TUBERCULOUS OPTIC NEURITIS
AN EXPERIMENTAL STUDY
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With the introduction of modern therapeutic agents, such as streptomycin, P.A.S., isoniazid and isoniazid combined with cortisone, into the treatment of tuberculous leptomeningitis, the mortality rate from this disease has been reduced to about 20 per cent. On the other hand, late complications in the central nervous system, unknown before the advent of this therapy, are now a frequent occurrence. Blindness caused by optic atrophy appearing in the course of treatment or as a later sequel, is one of the problems with which the neurosurgeon is concerned.

The present study was undertaken in order to try to find out whether the optic atrophy occurring in patients recovering from tuberculous meningitis following treatment results from: (a) local fibrosis of the pia-arachnoid producing constriction of the optic nerves and/or chiasm or constriction of the blood vessels supplying these structures, or (b) direct involvement of the same structures or of their vessels by the tuberculous process.

In a previous report evidence was submitted for the beneficial effect of isoniazid and, particularly of combined isoniazid-cortisone therapy in cases of well established exudative tuberculous leptomeningitis produced experimentally in rabbits. These studies showed that following the isoniazid therapy, the tuberculous process in the meninges subsided and was replaced by moderate to slight nondiffuse fibrous arachnoiditis, whereas the isoniazid-cortisone treatment resulted in complete disappearance of the meningitis without any signs of fibrosis of the pia-arachnoid.

MATERIALS AND METHODS

Twenty-eight rabbits weighing approximately 2 kg. each were divided into two groups of equal number: 14 animals, comprising the first group, were sensitized with killed bovine tubercle bacilli; after a positive tuberculin test was found in all of them, each received an intracisternal injection of approximately 100,000 tubercle bacilli of the Myco. tuberculosis bovis strain, suspended in 0.2 ml. of physiological saline, under sterile conditions. The culture used was sensitive to concentrations of 0.5 mg. per ml. of streptomycin and isoniazid. The second group of 14 animals was not sensitized with killed tubercle bacilli but otherwise was treated in the same way.

Treatment was started 15 days following the inoculation with live tubercle
bacilli, previous experiments having shown that by this time there is a well established tuberculous leptomenigitis in both sensitized and nonsensitized rabbits. 1

All the drugs were administered intramuscularly as follows:

Streptomycin: 8 nonsensitized and 3 sensitized animals each received 50 mg. daily.

Isoniazid: One nonsensitized and 8 sensitized animals each received 50 mg. daily.

Isoniazid-cortisone: 5 nonsensitized and 3 sensitized animals each received 50 mg. isoniazid and 15 mg. cortisone daily.

Animals were sacrificed at intervals varying between 10 and 133 days following the initiation of treatment. However, most of the animals treated with streptomycin died within 5 weeks following the induced infection. Treatment was continued up to the day before the animals died or were sacrificed.

In each animal, after fixation of the brain in 10 per cent formalin, the optic chiasm, together with the intracranial portions of the optic nerves, was excised and embedded in paraffin; sections were stained with hematoxylin and eosin, the Luxol fast blue method for myelin and Verhoeff’s modification of the Ziehl-Neelsen method for acid-fast bacilli.

PATHOLOGICAL FINDINGS

Macroscopic. No differences were observed between sensitized and nonsensitized animals. The appearance of the chiasm and optic nerves paralleled closely that of the whole base of the brain.

In animals examined during the early stages of all three types of treatment (6–10 days after commencement) the meninges enveloping the optic chiasm and optic nerves were thick, opaque and friable; occasionally, tubercles were clearly discernible. At later stages of treatment (30–133 days) the animals that received isoniazid showed fine thread-like adhesions between the two optic nerves (Fig. 1A), whereas in those treated with streptomycin the nerves were firmly bound to one another by adhesive arachnoiditis (Fig. 1B). However, in the animals that were treated with isoniazid plus cortisone, the leptomeninges were normal in appearance (Fig. 1C).

Histological. Again there were no apparent differences in the response of nonsensitized and sensitized animals to the various treatments instituted. The effect of these on the leptomeninges of the optic chiasm and optic nerves

Fig. 1. Optic chiasms of rabbits treated with (A) isoniazid for 18 days, (B) streptomycin for 20 days, (C) isoniazid plus cortisone for 45 days.