ACUTE ASEPTIC MENINGITIS IN CHILDREN

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As one of the acute medical emergencies demanding prompt diagnosis and effective treatment, purulent meningitis has received its fair share of attention, and practitioners are generally alert to this condition. Delay in diagnosis is still, however, responsible for an appreciable proportion of poor results, and the optimum therapy for each particular type is by no means decided. These problems have been discussed recently in this *Journal* by Esrachowitz[1] and Geefhuysen[2], and it is not our intention to review them.

In contrast to the purulent forms, aseptic meningitis has received little mention in this country. Bayer and Gear[3] reported on 100 cases in 1952. Smaller series associated with specific agents have been reported subsequently — 5 from Salisbury, Rhodesia, due to a Coxsackie B virus;[4] an outbreak of 58 cases associated with ECHO virus type 4;[5] 5 cases due to leptospira canicola[6]; and 8 cases due to ECHO virus type 9.[7] The condition was reviewed by one of us in 1959.[8]

During the years 1953 - 1960 inclusive, 161 patients with acute meningitis were admitted to the Addington Children's Hospital. Of these, 73 were of proved or presumed bacterial origin, and the remaining 88 were of the aseptic variety. (Cases of tuberculous meningitis have been excluded.) This means that 55% of cases of acute meningitis admitted to this hospital are of non-bacterial origin, and it is obviously of major importance to differentiate these cases from those of bacterial origin. Although in the majority of cases such differentiation is not difficult, in some 15% it may be impossible (even after watching their subsequent course), to say categorically into which class they fall.

Annual Incidence

The epidemic nature of outbreaks of aseptic meningitis is well recognized and is illustrated by the annual incidence shown in Table I.

TABLE I. ANNUAL INCIDENCE OF ASEPTIC MENINGITIS

Condition	*Year*							
	1953	1954	1955	1956	1957	1958	1959	1960
Cases of aseptic Meningitis	3	5	8	18	23	18	6	7
Cases of polio-myelitis	4	70	65	79	113	10	23	6

The high incidence in the years 1956 - 1958 coincided with epidemics elsewhere.

For interest the poliomyelitis notifications are included in this table. It will be seen that, although in some years a high incidence of poliomyelitis coincided with a high incidence of aseptic meningitis (e.g. 1956, 1957), and some overlap of these cases in both directions almost certainly occurred, in other years there was a high incidence of poliomyelitis with little 'non-polio' aseptic meningitis (e.g. 1954, 1955) and *vice versa* (1958). We are, at present, (early 1961) experiencing a minor epidemic of aseptic meningitis in spite of an almost complete absence of poliomyelitis. There is little doubt that the vast majority of cases of aseptic meningitis occurring in this area have been due to viral infections other than poliomyelitis.

Seasonal Incidence

Whereas the bacterial forms of meningitis occur throughout the year, with perhaps some slight predilection for the colder months, aseptic meningitis of viral aetiology occurs predominantly during the summer. This is illustrated in this series by Fig. I, which also shows (for comparison) the monthly incidence of poliomyelitis in Europeans in Durban over the same 8-year period. It will be seen that the majority of cases (in fact 73%) occurred in the months November to March. The chances of a case of acute meningitis occurring during these months being due to bacterial agents are only 18%, whereas over the rest of the year the chances are 71%. This is a striking difference.

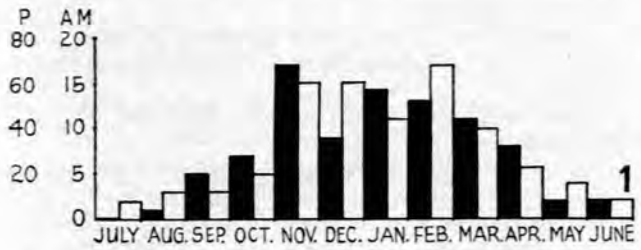

Fig. 1. Monthly incidence of aseptic meningitis (black) and poliomyelitis (white) over 8 years (1953 - 1960). A M = aseptic meningitis; P = poliomyelitis.

Age Distribution

The age distribution in this series of aseptic meningitis is shown in Table II and, for comparison, the bacterial cases are depicted in the same table.

It will be noted that aseptic meningitis is relatively uncommon under the age of 1 year, only 12·5% of cases falling into this age group. It is interesting to contrast this with the age distribution of the various forms of pyogenic meningitis. The higher incidence of pyogenic forms in the younger age groups is evident. We have no experience of aseptic meningitis in persons over the age of 13 years, but the impression gained from colleagues is that it is not nearly as common as in younger children.

TABLE II. AGE DISTRIBUTION OF VARIOUS FORMS OF MENINGITIS

Condition	*Age group*				
	< 6 Mo.	6 Mo. - 1 Yr.	1 Yr. - 5 Yr.	5 Yr. - 13 Yr.	Total
Aseptic meningitis	8	3	36	41	88
Meningococcal	5	5	6	2	18
H. influenzae	1	3	10	0	14
Pneumococcal	0	4	6	3	13
Unidentified	11	3	6	5	25
Total septic cases*	17	15	28	10	70

* Excluding one case each due to staphylococcus, *B. coli.* and enterococcus.

Race

This study is confined to European children and figures are not available for other races. Aseptic meningitis appears, however, to be uncommon in the Coloured community in Durban and rare in Africans and Indians.

Sex

Of the 88 cases 56 (63%) occurred in males and 32 (37%) in females. A similar high incidence in males was found in the septic cases — 45 males (64%) and 25 females (36%). We have no explanation to offer for this male predominance.

Presenting Symptoms

The incidence of the major presenting symptoms as seen in this series is shown in Table III.

TABLE III. PRESENTING SYMPTOMS IN ASEPTIC MENINGITIS

Symptom	*No. of cases*	%
Fever	78	89
Vomiting	61	69
Headache	59	67
Irritability	10	11
Convulsions	9	10
Muscular pains	8	9
Photophobia	4	5
Drowsiness	3	3
Sore throat	2	2
Rash	2	2

Fever, vomiting, and headache are by far the commonest symptoms encountered. Rather remarkable is the relatively high incidence of convulsions (9 cases). These were not confined to the lower age groups (only 3 of these children being under 3 years of age), nor were they always associated with high fever. Muscular pains affecting either the limbs or the abdominal muscles were complained of in 8 cases. The low incidence of skin rashes would seem to indicate that ECHO types 9 and 16 viruses were not common causative agents in this series, because in outbreaks due to these viruses a rash has been reported in from 18% to 60% of cases.

Symptoms had been present on admission for variable intervals from 12 hours to 7 days. The mean period was 2·3 days, which is almost identical with the mean for the septic cases, which was 2·4 days. One might have imagined that this period would be shorter for the septic group where symptoms are usually more dramatic.

Presenting Signs

Neck stiffness, usually associated with back stiffness, was the most frequently encountered sign, being present in 45 cases (51%). A positive Kernig's sign proved much less reliable and was found in only 19 cases (22%). Where the fontanelle was still open, increased tension was noted in 6 cases. In almost half the cases there were no signs apart from fever, and lumbar punctures were performed on the history alone. This is the type of case which is easily mistaken for influenza.

CSF Findings

1. *Cells.* All cases except 2 had an abnormal cellular content of the CSF at the initial lumbar puncture. The number of polymorphs ranged from 0 to 1,035 per c.mm., with a mean of 93. The lymphocytes ranged from 1 to 960 per c.mm., with a mean of 92. The distribution of the cell counts in 5 groups is shown in Table IV.

TABLE IV. CSF-CELL COUNTS IN ASEPTIC MENINGITIS

	Cells / c.mm.				
	0 - 10	11 - 50	51 - 100	101 - 200	>200
Polymorphs (No. of cases)	29	20	16	10	13
Lymphocytes (No. of cases)	19	36	12	9	12

Whereas only 13 cases (15%) had polymorph counts of over 200 per c.mm., in the septic group 77% of cases had polymorph counts in this range. Nevertheless, there is considerable overlap. When the polymorphs number over 500 per c.mm., aseptic meningitis is unlikely, and only 1 of our cases exceeded this figure. Counts of 5,000 per c.mm. and over have, however, been recorded.

2. *Protein.* The protein content of the initial CSF ranged from 10 to 90 mg. per 100 ml. with a mean of 47 mg. per 100 ml. It exceeded 40 mg. per 100 ml. in 26 cases (30%). In no less than 12 of the remaining cases the protein content was exactly 40 mg. per 100 ml., which some would regard as slightly raised in a child. In septic meningitis the protein is generally much higher, but in 14% of our cases it was below 40 mg. per 100 ml. at the initial lumbar puncture. Only very rarely does the protein rise above 100 mg. per 100 ml. in aseptic meningitis.

The globulin was raised in 30 of our aseptic cases (34%).

3. *Chloride.* This estimation does not appear to be of any diagnostic or prognostic value, the figures in this series ranging from 657 to 761 mg. per 100 ml.

4. *Sugar.* A low CSF sugar content is usually associated with tuberculous or septic meningitis or hypoglycaemia. In only 2 of our cases of aseptic meningitis was it below 50 mg. per 100 ml., being above this figure in the remaining 86 cases (92%). Nevertheless, in our septic cases the initial CSF sugar content was normal in 56%. It would seem, therefore, that the CSF-sugar level is not necessarily a reliable diagnostic sign.

Blood Leucocyte Count

This was recorded in only 44 cases. In these the total hite-cell count ranged from 5,000 to 15,000 per c.mm. with a mean of 10,000. In the septic cases the mean was 17,000. A polymorphonuclear leucocytosis is of considerable value in differentiating the septic cases.

Duration of Illness

The persistence of symptoms was very variable, from 1 to 14 days, although most cases improved rapidly. The mean duration of fever in hospital was 3½ days. The CSF remained abnormal for up to 2 months after the onset of the illness, and was still abnormal 1 week after admission to hospital in nearly half (47%) of the cases.

Virus Studies

There is, unfortunately, no virus laboratory in Natal. We were, nevertheless, able to have virus studies performed on 45 of our 88 cases.

Specimens of stool and CSF, and occasionally throat washings, were cultured for virus, and serum examined on admission and 10 days later for the presence of antibodies. (These investigations were performed almost entirely by the Poliomyelitis Research Foundation, Johannesburg, but a few were undertaken by the Union Health Department Laboratory in Durban during the short time that a virological department was in existence).

Four cases were clinically ascribed to mumps infection, on the basis either of parotid involvement or of family history, and in 3 of these the mumps complement-fixation test was positive.

Poliomyelitis virus type 1 was isolated in the stools of 4 patients — 1 in 1955, 1 in 1956 and 2 in 1957. None of these cases showed paresis.

Coxsackie B virus was isolated in only 1 case and in 1 other case an, as yet, unidentified enterovirus was cultured from the stool.

ECHO virus type 9 was isolated from the CSF of 2 patients (sisters).

Thus, in only 25% of the cases examined was the aetiology confirmed or revealed by virological studies. In 87% of the total cases the aetiology remained undetermined.

TREATMENT

There is no specific therapy for viral meningitis, and antibiotics are useless and should be avoided. However, where there is some doubt whether a particular case is, in fact, a viral meningitis, the child must, of course, be given the benefit of the doubt and treated accordingly. This problem is more liable to arise with the sporadic out-of-season case of viral meningitis than during an epidemic, when diagnosis is usually easy. The drug of choice in this series has been aspirin, given to relieve headache and to control the pyrexia. Frequently lumbar puncture was found to be of definite therapeutic value in the almost immediate relief of neck and back stiffness and headache.

Confinement to bed until the CSF has returned to normal is unnecessary provided the child is symptom-free. As mentioned previously, cells may persist in the CSF for many weeks after the symptoms have disappeared, and several of the children in this series returned to school without any ill-effects, although their spinal fluids still contained cells.

There are, of course, non-viral forms of aseptic meningitis which require specific treatment, but we have not encountered any such cases in Durban.

DISCUSSION

Aseptic meningitis is a syndrome of multiple and varied aetiology. This aspect has already been discussed, [8] and we do not propose to repeat it here. The majority of cases are, however, due to viral agents, and it might be preferable, when discussing this group, to label it 'meningitis of viral origin'.[9]

In recent years advances in laboratory techniques have shed considerable light on the aetiology of the condition. In one large American series of 430 cases, for example, the aetiology was established in 71%.[10] The commonest agent encountered was the Coxsackie B group of viruses (18%). Mumps accounted for 16%, ECHO viruses for 12%, and poliomyelitis viruses for 9%. A further 9% were due to lymphocytic choriomeningitis, and 4% to leptospirosis. In the face of such figures our poor virus-recovery rate merely serves to emphasize the need for suitable facilities in Natal.

The clinical picture as seen in this series conforms to that reported by others except in the incidence of convulsions. These are usually associated, particularly in the older child, with more serious conditions, and previously such cases were labelled acute encephalitis. However, the other clinical features in these cases with convulsions leave little doubt that they were, in fact, examples of viral meningitis. They all recovered rapidly and completely.

The clinical diagnosis of aseptic meningitis is usually not difficult, particularly during an epidemic, although it is probable that quite a number of mild cases are labelled influenza with no harm to the children concerned.

It is a common misconception that the lymphocytes exceed the polymorphs in the CSF in aseptic meningitis. This is not so in the early stages of the infection, and in 47% of our cases the polymorphs were in excess of the lymphocytes. Later a lymphocytic swing is expected. When the polymorph count is relatively high the question of septic meningitis arises; and even at lower figures this has to be considered. We have, for example, encountered proved meningococcal meningitis with only 2 polymorphs, and pneumococcal meningitis with only 20 polymorphs and 51 lymphocytes per c.mm. in the CSF. The finding of an organism, of course, abolishes all doubt, but in 25% of our septic cases no organism was found. This high figure is partly accounted for by treatment having been initiated before admission to hospital, which adds considerably to the difficulty of diagnosis, and possibly also to the inclusion of some cases of aseptic meningitis which, for the sake of safety, received treatment. Others, e.g. Smith,[11] have reported a similar high figure for this group of unproved bacterial meningitis. It is obviously better to err on the side of safety and to treat when in doubt, but the infliction of a course of unpleasant and potentially dangerous therapy on a child with a benign condition is, to say the least of it, undesirable. Our own experience indicates that increasing familiarity with aseptic meningitis enables a correct diagnosis to be made in a very high proportion of cases. For example, in 1956 we would never have left untreated a baby of 1 year presenting with a 2-hour history of fever and vomiting, and an initial CSF containing 1,035 polymorphs and 700 lymphocytes per c.mm., as was done in 1958.[8] In the final diagnosis of cases in which the laboratory findings are inconclusive, clinical assessment is of the utmost value.

The reassuring clinical picture is somewhat difficult to define, but in our experience the child with aseptic meningitis is just 'not as ill as his signs'. He is usually alert and aware of his surroundings in contrast to the apathy and listless irritability so often encountered in septic meningitis. Furthermore, the major symptoms and signs tend to retrogress much more rapidly in the aseptic cases.

Nevertheless, there remains a small percentage of cases in which there is doubt, and which, for safety, have to be treated as unidentified septic meningitis. In these the final answer is, therefore, not known. The possible, and graver, error of leaving untreated a case of bacterial meningitis has, somewhat surprisingly, not yet occurred in this hospital.

Viral meningitis, being a benign condition, requires no specific treatment. A watch has to be kept for the possible onset of paralysis in case one is dealing with poliomyelitis; and the possibility of a non-viral aetiology has always to be kept in mind, particularly in the absence of an epidemic. The question of septic meningitis has already been discussed. Tuberculous meningitis in the early stages can give rise to difficulty since the CSF findings may be very similar to those in aseptic meningitis. Leptospirosis occurs in this country[6] and must always be considered, particularly in the presence of suggestive clinical features, such as conjunctival injection, a biphasic illness, and severe muscular pains. On rare occasions toxoplasmosis may have to be considered in the differential diagnosis.

SUMMARY

A series of cases of acute aseptic meningitis in children is presented and discussed, and the age distribution is contrasted with that of bacterial meningitis.

Study of the annual and seasonal incidence shows that in certain years the disease assumed epidemic proportions and that the majority of cases occur in the summer months.

The commonest presenting symptoms were fever, vomiting, and headache; the incidence of convulsions was higher than in other reported series.

An analysis of the CSF contents is presented and these are compared with the findings in children suffering from bacterial meningitis.

The results of limited virus studies are discussed.

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