POSTGRADUATE COURSE

INFECTIONS OF THE CENTRAL NERVOUS SYSTEM REQUIRING EMERGENCY TREATMENT

Donald M. McLean, M.D.
The Research Institute of the Hospital for Sick Children, Toronto, Canada

Acute infections of the central nervous system always require prompt and adequate treatment. Before treatment is commenced, an accurate etiologic diagnosis should be established whenever possible. The familiar picture of acute pyogenic meningitis with rapid onset of high fever, headache, neck stiffness, vomiting and drowsiness or irritability requires no amplification, but meningitis should always be suspected in infants less than 12 months of age who become febrile and do poorly for no apparent reason. The presence of a few petechiae usually indicates possible meningococcemia, which should always be treated promptly with antibiotics, even though meningeal signs are minimal. However an overwhelming meningococcal septicemia may cause numerous petechiae and severe acute peripheral circulatory failure, which frequently may terminate fatally.

DIAGNOSTIC PROCEDURES

The most useful clinical diagnostic procedure in all cases of suspected infection of the central nervous system is lumbar puncture. Despite the presence of increased intracranial pressure in many instances, this procedure is safe if the child is held horizontally in the left or right lateral position. Cerebrospinal fluid containing 100 to 2,000 polymorphonuclear cells per cubic millimeter, with a glucose level below 50 mg/100 ml, is indicative of purulent meningitis, and Gram-staining of a smear of the fluid will frequently reveal the nature of the infecting organism. The combination of decreased glucose level, mixed polymorphonuclear plus lymphocytic cell response, and pellicle formation on holding cerebrospinal fluid overnight, is suggestive of tuberculous meningitis. Frequently acid-fast rods, morphologically typical of Mycobacterium tuberculosis, may be observed in smears of pellicles stained by the Ziehl-Neelsen method. The presence of 80% or more lymphocytes in cerebrospinal fluid in the presence of a normal glucose level is characteristic of aseptic meningitis due to viruses. A leukocyte count between 10 and 500/mm³ in cerebrospinal fluid is encountered more frequently in enterovirus infections, but counts between 500 and 5,000/mm³ occur commonly in mumps meningoencephalitis (Table I). Some cerebrospinal fluid should always be forwarded for culture of bacteria or viruses.

Frequently children with meningitis present with convulsions. At the Hospital for Sick Children, all children who have had a convulsion receive a lumbar puncture, except those patients who regularly develop a convulsion at the beginning of each febrile episode, or those who are known epileptics. The presence of polymorphonuclear cells in cerebrospinal fluid indicates meningitis. Convulsions must be controlled promptly by the intramuscular use of paraaldehyde or an ether anesthetic administered by open mask.

PYOGENIC MENINGITIS

In the case of pyogenic meningitis, three features in addition to convulsions require
prompt treatment: 1) the infecting organism, 2) dehydration and 3) shock, if present. This therapeutic regimen should be commenced in the emergency department of a hospital immediately after the diagnosis is made. An intravenous infusion is set up, and a solution containing 2 parts of a 5% solution of glucose and one part 0.85% saline solution, alternating with 5% glucose, is administered at the rate of 50 ml/lb/day. This is used for administration of antimicrobial therapy and corticosteroids if required. Vomiting ceases rapidly following withdrawal of all fluids by mouth. When dehydration is controlled, the rate of flow of fluids may be lessened, and the infusion is discontinued when the patient tolerates adequate amounts of fluids administered orally.

For hemophilus influenzae type B meningitis, the therapy of choice is chloramphenicol, 20 mg/lb, twice daily for 3 days, followed by 20 mg/lb/day intramuscularly. Chloramphenicol should be administered for a minimum of 7 days, and the temperature and clinical state of the patient should be normal at least 2 days before cessation of the therapy. The chloramphenicol may be combined with sulfisoxazole (Gantrisin) ½ gr/lb intravenously at once (up to 30 gr), and followed by ½ gr/lb up to 15 gr every 4 hours, or 6 gm per 24 hours. Sulfisoxazole should be administered intravenously at first, followed by oral administration subsequently.

For meningococcal infections sulfisoxazole should be administered as for H. influenzae infections. This may be combined with penicillin G crystalline, 500,000 units every 6 hours. In pneumococcal infections 2 million units of penicillin should be administered every 2 to 4 hours in combination with sulfisoxazole.

If the identity of the infecting organism is not known, the "unknown purulent meningitis" regimen of chloramphenicol and sulfisoxazole as for H. influenzae and penicillin as for meningococci should be instituted.

In staphylococcal meningitis, frequently

---

### TABLE I

**CEREBROSPINAL FLUID FINDINGS AND THERAPY IN MENINGITIS**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Polymorphonuclear cells (per mm³)</th>
<th>Lymphocytes (per mm³)</th>
<th>Protein (mg/100 ml)</th>
<th>Sugar (mg/100 ml)</th>
<th>Gram-stain</th>
<th>Peripheral Blood Findings</th>
<th>Antimicrobial Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilus influenzae, type B</td>
<td>100–4,000</td>
<td>40–100</td>
<td>0–50</td>
<td>0–50</td>
<td>Gram-negative rods</td>
<td>Neutrophilia</td>
<td>Chloramphenicol, 20 mg/lb q1h; sulfisoxazole, ½ gr/lb q4h*</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>100–2,000</td>
<td>40–100</td>
<td>0–50</td>
<td>0–50</td>
<td>Gram-negative diplococci</td>
<td>Neutrophilia</td>
<td>Sulfisoxazole, ½ gr/lb, q4h; Penicillin G, 500,000 units, q6h†</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>100–2,000</td>
<td>40–100</td>
<td>0–50</td>
<td>0–50</td>
<td>Gram-positive diplococci</td>
<td>Neutrophilia</td>
<td>Sulfisoxazole, ½ gr/lb, q4h; penicillin G, 1 X 10⁴ units q4h</td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>100–2,000</td>
<td>40–100</td>
<td>0–50</td>
<td>0–50</td>
<td>Gram-positive cocci in clusters</td>
<td>Neutrophilia</td>
<td>Methicillin, 50 mg/lb/day† and chloramphenicol or bacitracin, according to sensitivity of bacterium</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>100–2,000</td>
<td>40–100</td>
<td>0–50</td>
<td>0–50</td>
<td>Gram-negative rods</td>
<td>Neutrophilia</td>
<td>Chloramphenicol, 20 mg/lb q1h; sulfisoxazole, ½ gr/lb q4h</td>
</tr>
<tr>
<td>Enterovirus</td>
<td>10–500</td>
<td>40–100</td>
<td>60–100</td>
<td>0–100</td>
<td>No organisms</td>
<td>Leukopenia; relative lymphocytes</td>
<td>None</td>
</tr>
<tr>
<td>Mumps</td>
<td>100–5,000</td>
<td>40–100</td>
<td>60–100</td>
<td>0–100</td>
<td>No organisms</td>
<td>Leukopenia; relative lymphocytes</td>
<td>None</td>
</tr>
</tbody>
</table>

* Sulfisoxazole may be prescribed in addition to chloramphenicol.
† Penicillin may be prescribed in addition to sulfisoxazole.
† Trade names are Staphycillin or Celbenin.
the infecting organism is insensitive to penicillin G. Therefore methicillin (Celbenin), 50 mg/lb, may be administered every 6 hours; or chloramphenicol, bacitracin or other antibiotic may be prescribed according to the spectrum of antibiotic sensitivity of the organism.

Meningitis due to Escherichia coli is sometimes encountered, especially during the newborn period. Treatment is with chloramphenicol and sulfisoxazole as in H. influenzae meningitis.

In the case of aseptic meningitis due to mumps or enteroviruses, antibiotics should not be administered at all. However full supportive measures should be instituted, including intravenous infusion of fluids and electrolytes to control dehydration and salt loss due to vomiting.

In children with pyogenic meningitis who develop acute peripheral circulatory failure, cortisone, 5 mg/lb/day, or hydrocortisone sodium succinate (Solu-Cortef), 4 mg/lb/day, should be administered intravenously in four or more divided doses each day for 3 days, the maximum daily dosage being 300 mg cortisone or 250 mg hydrocortisone. This may be combined with administration of the adrenocorticotrophic hormone (Duracton), 20 to 40 units per day intramuscularly. It has been suggested that the adrenocorticotrophic hormone may antagonise the depressant effects of large doses of cortisone on the adrenal cortex. The organism found most frequently in meningitis complicated by shock is the meningococcus.

MEASLES ENCEPHALITIS

Encephalitis may supervene following an attack of measles in 1:250 to 1:700 cases. Signs of encephalitis, including irritability, drowsiness, convulsions or coma, frequently appear within 2 to 7 days after onset of morbilliform rash. Administration or gammaglobulin has had no effect on the course of the disease or the development of sequelae. Following the use of corticosteroids, the course of illness was shortened and the development of sequelae was lessened in some series, but other investigators observed little effect of corticosteroids on the duration of illness or occurrence of sequelae. At present at the Hospital for Sick Children the effect of corticosteroids on the clinical course and sequelae is under observation following admission of an unusually large number of patients with measles encephalitis between January and April, 1961. We have administered hydrocortisone, 4 mg/lb/day, in 4 or more divided doses until definite improvement is shown and consciousness is regained. Should coma persist for several weeks, corticosteroids should be continued until consciousness has been regained. Our early clinical impression is that more rapid improvement follows the use of corticosteroids in measles encephalitis, but no control patients who did not receive corticosteroids were studied during the 1961 outbreak.

In the case of uncomplicated measles, or measles with hyperpyrexia in the absence of encephalitic signs, administration of corticosteroids is inadvisable.

Between 1955 and 1960, 50 patients with measles encephalitis were admitted to the Hospital for Sick Children, 4 of whom subsequently died. In 35 cases the ages ranged between 4 and 7 years. In 38 instances symptoms of encephalitis supervened 2 to 4 days after onset of typical measles rash. The onset was abrupt with convulsions in 26 patients, 21 of whom were admitted comatose; but the onset was more insidious in 24 cases. Among 48 patients from whom cerebrospinal fluid was obtained, 37 had between 1 and 500 leukocytes/mm³. The cells were almost exclusively lymphocytes. However 19 spinal fluids had fewer than 10 leukocytes/mm³; 11 of these had none. Corticosteroids and/or corticotropin were administered to 17 patients, 11 of whom were discharged well, but 3 were discharged with some impairment, and 3 died. However only one patient developed long-standing sequelae. Of the 33 patients who received no corticoids, 25 were discharged well, 7 were incompletely recovered, and 1 died. On subsequent ex-
amination six patients had long-standing sequelae, but 27 had recovered completely. There was a tendency to retain patients on corticoid treatment in the hospital for longer periods than those who did not receive hormones.

A medical emergency may arise both in acute poliomyelitis and acute ascending polyneuritis (Guillain-Barré syndrome) following involvement of cord centers or bulbar nuclei which control respiration. Especially in the case of poliomyelitis, respiratory difficulty may become accentuated by pooling of secretions in the pharynx as a result of paralysis of striated muscle in the palate and pharynx. Hyperventilation and interrupted halting speech are characteristic early signs of respiratory muscle weakness, and these are followed by flaring of the alae nasae, recruitment of the accessory muscles of respiration, anxiety, restlessness and disorientation. Rising blood pressure may be observed, with increasing respiratory insufficiency, owing to accumulation of carbon dioxide in blood. (The use of mechanical apparatus in artificial respiration, such as the Bird respirator and the tank respirator, has been described elsewhere by Dr. A. W. Conn.) Paralysis of the palate and pharynx requires emergency treatment with elevation of the foot of the bed, nursing the patient in the prone or semi-prone position, and frequent suctioning of the pharynx. Occasionally maintenance of a clear airway in pharyngeal paralysis is impossible, and tracheotomy becomes necessary. Children with acute epiglottitis may sometimes present with pallor and ashen complexion without gross hyperemia of the buccal and epiglottis or croupy cough and stridor, but they are distinguished from those with poliomyelitis by the absence of neck stiffness or paralysis of skeletal musculature.

**GUILLAIN-BARRÉ SYNDROME**

Differentiation between acute poliomyelitis and Guillain-Barré syndrome includes the following points. 1) In poliomyelitis, paralysis usually is not distributed symmetrically, and characteristically the paralysis shows no further progression within a few hours after onset. In the Guillain-Barré syndrome paralysis is symmetrical, commencing in the distal portions of the lower extremities or occasionally in the upper extremities, and its level ascends steadily for several days, so that the upper limbs and diaphragm may be involved also. 2) In poliomyelitis the cerebrospinal fluid usually shows lymphocytosis, with the cell count ranging between 20 and 500/mm³, accompanied by a slightly increased protein content not exceeding 100 mg/100 ml. In the Guillain-Barré syndrome few cells are detected in the cerebrospinal fluid, but the protein level regularly becomes elevated to between 100 and 200 mg/ml. 3) Although poliovirus may be isolated regularly from stools of patients with acute poliomyelitis, it is extremely uncommon to isolate viruses from patients with the Guillain-Barré syndrome.

**SUMMARY**

Discussion of clinical recognition and differential diagnosis of purulent meningitis in children, and especially infants, is followed by an outline of therapeutic regimens currently employed at the Hospital for Sick Children. The clinical features and use of steroids in measles encephalitis are outlined. The differential diagnosis between poliomyelitis and the Guillain-Barré syndrome is discussed, together with points regarding early management of respiratory complications.

**REFERENCES**

POSTGRADUATE COURSE: INFECTIONS OF THE CENTRAL NERVOUS SYSTEM REQUIRING EMERGENCY TREATMENT

Donald M. McLean

*Pediatrics* 1961;28;1020

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://pediatrics.aappublications.org/content/28/6/1020