Bacterial Meningitis: Bugs' Story

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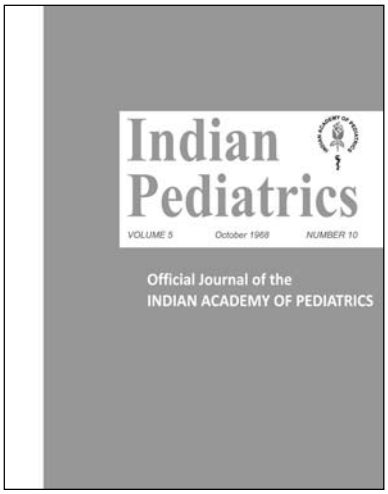
The October 1968 issue of Indian Pediatrics included three original research articles: ocular manifestations in tuberculous meningitis, evaluation of diagnostic methods for iron deficiency anemia, and changing patterns of purulent meningitis. Through this write-up, we highlight the changing pattern of acute bacterial meningitis in children over the past five decades.



THE PAST

The study by Vashi, *et al*. [1] described details of 69 children diagnosed as purulent meningitis admitted at JJ Hospital (Bombay, India) from January 1963 to June 1966. They obtained a detailed history regarding current and past symptoms, and conducted a detailed physical examination, especially of the central nervous system. This was followed by investigations such as complete blood count, cerebrospinal fluid (CSF) examination, tuberculin test, blood culture, throat swab, and *X*-rays of the chest, mastoid and sinuses. Special investigations like gastric lavage for acid-fast bacillus (AFB) stain, subdural tapping, pneumoencephalogram, and animal inoculation of CSF were performed in selected cases.

Acute bacterial meningitis contributed to 8% of total hospital admissions (1 case of purulent meningitis per 120 admissions in hospital). Majority (58%) of patients were below one year of age. The number of patients was more during the winter seasons closely paralleling the incidence of respiratory diseases. The mortality was quite high but showed a sequential decline over the study period – 59% in 1963, 33% in 1965, and 17% in first half of 1966. They attributed this trend to quicker diagnosis and quicker treatment. The mortality in neonates was to the tune of 62%. The presenting features were fever, vomiting, refusal to feed, headache, seizures and altered sensorium in form of irritability and delirium. The signs of meningeal irritation were present in 60-80% patients above 3 years of age, while cranial nerve palsies and hemiparesis were reported in 6-10% cases. The children <2 years of age showed bulging fontanelle (90% patients with open fontanelle). CSF findings showed increased pressure, pleocytosis, high protein content with low sugar content. A causative organism could be detected in 50% of cases; 20% grew menigococci on culture while pneumococci, coagulase-negative staphylococci, *Hemophilus influenzae*, *Staphylococcus aureus*, Pseudomonas and *E. coli* were also seen. Three patients showed a picture suggestive of partially treated pyogenic meningitis, later turning out to be tuberculous meningitis. Longer duration of treatment was required in patients with pneumococcal infection. In some cases, CSF had not cleared at discharge and on follow-up, the CSF normalized about one month after discharge. About one-thirds of patients could be followed-up for 6 months to 1 year. Neonates with subdural effusion seemed to be doing well. Hemiparesis was seen in five cases during the course of illness, out of which three had a complete remission within 3 weeks of follow up, while two had an improvement in 6-8 months. Two children with hydrocephalus succumbed to the illness. No complication of mental retardation or epilepsy was seen.

Historical background and past knowledge: Writers in the 17th and 18th centuries frequently referred to brain fever, phrensy, and cephalitis for patients who would today be classified as meningitis or encephalitis. Earliest described patients with 'phrensy' were defined as "those with continual raving, or a depravation of the chief faculties of the brain, arising from an inflammation of the meninges with a continual fever" by Thomas Willis in 1685 [2]. Meningococcal meningitis was first described

by Gaspard Vieusseux on a small outbreak in Geneva in 1805. The symptoms of meningitis were described by Russian physician Vladimir Kernig in 1882 and by Polish physician Jozef Brudzinski in 1909. The Kernig's sign and Brudzinski sign were described in 1882 and 1909, respectively [3]. Louis Pasteur identified the pneumococcus in 1881 while Anton Weichselbaum identified *Neisseria meningitidis* in 1887. In 1892-1893, Richard Pfeiffer reported on the isolation of what would later be called *Haemophilus influenzae*, and in 1882 Robert Koch identified *Mycobacterium tuberculosis* in tuberculous lesions from infected human tissues. The treatment with antiserum therapy for meningococcal meningitis began in 1906, but the introduction of penicillin therapy in 1944 provided the first effective treatment for meningitis. The introduction of a vaccine for *H. influenzae* type b (Hib) in the 1990s provided a marked reduction in the incidence of Hib meningitis.

THE PRESENT

In recent times, the advent of newer vaccines against Hib and Pneumococcus has changed the epidemiology of the disease as compared to the pre-vaccine era where both morbidity and mortality were quite high [4]. Highly effective antimicrobial therapy, when started early, results in good outcome. However, emerging problem of antibiotic resistance is of growing concern [5]. The phenomenon of indiscriminate antibiotic usage and frequent pre-treatment with antibiotics makes isolation of causative organism difficult and limits the choice of antibiotics. Hence, there is an increasing reliance on newer techniques like antigen detection by latex agglutination technique or DNA-based polymerase chain reaction (PCR).

Regarding changing trends in etiology of acute bacterial meningitis in children, *H. influenzae* type b was the leading cause of bacterial meningitis with high mortality among confirmed cases prior to the introduction of the pentavalent vaccine in India [6]. A recent hospital-based study from India documented that 82.9% of confirmed cases of childhood meningitis were positive for *S. pneumoniae*, 14.4% for *H. influenzae* type b, and remaining 2.7% cases were due to *N. Meningitides* [7].

Over the years, most countries have introduced vaccines against the common pathogens into their immunization schedules, which are also effective in preventing bacterial meningitis. The introduction of a pneumococcal conjugate vaccine in the US led to a decrease in the rate of infection by nearly 60% in children <5 years of age [8]. Hib vaccine introduction was followed by a dramatic decrease in the incidence of all invasive Hib disease, including meningitis. In a population-based observational study in England, annual incidence of *H. influenzae* meningitis, meningococcal disease and invasive pneumococcal disease showed a sharp decrease after the introduction of respective vaccines [9].

The Government of India has launched a program Mission Indradhanush on December 25, 2014 with an objective of increasing immunization coverage and to provide life-saving vaccines under Universal Immunization Program (UIP) to all children across the country free of cost. Pneumococcal conjugate vaccine was launched on May 13, 2017 and its introduction in the UIP is likely to have a great impact in further reducing child deaths from meningitis.

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