infections due to the Gram-negative bacilli, particularly *H. influenzae*, *Proteus*, *Pseudomonas pyocyanea*, and *Bact. coli*. The clinical disorders in which treatment has been most effective are septicaemias, meningitis, urinary-tract infections, and local (superficial) infections.

H. Influenzae Meningitis

The results of preliminary trials in the United States suggested that streptomycin might be particularly valuable in this condition; a standard scheme of treatment was therefore recommended in the present investigation.

Dosage.—*Intramuscular*, 20 mg. per 1 lb. (0.45 kg.) body weight daily in divided (four-hourly) doses; *Intrathecal* (in saline), 50–100 mg. initial dose, according to age, and 25–50 mg. on subsequent days. Treatment was continued for at least seven days after cerebrospinal fluid became sterile.

Results.—Forty-three cases were treated with streptomycin. Four of these also received sulphonamides, penicillin, or serum; in five others the C.S.F. was reported sterile before streptomycin injections were started. Of the remaining 34 cases, the infection was controlled in 25 (74%), while treatment failed in nine. There was no significant difference in age, duration, or C.S.F. changes between the two groups, but clinically the unsuccessful cases appeared to be more severe. Where typing was carried out the organism was found to be Pittman type b. When treatment was successful the C.S.F. usually became sterile within 24 hours of the first intrathecal injection. Streptomycin was effective in 13 cases which had relapsed on other treatment and in nine cases in which the infection had been present for two weeks or longer. Four patients relapsed after an initial response to streptomycin, but the organism remained sensitive and further treatment with streptomycin alone was successful. The principal cause of failure was the development of resistance by the organism; this occurred in seven of the nine failures, sensitivity changing from 0.5 to as high as 5,000 units in one to four days.

From this series it appears that streptomycin alone is probably as effective in *H. influenzae* meningitis as any other form of treatment at present available. The development of resistance is, however, a serious drawback, and it has been decided in future trials to use a combination of streptomycin, penicillin, and sulphonamides from the start.

Other Forms of Meningitis

Fourteen cases of meningitis due to penicillin-resistant bacteria have been treated with streptomycin. The causative organisms included *Bact. coli*, *Ps. pyocyanea*, *Staph. pyogenes*, *Proteus*, and *Str. faecalis*. In the majority of cases the meningitis developed after operation for cerebral abscess or cerebral tumour. The infection was controlled in 11 instances. Streptomycin is therefore a valuable new therapeutic agent in pyogenic meningitis due to penicillin-resistant organisms.

Other Infections

Septicaemias.—Five cases of subacute bacterial endocarditis due to *Str. viridans* or *H. influenzae* and one case of uncertain nature have been treated. With the exception

*Professor Sir Alexander Fleming (chairman), Professor Ronald V. Christie, Professor L. P. Garrod, Mr. R. Vaughan Hudson, Professor H. Raistrick, Dr. Robert Cruickshank, Dr. F. C. O. Valentine, Dr. F. R. Selbie, Professor Clifford Wilson (secretary).

of the latter, the response to streptomycin has been only temporary. Two cases of septicaemia without endocarditis due to *Ps. pyocyanea* or *Bact. coli* have responded satisfactorily.

Urinary-tract Infections.—A series of 61 patients with urinary-tract infection due to *Bact. coli, Ps. pyocyanea, Proteus, Staph. pyogenes,* and *Str. faecalis* has been investigated in 10 centres. In roughly half the cases the infection has been controlled by intramuscular administration of 3 g. of streptomycin daily for one to three days. Failure has almost always been due to the development of resistance. As with other antibacterial agents, streptomycin has a limited value where there is some underlying condition which is apt to lead to recrudescence of the infection.

Local Sepsis.—Fifty-five patients with local infections have been treated. These include a wide variety of lesions such as infected burns, operation wounds, superficial ulcers, sinuses, abscess cavities, and septic skin conditions. The bacterial causes were similar to those detailed in the preceding paragraph. Daily applications of a saline solution of streptomycin (2 mg. per ml.) have been used either alone or combined with intramuscular therapy. The results are favourable, particularly in superficial lesions, provided that all necrotic tissue is removed. The employment of a standard technique is essential. Streptomycin has been used effectively as a cover for skin-grafting. In a proportion of cases failure has been attributable to the development of resistance.

Respiratory Infections.—Chronic lung infections due to bronchiectasis and lung abscess (14 cases) have been treated by inhalation and intramuscular injection. Although a temporary reduction in bacterial content of the sputum has been noted the cases showed little if any clinical improvement. The results of a preliminary trial in whooping-cough were inconclusive. More experience is needed of *acute* lung infections due to penicillin-resistant organisms.

Intestinal-Tract Infections.—Forty-two cases of infantile diarrhoea have been treated by oral administration of 2–4 g. of streptomycin spread over seven days. Sensitive organisms rapidly disappear from the gut. As the infecting agent in this condition is not always the same it was to be expected that the results obtained in different centres would vary. Some centres report clinical benefit, but so far treatment has not been sufficiently controlled to warrant any definite conclusions. Further trials, in which streptomycin will be given to alternate cases, are being undertaken. A small number of cases of ulcerative colitis and of typhoid fever have been treated by oral and intramuscular administration with negative results.

Summary

In this series of cases streptomycin has often been successful in controlling the following infections : (1) Meningitis : *H. influenzae, Bact. coli, Ps. pyocyanea, Proteus,* and *Staph. pyogenes.* (2) Septicaemia : *Bact. coli* and *Ps. pyocyanea.* (3) Urinary tract infection : *Bact. coli, Proteus, Ps. pyocyanea, Str. faecalis,* and *Staph. pyogenes.* (4) Local sepsis: *Bact. coli, Proteus, Ps. pyocyanea, Staph. pyogenes,* and haemolytic streptococcus.

There have, however, been examples of almost every type of infection in which the micro-organisms rapidly became resistant. Courses of treatment should therefore be planned to exert the greatest possible influence from the beginning. The effect of combining streptomycin with other agents, such as the sulphonamides, is under investigation.

Owing to the short periods of administration toxic symptoms have been unusual and of slight importance. Urticarial rashes and skin irritation at the site of local application have occasionally been noted.

"C.B.11": A NEW ANALGESIC DRUG

PRELIMINARY COMMUNICATION

BY

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In experimental studies in human beings we have recently compared the pain-relieving properties of C.B.11 (4 : 4-diphenyl-6-morpho-linoheptan-3-one hydrochloride), pethidine, and physeptone (amidone). The method we used is a modification of that employed by Hewer and Keele (1947) in comparing the analgesic properties of physeptone, pethidine, and morphine. These authors, using a degree of ischaemic pain as their standard, found that the effects produced by 7.5 mg. of physeptone and morphine were equivalent to those of 75 mg. of pethidine. Because C.B.11 has been shown in recent studies (G. F. Somers, personal communication, 1947) to be a more effective analgesic than morphine in rats and of low toxicity we considered it was worthy of clinical trial in man.

Method

Ten volunteer medical students were trained to appreciate a degree of ischaemic pain produced by obstructing the blood flow to the arm by a sphygmomanometer cuff at a constant pressure of 220 mm. Hg. Following occlusion the subject contracted the flexor muscles of the forearm 60 times within the space of one minute. Contractions were then stopped and the ischaemia maintained, resulting in the development of a steadily increasing pain in the forearm. The degree of pain produced in five minutes was easily recognizable, and if the ischaemia was maintained it became intolerable in 10 to 15 minutes. The subjects were trained to recognize the level of pain reached in five minutes.

An intravenous injection of one of the three drugs under trial was then given into the opposite arm. On three separate occasions 5 mg. of C.B.11, 5 mg. of physeptone, or 50 mg. of pethidine was given, the order of injection being varied in different subjects. The analgesic effect of the drugs was estimated as follows: the degree of pain at the time of injection was tabulated as 100% ; an appreciable reduction of pain as 50% ; and reduction to a barely perceptible level as 20%. Records of the degree of pain experienced were made every minute until the pain again increased above the original level or it was evident that the quantity of drug given had not produced any analgesic effect. The results of the experiment are given in Table I.

TABLE I

	Pethidine 50 mg.	C.B. 11 5 mg.	Physeptone 5 mg.
Pain reduction to 20% ..	—	8	3
Pain reduction to 50% ..	—	1	3
No pain reduction	10	1	4

Discussion of Results.—In each case in which analgesia was produced the effect was apparent within two minutes and lasted as long with C.B.11 as with physeptone, the average duration being three minutes. After that period there was a rapid recrudescence of pain to above the original level with both drugs.

Side-effects.—With C.B.11 the injection was followed by transient dizziness, which did not last for more than five