

noticeable and persistent. A cinematograph record of the facies exists (Ministry of Health, 1948). A consultant neurologist made a provisional diagnosis of acute disseminated encephalomyelitis. By the next day (Oct. 14) there was marked deterioration, with a rising temperature and a tendency to accumulation of buccal secretions, but still no respiratory muscle involvement. Death, apparently due to bulbar failure, occurred rather suddenly the same evening.

Necropsy on Oct. 15 revealed a little focal haemorrhagic bronchopneumonia in the congested lungs, cloudy swelling and congestion of the liver and kidneys, and oedema and congestion of the spleen (all confirmed microscopically). The heart was normal, the air passages were clear, the pancreas and stomach were congested, and the urinary bladder was dilated. There was moderate oedema and congestion of the somewhat swollen brain and spinal cord.

Microscopical examination showed very severe perivascular "cuffing," mainly with lymphocytoid cells, and foci of acute inflammation and degeneration of parenchyma, in places almost purulent, in the basal ganglia, mid-brain, pons, and medulla—most severe in the mid-brain. The cerebral cortex in the left prefrontal, right Rolandic, and left occipital regions showed only oedema and congestion. The third and fourth cervical, fourth and eighth thoracic, and second lumbar segments of the spinal cord showed inflammation and degeneration of the grey matter, especially of the anterior horns, in which a considerable number of neurones were destroyed, and to a smaller extent of the white matter.

The findings were characteristic of acute polio-encephalomyelitis (A.B.B.).

The histological report was submitted to the consulting neurologist (Dr. T. Rowland Hill), who remarked: "A case of fulminating polio-encephalomyelitis in which, before death, it was not possible to demonstrate involvement of lower brainstem motor nuclei. There were signs of severe mid-brain lesions in that there were tonic fits of decerebrate rigidity and marked nystagmus. There was also a degree of flaccid weakness of the right lower extremity with markedly diminished reflexes. Bulbar palsy developed before death."

Specimens of the brain and cord were stored at the Virus Reference Laboratory, Colindale, in glycerol-saline for ten months at  $-10^{\circ}\text{C}$ . A 10% suspension of cord and medulla was then inoculated intracerebrally into one rhesus monkey under ether anaesthesia. The monkey developed typical signs of poliomyelitis ten days later and was killed with chloroform. Histological examination of the central nervous system showed lesions pathognomonic of poliomyelitis (F.O.MacC.).

### Summary

A case is recorded of acute encephalomyelitis of clinically undetermined aetiology, in which histological findings and virus isolation established the virus of poliomyelitis as the cause.

Our thanks are due to Dr. W. H. Bradley, of the Ministry of Health, for helpful suggestions.

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Hospital matrons and nurses from Belgium, Canada, Cyprus, Denmark, Egypt, Finland, France, Greece, Italy, the Netherlands, Norway, and the U.S.A. have recently attended a two weeks' course on nursing arranged by the British Council in Edinburgh. Sir Andrew Davidson, Chief Medical Officer of the Department of Health for Scotland, gave the opening lecture.

## STREPTOMYCIN IN DEVELOPMENT OF HYDROCEPHALUS IN TUBERCULOUS MENINGITIS\*

BY

S. N. DE, M.B., D.T.M., Ph.D.

(From the Department of Morbid Anatomy, University College Hospital Medical School, London)

[WITH PHOTOGRAVURE PLATE]

Since the introduction of streptomycin in the treatment of tuberculous meningitis several reports of hydrocephalus have appeared. Flory and his co-workers (1947) describe a case of relapse of tuberculous meningitis after cessation of streptomycin treatment in which an internal hydrocephalus was discovered at necropsy. Baggenstoss *et al.* (1947) record two fatal cases of tuberculous meningitis treated with intramuscular and subcutaneous streptomycin in which occurred heavy exudate at the base of the brain and moderate internal hydrocephalus. Wright and Rees (1948) report three cases of severe hydrocephalus associated with thick basal exudate after treatment with intramuscular and intrathecal streptomycin for at least eight weeks. Smith *et al.* (1948) describe two fatal cases with gross hydrocephalus after intramuscular, intrathecal, and intraventricular streptomycin; in two subjects who survived, ventriculography before treatment revealed some dilatation of the ventricles. In all of these cases exudate in the basal cisternae was found to be most intense.

An M.R.C. report (1948) includes 46 instances of hydrocephalus among 53 necropsies on cases of tuberculous meningitis treated with streptomycin by various routes. These studies led me, whilst interested in experimental hydrocephalus, to investigate the histological changes in the basal meninges in a small series of cases of tuberculous meningitis with the object of finding out if the administration of streptomycin had modified the lesion in any way that might lead to hydrocephalus.

### Materials and Methods

The leptomeninges from the undersurface of the pons were available for histological examination from eight cases of tuberculous meningitis; six of these were hydrocephalic, two were not. Seven had been treated with intramuscular and intrathecal streptomycin, with or without intraventricular streptomycin, for periods varying from 12 to 231 days, while only one (hydrocephalic) received no antibiotic treatment. Fig. A shows the dilatation of the anterior horns of the lateral ventricles in the frontal section of the brain of a case of tuberculous meningitis treated with streptomycin.

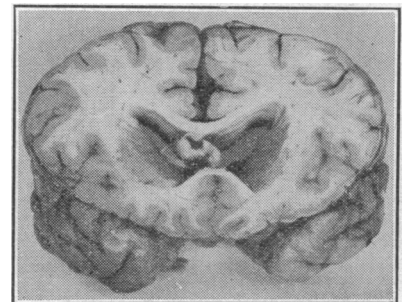


FIG. A.—Hydrocephalus in an infant following tuberculous meningitis treated with streptomycin.

The leptomeninges, with a piece of brain tissue, were cut out from the undersurface of the pons and fixed in 10%

\*Part of a thesis submitted to the University of London for the Doctorate of Philosophy.

formol-saline; the planes of section of the specimens were at right angles to the long axis of the brain. These were slowly dehydrated and embedded in paraffin, and thin sections were stained with Ehrlich's acid haematoxylin and eosin as well as with Weigert's iron haematoxylin and van Gieson's stain.

### Results

The basal subarachnoid space in all the hydrocephalic cases was completely blocked by a fibrinous exudate and thick tuberculous granulation tissue (Plate, Figs. 1 and 2). Two of the five treated cases showed some fibroblastic proliferation within the exudate, mainly directed against the fibrinous elements but also partly encircling some minute tubercles (Fig. 3). The other three gave no evidence of organization, nor was there any obvious histological modification of the lesions by streptomycin when compared with the lesions from the untreated case.

In the two non-hydrocephalic cases, both of which had been treated with streptomycin, the subarachnoid channels were patent in spite of the presence of meningitis (Fig. 4). The fibrinous exudate and the tubercles were there, but they were much less prominent. The lesions did not appear to have been essentially modified, nor was there any evidence of fibroblastic proliferation.

In three of the hydrocephalic cases the foramina of Luschka were found to be patent from the outside, and in one case histological section through this region showed the lateral recesses, including the foramina, to be unobstructed by tuberculous lesions.

### Discussion

Fibrosis of the tuberculous lesions is known to be a general response to streptomycin treatment both in miliary tubercles in man (Flory *et al.*, 1947; Baggenstoss *et al.*, 1947; M.R.C. Report, 1948) and in experimental lesions in guinea-pigs (Feldman *et al.*, 1945). This naturally aroused the suspicion that streptomycin, in the course of promotion of healing of tuberculous lesions in the meninges, might lead to fibrosis and adhesions, resulting in obstruction of the circulation of cerebrospinal fluid and consequent hydrocephalus.

The fact that intrathecal streptomycin had been given in many of the reported cases of hydrocephalus strengthened the view that leptomeningeal adhesions after such treatment were responsible for the blockage. But in the present investigation only two of the five streptomycin-treated cases showed some fibroblastic proliferation in the basal leptomeninges, and although this reaction did surround a few tubercles it seemed to be mainly directed along the fibrin threads in the exudate. Similarly, only one of the two hydrocephalic cases of Baggenstoss *et al.* (1947) and two of 46 hydrocephalic brains of the M.R.C. report (1948) showed any fibrosis in the meningeal exudate.

Further, Rich (1944) noted the presence of some degree of organization and repair in the meningeal lesions of the more protracted cases in pre-streptomycin days. Long ago Martin (1909) recorded scar tissue as replacing antecedent tuberculous lesions in the meninges in cases that had recovered from tuberculous meningitis, while Kramer and Stein (1931) also pointed out the tendency to fibrosis of the meningeal exudate in similar cases. These facts suggest that the formation of leptomeningeal adhesions has not always been responsible for the observed hydrocephalus, nor has it been especially brought about by treatment with streptomycin.

On the other hand, one of my cases of tuberculous meningitis which was not treated with streptomycin also

showed the presence of an internal hydrocephalus. A search through the older literature suggests that tuberculous meningitis by itself has long been suspected of being associated with hydrocephalus (Barther and Rilliet, quoted by Burr and McCarthy, 1900; Dandy and Blackfan, 1914; Rich, 1944; Martin and Elkinton, 1947; Bucy, 1948). Further, it has been possible to produce internal hydrocephalus in guinea-pigs after the introduction of *Mycobacterium tuberculosis* through the cisterna magna (De, 1949). It may therefore be concluded that tuberculous meningitis alone can give rise to hydrocephalus, and the prominence given to the condition since the introduction of streptomycin treatment is no doubt due to more careful examination of the brain in such cases.

The hydrocephalus found in association with tuberculous meningitis has mostly been of the communicating type (Wright and Rees, 1948; Smith *et al.*, 1948; M.R.C. report, 1948). In some of the brains of my series the foramina of Luschka were shown from outside to be free from any obstruction. In one case histological section confirmed this naked-eye finding. These observations support the findings of previous workers that the hydrocephalus is of the communicating type. Moreover, in all the hydrocephalic cases, treated and untreated, the wide subarachnoid space at the undersurface of the pons had been fully occupied by a fibrinous and caseous exudate with tuberculous granulation tissue; there appeared to be no room left for flow of any cerebrospinal fluid. On the other hand, the two non-hydrocephalic cases presented open subarachnoid passages in between the scanty exudate.

I have also found that the cisternal introduction of *M. tuberculosis* in guinea-pigs is followed by hydrocephalus associated with partial blockage of the cisterna pontis with considerable cellular proliferation, but in the rat this change is very slight and there is no evidence of blockage or of hydrocephalus (De, 1949). These facts also suggest that internal hydrocephalus in tuberculous meningitis is due to and occurs with obstruction of the basal subarachnoid by the tuberculous exudate, independent of any streptomycin treatment.

It should be noted in passing that in most of the present cases with streptomycin treatment the tuberculous lesions elsewhere in the body have shown some modification in the form of increase of collagen, and in one case almost complete replacement by lymphocytes. But in spite of the intrathecal administration the meningeal lesions failed to respond. Of course, in the two non-hydrocephalic cases the basal exudate was less intense, but it is difficult to decide if this is an effect of streptomycin, especially in the absence of any essential change in the histology. It is interesting to recall that the M.R.C. report (1948) recorded a similar finding in relation to the meningeal lesions where the fibrinous exudate around the lesions was suspected to shelter the bacilli from the effect of the antibiotic. Hinshaw and Feldman (1944), the originators of streptomycin therapy in tuberculosis, also realized that pathological characteristics of the local lesions can impose marked limitations in the treatment of clinical tuberculosis.

### Conclusions

Tuberculous meningitis can give rise to an internal hydrocephalus associated with complete blockage of the cisterna pontis by tuberculous granulation tissue and a copious fibrinous exudate, but independent of the development of cisternal fibrosis. There is no convincing evidence that streptomycin increases the chance of this complication by stimulating the production of reparative tissue.

I wish to thank Professor G. R. Cameron, F.R.S., for his help in the preparation of this paper, and Mr. McDonald for the photomicrographs reproduced in the photogravure plate.

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- of the Braasch cystoscope could not expel, prevented visualization and the bougies were not even glimpsed.
- As a last resort, 4-5 oz. (114-132 ml.) of liquid paraffin of a specific gravity of 850 was instilled into the bladder and the patient was asked to void. It was hoped that this manoeuvre, by bringing the fragments of the bougie more on a level with the internal urinary orifice, might effect their evacuation. At the first filling one fragment of the bougie came away, and at a subsequent filling, a couple of days later, the remaining fragments were voided. Doubtless the lubricating effect of the liquid paraffin played some small part in helping their expulsion. The above operations were carried out under penicillin-sulphonamide cover.
- It is quite possible that the use of liquid paraffin of low specific gravity, as described above, may prove helpful in securing the evacuation of other lighter-than-water foreign bodies not too large to be voided. The method seems so innocuous that it is worth a trial, and information regarding such trials would be very welcome.
- It is obvious that it would be simplicity itself to remove these fragments by cystotomy, but it seemed a pity to do this if it could be effected otherwise.
- It is a pleasure to acknowledge help from Dr. R. Collis, Dr. Norman Moore, Mr. Albert le Brocq, of the Greenmount Oil Co., Dublin, Dr. Dacre Hamilton, of Dublin University Medical School, and Mr. Morris, of the Irish Electro-Medical Co.

T. J. D. LANE, M.D.,

Genito-Urinary Department, Meath Hospital, Dublin.

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## Medical Memoranda

### Paraffin-wax in the Male Bladder

The following case of a foreign body in the bladder, and the method of evacuating it, may be of interest.

## CASE REPORT

One evening a young man, acting under an obsessive compulsive urge, fashioned a bougie, about 2½ in. (6.25 cm.) long by about ¼ in. (0.6 cm.) in diameter, out of candle droppings and passed it up his urethra, from whence it slipped into his bladder. The next morning he came to hospital complaining of pain and frequency and giving the above history. Cystoscopy showed the bougie, broken into three fragments, as three white rods floating in the water used for distending the bladder. A Braasch direct cystoscope was passed and efforts were made to grasp the fragments with a Bumpus specimen-taker. These efforts were unsuccessful, because the paraffin rods, floating at the top of the bladder, eluded capture by bobbing away. As the paraffin-wax from which this candle was made was capable of solution by liquid paraffin of medicinal quality of a specific gravity of 850 at a temperature of 120° F. (48.88° C.), it was decided to try dissolving the bougie. A piece of candle ¾ in. (1.9 cm.) long could be dissolved in 20 minutes, and it was hoped that solution of the bougie would be effected by washing out the bladder for an hour with the liquid paraffin at a temperature of 120° F. The bladder was accordingly filled with the specified liquid paraffin and emptied at two-minute intervals, 2 oz. (57 ml.) of the oil at 120° F. being used for each filling. The washings from the bladder undoubtedly contained fine particles of wax, but cystoscopy immediately afterwards showed no appreciable difference in the size of the rods. The possibility of melting them by using short-wave diathermy was inquired into, but as the elevation of temperature would not exceed 5° F. (2.8° C.) above blood heat the idea was abandoned.

In 1924 Wardhill, of Newcastle, described a technique for cystoscopy using liquid paraffin as a medium instead of water. The wax from which the bougie was made sank in liquid paraffin of a specific gravity of 850, and by using liquid paraffin instead of water and thus having the fragments of the bougie lying on the trigone instead of floating near the fundus it was hoped that the Braasch cystoscope and Bumpus specimen-taker, so useful in the extraction of foreign bodies heavier than water—stones, etc.—might do the trick. However, we met with failure again, because air bubbles, which the bubble extractor

### Histamine Desensitization in Ménière's Disease

The following case of moderately severe Ménière's disease responded so well to treatment by histamine desensitization that it is considered worth recording. This form of treatment in histamine-sensitive patients is most strongly recommended, as there is little doubt that it achieved success in this case. The result also supports the findings and experience of Miles Atkinson and others who have obtained success in the great majority of their cases.

## CASE REPORT

The patient, a high-ranking officer in the Royal Air Force, was posted abroad in November, 1946, to take command of a very important air-training project. Shortly after his arrival I was called one night to see him, as he was suffering from a sudden attack of intense vertigo, with nausea and vomiting, tinnitus, and deafness.

I arrived to find him quite prostrate, with extreme pallor, and covered with clammy sweat. He was vomiting repeatedly and complained of pronounced giddiness except in the prone position. His pulse was very rapid and barely palpable. There appeared to be a momentary loss of consciousness. I could not detect nystagmus, though this sign was evident in subsequent attacks. The cardiovascular, respiratory, and central nervous systems were clinically normal and I could find no evidence of focal sepsis. Little doubt remained that this was a case of Ménière's disease—a diagnosis supported by his previous history.

His wife informed me that he had suffered two previous attacks in England, the first some months previously and the second shortly before he left the United Kingdom. He had been seen then by two specialists, both of whom had confirmed a diagnosis of Ménière's disease. He had been taking 2 gr. (0.13 g.) of phenobarbitone twice daily for several months and had been given the usual instructions regarding reduced salt and fluid intake. I prescribed bromides and hyoscine, which gave some relief, but his attack continued practically throughout the night. He had completely recovered in 48 hours, but stated that his hearing was still somewhat impaired and that tinnitus was troublesome. It was known that he had

W. J. MATHESON: FIBROCYSTIC DISEASE OF THE PANCREAS

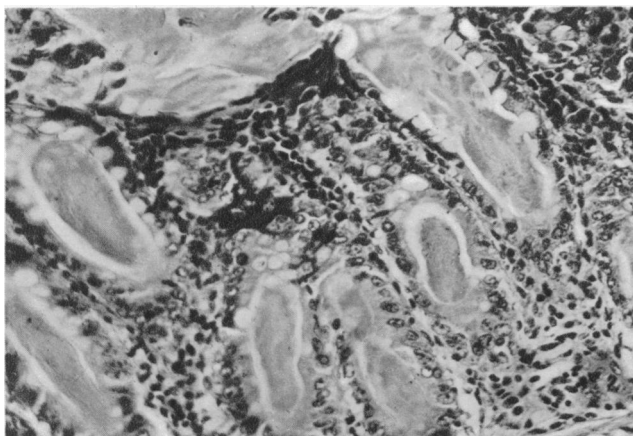


FIG. 1.—Appendix. Dilated glands filled with eosinophilic material, in places continuous with similar material filling the lumen. (× 190.)

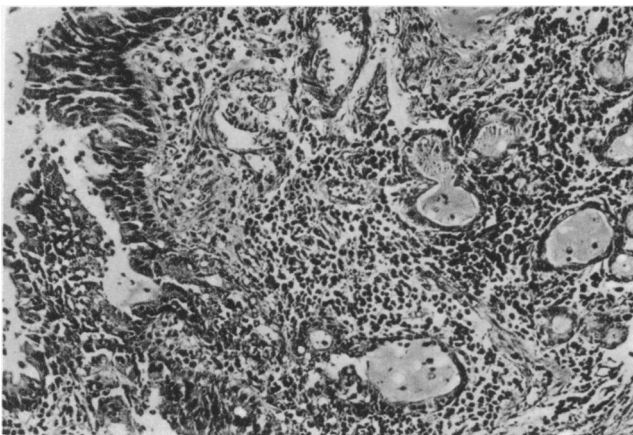


FIG. 2.—Bronchus showing dilated glands in wall. (× 105.)

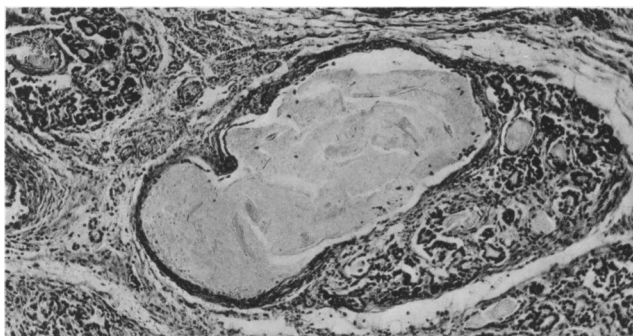


FIG. 3.—Pancreas. Grossly dilated duct lined by flattened cells and filled with eosinophilic material, as are the smaller ducts. (× 60.)

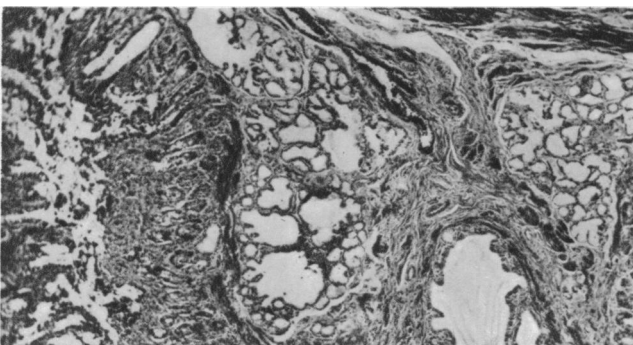


FIG. 4.—Duodenum showing dilated glands in wall. (× 90.)

S. N. DE: STREPTOMYCIN IN DEVELOPMENT OF HYDROCEPHALUS IN TUBERCULOUS MENINGITIS

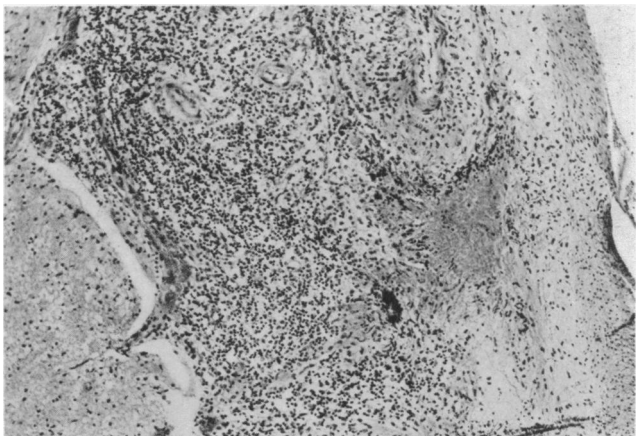


FIG. 1.—Complete blockage of cisterna pontis with tuberculous granulation tissue. Hydrocephalus followed meningitis not treated with streptomycin. H. and E. (× 65.)



FIG. 2.—Complete blockage of cisterna pontis with tuberculous granulation tissue. Hydrocephalus followed meningitis treated with streptomycin. H. and E. (× 25.)

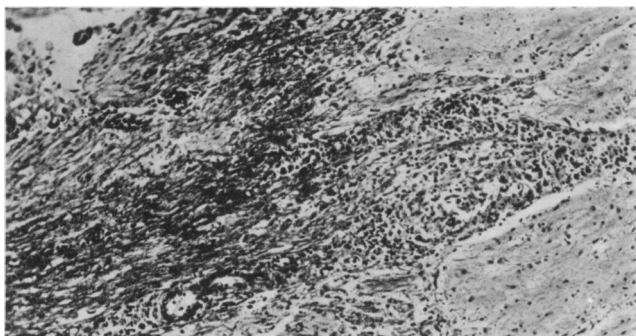


FIG. 3.—Fibroblasts and collagen fibres invading fibrin and tubercles within meningeal exudate. Hydrocephalus followed meningitis treated with streptomycin. H. and E. (× 65.)

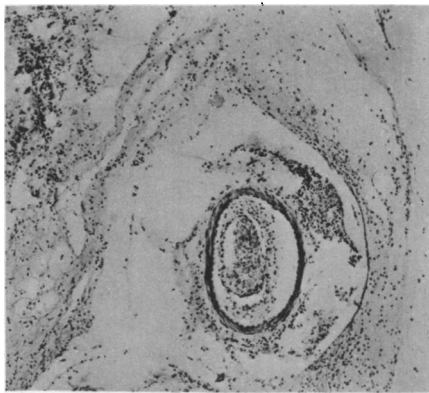


FIG. 4.—Patent sub-arachnoid channels within cisterna pontis. Tuberculous meningitis treated with streptomycin. No hydrocephalus. H. and E. (× 45.)