aid of antibiotics, radical removal of the abscess has become reasonably safe and is now the treatment of choice.^{1-8 19 20 22}

In 1969 Garfield,¹⁵ in reviewing 200 cases over 20 years, stated that the mortality rate of 40% was due to continuing inaccurate localisation of the abscess and inadequate use of antibiotics. He believed, also, that the results of assiduously repeated aspiration compared favourably with those of late excision. Localisation is no longer a problem because of the advances in neuroradiological techniques. Adequate antibiotic treatment is, of course, essential to control spread of contamination from the abscess. But we do not agree that the results of assiduously repeated aspiration compare favourably with those of later excision. Time and again it has been observed that aspiration does not always lead to improvement before excision, especially in acute cases. In chronic cases also sudden deterioration may occur after aspiration or ill-advised spinal tap, and the patient may be saved only by immediate excision.²⁰

It is generally believed that there is a close relation between mortality and depth of unconsciousness. In our group, the only death occurred in a patient who was alert (grade 1) on clinical presentation.

The incidence of epilepsy cannot be accurately estimated in this series because of the limited follow-up since epilepsy may develop several years after operation.¹² It was a presenting feature in three cases, and only one of the patients followed up has so far developed epilepsy; this constitutes 10% of the survivors with supratentorial abscesses—a very low incidence compared with that in other series.^{9 12 16} No relation was found between the severity of the neurological deficit and the development of epilepsy, and the patient who developed epilepsy was not taking prophylactic anticonvulsant medication. This type of treatment may be a factor and aspiration may be associated with higher incidence of seizures.²³

It has often been argued that total excision before encapsulation would lead to more severe neurological deficit than would repeated aspiration combined with massive antibiotic treatment and delayed excision if required.^{16 23} Our experience, like that of Ballantine and Shealy,⁶ has been that primary excision causes little or no postoperative deficit. Ballantine and Shealy⁶ found that eight out of nine patients had no postoperative deficit after primary excision of the brain abscess and the other improved over his preoperative status. Out of nine patients who had excision secondary to aspiration or evacuation, eight, although improved, had residual deficits and one patient was essentially unimproved neurologically. None of our patients became totally disabled because of paralysis. Neurological deficit when present

disappeared completely in all except two patients, who were left with hemiparesis in one case and cerebellar ataxia in the other. Visual field defects and speech disturbance also cleared up post-operatively.

In our hands primary excision has produced results so clearly superior to those from burrhole aspiration that we urge this method be adopted as the treatment of choice. It provides prompt internal decompression, permits careful inspection of the abscess cavity for daughter abscesses and allows their removal, and greatly shortens the length of the illness and need for hospital treatment. Most important, it greatly reduces both mortality and morbidity.

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References

- ¹ Sargent, P, *British Medical Journal*, 1928, **2**, 971.
- ² Sachs, E, *Annals of Surgery*, 1946, **123**, 785.
- ³ Fincher, E F, *Annals of Surgery*, 1946, **123**, 789.
- ⁴ Le Beau, J, *Journal of Neurosurgery*, 1946, **3**, 259.
- ⁵ Botterell, E H, and Drake, C G, *Journal of Neurosurgery*, 1952, **9**, 348.
- ⁶ Ballantine, H T, jun, and Shealy, C N, *Surgery, Gynecology and Obstetrics*, 1959, **109**, 370.
- ⁷ Ballantine, H T, jun, and White, J C, *New England Journal of Medicine*, 1953, **248**, 14.
- ⁸ Wright, R L, and Ballantine, H T, jun, *American Journal of Diseases of Children*, 1967, **114**, 113.
- ⁹ Kerr, F W L, King, R B, and Meagher, J N, *Journal of the American Medical Association*, 1958, **18**, 868.
- ¹⁰ Loeser, E, and Scheinberg, L, *Neurology*, 1957, **7**, 601.
- ¹¹ Kiser, J L, and Kendig, J H, *Journal of Neurosurgery*, 1963, **20**, 494.
- ¹² Joona, O V, Pennybacker, J B, and Turton, G K, *Journal of Neurology, Neurosurgery and Psychiatry*, 1951, **14**, 308.
- ¹³ Macewen, W, *Pyogenic Infective Disease of the Brain and Spinal Cord*. Glasgow, J. Maclehose and Sons, 1893.
- ¹⁴ Cairns, H, *Brain*, 1947, **70**, 251.
- ¹⁵ Garfield, J, *British Medical Journal*, 1969, **2**, 7.
- ¹⁶ Lewin, W, *British Medical Journal*, 1955, **1**, 631.
- ¹⁷ Carey, M E, Chou, S N, and French, L A, *Journal of Neurosurgery*, 1972, **36**, 1.
- ¹⁸ Liske, E, and Weikers, N J, *Neurology*, 1964, **14**, 294.
- ¹⁹ Krayenbuhl, H A, *Clinical Neurosurgery*, 1967, **14**, 25.
- ²⁰ Le Beau, J, et al, *Journal of Neurosurgery*, 1973, **38**, 198.
- ²¹ King, J E J, and Turney, F, *Annals of Surgery*, 1954, **139**, 587.
- ²² Samson, D S, and Clarke, K, *American Journal of Medicine*, 1973, **54**, 201.
- ²³ Beller, A J, Sahar, A, and Praiss, I, *Journal of Neurology, Neurosurgery and Psychiatry*, 1973, **36**, 757.

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Noxythiolin-resistant organisms in a district general hospital

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Summary

Twelve strains of *Pseudomonas aeruginosa*, three strains of *Klebsiella aerogenes*, and two strains of *Escherichia coli* were found to be resistant to noxythiolin. Some of the pseudomonads were isolated from patients in the same ward, not all of whom were on noxythiolin treat-

ment. The strains from these patients were indistinguishable from each other on phage typing, which suggested cross-contamination. No Gram-positive organism was found to be resistant to noxythiolin.

Noxythiolin should not be used before a disc diffusion sensitivity test has been performed to determine whether the organisms are sensitive to it. This is particularly important when pseudomonads are the offending organisms.

Introduction

Noxythiolin (N-hydroxymethyl-N-methylthiorea) decomposes in solution and works by liberating formaldehyde.¹ It has a

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Presence of persisting resistant and sensitive strains of *Ps aeruginosa* at different concentrations of noxythiolin over 18 hours. Sensitive strains are shown in parentheses

Hours	Noxythiolin (mg/ml)				
	25	12.5	6.2	3.1	1.5
0	+++ (+++)	+++ (+++)	+++ (+++)	+++ (+++)	+++ (+++)
1	+++ (+)	+++ (+)	+++ (+)	+++ (+)	+++ (+)
2	+++ (+)	+++ (+)	+++ (+)	+++ (+)	+++ (+)
4	+++ (+)	+++ (+)	+++ (+)	+++ (+)	+++ (+)
8	+++ (+)	+++ (+)	+++ (+)	+++ (+)	+++ (+)
18	+++ (+)	+++ (+)	+++ (+)	+++ (+)	+++ (+)
Presence of formaldehyde at end of test	+	+	+	+	+

very wide antibacterial spectrum,² and it has various clinical uses—for example, in intermittent catheterisation,³ peritonitis,⁴ and varicose ulcers.⁶ Although noxythiolin occasionally fails to eradicate organisms, in-vitro resistance to this agent has not been shown on clinical isolates.

Methods

During the investigation noxythiolin disc sensitivity tests were performed routinely on culture-positive specimens from patients who had either bladder washout or local spray with noxythiolin. The specimens were taken from catheter urine and bed sores. A 5-mg (Mast Laboratories Ltd) disc of noxythiolin was placed on a direct sensitivity test (Oxoid) agar plate containing 5% lysed defibrinated horse blood using either *Pseudomonas aeruginosa* (NCTC 10662) or *Escherichia coli* (NCTC 10418) as controls along with the organism under test. The size of the inoculum was standardised to give semi-confluent growth. Those strains showing growth right up to or within 2 mm of the disc margin were selected for study.

The minimum bactericidal concentrations (MBCs) were determined by making doubling dilutions of noxythiolin in water from 25 mg/ml down to 1.5 mg/ml. 0.01 ml of an 18-hour broth culture containing about 100 000 organisms was delivered into each tube. All the tubes were incubated and one loopful of each was subcultured on to blood agar plates at 0, 1, 2, 4, and 18 hours and the amount of growth was noted the next day.

At the end of the incubation period the broth cultures were tested for presence of formaldehyde by adding one drop of Schiff's reagent into each tube and noting the development of a purple colour. Schiff's reagent is a dilute solution of fuchsin hydrochloride (p-rosaniline) that has been decolorised by sulphur dioxide. This decolorisation is the result of a reaction between the p-rosaniline and sulphurous acid that destroys the quinonoid structure of the dye and produces a colourless compound. The aldehyde, by combining with the sulphurous acid, restores the quinonoid structure and hence the colour. The same test was applied after allowing the disc to diffuse into the agar medium and cutting out a block of agar which was shaken vigorously in 1 ml of sterile water before Schiff's reagent was added.

Results

There were 17 resistant isolates—12 strains of *Pseudomonas aeruginosa*, three of *Klebsiella aerogenes*, and two of *Escherichia coli*—all of which grew right up to or within 2 mm of the disc margin. No Gram-positive organism was resistant. The figure shows two resistant and two sensitive control organisms. The table summarises the results at different bactericidal concentrations. Formaldehyde was detected in all the tubes and in the block of agar cut out at the end of the incubation period.

The strains of *Ps aeruginosa* were isolated from 12 patients, only three of whom were having noxythiolin bladder washout. These three patients were in the same ward together with three other patients who were not being treated with noxythiolin but who grew the same organism from their catheter specimens of urine. The phage type of these strains of *Ps aeruginosa*, which were indistinguishable from each other, was 7/21/68/119 X. The infection in the three patients not receiving noxythiolin was probably due to cross-contamination, although no common source of infection could be traced.

Discussion

To simulate urinary tract infection the size of the inoculum

Zone of inhibition produced by two resistant and two sensitive control strains.

was standardised to 100 000 organisms. Although the urinary bladder has its own mechanism of clearing bacteria, the presence of pus cells, red cells, and other organic matter will no doubt hinder the performance of this antiseptic. As this experiment was performed under clean conditions it has shown clearly that if 25 mg/ml of noxythiolin is left in the bladder for half an hour to an hour it will fail to eradicate the resistant organisms. Even after 18 hours organisms grew in the presence of noxythiolin when the size of the inoculum was increased from 100 000 to 1 000 000 organisms. The recommended concentration of noxythiolin of 10 mg/ml may therefore not be adequate for several other purposes.

Although the mechanism of resistance is not known, more and more of these organisms are being encountered in units where noxythiolin is often used. The resistance has no connection whatsoever with the overall sensitivity pattern of the organisms concerned because even sensitive organisms have been found to be resistant to this antiseptic and vice versa. For example, several carbenicillin-, gentamicin-, and colistin-sensitive pseudomonads have been found to be resistant to noxythiolin. Since noxythiolin has a wide range of clinical uses—for example, in peritoneal lavage, bed sores, varicose ulcers, and bladder washouts—it is important to check the sensitivity of the pathogenic organisms before using noxythiolin, especially when pseudomonads are present.

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References

- Kingston, D, *Journal of Clinical Pathology*, 1965, **18**, 666.
- Haler, D, and Aebi, A, *Lancet*, 1961, **190**, 134.
- McFadyen, I R, *Clinical Trials Journal*, 1967, **4**, 654.
- Browne, M K, *Clinical Trials Journal*, 1967, **4**, 673.
- Browne, M K, and Stuller, J L, *British Journal of Surgery*, 1970, **57**, 37.
- McAusland, S D, *Practitioner*, 1963, **190**, 238.

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