

to the injection is encountered the needle tip may have been in the bladder; it is then withdrawn.

Details of the cases are given in the Table. No patient who started micturition after removal of the catheter was included in the series.

DISCUSSION

The intraprostatic injection therapy has opened up a new technique in the management of adenomatous enlargement of the prostate. The *modus operandi* of this relief is unknown. The rational fear of prostatic abscesses or urethral strictures appears to be unfounded. Abnormal vesical conditions, such as stones, bladder tumours, etc., are manifest contraindications.

The patients chosen initially for this treatment were unfit for general anaesthesia because of their poor general condition, and were confronted with some form of protracted tube drainage. Some of the patients had already started this unpleasant regimen. It is noted that after 11 months of catheter drainage one patient returned to normal urinary flow and has since married.

The part played by this treatment appears to be the relief of urinary retention, particularly in the older patients suffering from other serious disabilities. It remains unknown if the process of progressive enlargement of the prostate with increasing renal obstruction can be reversed or held stationary by this method.

The dramatic effect in the relief of retention observed in the series so far described suggests that this is a strong possibility.

In one patient, whose prostate was removed after two injections, the following changes occurred: "There are scattered interstitial haemorrhages with a few necrotic areas. Thrombosis of veins are noted, some of which are organizing."

The employment of this technique continues.

SUMMARY

Seventeen patients with retention of urine due to adenomatous prostatic enlargement were treated by direct injection of the prostate with a special solution. Micturition was resumed in all the patients. The average age of those treated was 74; the number of injections ranged from one to six, with an average of approximately two.

We would like to thank Mr. D. S. M. Barlow and Mr. D. H. C. Harland of the Luton and Dunstable Hospital for permission to publish their cases.

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Medical Memoranda

Herpes Simplex Virus Encephalitis Treated with Idoxuridine

Brit. med. J., 1967, 2, 419-420

CASE REPORT

An unmarried woman aged 41 with severe encephalitis had apparently been well until 18 September 1965, when she had a transient period of confusion which cleared after some hours. She then remained well and continued to work as a pork butcher for 10 days, when she complained of headache, rapidly followed by nausea and vomiting, and then had a single epileptic fit. Thereafter she became progressively more drowsy and less accessible, and on 30 September was admitted to a hospital in Cork. She was found to be drowsy but co-operative, with mild photophobia and meningism, bilateral ptosis, no other neurological deficit or papilloedema, a pyrexia of 100.2° F. (37.9° C.), and peripheral blood leucocytosis of 12,400. Lumbar puncture revealed clear C.S.F. under a pressure of 200 mm., containing 7 cells, mainly lymphocytes, with protein of 40 mg./100 ml. Bacteriological culture was negative. Because her level of consciousness continued to deteriorate without the development of localizing signs but with an increase in C.S.F. cell count to 130 lymphocytes and C.S.F. protein to 140 mg./100 ml., she was transferred to the Radcliffe Infirmary on 5 October for further investigation to exclude the presence of an intracranial space-occupying lesion of infective origin.

On admission she was in a state of muttering delirium with pyrexia of 102° F. (38.9° C.), mild meningism, no papilloedema, and normal pupillary size and reactions. There was no facial weakness and she moved all four limbs in response to painful stimuli. The tone of all limbs was variably increased; the tendon jerks were uniformly depressed, with bilateral extensor plantar responses. Overnight her condition altered slightly in that a minimal right facial weakness became evident and persistent right-sided hypertonus with hyperreflexia developed in her limbs. An E.E.G.,

however, showed only generalized slow-wave abnormality, and a left carotid angiogram was unremarkable except for slight displacement of the pericallosal artery to the left of the midline. Lumbar puncture was repeated and an air ventriculogram was then done via biparietal burr-holes; needle biopsy specimens of both parietal lobes were taken for virus culture, and both lateral ventricles were cannulated, specimens of clear C.S.F. being obtained from both sides. The air-contrast study was normal. The ventricular C.S.F. contained 8 cells/cu. mm. and 50 mg. of protein/100 ml., while the lumbar C.S.F. contained 80 cells/cu. mm. and 200 mg. of protein/100 ml.

The brain biopsy specimens and samples of right ventricular and lumbar C.S.F. were refrigerated overnight at 4° C., and next morning were inoculated into tissue cultures of primary human amnion and secondary monkey kidney. Lesions typical of herpes simplex were seen 24 hours later in the amnion cultures inoculated with the fluid from the right lateral ventricle. No virus was recovered from cultures of the brain and lumbar C.S.F., nor from throat swab or faeces. Complement-fixing and neutralizing antibody titres for herpes simplex virus were 1:64 and 1:256 respectively in blood collected the third day after the patient's admission; both titres rose twofold in the subsequent 14 days, and three months later had returned to the initial level.

Clinically her condition remained unaltered and when the positive virus culture was obtained it was decided to begin treatment with idoxuridine on 9 October—that is, on the 11th day after the onset of her acute symptoms. Though there was some left-hemisphere predominance, the clinical features left no doubt that both hemispheres were involved. It was thought that intracarotid perfusion was the most certain method of reaching the affected tissues. As the possible effects of idoxuridine on the cerebral tissue when given by direct intra-arterial perfusion were not known, and as it was necessary to maintain continuous cannulation of a major vessel for some days with the associated hazards of embolus formation from intravascular thrombosis, it was thought preferable to cannulate the right carotid artery in the first instance. Percutaneous puncture of the right internal carotid artery was carried out under radiological control and a polyethylene cannula inserted, radiographs being taken

after injection of contrast medium to confirm the position of the cannula.

A continuous slow perfusion with normal saline was set up, and once daily for a total of five days she was given 0.1% solution of idoxuridine in physiological saline, which had been prepared in the laboratory and made bacteria-free by filtration through a sintered glass filter. A total of 100 mg. was administered over a period of two hours on the first day and 100, 200, 200, and 400 mg. respectively at the same rate on the four succeeding days (a total dose of approximately 14 mg./kg.). No untoward effects were noted, and indeed it was thought that there was a minimal but definite improvement in her condition in that she became a little more responsive to painful stimuli and there was some decrease in the rigidity of her limbs. The cannula was removed without ill effect on the fifth day, and local pressure at the puncture site for 10 minutes was sufficient to prevent any possible haematoma formation.

The patient was transferred back to her referring hospital on 29 October. At this time she was conscious, and, though a little drowsy, appeared totally aphasic and demented, with increased tone in all limbs, more on the right than the left, with right hyperreflexia, but bilateral extensor plantar responses as before. She was being fed by a nasogastric tube and had an indwelling catheter in her bladder. There was no indication that the idoxuridine had had a therapeutic effect.

In the succeeding six months she made slow improvement until the stage was reached where she remained conscious but moderately confused, dysphasic, and quadriparetic, though she had regained sphincter control. She also had a single further epileptic fit.

DISCUSSION

Numerous cases of herpes simplex encephalitis have been reported in recent years. Previously, most cases were of the fulminating type and were diagnosed after death. Latterly there has been an increase in the number of severe cases diagnosed during life in adolescents and adults who survived the acute attack but not infrequently were left with signs and symptoms of residual brain damage of varying degree. Of the eight proved cases seen in this hospital since 1961 two were of the fulminating type in adult males and one was a 9-year-old girl who had completely recovered two years after the onset. None of the remaining five adult cases recovered. Three patients died 6 to 18 months after the onset, and two, including the present one, were still alive but more or less completely incapacitated. The preponderance of severe cases seen here is probably because this is a neurosurgical centre receiving cases of brain disease from a large area. Some of the reported cases appear to be primary infections and others probably encephalitis as a result of centrifugal spread of the virus from sites of chronic infection of the face or in the upper respiratory tract.

The only possible treatments are surgical decompression and specific attack on the virus with idoxuridine or similar drugs.

Calabresi (1963) injected up to 400 mg. of idoxuridine per kg. intravenously over a five-day period in an attempt to treat tumours, but a large proportion of patients developed stomatitis, alopecia, and leucopenia. More recently these side-effects have been reduced by the simultaneous inoculation of thymidine at another site in the body (Calabresi, 1965). Idoxuridine is said to interfere with D.N.A. synthesis only in actively dividing cells, so it was unlikely to affect neurones, but at the time this patient was diagnosed we had no information regarding the effect of idoxuridine in large doses on the central nervous system. The dose of idoxuridine used was almost certainly insufficient to produce a therapeutic effect on the affected brain, though it may have helped to limit spread of the virus. Tests for the presence of iodo-oxuridine in the lumbar C.S.F. two hours after administration on successive days showed that less than 20 $\mu\text{g./ml.}$ was present.¹ It is probable that idoxuridine passes the blood-brain barrier with difficulty, and it may be necessary to inject it into the ventricles (Calabresi, personal communication, 1966). H. R. Tyler inoculated "very large doses intravenously in an adult patient with herpes simplex virus encephalitis on whom decompression was also done, and the patient made a moderately good recovery" (Breedon *et al.*, 1966). It seems likely that a total dose of 100–200 mg./kg. over a five-day period may be required.

Though herpes simplex virus encephalitis is not a common disease at present and is not always severe in the patients seen in this hospital, facilities for its rapid diagnosis in the laboratory should be available in association with neurosurgical units, particularly now that investigation of specific chemotherapy with idoxuridine is possible.

We thank Mr. J. Pennybacker for permission to report this case; Mr. E. R. Hitchcock, Dr. D. W. G. Budd, and Dr. F. W. Wright for their clinical help; and Dr. D. M. Keating, of St. Finbarr's Hospitals, Cork, who referred the patient to this hospital. Our thanks are also due to Dr. T. A. Turnbull, of Smith Kline and French Ltd., for the supply of idoxuridine.

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¹ These tests were kindly done by Mr. K. J. Thrower in the Department of Clinical Biochemistry, using a Carey 14 spectrophotometer.