THE STREPTOMYCIN TREATMENT OF TUBERCULOUS MENINGITIS

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Streptomycin is the antibiotic principle prepared from *Streptomyces griseus*, and it is active against a wide range of bacteria. Its chief interest lies in its activity against *M. tuberculosis*. The scarcity of streptomycin in this country has led in the main to its use only in conditions for which no other form of treatment is available, and of these conditions in children tuberculous meningitis has received the most attention.

The toxicity of streptomycin is well known, and of the many toxic manifestations vestibular damage, skin rashes and damage to the kidneys are the most frequently seen. Of lesser importance and not calling for reduction of dosage of the drug are headache in the third week or so of treatment and transient numbness of the lips. It is difficult to assess the subjective effects of streptomycin in children, particularly as many of them have been so young, but with the dosage employed no toxic signs certainly due to the drug have been observed.

Intramuscular streptomycin is painful, the pain probably being due to the presence of impurities. It can be mitigated by the inclusion of a little novocain in the same syringe. With intrathecal injection of streptomycin some of the bigger patients have complained of pain in the back and legs when the lumbar route is used, while alarming reactions, with collapse and coma, have occasionally been seen following intracisternal injection. The amount of drug tolerated by the cysterna magna seems clearly to be less than that by the lumbar route.

Of fundamental importance in the streptomycin treatment of any tuberculous condition is the sensitivity of the particular organism to the drug. From primary isolation the great majority of strains of *M. tuberculosis* have an *in vitro* inhibitory level of one-eighth to half a unit of streptomycin per ml., a unit being one millionth of a gramme. The readiness with which the organism from treated pulmonary cases becomes drug-resistant seems to be rarer in meningitis, and strains recovered at autopsy after seven or more months continuous treatment with streptomycin have been found to have the same *in vitro* sensitivity as that of the primary isolation. For

testing sensitivity, isolation has to be made by culture or from a guinea pig, after which a standard suspension is prepared for inoculation into serial dilutions of streptomycin in Dubos's medium, where reading is made after ten days. Thus it may be six weeks or longer before the sensitivity of a strain is known.

As the earlier the disease is treated the better appear to be the results, it would be quite impossible to wait for sensitivity levels before commencing streptomycin therapy, and the dosage chosen is made on the assumption of a usual sensitivity of the organism to the drug. The aim is to maintain a constant inhibitory level in the blood, while the same level in the cerebrospinal fluid is maintained for varying periods according to the progress of the case.

With the dose of 0.02 gm. per lb. of body weight per day given in distilled water intramuscularly six-hourly, the blood levels have been consistently satisfactory. In occasional cases a transitory level of 64 units per ml. at the end of the first hour may be seen, and at six hours a level of 16 units is exceptionally found, but in the main the figures fall within the lined area in Fig. 1. It will be seen that six hours after the injection, levels of 2 to 8 units per ml. are present, an amount well in excess of the inhibitory $\frac{1}{2}$ unit.

An intramuscular injection every six hours for periods of six months or more can be a great trial both to patient and nursing staff, and the same daily amount of streptomycin given 12-hourly produces nearly as satisfactory blood levels. Fig. 2 shows the type of curve with this method of spacing, and even at 12 hours levels of 4 units may be seen. In one child of 11 years the calculated dose was 2 gm. per day, and as this upset the patient considerably the dose was halved, being given as 0.01 gm. per lb. of body weight per day 12-hourly: Fig 3 shows that there was still a therapeutic level at 12 hours, the 2 units per ml. in this case being eight times the *in vitro* inhibitory level for the particular organism.

In cases without meningitis, streptomycin penetrates only slightly into the cerebrospinal fluid after intramuscular injection, and levels of

Fig. 1. Blood levels obtained with 0.2 gm. per lb. of body weight per day given 6-hourly.

0.5 units per ml. of C.S.F. or less are found. But when meningitis is present higher levels, up to 2 and 4 and rarely 8 units, are seen. Fig. 4 shows the C.S.F. findings in a case of miliary tuberculosis which developed tuberculous meningitis while on intramuscular streptomycin, and demonstrates the greater facility with which the drug can cross an inflamed barrier. This higher streptomycin level is an almost constant finding, and is a reliable indication of meningeal inflammation. Such levels are above the average inhibitory amount for *M. tuberculosis*, and were the rationale for attempting to treat some cases of tuberculous meningitis by the intramuscular route alone.

Above the age of two years, a dose of 0.1 gm. of streptomycin diluted in saline is well tolerated when given intrathecally by the lumbar route, while under two half this amount should be given. Intracisternally and intraventricularly the irritant effects of streptomycin are more readily observed, and the amount injected should not exceed 0.05 gm. One hour after the injection of such amounts, the streptomycin level in the C.S.F., as might be expected, is very high and after 24 hours the levels are usually found within the range of 8 to 16 units per ml. of C.S.F.

The irritant effect of streptomycin on the theca is well illustrated when 0.1 gm. is injected into a normal thecal space. The results of such an injection by the lumbar route are shown in Fig. 5, when physiological saline was the diluting fluid. As it has been suggested that the cellular increase may be due to the saline and not the streptomycin, the lower half of Fig. 5 shows the result when streptomycin dissolved in normal cerebrospinal fluid is injected. In each case the considerable pleiocytosis was polymorphonuclear, and the cell count had returned to normal within a week. The protein in each case was rather higher than before

the streptomycin was given. The cellular rise is not seen to anything like the same extent in meningitis.

In many cases of established tuberculous meningitis under streptomycin therapy the cells and biochemistry have been followed daily as a routine, in the hope that some prognostic change might be observable. The daily variations in the cells and protein which may be seen in almost any case are depicted in Fig. 6. All that can be said is that these elements appear roughly to vary in the same direction; the day to day oscillation is so wide as to give little information of value for prognosis. The same may be said of daily sugar and chloride estimations. A general rise or fall in the protein and cells gives a rough indication of deterioration or improvement in the condition, and has proved to be more reliable than apparent clinical change. The cell differential count has shown a greatly predominant lymphocytosis, and possibly some of the polymorphs present are due to the streptomycin irritation already referred to. No alteration in the differential count, as distinct from the total count, has proved useful in prognosis.

A rising C.S.F. protein as a sign of impending block is well recognized. A prognostic point in this connection is a rising protein with falling cells when clinical improvement is occurring. Many cases which have done outstandingly well with streptomycin treatment have shown this divergence. Fig. 7 shows the C.S.F. in such a case, the patient having been treated for two months before the chart begins. At a point coinciding with clinical improvement the protein

Fig. 2. Blood levels obtained with 0.2 gm. per lb. of body weight given 12-hourly.

continued to rise while the cells fell. During a slight clinical relapse the two converged, but drew apart again as the patient improved. The child is now clinically cured, and has a C.S.F. chemically normal and with four lymphocytes per cu. mm. In a similar case while the cells were falling the protein rose to a peak of 7,000 mgm. before starting to fall.

There is no doubt that streptomycin itself may be the cause of some of the variation in protein. In a baby with coliform meningitis treated with intrathecal streptomycin for one week (Fig. 8), in spite of immediate sterilization of the fluid and clinical cure the protein remained raised, and 17 weeks after the streptomycin was given the C.S.F. protein level was still 75 mgm. This prolonged high level is almost certainly a streptomycin effect, as it is not seen in cases of purulent meningitis cured without streptomycin. Support for this view is lent by the findings after streptomycin is injected into a normal theca (Fig. 5), where an increase in protein is seen.

Streptomycin is excreted in the urine, and its concentration depends upon the system of dosage and the amount of urine passed. Therapeutic levels are found constantly even when the drug is given once daily, and figures of 500 and 1,000 units per ml. of urine are frequently seen.

The blood sedimentation rate nearly always falls in the initial stages of streptomycin treatment and rises again if the case fails to respond and death approaches. This is in interesting contrast to most untreated cases of tuberculous meningitis,

Fig. 4. Developing meningitis, showing concomitant increase in C.S.F. streptomycin.

where the sedimentation rate rises as the disease progresses and falls terminally.

Although we now know enough about streptomycin to be able to use it rationally there is so much individual variation from case to case of tuberculous meningitis that no stereotyped scheme of therapy can be expected to produce the same results. The following two cases illustrate some of the problems which are constantly being seen.

The first child, aged two, with miliary tuberculosis and meningitis, was treated for two months continuously with intramuscular streptomycin and for one month daily with the drug intrathecally followed by a rest of a week and then a further week's intrathecal course. In spite of a transient clinical improvement the cells and protein in the C.S.F. rose, and the child died two months after the commencement of treatment. Fig. 9 shows the radiological appearance of the lungs on admission. At autopsy the lungs felt soft and nodules were not palpable. Fig. 10 is an X-ray picture of the lungs postmortem, and although histological sections of the lungs showed miliary tubercles the sections of the enlarged paratracheal nodes showed only fibrosis. The meningitis appeared in no way to have been affected by the streptomycin therapy, and both macroscopically and histologically it was typical of the condition. The original strain of *M. tuberculosis* was sensitive to 0.5 unit of streptomycin, while that isolated at autopsy was resistant to 1,000 units per ml. This is one of the unusual instances where streptomycin resistance developed during the treatment of meningitis.

The most surprising postmortem finding in this

Fig. 3. Blood levels obtained with 0.1 gm. per lb. of body weight given 12-hourly.

	PROTEIN	CELLS
IN SALINE		
Before	16	3
24 hours after	32	1080
7 days after	40	3
IN C.S.F.		
Before	24	3
24 hours after	16	1316
7 days after	32	2

Fig. 5. Effect of 0.1 gm. of streptomycin on cells and protein when injected into a normal theca.

case was an early pyelonephritis. A full urine examination had been carried out weekly, and one week before death there was no albumin or pus in the specimen and the cultures were sterile. There were more than 1,000 units of streptomycin per ml. in the patient's urine, and the *Bact. coli* responsible for the condition was sensitive to 1 unit of streptomycin per ml. Thus we have an infection developing when the urine contains a thousand times the inhibitory dose of streptomycin to the organism.

The second case was a girl, aged six, with miliary tuberculosis but without meningitis either clinically or on the C.S.F. findings. Treatment by six-hourly intramuscular streptomycin was started. Routine lumbar puncture was performed weekly, and at the end of the second week the fluid was normal in all its constituents with a streptomycin content of 0.125 units per ml. At the end of the third week the cells and protein had risen and so had the level of streptomycin, and tubercle bacilli were present in the deposit. One week later the protein in the C.S.F. was 280 mgm. and there were 2 units of streptomycin per ml. Apart from slight irritability for a few days at the end of the second week there were no clinical signs to suggest the presence of meningeal inflammation.

As this level of streptomycin is sufficient to inhibit the growth of most strains of *M. tuberculosis* it was decided to treat the patient with intramuscular streptomycin alone. Tubercle bacilli were present for only a week, and for the next seven months weekly examination of the C.S.F. showed protein fluctuating around 200 mgm. and cells up to 250, while the streptomycin level was never less than 4 units per ml. Clinical meningitis was never manifest.

After seven months continuous intramuscular streptomycin six-hourly, the drug was withdrawn to see what would happen. Within four days tubercle bacilli had reappeared in the C.S.F. This isolation had the same streptomycin inhibitory level as the original strain grown, which was 0.25 units per ml. The patient was put on to intrathecal streptomycin as well as intramuscular, and for eight weeks has shown no change.

The points of particular interest in this case are that meningitis developed after intramuscular streptomycin was started, that there has never been any evidence of meningitis apart from the C.S.F. findings, and that in seven months of continuous treatment the streptomycin sensitivity of the infecting organism had not altered. Figs. 11 and 12 show the radiological improvement in the miliary process in the lungs during the period of treatment, with disappearance of mottling and resolution to within normal limits.

Points meriting some discussion are the diagnosis of tuberculous meningitis and the treatment of hydrocephalus during streptomycin treatment.

Diagnosis

All results indicate that the earlier streptomycin treatment is started the better the prognosis, so that the establishment of the diagnosis of tuberculous meningitis is of prime importance. The clinical diagnosis may be extremely difficult, particularly as some cases present with such slight signs of

Fig. 6. Tuberculous meningitis on intrathecal streptomycin treatment. Daily variation of cells and protein.

meningeal involvement. A contact history is the rule, and the Mantoux test is nearly always positive. There is occasionally an unfortunate tendency to discount the diagnostic value of a negative Mantoux reaction, although it appears to be a very rare finding in established cases. A point of clinical interest is the frequency of obstinate constipation. In one case, indeed, so much liquid paraffin was given for the constipation that a dermatitis developed, thought to be due to streptomycin. Withdrawal of the paraffin, however, and administration of vitamin A cleared the condition and exonerated the streptomycin.

Diagnosis on the C.S.F. findings may be difficult if *M. tuberculosis* is not seen, and raised protein and lymphocytes with a lowered sugar and chloride content are the usual but not invariable findings. A moderate lymphocytosis and slightly raised protein are constant findings of little diagnostic value alone as they occur in so many other conditions, notably poliomyelitis. Chlorides may be misleading. In one case of established tuberculous meningitis under treatment for six months the chloride level has never fallen below 700 mgm., while the low levels produced by vomiting, particularly in children, accompany so many other diseases. A reduced and falling sugar in the C.S.F. is possibly the most suggestive finding, while a normal level is evidence against tuberculosis. *M. tuberculosis* may be found in the spider's web clot which forms on standing, but may often be more readily seen in smears from the centrifuged deposit.

In a case illustrating how misleading the C.S.F.

Fig. 7. Divergence of cells and protein in C.S.F. during improvement of tuberculous meningitis with streptomycin.

Fig. 8. Persistence of high C.S.F. protein after 1 week's successful streptomycin treatment of coliform meningitis.

may be there was no contact history, the 1/1,000 Mantoux test was doubtful, and at all times the C.S.F. showed a high polymorph count. Clinically the child was more like an encephalitis than tuberculous meningitis, and after a month's treatment with streptomycin the drug was stopped under the impression that the diagnosis was wrong, particularly as tubercle bacilli had never been found in the C.S.F. A fortnight later a guinea pig inoculated with the fluid died with disseminated tuberculosis. In another case, a baby of six months, there was a family history of open tuberculosis, the Mantoux test was positive, and clinically there was a typical onset of tuberculous meningitis. The C.S.F. findings supported the diagnosis in that there were much lowered chlorides with raised protein and lymphocytes, but the sugar content was normal. After five days of streptomycin treatment the baby died, and at autopsy was found to have a cerebellar tumour, with no evidence of meningeal tuberculosis

In neither of these cases was the tubercle bacillus found in the C.S.F. on direct examination. On reviewing them in the light of subsequent knowledge it was realized that in the first case the continued polymorph rather than lymphocyte response in the C.S.F. was probably a streptomycin reaction, while in the second case insufficient importance had been attached to the normal sugar level. These cases are not cited as evidence to contraindicate the early commencement of streptomycin therapy when the diagnosis is only presumptive, but to show how difficult may be the diagnosis when all the clinical and pathological data have been assembled.

FIG. 9.—X-ray of chest of child dying with pyelonephritis, before treatment.

FIG. 10.—Postmortem X-ray of lungs of same child as in Fig. 9, two months after streptomycin treatment.

FIG. 11.—Miliary mottling of lungs of child who developed meningitis while on streptomycin treatment.

FIG. 12.—Same as Fig. 11, to show healing after six months on streptomycin.

Hydrocephalus

In cases of tuberculous meningitis treated with streptomycin coming to autopsy the incidence and degree of hydrocephalus has been striking. The cause of this complication seems to be the gelatinous exudate at the base of the brain interfering with the normal circulation of the C.S.F., and true internal hydrocephalus is seldom seen.

Increasing intracranial pressure may be inferred from increased C.S.F. pressure on lumbar tap and

sometimes by the onset of papilloedema. At times hydrocephalus develops so rapidly that in younger children skull measurements are sufficient to assure the diagnosis, and X-rays show greatly widened sutures.

The prolongation of life which streptomycin causes alters the clinical aspect of tuberculous meningitis markedly, so that in its chronic form it is almost a new disease, part of which is this tendency to hydrocephalus. The means by which

developing hydrocephalus can be treated are various, and are aimed at reducing the intracranial pressure.

Where there is no question of a block and the lumbar pressure is increased large amounts of fluid may be drained by the lumbar route, either by frequent puncture or by means of an indwelling lumbar catheter. When this method achieves poor clinical results, or when there are signs of blockage a catheter may be introduced through a burr hole in the skull into a lateral ventricle. The catheter may be left in the ventricle for varying periods of time, and through it excess of C.S.F. may be drawn off and streptomycin injected. A useful method is to leave the intraventricular catheter in place for a week, after which it is withdrawn and streptomycin is injected directly into the ventricle with a long needle. This may be done on alternate days with lumbar injection on the days when the ventricle is not used.

Occasionally surgery has been attempted, and a hole has been made in the tentorium cerebelli in order to allow a free escape of C.S.F. over the cerebral hemispheres. The relief gained by this means is only transitory, as the hole appears to be sealed off very quickly by exudate.

Another way of trying to reduce hydrocephalus is with anticoagulants. How these might work after the deposition of fibrin has occurred is not clear, although they could be expected to prevent the formation of further fibrin while the normal body mechanisms dealt with that already present. Heparin is the anticoagulant which has received the most attention, and it can be given intrathecally in doses up to 30 mgm. daily in children without harm. Unfortunately, if the usual intrathecal dose of 0.1 gm. of streptomycin is mixed with heparin an insoluble precipitate forms which contains the heparin. The C.S.F. 24 hours after the injection of 0.1 gm. of streptomycin has only 16-32 units per ml., and if heparin is mixed with such fluid no deposit occurs. But 24 hours after an adequate intrathecal dose of heparin, streptomycin added to the fluid still gives a precipitate, and it is necessary to wait for 48 hours before the two may be mixed safely. Thus, heparin is best used when no intrathecal streptomycin is being given, and if streptomycin is essential it cannot be given intrathecally more often than every third day.

Without large series of cases and controls the usefulness of such anticoagulants will be difficult to assess. Used prophylactically, there is no means of knowing what effect on the prevention of fibrin deposition the anticoagulant will have, as presumably some fibrin will be present before treatment starts, and some cases appear to resolve with no other treatment than streptomycin. Hydro-

cephalus developing while heparin was being given would suggest that the heparin was failing in its task, but as by no means all cases develop hydrocephalus even without heparin, its therapeutic value would be difficult to delimit. Little more can be said at the present with regard to the various anticoagulants which have been used than that the conception is sound and that they merit extended trial.

Conclusion

The prolongation of life and clinical improvement which streptomycin is able to effect in tuberculous meningitis are something quite new in the history of the disease, but the long period of both treatment and subsequent observation which will be necessary to evaluate the drug must delay any final conclusions as to its efficacy. Increasing experience is leading to increasing success, with almost every case treated presenting its own problems and teaching its individual lessons.

As the earlier the disease is treated the better will be the result, every effort must be made to establish the diagnosis as early as possible. Yet such encouraging results may be occasionally obtained even in comatose and apparently moribund children that almost any patient, however ill, is worth treating on the off chance that he may respond.

A greater problem is how long treatment should continue. The common practice is continuous intramuscular administration for an indefinite period, with an initial daily intrathecal course lasting between two and four weeks. But while the clinical pathology of streptomycin treatment has been well explored the ideal combination of intramuscular and intrathecal administration is not yet finally decided, and probably it varies from case to case. It is not known if a constant inhibitory streptomycin level in blood and C.S.F. is preferable to a series of peak levels, although as far as the C.S.F. is concerned the relative inefficiency of the constant C.S.F. level obtained by intramuscular administration alone favours the latter view. And whether, after the first period of intrathecal treatment, complete cessation of intrathecal injection, or a rest period followed by another and further daily courses, or single intrathecal injections increasingly spaced is the best regimen to follow, only experience will decide.

Constant watch must be maintained during treatment for signs of increasing intracranial pressure, which will necessitate other measures to prevent brain damage from hydrocephalus. But the development of hydrocephalus itself is no indication to stop treatment, as the most remarkable improvement, even to apparent normality, is sometimes seen after the demonstration

of such a degree of hydrocephalus that there seems to be scarcely any brain substance left.

In many cases of tuberculous meningitis streptomycin seems to maintain the condition of the patient when treatment was commenced, but little subsequent improvement is seen. Such experiences support the case for the inclusion of some adjuvant antibacterial agent with the streptomycin, in the hope that a synergistic action such as is seen with sulphonamide and penicillin might be found.

Finally, it must be realized that the streptomycin treatment of tuberculous meningitis cannot be lightly undertaken. Apart from full laboratory facilities for controlling the clinical pathology of a case much extra nursing is required, continuous

medical supervision is necessary, and from the patient's point of view there will be a course of intramuscular injections lasting for six months or more, apart from intrathecal and general supporting treatment. Only the fullest and continuing co-operation of everybody concerned can give streptomycin treatment the fair trial it deserves, and even in the most successful cases with apparent cure, prolonged subsequent observation is necessary owing to the possibility of relapse.

ADDENDUM

These observations were made at the Hospital for Sick Children, which was one of the centres taking part in the investigation by the Medical Research Council of streptomycin in tuberculosis.

NON-TUBERCULOUS MENINGITIS

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(1) PURULENT MENINGITIS

The treatment of purulent meningitis has undergone a great change in the past ten years. Before the introduction of sulphonamide therapy, the prognosis in all but meningococcal meningitis was very bad and there were very few recoveries. A radical transformation has been brought about by modern chemotherapy and even cases of influenzal meningitis with early and thorough treatment, may now be expected to recover, although hitherto they were almost always fatal. Nevertheless many patients with purulent meningitis still die, due largely to failure to diagnose the disease early enough and to inadequate treatment.

Diagnosis. The diagnosis of acute meningitis is not difficult although in infants the onset may be more insidious and typical meningeal signs absent. As a rule the onset is very acute, sudden high fever developing in a previously healthy child; drowsiness is an early symptom. Pain in the neck muscles

especially on flexion soon appears and Kernig's and Brudzinski's signs become positive.

If the child is untreated he becomes stuporose with marked neck retraction and in severe cases opisthotonus may develop. Vomiting follows as a result of rise in the intra-cranial pressure (in infants under two years the sutures may separate and hydrocephalus may develop).

It is not easy to distinguish one form of purulent meningitis from another, but if purpura and small haemorrhagic spots appear, the infection is probably due to the meningococcus. In infants, acute meningitis often does not present the typical syndrome outlined above. Neck stiffness may be absent, and Kernig's sign is often negative. Irritability, drowsiness, photophobia, bulging of the fontanelle in a child with unexplained fever are very suggestive of the onset of meningitis and a lumbar puncture should be carried out without delay.

DIFFERENTIAL DIAGNOSIS OF MENINGITIS

	Polymorphs	Mononuclears	Sugar	Chlorides	Protein
Tuberculous Meningitis		+	Decreased	Very low	+
Purulent Meningitis	+++		Absent	Slightly decreased	+
Virus Meningitis		+	Normal	Normal	+
Serous Meningitis	+		Normal	Normal	+

The following day was spent in Utrecht, a city with an old university and an excellent medical school. Again we were delighted by the versatility of our host who was a general surgeon in its widest sense, who could teach us much, yet was ever willing to listen. A delightful evening at our host's home in a fine old house, with the water lapping against its walls, ended a memorable day. To conclude our visit we drove out to the great dyke which makes the Zuyder Zee a fresh water sea by shutting it off from the ocean. The scenery, utterly flat and not even relieved by a windmill, soon lost its novelty and one could well imagine that in time it would engender agorophobia in the staunchest. There were depressing signs of German wantonness in the skeletons of wooden houses made uninhabitable by flooding. The dykes were destroyed as they retreated in 1945, not long before the surrender. However the Dutchman has not earned his reputation for stubbornness without cause and already a most ambitious rebuilding programme is well on the way to completion.

The Dutch, even as ourselves, seem to take the problem of recovery after the war very seriously, and in fact in some ways have been more successful than us. We have much in common and it is hoped that the exchange of medical knowledge and of doctors in the future will be even greater than in the past.

Aid for the Deaf

It is gratifying to learn that a committee has been set up to consider the three aspects of therapy for the deaf. Medical, surgical and instrumental. The greatest advances in these three aspects has been made in the surgical treatment of otosclerosis and in the construction of the present-day crystal microphone, with miniature valve amplifier, hearing aid.

The surgical approach is, of course, to be undertaken only by those taking the trouble to perfect the difficult technique, and the operation has no doubt come to stay, for its place in the treatment of otosclerosis is now proven without any doubt.

Although advances have been made in these three branches of therapy for the deaf, there still remains to be formed in this country, clinics set apart entirely for the treatment of the deaf, from infancy to old age. Thus within the one clinic there should be facilities for speech therapy, lip reading, hearing aid selection and maintenance, surgical treatment for those suitable for the operation, medical treatment for those who require it and finally and perhaps most important of all, facilities for further research in one or all of these three branches. Such clinics, I believe, are in existence in the Western Hemisphere but not in Europe.

E.R.G.P.

Paediatric Number

The July issue of the Journal was devoted to Paediatrics, but owing to the shortage of paper it was impossible to print all the articles. This month Dr. J. L. Henderson's paper on 'Infection in the Newborn Infant' has therefore been included in addition to the published contents.

Correction

In the article by Dr. I. A. B. Cathie on 'The Streptomycin Treatment of Tuberculous Meningitis' appearing in last month's issue of the Journal a typographical error occurs beneath a number of illustrations. In Figures I and II, 0.2 gm. per lb. of body weight should read : 0.02 gm. per lb. of body weight. In Figures III and V, 0.1 gm. per lb. of body weight should read : 0.01 gm. per lb. of body weight. We apologise for this error and hope that it has not proved misleading.