

TABLE XI.—Unimproved Cases and Causes of Death in Operated Series (55 Cases)

Group	No.	Unimproved	Died	
			Post-operative Due to Empyema	Due to Lung, etc.
II	2	2 (lung disease)	2 (shock; mitral stenosis) + (2 infection; 1 shock; 1 amyloid—late)	2
III	8 (all except 1 over 6 months)			
IV	5			
	15	2	10	3

Operative mortality = 18%.

Conclusion

Finally, I would like to stress the aetiological relationship between A.P. treatment and empyema mortality. The recorded incidence of empyema in A.P. treatment is very variable, and depends partly on the differences in treatment and partly on different definitions of an "empyema." Alexander (1937) quotes figures ranging from *nil* (Ulrici, 600 cases) to 21% (Hays, 151 cases). Frostad, in Norway, has estimated it at 10%, as an average figure, and in Söderhjelm's series it was given as "only 7.5%."

A consistent large series from one centre is available at Vardasen (Rogstad, 1948). Great care is taken in the selection of cases and in the technique of closed internal pneumolysis, the director undertaking them all himself. The empyema incidence there is only 6.4% (59 out of 918 patients). An attempt has been made to distinguish in the series between mortality due primarily to the empyema and that due to the spread of the tuberculous disease. So far as could be judged, death was due primarily to the empyema in 16 cases, or 1.7% of all those in whom an A.P. was induced. This not inconsiderable mortality is therefore due to the A.P. as a method of treatment, and should be borne in mind when the induction of a pneumothorax is being considered and weighed against the other methods of collapse of the lung. In certain cases the destruction and fibrosis of the lung indicate the need for a primary permanent method of collapse, such as that of thoracoplasty. It is certainly incorrect to induce an A.P. first in practically every case, as is sometimes done on the grounds that it is an easy and safe method of treatment and therefore should be given a trial.

The misleading factor about the risk of an A.P. (empyema being only one, although perhaps the worst, of the complications) is that the risk is spread over such a long period of time that it sometimes fails to impress itself sufficiently on the mind.

Summary

The results in a series of 74 cases of tuberculous empyema are discussed and analysed.

A staged thoracoplasty is the standard method of treatment used in all cases when the general condition permits, supplemented by a Schede and Roberts type of operation in a few, mostly chronic, cases. It should be carried out within six months of the onset of the empyema.

In cases without secondary infection and operated upon within six months, a limited thoracoplasty (up to seven ribs) is often satisfactory.

The treatment of progressive tuberculous pleurisy is discussed; if it does not respond to medical measures in about three months it is regarded as an "incipient empyema," best treated by a limited thoracoplasty.

The risk of the development of a tuberculous empyema with resulting mortality following A.P. treatment is discussed.

I would like to express my sincere thanks to Dr. Carl Semb for his personal kindness during a period of eight months spent in his department, and for suggesting the investigation. I would also like to thank the other members of the medical staff of Ullevål Hospital and Dr. Tuxen and others at Vardasen Sanatorium for their unfailing courtesy and friendliness; and, lastly, Sisters Halldis and Krohg without whose willing aid the investigation would not have been possible.

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PENICILLIN IN THE TREATMENT OF INFLUENZAL MENINGITIS

BY

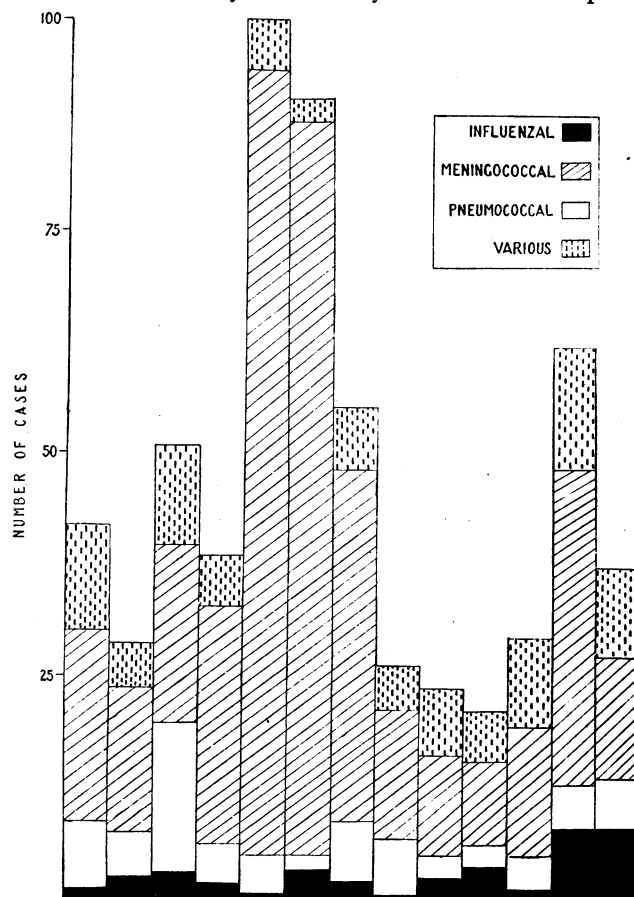
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The incidence of influenzal meningitis has increased recently (see the accompanying Chart) and the mortality from the disease has fallen very considerably with the use of sulphon-



Yearly incidence of cases of suppurative meningitis in the Children's Hospital, Birmingham

amides, Pittman type b specific rabbit antiserum, penicillin, and streptomycin. There is, however, at present no absolute answer to what is the best line of treatment to adopt.

Previous to the introduction of the sulphonamides, influenzal meningitis was usually fatal. With the use of sulphonamides alone the position was improved a little, but in America a big advance was made by Alexander's (1944) combined treatment with sulphadiazine and Pittman type b specific rabbit antiserum. Using this method she had 68 recoveries in a series of 87 cases. In this country, however, specific antiserum has not been freely available, and the main advance has been made with the use of sulphonamides and with penicillin. Gordon, Woodcock, and Zinnemann (1944) review reports of cases treated with sulphonamides and discuss the response to treatment in relation to the type of organism involved. They record two cases, due to strains not belonging to Pittman type b, which responded to sulphapyridine, and three cases, due to type b, of which only one responded to sulphapyridine. They conclude that prognosis and treatment depend primarily on the strain of the infecting organism. Gordon and Zinnemann (1945) tested the sensitivity of various strains of *H. influenzae* to penicillin and found that 31 of 48 respiratory strains were inhibited by concentrations of 2.5 units per ml. of medium, and 16 out of 18 strains isolated from cerebrospinal fluid were similarly inhibited. They conclude that *H. influenzae* strains are not insensitive to penicillin though the sensitivity is much lower than that of staphylococcal and streptococcal strains. Zinnemann (1946) surveys 20 cases of influenzal meningitis in relation to bacterial types. Of these, 19 were caused by type b. Of five treated with sulphonamides one recovered, while of 15 treated with sulphonamides and penicillin eight recovered. McIntosh and Drysdale (1945) report the case of a child aged 2½ years who developed *H. influenzae* meningitis (organism, Pittman type b) during convalescence from meningococcal meningitis and who recovered on treatment with penicillin and sulphamezathine.

Drysdale, McIntosh, and Brodie (1946) report recovery in a second case, that of a child of 20 months, treated with penicillin. In this case the organism (Pittman type b) was sensitive to penicillin but insensitive to sulphonamides. Forgacs, Hutchinson, and Rewell (1945) recommend that influenzal meningitis should be treated with a combination of penicillin and a sulphonamide, and report two cases, of which one recovered. Thomson, Bruce, and Green (1947) put on record four cases, of which three recovered; they advocate the use of intramuscular penicillin and an oral sulphonamide along with the intrathecal administration of 50,000 units of penicillin daily until the temperature has been normal for seven days. Gottlieb and Forsyth (1947) report four cases in infants, three of whom recovered on treatment with sulphadiazine by mouth and penicillin given intramuscularly and intrathecally. The strain of *H. influenzae* recovered from the cerebrospinal fluid was found to be insensitive to 10 units of penicillin per ml. of medium but sensitive to 100 units per ml. This justified their use of very large doses of penicillin, and they consider that high systemic dosage is essential in order to prevent relapses due to reinfection of the meninges. They recommend that 20,000–40,000 units should be given intrathecally daily and 120,000 units intramuscularly at three-hourly intervals.

More recently, reports have been made on the value of streptomycin. In the American literature Hoyne and Brown (1948) record 28 cases with only two deaths. All were given sulphadiazine, and in addition some received serum, some had serum and streptomycin, and some (17) had streptomycin. Twenty of the 26 who recovered had no intrathecal therapy, among them being 10 who received oral sulphadiazine and intramuscular streptomycin. These authors consider that not only is intrathecal therapy unnecessary but that it prolongs the time required for recovery.

Case	Age in Years	Sex	No. of Days Ill Before Admission	Cerebrospinal Fluid—First Examination					Penicillin Units (Thousands) Daily × No. of Days		Sulphadiazine Daily Dose × No. of Days	Result	
				Cells per c.mm.	Sugar (mg./100 ml.)	Protein (mg./100 ml.)	Organism		I.M.	I.T.			
							Seen	Cultured					
1	1 3/12	F	2	2,610	0	50	+	+	80 × 2 240 × 29 - 80 × 37	20 × 6 40 × 7 40 × 12	83.5 g. × 29	Cured	
2	1	F	8	215	0	90	+	+			50 g. × 21	Died after 36 days	
3	7/12	F	14–21	1,000	0	340	+	0	64 × 4 240 × 28 320 × 17	10 × 11 20 × 2 40 × 8	69 g. × 27	Alive M.D.	
4	1 3/12	F	3	577	0	120	+	+			105 g. × 36	Cured	
									Clinical evidence of recurrence of meningitis				
5	2	F	5	80,000	—	—	+	+	800 × 14 1,200 × 5 400 × 2	60 × 6 40 × 2	4 g. × 1	Died within 48 hours	
6	4½	M	1	5,600	0	200	+	+	960 × 21	40 × 5	32 g. × 10	Cured	
7	1 5/12	M	1	2,100	83	15	(6 months later)	+	+	960 × 20	40 × 10	67 g. × 16	"
					0	160				Omit 4 days 40 × 4 (Probably unrec.)			
8	5	M	1	12,800	0	350	+	+	960 × 23	40 × 16	112 g. × 20	"	
				150	44	35	(43rd day)						
9	2	F	2	14,000	22	25	(3 months later)	+	0	480 × 1 960 × 10 480 × 9	40 × 8 Convulsion after 5th dose	60 g. × 15	"
				50	11	100				40 × 4			
10	1 9/12	M	14	1,400	33	30	+	+	320 × 5 960 × 12 100—1 dose	40 × 4	52 g. × 14	"	
							(On 19th day in hospital)			Omit for 2 wks			
11	2½	M	1	7,500	0	240	+	0	120 × 2 320 × 14	40 × 1	2 g.	Died in 4 hours	
12	10/12	M	10	380 80 white 590 red	0	55	+	0		40 × 3	79 g. × 18	Cured	
					35		(On 4th day of treatment)			Convulsion after 3rd dose			
13	2½	M	6	2,540	21	90	+	0	480 × 4 480 × 4	40 × 4	96 g. × 24	"	
				70	30.5	35	(On 5th day of treatment)			Then given streptomycin			
14	6	M	3	6,000	41	200	+	+	400 × 1	40 × 1	8 g. × 7	"	
15	1 5/12	F	7	5,000	82	186	+	+	Then streptomycin	Streptomycin	40 g. × 9	"	

Organism typed in 3 cases only—Type b.

In a report in the *American Journal of Diseases of Children* (1948) of a discussion (in the Transactions of the American Pediatric Society) on the value of streptomycin Alexander states that the use of streptomycin alone in the treatment of influenzal meningitis led to complete recovery when the infection was mild or of average severity; when the infection was severe the result was disappointing, the chief cause of failure being the development of resistance by the organism. In the same discussion Weech reported that he had found Pittman type b to be just as susceptible to penicillin as to streptomycin, while Hodes found that each of 12 strains isolated from patients suffering from influenzal meningitis was more susceptible to penicillin than to streptomycin.

In this country Wilson (1948), in a summary of a report to the Medical Research Council on the use of streptomycin in influenzal meningitis, states that the principal cause of failure was the development of resistance by the organism; this occurred in seven out of nine failures, the sensitivity changing from 0.5 unit to as high as 5,000 units in one to four days. This development of resistance is a serious drawback, and Wilson remarks that "it has been decided in future trials to use a combination of streptomycin, penicillin, and sulphonamides from the start." Smythe (1948) reports 12 cases treated with streptomycin, 10 of which had received previous treatment with penicillin and sulphadiazine. In all of these cases the preliminary dosage of penicillin was not high. He concluded that "streptomycin gave good results in mild and moderately severe cases but was unsatisfactory in three severe cases." Roscoe and Gleason-White (1948) report four cases treated with streptomycin. In their one fatal case the organism was resistant to streptomycin, and in one of their successful cases the infection was first controlled with intramuscular penicillin, 100,000 units followed by 50,000 units three-hourly for two days and then 25,000 units four-hourly. Relapse occurred on the 15th day, and this was controlled by streptomycin. In the light of the experience of Gottlieb and Forsyth and of our own experience we do not consider that this case indicates a failure of penicillin to cure the disease but that it emphasizes the need for continued high dosage. It is to this point that we particularly wish to draw attention.

Report of 15 Cases

Fifteen cases of influenzal meningitis were treated in the Birmingham Children's Hospital. Two were admitted at the end of 1946, two in March, 1947, and 11 between November, 1947, and July, 1948. Six in the last group were under our care, and for permission to include the other cases in this report we are indebted to our colleagues. Case 1 has already been reported (Gerard, 1947). Twelve of the 15 children are alive, and all are quite well with one exception (Case 3), who is spastic and mentally defective. Details of the cases are summarized in the Table and reports are given below. The incidence of influenzal meningitis among admissions to the hospital is shown in the Chart.

Types of Cases

An evaluation of any line of therapy must take into account the age of the patient, the initial severity of the infection, and the duration of the illness before treatment is begun. It is well established that the mortality is highest in infants. The initial severity can be estimated roughly by the rate of progress to a comatose state, but, apart from that, clinical signs are of uncertain value; chief among laboratory tests is the amount of reducing substance in the cerebrospinal fluid.

Age.—Of the patients whose cases are here recorded two were under 1 year, eight were between 1 and 2 years, four were between 2 and 5 years, and one was over 5 years.

Initial Severity and Duration of Illness

Severe Type.—Cases 6, 7, 8, and 11 were admitted within 24 hours of the onset of illness, and all were comatose or semicomatose. In the cerebrospinal fluid the cell count was high—2,000–12,000 per c.mm.—and no sugar was present. Three of these patients recovered, and one (Case 11) died within four hours of admission. Cases 1, 4, 9, and 14 were admitted on the second or third day of the illness and were comatose or semicomatose; the cell count in the cerebrospinal fluid was 577–4,000, and sugar was present in two; all recovered. Case 2, aged 1 year, was admitted to hospital on the eighth day of her illness, during the first four days of which "she could not be roused"; she died five weeks after admission. A second (Case 3), aged 7 months, had been ill for two to three weeks and had "seemed far away" for two weeks; she survived, but with permanent cerebral damage. A third (Case 5), aged 2 years, was admitted on the fifth day of illness and died two days later. These three cases draw attention to the difficulty in diagnosing meningitis in very young children and emphasize the disaster consequent on delay in starting adequate treatment.

Less Severe Type.—Case 12, aged 10 months, was admitted on the 10th day of illness; he appeared to have pain in the head, and resisted flexion of the neck, but he was "lively and active." In the cerebrospinal fluid the cell count was 380, sugar was absent, and the protein was 55 mg. per 100 ml. Case 10, aged 1 year 9 months, had been ill for two weeks before admission and was actually under observation in hospital for nearly three weeks before meningeal signs appeared; after some improvement on treatment with relatively small doses of penicillin for pyrexia of unknown origin, a sudden rise in temperature on the 17th day induced us to have a second blood culture, the first, on his admission to hospital, having proved to be sterile. A pure growth of *H. influenzae* was obtained. Lumbar puncture was carried out on the 19th day, neck rigidity having appeared; the fluid contained 1,400 cells, 33 mg. sugar, and 30 mg. protein per 100 ml.; *H. influenzae* was cultured. These two cases demonstrate the long bacteraemic phase which may precede the meningeal phase; in neither case was the meningitis severe, and both patients recovered.

Treatment and Results

The line of treatment adopted has varied somewhat according to the physician responsible for the case and according to experience gained. That and the results obtained will be discussed under three headings.

1. Sulphadiazine and Penicillin (11 cases)

(a) Three of these patients died. One (Case 11), aged 2½ years, admitted in coma after 24 hours' illness, died before more than one dose of penicillin had been given. Another (Case 2), aged 1 year, had a severe infection and had been ill for eight days; she was comatose on admission. She was given intrathecal penicillin, 40,000 units daily for 12 days, and intramuscular penicillin, 10,000 units three-hourly for 36 days. Irreparable damage may have been done during the eight days before admission, but in any event the intramuscular dose was inadequate. She died on the 36th day of treatment. The third (Case 5) was semicomatose on admission, after having been ill for five days; she was given one dose of 40,000 units of penicillin intrathecally and 50,000 units three-hourly intramuscularly. This dosage we regard as inadequate. She died within 48 hours of admission.

(b) One (Case 3) recovered, but had received permanent cerebral damage. She was 7 months old, and had been ill for two to three weeks before admission. Again irreparable damage may have already been done, but doses of only 10,000 units were given intrathecally and 8,000 units, later increased to 30,000 units three-hourly, intramuscularly.

(c) Seven cases recovered completely. Six of them were of the severe type, comatose or semicomatose on admission; three were admitted within 24 hours of the onset of illness and three within two to three days; the seventh case had a long bacteraemic phase and the meningitis was not severe. Case 1 (Gerard, 1947), the first in the series, had a relatively low intramuscular dosage over a period of four weeks and required

intracisternal as well as intraventricular penicillin. Case 4 had 40,000 units of penicillin intrathecally for eight days and intramuscular penicillin, 320,000 units daily, for 17 days. After an immediate good response there was a recurrence of meningitis at the end of the third week, and this was controlled completely by much larger dosage. Cases 6, 7, 8, and 9 were given 40,000 units intrathecally daily and 960,000 units intramuscularly in three-hourly doses. In no case was there any evidence of meningeal reinfection after the illness was once under control, and in no case was intracisternal or intraventricular therapy required. In one case a severe convulsion occurred after the fifth intrathecal injection, but with no ultimate ill effect.

In this last group the cerebrospinal fluid became sterile on the third to fifth day, clinical improvement was apparent in two to three days, and the meningitis seemed to be well under control by the end of a week, though the temperature did not settle completely so long as intramuscular penicillin was given. Also the cell count in the cerebrospinal fluid did not return to normal while the patient was under treatment. This was presumably due to reaction to the penicillin, but in those patients whose C.S.F. has been examined several months after cessation of treatment an ultimate return to normal is indicated. The persistence of pyrexia and cellular reaction, however, made it difficult to decide when to stop treatment: we may have given an unnecessary amount of intrathecal penicillin. There seems to be no need to continue this for more than a week after the fluid is sterile, provided adequate intramuscular penicillin, 960,000 units daily, is continued for about three weeks.

2. *Sulphadiazine, Penicillin, and Streptomycin* (3 cases).—In Cases 12 and 13 a change was made from penicillin to streptomycin on the fourth and fifth day respectively, but in each case improvement in the C.S.F.—a fall in cells from 380 to 80 and a rise in sugar from 0 to 35 mg. per 100 ml. in one, and a fall in cells from 2,540 to 70 and a rise in sugar from 21 mg. to 30.5 mg. per 100 ml. in the other—had already taken place. The second patient had a convulsion after one of the intrathecal injections of penicillin. In the third (Case 14), a change to streptomycin was made on the second day of treatment. In none of these cases can it be said that penicillin had failed: it had not been given time to succeed. All recovered.

3. *Sulphadiazine and Streptomycin*.—One patient (Case 15) was treated with this combination with complete success.

Conclusion

We submit that these cases show that penicillin, combined with oral sulphadiazine, given in adequate dosage—960,000 units daily for three weeks in three-hourly doses intramuscularly, and 40,000 units daily intrathecally for about seven days after the cerebrospinal fluid is sterile—provides an effective remedy in the treatment of severe as well as of moderately severe cases of influenzal meningitis. The facts that streptomycin is not freely available at present and that the organism is known to develop resistance render streptomycin less generally useful.

We wish to express thanks to our colleagues for permission to include their cases in this survey, to the resident medical staff for their help in carrying out the treatment, and to the nursing staff for their great care of the patients. We are also indebted to Dr. Rogers for the pathological reports and to Miss E. Hickmans for the biochemical reports.

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A STUDY OF THE POST-WAR INCIDENCE OF BREAST-FEEDING

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This investigation was carried out in order (1) to study the real incidence of breast-feeding in the town of Hitchin, North Hertfordshire (population 20,710); (2) to analyse the reasons for early weaning; and (3) to consider any existing correlation of age and parity, place of confinement, effect of vitamin supplements, mixed feeding, and housing.

Opinions of previous investigators have varied considerably on the trend in breast-feeding. Spence (1938) reported a definite decline; Robinson (1939) stressed the tendency towards a shortening of the duration; Hughes (1942), reviewing the incidence of breast-feeding in a small mining community, found that 31% of babies were weaned by the second week. It has recently been stated that not more than half the babies in Britain are breast-fed for longer than three months (Waller, 1947).

Material and Method

The survey was restricted to mothers living in Hitchin who were confined locally between Jan. 1, 1946, and Dec. 31, 1947, and who spent at least six antenatal months in the district. By such selection it was hoped that variations in antenatal and post-natal care, modes of management in infant-feeding, and fluctuations in the availability of extra rationed goods would be equalized.

In order to obtain a comprehensive survey it was obvious that the records of antenatal and infant welfare clinics alone would be inadequate. A detailed questionnaire was therefore prepared and mothers in the above category were interviewed individually. The questions were worded so that a "social history" of each infant could be built up. A complete picture of environmental conditions possibly affecting its intrauterine and extrauterine life until the age of 6-9 months was obtained. Out of all the visits paid, in only one instance was the required information refused.

The results of the questionnaire, taken in conjunction with the relevant records in the clinics and the reports of the health visitors, provide the basis of this study.

Results

Omitting infant deaths, removals from the district, and mothers who were confined elsewhere, the total available for investigation was 546. The number successfully interviewed was 545. Of these, 58.7% were in regular attendance at the infant welfare centre. This figure is regarded as satisfactory, since over 30% of mothers with children born in 1946-7 are living in an area of the town almost two miles from the centre, and their regular attendance would be a matter of great inconvenience to them.

Deliveries.—These were carried out in the County Council Maternity Home (161), two private nursing-homes (230), the