SPINAL WASH-OUTS IN THE TREATMENT OF PURULENT MENINGITIS

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The special physiological and anatomical peculiarities of the central nervous system constitute great impediments in the way of maximal action of penicillin in purulent meningitis. In the first place there is a blood-C.S.F. barrier to penicillin penetration. In spite of some favourable reports on the exclusive use of systemic penicillin, increasing experience shows that even in large doses it is not reliable enough for intrathecal administration to be dispensed with. In the present series, doses of 200,000 units intravenously in adults produced no detectable penicillin in the C.S.F. within two hours, nor did 200,000 units intramuscularly to a child aged 2 years. Further evidence on this point is given by the work of McAdam *et al.* (1945); Smith, Duthie, and Cairns (1946); and Kinsman and d'Alonzo (1946). Schwemlein *et al.* (1946) showed that an intravenous infusion of 25 million units of penicillin in 24 hours given in the treatment of syphilis produced only 0.04–0.55 unit per ml. in the C.S.F. So much for the efficacy of this barrier. Secondly, as the C.S.F. becomes purulent the pia and arachnoid tend to adhere. Apart from the liability of these adhesions to produce hydrocephalus, if C.S.F. pathways are blocked they produce cesspools beyond them inaccessible to intrathecal penicillin. Thirdly, the thick plaques of adhesions themselves form areas resistant to penicillin penetration and become admirable niduses where organisms thrive unperturbed; and, what is more, they lead to thromboses of adjoining veins with extending focal lesions and consequent fatal termination.

Experience with the present series gradually gave an impression of the overriding importance not only of the second but of the third factor in the majority of the fatal cases. Of over 40 patients observed or treated personally, the five that died directly from the meningitis and came to necropsy all showed thick, creamy, and sometimes almost organized adhesive exudates. Pneumococcal, streptococcal, staphylococcal, and influenzal varieties are included.

Contrary to expectation, only one of these five cases showed evidence of a block that would interfere with the free flow of penicillin and could be blamed for progressive meningitis beyond. Thick intensive exudate of pus at the base of the brain matted everything together, with resultant non-communicating hydrocephalus. In the four remaining cases no such blocks were found, but fibro-purulent exudates formed scattered and sometimes confluent plaques, covering large areas of the brain surface and sometimes of the spinal cord.

Spinal Wash-outs

Thus it was in the post-mortem room that the idea of combating the formation of these plastic exudates by 'further means first arose. Some cases pass the precipitation stage before coming under medical care, but others undergo that stage immediately after. The use of spinal wash-outs was considered and its possibilities were explored.

Only the cases treated after the adoption of spinal wash-outs are included here. They number eight, and have a miscellaneous pathology (Table I). The ages ranged from 13 months to 39 years. The series comprises one case of pneumococcal meningitis, two influenzal, one staphylococcal, one streptococcal, one aseptic following rupture of an old sterile brain abscess, and two cases the pathogenic organisms of which were not isolated. All were treated

TABLE I.—Analysis of Cases

Case No.	Age and Sex	Organism	First seen after Onset	Result	Re-lapses	Focus	No. of Wash-outs
1	3 M.	?	24 hrs.	Recovered	0	?	1
2	2 M.	<i>H. strept.</i>	7 days	"	1	Ears	1
3	29 F.	<i>Staph. aureus</i>	48 hrs.	Died	0	Empyema	1
4	1 1/12 M.	<i>H. Influenzae</i>	48 hrs.	"	1	?	0
5	39 M.	?	7 days	Recovered	0	?	3
6	8 M.	Pneumococcal	About 7 days	Died	0	?	4
7	1 2/12 M.	<i>H. Influenzae</i>	7 days	Recovered	1	?	13
8	20 M.	Aseptic (ruptured abscess)	Same day	"	1	Old brain abscess	3

with sulphamezathine, 15,000 units of intramuscular penicillin three-hourly, and varying doses of intrathecal penicillin. They were first seen 1 to 7 days from the onset. Five recovered and three died. Of these three, one died of other causes, and necropsy showed no meningitis; one died because the infecting haemophilus acquired penicillin resistance; and the third (pneumococcal), admitted in coma and with hemiplegia, showed thick exudates on both hemispheres. The existence of the hemiplegia prior to admission constitutes evidence of the antecedent formation of the plastic exudate, and hence the expected lack of response.

Technique of Spinal Wash-outs

The two-needle method was rejected as ineffective except for the space between the needles, but the washing effect through one needle was considered worth investigating. On consulting the available literature later, no specific mention was found of the one-needle method of spinal lavage.

The following were fitted in series—a vacoliter of Hartmann's solution, a glass connexion, a 3–4 in. (7.5–10 cm.) rubber tube with a clamp, a rubber stopper with inlet and outlet glass tubes, a 20-ml. syringe barrel (filled by releasing the clamp), a long piece of Ryle's tubing, and a metal connexion for the lumbar puncture needle. The connected apparatus was attached to a metal pole clamped to the L.P. trolley (Fig. 1). The Ryle's tubing was clamped with forceps till in use. Irrigations were performed by connecting the apparatus to the L.P. needle in situ, and repeated in 20 ml. till the return fluid became clear. The technique was tried, and improved, on two cases. One was a child of 3 years (organism not isolated), the other a child aged 2 with a relapsed streptococcal meningitis. The method was successful in both.

FIG. 1.—Method of fitting the lavage apparatus to the L.P. trolley.

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Effectiveness of a Wash-out

The effectiveness of each irrigation in reducing the C.S.F. cell count was next studied. The third case was that of a female aged 29 with staphylococcal meningitis and empyema. The cerebrospinal fluid was turbid under a pressure of 300 mm. H₂O. Queckenstedt's test was normal. Wash-outs of 40 ml. were absorbed easily, and were repeated three times, so that 120 ml. was used altogether. A second specimen was taken at the very end, just before the dose of intrathecal penicillin. The count of the pre-lavage specimen was 1,335 cells per c.mm., while on the post-lavage specimen it was 430.

After 8,000 units of penicillin in 40 ml. of distilled water, introduced into the free tube of the rubber stopper, were allowed to seep in through the same apparatus, a steady fall of C.S.F. pressure was noted. The explanation lay evidently in the reduced osmotic pressure consequent on the removal of excess proteins, fibrin, etc., and the dilution of the C.S.F. by the addition of 40 ml. of dilute penicillin. In a quarter of an hour the pressure fell from 250 mm. to 50 mm. H_2O . On the second day the C.S.F. pressure was 100 mm. H_2O : 180 ml. was used in spinal lavage, and pre- and post-lavage counts were 375 and 50 cells per c.mm. respectively.

The same phenomenon of rapid absorption of the diluted C.S.F. was noted on this and subsequent occasions. Concurrent with the fall in manometric reading there was increasing concentration in the C.S.F. cell count. Specimens taken 1/4-hourly showed a rising count of 12, 20, 38 cells per c.mm. It became a practice to leave the pressure after a wash-out at 300 mm. H_2O . This brought the final pressure to 80–120 mm. H_2O . Lower pressures were avoided with an inflamed pia-arachnoid, as that would approximate the two layers and promote adhesions.

The wash-outs seem to have solved the problem of increased C.S.F. pressure in meningitis, since in a total of 30 of them not once was the pressure markedly high after the first wash-out. On the third day it was 130 mm. H_2O , and the cellular count 109 per c.mm.; on the fourth the corresponding figures were 50 and 12. Wash-outs performed on these two occasions showed that they do not provoke pleocytosis when aseptic.

Further Trials

The fourth case was that of a child of 13 months with influenzal meningitis. Lumbar puncture produced only two beads of thick pus. Aspiration was tried without effect. Spinal wash-outs were attempted, but the fluid would not go in freely. Penicillin was given intrathecally, and the following day no more could be done than on the first. The *Haemophilus influenzae* isolated was penicillin-sensitive. The child improved, and was apyrexial for a few days. It soon relapsed, and as there was the same difficulty with the lumbar puncture the ventricles were tapped four hours after an intrathecal dose of penicillin. Fluid from the ventricles, however, contained more than 8 units of penicillin per c.mm., and the thick perispinal exudate formed no block to the passage of penicillin as was feared, but the haemophilus was shown to have acquired much greater resistance to penicillin. The child died next day. Necropsy revealed thick pus below the tentorium and surrounding the spinal cord. Small concentrations of penicillin were found on the brain surface at necropsy.

In the fifth case of purulent meningitis the organism eluded isolation, but response to treatment and spinal lavage was quick. On one occasion the

FIG. 2.—Case 5. C.S.F. cell count after 20-ml. wash-out.

FIG. 3.—Case 5. C.S.F. cell count after a further wash-out of 40 ml.

FIG. 4.—Case 6. Effect of wash-out on the first day of admission.

FIG. 5.—Case 6. Effect of wash-out on the second day of admission.

respective cell counts were: before irrigation, 580 per c.mm.; after, 70, 210, 525, 650 (Fig. 2). Another irrigation with 40 ml. was given and counts on pre-, mid-, and post-lavage specimens were 50, 325, and 375 respectively, showing even better mixing (Fig. 3).

The sixth case was that of a boy of 8 years with pneumococcal meningitis admitted in coma with right-sided hemiplegia. The effect of the wash-outs on the first and second days is shown in Figs. 4 and 5 respectively. On the third day the C.S.F. did not flow freely; Queckenstedt's test became abnormal and lavage impossible. Ventricular puncture gave a freer flow of C.S.F. but no evidence of increased pressure, and no improvement followed. The next day the same difficulty was met with during lumbar puncture, and a large dose of 50% dextrose intravenously to relieve a supposed tonsillar herniation had no effect. The L.P. needle was shifted two spaces higher up, and the C.S.F. flow and Queckenstedt's test were here normal. To exclude a delayed effect of the injection, another L.P. needle was introduced in the lower spaces, but the same initial state of affairs was still evident, and a spinal block was diagnosed. The child died two days later; necropsy revealed no convincing hydrocephalus, no herniation, and no organic blocks above the foramen magnum, but there were thick purulent exudates over the convexity of the hemispheres. Unfortunately the spinal cord was not exposed.

Cerebrospinal Fluid Clearance

The seventh patient was a child of 14 months with influenzal meningitis and very turbid C.S.F. (4,600 cells per c.mm.). The organism was only slightly sensitive to penicillin, and it was felt that the effect of repeated wash-outs might show to better advantage here. Six daily wash-outs were done and progress was satisfactory. A relapse followed, and 7 more daily wash-outs were given. The child recovered fully.

The effect of these wash-outs on pus clearance was studied in this case. All wash-out fluid drained was collected, mixed, and measured. A cell count on a specimen of it gave an idea of the amount of pus removed. Further, the number of millilitres of purulent C.S.F. cleared of pus could be calculated on the same lines as that of urea clearance of the blood. The results of the first six wash-outs are shown in Table II.

Leaking Cerebral Abscess

The eighth patient was a young man of 20 years who had had a cerebral abscess on the right side drained

TABLE II

Wash-out	Pre-lavage Count (cells/c.mm.)	Average Count of Return Fluid (cells/c.mm.)	Post-lavage Count (cells/c.mm.)	Total Cells Removed	C.S.F. Cleared (ml.)
First ..	4,600	3,125	1,350	246,000,000	53.5
Second ..	3,020	1,740	1,200	166,000,000	55.2
Third ..	1,340	450	440	44,000,000	33.5
Fourth ..	845	275	230	32,000,000	38.6
Fifth ..	510	127	102	24,000,000	48.5
Sixth ..	390	130	100	26,000,000	69.0

successfully two years previously. On Jan. 12, 1946, he had convulsions culminating in status epilepticus, which later became strictly right-sided. The C.S.F. was acellular and sterile. The next day severe symptoms and signs of meningitis developed and the convulsions ceased. Rupture of a left-sided abscess was suspected, and the C.S.F. was now purulent (8,000 cells/c.mm.) and under pressure. Table III shows the effect of successive daily wash-outs on this patient. The third wash-out is peculiar in that the average count of the return fluid and the post-lavage count are both higher than the initial count. The abscess must have leaked during the procedure. The patient considerably improved. Six hours after the fourth lumbar puncture (603 cells per c.mm.) he suddenly developed an acute exacerbation, and the C.S.F. contained 2,700 cells per c.mm. Further leakage must have occurred. All specimens of C.S.F. during the illness were sterile. The patient recovered.

TABLE III

Wash-out	Pre-lavage Count (cells/c.mm.)	Average Count of Return Fluid (cells/c.mm.)	Post-lavage Count (cells/c.mm.)	Total Cells Removed	C.S.F. Cleared (ml.)
First ..	8,000	4,000	3,200	488,000,000	61
Second ..	6,300	1,330	700	385,000,000	61
Third ..	1,365	2,180	1,700	215,000,000	157
Fourth ..	603	246	197	27,000,000	45

Pain in Spinal Wash-outs

The most frequent cause of pain was the low temperature of the solution. Warming the fluid obviated the pain in the majority, but some complained of discomfort or headache when there was much variation in the C.S.F. pressure, and wash-outs then had to be restricted to 20 ml. at a time. Another cause of pain may be the position of the needle-point in the spinal theca. On the whole, spinal wash-outs performed by allowing fluid to seep in by gravity are not often painful, and the pain is less than that caused by mixing the C.S.F. with the injected penicillin several times in a 20-ml. syringe as recommended by some authorities.

Discussion

Merritt and Fremont-Smith (1937) express themselves as follows: "The conception of acute purulent meningitis as an abscess of the ventriculo-subarachnoid space has previously been presented. It is a well-known principle that the best treatment for an abscess is free drainage. . . . Continuous drainage of the fluid . . . is especially valuable. Irrigation of the subarachnoid space through a needle in the cisterna magna and out through a needle in the lumbar space, or vice versa, will often prevent development of subarachnoid block."

For the reason given earlier, the one-needle method described here was preferred. It is felt that penicillin has not done away with the necessity for preventing deposit formation. Smith, Duthie, and Cairns (1946) state that "the subarachnoid space may become blocked in the early stages of the illness by the rapid deposition of thick fibrinous pus. . . . On the second or third day after the first injection of penicillin most patients show an increase in the

cells in the C.S.F. . . . It is at this stage that there is most danger of the subarachnoid space becoming blocked." Jepson and Whitty (1946) feel that "the post-mortem appearances tempt one to search for some means of increasing C.S.F. circulation, especially through the basal cisterns."

These views are similar to those that led to the present work on the merits, practicability, and effectiveness of spinal irrigations. Jepson and Whitty also state that "withdrawal of much fluid from lumbar sac or cistern remains of doubtful value in view of the possibility of encouraging herniation through the tentorial hiatus or foramen magnum, especially when cerebral oedema is present, although in our experience withdrawal of 30 to 40 ml. by the lumbar route has had no untoward consequences." Withdrawal of similar amounts had no ill effects in the present series of cases. It is felt that the fear of herniation in uncomplicated meningitis has been exaggerated unduly. The frequent use by earlier workers of the double-needle method of spinal irrigation and forced drainage suggests that this is not a serious possibility. Merritt and Fremont-Smith caution people against the removal of large amounts of C.S.F. in cases with increased intracranial tension, except in patients with meningitis, when "as much fluid should be removed as it is possible to obtain." Katzenelbogen (1935) states that "forced drainage was demonstrated by several workers to be innocuous and well tolerated by patients."

If apprehension is felt about the reduction of pressure—for example, in traumatic cases, where cerebral oedema is suspected—a preliminary hypertonic injection may be given. The spinal wash-out should then not be delayed, not only for fear of the pressure rising again but because of the concentrating effect on the C.S.F. and the consequent precipitation of thick exudates. It is felt that this measure will rarely be needed in uncomplicated meningitis.

Of the 30 wash-outs performed none resulted in contamination, as shown by frequent cultures. Apart from clearing pus and organisms, and restoring osmosis to normal, the irrigating fluid may break up commencing adhesions. The C.S.F. pressure is kept down.

Summary

The shortcomings of penicillin in purulent meningitis are discussed.

The seriousness of the formation of deposits of plaques from fibro-purulent exudates is emphasized. These result in occluded areas inaccessible to intrathecal penicillin and, because of adjoining thromboses, inaccessible to systemic penicillin.

The possibilities of spinal irrigation by a single-needle method, as a preventive measure against these adhesions, are explored.

A safe aseptic technique is described, and its effectiveness is demonstrated. A C.S.F. cellular clearance is calculated.

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