Personal Practice

Acute Bacterial Meningitis

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Acute bacterial meningitis (ABM) remains a common life threatening condition in children. In a multicentric survey in India, ABM constituted 1.5% of admissions in pediatric wards and the mean case fatality was 16%(1). Even though the mortality on account of this formidable disease has decreased over the years with the availability of potent antibiotics, a significant number of patients are left with neurological sequelae(2). The ultimate outcome rests on a number of factors besides control of infection and recent research on animal models has given insight into pathogenesis which may lead to development of innovative therapeutic strategies(3,4).

Epidemiology

ABM is essentially a disease of young children, mainly due to attenuated immunologic response in this age group. Nearly 95% of cases occur between 1 month and 5 years of age(5). Poor socio-economic condition, overcrowding, recent colonization with pathogenic bacteria, close contact with patients, splenic dysfunction, and cerebrospinal fluid (CSF) communications (congenital or acquired) across the mucocutaneous barrier are some of the host factors which increase the risk of meningitis(6,7). The widespread use of conjugate vaccine against *Haemophilns influenzae* type b in many developed countries has lead to decline in number of cases of meningitis(8).

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Etiology

Etiology of ABM is related to the age of the patient with the background of several host factors. During the first 2 months of life, *Escherichia coli* Kl and other Gram negative enteric bacilli, group B *Streptococcus* and *Listeria monocytogenes* are the usual offending organisms. In children between 2 months to 12 years, bacterial meningitis is primarily due to *H. influenzae* type b, *Streptococcus pneumoniae* and *Neisseria meningitidis.* The incidence and relative frequency of these bacteria differ markedly depending on geographic areas, genetic factors and usage of *H. influenzae* type b vaccine. Meningitis in infants between the age of 1-3 months may be due to pathogens found both in neonates and older children.

In children with severe malnutrition, compromised immunity or anatomical defects, infection can occur with other microbes like *Staphylococcus, Salmonella, Pseudomonas, etc.* Reports from developing countries indicate that a sizeable proportion of cases presumed to be bacterial in nature fail to demonstrate any pathogen(9,10).

Pathogenesis and Pathology

The mucosal surfaces in the nasopharynx are the initial site of colonization for the common meningeal pathogens. The exact mechanism by which bacteria invade CNS is not clear. For some organisms,

specific surface components as Kl polysaccharide antigen of E. coli are essential for attachment to mucosal surface and specific virulence(11). Invasion across the nasopha-ryngeal mucosa takes place by an endocytic process or through intercellular route by separation in apical tight junction of columnar epithelial cells(12). The sequence of events leading to inflammation and resultant damage is summarized in *Fig. 1*(11,13).

The fundamental pathological change in ABM is inflammation of leptomeninges with a meningeal exudate of varying thickness encasing the brain. The exudate extends into Virchow Robin spaces along the penetrating vessels. Involvement of vessels leads to phlebitis or arteritis and softening or necrosis of corresponding vascular territory. Cerebral edema develops early in the course of ABM and together with acute hydrocephalus it may be responsible for intracranial hypertension. Intracranial pressure (ICP) is maximally increased within first 48 hours. This in turn impedes cerebral perfusion resulting in neuronal injury. Nearly 30% of infants and children with ABM have a decreased cerebral blood flow (CBF) ranging from 30-70%(14).

Clinical Features

Early symptoms of meningitis in young children are often vague and ill defined. In general, younger the infant the more non-specific are the symptoms. The main symptoms which are highly suggestive of a diagnosis of ABM in infants are fever (with or without vomiting), alteration of behavior (infant becomes lethargic or drowsy, irritable, feeds poorly), a high pitched cry, seizures and a full or tense anterior fontanelle. Specific signs of meningeal irritation are hardly ever present in infants below the age of 2 years. In older children, classical

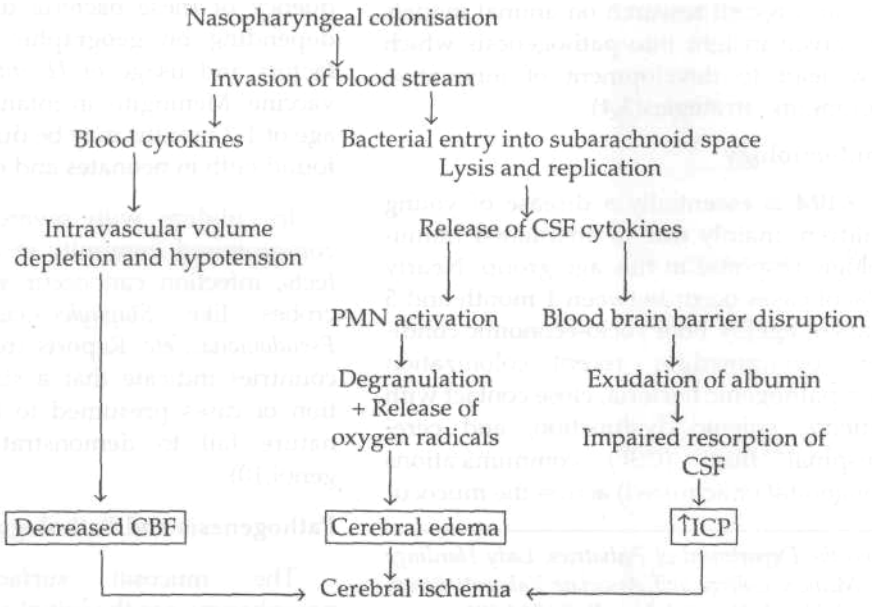

Fig. 1. Sequential steps in pathogenesis and pathophysiology of bacterial meningitis (Adapted from 11, 13). CBF-Cerebral blood flow; CSF-Cerebrospinal fluid; ICP-Intra-cranial pressure. PMN-Polymorphonuclear.

signs and symptoms of meningitis like fever, headache, vomiting, photophobia, neck stiffness and the meningeal signs are likely to be present. Neck stiffness is the most important of all meningeal signs and earliest to appear. It becomes more marked if tested while the patient sits up with knees extended. Kernig sign and Brudzinski sign are other meningeal signs. The meningeal signs are due to reflex muscle spasm in reaction to pain on stretching of contents of spinal cord. These signs may be absent in comatose patients.

The second mode of presentation is acute and fulminant in which manifestations of sepsis and meningitis develop rapidly associated with severe brain edema and raised ICP. This type of presentation is seen most often with *N. meningitidis*. Petechial hemorrhages appearing on the skin which rapidly coalesce producing areas of purpura are considered hallmark of this disease, although they may be seen in meningitis due to other organisms also. Profound hypotension and fatal shock has been reported in many series(15,16).

Seizures occur in about 30-40% cases of ABM. A high concentration of tumour necrosis factor (TNF) has been associated with occurrence of seizures(17). Alterations of mental status and reduced level of consciousness is common and is due to increased intra-cranial pressure (ICP), cerebritis or hypotension. Papilledema is uncommon in uncomplicated acute meningitis and when present suggests a more chronic process such as presence of intracranial abscess, subdural empyema or occlusion of dural venous sinus. Focal neurologic signs may be due to vascular occlusion, abscess formation or cortical infarction. Overall 14% of children of bacterial meningitis have focal neurological signs(2).

Reactive thrombocytosis is common during recovery from meningitis and implies favorable prognosis for survival(18).

Complications of Acute Bacterial Meningtitis

Complications of ABM can develop early in the course of illness or later after several days of therapy or may be noticed on follow up *(Table I)*.

Systemic Complications

Peripheral circulatory failure is a sudden life threatening complication of meningitis. It occurs most commonly with meningococcal infection but can accompany other types of infection. Antibiotic therapy may initially aggravate hypotension, hence intensive monitoring is required in the initial

TABLE *I*—*Complications and Sequelae of ABM.*

Complications	
Neurological	
	• Increased ICP
	• Seizures
	• Extra-axial fluid collection
	• Ventriculitis
	• Cranial nerve palsies
	• Hemi/quadriparesis
	• Hearing loss
	• Hydrocephalus
Systemic	
	• Peripheral circulatory failure
	• Disseminated intravascular coagulation
	• Syndrome of inappropriate secretion of anti-diuretic hormone (SIADH).
	• Arthritis
Sequelae	
	• Mental retardation
	• Seizures
	• Sensorineural hearing loss
	• Visual impairment
	• Behavioral problems
	• Motor deficits
	• Hydrocephalus
	• Learning disabilities

period(19). Other manifestation of acute bacterial sepsis may be seen as coagulopathy, acidosis and hypoglycemia.

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is seen in 30-50% of cases of ABM. It leads to cerebral edema and hyponatremic seizures. Later in course of therapy, central diabetes insipidus may develop as a result of hypothalamic or pituitary dysfunction(5).

Pneumonia, pericarditis and *arthritis* occur occasionally. *Prolonged fever* (> 10 days) is seen in some cases due to intercurrent viral infection, secondary bacterial infection, thrombophlebitis or a drug reaction. Secondary fever that is seen after an initial afebrile period is usually due to nosocomial infection.

Neurological Complications

Increased intracranial tension is present in almost all cases of ABM initially though only 1-3% of cases have persistent hydrocephalus(20). When ICP is very high, herniation of brain tissue may occur at the incisura or at foramen magnum and may lead to sudden respiratory arrest, sudden death or persistent vegetative state.

Seizures occur in about 30-40% of children with meningitis. Generalized seizures occuring within first four days are of no prognostic significance. Seizures that present after 4th day and those that are difficult to treat and those that appear late in the course of meningitis are associated with poor prognosis(5). Children with focal convulsions are more likely to have neurologic sequelae of meningitis. Causes of late onset seizures include cerebritis, subdural effusion, vascular thrombosis and abscess formation.

Subdural effusion develops in 10-30% of patients with meningitis and are more common in *H. influenzae* meningitis. These effusions are asymptomatic in 85-90% of cases. Effusions usually resolve during treatment and aspiration is required only in presence of increased ICP or a depressed level of consciousness. Subdural empyema requires more aggressive treatment in form of repeated tapping or operative treatment.

Alteration in level of consciousness and focal abnormalities like motor weakness and impaired vision may be seen during acute phase of illness. *Mental, retardation* is seen in upto 4.2% of cases(2). Intellectual and academic performance of children suffering form ABM due to *H. influenzae* did not differ from controls, though these children differed in need for special educational assistance, comprehension and reading(21). *Cranial nerve dysfunction* is transient with the exception of involvement of auditory and vestibular nerve complex. *Sensorineural hearing loss* is the most common sequele of ABM. Nearly 10%-25% of cases of ABM are left with permanent sensorineural hearing loss (SNHL)(2,22). The patients of ABM should have audiologic evaluation after recovery. Rarely visual loss due to involvement of optic nerve may occur.

Diagnosis

Since the clinical features of meningitis are non-specific specially in infants a lumbar puncture should be performed at the earliest suspicion of meningitis. Occasionally LP may have to be postponed due to clinically important cardiorespiratory compromise, signs of increased intracranial pressure and infection in the area that needle will traverse to obtain CSF. Lumbar puncture should not be withheld in cases of thrombocytopenia if the administration of platelets provides safety from bleeding(19). Clinical signs of raised ICP are the best guide to withhold a lumbar puncture as even a normal CT scan does not rule out the imminent risk of coning(23). In case LP is deferred, empirical antimeningitic treat-

ment should be started after taking blood culture.

LP in Children with Febrile Seizures

A seizure associated at onset of meningitis may not be distinguishable from simple febrile convulsion. It is therefore advocated that LP be routinely done in all infants/young children after an initial febrile seizure to exclude cases of occult meningitis. The cut-off age for routine LP has been suggested as 18-24 months. However, it can be argued that a vast majority of children who have seizures with fever do not have meningitis and a skilled physician can identify an odd case of meningitis amongst these cases. Lethargy, irritability, vomiting and presence of complex febrile seizures are strong indicators of meningitis in febrile infants with seizures(24). Caution should be exercised in withholding LP in infants with seizures with fever and only be withheld if the patient is well and alert on examination and can be observed for the next few hours. In patients who have been pretreated with antibiotics or anticonvulsants the signs are masked and hence they must be subjected to LP.

CSF *Examination*

CSF examination includes a naked eye examination, pressure, microscopy-total and differential leukocyte count, Gram's stain, estimation of proteins and glucose and CSF culture. The CSF should be examined immediately after doing the LP since the cell count tends to fall over a period of time and may be falsely low after 30-60 min. The normal CSF of children contains less than 6 WBCs/mm^3 and in 95% of cases there are no polymorphonuclear (PMN) leukocytes(25). Hence presence of more than a single polymorphonuclear leukocyte in a child over 6 weeks of age is suggestive of ABM. However, CSF lymphocytosis may be a predominant feature in 10-13% of cases(26). CSF lymphocytosis is believed to represent an early phase of infection and repeat CSF examination in these cases will show a PMN predominance(27). Prior antibiotic therapy also results in lymphocytosis.

Protein in CSF is raised (normal value 40 mg/dl after 2nd month of life) in all cases of ABM. In patients of ABM, CSF glucose and ratio of CSF to blood glucose (normally about 66%) are low (19).

Gram stain of the smear is useful for detection of organisms and positivity depends on the number of organisms present(28). Flouroscent staining of bacterial DNA with acridine orange may show the bacterial morphology in cases where Gram stain is negative(5). Bacterial characteristics on Gram stain are usually not affected by previous antibiotic use of 44 to 68 h(29). CSF culture provides a confirmatory evidence of ABM and is essential for selecting appropriate antibiotic for the etiological organisms. The rate of bacterial isolation is affected by antibiotic use prior to lumbar puncture, further rate of isolation is increased if direct plating of CSF is done at bedside.

If a lumbar puncture is traumatic, a total cell count is performed and repeated after lysing RBC,s with acetic acid. If the total number of WBCs compared with number of RBCs exceed the value in whole blood the presence of CSF pleocytosis can be assumed. For every 1000 RBCs in CSF, 1 mg of protein per decilitre can be substracted(19). Further, studies have shown that abnormalities such as low glucose or positive Gram's stain are indicators independent of contamination with blood and none of the cases of ABM will be missed if all these are carried out.

Indications for Repeat Lumbar Puncture

A repeat spinal tap is not indicated in

uncomplicated ABM due to common meningeal pathogens. It should be done in case of: *(i)* strong clinical suspicion of ABM with normal CSF at the onset; *(it)* Poor clinical response to therapy of 48-72 hours; and *(Hi)* Unusual offending organism. Similarly the end of therapy LP is not essential if the course of illness is uncomplicated(30,31). The information provided at end of therapy is not useful in predicting which patient will have recurrent disease and complications.

Changes in CSF During Therapy

The white cell count often increases 24 hours after initiation of antibiotic therapy decreasing markedly thereafter. The percentage of polymorphonuclear cells does not decrease until after 48-72 hours of starting treatment. CSF protein level decreases throughout the therapy. CSF glucose resolves in the majority of patients by 24 hours. CSF culture is usually sterile within 24-48 h of appropriate antibiotic therapy.

Rapid Diagnostic Tests

Various rapid diagnostic tests including counter immunoelectrophoresis (CIE), latex particle agglutination and enzyme linked immunosorbent assay are used for detection of bacterial antigen. Antigen is consistently detected from CSF in patients with ABM. Latex particle agglutination kits are commercially available for detecting the polysaccharide antigen of *H. influenzae* type b, *S. pneumonia, N. meningitidis* and Group B *Streptococci* and are most widely used. Latex has a sensitivity of 90-95% compared to 80-85% for CIE (32). Tests which detect specific antibodies in the CSF include antipolyribose phosphate Hib antibody and IgM antibodies to *N. meningtidis* group A(33). Due to high costs these tests should be reserved for those cases in whom Gram's stain fails to reveal the causative agents and for delayed diagnosis of partially treated meningitis(34,35).

Various non-specific markers of CSF inflammation, break down of blood brain barrier and the type of inflammation have been investigated for diagnosis of ABM. These non-specific markers include C-reactive proteins, CSF lactic acid, lactate dehydrogenase, limulus lysate test, CSF aminoacidgram, SGOT, CPK, serum muramidase, estimation of granulocyte colony-stimulating factor in CSF (G-CSF) and fibronectin concentration.

Blood Culture

Blood culture is positive in 80-90% of cases of childhood meningitis(5). Gram's stain of buffy coat from blood or petechial lesion may also help in the early identification of organisms.

Radiological Studies

Sonography in infants with open anterior fontanelle and computed tomography of head are the non-invasive imaging modalities to detect early structural changes and follow up children with ABM(36). Contrast enhanced CT is useful in delineating suppurative collections like subdural empyema(37). However, for patients without atypical features there is no need to recommend CT of brain(38). These investigations should be considered in patients with: (z) signs of increased intracranial tension, *(ii)* focal neurological deficits, *(Hi)* prolonged fever during therapy, *(iv)* recurrent/focal seizures *(v)* prolonged depression of consciousness, and *(vi)* increased head circumference.

Differential Diagnosis

Several diseases particularly aseptic meningitis, tuberculous meningitis, brain abscess and lead encephalopathy may present with signs and symptoms suggestive of ABM. A careful examination of CSF, Gram's/acridine orange staining and CSF culture usually confirm diagnosis of ABM

in most of the cases. Even though partial treatment of meningitis with oral or systemic antibiotics may not completely alter the CSF profile in ABM, it may sometimes pose a diagnostic problem. However CSF pleocytosis, increase in proteins and low glucose levels still persist and indicate a diagnosis of ABM. In such cases CSF, blood and urine should be tested for bacterial antigen in order to establish the etiological diagnosis.

Treatment

Treatment can be broadly categorized into: (1) Antibiotic therapy; (2) Supportive care and (3) Adjuvant therapy.

Antibiotic Therapy

Selection of Initial Antibiotic Therapy

The antibiotic regimen should be such that covers all the likely pathogens anticipated according to the age of the child, combination should not be antagonistic and it should achieve bactericidal concentrations in the CSF. Later the treatment can be modified depending upon the result of Gram stain and CSF culture. Various antibiotics used in initial therapy and subsequent treatment are shown in *Table II.*

Third generation cephalosporins are the preferred initial antibiotics for meningitis as they are effective against most bacteria causing meningitis including resistant *H. influenzae* type b and penicillin resistant strains of *S. pneumoniae(5,39).* However, due to high cost, combination of penicillin and choramphenicol or ampicillin and chloramphenicol is often used as initial therapy. Chloramphenicol when used alone has been found to be as effective as in combination with penicillin or ampicillin(10). Also oral administration of chloramphenicol is known to acheive comparable CSF levels to that obtained after IV administration(40). However, since the minimum bactericidal concentration of chloramphenicol is higher than the minimum inhibitory concentration against antibiotic resistant pneumococci, it should not be used to treat meningitis with these strains(41). Subsequent therapy depends on the organism isolated and its antibiotic sensitivity. For penicillin resistant pneumococci, combination of vancomycin with cephalosporins or rifampicin should be used. A small number of anecdotal reports have shown that imipenem cilastatin has yielded clinical cure without complications in pneumococcal meningitis in pediatric patients. Meropenem another carbapenem has good *in vitro* activity and may be available soon for use. In India, the exact incidence of resistant pneumococci is not known. High dose of cefotaxime or ceftriaxone (250-300 mg/kg) can be tried before adding vancomycin, as strains with mild and intermediate resistance are sensitive to these(41). For multiple drug resistant staphylococci, several floroquinolones are found to be highly effective *in vitro;* however, poor CSF penetration and rapid emergence of resistance has markedly limited its usefulness in meningitis(42).

Duration of Therapy

The duration of antimicrobial therapy is based on the causative agent, and clinical response *(Table II).* Longer duration of treatment is required in cases of complications such as subdural empyema, prolonged fever, persistence of meningeal signs or development of nosocomial infections. In such cases discontinuation of antimicrobial therapy is individualized.

Supportive Therapy

The first 3-4 days of treatment are critical because life threatening complications of meningitis occur most frequently during this period. It is advisable to manage infants and children with meningitis in hos-

TABLE II–*Initial and Subsequent Therapy in Cases of Bacterial Meningitis*

[A] Initial Empiric Therapy

Age	Suspected pathogen	Drug of choice*	Alternative choice
0-2 months	• Gram negative enteric bacilli • *L. monocytogenes* • *Group B streptococcus*	Ampicillin + Cefotaxime	Ampicillin + Aminoglycoside
2 months to 12 years	• *H. influenzae* • *S. pneumoniae* • *N. meningitidis*	Ceftriaxone or Cefotaxime	Ampicillin + Chloramphenicol

[B] Subsequent Antibiotic Therapy in children 2-12 months

Pathogen	Drug of choice	Alternative choice	Duration of therapy
Pathogen unknown	Ceftriaxone	Ampicillin + Chloramphenicol	(days) 14 days
H. influenzae type b	Ceftriaxone	Chloramphenicol + Ampicillin	10
S. pneumoniae			
• Penicillin sensitive	Crystalline penicillin	Chloramphenicol	14
• Penicillin resistant	Ceftriaxone + Vancomycin/Rifampicin	–	14
N. meningititids	Crystalline penicillin	Ceftriaxone/ Chloramphenicol	7-10
Staphylococci	Nafcillin	Vancomycin	2-3 weeks

** Dosage Schedule: (All drugs to be given intravenously)*

Ampicillin	(300 mg/kg/24 hours, in 4 divided doses)
Ceftriaxone	(100 mg/kg/24 hours, in 2 divided doses)
Cefotaxime	(200 mg/kg/24 hours, in 4 divided doses)
Chloramphenicol	(100 mg/kg/24 hours, in 4 divided doses)
C. penicillin	(300, 000 units/kg/24 hours, in 4-6 divided doses)
Vancomycin	(60 mg/kg/24 hours, in 3-4 divided doses)
Nafcillin	(150-200 mg/kg/24 hours, in 4-6 divided doses)

pital that has staff with expertise; in caring for infants and children who are critically ill. Vital signs of patients should be monitored regularly during the first 24-28 hours of treatment. Urine specific gravity, body weight and electrolytes are measured every 12-24 h for the first two days. Neurological examination should be performed initially and daily throughout hospitalization(19).

In normovolemic patients fluids are restricted to two third of maintenance until raised ICP and SIADH are excluded(39). Fluid administration may be returned to normal when serum sodium level is normal. However, it is equally important to maintain systemic blood pressure which in turn maintains cerebral blood flow. Patients with evidence of dehydration must

be given volume replacement. Concurrence of shock and cerebral edema is a therapeutic dilemma. The treatment of hypotension with fluids and vasoactive agents must take priority in such cases and the cerebral perfusion pressure should not be permitted to fall below 30 mm Hg(43). A recent study has shown that restriction of fluid does not improve outcome of bacterial meningitis(44).

Intracranial pressure can be reduced by elevating the head end of the bed by 30° to maximize venous drainage. Mannitol (0.5-1 g/kg) is traditionally used to reduce ICP. Oral glycerol has been evaluated in children with ABM. Patients were randomized to receive IV dexamethasone, oral glycerol, dexamethasone plus glycerol or neither. Although the study was not placebo controlled the group receiving glycerol had significantly lower audiological or neurological sequelae(45). Hyperventilation to maintain the arterial PCO_2 between 27-30 mm of Hg may also be used to reduce ICP. However, in patients with cerebral edema hyperventilation may be counter productive as it causes reduction of already compromised CBF with resultant ischemic damage.

Seizures are common during the course of bacterial meningitis. Metabolic complications like hyponatremia, hypocalcemia and hypoglycemia must be excluded and specific therapy instituted if present. Immediate management of seizures include intravenous diazepam (0.1-0.2 mg/kg/dose) or lorazepam (0.05 mg/kg/dose). This is followed by a loading dose of phenytoin (15 mg/kg) and then maintenance dose of 5 mg/kg/24 h for further control of seizures. Phenytoin is preferred over phenobarbitone because it causes less CNS depression and allows assessment of sensorium. Anticonvulsants can be discontinued after a few days unless there is evidence of persistent seizure activity.

Adjunct Therapy

Improvement in our understanding of the pathophysiology of ABM has lead to the development of therapeutic approaches to modulate the inflammatory cascade to reduce the incidence of sequelae and death. Adjunctive anti-inflammatory agents in treatment of bacterial meningitis include corticosteroids and newer anti-inflammatory drugs which are still in experimental stage(4).

Corticosteroids

Corticosteroids have been used with objective of blocking secondary release of cytokines and toxic intermediaries from the brain cells and are also presumed to stabilize altered vascular permeability. A number of trials were conducted in the last decade to evaluate the role of dexamethasone (0.15 mg/kg every 6 hours for 2-4 days). The benefit of dexamethasone use in these studies was only moderate and limited to decrease in frequency of audiologic sequelae in meningitis due to Hib(46-48). The mortality rate and other neurologic sequele were not reduced. The effect of dexamethasone in treatment of neonatal meningitis and menimgococcal meningitis has not been evaluated and its efficacy in pneumococcal meningitis has not been conclusively proved. There is also a risk of upper gastrointestinal bleeding with use of dexamathasone. The decreased penetration of vancomycin into CSF in animals with experimental meningitis is another cause of concern(41). The Disease Committee of American Academy of Pediatrics has recommended dexamethasone use in meningitis due to Hib and its use may be considered for other cases(49). In the light of these observations, the need for dexamethasone should be assessed on individual basis.

Other Potential Adjuncts

Anti-endotoxin antibodies have been

produced by monoclonal antibody technology and appear to have beneficial role in ABM caused by Gram negative organisms. Monoclonal antibodies against TNF, IL-IB and against CD 18 cells may help in reducing inflammation as shown in experimental studies(4). Non steroidal antinflammatory agent, *e.g.,* indomethacin inhibit synthesis of prostaglandins from arachidonic acid via cycloxygenase pathway and can thereby reduce brain edema. Preliminary results of pentoxifylline-a methylxanthine phosphodiesterase inhibitor indicate that it reduces some of the inflammatory indices of ABM in animal model. Superoxide dismutase and catalase decrease brain edema and injury by acting as scavengers for reactive oxygen species. Role of all these is still at experimental stage and further trials are required to define their use in meningitis in humans.

Prognosis

The prognosis of a patient with pyogenic meningitis depends on many factors including age, causative micro-organism, bacterial density, intensity of host's inflammatory response and time taken to sterilize the CSF(19). Case fatality is reported to be 3-6% in developed countries(4) but higher mortality (16%) is reported from developing countries(l).

Neurodevelopmental sequelae are seen in 10-20% of patients(5,20). The sequelae of bacterial meningitis may improve with time and even resolve completely. The potential for recovery is attributed to the plasticity of brain. Persistence of fever, neck rigidity and reluctance to leave the supine position beyond the first week was associated with risk of neurologic complication or sequelae(50). Prognosis is poorest among infants less than 6 months, in those with delayed sterilization of the CSF, seizures beyond 4th day of hospital stay, coma, focal neurological signs on presentation, SIADH, *Salmonella* or *Pseudomonas* infection.

Prompt diagnosis and treatment of ABM remains a clinical challenge for all pediatricians. It is widely believed that any delay in diagnosis may be associated with increased number of' sequelae and poor outcome. Interestingly a prospective study and a retrospective analysis which examined the relationship between the length of prediagnostic illness and neurologic abnormalities showed that outcome was not affected by duration of illness before hospitalization(51,52).

Prevention

Prevention of ABM is possible with (z) prevention of secondary cases with antibiotic chemoprophylaxis of index case and close contacts, and *(it)* vaccination of susceptible population with specific vaccines.

Chemoprophylaxis

Rifampicin prophylaxis for Hib is recommended (20 mg/kg daily for 4 days) for all household contacts -of an index case as well as the index case when at least one contact is younger than 4 years of age, regardless of immunization status of the contact. The index case should receive chemoprophylaxis at or near the completion of therapy.

For *N. meningitidis,* chemoprophylaxis is recommended for all close contacts regardless of age and immunization status. If the organism is sensitive to sulfonamides, chemoprophylaxis can be given with sulfisoxazole (500 mg every 12 hours for children 1-12 years, and 1 g every 12 hours for contacts over 12 years for 2 days). Alternatively rifampicin (10 mg/kg every 12 hours for 2 days) can be given. Ceftriaxone (250 mg intramuscularly as a single dose) is an effective chemoprophylactic agent in pregnant women. No prophylaxis for

S. pneumoniae is required for normal hosts.

Vaccination

Immunization with *H. influenzae* type b vaccines-HIB OC (3 doses I/M at 2, 4, 6 months and a booster at 15 months) or PRP-OMP (2 doses I/M at 2, 4 months and booster at 12 months) are recommended. Mass immunization with a quadrivalent meningococcal vaccine against serogroup A,C, Y and W135 has been used to control outbreaks. Group B polysacoharide is poorly immunogenic and has not been useful for development of vaccine. Therefore vaccines based on outer membrane protein are currently being evaluated for their efficacy(53). Selective immunization with meningococcal vaccine is also recommended for children older than 2 years who are at high risk of infection. The clinical efficacy of pneumococcal vaccine is yet to be established. Although improvement of treatment strategies has given encouraging results, prevention of bacterial meningitis by development and introduction of combined conjugate vaccine against the common causative pathogens will be the major challenge of next decade.

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