GOOD MORNING

Acute Bacterial Meningitis

Bacterial meningitis is one of the most potentially serious infections occurring in infants and older children. This infection is associated with a high rate of acute complications and risk of .long-term morbidity

The incidence of bacterial meningitis is sufficiently high in febrile infants that it should be included in the differential diagnosis of those with altered mental status and other .evidence of neurologic dysfunction

ETIOLOGY

The most common causes of bacterial meningitis in children older than mo of age in the United States are Streptococcus pneumoniae and 1 Neisseria meningitidis. Bacterial meningitis caused by S. pneumoniae and Haemophilus influenzae type b has become much less common in developed countries since the introduction of universal immunization against these pathogens beginning at 2 mo of age. Infection caused by S. pneumoniae or H. influenzae type b must be considered .in incompletely vaccinated individuals or those in developing countries ,Those with certain underlying immunologic (HIV infection ,immunoglobulin [Ig] G subclass deficiency) or anatomic (splenic dysfunction cochlear defects or implants) disorders also may be at .increased risk of infection caused by these bacteria

Alterations of host defense resulting from anatomic defects or immune deficits also increase the risk of meningitis from less-common ,pathogens such as Pseudomonas aeruginosa, Staphylococcus aureus coagulase-negative staphylococci, Salmonella spp., anaerobes, and Listeria .monocytogenes

PATHOLOGY AND PATHOPHYSIOLOGY

A meningeal purulent exudate of varying thickness may be distributed around the cerebral veins, venous sinuses, convexity of the brain, and cerebellum, and in the sulci, sylvian fissures, basal cisterns, and spinal cord. Ventriculitis with bacteria and inflammatory cells in ventricular fluid may be present (more often in neonates), as may subdural effusions . .and, rarely, empyema

Vascular and parenchymal cerebral changes characterized by polymorphonuclear infiltrates extending to the subintimal region of the small arteries and veins, vasculitis, thrombosis of small cortical veins, occlusion of major venous sinuses, necrotizing arteritis producing subarachnoid ,hemorrhage

,Cerebral infarction, resulting from vascular occlusion because of inflammation vasospasm, and thrombosis, is a frequent sequela. Infarct size ranges .from microscopic to involvement of an entire hemisphere

,Inflammation of spinal nerves and roots produces meningeal signs and inflammation of the cranial nerves produces cranial neuropathies .of optic, oculomotor, facial, and auditory nerves

Increased intracranial pressure (ICP) also produces oculomotor nerve palsy because of the presence of temporal lobe compression of the nerve during tentorial herniation. Abducens nerve palsy may be a nonlocalizing sign of elevated .ICP

,Increased ICP is a result of cell death (cytotoxic cerebral edema) cytokine-induced increased capillary vascular permeability (vasogenic cerebral edema), and, possibly, increased hydrostatic pressure (interstitial cerebral edema) after obstructed reabsorption of CSF in the .arachnoid villus or obstruction of the flow of fluid from the ventricles ICP may exceed 300 mm H2O. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) may produce excessive water retention ,and potentially increase the risk of elevated ICP . Furthermore if the fontanels are still patent, increased ICP is not always .dissipated

Hydrocephalus can occur as acute complication of meningitis. It most often takes the form of a communicating hydrocephalus caused by adhesive thickening of the arachnoid villi around the cisterns at the base of the brain. Thus, there is interference with the

normal resorption of CSF. Less often, obstructive hydrocephalus develops

after fibrosis and gliosis of the aqueduct of Sylvius or the foramina of Magendie and .Luschka

Raised CSF protein levels are partly a result of increased vascular

permeability of the blood–brain barrier and the loss of albumin-rich

fluid from the capillaries and veins traversing the subdural space. Continued

transudation may result in subdural effusions, usually found in

.the later phase of acute bacterial meningitis

Hypoglycorrhachia(reduced CSF glucose levels) is attributable to decreased glucose .transport by the cerebral tissue

Damage to the cerebral cortex may be a result of the focal or diffuse

,effects of vascular occlusion (infarction, necrosis, lactic acidosis)

hypoxia, bacterial invasion (cerebritis), toxic encephalopathy (bacterial

.toxins), elevated ICP, ventriculitis, and transudation (subdural effusions)

These pathologic factors result in the clinical manifestations of

impaired consciousness, seizures, cranial nerve deficits, motor and

.sensory deficits, and later psychomotor retardation

CLINICAL MANIFESTATIONS

The onset of acute meningitis has 2 predominant patterns. The more dramatic and, fortunately, less common presentation is sudden onset with rapidly progressive manifestations of shock, purpura, disseminated intravascular coagulation, and reduced levels of consciousness often resulting in progression to coma or death within 24 hr. More often, meningitis is preceded by several days of fever accompanied by upper respiratory tract or gastrointestinal symptoms, followed by nonspecific .signs of CNS infection, such as increasing lethargy and irritability

The signs and symptoms of meningitis are related to the nonspecific findings associated with a systemic infection and to manifestations of meningeal irritation. Nonspecific findings include fever, anorexia and ,poor feeding, headache, symptoms of upper respiratory tract infection myalgias, arthralgias, tachycardia, hypotension, and various cutaneous .signs, such as petechiae, purpura, or an erythematous macular rash

Meningeal irritation is manifested as nuchal rigidity, back pain, Kernig sign (flexion of the hip 90 degrees with subsequent pain with extension of the leg), and Brudzinski sign (involuntary flexion of the knees and hips after passive flexion of the neck while supine). In children, particularly in those younger than 12-18 mo, Kernig and Brudzinski signs are not consistently present. Indeed fever, headache, and nuchal rigidity .are present in only 40% of adults with bacterial meningitis

Increased ICP is suggested by headache, emesis, bulging fontanel or diastasis of the sutures, oculomotor (anisocoria, ptosis) or abducens (widening) ,nerve paralysis, hypertension with bradycardia, apnea or hyperventilation decorticate or decerebrate posturing, stupor, coma, or signs of .herniation

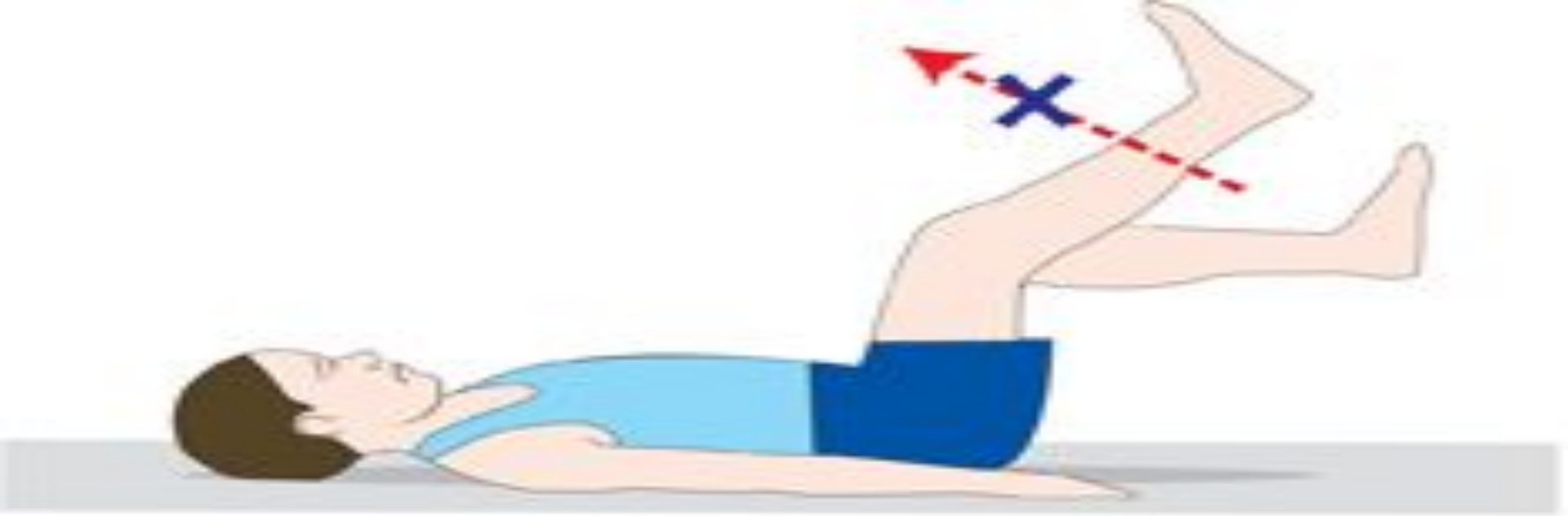
Papilledema is uncommon in uncomplicated meningitis and should suggest a more chronic process, such as the presence of an intracranial abscess, subdural empyema, or occlusion of a dural venous .sinus. Focal neurologic signs usually are a result of vascular occlusion Cranial neuropathies of the ocular, oculomotor, abducens, facial, and ,auditory nerves may also be the result of focal inflammation. Overall approximately 10-20% of children with bacterial meningitis have focal .neurologic signs

Seizures (focal or generalized) caused by cerebritis, infarction, or .electrolyte disturbances occur in 20-30% of patients with meningitis Seizures that occur on presentation or within the 1st 4 days of onset are usually of no prognostic significance. Seizures that persist after the 4th day of illness and those that are difficult to treat may be associated .with a poor prognosis

Alterations of mental status are common among patients with meningitis and may be the consequence of increased ICP, cerebritis, or hypotension; manifestations include irritability, lethargy, stupor, obtundation, and coma. Comatose patients .have a poor prognosis

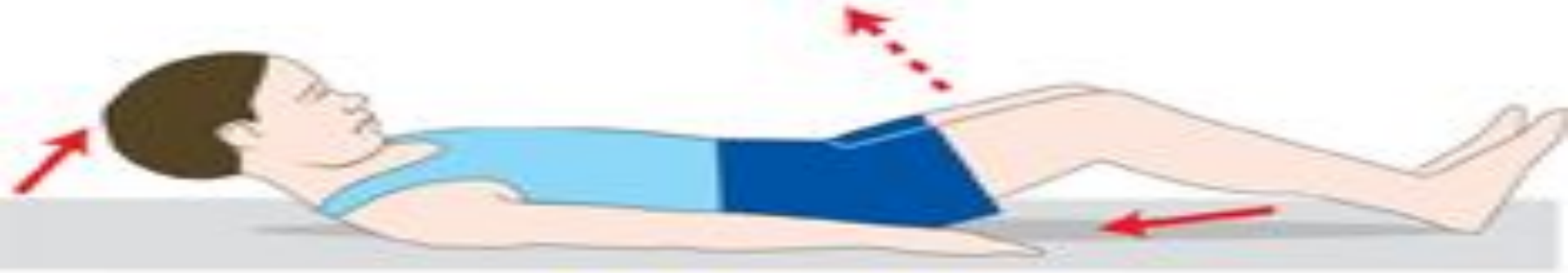
Additional manifestations of meningitis include photophobia and tache cérébrale, which is elicited by stroking the skin with a blunt

.object and observing a raised red streak within 30-60 sec



Kernig Sign

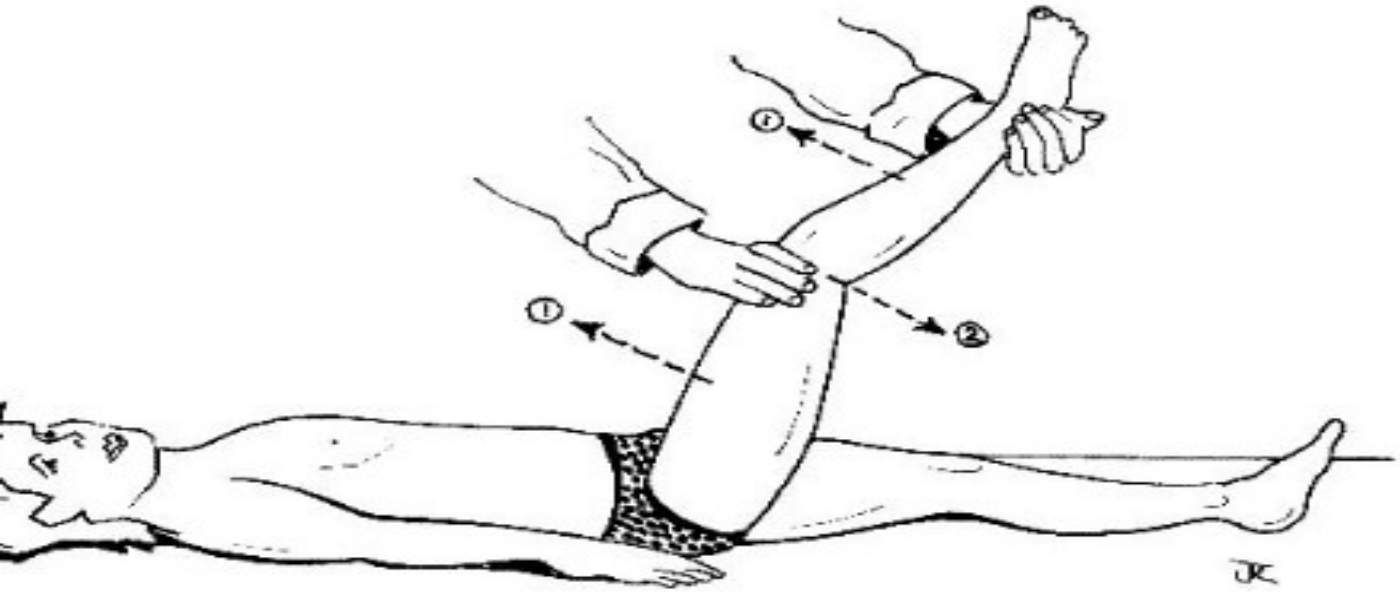
When the hips are flexed at 90 degrees, attempting to extend the leg at the knee past 135 degrees causes pain and/or extensor spasm.

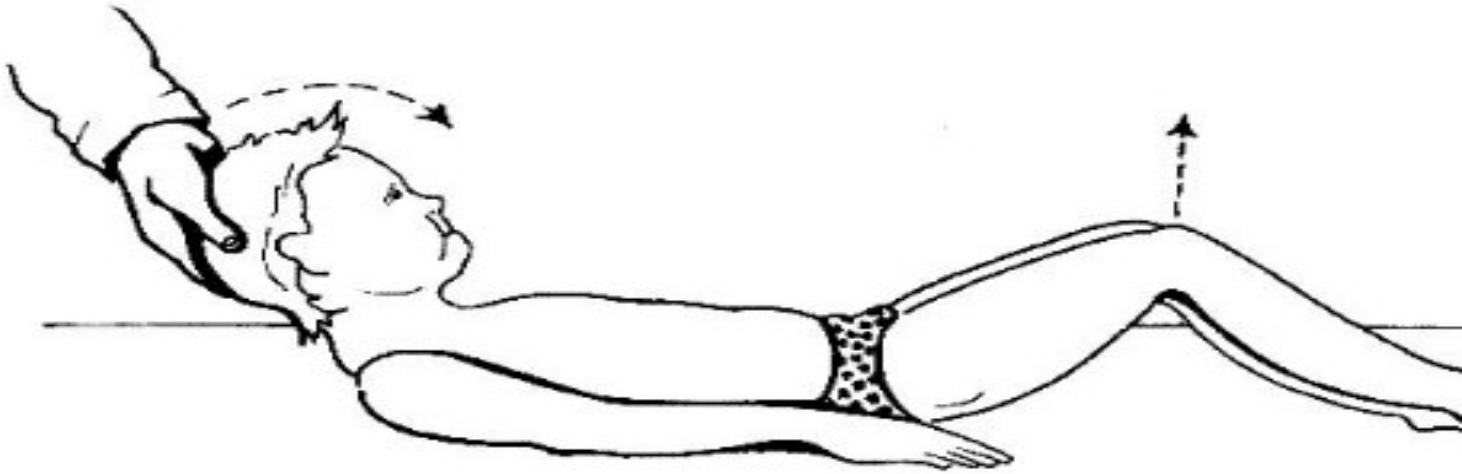


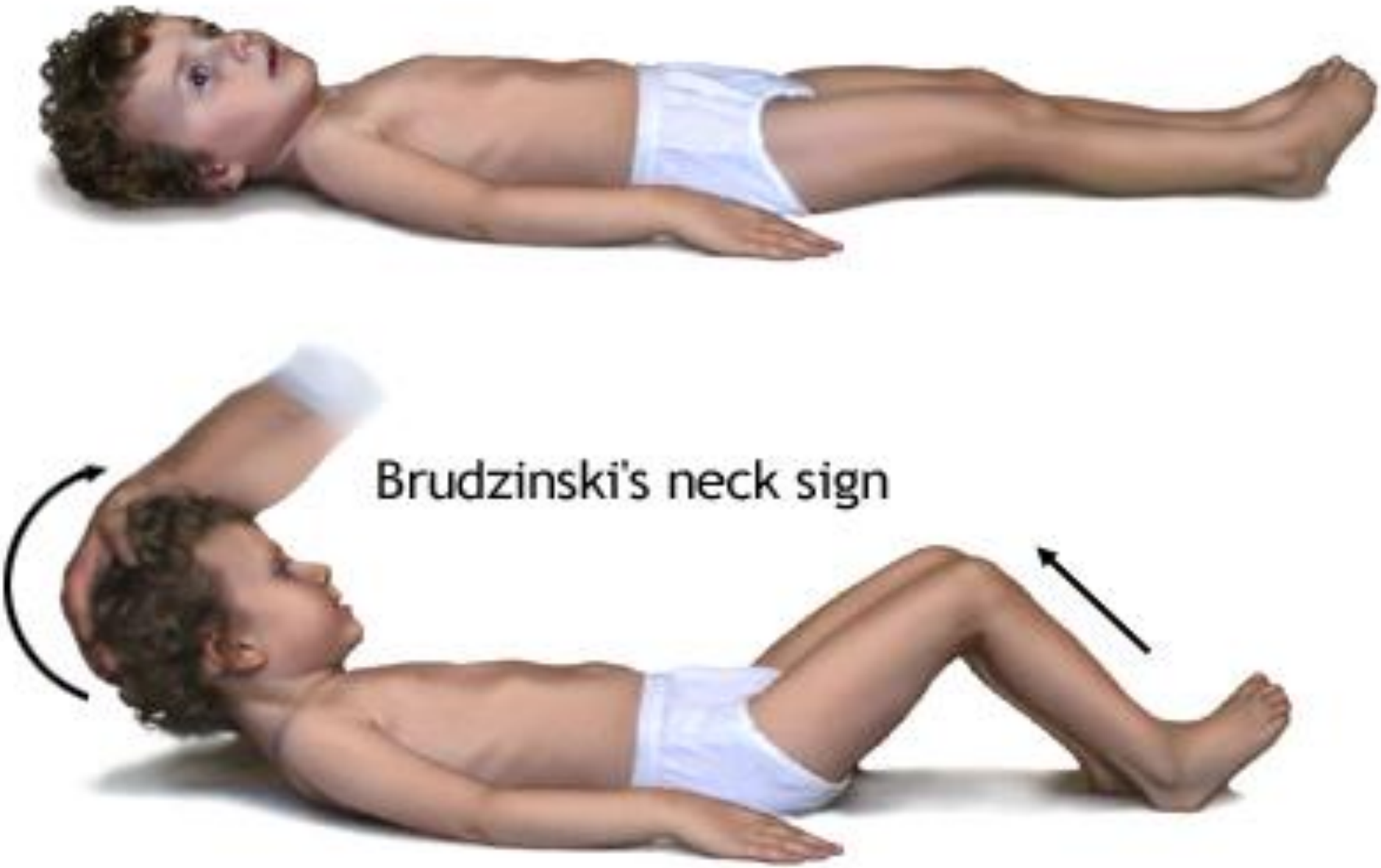
Brudzinski Sign

Flexion of the neck while laying supine causes involuntary hip and knee flexion.

Kernig's and Brudzinski's tests






Brudzinski's neck sign

DIAGNOSIS

The diagnosis of acute pyogenic meningitis is confirmed by analysis of the CSF, which typically reveals microorganisms on Gram stain and culture, a neutrophilic pleocytosis, elevated protein, and .reduced glucose concentrations

LP should be performed when bacterial meningitis is .suspected

;Contraindications for an immediate LP include

evidence of increased ICP (other than a (1)

bulging fontanel), such as 3rd or 6th cranial nerve palsy with a

depressed level of consciousness, or hypertension and bradycardia with

.respiratory abnormalities

severe cardiopulmonary compromise requiring prompt resuscitative measures (2)
for shock or in patients in whom positioning for the LP would further compromise

.cardiopulmonary function

.infection of the skin overlying the site of the LP (3)

.Thrombocytopenia is a relative contraindication for LP

.If an LP is delayed, empirical antibiotic therapy should be initiated

CT scanning for evidence of a brain abscess or increased ICP should

not delay therapy. LP may be performed after increased ICP has been

.treated or a brain abscess has been excluded

Blood cultures should be performed in all patients with suspected meningitis. Blood cultures reveal the responsible .bacteria in up to 80-90% of cases of meningitis

,Elevations of the C-reactive protein

erythrocyte sedimentation rate, and procalcitonin have been used to differentiate bacterial (usually elevated) from viral .causes of meningitis

Lumbar Puncture

The CSF leukocyte count in bacterial meningitis usually is elevated to >1,000/mm3 and, typically, there is a neutrophilic predominance Turbid CSF is present when the CSF leukocyte count .(75-95%) exceeds 200-400/mm3. Normal healthy neonates may have as many as 30 leukocytes/mm3 (usually <10), but older children without ;viral or bacterial meningitis have <5 leukocytes/mm3 in the CSF in both age groups there is a predominance of lymphocytes or .monocytes

A CSF leukocyte count <250/mm3 may be present in as many as 20% of patients with acute bacterial meningitis; pleocytosis may be absent in patients with severe overwhelming sepsis and meningitis and is a poor prognostic sign. Pleocytosis with a lymphocyte predominance ;may be present during the early stage of acute bacterial meningitis conversely, neutrophilic pleocytosis may be present in patients in the .early stages of acute viral meningitis

The shift to lymphocyticmonocytic predominance in viral meningitis invariably occurs within 8-24 hr of the initial LP. The Gram stain is positive in 70-90% of .patients with untreated bacterial meningitis

A diagnostic conundrum in the evaluation of children with suspected bacterial meningitis is the analysis of CSF obtained from children already receiving antibiotic (usually oral) therapy. This is an important issue, because 25-50% of children being evaluated for bacterial .meningitis are receiving oral antibiotics when their CSF is obtained

CSF obtained from children with bacterial meningitis, after the initiation of antibiotics, may be negative on Gram stain and culture. Pleocytosis with a predominance of neutrophils, elevated protein level, and a reduced concentration of CSF glucose usually persist for several days .after the administration of appropriate intravenous antibiotics

A traumatic LP may complicate the diagnosis of meningitis. Repeat LP at a higher interspace may produce less hemorrhagic fluid, but this fluid usually also contains red blood cells. Interpretation of CSF leukocytes and protein concentration are affected by LPs that are traumatic, although the Gram stain, culture, and glucose level may not be influenced. Although methods for correcting for the presence of red blood cells have been proposed, it is prudent to rely on the bacteriologic results rather than attempt to interpret the CSF leukocyte

,and protein results of a traumatic LP. Children with seizure particularly those with fever associated status epilepticus do not have a CSF pleocytosis in the absence of CNS infection or inflammatory .disease

Differential Diagnosis

Other infectious agents e.g. viral, TB, fungal, parasitic; bacterial parameningial infection; postinfectious, systemic or immunologically mediated process; malignancy; drugs; miscellaneous e.g. poisoning, intracranial .hemorrhage

TREATMENT

Antibiotic Therapy

The initial (empirical) choice of antibiotic therapy for meningitis should be given in high dose & should cover the most common .pathogens until the result of culture become available

Vancomycin (60 mg/kg/day ÷ 4)and

3rd generation cephalosporins e.g. Cefotaxime (200-300 .mg/kg/day ÷ 3,4) or Ceftriaxone (100 mg/kg/day once or twice)

If patient is immunocompromised or gram-negative bacterial meningitis is suspected, initial therapy may be with Ceftazidime (150 mg/kg/day ÷ 3), an aminoglycoside e.g. Gentamicin (5-7.5 mg/kg/day ÷ 3) or Amikacin (20-30 mg/kg/day ÷ 3), or Meropenem

Duration of antibiotic Rx in uncomplicated meningitis as follows:- N. meningitidis for 5-7 days. H. influenza for 7-10 days. S. pneumonia for 10-14 days; whereas Gram-negative bacilli e.g. E. coli or P. aeruginosa either 3 wk or at least 2 wk after CSF .sterilization

Supportive Care

Repeated medical and neurologic assessments especially in the 1st 72 hr.1 .1
e.g. chart for vital signs, fluid input & urine output, pupillary reflexes, level of .consciousness

Patients should initially receive nothing by mouth. Shock should be treated .2 .2
with fluid resuscitation +/_ inotropic agents; whereas if there is no hypotension, IV fluid should be restricted to half or two thirds of maintenance until it can be established that ↑ ICP or SIADH is not present, .then full maintenance can be given

,ICP can be treated by: head elevation, restriction of IV fluid ↑ .3
furosemide (1 mg/kg) or mannitol (0.5–1.0 g/kg), and endotracheal
↓ intubation with hyperventilation. Glycerol has also been used to
.cerebral edema by ↑ plasma osmolality & enhance cerebral circulation

Seizures should be treated with IV diazepam (0.1–0.2 mg/kg/dose) or .4
lorazepam; for maintenance Rx of seizures, give phenytoin which is
better than phenobarbital because it produces less CNS depression that permits .assessment of patient's level of consciousness

Corticosteroids

/Data support the use of intravenous dexamethasone, 0.15 mg/kg dose given every 6 hr for 2 days, in the treatment of children older than 6 wk with acute bacterial meningitis caused by H. influenzae type b. Among children with meningitis caused by H. influenzae ,type b, corticosteroid recipients have a shorter duration of fever lower CSF protein and lactate levels, and a reduction in sensorineural .hearing loss

,Early steroid treatment of adults with bacterial meningitis especially those with pneumococcal meningitis, results in .improved outcome

Corticosteroids appear to have maximum benefit if given 1-2 hr before antibiotics are initiated. They also may be effective if given .concurrently with or soon after the first dose of antibiotics

,Complications of corticosteroids include gastrointestinal bleeding .hypertension,hyperglycemia, leukocytosis, and rebound fever after the last dose

COMPLICATIONS

During the treatment of meningitis, acute CNS complications

Seizures 2.increased ICP 3. cranial nerve palsies 4. stroke 5. cerebral or cerebellar .1 .herniation 6.thrombosis of the dural venous sinuses

Collections of fluid in the subdural space develop in 10-30% of .patients with meningitis and are asymptomatic in 85-90% of patients

Subdural effusions are especially common in infants. Symptomatic ,subdural effusions may result in a bulging fontanel, diastasis of sutures enlarging head circumference, emesis, seizures, fever, and abnormal results of cranial transillumination. CT or MRI scanning confirms the presence of a subdural effusion. In the presence of increased ICP or a depressed level of consciousness, symptomatic subdural effusion . should be treated by aspiration through the open fontanel .Fever alone is not an indication for aspiration

SIADH occurs in some patients with meningitis, resulting in hyponatremia and reduced serum osmolality. This may exacerbate cerebral edema or result in hyponatremic seizures

Fever associated with bacterial meningitis usually resolves within days of the onset of therapy. Prolonged fever (>10 days) is noted 5-7 in approximately 10% of patients. Prolonged fever is usually caused by ,intercurrent viral infection, nosocomial or secondary bacterial infection thrombophlebitis, or drug reaction. Secondary fever refers to the recrudescence of elevated temperature after an afebrile interval. Nosocomial infections are especially important to consider in the evaluation of these patients. Pericarditis or arthritis may occur in patients being .treated for meningitis, especially that caused by N. meningitidis Involvement of these sites may result either from bacterial dissemination .or from immune complex deposition

Thrombocytosis, eosinophilia, and anemia may develop during therapy for meningitis. Anemia may be a result of hemolysis or bone marrow suppression. Disseminated intravascular coagulation is most often associated with the rapidly progressive pattern of presentation and is noted most commonly in patients with shock and purpura. The combination of endotoxemia and severe hypotension initiates the coagulation cascade; the coexistence of ongoing thrombosis may .produce symmetric peripheral gangrene

PROGNOSIS

Appropriate antibiotic therapy and supportive care have reduced the .mortality of bacterial meningitis after the neonatal period to <10% .The highest mortality rates are observed with pneumococcal meningitis Severe neurodevelopmental sequelae may occur in 10-20% of Patients. The prognosis is poorest among infants younger than 6 mo and in those with high concentrations of bacteria/bacterial products in their CSF. Those with seizures occurring more than 4 days into therapy or with coma or focal neurologic signs on presentation have an increased risk of long-term .sequelae

The most common neurologic sequelae include hearing loss, cognitive ,impairment, recurrent seizures, delay in acquisition of language visual impairment, and behavioral problems. Sensorineural hearing loss is the most common sequela of bacterial meningitis and, usually, is already present at the time of .initial presentation

It is a result of cochlear infection and occurs in as many as 30% of patients with pneumococcal meningitis, 10% with meningococcal, and 5-20% of those with H. influenzae type b meningitis. Frequent reassessment on an outpatient basis is indicated for patients who have a hearing .deficit

PREVENTION

.It is either by vaccination or antibiotic prophylaxis

S. pneumonia; by vaccination with 7-valent (which is now replaced with 13-valent) conjugate pneumococcal vaccine is recommended for children < 2 yr of age and those at high risk e.g. asplenia or .immunodeficiency. No antibiotic Px is required

H. influenza type b; Conjugated vaccines for Hib started at 2 mo of age. Rifampin Px should be given to all house-hold contacts (except .pregnant women) in dose 20 mg/kg once for 4 days

N. meningitides; Quadrivalent conjugated vaccine is recommended for high-risk children > 2 yr, asplenia, deficiencies of terminal complement proteins, & college freshmen. Rifampin Px in dose 20 mg/kg ÷ 2 for 2 days; ciprofloxacin or ceftriaxone (single dose) also can be given. They should be given to all contacts (regardless of immunization status) e.g. household, daycare center, nursery school contacts, and health care workers who have direct exposure to oral secretions of patients as well as the index case. Vaccine also may be used as an adjunct with chemoprophylaxis for exposed contacts or during .epidemics of meningococcal disease

THANKS