THE TREATMENT OF TUBERCULOUS MENINGITIS.*

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The purpose of this paper is to review our experiences with streptomycin in the treatment of tuberculous meningitis during the period September, 1947, to March, 1950. The cases reviewed are 94 in number, occurring consecutively, all of them bacteriologically proved. Several cases admitted on or after April 1st, 1950, are omitted from this survey, as insufficient time has elapsed to justify an assessment of their progress or their chance of ultimate recovery or survival.

Before dealing in detail with the 94 cases treated in our wards during two and a half years it is relevant to mention that prior to the introduction of streptomycin 297 cases of tuberculous meningitis were treated in the same wards during the period September, 1934, to September, 1947. All of these cases died in deepening coma within two or three weeks of admission. In evaluating the effect of streptomycin it is necessary to bear this fact in mind. For the first time in medical history we have in our hands a preparation which can arrest the tuberculous process, even when it occurs in the brain. One in every four or five cases recovers from the disease, provided treatment is not too long delayed or too soon abandoned.

I do not need to tell this audience of experts on tuberculosis that in considering the granulomatous process initiated by Koch's bacillus it is impossible to speak of recovery, much less of cure, unless cases are followed up for many months after apparent arrest of signs and symptoms. Publication of earlier reviews from other countries has tended to give an unduly optimistic account of the benefits of streptomycin, which prolonged observation of cases would have modified.

We began this work nearly three years ago with little guidance as to the optimum dosage and correct routes of administration of streptomycin. The drug was difficult to obtain, and very expensive. Dosage, as is usual with new remedies, was tentative, and we now know excessive, just as that of penicillin was, when it was introduced, grossly inadequate. The route of administration—intramuscular or intrathecal—was also speculative, and even when it was found essential to give at least some of the drug intrathecally, there was no unanimity as to how long intrathecal therapy should be continued. Our earlier experiences were, therefore, a little groping, but we soon realized that prolonged intrathecal therapy was necessary. The prolongation of life which the new remedy brought, as compared with the rapid death of the pre-streptomycin days, was also very obvious. This delaying action of streptomycin, permitting the patient to live for several months in comparative comfort, during which the relatives accustom themselves to an eventual bereavement, is not the least of the advantages of streptomycin in the treatment of a condition hitherto rapidly and invariably fatal.

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We have treated, in all, 94 cases, of whom to-day 19 may be regarded as cures—a recovery rate of a little more than 20 per cent. We find that children under two years of age rarely survive. Of 14 cases in this age-group, 13 died and the survivor has been only four months under treatment and, although apparently well, ultimate cure cannot yet be guaranteed. Curiously enough, our best age-group was from 2-4 years, in which we had 17 cases, of whom 5 recovered. The 5-9 year age-group, which furnished 20 cases, gave 5 recoveries. The next quinquennial age-grouping (10-14 years) yielded only one recovery out of 6 cases, and of the remaining patients (15 years or over) 7 recovered out of 37 treated.

There was no statistically significant difference between the sexes, either in incidence or fatality.

At least two out of every five of these 94 cases were known to have had prolonged contact with an open case of phthisis within three months of the onset of meningeal symptoms. In many more, such an association was suspected. The tubercle bacilli isolated from the cerebro-spinal fluids were typed in several instances: all were of the human type.

Other tuberculous lesions were present in many cases. These lesions always antedated meningeal involvement. It should be mentioned that many of the acutely ill patients who died within a few weeks of coming under treatment may have had miliary or other pulmonary involvement, but their clinical condition did not, on humane grounds, permit of their transport to the X-ray Department for radiographic investigation.

Among the 94 cases treated the following non-meningeal tuberculous lesions were found in 21 cases.

Pulmonary tuberculosis: primary 8, ulcerative 3, miliary 7.

| Tuberculosis of joints | 1 |
| " glands | 1 |
| " abdomen | 1 |

In all cases the non-meningeal lesions improved while under treatment; this was especially noticeable in the miliary cases.

Choroid tubercles were not seen in any uncomplicated case of tuberculous meningitis. When the meningitis supervened on miliary tuberculosi, choroidal tubercles were seen in three cases.

**Rationale of Treatment.**

The system of treatment which we have adopted for some two years now is as follows:

1. All cases, irrespective of age or weight, receive 500 mgms. streptomycin twice daily intramuscularly, for at least six months.

2. Daily intrathecal therapy of 100 mgms. dissolved in a few c.c.s. of saline is given for at least six weeks after admission, and, if necessary, is continued for 3 to 4 months until clinical improvement with remission of meningitic signs justifies withdrawal. After each 7 days the intrathecal therapy is remitted for three days in order to prevent the back becoming unduly sore. If clinical improvement allows, after the sixth week, the intrathecal therapy is given on alternate days and still later, on every third day. When intrathecal therapy is finished check spinal punctures are done every 10 days until intramuscular streptomycin treatment is