

duodenum were visualized. A perforation 5 mm. in diameter was seen in the anterior wall of the first part of the duodenum. This was closed by placing three Lembert type sutures of chromic catgut through healthy tissue wide of the ulcer and tying them over a piece of omentum which was drawn over the defect. A Penrose drain was placed at the site of the perforation and brought out through the lateral end of the wound. The abdomen was closed in layers with interrupted chromic catgut. Postoperatively the patient was given penicillin for 4 days and continuous gastric suction was maintained for 24 hours with intravenous amigen and glucose as parenteral feedings. The patient was allowed up in 24 hours and started on a Sippy diet which was quickly increased to a convalescent ulcer regimen. He was discharged from hospital on the tenth postoperative day with the wound soundly healed and free from complaints. He has since been followed in the outpatient clinic and has remained well.

COMMENT

1. This case is believed to be the oldest on record of successful closure of a perforated peptic ulcer.
2. Early ambulation is important in preventing the pulmonary and cerebral complications so frequent in the aged.

REFERENCES

1. SANDELL, D. H.: *Brit. M. J.*, 1: 210, 1936.
2. GRAHAM, R.: *Surg., Gyn. & Obst.*, 62: 235, 1937.
3. TANNER, N. C.: *Brit. M. J.*, p. 563, May 8, 1943.
4. ASHTON, G. W.: *Med. J. Australia*, 1: 130, 1944.

TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN

C. B. Rich, M.D., F.R.C.P.[C.] and
A. J. Samuels, B.Sc., M.D.*

Edmonton, Alta.

The literature contains references to 13 cases of tuberculous meningitis which have been favourably affected by streptomycin, of which two are symptom free.^{1 to 5} These and others perhaps as yet unreported indicate that means of combating this heretofore fatal disease is now at hand. The fact that residual brain damage is simultaneously reported cannot be held an argument for withholding this drug. As Hinshaw *et al.* conclude, the overall accomplishment is the prolonging of life and the alteration of the usual course of tuberculous meningitis, and the fact that 2 infants are symptom-free is the goal at which to aim.

Hinshaw, Pyle and Feldman⁶ assess streptomycin as of greatest value in those conditions where a temporary suppression of the infection may enable the patient to gain ascendancy over

his disease. In support of this claim is the report of Baggenstoss, Feldman and Hinshaw⁷ who studied the post mortem specimens of four fatal cases of miliary tuberculosis. They claim that in one case meningitis was apparently inhibited, and was prevented or cured in two other cases. In this particular series, the dosage of streptomycin had varied between 56 to 60 gm. over a period of 2 months, 248 gm. over 3½ months, and 242 gm. over 6 weeks, given both intrathecally and intramuscularly.

They further report that they could find no histological evidence of any effect of streptomycin, other than a possible renal tubule damage in one case. It is therefore held that the more significant residual neurological disturbances are the product of tuberculous meningitis inadequately controlled and not the toxic effect of streptomycin. Until a better agent is made available the one presently at hand must be energetically used.

CASE HISTORY

The following case is reported as an example of the problems in the management of tuberculous meningitis.

K.G., aged 2½ years, had been ill for 10 days prior to admission to hospital on April 2, 1947. He had become ill-tempered, easily irritated, and refused his food. Pain in the chest, moderate fever and constipation progressively developed. On the day of admission neck rigidity and vomiting began, and the patient was admitted for observation.

The past history and family history were not contributory. Tuberculous contacts were sought for and not found. Physical examination revealed an irritable, whimpering child demonstrating photophobia, and vomiting his food two or three times during the day. There was neck rigidity and a positive Kernig's sign. The pupils were moderately dilated but reacted sluggishly to light. No gross lesions were found in the chest.

The deep reflexes were hyperactive throughout, with ankle clonus, spastic paralysis, and extensor plantar Babinski response on the left side. Examination of the cerebrospinal fluid revealed an initial pressure of 530 mm. c.s.f. The fluid had a ground-glass appearance and developed a coagulum on standing. No acid-fast organisms were found in the Ziehl-Neelsen stain of the coagulum smear. The cell count on the sample of spinal fluid was 245 cells, mostly lymphocytes. Subsequent biochemical examination reported glucose 15 mgm. %; chlorides 685 mgm. % which eventually dropped as low as 596 mgm. %; protein 112 mgm. % (see Table I).

An x-ray of the chest revealed a primary bronchopneumonic process in the right upper lobe. A Mantoux test was strongly positive, and a guinea pig inoculation of an early specimen of cerebro-spinal fluid was subsequently as positive for tuberculosis.

Streptomycin was given, in a dosage of 25 mgm. intrathecally daily for the first two days, and increased to 50 mgm. for the next 10 days before rising to 100 mgm. daily. At one time, however, as much as 300 and 500 mgm. were being given alternate days intrathecally. At the same time 50 to 150 mgm. were given intramuscularly every three hours. From this experience, as well as the literature, it would appear that 300 mgm. intrathecally should be given daily, until the fall in the initial spinal fluid pressure, the drop in the temperature, the return of the spinal fluid cell count

* Referred from the Surgical Service of Dr. M. Weinlos, F.R.C.S.[C.], Misericordia Hospital, Edmonton, Alberta.

and differential to normal limits indicate that a balance must now be struck between continued suppression of the tuberculous process and the avoidance of a possible chemical meningitis. In this case, towards the end, it was felt that the continued high dosage of streptomycin might be contributing to a persistence of spinal fluid cell count of the magnitude of 40 to 50 cells.

The total dosage of streptomycin amounted to 7.0 gm. intrathecally, and 70.0 gm. intramuscularly over a period of 4 months, necessitating 41 lumbar spinal taps. A dosage of 15 gm. was continued, q. 6 h. intramuscularly till December 16.

resolved the spinal block, and minimized the resultant hydrocephalus.

In this case, the temperature returned to normal within 30 days, and remained within normal limits but for occasional elevations to 100 degrees for one day.

Nursing care was that of a totally incapacitated infant, with the problem of maintaining adequate fluid intake as well as daily bowel evacuation. During the course of active treatment the patient contracted chicken pox which was prevalent among the nursing staff, but apparently this had no significant effect on the course of the disease.

TABLE I.
LABORATORY FINDINGS IN SPINAL FLUID WITH OBSERVATIONS ON CLINICAL PROGRESS.

Date	Init. c.s.f. pressure in mm. c.s.f.	Cell total %	Count lymphs. %	Prot. mgm. %	Gluc. mgm. %	Chlor. mgm. %	Streptomycin intrathecal	Remarks
April 4	530	245	most	112	15	685	...	
5	300	177	93	
6	...	200	79	25 mgm.	
7	430	232	81	25	
8	490	15	596	50	
9	470	50	
10	370	105	66	775	50	Rt div. strab.
11	320	132	69	...	34	694	50	Papilloedema
12	50	
13	370	50	Blind?
14	135	50	
16	240	50	
18	235	82	40	50	
19	140	48	70	100	Cephalic scream.
21	175	240	15	65	35	700	100	Blind! Deaf?
23	295	215	11	
25	220	190	12	300	Chicken pox
27	240	200	
29	240	300	Difficulty swallowing
May 1	165	107	65	300	Hearing?
3	125	380	27	300	
5	215	300	Spinal block
6	185	93	500	Hears well!
8	215	500	
10	135	500	Conus coma?
12	160	106	34	760	500	for 24 hr.
14	120	500	
17	500	
19	90	50	75	500	
22	90	125	40	300	Dynamics normal
26	170	88	43	300	Muttering!
30	140	77	28	300	
June 2	130	30	34	300	Pupils contract
11	110	77	86	500	
19	160	49	80	Discontinued	
25	130	35	35	
July 23	130	2	..	68	50	775	...	
August 12	175	10	

It is highly probable that the early dosage of streptomycin was inadequate, and it may be that less residual neurological damage would have resulted if the early dosage had been higher. Hinshaw, *et al.*¹ recommend that 100 to 200 mgm. streptomycin in 1 to 5 c.c. c.s.f. or normal saline be administered intrathecally or cisternally daily.

At each intrathecal injection, the spinal fluid pressure was cautiously reduced to within normal limits, and the streptomycin then introduced. In spite of this a certain degree of hydrocephalus resulted from the increased intracranial pressure, as seen by repeated x-rays of the skull. Partial and, over a period of 10 days, probably complete spinal block was a problem, but it was felt that the block was relieved by daily injection of streptomycin after cautious manipulation of the spinal fluid even against some degree of resistance. The daily effort to maintain a near-normal intracranial pressure perhaps

It should be emphasized that at the height of the disease and for some weeks, this patient was in a completely vegetative state. He was apparently blind and deaf, able only to swallow food put in his mouth. At the present time (January 5, 1948) he can both see and hear. He plays at about the same level as an eighteen months' child. (He is now 3 years). He seems happy and contented, and is of normal weight and height. However, residual weakness of the left arm remains and he is unable to sit up. No attempt is made to speak, and the child's eyes

lack the glint of awareness and intelligence.

An x-ray dated December 16, shows resolution and some degree of calcification of the tuberculous lesion in the right upper lobe.

SUMMARY

Fourteen cases of suppressed tuberculous meningitis are now reported in the literature. Of these, two are considered by their authors to be entirely symptom-free, while the others admittedly have residual neurological signs and symptoms which include mental deterioration, blindness, deafness, cerebellar disturbances and various paralyses.

Herein is presented the case of a 2½ year old infant with conclusively proved tuberculous meningitis treated with streptomycin. Nine months after initiation of therapy, the intracranial inflammatory process appears to have been suppressed, and the child continues to progress.

The problems of management of the acute stage as well as the post-inflammatory stage which, prior to the advent of streptomycin, did not present themselves, are described. Tuberculous meningitis, if the patients are not open sources of infection may well be handled in general hospitals if other facilities are not available. It requires early diagnosis and immediate institution of adequate therapy.

It is suggested that an initial dosage of 300 mgm. streptomycin intrathecally be given daily, concomitantly with 2 to 4 grams intramuscularly. Changes in dosage should be made on a basis of: (a) Initial spinal pressure on the day of therapy; (b) daily temperature; (c) cerebrospinal fluid cell count and differential.

Increased intracranial pressure maintained over long periods of time appears to be of great significance in the prognosis of those cases successfully suppressed.

We desire to express our appreciation for the devoted care and attention given unstintingly by the Nursing Staff of the Pædiatric Service of the Misericordia Hospital. We wish further to thank the City Relief Department and the Edmonton Chapter of the Canadian Red Cross Society for their contribution of funds adequate to supply the necessary amount of streptomycin.

REFERENCES

1. HINSHAW, H. C., FELDMAN, W. H. AND PFEUTZE, K. H.: *J. Am. M. Ass.*, 132: 773, 1946.
2. KRAPCHIK, L. L.: *J. Am. M. Ass.*, 132: 375, 1946.
3. COOKE, R. E., DUNPHY, D. L. AND BLAKE, F. G.: *Yale J. Biol. & Med.*, 18: 221, 1946.
4. Clin. Path. Conf., Willard Park Hospital, N.Y., *Arch. Pædiat.*, 64: 210, 1947.
5. Clin. Path. Conf., Willard Park Hospital, N.Y., *Arch. Pædiat.*, 64: 42, 1947.
6. HINSHAW, H. C., PYLE, M. M. AND FELDMAN, W. H.: *Am. J. Med.*, 2: 429, 1947; *abst. J. Am. M. Ass.*, 134: 1122, 1947.
7. BAGGENSTOSS, A. H., FELDMAN, W. H. AND HINSHAW, H. C.: *Proc. Staff Meet. Mayo Clin.*, 22: 265, 1947.

THE USE OF BAL (2, 3 DIMERCAPTOPROPANOL) IN ARSENICAL ENCEPHALOPATHY*

C. W. E. Danby, M.D.

Montreal, Que.

The use of BAL (2, 3 dimercaptopropanol) in the treatment of certain toxic manifestations seen in arsenotherapy appears to be of significant value. A short and comprehensive review of the compound and its clinical applications has been written by Eagle¹ who reported a 20% mortality rate in cases of toxic encephalopathy treated by BAL. In 8% of these patients treatment had been delayed from 9 to 72 hours. Cohen *et al.*² report one case of encephalopathy due to arsenotherapy which was treated successfully by BAL. In view of Tzanck's³ report that 75% of patients with severe encephalopathy have a fatal outcome, it may be reasoned that BAL does have a real curative effect if given early and in adequate amounts.

The following cases are reported as examples of arsenical encephalopathy which were treated by BAL. The product used was 10% solution of BAL in peanut oil containing 20% benzyl benzoate.

CASE 1

L.T., a coloured male, aged 24, was admitted July 16, 1945, with a primary sore and an early secondary syphilide. Examination showed a small adult negro 5' 7" tall, weighing 120 pounds. The only abnormalities were an indurated ulcer on the glans penis near the meatus with right inguinal lymphadenopathy and an erythematopapular eruption on the arms, legs and chest. Blood pressure was 110/74. Laboratory investigation showed urinalysis negative, blood urea nitrogen 13 mgm. %, van den Bergh 0.1 mgm. fasting blood sugar 0.100 gm., urobilinogen present in 1:200 dilution of urine, prothrombin time 17 seconds, a normal electrocardiogram and a normal x-ray of the chest. Treatment was begun on July 18 with mapharsen 240 mgm. daily in 2,400 c.c. of 5% dextrose solution intravenously for 8 hours. This was continued for a total of 1,200 mgm. of mapharsen during 5 days. In addition he was given ascorbic acid 300 mgm. daily, crude liver extract 1 c.c. daily and bismuth subsalicylate 2 c.c. on the first, third and fifth days. Apart from some nausea on the first day there was no sign of reaction until the fifth day when the temperature rose to 100°. On the sixth day routine lumbar puncture was performed and the spinal fluid showed no abnormality. Fever continued at 100 to 102° with no complaint from the patient until the ninth day when he suffered a convulsive clonic seizure at 10.00 p.m. Lumbar puncture was repeated and the spinal fluid showed Pandy positive and 16 lymphocytes. Sodium amylal 3¼ grains and 60 c.c. of 50% dextrose intravenously was administered. Another convulsion occurred at 2.45 p.m. and the intravenous dextrose was repeated. Beginning at 3.45 p.m. BAL was administered in a dosage of 3 mgm./kg. body weight every four hours for five doses during the first 24 hours, then once daily

* From the Department of Dermatology, Montreal General Hospital, Montreal, Quebec.