

## **RECURRENT MENINGITIS IN CHILDHOOD\***

**(Hacettepe Series of 53 cases)**

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Bacterial meningitis in childhood carries a 10-15% mortality rate and can cause significant neurological damage in the children who recover<sup>1</sup>. Inadequate antibacterial treatment in these patients may lead to further attacks. Congenital and acquired gross anatomic defects of the central nervous system, parameningeal foci of infection (sinus or mastoid) and impaired antibacterial or immune responses can also cause recurrences<sup>2-5</sup>. It is obvious that repeated episodes of bacterial meningitis increase both the sequelae and the mortality rate. Prevention of the predisposing factors requires cure of the infection, closure (insofar as possible) of any anatomic defects and repair of any defects in the dura mater. The success of treating recurrent meningitis ultimately depends not only on the appropriate use of antibiotics during the recurrence itself but also on the effective treatment of its cause. A paramount problem in cases of recurrent meningitis is therefore determining the cause of the recurrence<sup>4</sup>.

The aim of this study, based on the investigation of patients treated for recurrent meningitis at Hacettepe Children's Hospital over a ten-year period, is to determine the cause of recurrence and to compare various diagnostic methods, the results of treatment and the prognosis in available follow-up patients.

### **Material and Methods**

A total of 53 patients with recurrent meningitis were studied at Hacettepe Children's Hospital from 1969 to 1979. Thirty-nine of the 53 were boys (73%) and 14 were girls (27%). The ages of the patients ranged from 0 to 17 years. In establishing past history, questions relating to head trauma in particular were asked of the patients or parents. In the physical examination, midline defect and parameningeal foci of infection were especially sought. In addition to the routine laboratory tests, a

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number of special tests selected on the basis of each patient's history and physical findings were performed, such as CAT scan of the brain, isotopic cisternography or brain scintigraphy, myelography, angiography, pneumoencephalography and ventriculography.

## Results

Six (11%) of the 53 patients died, 12 (22%) showed neurological sequelae and the remaining 35 (67%) recovered. Recurrences of meningitis ranged from 2 to 11 times, as shown in Table I. The following were found as predisposing factors contri-

TABLE I  
OUTCOME OF THE 53 RECURRENT MENINGITIS CASES

| Number of<br>recurrences<br>of meningitis | Number of<br>cases | Outcome           |                          |              |
|-------------------------------------------|--------------------|-------------------|--------------------------|--------------|
|                                           |                    | Total<br>recovery | Neurological<br>sequelae | Exitus       |
| 2                                         | 33                 | 23                | 7                        | 3            |
| 3                                         | 9                  | 6                 | 2                        | 1            |
| 4                                         | 4                  | 2                 | 1                        | 1            |
| 5                                         | 5                  | 3                 | 2                        | —            |
| 9                                         | 1                  | —                 | —                        | 1            |
| 11                                        | 1                  | 1                 | —                        | —            |
| Total and<br>percent                      | 53                 | 35<br>(66.1%)     | 12<br>(22.6%)            | 6<br>(11.3%) |

buting to recurrence: head trauma (28 cases); infections such as sinusitis, otitis media, mastoiditis and brain abscess (14 cases); subdural collections (2 cases); dermoidal sinus (2 cases); immunological deficiency (one case of Bruton's disease); splenectomy due to hemolytic anemia (one case) and Mollaret's meningitis (one case). It was not possible to determine the predisposing factors in four cases (Table II).

*Physical examination (acute stage):* The attacks, which occurred suddenly, consisted of headaches, neck pains and stiffness persisting for several days, vomiting, fever and changes of consciousness. The Kernig and Brudzinski signs were usually positive. Some of the patients had motor deficits and paresis or paralysis of the cranial nerves (Table III).

TABLE II  
**PREDISPOSING FACTORS OF RECURRENT MENINGITIS IN THE  
 HACETTEPE SERIES**

|                                             | <u>Number of cases</u> |
|---------------------------------------------|------------------------|
| — Head trauma                               | 28                     |
| Location of the fracture in the skull x-ray |                        |
| Frontal bone                                | 5                      |
| Orbita                                      | 2                      |
| Petrous bone                                | 2                      |
| Temporal bone                               | 1                      |
| Ethmoid bone                                | 1                      |
| — Focal infections*                         | 14                     |
| Otitis media                                | 5                      |
| Mastoiditis                                 | 5                      |
| Sinusitis                                   | 7                      |
| Brain abscess                               | 2                      |
| — Dermoidal sinus                           | 2                      |
| — Subdural collections                      | 2                      |
| — Immunological disorder                    | 1                      |
| — Splenectomy due to hemolytic anemia       | 1                      |
| — Mollaret's meningitis <sup>18</sup>       | 1                      |
| — Unknown causes                            | 4                      |

\* Some patients have more than one focal infection.

**Laboratory examination:** The changes in spinal fluid during the acute phase were characterized by pleocytosis with predominance of polymorphonuclear neutrophils, increased protein levels and decreased sugar levels—typical findings of purulent meningitis.

**Bacteriological examination:** Some of the patients had been treated by antibiotics before admission to the hospital. In such instances it was impossible to grow the microorganism in cerebrospinal fluid (CSF). However, the microorganism was isolated in CSF in 22 patients. The following were found: pneumococcus (10 cases), *E. coli* (2 cases), pyocyanic (2 cases), *Staphylococcus aureus* (2 cases),

Klebsiella (2 cases), Neisseria meningitidis (2 cases), Pseudomonas (2 cases) and Salmonella paratyphi A (1 case) (Table III). Some of the pertinent laboratory findings are summarized in Table IV.

*Treatment:* Penicilline crystalise (500.000 U/kg/day) and chloramphenicol (100 mg/kg/day) were given intravenously to all patients during the acute phase. In addition to antibiotics, a surgical operation for brain abscess was performed on two patients and subdural punctures were done in another two patients. After the acute phase prophylactic penicillin (Penadur) was given to patients on a long-term basis.

TABLE III

**CLINICAL SYMPTOMS AND SIGNS AND MICROORGANISMS  
OBSERVED IN RECURRENT MENINGITIS IN THE HACETTEPE SERIES**

| <u>Symptoms and signs</u>    | <u>Number of cases</u> |
|------------------------------|------------------------|
| Convulsion                   | 16                     |
| Motor deficits               | 7                      |
| Cranial nerve paralysis      | 14                     |
| VIIth Nerve                  | 7                      |
| Central type paralysis       | 1                      |
| VIIIth Nerve                 | 3                      |
| VIth Nerve                   | 2                      |
| IIIrd Nerve                  | 1                      |
| Aphasia                      | 2                      |
| Cortical blindness           | 1                      |
| Diplopia                     | 1                      |
| <u>Microorganisms in CSF</u> |                        |
| Pneumococcus                 | 10                     |
| E. coli                      | 2                      |
| Pyocyanic                    | 2                      |
| Staphylococcus aureus        | 2                      |
| Klebsiella                   | 2                      |
| Neisseria meningitidis       | 2                      |
| Pseudomonas                  | 1                      |
| Salmonella paratyphi A       | 1                      |

TABLE IV  
**LABORATORY FINDINGS IN THE HACETTEPE SERIES OF  
 RECURRENT MENINGITIS**

| <u>Laboratory tests</u>             | <u>Abnormalities</u>                       | <u>Number of cases</u> |
|-------------------------------------|--------------------------------------------|------------------------|
| X-ray — skull                       | Fracture                                   | 11                     |
|                                     | Mastoiditis                                | 8                      |
|                                     | Sinusitis                                  | 8                      |
|                                     | Increased intracranial pressure            | 6                      |
|                                     | Spinal defect                              | 1                      |
| — vertebrae                         |                                            |                        |
| Computerized axial tomography (CAT) | Right frontal tumor                        | 1                      |
|                                     | Ventricular dilatation and frontal atrophy | 1                      |
| Isotopic cisternography             | Blockage of CSF circulation                | 6                      |
|                                     | Leak of CSF                                | 4                      |
|                                     | Hydrocephaly                               | 2                      |
| Brain scintigraphy                  | Tumor                                      | 3                      |
| Angiography                         | Hydrocephaly                               | 5                      |
| Myelography                         | Blockage                                   | 3                      |
| Venography                          | Lateral sinus thrombosis                   | 1                      |
| Immunological tests                 | Immunological deficiency                   | 1                      |

## Discussion

The success of any antibiotic in the treatment of bacterial meningitis depends on its antibacterial properties and the concentration that remains in the blood and CSF after systemic administration. With modern antibiotics, the majority of cases can be treated without serious complications<sup>4,6</sup>. Even with proper treatment, however, certain factors can predispose to further attacks in some patients. These include congenital or acquired anatomic defects in dura mater or in the bone adjacent to the dural defect (such as meningocele, meningomyelocele, encephalocele, encephalocystocele, dermoid sinus, intracranial epidermoid cysts) and parameningeal focal infections, immunological deficiency, sickle cell anemia, leukemia, lymphoma, asplenia and splenectomy<sup>2-16</sup>. Whitecar et al<sup>17</sup> also discussed the infectious agent of *Diplococcus pneumoniae*, without establishing the source of origin.

In this series, 28 of the 53 patients with recurrent meningitis (53%) had a history of head trauma occurring anywhere from a few days to several years before the

attacks. Eleven of the 28 patients with head trauma had fractures, of which five were located in the frontal area as seen in the skull x-rays (Table II). The trauma leading to recurrent meningitis may not necessarily have been severe, however. In some cases the head trauma had seemed so insignificant that it had been forgotten by the patients or parents and only recalled as a result of extensive questioning. The presence of fracture might also be clinically or radiologically obscure. Experience suggests that careful and specifically directed questions are often necessary to elicit reports of significant trauma in many patients. Although cerebrospinal rhinorrhea or otorrhea is an important clue, these signs are often lacking even in the presence of skull fracture with dural tears and may be missed in the absence of careful history. The dural defect may not be found despite careful studies, including surgical exploration in some patients. In such patients radioactive studies should be done in order to show the leak. In the Hacettepe series, cisternography revealed CSF leakage in four patients who had dural defect, including one with no known history of head trauma, and the blockage of CSF circulation in 6 patients (Table IV).

Meningitis may recur even after successful surgery (such as surgery to repair anatomic defects, operations on parameningeal foci of infection, or surgical intervention for space-occupying lesions in the brain). In the Hacettepe series, meningitis occurred repeatedly in three patients who had had brain operations.

The second most important predisposing factor in this series, involving 14 cases or 26% of the total, was infection, including otitis media, mastoiditis, sinusitis and brain abscess. Therefore, infection should be looked for carefully. Pneumococci were found in the CSF of 10 patients (45%). *Pneumococcus* takes first place among microorganisms reported in the literature followed by *Hemophilus influenzae* and *Staphylococcus*.

Dermal sinus tracts originating in the midline may expose the spinal or cerebral subarachnoid space to the skin surface, and superimposed infection can lead to a further attack of meningitis. It has been recommended that the scalp be shaved at the midline and that the midline skin be inspected from the bregma over the vertex and suboccipital area to the tip of the coccyx. Careful inspection may reveal a sinus opening, an area of inflammation of the soft tissues, tufts of hair or an abnormal discharge<sup>7</sup>.

In this series, two patients with dermoid sinus were followed and treated surgically, after which the meningitis did not recur.

Other causes of recurrence revealed in this study were: immunologic disorder, subdural collections, splenectomy due to hemolytic anemia and Mollaret's meningitis<sup>18</sup>. These predisposing factors must be considered among the causes of recurrence if there is no history of head trauma or infections and no clue of dural defect. In the absence of these, pertinent laboratory methods have to be used.

Relatively high rates of mortality (11%) and neurological sequelae (22%) were found in our study. These rates could be decreased if in addition to the antibiotic treatment in acute stages the causes of recurrence were identified and treated. It is therefore very important to take careful and detailed histories and to make complete physical and neurological examinations. Pertinent laboratory methods should be selected to reveal the cause of recurrence. In some cases it is impossible to identify the cause even with complete studies. Continuous prophylactic antibiotics should be helpful in preventing further attacks.

## Summary

In this study, 53 cases (39 boys and 14 girls) with recurrent meningitis seen at Hacettepe Children's Hospital were evaluated. Six (11%) patients died and 12 (22%) showed neurological sequelae. Recurrences of meningitis ranged from 2 to 11 times. Head trauma (28 cases), infection (14 cases), subdural collection (2 cases), dermoidal sinus (2 cases), immunological deficiency (1 case), hemolytic anemia and splenectomy (1 case) and Mollaret meningitis (1 case) were the identifiable causes of recurrence. Pneumococcus was isolated in the CSF of 45% of the cases for which the culture was grown. Various methods to determine the cause of recurrence and appropriate treatment in addition to antibiotics were discussed.

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