BACTERIAL MENINGITIS IN SPINA BIFIDA CYSTICA

A REVIEW OF 37 CASES

BY

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Meningitis is a well-known complication of meningocele, but the problems of its diagnosis and treatment have so far received scant attention. Some children with meningocele have a small neurological deficit and no hydrocephalus. Others with hydrocephalus may benefit from modern treatment and grow up to lead normal lives. The problem of meningitis in meningocele is, therefore, worthy of study. It is well known that purulent neonatal meningitis in anatomically normal children is a difficult diagnostic problem, and despite the advent of antibiotics it still carries a high mortality and grave sequelae in some of the survivors (Watson, 1957; Ziai and Haggerty, 1958; Groover, Sutherland and Landing, 1961). In the present paper we describe 37 cases of bacterial meningitis in children with spina bifida cystica.

Background

A combined surgical, medical and orthopaedic study of the problems of spina bifida has been in progress in the Sheffield Children's Hospital for several years. Cases are referred to this hospital from a wide area. The majority of the children are referred in the neonatal period, many of them within 24 hours of birth, and they are admitted under the surgical care of Mr. R. B. Zachary. As far as possible the babies are treated in one surgical ward, so that the nursing staff gain experience in the special techniques of their care, but this is not always possible and they may be nursed in other wards. The general policy is to administer a broad-spectrum antibiotic and to repair the meningocele immediately after admission. This is done irrespective of the severity of the neurological involvement or of the presence of hydrocephalus. Very wide meningoceles in which adequate skin cover is not feasible without undue tension, and obviously infected lesions in which there is a danger of burying pus, are left to granulate and epithelialize.

When the back wound has healed, air ventriculography is performed for the detection of hydro-

cephalus. If present, this may be treated with a ventriculo-caval shunt (Spitz-Holter valve).

Present Investigation

Criteria for Inclusion. The term 'meningitis' is used, though this expression may not be strictly accurate in all cases. In anatomically normal children meningitis usually includes infection of the meninges and the lining of the cavities of the brain. In children with spina bifida cystica, who are likely to have congenital obstruction to the cerebrospinal fluid pathways, there may be 'meningitis' arising from an infected meningocele without infection of the ventricles, or the other way round. Alternatively, the ventricles may be involved alone as a result of infection introduced by ventriculography or the insertion of a Spitz-Holter valve. Ante-mortem diagnosis was made usually on examination of cerebrospinal fluid obtained from the lateral ventricles, the lumbar theca not being available because of the spinal lesion. Strictly speaking, therefore, we usually refer to 'ventriculitis', rather than meningitis. Since, however, the majority of these cases have meningitis also, it would be pedantic to introduce a new term. For this reason, but bearing in mind its limitations in these children, we use the term 'meningitis'.

The cases belong to two groups. Group I consists of 33 cases; in these the meningitis appeared to be related to the meningocele or to the procedures involved in the investigation and treatment of associated hydrocephalus. Meningitis in this group was diagnosed during life if there was a marked polymorphonuclear pleocytosis in the lateral ventricular cerebrospinal fluid with the subsequent isolation of an organism, or at autopsy on evidence of infection of the meninges and lateral ventricles. Group II consists of four children who developed pyogenic meningitis apparently unrelated to the spina bifida cystica or to the hydrocephalus.

Group I

This series is drawn from 262 consecutive cases of

TABLE 1

TIMETABLE OF 32 CASES OF MENINGITIS IN ASSOCIATION WITH SPINA BIFIDA CYSTICA*

	Range	50%	Average
Age on admission Age at repair of spina bifida (27 cases)	Day of birth to 2 months	Within 48 hours of birth	8 days
Age at diagnosis of meningitis	4 days to 4½ months	Within first 28 days of life	35 days

* One infant first admitted at 8 months of age is not included.

TABLE 2

AETIOLOGICAL GROUPS (33 CASES)

	Number at Risk	Cases of Meningitis		Died
		Number	%	
Unrelated to ventriculography or ventriculo-caval shunt . .	262	25	9.5	17
Related to ventriculography . .	207	3	1.4	2
Related to ventriculo-caval shunt	109	5	4.6	5

TABLE 3

TIME OF ONSET RELATED TO AETIOLOGICAL FACTORS

Cases	Time
Unrelated to ventriculography or ventriculo-caval shunt	Meningomyelocele repaired (21 cases); interval between operation and diagnosis 1 day to 8 weeks Meningomyelocele not re- paired (four cases); age of diagnosis { 4 weeks 4½ weeks 6 weeks P.M. at 4 weeks
Related to ventriculography (three cases); interval between ventriculography and diagnosis	{ 3 days 4 days 4 days
Related to ventriculo-caval shunt (5 cases); interval between insertion and diagnosis . .	{ 3 days 5 days 6 days 7 days 8 days

spina bifida cystica (meningomyelocele 249; meningoceles 13) admitted to the Sheffield Children's Hospital from January 1959 to the end of April 1961. Thirty-three cases of purulent meningitis have been diagnosed according to the criteria stated above, an incidence of 12%. One child developed meningitis due to *Strep. faecalis* early in the newborn period, from which she recovered completely. After the insertion of Spitz-Holter valve she developed meningitis due to *Ps. pyocyanea*. This child is counted as two cases.

Six of the 32 infants had no detectable paralysis at the onset of the meningitis, but 14 had complete flaccid paraplegia. The remaining 12 had variable degrees of partial paraplegia.

Only two infants were premature. An adequate antenatal history was available from 26 mothers. Pregnancy was apparently normal in 17, five mothers had toxæmia, two had early spontaneous rupture of the membranes and one had a threatened abortion. Natal history was recorded in 30 cases and in 25 delivery was apparently normal.

There were 22 females and 10 male children. There was no difference in the sex incidence in the 262 cases of spina bifida cystica.

One child was admitted at the age of 8 months following rupture of the meningocele sac. This lesion was repaired immediately after admission, and two weeks later meningitis supervened. Table 1 shows the relative ages at the times of admission, meningocele repair and diagnosis of meningitis in the other 31 children. All were admitted under 2 months of age, half of them within 48 hours of birth (average 8 days). Of the 32 children of this series, 27 had the meningocele repaired before the onset of the meningitis; in five the lesions had been left to granulate. The meningocele was repaired within 48 hours of birth in 16 cases and from 3 days to 2 months of age in the remainder (average 8 days). Meningitis was diagnosed between 4 days to 4 months of age, half being within the first 28 days of life (average 35 days).

Aetiological Groups (Tables 2 and 3). Five of the cases occurred among the 109 children who were treated with ventriculo-caval shunts (Spitz-Holter valve), an incidence of 4.6% of those at risk. In these cases, the spinal lesion had healed (four had been repaired, one had granulated) and the meningitis occurred three to eight days postoperatively.

In three infants with a healed spinal lesion (all repaired) meningitis occurred three to five days after air ventriculography, and these cases could be ascribed to that procedure. This represents an incidence of 1.4% in those submitted to ventriculography.

The 25 remaining cases (21 repaired, four granulated) occurred in children without ventriculo-caval shunts and unrelated to ventriculography, an incidence of 9.5% of the total 262 infants at risk. Meningitis was diagnosed between one day and eight weeks postoperatively (11 within two weeks) in the 21 in whom the meningocele was repaired. Three children of this group had had a ventriculogram two and a half, three and seven weeks respectively before the onset of the meningitis. It was

not thought that the meningitis was caused by the ventriculogram.

Further Factors in Aetiology. At the time of the onset of the meningitis 18 infants were still on prophylactic antibiotic treatment. This was usually tetracycline in an average dose of 20 mg./lb. body-weight/day. When the meningitis developed, 12 infants were no longer receiving an antibiotic.

Table 4 shows that after repair of the meningo-myelocele first intention healing occurred less frequently, and sepsis and cerebrospinal fluid leakage occurred more frequently in cases developing meningitis as compared with the same number of infants who did not develop meningitis.

Table 5 shows the organisms involved in the infected meningo-myelocele wounds in the 20 cases in which this is known. *Staph. aureus* and *Esch. coli* predominate. Within three days of the diagnosis of the meningitis 12 wound swabs were taken. Nine showed the same organism on the back and in the cerebrospinal fluid, but three did not.

The spina bifida cystica was a meningo-myelocele in all but one of the infants. The exception was a child with a thoracic meningocele who developed *Staph. aureus* meningitis after the insertion of a Spitz-Holter valve.

Table 6 shows the incidence of meningitis in relation to the site of the spina bifida cystica. It is seen that all the 25 cases which were unrelated to ventriculo-caval shunt or ventriculography (i.e. presumably due to an ascending infection from the meningo-myelocele) occurred in infants whose spinal lesions involved the napkin area. There was one case which occurred among 36 children in whom the spina bifida extended no lower than the thoracic spine. This was a child who developed meningitis after the insertion of a Spitz-Holter valve.

The Figure shows the distribution of cases as they occurred week by week during 1960 and 1961. It indicates a tendency to bunching, the possible reasons for which will be discussed later.

Clinical Features. Much of this study is retrospective, and the clinical features in a number of cases have not been recorded in sufficient detail. Table 7 shows the incidence of the important clinical features as compared with the incidence in the same number of 'control' infants of the corresponding age group. At no time has the absence of the record of a clinical feature been taken to indicate the absence of that feature in the child. Only a definite positive or negative record has been counted. The 'control' infants have been selected only in as much as they were infants with meningo-

TABLE 4
WOUND HEALING IN 25 CASES OF MENINGITIS AND 25 CONTROLS

	First Intention Healing	Wound Sepsis	C.S.F. Leakage
Meningitis ..	5	17	15
Controls ..	18	7	4

TABLE 5
BACTERIOLOGY OF THE MENINGOMYELOCELE WOUND IN 20 CASES

Organism	Number of Isolations*
<i>Staph. aureus</i> ..	13
<i>Esch. coli</i> ..	12
<i>Proteus morgani</i> ..	5
<i>Ps. pyocyanea</i> ..	4
<i>Staph. albus</i> ..	3
<i>β haem. Streptococcus</i> ..	3
<i>C. albicans</i> ..	1

* Often in combination.

TABLE 6
INCIDENCE OF ASCENDING MENINGITIS IN RELATION TO THE SITE OF THE SPINA BIFIDA CYSTICA (25 CASES)

Site of Spina Bifida Cystica	Number	Cases of Meningitis	
		Number	%
Encephalocele ..	36	0	0
Cervical ..			
Thoracic ..			
Thoraco-lumbar ..	142	15	11
Lumbar ..			
Thoraco-lumbo-sacral ..	84	10	12
Lumbo-sacral ..			
Sacral ..			

TABLE 7
CLINICAL FEATURES OF CASES OF MENINGITIS COMPARED WITH CONTROLS

	Cases of Meningitis	Controls
Generally unwell ..	21/22	7/22
Pyrexia ..	26/31	13/31
Poor feeding ..	13/19	5/19
Vomiting ..	10/20	10/20
Convulsions ..	17/32	1/32

myelocele but without meningitis, and on whom adequate clinical notes were made.

The features most commonly found at the onset of meningitis were a poor general condition, pyrexia and poor feeding activity. A poor general appearance was considerably commoner in the infants with meningitis than in the control group. A pyrexia of greater than 99° F. (37° C.) (excluding the first postoperative day) was found twice as often amongst the cases of meningitis as it was amongst the control

FIG.—Chronological distribution of cases, showing tendency to bunching.

group. In general the pyrexia of meningitis was high and persistent, unlike that which occurred in the controls, which was usually low grade and intermittent. A subnormal temperature was present in two of the cases and in one control with pneumonia. The temperature was normal in only three of the cases of meningitis. Pyrexia was the commonest first sign of meningitis to be observed.

Poor feeding was commoner in the infants with meningitis than it was in the controls, but vomiting occurred with equal frequency in the two groups.

Convulsions were present in over half the children with meningitis, but in most cases this was a late feature. Only one case of convulsions was found in 32 control children. The fits in this child were transient and due to overheating in an incubator.

The frequency of neck stiffness and head retraction in meningomyelocele made these features of limited value in the diagnosis of meningitis.

The character of the anterior fontanelle as an indication in children with congenital hydrocephalus was found to be unreliable. Some of the infants with meningitis had soft or flat fontanelles, whereas many of the control infants had bulging fontanelles. A very tense fontanelle was sometimes an indication of the onset of meningitis.

A rapidly rising head circumference was often

found to indicate progressive congenital hydrocephalus in the absence of meningitis. In some cases of meningitis, however, there was no unusual rise in head circumference at the time of the onset of the meningitis.

Cerebrospinal Fluid Characteristics. The pleocytosis at the diagnostic ventricular puncture varied from 50-8,000 white cells/c.mm., polymorphs predominating. The initial protein content varied from 20 mg./100 ml. to 1.2 g./100 ml. The initial sugar content was usually negligible, but sometimes it fell within the range found in our laboratory in uninfected cerebrospinal fluid obtained from hydrocephalic infants at routine ventriculography (10 mg./100 ml.-56 mg./100 ml. in 14 specimens).

Gram-negative organisms were found in 22 cases and Gram-positive organisms in 11 (Table 8). *Esch. coli* was by far the commonest organism, being responsible for 12 cases. Mixed infection occurred in one infant, the organisms being *Aerobacter aerogenes* and *Ps. pyocyanea*.

The organisms in the three cases attributed to ventriculography were *Ps. pyocyanea* in two and *Staph. aureus* in one. The five cases associated with the insertion of a Spitz-Holter valve were due to *Staph. aureus* in three, *Ps. pyocyanea* in one and

Strep. faecalis in one. *Esch. coli* was responsible for half the cases unrelated to ventriculography or ventriculo-caval shunts.

Other Investigations. Blood was taken for culture in only five cases, with positive results in three. Two were in children with functioning ventriculo-caval shunts and these both showed the expected septicaemia. The third positive result was from a child with *Esch. coli* meningitis who did not have a ventriculo-caval shunt. Two others without shunts had sterile blood cultures.

The haemoglobin level was generally well maintained despite prolonged illness. The leucocytosis in the peripheral blood varied from 10,000 to 54,000 cells/c.mm., polymorphs usually predominating. Four infants had urinary infections.

Treatment. With the exception of one child who died at home, all received systemic antibiotic treatment appropriate to the *in vitro* sensitivities of the causative organisms. Antibacterial agents used were penicillin, streptomycin, sulphadimidine, tetracycline, chloramphenicol, polymyxin, erythromycin and novobiocin, singly or in combination. In addition, treatment included daily intraventricular instillations of a combination of one or more antibiotics with 10 mg. of hydrocortisone hemisuccinate. Antibiotics used by the intraventricular route were soluble penicillin (5,000 to 10,000 units per dose), streptomycin (10-25 mg.), chloramphenicol (5-10 mg.), polymyxin (15,000-50,000 units), erythromycin (20 mg.) and neomycin (25 mg.). Courses of intraventricular treatment ranged from one dose (the child dying rapidly after diagnosis) to 50 consecutive daily doses. One child with relapsing meningitis had a total of 103 intraventricular instillations before a final cure.

Progress. Of the 24 fatal cases diagnosed during life, three died within 24 hours, eight died within one week, 17 died within one month and all but one died within three months of diagnosis. The remaining child had recovered from meningitis due to *Staph. aureus*, but died eight months later from a prolonged staphylococcal septicaemia.

The course of the disease was followed by observing the changes in the ventricular fluid. Intraventricular therapy was continued until death, or in the survivors until the cerebrospinal fluid was persistently sterile. Relapse after an apparent cure was common. This was diagnosed by a return of a cerebrospinal fluid pleocytosis or positive culture. Children with relapse received further courses of systemic and intraventricular treatment.

TABLE 8
ORGANISMS ISOLATED FROM THE C.S.F.

Causative Organisms	Number	Died
Gram-negative { <i>E. coli</i> <i>Ps. pyocyanea</i> * <i>Aerobacter aerogenes</i> * <i>Proteus morgani</i>	{ 12 7 2 1 } 22	{ 9 6 3 1 } 18
Gram-positive { <i>Staph. aureus</i> <i>β haem. Strep.</i> <i>Strep. faecalis</i>	{ 6 3 2 } 11	{ 4 1 1 } 6
Organism unknown (died at home) ..	1	1

* One case with combined infection is included in both groups.

In the survivors initial courses of intraventricular treatment varied from four to 37 days. Two of the survivors relapsed once and were given further intraventricular treatment for six and 10 days respectively. One survivor relapsed three times and was treated with continuous systemic and intermittent intraventricular therapy for nearly four months before relapse no longer occurred.

Detailed description of the cerebrospinal fluid changes during the treatment of meningitis, with special reference to antibiotic assays, will form the subject of a separate communication.

Outcome. Eight children (25%) are alive. One infant who survived one attack of meningitis succumbed to a second attack due to another organism.

Four survivors are now over 6 months of age and four others are over 1 year of age. At the last assessment one had a D.Q. (Gesell) of 90, two a D.Q. of 70-80, two a D.Q. of 50-70 and two were aments. One child is being followed up at another hospital and is apparently 'not greatly retarded'. Seven had gross hydrocephalus at the termination of the meningitis and were treated with ventriculo-caval shunts. The head circumference in five is still excessive. Additional neurological damage sustained as a result of the meningitis includes a spastic quadriplegia in one of the aments, and severe optic atrophy and apparent blindness in the other. None has convulsions.

Of the 22 infections with Gram-negative organisms 18 were fatal, as compared with six deaths in the 11 infections due to Gram-positive organisms (Table 8). There were four deaths due to *Staph. aureus* infection. In three there was a generalized staphylococcal septicaemia, and the fourth child was moribund from gross hydrocephalus before the onset of the meningitis. In two of the fatal cases with staphylococcal septicaemia a functioning Spitz-Holter valve was *in situ*. The death of the infant with β -haemolytic streptococcal meningitis

was due to a supervening respiratory infection. In the infant who died with *Strep. faecalis* meningitis a functioning Spitz-Holter valve was *in situ*, and the child died with a septicaemia. All five cases associated with the insertion of Spitz-Holter valves were fatal.

Autopsies were performed on all the fatal cases. This material forms part of a special study by Dr. J. L. Emery who will report it separately.

Group II

This consists of four cases in which the meningitis was apparently unrelated to the spina bifida cystica or to the procedures involved in the investigation and treatment of hydrocephalus. The first was a case of pneumococcal meningitis which occurred four months after the repair of a thoraco-lumbar meningocele, two and a half months after a ventriculogram and two months after the insertion of a Spitz-Holter valve. The ventriculo-caval shunt was functioning and pneumococci were isolated on blood culture. The valve was left *in situ*, and the infant made a good recovery on systemic and intraventricular penicillin. At 1 year of age her D.Q. was 70, and her head circumference was within the normal range. The second was a case of meningococcal meningitis occurring five months after the repair of a sacral meningocele. At the time of the repair this boy's head was growing at a normal rate. He was not investigated further, and so hydrocephalus was not excluded. He recovered from the meningitis on penicillin and sulphadimidine treatment, but after this illness his head started to enlarge at an abnormal rate. A ventriculogram now showed gross hydrocephalus which has since been successfully treated by a ventriculo-caval shunt. At 2 years of age he is retarded with a D.Q. of about 50. The third case was a girl with a repaired encephalocele. A ventriculogram showed a non-communicating hydrocephalus which was treated with a Spitz-Holter valve. Three months later she was admitted moribund and died soon after admission. At autopsy she was found to have meningitis over the base and vertex of the brain but no infection of the ventricles. This was in keeping with the observation that the hydrocephalus was non-communicating. No organism was recovered from the lateral ventricular cerebrospinal fluid. The fourth case was a 2-year-old boy with a repaired lumbar meningocele, who was admitted with a one-day history of feverish illness. On admission he was pyrexial with neck stiffness and a tense bulging anterior fontanelle. Surprisingly the ventricular fluid was normal, but a cisternal tap produced turbid fluid from which pneumococci were cultured.

He was treated with systemic penicillin and three instillations of soluble penicillin through cisternal punctures. Throughout his illness and recovery, the ventricular fluid remained normal. He made a full recovery and apparently has no sequelae*.

These four children had all been well up to the onset of their acute illness. The spinal lesion was firmly healed in three of them and although in the fourth case there was some ulceration in the meningocele, pneumococci were not isolated from this lesion. For these reasons and in view of the pathogens involved, it seems reasonable not to attribute the meningitis to ascending infection from the spina bifida.

Discussion

Localized infection of the spinal meninges probably occurs in all cases of infected meningocele. This infection may spread up the theca to produce varying degrees of spinal meningitis and if it enters the cranium, cerebral meningitis results. The antemortem diagnosis of meningitis depends upon finding altered cerebrospinal fluid, but there are some problems in this connexion peculiar to cases of meningocele. The availability of sites for obtaining specimens of cerebrospinal fluid is severely limited. The lumbar theca cannot usually be used owing to the presence of the spinal lesion, and cisternal puncture is hazardous in view of the likely presence of an Arnold-Chiari deformity. The only site from which cerebrospinal fluid is always available is a lateral ventricle, but there may be disadvantages in relying on this fluid in children with likely obstruction of the cerebrospinal fluid pathways. Thus the ventricular fluid may be normal in cases of meningitis in which the aqueduct of the fourth ventricular foramina is not patent. This is illustrated by the last two cases in Group II of this series.

Detailed study of the autopsy material of cases of meningocele is not yet complete. In addition, some children died at home and autopsy was not performed. Consequently, the total incidence of meningitis in the newborn period is not fully determined, and the figure of 32 affected children out of a total of 262 at risk (12%) represents a minimal incidence. Thus 45 other children (who either died at home or in whom autopsy evidence is not yet complete) have died without meningitis being definitely excluded (Table 9). Of these children, 17 had normal ventricular fluid just before death, but meningitis without involvement of the ventricles has not been excluded.

* Later he died in another hospital of 'fulminating cystitis'.

TABLE 9

INCIDENCE OF MENINGITIS AND OF MORTALITY IN RELATION TO YEAR OF ADMISSION

Year	Total Admissions	Cases of Meningitis	Death From Meningitis	Death <i>Not</i> Due to Meningitis	Death Due to Unknown Causes	Total Deaths
1959	118	5	5	12	22 (6)	39
1960	104	19	12	8	20 (9)	40
1961 (Jan. to April 30)	40	9	7	2	3 (2)	12
Total	262	33	24	22	45 (17)	91

Figures in parenthesis indicate infants with normal ventricular cerebrospinal fluid immediately preceding death.

The investigation of these children during 1959 was less complete than subsequently, and the apparent low incidence of meningitis in that year probably represents a failure of diagnosis. The total death rates for 1959 and for 1960 are remarkably similar, being 36% and 38% respectively, and meningitis probably occurred as frequently in 1959 as later. It is reasonable to believe, therefore, that the incidence of meningitis was probably higher than 12%, but perhaps not greatly in excess of this figure. MacNab (1957) reported an incidence of meningitis of 18% in about 160 cases of meningocele. Known cases of meningitis in our series form 26% of all deaths. MacNab (1957) reported that 'the complications of meningitis and leakage of cerebrospinal fluid from meningocele account for 26% of deaths'.

There has been no previous large series describing the features of meningitis associated with meningocele. As half our patients were less than 28 days old and the rest (with one exception) were under the age of 4 months, we have compared some of our findings with accounts of neonatal meningitis in anatomically normal infants.

The non-specificity of the clinical picture and the difficult diagnostic problem of neonatal meningitis are well known (Watson, 1957; Ziai and Haggerty, 1958; Groover *et al.*, 1961). In the Groover *et al.* series of 39 patients, a diagnosis of meningitis was not suggested until some type of therapy had been given in 14 cases, and in 10 cases diagnosis was not made until autopsy. Additional difficulties are present in children with meningocele. A suppurating lesion on the back is an adequate reason for pyrexia and ill health. Neck stiffness and head retraction may be present in cases of Arnold-Chiari deformity without meningitis (Perret and Meyers, 1960). A bulging fontanelle or a rapidly increasing head size may be due to congenital hydrocephalus. Conversely, if a functioning ventriculo-caval shunt is *in situ*, an otherwise tense

fontanelle might be made soft. A poor general appearance with no localizing signs is sufficient indication to investigate the cerebrospinal fluid. Poor feeding activity and a persistent pyrexia of over about 100° F. (38° C.) are also features demanding immediate investigation.

There is general agreement about the poor prognosis in neonatal meningitis. The evidence that infection by any particular organism or by any group of organisms (e.g. Gram-negative bacilli) carries a different prognosis is poor and conflicting, largely due to smallness of numbers and because continually differing methods of treatment are adopted. For example, Watson (1957) found that in his series, in three-quarters of which coliform organisms were the infecting agents, the prognosis was poor. In our own series Gram-negative bacilli were responsible for two-thirds of the cases and the mortality in these was also higher (18 out of 22) than in those due to Gram-positive cocci (six out of 11). These differences are not statistically significant, and it is not surprising that such differences were not present in the series of Ziai and Haggerty (1958) and Groover *et al.* (1961). Such groupings may also hide the importance of individual pathogens, such as *Ps. pyocyanea* in the Gram-negative and *Staph. aureus* in the Gram-positive group.

Out of our seven *Ps. pyocyanea* cases, two were associated with ventriculography and one with the insertion of a Spitz-Holter valve. In addition, two further cases occurred two to three weeks after ventriculography. As expected, this organism appeared to be closely related to medical procedures involving ventricular puncture. Of the six *Staph. aureus* cases, three followed the insertion of a Spitz-Holter valve and one followed ventriculography. This experience is in accord only with the increasing recognition that shunting operations for hydrocephalus are frequently complicated by staphylococcal meningitis (Karelitz, Desposito, Spinner and Isenberg, 1960). *Ps. pyocyanea* and *Staph. aureus*

TABLE 10

REPRESENTATIVE RESULTS OF TREATMENT OF NEONATAL MENINGITIS IN ANATOMICALLY NORMAL INFANTS COMPARED WITH RESULTS IN THIS SERIES

Authors	Years of Series	No. of Cases	Mortality Rate (%)	Sequelae Rate (%)	Survivors With No Sequelae (%)
Watson (1957)	1950-1955	45	64	11	24
Ziai and Haggerty (1958)	1932-1957	83	75	9	17
Groover <i>et al.</i> (1961)	1948-1959	39	67	5	28
Present series	1959-1961	33	75		

were between them responsible for seven of our eight cases attributed to medical intervention.

Table 10 compares the mortality rate in this series with that in three series of neonatal meningitis in anatomically normal children. Perhaps part of the reason that the survival rate amongst our children with severe congenital deformities approached those in the other series is that half the children were up to 4 months of age. Many of them, however, were severely debilitated by a suppurating meningo-myelocoele, and their chronological age by no means reflected their maturity. The use of intraventricular therapy in these children was presumably responsible in part for their survival. Most of them had some degree of hydrocephalus at the onset of their meningitis and intraventricular instillations could be carried out with relative ease. Nevertheless, the results of our intraventricular treatment cannot be claimed to be successful. The problems of achieving continuous bactericidal antibiotic levels in the cerebrospinal fluid are being investigated at the moment. Clifford and Stewart (1961) have recently reported three survivors out of four cases of *Ps. pyocyanea* meningitis in children with meningo-myelocoele using intraventricular instillations of a new derivative of polymyxin B.

It is not easy to assess the sequelae in infants already handicapped by congenital neurological defects. It is noteworthy, however, that only one of our eight survivors attained a D.Q. of 90. In our large series of hydrocephalus associated with meningo-myelocoele, more than half attained a D.Q. of 90 or over with a period of observation of one year (Lorber, 1961).

No form of treatment will ever be as effective as prevention. Operative technique and nursing care are of paramount importance in preventing wound sepsis and postoperative cerebrospinal fluid leakage (Ingraham and Matson, 1954). The bunching of cases (shown in the Figure) seemed to correspond to times when the pressure of work on the nursing staff was unusually high and there was perhaps the inevitable fall in nursing standards. The use of various prophylactic antibiotics is being investigated, but it seems unlikely that antibiotics alone will ever

be very effective under the conditions of meningo-myelocoele wound healing.

Of the 32 children in this series, 27 had their meningo-myelocoele repaired, half of them within the first 48 hours of life. Heimburger (1953) urges early operation on a number of counts, one being that meningitis remains a danger at least until the spinal lesion is covered with healthy skin. Our series presents no evidence for or against this view. The preponderance of cases in infants with a repaired meningo-myelocoele merely reflects the fact that repair was carried out on admission in nearly all our cases. It is our impression that following cerebrospinal fluid leakage through an infected meningo-myelocoele, meningitis is particularly liable to occur when the leakage ceases, either spontaneously or after closure. For this reason we do not advocate secondary closure of meningo-myelocoeles which are obviously infected.

Summary

Out of a consecutive series of 262 infants with spina bifida cystica, 37 developed bacterial meningitis. The 33 cases in Group I were directly related either to ascending infection from the meningo-myelocoele (25 cases), or the investigation (three cases), or treatment (five cases) of the associated hydrocephalus. In the remaining four cases (Group II), the meningitis occurred late and without any definite relation to the anatomical disorders. Of the Group I cases, 32 were under 4 months of age and half were under 28 days of age. The use of prophylactic antibiotic treatment did not prevent meningitis. Ascending meningitis occurred only in infants whose meningo-myelocoele involved the napkin area. The non-specificity of the clinical picture, and the overlap of signs of progressive hydrocephalus with acute meningitis made diagnosis difficult. An added diagnostic difficulty was the inaccessibility of the spinal theca for obtaining specimens of cerebrospinal fluid. The cerebrospinal fluid changes were typical of pyogenic meningitis. The positive cultures obtained produced Gram-negative bacilli in 22 in Group I, the commonest organism being *Esch. coli* (12 cases). *Ps. pyo-*

cyanea was responsible for seven cases. Gram-positive cocci were detected in 11, out of which six were *Staph. aureus*. *Ps. pyocyanea* and staphylococcal infections were responsible for seven out of eight cases which were the result of procedures for the investigation and treatment of the associated hydrocephalus.

Antibiotic treatment appropriate to the nature and sensitivity of the organism was given by the systemic and intraventricular routes. Intraventricular hydrocortisone was used in each case.

There were eight survivors in Group I, of whom only one shows a normal mental development. There were three survivors in Group II (two cases of pneumococcal and one of meningococcal meningitis).

Although these results are poor, they are not very different from those obtained generally in neonatal meningitis in anatomically normal children. Advances in the prevention of the meningitis hold out better hopes of success than different methods of treatment in established cases.

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Addendum

In January 1962, in Group I, seven children (22%), are known to be alive. One infant who was alive (an ament) at the time the paper was submitted died at 8 months of age with extreme hydrocephalus, persistent basal exudate and blockage of the proximal end of the ventriculo-caval shunt by a thrombosis in the jugular vein. Another child, who was to be followed up at another hospital, has not been seen after 6 months of age, but according to his mother he is well at 2 years. Of the six remaining survivors, one showed remarkable improvement and was demonstrated at a clinical meeting of the Royal Society of Medicine (Lorber, November 1961). This infant was developing rapidly, and by 1 year of age her I.Q. rose to about 70 (from 50 at 6 months). She recovered her vision. She has no neurological sequelae now, in spite of 103 intraventricular injections which resulted in two large cysts in the cerebral white matter communicating with the anterior horn of the lateral ventricles (Grainger and Lorber, 1962). The other five survivors have all been followed up from 12 to 24 months of age. Their D.Q. (Gesell) are all within 70 to 80. None had deteriorated, and three had improved since the previous estimate. All but one had been treated with ventriculo-caval shunt. The head circumference of the unoperated infant and of two others is still above the 90th percentile, although their heads are no longer growing excessively. Three now have normal or small normal heads.