40 Current Status and Management of Community Acquired Meningitis

Abstract: Community acquired meningitis is associated with high mortality and morbidity. Bacterial meningitis is often a medical emergency, whereas viral meningitis often mild and remains unrecognized. In the past, the three most frequent bacterial pathogens of community acquired meningitis were *H.influenzae, N.meningitides* and *S.pneumoniae*. With the use of *H.influenzae* type b conjugate vaccine- incidence of *H.influenzae* meningitis in infants and children have dramatically reduced. *S.pneumoniae* is the most common cause of meningitis in adults. Listeria monocytogenes causes bacterial meningitis more in immunocompromised, pregnancy and older persons. During childhood and adolescence commonest organisms *N.meningitidis* followed by *S.pneumoniae*. Principle viruses identified causing meningitis are enteroviruses, herpesviruses, varicella zoster virus, flaviviruses, adenoviruses, etc. .Patients commonly present with fever,confusion, lethargy, headache, vomiting and irritability. Neck stiffness present only in 50% cases. Meningococcal disease often associated with petechial or purpuric skin rashes. Viral meningitis are often mildly symptomatic. Common neurological complications are cranial nerve dysfunction, seizure, focal cerebral signs and sensory neural deafness. Lumbar puncture is the most crucial investigation. Gram staining often revealed organisms and help in therapy. CT scan not mandatory,but needed if there is focal signs or features of raised intracranial tension. PCR more useful in diagnosing organisms in viral meningitis. Vancomycin and third generation cephalosporin is drug of choice if *S.pneumoniae* is suspected organism. For *N.meningitidis* and *H.influenzae* meningitis third generation cephalosporin is drug of choice. *L.monocytogenes* is susceptible to ampicillin. No specific antiviral therapy in case of viral meningitis except herpes simplex. Chemoprophylaxis is indicated for *N.meningitidis* and *H.influenzae* but not against *S.pneumonia*.

INTRODUCTION

Community acquired meningitis is associated with high mortality and morbidity. Epidemiology of community acquired meningitis has changed over the last 15 years due to advent of new vaccines and development of antibiotics resistance. Bacterial meningitis would appear to be the most frequent, but viral etiologies are very often poorly recognized.

Bacterial meningitis is a medical, neurological and sometimes neurosurgical emergency that requires a multidisciplinary approach. Bacterial meningitis has an annual incidence of 4 to 6 cases per 100000 adults. Diagnosis is often considered but the disease may be difficult to recognize. Recommendations for antimicrobial therapy are changing as a result of development of antibiotics resistance.

On the contrary viral meningitis is benign and less life-threatening. Previously it was termed as aseptic meningitis, because no bacterial pathogen can be isolated or identified from these group of patients. But with the advent of science of virology and molecular biologic technique specific virus can be isolated from CSF of patient with aseptic meningitis syndrome. Unfortunately, owing to the pathophysiology of many viral infections, relative inaccessibility and expense of viral isolation procedures and a lack of interest in pursuing etiologic diagnosis in non-life-threatening illnesses, diagnosis often rests on clinical ground and frequently missed.

PATHOGENS

In the past, the three most frequent bacterial pathogens of community acquired meningitis were *H.influenzae, N.meningitidis, S. pneumoniae.* With the use of *H. influenzae* type b conjugate vaccine-dominant position of *H. influenzae* as leading cause of meningitis in infants and children have dramatically altered, as a result frequency of *S.pneumonia*, and *N.meningitidis* have increased. Other bacterial causes in this age group have been group b streptococci, listeria monocytogenes and enteric gram-negative bacilli.

S. pneumoniae is the most common cause of meningitis in adults accounting more than half of the cases.There are many predisposing factors such as pneumococcal pneumonia, otitis media, sinusitis, diabetes, alcoholism, splenectomy, complement deficiency, etc. *N.meningitidis* account for 25% of all cases of bacterial meningitis and up to 60% of cases in children and young adults between 2 to 20 years. Infection may be initiated by nasopharyngeal colonization which can result in asymptomatic carrier state or invasive meningococcal disease. Listeria monocytogenes have assumed an increasing role in bacterial meningitis in immunocompromised, pregnancy, above 60 years and other vulnerable persons at risk.Infection are spread by ingesting food contaminated by Listeria. Enteric gram- negative bacilli are increasing common cause of meningitis in individuals with chronic and debilitating disease such as diabetes, alcoholism, cirrhosis, etc. In series of cases of bacterial meningitis, 6 to 10% of cases are of unknown causes.[1]

Frequency of various bacterial species in community acquired meningitis are age-related. In neonate's group B streptococci, L monocytogenes, *E. coli* are leading causes. From ages. 2 to 23 months leading etiologies are *S.pneumonia*, followed by *N.meningitidis*. During childhood and adolescence *N.meningitidis* followed by *S.pneumoniae.* In older age group *S.pneumoniae* and *L.monocytogenes* are dominant organisms.

About 1% cases of bacterial meningitis are polymicrobial infection. Rarely unusual bacterial species of zoonotic importance may produce meningitis in humans. Such as brucella, francisella tularensis, streptococcus suis, etc.

Many viruses can cause acute meningitis and epidemiology of specific syndromes differ with the etiologic agents. Principle viruses identified are enteroviruses (coxsackievirus, echovirus, poliovirus), herpes viruses, herpes simplex virus type 1 and 2, varicella zoster virus, flaviviruses, adenoviruses, paramyxoviruses. Enteroviruses are responsible for more than one-half of the cases of acute meningitis. Majority of viral meningitis occur in infants, young children, adolescents,

however, no age group is spared. Enteroviruses causes infection during summer and fall, whereas mumps, measles and varicella-zoster meningitis peak in the winter and spring months. Enteroviruses spread by both fecal-oral and respiratory routes from person to person. Adenovirus spread by respiratory route.

CLINICAL MANIFESTATIONS

In community acquired bacterial meningitis antecedent upper respiratory tract infection is common(40%), another 10-15% of patients have an ill defined prior illness. 25 to 75% patients have a acute onset within 24 hours with headache, lethargy and confusion. Other patients may have more prolonged respiratory tract or ear symptoms and meningeal symptoms develop slowly. Prodromal symptoms are prolonged in case of *L.monocytogenes*. Infection, fever, vomiting, irritability, lethargy, headache are features in most patients. Neck stiffness is a symptom in less than 50% of cases. Myalgia, backache are more common in meningococcal meningitis. Photophobia is more often associated with viral meningitis. Diagnostic dilemma more common in infants. Fever and vomiting may be the only features and nuchal rigidity may be absent. Bulging of fontanelle may be present or absent. In adult diagnostic confusion may occur in patients who are obtunded because of other illness (pneumonia, congestive heart failure).

A petechial or purpuric rash predominantly on the extremities almost always indicates a meningococcal disease. About 50% patients with meningococcal disease have skin lesion. Maculopapapular rash or large purpuric area with necrotic centres may also develop. Rarely such lesion may occur in other types of meningitis. Macular or petechial skin lesions may occur with enteroviral aseptic meningitis.

Features common to cases of acute viral meningitis include headache, fever photophobia, irritability, mild to moderate meningismus. These may be accompanied by findings that are more specific for a given disease such as parotitis in mumps, zosteriform eruption in zoster, vesiculo-pustular eruption in varicella, asymmetric paralysis in poliomyelitis, gastrointestinal disturbance and rash in enteroviral illness. Evidence of more severe meningeal irritation such as Kernig's sign and Brudzinski's sign generally absent. Mild degree of lethargy, drowsiness common but presence of stupor, coma, marked confusion direct to consider alternative diagnosis. Seizures, focal neurological signs do not present in uncomplicated viral meningitis, but its presence indicate parenchymal involvement.

NEUROLOGIC COMPLICATIONS

Cranial nerve dysfunction is noted in 20% of patients. Cranial III, IV, VI nerves are most often involved. Seizures may occur in 15 to 30% of cases.

Seizures may be focal or generalized. It is more common in *S.pneumoniae* patients and alcoholism is a confounder. Focal cerebral signs (hemiparesis, quadriparesis, visual field defects, disorder of conjugate gaze) occur in 10 to 20% patients with meningitis, more frequently with pneumococcal than other type of community acquired meningitis.[2] They occur more frequently in early stage than later. Cerebral edema (34%) and hydrocephalus (29%), sagittal sinus thrombosis are other common complications.

Late complications like sensoryneural deafness is noted with *H.influenzae, S.pneumoniae* infection more in children(10%).Vasculitis-induced infraction of cranial nerves and necrosis of cells in the organ of corti may be responsible for such permanent deafness. Other major neurodeficits are hemiparesis, quadriparesis, mental retardation, blindness. Late onset epilepsy may occur in patients who have permanent cerebral dysfunction.

NON-NEUROLOGIC COMPLICATIONS

Shock may develop early in the course of acute bacterial meningitis as a consequence of bacteremia more in meningococcemia-meningitis or in pneumococcal bacteremia in asplenic patients.

Coagulation disorder may complicate bacteremias. It may be thrombocytopenia or disseminated intravascular coagulation. Rarely endocarditis or pyogenic arthritis or serum sickness like syndrome can occur.

Usually fever subsides after 2 to 5 days of proper antimicrobial therapy. Occasionly fever persist for 8 to 10 days or longer or recurs after initial defervescence. Such a febrile course suggest inadequate antimicrobial therapy, ventricular empyema, subdural effusion, ventriculitis, sagittal sinus thrombosis, drug fever or serum sickness like syndrome. Re-evaluation of CSF findings with brain imaging should be considered.

LABORATORY FEATURES

Critical to the diagnosis is examination of CSF. Lumbar puncture (LP) is safe in the absence of raised intracranial pressure. CSF profile help to differentiate meningitis from encephalitis and viral from bacterial meningitis. However, CSF, profile may vary early in viral infection (with initial neutrophilic predominance) and after antibiotic treatment of bacterial meningitis which may render the Gram stain negative and protein level normal. These factors do not to significantly affect the opening pressure, cell count or CSF/serum glucose ratio. CSF profile also appear normal at presentation in about 3% cases of bacterial meningitis.

CSF value characteristics of acute pyogenic meningitis include pleocytosis of 100-5000 cells/mm^3, increased opening pressure(>180 mm H_2O in 90%), elevated protein level(>45 mg/dl), decreased glucose concentration (<40 mg/dl), and/or CSF/serum glucose ratio of <0.4 in

~ 60%. Gram staining of centrifused CSF-that revealed infecting agent in 60-90% of cases.[3] In community acquired meningitis in adults 13% cases are culture negative. CSF/serum glucose ratio particularly helpful in case of hyperglycemia or dextrose therapy in emergency.

If LP is delayed due to neuroimaging, after obtaining blood culture empirical antibiotics should be started immediately. Antibiotics therapy few hours before LP examination do not alter CSF WBC count or glucose concentration nor visualization of organisms by Gram staining.

Latex agglutination and PCR technique may be used to detect organisms, particularly who received prior antimicrobial therapy. Sensitivity of latex particle agglutination in detecting antigen of common strains of bacteria from CSF varies among organisms. *H.influenzae* antigen can be detected in 95% of cases, *N.meningitidis* in 64 to 78% of cases, and *S.pneumonia* in 67% if cases.[4] Specificity of this test is 95 to 100%. But use of PCR technique not useful in bacterial meningitis as they are in viral meningitis and also is limited by its cost and time consuming and technically demanding nature. The litmus amebocyte lysate assay is a rapid diagnostic test for detecting gram-negative endotoxin in CSF.Various chemical and enzymatic changes have been noted in CSF of patients with acute bacterial meningitis. They are useful in differentiating in bacterial meningitis from viral meningitis. Increase serum lactate >3.9 mm are usually observed in bacterial meningitis and levels are lower in patients with aseptic meningitis. Elevated level of procalcitonin have been found as a marker of acute bacterial meningitis and have been used to differentiate bacterial from viral meningitis.

Blood culture from patients with community acquired meningitis often reveal the pathogen: 90% in case of *H.influenzae,* 80% in case of *S.pneumoniae* and 90% of *N.meningitidis*. Bacteremic skin lesions associated with highly invasive organisms may reveal the agent on Gram-stained smear. Peripheral leukocyte count usually elevated. Hyponatremia in the course of meningitis is due either to complications of SIADH or to inappropriate fluid administration.

In the absence of a focal neurologic findings or a history suggestive of intracranial mass lesion in a patient suggestive of community acquired meningitis –diagnostic lumbar puncture and therapy should not be deferred, pending a CT scan brain. When history, clinical setting, physical examination (papilledema, focal cerebral findings) suggest a suppurative intracranial collection cranial CT should be carried out without delay – before lumbar puncture.

Variety of abnormalities is detected by CT brain. Contrast enhancement of leptomeninges, ventricular lining, cerebral edema, widening of subarachnoid space, multifocal enhancing lesion, subdural effusion, empyema, hydrocephalus, etc.

Sagittal sinus thrombosis a rare complication are detected by MRI. Among clinical features in those with abnormal CT findings more prevalent are age>60 years, h/o CNS lesion, abnormal consciousness, seizure, visual field abnormality, aphasia and other focal deficits.

CT scan brain should not be routine but should be used as indicated by clinical setting, neurologic findings and clinical course.

Most important laboratory test for diagnosing viral meningitis is CSF study. Typically CSF shows lymphocytic pleocytosis (25 to 500 cells/μl), normal or mildly elevated protein level, normal glucose level and normal or mildly elevated CSF oncotic pressure(100 to 350 mm Hg). PMN may predominate in first 48 hours of illness. Organisms are not seen on Gram's stain or acid-fast stained smears or India ink preparations. PCR amplification of viral nucleic acid has become the single most important method of diagnosing viral infection. Result of viral culture is disappointing. Serology for some viruses are less useful, because prevalence of antibody seropositivity is high in general population. Diagnosis of acute viral infection can be made by documentation of seroconversion between acute phase and convalescent sera(usually taken after 2 to 4 weeks). Agarose electrophoresis demonstrating oligoclonal bands is useful in some cases.

TREATMENT

Treatment of Bacterial Meningitis

Therapy of acute bacterial meningitis involves:

a. Rapid identification of the pathogen.
b. Prompt institution of antimicrobials.
c. Prevention and management of neurologic and systemic complications.
d. Study of predisposing factors.

Efficacy of antimicrobial therapy in bacterial meningitis depends on number of factors such as antimicrobial susceptibility, bactericidal activity, capacity to penetrate blood-brain barrier, effectiveness of various mode of antimicrobials to achieve desired concentration in CSF. Most antibiotics used in the treatment of meningitis except chloramphenical and rifampicin do not readily penetrate blood-brain barrier. β-lactum antibiotics penetrate at desired levels when only meninges are inflamed. Clindamycin, erythromycin and first and second generation cephalosporins never achieved effective bactericidal concentrations, so should not be used in the treatment of community acquired meningitis. β-lactum, aminoglycosides, vancomycin should be used in intermittent intravenous bolus dose rather than continuous administration.

Streptococcus pneumoniae

Penicillin G and ampicillin had been the drugs of choice for meningitis for many decades due to high susceptibility. But in the last two decades from various parts of the world upto 40-50% of strains with moderate to high degrees of resistance have been reported.[5] Multiple antimicrobial resistance was also common among penicillin resistant isolates. In view of increasing resistance, penicillin should not be used as the drug of choice in empiric treatment of bacterial meningitis when *S. pneumoniae* is likely pathogen. So in 1980s third generation cephalosporin such as cefotaxime or ceftriaxone in high doses have been used as initial treatment in suspected cases.

Again in 1990s emergence of relatively resistant strains to third generation cephalosporin thrown new therapeutic problems. Such treatment failure have attributed to recommend vancomycin in addition to third generation cephalosporin as initial treatment of meningitis when *S. pneumoniae* is suspected. Though penetration of vancomycin in poor but in inflamed meninges therapeutic concentration is 4-8 fold higher than the minimum bactericidal concentration and are

adequate for bacterial clearance. Co-administration of dexamethasone reduce the penetration by 29%, but with higher doses of vancomycin therapeutic concentration in CSF achieved even if steroid is coadministered. Vancomycin resistance not observed till now. Rifampicin is added with vancomycin if meningitis is due to highly penicillin and cephalosporin resistant S pneumoniae.[6]

For several decades chloramphenicol has been the alternative treatment for pneumcoccal meningitis in the highly β-lactam allergic patients. But in a South African study of pneumococcal meningitis due to strain that were both penicillin resistant and chloramphenicol susceptible, 80% children who were treated initially with chloramphenical had an unsatisfactory results. Poor outcome was due to inadequate bactericidal activity of chloramphenicol against penicillin resistant strains.[7] So chloramphenicol alone should not be used as was in the past.

Neisseria meningitides

Penicillin or ampicillin remains the antimicrobial of choice for treatment of meningitis caused by *N.meningitidis*. Strains which are resistant to Penicillin or ampicillin, cefotaxime or ceftriaxone are drugs of choice.

Haemophilus influenzae

Ampicillin was the drug of choice in the treatment of *H.influenzae* meningitis from the late 1960s to 1970s .The emergence of resistant strain (approx 30% in USA) compelled to change of therapy. Cefotaxime or ceftriaxone have become the drug of choice for treatment of *H. influenzae* meningitis. Resistance to cefotaxime or ceftriaxone has not been yet reported as a problem.

L. monocytogenes

Reference treatment is ampicillin (200-400 mg/kg day) for 21 days.Alternative is co-trimoxazole 960 mg every 12 hours for 3 weeks.

Empirical Therapy: Choice of Antibiotics

Initial antimicrobial treatment of acute bacterial meningitis of unknown cause is based on coverage of the likely pathogens, as suggested by the age of the patient, clinical setting, predisposing factors. In adults *S.pneumoniae, N.meningitidis, L.monocytogenes* are responsible for most cases of community acquired meningitis.so combination of vancomycin with cefotaxime or ceftriaxone (with or without rifampicin) remains the initial therapy of choice. Role of *H. influenzae* and Enterobacteriaceae in 5 to 10% cases further support the use of cefotaxime or ceftriaxone in initial combination therapy. In view of relative insusceptibility of *L.monocytogenes* to third generation cephalosporins, ampicillin should be added. Patients allergic to ampicillin, trimethoprim-sulfamethoxazole may be the alternative (Table 1).

Doses Schedule

Table 2 gives the details of drugs and usage as advocated by various agencies

Duration of Antimicrobial Therapy

Treatment of meningococcal meningitis 7 days is adequate (for 5 days after patient becomes afebrile).

Treatment of *H.influenzae* meningitis should be given for 7 to 10 days(7 days after patient became afebrile).

Meningitis due to *S. pneumoniae* should be treated for at least 14 days.

Meningitis due to *L. monocytogenes* should get therapy with ampicillin for at least 21 days.

Other Aspects of Therapy

Patients need constant attention to prevent aspiration and hypoxia. Seizures should be early recognized and treated with anticonvulsants.

Initial fluid management of patients with bacterial meningitis involves careful evaluation of state of hydration. Shock requires fluid replacement to maintain systemic blood pressure and sustain cerebral perfusion. Hyponatremia has been observed and attributed to SIADH. Frequency of SIADH in bacterial meningitis varies widely from 4 to 88%.[8] This led to conservative fluid therapy early in the management. So maintenance plus replacement fluids can be administered in the initial 24 to 48 hours, but with subsequent monitoring for SIADH.

Coagulopathies such as disseminated intravascular coagulation may develop in more severely ill patients particularly with meningococcemia-meningitis syndrome.

Markedly elevated CSF pressures are observed in about 5% of cases in the absence of any mass lesion. Such elevated pressure are due to result of cerebral edema, complicating cerebral herniation. Measures that can be taken to reduce ICP are elevation of head of the bed to 30 degrees, intubation and hyperventilation, intravenous mannitol.

Adrenocortical insufficiency another complication should be looked for and to be treated by corticosteroids.

Role of Corticosteroid

Corticosteroids reduce the intense leukocyte responses, CSF outflow resistance, and development of brain edema. Dexamethasone has been shown to improve outcome in pneumococcus but not in meningococcal meningitis. Steroid also reduce neurological and audiological sequelae in *H. influenzae* meningitis.No role of steroid in viral encephalitis.Recommended dose is IV Dexamethasone 8 mg qds (0.15 mg/kg 6 hourly) for 4 days. This should be administered before or with the first dose of antibiotic in suspected meningitis.

Contraindications in the use of steroid are:

- Viral meningitis
- Patient where diagnosis is in doubt
- Patients already treated with antibiotics
- Patient with sepsis
- Immunocompromised patients.

Another point of concern is steroid reduce the concentration of vancomycin in CSF, so higher doses needed to achieve therapeutic concentration of vancomycin.

Adjuvant Intrathecal Therapy

Intrathecal therapy is unnecessary for common types of community acquired meningitis. Occasionally with refractory meningitis caused by gram negative bacilli, adjuvant use of intrathecal or intraventricular aminoglycosides might be considered. Adjuvent use of intrathecal vancomycin occasionly needed in meningitis caused by methicillin resistant *S. aureus* or coagulase negative staphylococci, that do not satisfactorily responded to intravenous vancomycin.

Repeat Lumbar Puncture

Analysis of CSF should be repeated only in those patients who do not improve clinically after 48 hours of appropriate antimicrobial therapy.

Decline in Consciousness

For patients who fail to improve after appropriate antimicrobial therapy, should undergone brain imaging. Inflammatory process in brain causes increased permeability of blood-brain barrier and causes brain edema. On imaging early signs of brain edema are disappearance of sylvian fissure

and narrowing of ventricular size, In advanced stage basal cisterns and sulci may become obliterated. Seizures and hydrocephalus are other causes of deteriorating consciousness.

If neuroimaging does not reveal any abnormality repeat lumbar puncture should be done. On the basis of Gram's staining and culture choice of antibiotics should be reviewed.

Focal Neurologic Abnormality

Signs of cerebral infraction and cytotoxic edema on cranial imaging suggest septic arteritis, venous thrombophlebitis or thromboembolic events. Subdural empyema, focal seizures, epilepsia partialis continua are other focal complications following meningitis. Abnormality of cranial nerves are caused by meningeal inflammatory process or by an increase in cerebrospinal fluid pressure. Most frequent cranial nerve abnormality is eighth nerve involvement.

Outcome

Community acquired meningitis caused by *S. pneumoniae* case fatality rate is as high as 19 to 37%.[9] In upto 30% of survivor long-term neurologic sequelae develop including hearing loss and other focal neurologic abnormality. In case of meningococcal meningitis mortality around 3 to 13% and morbidity 3 to 7%, much lower than pneumococcal meningitis. For Listeria meningitis prognosis is poor, with 33% mortality and 33% sequelae. Mortality in case of *H.influenzae* meningitis is 3 to 7%. Outcome of viral meningitis in case of adult is excellent. Outcome in infants and in neonates is less certain. Residual sequele may persist.

Treatment for Viral Meningitis

There is no specific antiviral therapy for viral meningitis. Adenine arabinoside and acyclovir which are somewhat useful in herpes simplex and varicella-zoster encephalitis are probably not necessary in cases of uncomplicated meningitis. Intravenous acyclovir may be given (30 mg/kg per day in three divided doses) for 7 days in complicated and in immunocompromised patients. Oral acyclovir (800 mg five times day), famciclovir (500 mg tid), valacyclovir (1000 mg tid) for a week may be tried in less severely ill cases.

Prevention

Chemoprophylaxis is indicated for *N.meningitidis* and *H.influenzae* aiming to prevent secondary disease in close contacts of infected people by eradicating nasopharyngeal colonization.There is no evidence that chemoprophylaxis for *S.pneumonia* is useful.

Close contacts of meningococcal disease is 500 to 800 times at risk than the endemic rate for meningococcal disease in general population. Rifampicin is recommended in a dose 600 mg orally every 12 hours for 2 days in adults (10 mg/kg every 12 hours for children over 1 month of age, and 5 mg/kg every12 hour under 1 month of age). Rifampicin is contraindicated in pregnancy and in severe liver disease. Alternative is single dose ciprofloxacin 500-750 mg for adults. But it is contraindicated in children and in pregnancy due to potential side effects on growing cartilage. In this group ceftriaxone (250 mg intramuscular in adults and 125 mg in children) is preferred. Recently in a study in Egypt single dose azithromycin(500 mg) found to be effective.

If an unvaccinated child <4 years of age lives in the same household as the patient, rifampicin prophylaxis should be given to the entire household (except pregnant)for 4 days. Doses are:

Oral doses:

1-3 months	10 mg/kg once daily for 4 days
3 months-12 years	20 mg/kg once daily for 4 days(max 600 mg)

>12 years/adult 600 mg once daily for 4 days

Because nasopharyngeal carriage may reappear after discontinuation of antimicrobial therapy for systemic infection, index patient should receive rifampicin before hospital discharge.

Vaccination

Vaccination against *H.influenzae* type b with conjugate vaccine has dramatically reduced the incidence of *H.influenzae* meningitis. Polysaccharide vaccine against *N.meningitidis* can protect patient over 2 years against serotypes A, C, Y and W-135.[10] Live attenuated VZV vaccine now available with 70-90% efficacy.

Newer Directions

Recent advances in experimentally induced bacterial meningitis in animals include the role of oxygen-glucose deprivation of hippocampal neurons as a complication of meningitis, the role of nuclear factor B1 and brain derived neurotropic factor.

Use of agents that block the action of polynuclear cells or cytokines has been promising in the experimental meningitis in animal model. A recent clinical trial of a protein that increases bacterial permeability has shown promising result in 26 children with severe meningococcemia. Experimental drug pleconaril has shown efficacy against enteroviral infection. Since most of the cases of enteroviral infections are benign and self limited, indication of pleconaril is yet to be defined. Progress is to be more likely in the field of vaccine in terms of more use of available vaccines and development of new vaccines, so that incidence of this devastating disease can be lowered.

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MULTIPLE CHOICE QUESTIONS

1. **Commonest organism causing bacterial meningitis in adult is:**
   A. *S.pneumoniae* B. *N.meningitidis*
   C. *H.influenzae* D. *L.monocytogenes*
2. **Commonest organisms causing bacterial meningitis in children is:**
   A. *S.pneumoniae* B. *N.meningitidis*
   C. *H.influenzae* D. *L.monocytogenes*
3. ***L.monocytogenes* causes infection more in:**
   A. Pregnancy B. Elderly
   C. Immunocompromised D. All of the above
4. **In meningitis neck stiffness found in:**
   A. All cases B. 10% cases
   C. 50% cases D. 80% cases
5. **Petechial/purpuric rash found in following infection:**
   A. Meningococcal B. Pneumococcal
   C. *H.influenzae* infection A. All
6. **Sensory neural deafness occur in following infection:**
   A. *H.influenzae* B. *N.meningitidis*
   C. *S.pneumoniae* D. *L.monocytogenes*
7. **PCR study of CSF more useful in diagnosing:**
   A. Viral meningitis B. Bacterial meningitis
   C. Both D. None
8. **Sagittal sinus thrombophlebitis best diagnosed by:**
   A. CT scan B. MRI
   C. CSF study D. None
9. **Drug of choice in *L.monocytogenes* is:**
   A. Ampicillin B. Cefotaxime
   C. Vancomycin D. Penicillin
10. **Prophylaxis not indicated in:**
    A. *S.pneumoniae* B. *N.meningitidis*
    C. *H.influenzae* D. *L.monocytogenes*

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1. A 2. B 3. D 4. C 5. A 6. A 7. A 8. B 9. A 10. A