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### THE EFFECT OF NEOMYCIN IN *B. PROTEUS* CYSTITIS COMPLICATING TUBERCULOUS MENINGITIS

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Retention of urine associated with tuberculous meningitis is very uncommon in children, and when there is an added complication of *B. proteus* cystitis these conditions together present a serious medical problem. We can find no record in the medical literature of a patient suffering from a combination of these infections, and the object of this report is to describe such a case.

Waisbren and Spink<sup>1</sup> described 17 cases of urinary infection due to *B. proteus*, which were favourably affected by neomycin and 7 patients with tuberculosis—5 of whom had meningeal involvement. These showed no beneficial response to neomycin, alone or in combination with other antimicrobial agents such as sulphadiazine, aureomycin, streptomycin, dihydrostreptomycin and Promizole. The authors concluded that although infections due to *B. proteus* were favourably affected by neomycin the ototoxic and nephrotoxic effect of this drug precluded its recommendation for general use.

Garfield *et al.*<sup>2</sup> listed 62 infections with organisms sensitive to neomycin and completely or partially resistant to other antibiotics. Amongst these is mentioned one case of cystitis due to *B. proteus*, but details of this case are not given. One of the 10 cases described in detail had a urinary infection from which a mixed growth of proteus, pseudomonas and non-haemolytic streptococci was obtained. In this case only the proteus was eliminated by neomycin.

Kadison *et al.*<sup>3</sup> listed the organisms against which neomycin was found to be active. They mention that neomycin, in acting on *B. proteus*, differs from the polymyxins.

#### CASE REPORT

M.M., a Bantu girl aged 7 years, was admitted to the McCord Zulu Hospital on 23 January 1956 complaining of severe cough, headache and abdominal pain. On examination she was found to be irritable and restless, with marked neck rigidity and positive Kernig's and Brudzinski's signs. The CSF was sent for examina-

tion on 3 occasions but each time arrived at the laboratory clotted. On 27 January a protein content of 3.8 g.% was found. X-ray of the lungs showed a right hilar flare and infiltration at the left base. The Mantoux test (1/1000) was positive. A diagnosis of tuberculous meningitis was made.

The following treatment was instituted at the McCord Zulu Hospital on 23 January: (1) Streptomycin, 0.5 g. twice daily by intramuscular injection, (2) procaine penicillin, 300,000 i.u. daily by intramuscular injection (discontinued on 4 February), and (3) INH 100 mg. three times a day.

On 29 January the patient developed retention of urine and required catheterization daily until a Foley's self-retaining catheter was inserted on 1 February. She was then also given Sulphatriad, 1 tablet 4-hourly. The meningitis remained unchanged; the CSF clotted as soon as it was obtained, and because of this she was put on ACTH, 0.5 c.c. daily, starting on 2 February. By 9 February she was less irritable.

On 2 March 1956 she was transferred to King George V Hospital.

On admission the child's weight was only 28½ lb. She was fully conscious but obviously meningitic, with neck stiffness, positive Kernig's sign and marked irritability. She still had retention of urine and arrived with the Foley's catheter *in situ*.

The CSF findings on admission were 83 cells per c.mm., all lymphocytes; increased globulin; protein 920 mg.%; chloride 696 mg.%; sugar 55 mg.%. The diagnosis of tuberculous meningitis was later confirmed by a positive biological test and a positive serum CSF bromide ratio of 0.94 (Hunter<sup>4</sup>).

A catheter specimen of urine showed: Albumin+, pus cells + + + +, red blood cells +; reaction acid.

On culture the urine gave a mixed growth of Gram negative and Gram positive bacilli, which were not further identified but which were found to be sensitive to achromycin, chloromycetin and terramycin.

#### Treatment and Progress

1. For the tuberculous meningitis: 10 i.u. of ACTH powder was given 6-hourly by intramuscular injection until 27 July (i.e. 4½ months), and 50 mg. of INH 6-hourly, 5 gr. of potassium chloride four-hourly and additional vitamin B were given.

2. For the cystitis: one Gantrisin tablet 6-hourly, 5 gr. of potassium citrate 4-hourly and bladder wash-outs of potassium permanganate.

4 March (i.e. 2 days after admission). Urine was leaking from

around the catheter, which was therefore removed and 6-hourly catheterization instituted.

5 March. The patient began to pass urine into the bed. Catheterization was discontinued but bladder wash-outs were continued.

6 March. Catheter specimen of urine showed: Albumin trace, pus cells +++; reaction alkaline.

12 March. The culture report on a catheter specimen of urine was as follows: 'Culture gave growth of *B. proteus*, insensitive to penicillin, streptomycin, achromycin, chloromycetin, terramycin, ilotycin and aureomycin'.

15 March. A further catheter specimen of urine showed: Albumin trace, pus cells ++; reaction acid. Culture from the urine gave a growth of *B. proteus* with the same sensitivity results as the specimen of 12 March.

16 March. Some neomycin was supplied by Messrs. Upjohn. The *B. proteus* was tested against this antibiotic and found to be sensitive.

Two mice injected intraperitoneally with the *B. proteus* were dead the following morning.

17 March. Neomycin, 17 mg. in 5 ml. of distilled water was injected into the bladder daily for 3 days.

18 March. The patient passed urine into the bed-pan for first time. Gantrisin and pot. cit. were discontinued.

19 March. She also received 12.5 mg. of neomycin 6-hourly by intramuscular injection for 8 doses (which was all that was available).

20 March. Catheter specimen of urine was sterile after this very small dose of neomycin.

26 March 1956. A non-catheter specimen of urine showed no abnormality.

*Progress of the Tuberculous meningitis.* A steady improvement occurred except for a fluctuation of the lumbar protein in the presence of a completely normal cisternal CSF, probably due to local disorder in the spinal sub-arachnoid space. The patient is now perfectly normal in all other respects, but is still receiving treatment with INH in this hospital.

#### DISCUSSION

During the year 1956 there were 7 cases of urinary infection with *B. proteus* in King George V Hospital in a total of 2,306 patients admitted. All the proteus strains were sensitive to chloromycetin except the one isolated from the case here described.

The virulence of *B. proteus* to laboratory animals is vari-

able.<sup>5,6</sup> The strain grown from this case was virulent, killing mice on intraperitoneal injection. It is therefore very doubtful if the present state of this patient would have been so satisfactory had the urinary infection not cleared up so quickly.

Nephrotoxic complications occur with neomycin<sup>1</sup> and it therefore appears advisable to limit its parenteral administration. It is excreted in the urine very quickly. Kadison *et al.*<sup>3</sup> found that 200 units of neomycin injected intravenously in man produced a concentration of 7 units per ml. in 2 hours and that the effective inhibitory dose was 1.05 units per ml. test medium. Where the organism is sensitive to neomycin a short parenteral course combined with topical therapy should be effective—as indeed it proved to be in our case.

#### SUMMARY AND CONCLUSION

A case of tuberculous meningitis with urinary retention complicated by a *B. proteus* cystitis is described. Neomycin was extremely effective in the small doses used.

We wish to thank Dr. B. A. Dormer for making this work possible, and Messrs. Upjohn for supplying the neomycin. We also wish to thank the Medical Superintendent of the McCord Zulu Hospital, Durban, for permission to use his records.

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