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Purulent meningitis in infancy and childhood

By

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Clinical features, humoral immunity and EEG findings in infants and children suffering from purulent meningitis are discussed on the basis of data collected in the last 10 years. Purulent meningitis is a grave disease with a bad prognosis and a mortality rate of 47 and 12% in infancy and in childhood, respectively. Beyond the importance of early diagnosis and adequate treatment, the use of immunological tests and EEG findings is emphasized.

Purulent meningitis is a considerable factor of morbidity and fatality rate not only in the newborn but also in the postnatal period of life [2, 11]. DUREUX et al. [4] reported a fatality rate of 15.5% in a material of 110 patients aged between 1 month and 2 years. Of these, 68.1% recovered without, and 16.1% with, residual damage. Among patients of 2—14 years the mortality rate is 10%.

Purulent meningitis in the newborn infant has been dealt with in a previous paper [7]. The postneonatal period has some different characteristics, so we found it justified to analyze our cases subdivided into infant (28 days to 1 year) and children (1—14 years) groups.

PATIENTS AND FINDINGS

During the ten years between January 1, 1964, and December 31, 1973, 17 infants and 17 children were admitted with meningitis. Age and sex of these patiens are given in Table I.

TABLE I

Age	Male	Female	Total
1—6 months	6	5	11
7—12 months	4	2	6
1—4 years	8	4	12
5—12 years	4	1	5
Total	22	12	34

Two age-peaks can be seen, one between 1 and 6 months and a second between 1 and 4 years. The liability to infection of the first group will be discussed later in connection with immunological findings, the susceptibility in the 1- to 4-year age group has been pointed out in several WHO publications and also by us. The mortality rate is higher in boys (65%) than in girls.

The presenting symptoms and those

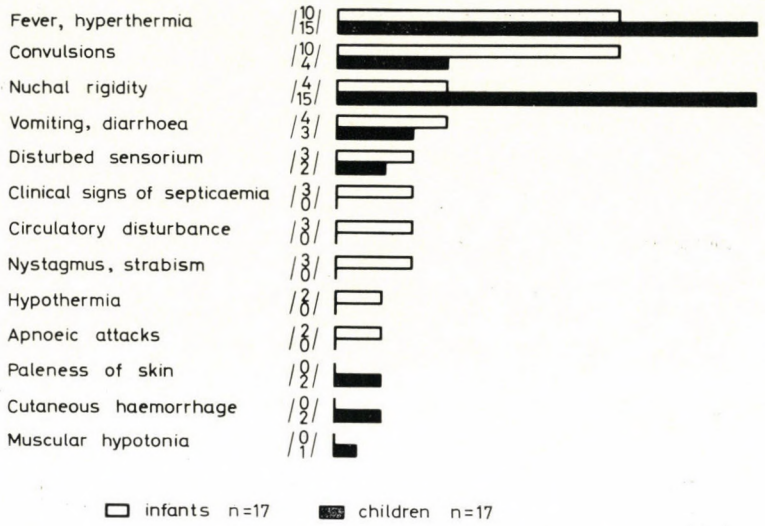

FIG. 1. First symptoms of the disease

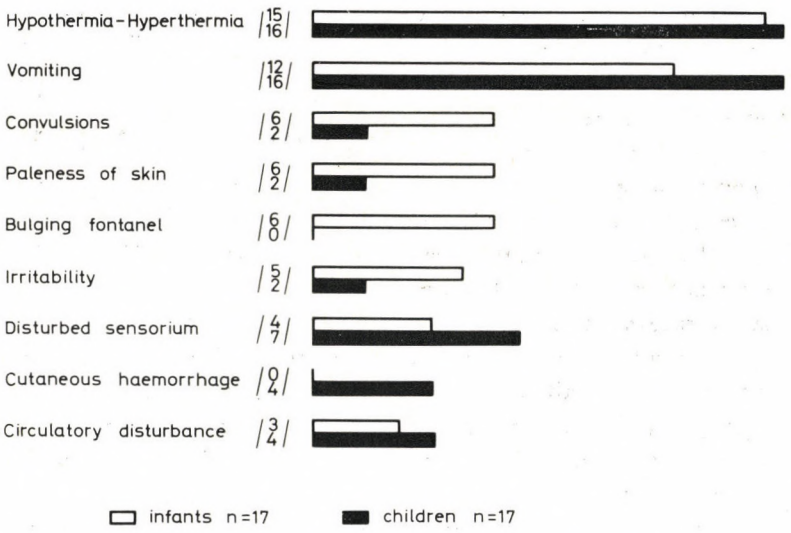

FIG. 2. Main symptoms of the disease

observed in the course of the disease are shown in Figs 1 and 2.

As presenting symptoms, fever and vomiting were dominating in both infants and children. Convulsions, paleness, irritability were frequently seen in the infants, while sensorial disturbances, circulatory disturbances and haemorrhagic skin lesions (accompanying meningococcal menin-

gitis) were more characteristic in childhood.

In infancy, the clinical course was characterized by repeated convulsions and fever and in children by fever and nuchal rigidity. Other symptoms were infrequent and non-specific.

Upper respiratory tract infections accompanied the disease frequently in both groups. Adenoiditis, suppurative otitis media, pneumonia in 5 cases, thigh abscess (due to intramuscular injections?) in 2 cases were seen in the infants. In the children, adenoiditis, tonsillitis in 3 cases, pneumonia in 2 cases and in one case sinus empyema complicated the disease.

Organisms cultured from the CSF are shown in Table II.

Ten of the patients with purulent meningitis died. All the cases are grouped according to age and causative agent in Table III.

The case fatality rate of purulent infantile meningitis amounted to 47%, nearly as high as in the neonatal period. Mortality was considerably lower in children; in this group two patients died, both were 1½ years old. Girls and boys were affected in a ratio of 4 : 6.

Table IV shows the time elapsed before death and Table V the age, sex, infecting agents and their resistance, antibiotics, outcome of the disease, number of days spent in hospital and postmortem diagnoses.

All the 13 meningococcal meningitis patients were sensitive to penicillin, and 11 to chloromycetin, 7 to tetracycline and erythromycin 5 to streptomycin, 3 to methicillin and

Table II

Causative agents of meningitis cultured from the cerebrospinal fluid

	1—12 months	1—12 years
Meningococcus	5	8
Pneumococcus	6	2
Haemophilus influenzae	1	1
Klebsiella	1	0
Non-identifiable	0	1
No pathogen isolated	4	5

Table III

Correlation of fatality rate with type of bacterium cultured from CSF

	1—12 months	1—12 years	Total
Pneumococcus	4	1	5
Haemophilus influenzae	1	0	1
Klebsiella	1	0	1
Non-identifiable	0	1	1
No pathogen isolated	2	0	2
Fatality rate	8/17	2/17	10/34

TABLE IV

Time before death

	< 24 hrs	1—3 days	4—6 days	> 6 days
1—12 months	5	0	1	2
1—12 years	1	0	1	0

2 to oxacillin. Sensitivity to gentamycin and kanamycin also occurred. From 8 pneumococcus cases the bacterium was sensitive to penicillin and chloromycetin in 6, to erythromycin in 4, tetracycline in 3, oxacillin and methicillin in 2 instances. Both H. influenzae cases showed sensitivity to chloromycetin.

The results of immunoglobulin estimations are seen in Table VI where normal values for infants and children are also given.

Hypogammaglobulinaemic IgG levels have been found in 4 infants (Fig. 3). The serum IgG level was especially low (40 mg/100 ml) in a seven months old infant with pneumococcal meningitis.

The serum IgM level was considerably elevated in almost every patient but two; both of these patients died.

Continuous EEG recordings were made in 4 infants and 8 children in the resting state.

Meningococcal meningitis caused a change of slight or medium degree in background activity; it manifested itself mainly with a rapidly reversible symmetrical delta activity. Haemophilus influenzae meningitis in the beginning of the disease caused somewhat more severe changes, usually a diffuse, rather symmetrical delta

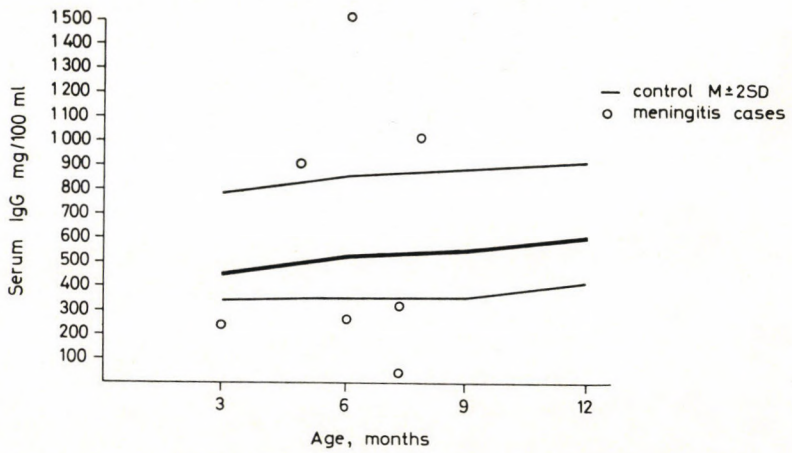

FIG. 3. Serum IgG levels in patients with meningitis

activity, which gradually disappeared. In pneumococcal meningitis first a paradoxically normal curve was seen, then the EEG displayed focal changes, occasionally combined with spike and spike-wave activities without clinical convulsions. The focal signs persisted for a long time during the course of the disease.

Discussion

The majority of our observations confirmed the data in the literature concerning the history, clinical symptoms, prognosis and frequency of bacteria [1, 5].

General considerations. Purulent meningitis after the neonatal age was more frequent in the first than in the second half of the first year. In the 1—14- year age group it affected mainly children 1—4 years of age, later it became less frequent. The morbidity rate was higher in boys than in girls in every age group.

Symptomatology. The importance of fever, especially of extremes in the type of fever cannot be overemphasized. In addition, vomiting in infants and sensory and circulatory disturbances in children drew attention to the disease of the central nervous system. Thus, a lumbar puncture must be performed without delay in every case presenting even the slightest sign of meningeal irritation. As far as the previous or complicating diseases are concerned, respiratory tract infections stood in the first place.

Examination of the cerebrospinal fluid including its cytology is essential. In infants, pneumococcus and meningococcus, in 1—2 years old children, meningococcus were the most frequently occurring microorganisms. In some cases of so-called sterile meningitis, meningococcus was assumed as the causative organism.

In four infants, very low serum IgG concentrations (40—240—260—320 mg/100 ml) were found at the time of diagnosing the meningitis. There was one substantial difference between these and the neonatal cases: in neonates the high frequency of perinatal infections, in children the threatening physiological hypogammaglobulinaemia was the main danger. The transitory hypogammaglobulinaemia manifesting itself with severe infection, a well-known occurrence, can be differentiated from malignant congenital immune deficiency states by the slowly increasing IgG level. The normal catabolism of maternal IgG and the rate of endogenous synthesis are not well-balanced, so the period of normal transitory hypogammaglobulinaemia may be prolonged. This was seen in one of our four infants where purulent meningitis had started at 7 months and systematic gammaglobulin substitution was necessary until 20 months of age.

The increase in the serum IgM level was mostly considerable with the exception of the two lethal cases which were not able to produce sufficient amounts of IgM. Jones et al. [6] found a family with 9 children in 8

TABLE V

Initials, age and sex of the patients investigated, infecting agents, antibiotic sensitivity, treatment, length of hospital case, outcome of the disease and necropsy findings

Patient	Age	Sex	Bacterium	Sensitivity	Antibiotic treatment	No. of days in hospital	Outcome	Necropsy
B. J.	5 months	female	Not isolated		P., T.	1	Died	Meningitis, purulent
V. J.	2 months	male	Pneumococcus	Ce., Methi.,	Ce., Methi.	24	Died	Septicaemia Osteomyelitis Pulmonary haemorrhage Meningitis, purulent
K. J.	4 years	male	Not isolated		P., Ery., Sulpha	21	Survived	
M. F.	1½ years	male	Pneumococcus	P., Chl., Ery.	Methi., T. i. th. P.	5	Died	Meningitis, purulent Atelectasis, focal Septicaemia
B. M.	10 years	female	Not isolated		P., Chl., Sulpha	21	Survived	
M. E.	6 months	female	Meningococcus	P., T., Str., Chl., Methi., Genta., Neo., Ery., Ce.	P., Chl.	33	Survived	
B. M.	2 months	female	Pneumococcus	P., T., Str., Chl.	P., Str., Chl. i. th. P.	64	Survived	
Sz. G.	1½ years	male	Pneumococcus	P., T., Chl., Ery., Ce., Oxa., Sulpha	P.	59	Survived	
I. J.	3 months	male	H. influenzae	Chl., P.	Chl., P.	1	Died	Meningitis, purulent Pneumonia
O. A.	13 months	female	Meningococcus	P., Chl.	P., Chl.	33	Survived	
T. Z.	5 years	male	Meningococcus	P., T., Chl., Methi., Genta., Nevi., Ery., Kana., Oxa.	P., Chl.	18	Survived	
Cs. J.	2½ years	male	Meningococcus	P., Chl., Ery., Ce.	P., Chl.	64	Survived	
S. É.	1½ years	female	Not isolated		Ce., Methi.	1	Died	Meningitis, purulent Laryngotracheobronchitis
K. J.	2 months	male	Not isolated		P., T.	5	Died	Meningitis, purulent

D. F.	12 years	male	Not isolated		P., Chl.	28	Survived	
D. Z.	7 years	male	Meningococcus	P., T., Methi., Ery.	P.	26	Survived	
B. M.	4 months	male	Klebsiella	T., Methi. Ce., Fu.	P., Str., i. th. P.	1	Died	Otitis media Meningitis, purulent
K. B.	12 years	male	Meningococcus	P., Str.	P., Str.	14	Survived	
R. J.	2 years	female	Meningococcus	P., Str., T., Neo., Ery.	P., Methi., T., Ery.	24	Survived	
B. T.	2 years	male	Meningococcus	P.	P.	16	Survived	
Ny. T.	7 months	male	Pneumococcus	P., T., Methi., Genta. Ery., Ce., Fu.	P. i. th. P.	66	Survived	
N. A.	3½ months	male	Not isolated		P., Chl.	35	Survived	
H. I.	3 months	female	Pneumococcus	P., Au.	P., Methi. i. th. P.	1	Died	Meningitis, purulent
B. G.	2 years	male	Not isolated		P., Chl.	23	Survived	
F. M.	3 years	female	Not isolated		P.	14	Survived	
B. K.	10 months	male	Not isolated		P., Chl.	18	Survived	
K. I.	7 months	male	Meningococcus	P., Chl.	P., Chl.	50	Survived	
Á. É.	13 months	female	Meningococcus	P., Str., T., Chl., Neo., Ery., Si., Oxa.	P.	19	Survived	
L. B.	14 months	male	Meningococcus	P., T., Chl., Str., Neo., Ery.	P., Sulpha.	30	Survived	
O. J.	8 months	male	Pneumococcus	Oxa., Chl., Si, Fu.	P., Chl. Oxa.	1	Died	Meningitis, purulent Otitis supp. Pneumoc. pneumonia. Patency of duct. arteriosus
K. Gy.	1½ years	female	H. influenzae	Neo., Chl., Ery., Fu.	Chl., Ery., Sulpha., Deco.	65	Survived	
H. Cs.	2 years	male	Meningococcus	P., Chl.	P., Chl.	21	Survived	
E. L.	6 months	female	Pneumococcus	P.	P.	6	Died	Meningitis, purulent Pyelonephritis
B. L.	5 months	male	Meningococcus	P., Chl., T.	P., Chl.	30	Survived	

Abbreviations: P: penicillin Str: streptomycin Methi: methicillin Neo: neomycin Nevi: nalidixic acid Deco: decomycin
Chl: chloramphenicol Ce: cefaloridine Oxa: oxacillin Kana: kanamycin Ery: erythromycin Sulpha: sulphonamides
T: tetracycline Fu: furadantin Si: sigmamycin Genta: gentamycin Au: aureomycin

TABLE VI

Serum immunoglobulins in infants and children with purulent meningitis

Age	Serum IgG, mg/100 ml	Serum IgA, mg/100 ml	Serum IgM, mg/100 ml	Microorganism and outcome
Control				
3—5 months	460 (340— 790)	11 (5—44)	47 (20— 88)	
6—8 months	510 (250— 850)	16 (6—47)	50 (30—100)	
1—2 years	600 (400— 900)	25 (8— 34)	60 (30—120)	
7> years	1100 (750—1500)	125 (50—308)	90 (56—200)	
Patients				
3 months	240	20	36	H. influenzae Died
5 months	900	168	160	Meningococcus Survived
6 months	2280	—	40	Pneumococcus Died
6 months	260	—	96	Meningococcus Survived
7 months	40	40	96	Pneumococcus Survived
7 months	320	40	98	Meningococcus Survived
8 months	1000	80	78	Pneumococcus Died
1½ years	840	96	304	Pneumococcus Survived
2 years	1640	280	164	Meningococcus Survived
2 years	1320	60	116	Meningococcus Survived
7 years	760	—	100	Meningococcus Survived

of whom low serum IgM concentrations were associated with low meningococcal antibody-titres; 3 of the 8 children contracted meningococcal meningitis.

EEG findings. It is generally accepted that in the early stage of purulent meningitis the main signs are a change of background activity and a 1.5—2.0 c/sec delta activity with variable localization, amplitude and extent [3, 8]. PLANTUREUX [9] emphasized the correlation between the change of consciousness and EEG activity. Other authors [4, 8] pointed out that among cases of meningitis, the meningococcal disease causes the slightest electric changes, and these are readily reversible. This observation is the more important as culturing meningococcus from the CSF is not always successful and in these

cases a rapidly improving EEG as an indirect sign may be helpful in diagnosing meningococcal infection. The EEG findings show a rather close correlation with the kind of causative microorganism, and are naturally influenced by the length of the period elapsed before instituting therapy. One of the most important roles of the EEG is its ability to assess the activity of the process. According to our experience, in the presence of continuous high-voltage delta activity antibiotic treatment should by all means be continued. The appearance of spike potentials does not necessarily mean an epileptogenic focus; in the majority of cases they are not accompanied by convulsions but are reliable signs of developing complications and of damage, and need continuous checking for a long time during convalescence and after recovery.

Therapy. Having made the diagnosis by lumbar puncture, symptomatic and antibiotic treatment should be started without delay. If bacterial identification from the CSF is unsuccessful or the result is dubious, the following regime is recommended.

1. Combination of penicillin + gentamycin or kanamycin, especially in young infants, in view of the high probability of *E. coli* and other Gram-negative infections.

2. Combination of penicillin + chloromycetin.

3. Ampicillin alone or together with some other antibiotic.

If sensitivity in vitro does not correspond to the previously chosen antibiotic or if there is no clinical effect, another antibiotic should be given. The duration of treatment is guided by the clinical symptoms, the blood and CSF biochemical tests, and by the type of the microorganism. The lumbar puncture has to be repeated after 24—48 hours and before the discontinuation of therapy. Subdural collections of fluid, mainly in infancy, are frequent complications.

In meningococcal meningitis the therapy of choice is penicillin-G. The recommended dose is 400 000 units per kg body weight per 24 hours, given in 6 equal intravenous doses injected over 2—10 minutes or in continuous drip. Intramuscular administration is also effective but painful and may cause local tissue damage. Sulphonamides for early treatment are recommended only if intravenous administration is possible; after the 2nd or 3rd day they may be given in doses of 100 mg/kg for 8—10 days.

In pneumococcal meningitis, the most effective antibiotic is penicillin-G in high doses: 4—12 million U/day in infusion. This high dose is to be maintained at least for 10—14 days. Further management is guided by the clinical picture and CSF findings and treatment should not be discontinued on the basis of one negative CSF finding since relapses occur frequently.

In Haemophilus influenzae meningitis, chloromycetin and ampicillin are the most effective drugs. The starting dose of chloromycetin is

200 mg/kg/day in the first days, 100 mg/kg/day later, divided in 4 doses and administered intramuscularly. In later stages, oral treatment is also possible. Ampicillin is given in doses of 300 mg/kg/day and later 150 mg/kg/day, for two weeks at least [1].

Resistance against penicillin is common in staphylococcal meningitis. The drug of choice is semi-synthetic penicillin (methicillin, oxacillin, etc.) given intravenously for 2—3 days. If necessary, on the basis of the sensitivity tests, some new antibiotic has to be started and given for 8—10 days until the clinical symptoms disappear.

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